Presidenza del Consiglio dei Ministri

DIPARTIMENTO DELLA PROTEZIONE CIVILE

COMITATO TECNICO SCIENTIFICO EX OO.C.D.P.C. 03/02/2020, N. 630; 18/04/2020, N. 663; 15/05/2020, N. 673

Verbale n. 94 della riunione tenuta, presso il Dipartimento della Protezione Civile, il giorno 07 luglio 2020

	PRESENTE	ASSENTE
Dr Agostino MIOZZO	X	
Dr Fabio CICILIANO	X	
Dr Massimo ANTONELLI	X	
Dr Giovannella BAGGIO	IN VIDEOCONFERENZA	
Dr Roberto BERNABEI		X
Dr Silvio BRUSAFERRO	IN VIDEOCONFERENZA	
Dr Elisabetta DEJANA	IN VIDEOCONFERENZA	
Dr Mauro DIONISIO	IN VIDEOCONFERENZA	
Dr Ranieri GUERRA	X	
Dr Achille IACHINO	IN VIDEOCONFERENZA	
Dr Sergio IAVICOLI	X	
Dr Giuseppe IPPOLITO	X	
Dr Franco LOCATELLI	IN VIDEOCONFERENZA	
Dr Nicola MAGRINI	PRESENTE Ammassari in rappresentanza di AIFA	
Dr Francesco MARAGLINO		X
Dr Rosa Marina MELILLO	IN VIDEOCONFERENZA	
Dr Nausicaa ORLANDI		X
Dr Flavia PETRINI	IN VIDEOCONFERENZA	
Dr Kyriakoula PETROPULACOS	IN VIDEOCONFERENZA	
Dr Giovanni REZZA		X
Dr Luca RICHELDI	IN VIDEOCONFERENZA	
Dr Giuseppe RUOCCO		X
Dr Nicola SEBASTIANI	X	
Dr Andrea URBANI		X
Dr Alberto VILLANI	IN VIDEOCONFERENZA	
Dr Alberto ZOLI		X

È presente la Dr Adriana Ammassari in rappresentanza di AIFA (in videoconferenza).

È presente il Dr Giovanni Baglìo in rappresentanza del Sig. Vice Ministro della Salute Pierpaolo Sileri (in videoconferenza).

È presente il Dr Luigi Bertinato di ISS (in videoconferenza).

La seduta inizia alle ore 15,10.

QUESITI DEL MINISTERO DELL'ISTRUZIONE RELATIVI ALL'INIZIO DEL NUOVO ANNO SCOLASTICO

Il CTS condivide con il Ministro dell'Istruzione alcuni aspetti da affrontare relativamente alla ripresa del prossimo anno scolastico per le scuole di ogni ordine e grado. A tal fine, a margine dell'audizione del 02/07/2020 con le diverse rappresentanze sindacali che hanno illustrato alcuni aspetti relativi alle misure di contenimento del contagio da SARS-CoV-2 e dell'impatto che queste potrebbero avere sul mondo della scuola, in data 03/07/2020 sono pervenute dal Sig. Ministro dell'Istruzione al CTS alcune istanze (allegato) che vengono riscontrate con le osservazioni che di seguito si riportano:

- In riferimento al distanziamento previsto, il metro di distanza deve intendersi solo in condizione statica o anche in movimento? Qualora, infatti, non sia possibile garantire il metro previsto durante gli spostamenti che avvengono all'interno o all'esterno della classe, è sufficiente il solo utilizzo della mascherina?

- Il previsto distanziamento di un metro è da intendersi, relativamente alla configurazione del *layout* delle aule, nel senso della necessità di prevedere un'area statica dedicata alla "zona banchi". Nella zona banchi il distanziamento minimo di 1 metro tra le rime buccali degli studenti dovrà essere calcolato dalla posizione seduta al banco dello studente, avendo pertanto riferimento alla situazione di staticità. Con riferimento alla "zona cattedra", nella definizione del *layout* resta imprescindibile la distanza di 2 metri lineari tra il docente e l'alunno nella "zona interattiva" della cattedra, identificata tra la cattedra medesima ed il banco più prossimo ad essa. L'utilizzo della mascherina è necessario in situazioni di movimento e in generale in tutte quelle situazioni (statiche o dinamiche) nelle quali non sia possibile garantire il distanziamento prescritto. In coerenza con il documento tecnico approvato nella seduta n. 82 del 28/05/2020 e con le integrazioni approvate nella seduta n. 90 del 22/06/2020, il CTS ribadisce che la eventuale rivalutazione circa la possibilità di rendere non obbligatorio l'uso delle mascherine potrà essere valutata soltanto all'esito dell'analisi degli indici epidemiologici relativi alla diffusione del virus SARS-CoV-2 osservati nell'ultima settimana del mese di agosto p.v.

- In relazione al metro di distanziamento previsto, è possibile indicare il valore in metri quadri dello spazio di occupazione di ciascun studente?
  - Il distanziamento fisico (inteso come distanza minima di 1 metro fra gli alunni, tra le rime buccali) rimane un punto di primaria importanza nelle azioni di prevenzione. Come indicato nel documento tecnico del 28 maggio e nell'aggiornamento del 22 giugno *"il layout delle aule destinate*

alla didattica andrà rivisto con una rimodulazione dei banchi, dei posti a sedere e degli arredi scolastici, al fine di garantire il distanziamento interpersonale di almeno 1 metro", inoltre "*va prestata la massima attenzione al layout della zona interattiva della cattedra prevedendo tra l'insegnante e il banco/o i banchi uno spazio idoneo di almeno 2 metri.*" Pertanto, nella definizione del layout resta imprescindibile la distanza di 1 metro lineare tra gli alunni e di 2 metri lineari tra il docente e l'alunno nella zona interattiva della cattedra. Per tale motivo non viene indicato un valore in metri quadri dello spazio di occupazione dello studente in quanto tale parametro adottato singolarmente, potrebbe non garantire il distanziamento minimo lineare essenziale sopra ricordato.

- Quando uno studente o il personale scolastico dovesse presentare, all'interno della sede scolastica, dei sintomi riconducibili al virus Covid19, quali sono le procedure da adottare? È possibile la predisposizione di un unico protocollo sanitario valido su tutto il territorio nazionale? Quale deve essere il ruolo della ASL, del pediatra e del medico di base in caso di individuazione di soggetti positivi?
    - Il Documento tecnico, nell'aggiornamento del 22 giugno u.s., alla sezione "Misure di controllo territoriale" - di seguito riportata - ha individuato la procedura da adottare nel contesto scolastico in coerenza con quanto già individuato nel "Protocollo condiviso di regolamentazione delle misure per il contrasto e il contenimento della diffusione del virus Covid-19 negli ambienti di lavoro" del 24 aprile 2020 (punto 11 - Gestione di una persona sintomatica in azienda). "*Misure di controllo territoriale - In caso di comparsa a scuola in un operatore o in uno studente di sintomi*

suggestivi di una diagnosi di infezione da SARS-CoV-2, il CTS sottolinea che la persona interessata dovrà essere immediatamente isolata e dotata di mascherina chirurgica, e si dovrà provvedere al ritorno, quanto prima possibile, al proprio domicilio, per poi seguire il percorso già previsto dalla norma vigente per la gestione di qualsiasi caso sospetto. Per i casi confermati le azioni successive saranno definite dal Dipartimento di prevenzione territoriale competente, sia per le misure quarantenarie da adottare previste dalla norma, sia per la riammissione a scuola secondo l'iter procedurale altrettanto chiaramente normato. La presenza di un caso confermato necessiterà l'attivazione da parte della scuola di un monitoraggio attento da avviare in stretto raccordo con il Dipartimento di prevenzione locale al fine di identificare precocemente la comparsa di possibili altri casi che possano prefigurare l'insorgenza di un focolaio epidemico. In tale situazione, l'autorità sanitaria competente potrà valutare tutte le misure ritenute idonee. Questa misura è di primaria importanza per garantire una risposta rapida in caso di peggioramento della situazione con ricerca attiva di contatti che possano interessare l'ambito scolastico. Sarebbe opportuno, a tal proposito, prevedere, nell'ambito dei Dipartimenti di prevenzione territoriali, un referente per l'ambito scolastico che possa raccordarsi con i dirigenti scolastici al fine di un efficace contact tracing e risposta immediata in caso di criticità". Tale previsione sarà altresì utile per tutti i raccordi di competenza dell'Autorità sanitaria previsti dalla normativa vigente. Gli esercenti la potestà genitoriale in caso di studenti adeguatamente e prontamente informati si raccorderanno con il medico di medicina generale o pediatra di libera scelta per quanto di competenza. Nel contesto delle iniziative di

informazione rivolte agli alunni, genitori e personale scolastico sulle misure di prevenzione e protezione adottate, si ravvisa l'opportunità di ribadire la responsabilità individuale e genitoriale.

- È possibile attivare una collaborazione tra le istituzioni scolastiche e le ASL territorialmente competenti, prevedendo l'individuazione di un referente e/o di una struttura locale specificatamente dedicata, volta ad assistere e supportare le scuole nell'attuazione delle misure di prevenzione e contenimento del contagio dal Covid-19?
    - Il Documento tecnico nell'aggiornamento del 22 giugno u.s. ha già indicato - come specificato nella risposta precedente - nel contesto delle "Misure di controllo territoriale" l'opportunità di prevedere, nell'ambito dei Dipartimenti di prevenzione territoriali, un referente per l'ambito scolastico che possa raccordarsi con i dirigenti scolastici al fine di un efficace *contact tracing* e risposta immediata in caso di criticità. Pertanto, è già prevista l'attivazione della collaborazione citata nella domanda. Tale sistema di raccordo tra sistema scolastico e sistema sanitario nazionale è una misura innovativa di grande rilievo, soprattutto nel contesto emergenziale in atto, per supportare le Istituzioni scolastiche nella realizzazione dei compiti assegnati per l'effettuazione di un anno scolastico in piena sicurezza. Tale sistema di monitoraggio e di allerta precoce attivato sul territorio nazionale consentirà di individuare situazioni locali meritevoli di misure di contenimento della diffusione epidemica, che potranno interessare specifiche realtà scolastiche locali, a tutela della salute dei lavoratori e degli studenti.

- Si ritiene necessaria l'obbligatorietà della figura del medico competente per la sorveglianza sanitaria ordinaria presso ogni sede scolastica?
    - Fermo restando quanto previsto dal D.Lgs 81/08 e successive modifiche e integrazioni -che prevede la sua applicazione *a tutti i settori di attività, privati e pubblici, e a tutte le tipologie di rischio* - nonché quanto previsto dalla specifica normativa ministeriale, nello specifico, per quanto concerne il quesito posto in tema dell'obbligatorietà della figura del medico competente per la sorveglianza sanitaria ordinaria presso ogni sede scolastica, si rappresenta che tale obbligo di nomina del medico competente è subordinato all'esito del processo di valutazione dei rischi che è specifica responsabilità del datore di lavoro. Pertanto, solo qualora la citata valutazione evidenzi la presenza di uno dei rischi "normati" dal D.Lgs 81/08 e s.m.i e che prevedano l'obbligo di sorveglianza sanitaria, è necessario nominare il medico competente. Va precisato che il contesto attuale emergenziale non introduce elementi di novità rispetto alla previsione di sorveglianza sanitaria ordinaria, mentre per quella definita come sorveglianza sanitaria "eccezionale", si rimanda al quesito specifico successivo.
- In merito alle operazioni di pulizia degli ambienti scolastici, tenuto conto che diversamente dagli esami di stato il numero dei presenti nelle scuole sarà a settembre molto elevato, è possibile indicare le modalità e la periodicità con cui esse devono avvenire? Con particolare riferimento ai servizi igienici, è possibile specificare le modalità e la frequenza per lo svolgimento delle pulizie ed il numero minimo di bagni necessari in rapporto al numero totale degli studenti e del personale scolastico di ciascun istituto?

- Si riportano di seguito le indicazioni presenti nel Documento tecnico del 28 maggio u.s., riguardanti le modalità e periodicità delle operazioni di pulizia: *"Le operazioni di pulizia dovranno essere effettuate quotidianamente secondo le indicazioni dell'ISS previste nella Circolare del Ministero della Salute "Indicazioni per l'attuazione di misure contenitive del contagio da SARS-CoV-2 attraverso procedure di sanificazione di strutture non sanitarie (superfici, ambienti interni) e abbigliamento" in particolare nella sezione "Attività di sanificazione in ambiente chiuso" di cui un estratto è in Allegato 1. Nello stesso allegato è riportato un estratto con i principi attivi indicati per le varie superfici tratto da Rapporto ISS COVID-19 n. 19/2020 - "Raccomandazioni ad interim sui disinfettanti nell'attuale emergenza COVID-19: presidi medico-chirurgici e biocidi. Versione del 25 aprile 2020". A riguardo si precisa che per sanificazione si intende l'insieme dei procedimenti e operazioni atti ad igienizzare determinati ambienti e mezzi mediante l'attività di pulizia e di disinfezione. Poiché la scuola è una forma di comunità che potrebbe generare focolai epidemici in presenza di un caso, a causa della possibile trasmissione per contatto, la pulizia con detergente neutro di superfici in locali generali, in presenza di una situazione epidemiologica con sostenuta circolazione del virus, andrebbe integrata con la disinfezione attraverso prodotti con azione virucida. Nella sanificazione si dovrà porre particolare attenzione alle superfici più toccate quali maniglie e barre delle porte, delle finestre, sedie e braccioli, tavoli/banchi/cattedre, interruttori della luce, corrimano, rubinetti dell'acqua, pulsanti dell'ascensore, distributori automatici di cibi e bevande, ecc. Qualora vengano usato prodotti disinfettanti, e qualora la struttura educativa*

ospiti bambini al di sotto dei 6 anni, si raccomanda di fare seguire alla disinfezione anche la fase di risciacquo soprattutto per gli oggetti, come i giocattoli, che potrebbero essere portati in bocca dai bambini. I servizi igienici sono dei punti di particolare criticità nella prevenzione del rischio. Pertanto, dovrà essere posta particolare attenzione alle misure già poste in essere dalle scuole per la pulizia giornaliera dei servizi igienici con prodotti specifici". Si ravvisa l'opportunità di verificare la funzionalità ed efficienza dei servizi igienici, assicurandone eventuale ripristino prima dell'avvio dell'anno scolastico.

- È possibile dettagliare i dispositivi di protezione che devono indossare le seguenti tipologie di lavoratori?
    - Collaboratori scolastici nelle attività di pulizia e detersione di cui alle indicazioni dell'ISS previste nel documento dell'8 maggio 2020 nella sezione relativa a "Opzioni di sanificazione tutti i tipi di locali" riportato in allegato 1;
        - Per i collaboratori scolastici impegnati nelle attività di pulizia e detersione si rimanda a quanto indicato nella citata Circolare del Ministero della Salute "Indicazioni per l'attuazione di misure contenitive del contagio da SARS-CoV-2 attraverso procedure di sanificazione di strutture non sanitarie (superfici, ambienti interni) e abbigliamento". In particolare "*bisogna indossare sempre guanti adeguati per i prodotti chimici utilizzati durante la pulizia e la disinfezione, ma potrebbero essere necessari ulteriori dispositivi di protezione individuale (DPI, specie per i prodotti ad uso professionale) in base al prodotto*". Pertanto, la scelta del

dispositivo è esclusivamente correlata allo specifico prodotto utilizzato, come peraltro avviene già di norma e come previsto dagli specifici documenti di valutazione del rischio.

- Docenti/ATA nel caso di gestione di un eventuale caso sospetto da COVID;
  - Per i Docenti/ATA, nella gestione di un eventuale caso sospetto, è sufficiente mantenere il distanziamento di almeno un metro e utilizzare la mascherina chirurgica.
- Personale amministrativo nelle attività di ricevimento front office e nella gestione del cartaceo con spray idro alcolico.
  - Per il personale amministrativo nelle attività di ricevimento *front office* è sufficiente la mascherina chirurgica.
- Relativamente al prospettato utilizzo nella gestione del cartaceo da parte di personale amministrativo di "spray idro alcolico", si rappresenta che in nessuno dei documenti tecnici del CTS è stato previsto un tale utilizzo che, pertanto, si ritiene non necessario.

- Possono essere fornite indicazioni precise per la gestione dei laboratori tecnico-pratici degli istituti superiori, soprattutto per ciò che riguarda le misure di prevenzione del rischio da interferenze e da contagio tramite superfici?
  - Per la gestione dei laboratori tecnico-pratici degli Istituti superiori si rimanda al Documento di valutazione dei rischi, nonché all'ulteriore documentazione in materia di sicurezza sul lavoro, che ciascuna Istituzione scolastica dovrà integrare in collaborazione con il Responsabile del servizio di prevenzione e protezione, ferme restando le indicazioni già fornite in altri contesti circa la pulizia e la disinfezione delle superfici da

contatto quando le postazioni vengono utilizzate da utenti diversi . Dovranno altresì essere assicurati adeguati ricambi d'aria.

- È necessario predisporre delle misure di pulizia e igienizzazione specifiche presso ogni sede scolastica in occasione della riapertura di settembre?
    - In via preliminare il Dirigente scolastico assicurerà, prima della riapertura della scuola, una pulizia approfondita, ad opera dei collaboratori scolastici, dei locali della scuola destinati alla didattica e non, ivi compresi androne, corridoi, bagni, uffici di segreteria e ogni altro ambiente di utilizzo. Non sono necessarie misure ulteriori analogamente a quanto già previsto per l'effettuazione degli esami di stato dello scorso mese di giugno.
- Chi cura il reperimento e la distribuzione di mascherine per il personale scolastico e per gli studenti in condizione di lavoratori (ad es. per attività di laboratorio)? Sarà cura del dirigente scolastico o della Protezione Civile? Analogamente, per quanto riguarda i banchi monoposto, chi ne cura il reperimento?
    - Fermo restando che tale domanda non ricade nelle specifiche competenze del CTS, si rappresenta che sulla base di specifiche informazioni ricevute nel corso di audizione del Commissario straordinario per l'emergenza, lo stesso curerà la fornitura di mascherine chirurgiche alle scuole sia per il personale scolastico che per gli studenti in condizioni di lavoratori. Inoltre, il Commissario straordinario per l'emergenza curerà l'acquisizione di banchi monoposto secondo il fabbisogno stimato dal Ministero dell'Istruzione.

- È possibile chiarire le condizioni di utilizzo delle mascherine rispetto alla fascia di età dello studente? Con particolare riferimento agli alunni della scuola dell'infanzia quali sono le indicazioni sulle modalità di inserimento e accompagnamento da parte dei genitori o di altre figure parentali?
    - Tutti gli studenti di età superiore ai sei anni dovranno indossare una mascherina chirurgica o di comunità di propria dotazione, fatte salve le dovute eccezioni (ad es. attività fisica, pausa pasto). Inoltre, in coerenza con quanto disciplinato dal comma 3, art. 3 del DPCM 17 maggio 2020 "non sono soggetti all'obbligo i bambini al di sotto dei sei anni, nonché i soggetti con forme di disabilità non compatibili con l'uso continuativo della mascherina ovvero i soggetti che interagiscono con i predetti." Va in ogni caso sottolineato, come già richiamato nei documenti tecnici, il ruolo degli esercenti della responsabilità genitoriale nel preparare e favorire un allenamento preventivo ai comportamenti responsabili degli studenti. La presenza di genitori o di altre figure parentali nella scuola dell'infanzia dovrà essere limitata al minimo indispensabile. Sarà cura delle singole scuole definire le modalità di inserimento e accompagnamento sulla base delle condizioni logistiche e organizzative specifiche di ciascuna realtà scolastica.
- È possibile dettagliare maggiormente le modalità e le misure igienico-sanitarie da predisporre nell'ambito della refezione scolastica (anche nel caso di consumo del pasto in classe)?
    - Per il consumo del pasto in refettorio valgono le stesse misure di distanziamento fisico di almeno 1 metro già indicate per gli altri locali destinati alla didattica. Per il consumo del pasto in classe dovrà essere

mantenuta la normale disposizione e distanziamento già previsti per le ore di didattica. Riguardo alle misure igienico sanitarie si rimanda alle misure già in essere per la refezione scolastica.

- Per i percorsi per le competenze trasversali e l'orientamento (già alternanza scuola lavoro) si pone un problema di responsabilità da parte della scuola che invia gli studenti presso aziende ed enti. A quali regole devono attenersi questi ultimi soggetti?
    - Allo stato attuale tutte le aziende hanno l'obbligo di attuare quanto previsto nel "Protocollo condiviso di regolamentazione delle misure per il contrasto e il contenimento della diffusione del virus Covid-19 negli ambienti di lavoro" del 24 aprile 2020. È evidente che i raccordi tra la scuola con le figure della prevenzione degli Enti ospitanti gli studenti e la garanzia dell'adeguata informazione agli stessi dovrà essere curata, anche nell'ottica del contesto emergenziale e dell'effettivo periodo di effettuazione. Valgono comunque le regole dell'ente ospitante.
- Possono essere fornite indicazioni chiare sull'autorità medica competente a certificare la condizione di "fragilità" dei lavoratori?
    - La tutela dei "lavoratori fragili" si estrinseca attraverso la sorveglianza sanitaria eccezionale di cui all'art. 83 del Decreto Legge del 19 maggio 2020 n. 34 (attualmente in corso di conversione in Legge), assicurata dal datore di lavoro ed effettuata dal "medico competente" ove presente; in assenza del medico competente, il datore di lavoro potrà nominarne uno *ad hoc* per il solo periodo emergenziale o rivolgersi ai servizi territoriali dell'Inail che vi provvedono con propri medici del lavoro.

PROGRAMMA DI SCREENING E DI CONTROLLO SIEROLOGICO DEL PERSONALE DOCENTE E NON DOCENTE PER LA RICERCA DI ANTICORPI ANTI-SARS-COV-2 E RELATIVA PROCEDURA AD EVIDENZA PUBBLICA DA PARTE DELLA STRUTTURA DEL COMMISSARIO STRAORDINARIO PER L'ATTUAZIONE E IL COORDINAMENTO DELLE MISURE DI CONTENIMENTO E CONTRASTO DELL'EMERGENZA EPIDEMIOLOGICA COVID-19 PER UNA EVENTUALE

Il CTS nella seduta n. 90 del 22/06/2020 ha raccolto dal Sig. Presidente del Consiglio dei Ministri e dal Sig. Ministro della Salute un quesito relativo ad un eventuale programma di screening o di controllo sierologico per il personale della scuola prima dell'apertura del prossimo anno scolastico.

Nella seduta n. 91 del 23/06/2020, il Commissario straordinario per l'attuazione e il coordinamento delle misure di contenimento e contrasto dell'emergenza epidemiologica COVID-19 ha chiesto al CTS informazioni relative alle caratteristiche dei test diagnostici da impiegare nello screening.

Il CTS, nella seduta n. 92 del 02/07/2020 ha sottolineato che l'identificazione di test rapidi per la ricerca di IgG/IgM da eseguire su sangue capillare deve essere improntata al reperimento di dispositivi medici in vitro connotati da sufficiente affidabilità, garantita dalla presenza di Certificazione CE con sensibilità superiore al 92% e specificità superiore al 95%[1,2,3]. Il CTS indica al Commissario straordinario

1 Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Spijker R, Taylor-Phillips S, Adriano A, Beese S, Dretzke J, Ferrante di Ruffano L, Harris IM, Price MJ, Dittrich S, Emperador D, Hoo. L, Leeflang MMG, Van den Bruel A – Cochrane COVID-19 Diagnostic Test Accuracy Group Antibody tests for identification of current and past infection withSARS-CoV-2 (Review) – Cochrane Database Syst Rev. 2020 06 25; 6:CD013652 (allegato).

2 Kumleben N, Bhopal R, Czypionka T, et al. Test, test, test for COVID-19 antibodies: the importance of sensitivity, specificity and predictive powers – Public Health, 2020; 185: 88-90 (allegato).

3 Lucy A. McNamara, Stacey W. Martin – Principles of Epidemiology and Public Health, in Principles and Practice of Pediatric Infectious Diseases (Fifth Edition), Elsevier, 20

l'inserimento del criterio relativo alla celerità dei tempi di ottenimento della risposta dei test quale parametro aggiuntivo da tenere in considerazione per la valutazione delle offerte.

Il Commissario straordinario per l'attuazione e il coordinamento delle misure di contenimento e contrasto dell'emergenza epidemiologica COVID-19 ha trasmesso al CTS la bozza dell'indizione di gara ad evidenza pubblica (allegato).

Il CTS, in relazione al programma attuativo dell'indagine di screening, in assenza di una proposta operativa, raccomanda alle Istituzioni competenti di procedere con urgenza alla sua elaborazione, tenendo conto anche delle criticità emerse durante l'attuazione dell'indagine sieroepidemiologica nazionale.

PROCEDURE DI CONTENIMENTO DEL CONTAGIO DA SARS-COV-2 PER LA RIPRESA DELLE ATTIVITÀ DEL NAVIGLIO MERCANTILE RELATIVO ALLE NAVI DA CROCIERA

Il CTS analizza il documento della "Misure per la gestione dell'emergenza epidemiologica da covid-19 a bordo delle navi da crociera" trasmesso dal Ministero delle Infrastrutture e dei Trasporti (allegato).

Al riguardo, il CTS ritiene di esprimere le seguenti osservazioni:

- Al paragrafo B, punto 3 "Protezione personale e prevenzione delle infezioni" si fa riferimento al lavaggio delle mani con acqua calda e sapone o con soluzioni a base di alcol (almeno 60%). Il CTS indica come riferimento per tale dato il documento di ECDC "Guidelines for the use of non-pharmaceutical measures to delay and mitigate the impact of 2019-nCoV" (allegato);
- Al paragrafo B, punto 3 "Protezione personale e prevenzione delle infezioni" si legge che "il marittimo deve mantenere una distanza di almeno un metro dalle

altre persone, in particolare da quelle che tossiscono o starnutiscono o possono avere la febbre". Si sottolinea che qualsiasi passeggero che presenti sintomi compatibili con COVID-19 deve essere isolato e non permanere, quindi, a contatto con altre persone.

- Al paragrafo C "Misure adottate a terra prima dell'imbarco", come prerequisito di imbarco il CTS ritiene di poter considerare l'ipotesi del test molecolare obbligatorio per tutti i passeggeri che nei 14 giorni antecedenti si siano recati o siano transitati in uno dei Paesi con trasmissione sostenuta del virus SARS-CoV-2 (ad incidenza cumulativa superiore a quella nazionale, attualmente stabilita in 16 casi per 100.000 abitanti).
- Al paragrafo B, punto 4 "Test e trattamento" si fa riferimento alla diagnosi di infezione da nuovo coronavirus. Osserviamo che la diagnosi viene effettuata solo tramite tamponi (PCR) su campioni prelevati dalle alte (e basse) vie respiratorie come indicato dalla Circolare del Ministero della Salute n. 0011715 del 03/04/2020.
- I test sierologici non possono, allo stato attuale dell'evoluzione tecnologica, sostituire il test molecolare nell'attività diagnostica, come peraltro ribadito dalla Circolare del Ministero della Salute n. 0016106 del 09/05/2020.
- Al paragrafo D, punto 1 lett. c) "Autodistanziamento a bordo" il CTS sottolinea che, come peraltro previsto dall'ultimo documento di Healthy Gateways (allegato), si consiglia ai passeggeri di evitare l'uso degli ascensori. Si raccomanda, altresì, di rivedere e ridurre la capacità massima degli ascensori in base alla guida del distanziamento fisico. Poiché si prevede sia necessario considerare comunque l'eventuale utilizzo degli ascensori per particolari circostanze, si raccomanda l'adeguato distanziamento fisico, l'utilizzo delle

maschere facciali e la disponibilità di soluzioni a base alcolica all'ingresso di ogni ascensore. Gli ascensori devono essere puliti regolarmente con particolare attenzione alle superfici che vengono toccate frequentemente.

- Al paragrafo D, punto 1 lett. h) viene indicato di organizzare il funzionamento dei sistemi HVAC per massimizzare la circolazione dell'aria fresca nel sistema. Il CTS osserva che è necessario, altresì, prevedere che tutte le unità di trattamento dell'aria vengano commutate dal ricircolo al 100% di aria esterna chiudendo le serrande di ricircolo; nel caso non sia possibile arrestare completamente il ricircolo dell'aria dovrebbe essere previsto l'utilizzo di filtri HEPA. Le strutture mediche e le aree di isolamento devono essere collegate a UTA separate. Se nelle strutture mediche della nave vengono svolte procedure che generano aerosol, tali aree dovrebbero essere a pressione negativa ed ottenere 10 ricambi d'aria all'ora; l'aria di ritorno da tali strutture dovrebbe essere filtrata in HEPA o scaricata all'esterno.
- Al paragrafo D, punto 1 lett. i) viene indicato di far riferimento alla normativa vigente nazionale, unionale ed internazionale per quanto riguarda l' "utilizzo di ristoranti, bar, discoteche, SPA, teatri, negozi di bordo, cinema, sale giochi, casinò, palestre ecc.". il CTS ritiene che il documento a cui far riferimento a tal proposito sia "Interim guidance for preparedness and response to cases of COVID-19 at points of entry in the European Union (EU)/ EEA Member States (MS). Interim advice for restarting cruise ship operations after lifting restrictive measures in response to the COVID-19 pandemic" (allegato).
- In riferimento alle nursery ed alle aree gioco per bambini si raccomanda di utilizzare il documento "European Manual for Hygiene Standards and

Communicable Disease Surveillance on Passenger Ships" reperibile al link http://www.shipsan.eu /Home/EuropeanManual.aspx.

- Al paragrafo D, punto 2 "Misure per la gestione dei rischi durante l'imbarco" viene considerata la possibilità di richiedere agli equipaggi di completare un periodo di auto-distanziamento per i primi 14 giorni a bordo della nave dopo l'imbarco. Il CTS osserva, invece, che la procedura pre-imbarco dovrebbe prevedere che i marittimi vengano sottoposti a tampone pre-imbarco. Tale tampone dovrebbe essere poi ripetuto ad intervalli regolari di 15 giorni al 50% del personale navigante, al fine di coprire l'intero equipaggio ogni 30 giorni.
- Al paragrafo E "Gestire un focolaio di COVID-19 a bordo della nave", il CTS osserva che, in premessa, è necessario prevedere che tutte le persone che intendano lavorare a bordo (ufficiali di bordo e membri dell'equipaggio) completino la formazione sul COVID-19. Gli operatori di linea devono formare il proprio equipaggio a riconoscere segni e sintomi compatibili con COVID-19. L'equipaggio deve conoscere le procedure da seguire quando un passeggero o un membro dell'equipaggio mostra segni e sintomi di COVID-19. Ogni membro dell'equipaggio deve essere addestrato, in relazione al proprio ruolo e alle proprie responsabilità, ad attuare le misure previste dal piano di contingenza. Dovrebbero essere, inoltre, effettuate esercitazioni prima di riprendere le operazioni e poi ogni 30 giorni per testare la formazione di tutto il personale su:
  - segni e sintomi riferibili a COVID-19;
  - misure di distanziamento fisico;
  - gestione delle folle;
  - uso dei DPI;

- protocolli per pulizia e disinfezione;
- procedure relative alla prevenzione, alla sorveglianza e alla risposta a eventuali focolai a bordo.

Ciascun membro dell'equipaggio deve segnalare immediatamente la comparsa di qualsiasi segno o sintomo anche sospetto di COVID-19 e non deve recarsi a lavoro.

- Al paragrafo E, punto 2 "Definizione di un caso sospetto di COVID-19" si suggerisce di far riferimento alla Circolare del Ministero n. 0007922 del 09/03/2020

PROCEDURE DI SICUREZZA PER LA RIPRESA DELLE MANIFESTAZONI CICLISTICHE

Il CTS, al fine di acquisire informazioni sull'analisi preliminare dell'impatto globale dello sport del ciclismo sul Paese con lo scopo di dare risposte coerenti con il principio di massima precauzione per le azioni di contenimento del contagio, procede all'audizione del Presidente e del Segretario della Federazione Ciclistica Italiana nonché del Presidente e del Segretario della Commissione Tutela della Salute della medesima federazione.

Anche alla luce dell'analisi dei documenti pervenuti dall'Ufficio per lo Sport della Presidenza del Consiglio dei Ministri concernenti la proposta di adeguamento del protocollo di attuazione per la ripresa degli allenamenti e le raccomandazioni per la ripresa delle gare di tutte le categorie della Federazione Ciclistica Italiana avvenuta durante la seduta del CTS n. 93 del 03/07/2020, il CTS ritiene di fornire le seguenti osservazioni, relative, rispettivamente, alla componente dilettantistica ed alla componente professionistica dello sport del ciclismo.

In via preliminare, il CTS rappresenta che la tematica degli sport di contatto, ai quali anche lo sport del ciclismo può considerarsi analogo per modalità di estrinsecazione delle aggregazioni quando gli atleti si muovono "in gruppo", è stata già affrontata nella seduta n. 91 del 23/06/2020, confermando che, in considerazione dell'attuale situazione epidemiologica nazionale, con il persistente rischio di ripresa della trasmissione virale in cluster determinati da aggregazioni certe, debbano essere rispettate le prescrizioni relative al distanziamento fisico e alla protezione individuale.

Inoltre, già nella seduta n. 76 del 18/05/2020, il CTS, ai sensi dell'art. 1 co. 1 lett. e) del DPCM 17/05/2020, validò il documento inviato dall'Ufficio dello Sport della Presidenza del Consiglio dei Ministri relativo alle Linee Guida per lo sport di base che già illustrava la criticità correlata alla condizione che "... *lo spostamento d'aria causato dall'atleta e/o il posizionamento in scia, possono facilitare la contaminazione da droplet su distanze maggiori rispetto alla misura canonica di distanziamento sociale. In queste circostanze, più elevato è il vento, maggiore sarà il distanziamento richiesto per garantire le condizioni di sicurezza* ...". Questa condizione, tipica dei ciclisti posti "in scia", rappresenta una importante modalità di trasmissione del *droplet* soprattutto se si considera l'incremento degli indici ventilatori, tipici degli sport che, come il ciclismo, richiedono un forte e prolungato impegno muscolare.

Dall'analisi del documento relativo alla ripresa delle attività sportive del ciclismo dilettantistico e sentiti i rappresentanti della Federazione Ciclistica Italiana che hanno circostanziato le attività previste in ambito sanitario per le componenti professionistica e dilettantistica, il CTS rileva l'assenza di modalità di gestione o di precauzione ovvero di modelli organizzativi tali da consentire un'adeguata azione di prevenzione o di contenimento di eventuali contagi sostenuti dal virus SARS-CoV-2.

La proposta relativa esclusivamente all'esibizione di una autocertificazione che ciascun atleta dovrebbe esibire all'approssimarsi della gara non può certamente costituire garanzia nel controllo del contagio.

Per la componente professionistica, il CTS ritiene di formulare le seguenti considerazioni medico/scientifiche:

1. Il CTS prende atto che gli allenamenti e le gare con atleti che si muovono "in gruppo" e "in scia" sono parte imprescindibile dello sport del ciclismo.
2. Il controllo clinico/diagnostico proposto dal documento fa riferimento esclusivamente agli atleti. Ciò appare una misura parziale ai fini del contenimento del virus SARS-CoV-2, poiché esclude dall'effettuazione del tampone rino-faringeo tutte le persone del gruppo squadra che, a qualsiasi titolo, sono poste a stretto contatto con gli atleti, coerentemente alle indicazioni che il CTS ha già fornito in merito alle misure per il contenimento epidemico nello sport del giuoco del calcio professionistico per le squadre di serie A.
3. Nelle corse a tappe, inoltre, gli atleti dovrebbero evitare ogni contatto con persone non sottoposte alle medesime procedure di controllo diagnostico. Qualora, durante il periodo di gara, anche un solo membro dell'equipe risulti positivo al test molecolare per SARS-CoV-2, tutti gli altri componenti del gruppo (compreso gli atleti) dovranno da quel momento, per ovvie ragioni di prevenzione della diffusione epidemica, non avere contatti con qualsiasi altro soggetto esterno per 14 giorni.
4. In questi casi, il CTS raccomanda l'esecuzione del tampone rino-faringeo per la ricerca di SARS-CoV-2 ogni 120 ore, indipendentemente dal fatto che, nell'ambito della competizione, si tratti di un giorno di gara o di riposo.
5. Il CTS, infine, riafferma che l'intera delegazione sportiva (ciclisti, personale dirigente, assistenti, maestranze e tutti gli altri lavoratori a qualsiasi titolo coinvolti) rimarrà posta, com'è ovvio, sotto il controllo sanitario e la

responsabilità dell'Autorità Sanitaria Locale su cui ricade la competenza della competizione.

Atteso che lo sport del ciclismo, prevedendo una strettissima contiguità tra gli atleti, è un'attività intrinsecamente connotata da un elevato rischio di diffusione di contagio e che tutte le sopra indicate considerazioni vengano rispettate in maniera puntuale, il CTS, limitatamente alla componente professionistica dello sport del ciclismo, ritiene di esprimere un parere tecnico non ostativo alla strategia ipotizzata dalla Federazione Ciclistica Italiana, raccomandando di estendere a tutto il gruppo squadra e eventualmente agli atleti provenienti da Paesi stranieri le attività di monitoraggio sanitario lasciando, per ovvia competenza di funzione istituzionale, la decisione finale nel merito al Ministro competente.

Per la componente dilettantistica, alla luce di quanto espresso, il CTS rimanda alla Federazione Ciclistica Italiana la eventuale redazione di un documento maggiormente esaustivo che consenta di comprendere quali siano le attività di prevenzione poste in essere relativamente alla diffusione del virus SARS-CoV-2.

QUESITI PROVENIENTI DA DIVERSI DICASTERI SU TEMATICHE CONCERNENTI IPOTESI DI RIMODULAZIONE DELLE MISURE CONTENITIVE

Il CTS ha elaborato durante la sua attività diversi documenti tecnici e pareri per alcuni settori di maggiore complessità, finalizzati a supportare il processo decisionale del Governo, di altre istituzioni centrali e degli enti territoriali attraverso analisi e proposte di soluzioni tecnico-organizzative che consentissero una modulazione contestualizzata con il coinvolgimento delle autorità competenti, così come peraltro sancito dall'allegato n. 10 del DPCM dell'11/06/2020.

Il CTS rileva che pervengono richieste di pareri, quesiti, istanze provenienti da Autorità nazionali e locali, Ministeri, categorie professionali, associazioni di categoria, enti, istituzioni e organismi diversi circa la riapertura di attività e la

rimodulazione degli interventi relativi al contenimento del contagio da SARS-CoV-2 proiettati in ambiti locali che, molto spesso, risultano di difficile interpretazione a causa delle differenze – talora anche sostanziali – delle normazioni regionali.

Il CTS evidenzia che alcune Amministrazioni locali adottano in maniera autonoma e non coordinata iniziative che talora determinano disorientamento nei cittadini, anche attraverso una non corretta attività di comunicazione istituzionale che è apparsa in più di un'occasione ondivaga e imprecisa.

Al riguardo, il CTS ritiene che solo un'azione condivisa e coordinata – anche degli enti locali – può consentire la migliore gestione della contingenza epidemica, anche in riferimento agli attuali indici epidemiologici.

Nella considerazione che la Conferenza permanente per i rapporti tra lo Stato, le Regioni e le Province autonome ha il compito di dare attuazione alla collaborazione istituzionale tra lo Stato e le autonomie locali, il CTS ritiene che tali iniziative potrebbero essere meglio rappresentate in quella sede, attraverso l'elaborazione di un documento di riferimento.

Il CTS rimanda, all'esito di un'analisi più approfondita in tal senso, la eventuale trattazione dei documenti pervenuti relativi al trasporto pubblico locale delle Regioni Liguria, Piemonte, Lombardia, Veneto, Friuli Venezia Giulia trasmesso dal Ministero delle Infrastrutture e dei Trasporti (allegato) e della Conferenza Episcopale Italiana trasmesso dal Ministero dell'Interno (allegato).

ATTIVITÀ DEL COMITATO TECNICO SCIENTIFICO

Il CTS, già alla luce dell'emanazione del Decreto Legge 16/05/2020, n. 33, che sanciva dal punto di vista normativo il passaggio alla seconda fase delle azioni di

rimodulazione delle misure di contenimento del contagio, ha iniziato un dibattito interno interrogandosi sulle proprie funzioni e attribuzioni, al fine di un eventuale processo di rimodulazione del suo mandato e della sua azione complessiva.

In considerazione del fatto che il DPCM 11/06/2020 attualmente in vigore stabilisce le misure di prevenzione e contenimento del contagio da SARS-CoV-2 delle attività produttive, commerciali e sociali, fino al 14/07/2020, proiettando eventuali potenziali criticità con le decisioni di prossima adozione, durante la riunione odierna si è svolto un nuovo confronto interno relativo all'eventuale ruolo futuro ed alla funzione che il Comitato potrà avere nelle settimane e nei mesi a venire a supporto del Ministro della Salute e del Governo.

Il dibattito si è concluso con la unanime proposta di richiedere al Sig. Ministro della Salute una urgente interlocuzione al fine di definire eventuali revisioni nell'organizzazione e/o nel mandato del CTS, così come peraltro già indicato dallo stesso Sig. Ministro nelle sedute n. 89 del 16/06/2020 e n. 90 del 22/06/2020, allorquando fu da lui rappresentata l'esigenza di porre all'ordine del giorno del CTS il dibattito sulle diverse funzioni ed attribuzioni di una nuova struttura di supporto. Questa nuova realtà, in un futuro a medio-lungo termine, dovrebbe agire nell'ottica di un'ampia strategia complessiva nella *preparedness* e nella gestione delle contingenze di natura sanitaria, salvaguardando il modello di intervento concepito in sede di CTS con il suo notevole patrimonio di conoscenza che ha consentito al Paese di superare la fase di crisi, grazie all'azione sinergica delle Istituzioni che hanno partecipato in maniera coordinata alla gestione dell'emergenza.

PARERI

- Il CTS ratifica il seguente parere di ISS, sulla base delle evidenze documentali:
    - Integrazione mascherine Tunisia babygriffes – importatore Agmin (donazione ambasciata):
        - Con riferimento alla documentazione integrativa ricevuta per le Mascherine LNI della ditta Babygriffes si osserva che:
            - è adesso presente il numero identificativo di registrazione sul database NSIS del Ministero della Salute ove è indicato che si tratta di mascherine non sterili, di classe I;
            - dal punto di vista tecnico è adesso presente, con esito favorevole, la documentazione relativa ai Requisiti di Prestazione previsti per le mascherine di tipo I dalla norma UNI EN 14683:2019 quali Efficienza di Filtrazione Batterica, Traspirabilità e Pulizia Microbica;
            - continuano a non essere presenti i dati relativi alle prove di Biocompatibilità con la cute previste dalla norma UNI EN 10993 (citotossicità, sensibilizzazione, irritazione) né è presente, in sostituzione di dette prove, una valutazione del rischio su base bibliografica relativamente alla biocompatibilità di detti DM;
            - per quanto concerne il Sistema di Qualità posseduto dal fabbricante, sono state elencate ed è presente una autocertificazione che indica l'applicazione di alcune

procedure operative per l'approvazione delle materie prime e delle varie fasi di produzione.

- Il CTS acquisisce il parere FAVOREVOLE della Commissione Consultiva Tecnico Scientifica di AIFA su emendamento allo studio clinico ACALABRUTINIB Acerta Pharma (allegato).

Il CTS conclude la seduta alle ore 17,50.

	PRESENTE	ASSENTE
Dr Agostino MIOZZO		
Dr Fabio CICILIANO		
Dr Massimo ANTONELLI		
Dr Giovannella BAGGIO	**IN VIDEOCONFERENZA**	
Dr Roberto BERNABEI		**X**
Dr Silvio BRUSAFERRO	**IN VIDEOCONFERENZA**	
Dr Elisabetta DEJANA	**IN VIDEOCONFERENZA**	
Dr Mauro DIONISIO	**IN VIDEOCONFERENZA**	
Dr Ranieri GUERRA		
Dr Achille IACHINO	**IN VIDEOCONFERENZA**	
Dr Sergio IAVICOLI		
Dr Giuseppe IPPOLITO		
Dr Franco LOCATELLI	**IN VIDEOCONFERENZA**	
Dr Nicola MAGRINI	**PRESENTE Ammassari in rappresentanza di AIFA**	
Dr Francesco MARAGLINO		**X**
Dr Rosa Marina MELILLO	**IN VIDEOCONFERENZA**	
Dr Nausicaa ORLANDI		**X**
Dr Flavia PETRINI	**IN VIDEOCONFERENZA**	
Dr Kyriakoula PETROPULACOS	**IN VIDEOCONFERENZA**	
Dr Giovanni REZZA		**X**

Presidenza del Consiglio dei Ministri

DIPARTIMENTO DELLA PROTEZIONE CIVILE

COMITATO TECNICO SCIENTIFICO EX OO.C.D.P.C. 03/02/2020, N. 630; 18/04/2020, N. 663; 15/05/2020, N. 673

Dr Luca RICHELDI	**IN VIDEOCONFERENZA**	
Dr Giuseppe RUOCCO		**X**
Dr Nicola SEBASTIANI		
Dr Andrea URBANI		**X**
Dr Alberto VILLANI	**IN VIDEOCONFERENZA**	
Dr Alberto ZOLI		**X**

Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Antonelli Massimo <Massimo.Antonelli@unicatt.it>

mer 08/07/2020 22:11

A:Segreteria CTS <segreteria.cts@protezionecivile.it>;

Cc:cts <cts@protezioneciville.it>;

Approvo
Grazie
MA

Inviato da iPhone

> Il giorno 8 lug 2020, alle ore 21:17, Segreteria CTS <segreteria.cts@protezionecivile.it> ha scritto:
>
> gentili colleghi,
>
> reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).
>
> per la vostra nuova (ed urgente) approvazione del verbale emendato.
>
> grazie per la pazienza.
>
> fabio
>
> <verbale CTS 94 del 07-07-2020.pdf>

Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Giovannella Baggio <giovannella.baggio@gmail.com>

mer 08/07/2020 23:10

A:Segreteria CTS <segreteria.cts@protezionecivile.it>;

Cc:cts <cts@protezionecivile.it>;

Approvo.
Buona notte!
Giovannella

Il Mer 8 Lug 2020, 21:17 Segreteria CTS <segreteria.cts@protezionecivile.it> ha scritto:

gentili colleghi,

reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).

per la vostra nuova (ed urgente) approvazione del verbale emendato.

grazie per la pazienza.

fabio

Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Silvio Brusaferro <silvio.brusaferro@iss.it>

gio 09/07/2020 08:56

A: Segreteria CTS <segreteria.cts@protezionecivile.it>; cts <cts@protezionecivile.it>;

approvo

Silvio Brusaferro
Presidente Istituto Superiore di Sanità - Roma
President of Istituto Superiore di Sanità - Rome
Viale Regina Elena 299 – 00161 Roma - Italy
silvio.brusaferro@iss.it

Da: Segreteria CTS <segreteria.cts@protezionecivile.it>
Data: mercoledì 8 luglio 2020 21:17
A: cts <cts@protezionecivile.it>
Oggetto: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

gentili colleghi,

reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).

per la vostra nuova (ed urgente) approvazione del verbale emendato.

grazie per la pazienza.

fabio

Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Elisabetta Dejana <elisabetta.dejana@ifom.eu>

gio 09/07/2020 09:13

A:Segreteria CTS <segreteria.cts@protezionecivile.it>; cts <cts@protezionecivile.it>;

Approvo.

Elisabetta Dejana

Segreteria CTS (segreteria.cts@protezionecivile.it) wrote:
>
> gentili colleghi,
>
>
> reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).
>
>
> per la vostra nuova (ed urgente) approvazione del verbale emendato.
>
>
> grazie per la pazienza.
>
>
> fabio
>

R: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Dionisio Mauro <m.dionisio@sanita.it>

gio 09/07/2020 09:21

A: Segreteria CTS <segreteria.cts@protezionecivile.it>;

Approvo il verbale emendato
Buona giornata
Mauro Dionisio

Ministero della Salute
Direzione Generale della Prevenzione Sanitaria

Dott. Mauro Dionisio
Direttore Ufficio 3 – Coordinamento USMAF - SASN

Viale Giorgio Ribotta, 5 - 00144 Roma
tel. 06 5994 2714 email: [r.biribicchi@sanita.it]***m.dionisio@sanita.it***

Da: Segreteria CTS <segreteria.cts@protezionecivile.it>
Inviato: mercoledì 8 luglio 2020 21:17
A: cts <cts@protezionecivile.it>
Oggetto: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020
Priorità: Alta

gentili colleghi,

reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).

per la vostra nuova (ed urgente) approvazione del verbale emendato.

grazie per la pazienza.

fabio

Re: [EXT] EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

GUERRA, Raniero <guerrar@who.int>

mer 08/07/2020 22:38

A: Segreteria CTS <segreteria.cts@protezionecivile.it>;

Cc: cts <cts@protezionecivile.it>;

Va bene
Rg

Ranieri Guerra
Assistant Director-General
World Health Organization
Tel: +4122 791 36 00
E-mail: guerrar@who.int
http://www.who.int/en/

> On 8 Jul 2020, at 21:17, Segreteria CTS <segreteria.cts@protezionecivile.it> wrote:
>
> gentili colleghi,
>
> reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).
>
> per la vostra nuova (ed urgente) approvazione del verbale emendato.
>
> grazie per la pazienza.
>
> fabio
>
> <verbale CTS 94 del 07-07-2020.pdf>

Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

a.iachino@sanita.it

gio 09/07/2020 06:52

A:Segreteria CTS <segreteria.cts@protezionecivile.it>;

Approvo

Ottieni Outlook per Android

Da: Segreteria CTS <segreteria.cts@protezionecivile.it>
Inviato: Mercoledì 8 Luglio 2020, 21:17
A: cts
Oggetto: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

gentili colleghi,

reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).

per la vostra nuova (ed urgente) approvazione del verbale emendato.

grazie per la pazienza.

fabio

Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Iavicoli Sergio <s.iavicoli@inail.it>

mer 08/07/2020 22:04

A:Segreteria CTS <segreteria.cts@protezionecivile.it>; cts <cts@protezionecivile.it>;

Concordo

SI

Scarica Outlook per iOS

Da: Segreteria CTS <segreteria.cts@protezionecivile.it>
Inviato: Wednesday, July 8, 2020 9:17:15 PM
A: cts <cts@protezionecivile.it>
Oggetto: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

gentili colleghi,

reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).

per la vostra nuova (ed urgente) approvazione del verbale emendato.

grazie per la pazienza.

fabio

R: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Ippolito Giuseppe <giuseppe.ippolito@inmi.it>

mer 08/07/2020 22:21

A:Segreteria CTS <segreteria.cts@protezionecivile.it>;

Cc:cts <cts@protezionecivile.it>;

La mia approvazione era riferita al Verbale N. 94 DEL 7/7/2020

Giuseppe Ippolito MD, MSc (HCMO), FRCPE
Scientific Director
National Institute for
Infectious Diseases Lazzaro Spallanzani
Via Portuense, 292
00149 Rome
Italy
phone ++39-06-5594223
fax ++39-06-5594224
mobile ++39 328 3705118
Skype: g.ippolito
office e-mail: giuseppe.ippolito@inmi.it
home e-mail: giuseppe.ippolito.rm@gmail.com

Da: Antonelli Massimo <Massimo.Antonelli@unicatt.it>
Inviato: mercoledì 8 luglio 2020 21:36
A: Segreteria CTS <segreteria.cts@protezionecivile.it>
Cc: cts <cts@protezionecivile.it>
Oggetto: Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Approvo
Grazie
MA

Inviato da iPhone

> Il giorno 8 lug 2020, alle ore 21:17, Segreteria CTS <segreteria.cts@protezionecivile.it> ha scritto:
>
> gentili colleghi,

R: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Locatelli Franco <franco.locatelli@opbg.net>

gio 09/07/2020 09:57

A Brusaferro Silvio <silvio.brusaferro@iss.it>; Segreteria CTS <segreteria.cts@protezionecivile.it>; cts <cts@protezionecivile.it>;

Approvo il verbale e l'emendamento.
FL

Prof. Franco Locatelli
Full Professor of Pediatrics
Sapienza, University of Rome
Director
Department of Pediatric Hematology and Oncology
IRCCS Ospedale Pediatrico Bambino Gesù
Piazza Sant'Onofrio, 4
00165 Rome
Italy

Phone: +39 06 68592678/2129
Fax: +39 06 68592292
e-mail: franco.locatelli@opbg.net

Da: Silvio Brusaferro <silvio.brusaferro@iss.it>
Inviato: giovedì 9 luglio 2020 08:56
A: Segreteria CTS <segreteria.cts@protezionecivile.it>; cts <cts@protezionecivile.it>
Oggetto: Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

approvo

Silvio Brusaferro
Presidente Istituto Superiore di Sanità - Roma
President of Istituto Superiore di Sanità - Rome
Viale Regina Elena 299 – 00161 Roma - Italy
silvio.brusaferro@iss.it

Da: Segreteria CTS <segreteria.cts@protezionecivile.it>
Data: mercoledì 8 luglio 2020 21:17
A: cts <cts@protezionecivile.it>
Oggetto: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

gentili colleghi,

reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).

RE: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Ammassari Adriana <A.Ammassari@aifa.gov.it>

gio 09/07/2020 09:05

A: Segreteria CTS <segreteria.cts@protezionecivile.it>; cts <cts@protezionecivile.it>;

Approvo
AA

Dott.ssa Adriana Ammassari
Innovazione e strategia del farmaco
AIFA

Da: Segreteria CTS [segreteria.cts@protezionecivile.it]
Inviato: mercoledì 8 luglio 2020 21.17
A: cts
Oggetto: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

gentili colleghi,

reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).

per la vostra nuova (ed urgente) approvazione del verbale emendato.

grazie per la pazienza.

fabio

Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Rosa Marina Melillo <rosmelil@unina.it>

gio 09/07/2020 08:47

A: Antonelli Massimo <massimo.antonelli@unicatt.it>;

Cc: Segreteria CTS <segreteria.cts@protezionecivile.it>; cts <cts@protezionecivile.it>;

Approvo

Grazie

Rosa Marina Melillo

Inviato da iPhone

> Il giorno 9 lug 2020, alle ore 01:30, Antonelli Massimo <Massimo.Antonelli@unicatt.it> ha scritto:
>
> Approvo
> Grazie
> MA
>
> Inviato da iPhone
>
> > Il giorno 8 lug 2020, alle ore 21:17, Segreteria CTS <segreteria.cts@protezionecivile.it> ha scritto:
> >
> > gentili colleghi,
> >
> > reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).
> >
> > per la vostra nuova (ed urgente) approvazione del verbale emendato.
> >
> > grazie per la pazienza.
> >
> > fabio
> >
> > <verbale CTS 94 del 07-07-2020.pdf>

Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Flavia Petrini <flavia.petrini@unich.it>

gio 09/07/2020 07:47

A:Segreteria CTS <segreteria.cts@protezionecivile.it>;

Cc:cts <cts@protezioneciville.it>;

Priorità: Alta

Concordo
FP

Il giorno 8 lug 2020, alle ore 21:17, Segreteria CTS <segreteria.cts@protezionecivile.it> ha scritto:

gentili colleghi,

reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).

per la vostra nuova (ed urgente) approvazione del verbale emendato.

grazie per la pazienza.

fabio
<verbale CTS 94 del 07-07-2020.pdf>

Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Petropulacos Kyriakoula <Kyriakoula.Petropulacos@regione.emilia-romagna.it>

gio 09/07/2020 08:49

A Segreteria CTS <segreteria.cts@protezionecivile.it>;

Approvo

Da: Segreteria CTS <segreteria.cts@protezionecivile.it>
Data: mercoledì 8 luglio 2020 21:17
A: cts <cts@protezionecivile.it>
Oggetto: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

gentili colleghi,

reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).

per la vostra nuova (ed urgente) approvazione del verbale emendato.

grazie per la pazienza.

fabio

Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Luca Richeldi <luca.richeldi@policlinicogemelli.it>

mer 08/07/2020 21:22

A:Segreteria CTS <segreteria.cts@protezionecivile.it>;

Grazie Fabio, approvo.

Luca

Prof. Luca Richeldi
Università Cattolica del Sacro Cuore

Da: Segreteria CTS <segreteria.cts@protezionecivile.it>
Data: mercoledì 8 luglio 2020 21:17
A: cts <cts@protezionecivile.it>
Oggetto: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

gentili colleghi,

reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).

per la vostra nuova (ed urgente) approvazione del verbale emendato.

grazie per la pazienza.

fabio

5X1000

Re: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Stefano Palomba <stefano.palomba@gmail.com>

gio 09/07/2020 09:03

A:Segreteria CTS <segreteria.cts@protezionecivile.it>;

Igesan, Approva

Il Gio 9 Lug 2020, 07:54 Segreteria CTS <segreteria.cts@protezionecivile.it> ha scritto:

Da: Segreteria CTS
Inviato: mercoledì 8 luglio 2020 21:17
A: cts
Oggetto: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

gentili colleghi,

reinvio il verbale n. 94 del 7/7/2020 con alcuni emendamenti relativi ai quesiti sulla scuola richiesti dal ministero dell'istruzione (definizione precisa della "zona banchi" e della "zona interattiva della cattedra", introduzione di un caveat relativo all'obbligo dell'uso delle mascherine da aggiornarsi all'esito degli indici epidemiologici rilevati a fine agosto).

per la vostra nuova (ed urgente) approvazione del verbale emendato.

grazie per la pazienza.

fabio

R: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

Villani Alberto <alberto.villani@opbg.net>

gio 09/07/2020 08:55

A:Segreteria CTS <segreteria.cts@protezionecivile.it>;

Approvo
Alberto Villani

Alberto Villani, MD PhD
Responsabile Unità Operativa Complessa
Pediatria Generale e Malattie Infettive
Unità di Ricerca Patogenesi e Terapie Innovative in Infettivologia
Dipartimento Pediatrico Universitario - Ospedaliero
Tel. +39.06.6859.2758 - 2744
Fax +39.06.6859.2914
Ospedale Pediatrico Bambino Gesù
Piazza Sant'Onofrio, 4 - 00165 Roma

Da: Segreteria CTS <segreteria.cts@protezionecivile.it>
Inviato: mercoledì 8 luglio 2020 21:17
A: cts <cts@protezionecivile.it>
Oggetto: EMENDAMENTO - Verbale N. 94 DEL 7/7/2020

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per la vostra nuova (ed urgente) approvazione del verbale emendato.

grazie per la pazienza.

fabio

Il Ministro della Salute

ALLEGATO N. 1

faccio riferimento all'acclusa nota prot. 4477 del 3 luglio 2020, con la quale il Ministro dell'istruzione ha trasmesso a questo Dicastero alcuni quesiti concernenti l'applicazione delle misure di sicurezza nelle istituzioni scolastiche, sui quali acquisire il parere del Comitato tecnico-scientifico.

Tanto premesso, Ti chiedo di voler sottoporre i predetti quesiti alle valutazioni di codesto Comitato, al fine di poter fornire un riscontro all'unita richiesta.

L'occasione mi è gradita per porgerTi cordiali saluti.

Roberto Speranza

Dott. Agostino Miozzo
Coordinatore Comitato tecnico scientifico
Dipartimento della protezione civile
Presidenza del Consiglio dei ministri

e p.c.

Dott. Angelo Borrelli
Capo del Dipartimento della protezione civile
Presidenza del Consiglio dei ministri

Ministero dell'Istruzione
Il Ministro

Gentile Ministro, Caro Roberto,

ti invio in allegato i nuovi quesiti da trasmettere al Comitato Tecnico Scientifico, emersi nel corso dell'incontro del 2 luglio u.s., che si è svolto presso la sede del Comitato stesso, a cui hanno partecipato i rappresentanti delle Organizzazioni Sindacali.

Colgo l'occasione per ringraziare, ancora una volta, te e il Comitato per la disponibilità dimostrata.

Lucia Azzolina

On. Roberto Speranza
Ministro della Salute
ROMA

Visto dal funzionario responsabile

- In riferimento al distanziamento previsto, il metro di distanza deve intendersi solo in condizione statica o anche in movimento? Qualora, infatti, non sia possibile garantire il metro previsto durante gli spostamenti che avvengono all'interno o all'esterno della classe, è sufficiente il solo utilizzo della mascherina?

- In relazione al metro di distanziamento previsto, è possibile indicare il valore in metri quadri dello spazio di occupazione di ciascun studente?

- Quando uno studente o il personale scolastico dovesse presentare, all'interno della sede scolastica, dei sintomi riconducibili al virus Covid19, quali sono le procedure da adottare? E' possibile la predisposizione di un unico protocollo sanitario valido su tutto il territorio nazionale? Quale deve essere il ruolo della ASL, del pediatra e del medico di base in caso di individuazione di soggetti positivi?

- E' possibile attivare una collaborazione tra le istituzioni scolastiche e le ASL territorialmente competenti, prevedendo l'individuazione di un referente e/o di una struttura locale specificatamente dedicata, volta ad assistere e supportare le scuole nell'attuazione delle misure di prevenzione e contenimento del contagio dal Covid-19?

- Si ritiene necessaria l'obbligatorietà della figura del medico competente per la sorveglianza sanitaria ordinaria presso ogni sede scolastica?

- In merito alle operazioni di pulizia degli ambienti scolastici, tenuto conto che diversamente dagli esami di stato il numero dei presenti nelle scuole sarà a settembre molto elevato, è possibile indicare le modalità e la periodicità con cui esse devono avvenire? Con particolare riferimento ai servizi igienici, è possibile specificare le modalità e la frequenza per lo svolgimento delle pulizie ed il numero minimo di bagni necessari in rapporto al numero totale degli studenti e del personale scolastico di ciascun istituto?

- E' possibile dettagliare i dispositivi di protezione che devono indossare le seguenti tipologie di lavoratori?
  1) collaboratori scolastici nelle attività di pulizia e detersione di cui alle indicazioni dell'ISS previste nel documento dell'8 maggio 2020 nella sezione relativa a "Opzioni di sanificazione tutti i tipi di locali" riportato in allegato 1;
  2) Docenti/ATA nel caso di gestione di un eventuale caso sospetto da COVID;
  3) personale amministrativo nelle attività di ricevimento front office e nella gestione del cartaceo con spray idro alcolico.

- Possono essere fornite indicazioni precise per la gestione dei laboratori tecnico-pratici degli istituti superiori, soprattutto per ciò che riguarda le misure di prevenzione del rischio da interferenze e da contagio tramite superfici?

- E' necessario predisporre delle misure di pulizia e igienizzazione specifiche presso ogni sede scolastica in occasione della riapertura di settembre?

- Chi cura il reperimento e la distribuzione di mascherine per il personale scolastico e per gli studenti in condizione di lavoratori (ad es. per attività di laboratorio)? Sarà cura del dirigente scolastico o della Protezione Civile? Analogamente, per quanto riguarda i banchi monoposto, chi ne cura il reperimento?

- E' possibile chiarire le condizioni di utilizzo delle mascherine rispetto alla fascia di età dello studente? Con particolare riferimento agli alunni della scuola dell'infanzia quali sono le indicazioni sulle modalità di inserimento e accompagnamento da parte dei genitori o di altre figure parentali?

- E' possibile dettagliare maggiormente le modalità e le misure igienico sanitarie da predisporre nell'ambito della refezione scolastica (anche nel caso di consumo del pasto in classe)?

- Per i percorsi per le competenze trasversali e l'orientamento (già alternanza scuola lavoro) si pone un problema di responsabilità da parte della scuola che invia gli studenti presso aziende ed enti. A quali regole devono attenersi queste ultimi soggetti?

- Possono essere fornite indicazioni chiare sull'autorità medica competente a certificare la condizione di "fragilità" dei lavoratori?

ALLEGATO N. 2

Cochrane Library

Cochrane Database of Systematic Reviews

Antibody tests for identification of current and past infection with SARS-CoV-2 (Review)

Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Spijker R, Taylor-Phillips S, Adriano A, Beese S, Dretzke J, Ferrante di Ruffano L, Harris IM, Price MJ, Dittrich S, Emperador D, Hooft L, Leeflang MMG, Van den Bruel A, Cochrane COVID-19 Diagnostic Test Accuracy Group

Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Spijker R, Taylor-Phillips S, Adriano A, Beese S, Dretzke J, Ferrante di Ruffano L, Harris IM, Price MJ, Dittrich S, Emperador D, Hooft L, Leeflang MMG, Van den Bruel A.
Antibody tests for identification of current and past infection with SARS-CoV-2.
Cochrane Database of Systematic Reviews 2020, Issue 6. Art. No.: CD013652.
DOI: 10.1002/14651858.CD013652.

TABLE OF CONTENTS

[Diagnostic Test Accuracy Review]

Antibody tests for identification of current and past infection with SARS-CoV-2

Jonathan J Deeks[1,2], Jacqueline Dinnes[1,2], Yemisi Takwoingi[1,2], Clare Davenport[1,2], René Spijker[3,4], Sian Taylor-Phillips[1,5], Ada Adriano[1], Sophie Beese[1], Janine Dretzke[1], Lavinia Ferrante di Ruffano[1], Isobel M Harris[1], Malcolm J Price[1,2], Sabine Dittrich[6], Devy Emperador[6], Lotty Hooft[4], Mariska MG Leeflang[7,8], Ann Van den Bruel[9], Cochrane COVID-19 Diagnostic Test Accuracy Group[1]

[1]Test Evaluation Research Group, Institute of Applied Health Research, University of Birmingham, Birmingham, UK. [2]NIHR Birmingham Biomedical Research Centre, University Hospitals Birmingham NHS Foundation Trust and University of Birmingham, Birmingham, UK. [3]Medical Library, Amsterdam UMC, University of Amsterdam, Amsterdam Public Health, Amsterdam, Netherlands. [4]Cochrane Netherlands, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands. [5]Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, UK. [6]FIND, Geneva, Switzerland. [7]Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands. [8]Biomarker and Test Evaluation Programme (BiTE), Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands. [9]Department of Public Health and Primary Care, KU Leuven, Leuven, Belgium

Contact address: Jonathan J Deeks, j.deeks@bham.ac.uk.

Editorial group: Cochrane Infectious Diseases Group.
Publication status and date: New, published in Issue 6, 2020.

Citation: Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Spijker R, Taylor-Phillips S, Adriano A, Beese S, Dretzke J, Ferrante di Ruffano L, Harris IM, Price MJ, Dittrich S, Emperador D, Hooft L, Leeflang MMG, Van den Bruel A. Antibody tests for identification of current and past infection with SARS-CoV-2. *Cochrane Database of Systematic Reviews* 2020, Issue 6. Art. No.: CD013652. DOI: 10.1002/14651858.CD013652.

ABSTRACT

Background

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus and resulting COVID-19 pandemic present important diagnostic challenges. Several diagnostic strategies are available to identify current infection, rule out infection, identify people in need of care escalation, or to test for past infection and immune response. Serology tests to detect the presence of antibodies to SARS-CoV-2 aim to identify previous SARS-CoV-2 infection, and may help to confirm the presence of current infection.

Objectives

To assess the diagnostic accuracy of antibody tests to determine if a person presenting in the community or in primary or secondary care has SARS-CoV-2 infection, or has previously had SARS-CoV-2 infection, and the accuracy of antibody tests for use in seroprevalence surveys.

Search methods

We undertook electronic searches in the Cochrane COVID-19 Study Register and the COVID-19 Living Evidence Database from the University of Bern, which is updated daily with published articles from PubMed and Embase and with preprints from medRxiv and bioRxiv. In addition, we checked repositories of COVID-19 publications. We did not apply any language restrictions. We conducted searches for this review iteration up to 27 April 2020.

Selection criteria

We included test accuracy studies of any design that evaluated antibody tests (including enzyme-linked immunosorbent assays, chemiluminescence immunoassays, and lateral flow assays) in people suspected of current or previous SARS-CoV-2 infection, or where tests were used to screen for infection. We also included studies of people either known to have, or not to have SARS-CoV-2 infection.

We included all reference standards to define the presence or absence of SARS-CoV-2 (including reverse transcription polymerase chain reaction tests (RT-PCR) and clinical diagnostic criteria).

Data collection and analysis

We assessed possible bias and applicability of the studies using the QUADAS-2 tool. We extracted 2x2 contingency table data and present sensitivity and specificity for each antibody (or combination of antibodies) using paired forest plots. We pooled data using random-effects logistic regression where appropriate, stratifying by time since post-symptom onset. We tabulated available data by test manufacturer. We have presented uncertainty in estimates of sensitivity and specificity using 95% confidence intervals (CIs).

Main results

We included 57 publications reporting on a total of 54 study cohorts with 15,976 samples, of which 8526 were from cases of SARS-CoV-2 infection. Studies were conducted in Asia (n = 38), Europe (n = 15), and the USA and China (n = 1). We identified data from 25 commercial tests and numerous in-house assays, a small fraction of the 279 antibody assays listed by the Foundation for Innovative Diagnostics. More than half (n = 28) of the studies included were only available as preprints.

We had concerns about risk of bias and applicability. Common issues were use of multi-group designs (n = 29), inclusion of only COVID-19 cases (n = 19), lack of blinding of the index test (n = 49) and reference standard (n = 29), differential verification (n = 22), and the lack of clarity about participant numbers, characteristics and study exclusions (n = 47). Most studies (n = 44) only included people hospitalised due to suspected or confirmed COVID-19 infection. There were no studies exclusively in asymptomatic participants. Two-thirds of the studies (n = 33) defined COVID-19 cases based on RT-PCR results alone, ignoring the potential for false-negative RT-PCR results. We observed evidence of selective publication of study findings through omission of the identity of tests (n = 5).

We observed substantial heterogeneity in sensitivities of IgA, IgM and IgG antibodies, or combinations thereof, for results aggregated across different time periods post-symptom onset (range 0% to 100% for all target antibodies). We thus based the main results of the review on the 38 studies that stratified results by time since symptom onset. The numbers of individuals contributing data within each study each week are small and are usually not based on tracking the same groups of patients over time.

Pooled results for IgG, IgM, IgA, total antibodies and IgG/IgM all showed low sensitivity during the first week since onset of symptoms (all less than 30.1%), rising in the second week and reaching their highest values in the third week. The combination of IgG/IgM had a sensitivity of 30.1% (95% CI 21.4 to 40.7) for 1 to 7 days, 72.2% (95% CI 63.5 to 79.5) for 8 to 14 days, 91.4% (95% CI 87.0 to 94.4) for 15 to 21 days. Estimates of accuracy beyond three weeks are based on smaller sample sizes and fewer studies. For 21 to 35 days, pooled sensitivities for IgG/IgM were 96.0% (95% CI 90.6 to 98.3). There are insufficient studies to estimate sensitivity of tests beyond 35 days post-symptom onset. Summary specificities (provided in 35 studies) exceeded 98% for all target antibodies with confidence intervals no more than 2 percentage points wide. False-positive results were more common where COVID-19 had been suspected and ruled out, but numbers were small and the difference was within the range expected by chance.

Assuming a prevalence of 50%, a value considered possible in healthcare workers who have suffered respiratory symptoms, we would anticipate that 43 (28 to 65) would be missed and 7 (3 to 14) would be falsely positive in 1000 people undergoing IgG/IgM testing at days 15 to 21 post-symptom onset. At a prevalence of 20%, a likely value in surveys in high-risk settings, 17 (11 to 26) would be missed per 1000 people tested and 10 (5 to 22) would be falsely positive. At a lower prevalence of 5%, a likely value in national surveys, 4 (3 to 7) would be missed per 1000 tested, and 12 (6 to 27) would be falsely positive.

Analyses showed small differences in sensitivity between assay type, but methodological concerns and sparse data prevent comparisons between test brands.

Authors' conclusions

The sensitivity of antibody tests is too low in the first week since symptom onset to have a primary role for the diagnosis of COVID-19, but they may still have a role complementing other testing in individuals presenting later, when RT-PCR tests are negative, or are not done. Antibody tests are likely to have a useful role for detecting previous SARS-CoV-2 infection if used 15 or more days after the onset of symptoms. However, the duration of antibody rises is currently unknown, and we found very little data beyond 35 days post-symptom onset. We are therefore uncertain about the utility of these tests for seroprevalence surveys for public health management purposes. Concerns about high risk of bias and applicability make it likely that the accuracy of tests when used in clinical care will be lower than reported in the included studies. Sensitivity has mainly been evaluated in hospitalised patients, so it is unclear whether the tests are able to detect lower antibody levels likely seen with milder and asymptomatic COVID-19 disease.

The design, execution and reporting of studies of the accuracy of COVID-19 tests requires considerable improvement. Studies must report data on sensitivity disaggregated by time since onset of symptoms. COVID-19-positive cases who are RT-PCR-negative should be included as well as those confirmed RT-PCR, in accordance with the World Health Organization (WHO) and China National Health Commission of the People's Republic of China (CDC) case definitions. We were only able to obtain data from a small proportion of available tests, and action is needed to ensure that all results of test evaluations are available in the public domain to prevent selective reporting. This is a fast-moving field and we plan ongoing updates of this living systematic review.

PLAIN LANGUAGE SUMMARY

What is the diagnostic accuracy of antibody tests for the detection of infection with the COVID-19 virus?

Background

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus that spreads easily between people in a similar way to the common cold or 'flu. Most people with COVID-19 have a mild to moderate respiratory illness, and some may have no symptoms (asymptomatic infection). Others experience severe symptoms and need specialist treatment and intensive care.

The immune system of people who have COVID-19 responds to infection by developing proteins that can attack the virus (antibodies) in their blood. Tests to detect antibodies in peoples' blood might show whether they currently have COVID-19 or have had it previously.

Why are accurate tests important?

Accurate testing allows identification of people who might need treatment, or who need to isolate themselves to prevent the spread of infection. Failure to detect people with COVID-19 when it is present (a false negative result) may delay treatment and risk further spread of infection to others. Incorrect identification of COVID-19 when it is not present (a false positive result) may lead to unnecessary further testing, treatment, and isolation of the person and close contacts. Correct identification of people who have previously had COVID-19 is important in measuring disease spread, assessing the success of public health interventions (like isolation), and potentially in identifying individuals with immunity (should antibodies in the future be shown to indicate immunity).

To identify false negative and false positive results, antibody test results are compared in people known to have COVID-19 and known not to have COVID-19. Study participants are classified as to whether they are known or not known to have COVID-19 based on criteria known as the 'reference standard'. Many studies use samples taken from the nose and throat to identify people with COVID-19. The samples undergo a test called reverse transcriptase polymerase chain reaction (RT-PCR). This testing process can sometimes miss infection (false negative result), but additional tests can identify COVID-19 infection in people with a negative RT-PCR result. These include measuring clinical symptoms, like coughing or high temperature, or 'imaging' tests like chest X-rays. People known not to have COVID-19 are sometimes identified from stored blood samples taken before COVID-19 existed, or from patients with respiratory symptoms found to be caused by other diseases.

What did the review study?

The studies looked at three types of antibody, IgA, IgG and IgM. Most tests measure both IgG and IgM, but some measure a single antibody or combinations of the three antibodies.

Levels of antibodies rise and fall at different times after infection. IgG is the last to rise but lasts longest. Levels of antibodies are usually highest a few weeks after infection.

Some antibody tests need specialist laboratory equipment. Others use disposable devices, similar to pregnancy tests. These tests can be used in laboratories or wherever the patient is (point-of-care), in hospital or at home.

We wanted to find out whether antibody tests:

- are accurate enough to diagnose infection in people with or without symptoms of COVID-19, and

- can be used to find out if someone has already had COVID-19.

What did we do?

We looked for studies that measured the accuracy of antibody tests compared with reference standard criteria to detect current or past COVID-19 infection. Studies could assess any antibody test compared with any reference standard. People could be tested in hospital or the community. Studies could test people known to have – or not to have – or be suspected of having COVID-19.

Study characteristics

We found 54 relevant studies. Studies took place in Asia (38), Europe (15), and in both USA and China (1).

Forty-six studies included people who were in hospital with suspected or confirmed COVID-19 infection only. Twenty-nine studies compared test results in people with COVID-19 with test results in healthy people or people with other diseases.

Not all studies provided details about participants' age and gender. Often, we could not tell whether studies were evaluating current or past infection, as few reported whether participants were recovering. We did not find any studies that tested only asymptomatic people.

Main results

Our findings come mainly from 38 studies that provided results based on the time since people first noticed symptoms.

Antibody tests one week after first symptoms only detected 30% of people who had COVID-19. Accuracy increased in week 2 with 70% detected, and was highest in week 3 (more than 90% detected). Little evidence was available after week 3. Tests gave false positive results in 2% of those without COVID-19.

Results from IgG/IgM tests three weeks after symptoms started suggested that if 1000 people had antibody tests, and 50 (5%) of them really had COVID-19 (as we might expect in a national screening survey):

- 58 people would test positive for COVID-19. Of these, 12 people (21%) would not have COVID-19 (false positive result).

- 942 people would test negative for COVID-19. Of these, 4 people (0.4%) would actually have COVID-19 (false negative result).

If we tested 1000 healthcare workers (in a high-risk setting) who had had symptoms, and 500 (50%) of them really had COVID-19:

- 464 people would test positive for COVID-19. Of these, 7 people (2%) would not have COVID-19 (false positive result).

- 537 people would test negative for COVID-19. Of these, 43 (8%) would actually have COVID-19 (false negative result).

We did not find convincing differences in accuracy for different types of antibody test.

How reliable were the results of the studies of this review?

Our confidence in the evidence is limited for several reasons. In general, studies were small, did not use the most reliable methods and did not report their results fully. Often, they did not include patients with COVID-19 who may have had a false negative result on PCR, and took their data for people without COVID-19 from records of tests done before COVID-19 arose. This may have affected test accuracy, but it is impossible to identify by how much.

Who do the results of this review apply to?

Most participants were in hospital with COVID-19, so were likely to have more severe disease than people with mild symptoms who were not hospitalised. This means that we don't know how accurate antibody tests are for people with milder disease or no symptoms.

More than half of the studies assessed tests they had developed themselves, most of which are not available to buy. Many studies were published quickly online as ‘preprints’. Preprints do not undergo the normal rigorous checks of published studies, so we are not certain how reliable they are.

As most studies took place in Asia, we don't know whether test results would be similar elsewhere in the world.

What are the implications of this review?

The review shows that antibody tests could have a useful role in detecting if someone has had COVID-19, but the timing of when the tests are used is important. Antibody tests may help to confirm COVID-19 infection in people who have had symptoms for more than two weeks and do not have a RT-PCR test, or have negative RT-PCR test results. The tests are better at detecting COVID-19 in people two or more weeks after their symptoms started, but we do not know how well they work more than five weeks after symptoms started. We do not know how well the tests work for people who have milder disease or no symptoms, because the studies in the review were mainly done in people who were in hospital. In time, we will learn whether having previously had COVID-19 provides individuals with immunity to future infection.

Further research is needed into the use of antibody tests in people recovering from COVID-19 infection, and in people who have experienced mild symptoms or who never experienced symptoms.

How up-to-date is this review?

This review includes evidence published up to 27 April 2020. Because a lot of new research is being published in this field, we will update this review frequently.

SUMMARY OF FINDINGS

Summary of findings 1. What is the diagnostic accuracy of antibody tests, for the diagnosis of current or prior SARS-CoV-2 infection?

Question	What is the diagnostic accuracy of antibody tests, for the diagnosis of current or prior SARS-CoV-2 infection?
Population	Adults or children suspected of • current SARS-CoV-2 infection • prior SARS-CoV-2 infection or populations undergoing screening for SARS-CoV-2 infection, including • asymptomatic contacts of confirmed COVID-19 cases • community screening

Index test	Any test for detecting antibodies to SARS-CoV-2, including:
	• laboratory-based methods
	  * ELISA
	  * CLIA
	  * other laboratory-based methods
	• rapid tests; lateral flow assays, including
	  * tests that can be used at point-of-care, such as CGIA
	  * rapid diagnostic tests, such as FIA

Target condition	Detection of • current SARS-CoV-2 infection • prior SARS-CoV-2 infection
Reference standard	RT-PCR alone, clinical diagnosis of COVID-19 based on established guidelines or combinations of clinical features and for non-COVID-19 cases, the use of pre-pandemic sources of samples for testing
Action	The current evidence-base for antibody tests is inadequate to be clear about their utility (mainly because of small numbers of small studies for each test, few data available outside of acute hospital settings, and many issues in likely bias and applicability of the studies). The sensitivity of antibody tests is too low early in disease for use as a primary test of diagnosis, but they may have value for late diagnosis, for identifying previous infection, and for sero-prevalence studies.
Limitations in the evidence	
Risk of bias	**Participant selection:** high risk of bias in 48 studies (89%) **Application of index tests:** high risk of bias in 14 studies (26%) **Reference standard:** high risk of bias in 17 studies (31%) **Flow and timing:** high risk of bias in 29 studies (54%)
Concerns about applicability of the evidence	**Participants:** high concerns in 44 studies (81%) **Index test:** high concerns in 17 studies (31%) **Reference standard:** high concerns in 33 studies (61%)
Findings	

- We included 54 studies evaluating 15,976 samples. 8256 samples were from COVID-19 cases.
- Data were not available for most antibody tests that have regulatory approval.
- Most studies reported on detection of IgG, IgM, or IgG/IgM antibodies.
- Test sensitivity was strongly related to time since onset of symptoms, with low sensitivity between 1 and 14 days, and sensitivity for IgG/IgM tests exceeding 90% between 15 and 35 days. Little evidence was available beyond 35 days.
- Specificity was high (> 98%) for all types of antibody. There was some variation in sensitivity between test methods, with laboratory-based methods appearing to outperform (point-of-care) tests using disposable devices.
- Small sample sizes, low numbers of studies and concerns and bias and applicability hinder trustworthy comparisons being made between test brands.

Quantity of evidence	**Number of studies**	**Total participants or samples**		**Total cases**
	54	15,976		8526
	Sensitivity (95% CI) ***Studies (TP/COVID cases)***			**Specificity (95%CI)** ***Studies (FP/non-COVID cases)***
	Days 8-14	**Days 15-21**	**Days 22-35**	**All time points**
IgG	66.5% (57.9 to 74.2)	88.2% (83.5 to 91.8)	80.3% (72.4 to 86.4)	99.1% (98.3% to 99.6%)
	22 (766/1200)	22 (974/1110)	12 (417/502)	44 (159/6136)
IgM	58.4% (45.5 to 70.3)	75.4% (64.3 to 83.8)	68.1% (55.0 to 78.9)	98.7% (97.4% to 99.3%)
	21 (724/1171)	21 (800/1074)	11 (378/507)	41 (183/6103)
IgG/IgM*	72.2% (63.5 to 79.5)	91.4% (87.0 to 94.4)	96.0% (90.6 to 98.3)	98.7% (97.2% to 99.4%)
	9 (441/608)	9 (636/692)	5 (146/152)	23 (78/5761)
Numbers applied to a hypothetical cohort of 1000 patients, using summary data for IgG/IgM at days 15 to 21 as an exemplar (sensitivity 91.4% (87.0 to 94.4) and specificity 98.7% (97.2 to 99.4))				
Prevalence of COVID-19	**TP (95% CI)**	**FP (95% CI)**	**FN (95% CI)**	**TN (95% CI)**
2%	18 (17 to 20)	13 (6 to 27)	2 (1 to 3)	967 (953 to 974)
5%	46 (44 to 47)	12 (6 to 27)	4 (3 to 7)	938 (923 to 944)
10%	91 (87 to 94)	12 (5 to 25)	9 (6 to 13)	888 (875 to 895)
20%	183 (174 to 189)	10 (5 to 22)	17 (11 to 26)	790 (778 to 795)
50%	457 (435 to 472)	7 (3 to 14)	43 (28 to 65)	494 (486 to 497)

CGIA: colloidal gold immunoassays; **CI:** confidence interval; **CLIA:** chemiluminescence immunoassays; **ELISA:** enzyme-linked immunosorbent assays; **FIA:** fluorescence-labelled immunochromatographic assays; **FN:** false negative; **FP:** false positive; **RT-PCR:** reverse transcription polymerase chain reaction; **TN:** true negative; **TP:** true positive; * Positive if either IgG or IgM positive.

BACKGROUND

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus and resulting COVID-19 pandemic present important diagnostic evaluation challenges. These range from understanding the value of signs and symptoms in predicting possible infection, assessing whether existing biochemical and imaging tests can identify infection and people needing critical care, and evaluating whether new diagnostic tests can allow accurate rapid and point-of-care testing, either to identify current infection, rule out infection, identify people in need of care escalation, or to test for past infection and immunity.

We are creating and maintaining a suite of living systematic reviews to cover the roles of tests and characteristics in the diagnosis of COVID-19. This review summarises evidence of the accuracy of COVID-19 antibody tests; both laboratory-based tests and point-of-care tests.

Target condition being diagnosed

COVID-19 is the disease caused by infection with the SARS-CoV-2 virus. The key target conditions for this suite of reviews are current SARS-CoV-2 infection, current COVID-19 disease, and past SARS-CoV-2 infection.

Antibody tests are being considered and evaluated for both:

- identification of past SARS-CoV-2 infection, and
- current infection.

For current infection the severity of the disease is of importance. SARS-CoV-2 infection can be asymptomatic (no symptoms); mild or moderate (symptoms such as fever, cough, aches, lethargy but without difficulty breathing at rest); severe (symptoms with breathlessness and increased respiratory rate indicative of pneumonia); or critical (requiring respiratory support due to severe acute respiratory syndrome (SARS) or acute respiratory distress syndrome (ARDS). People with COVID-19 pneumonia (severe or critical disease) require different patient management, and it is important to be able to identify them. There is no consideration that antibody tests are able to distinguish severity of disease, thus, in this review, we consider their role for detecting SARS-CoV-2 infection of any severity (asymptomatic or symptomatic).

Index test(s)

Antibody tests

This review evaluates serology tests to measure antibodies to the SARS-CoV-2 virus. Antibodies are formed by the body's immune system in response to infections, and can be detected in whole blood, plasma or serum. Antibodies are specific to the virus, and therefore can be used to differentiate between different infections. There are three types of antibody created in response to infection: IgA, IgG and IgM; these rise and fall at different times after the onset of infection. IgG is used in most antibody tests as it persists for the longest time and may reflect longer-term immunity, although it is the last to rise after infection. Many tests assess both IgG and IgM. IgM typically rises quickly with infection and declines soon after an infection is cleared. Alternatively tests may combine IgA with IgG, or measure all antibodies (IgA, IgG and IgM).

Antibody tests are available for laboratory use including enzyme-linked immunosorbent assay (ELISA) methods, or more advanced chemiluminescence immunoassays (CLIA). There are also laboratory-independent, point-of-care lateral flow assays, which use disposable devices, akin to a pregnancy test, that use a minimal amount of blood on a testing strip. Antibody detection is indicated by visible lines appearing on the test strip, or through fluorescence, which can be detected using a reader device. Many of these tests are known as colloidal gold-based immunoassays, as they use COVID-19 antigen conjugated to gold nanoparticles.

Following the emergence of COVID-19 there has been prolific industry activity to develop accurate antibody tests. The Foundation for Innovative Diagnostics (FIND) and Johns Hopkins Centre for Health Security have maintained online lists of these and other molecular-based tests for COVID-19. At the time of writing (21 May 2020), FIND listed 279 antibody tests, 196 of which are produced by commercial companies and are commercially available. Reguatory approval in the European Union (EU; CE-IVD) had been awarded to 185 on the list, whereas in China only seven had been approved, and eight by the FDA (US Food and Drug Administration). For a period of time the FDA allowed commercialisation of antibody tests in the USA without FDA approval, resulting in around 100 tests being placed on the market. Both the content of the list, and these figures will increase over time.

Clinical pathway

Broadly speaking, there are four considered uses of antibody tests.

1. In diagnosis of acute suspected COVID-19 in patients who presented with symptoms, particularly where molecular testing had failed to detect the virus.
2. In assessment of immune response in patients with severe disease.
3. For individuals to assess whether they have had a SARS-CoV-2 infection and have an immune response.
4. In seroprevalence surveys for public health management purposes.

For 1, the standard approach to diagnosis of COVID-19 is through a reverse transcription polymerase chain reaction (RT-PCR) test, which detects the presence of virus in swab samples taken from nose, throat or fluid from the lungs. However, the test is known to give false negative results, and can only detect COVID-19 in the acute phase of the illness. Both the World Health Organization (WHO) and the China CDC (National Health Commission of the People's Republic of China), have produced case definitions for COVID-19 that include RT-PCR-negative cases that display other convincing clinical evidence (Appendix 1). The most recent case definition from the China CDC includes positive serology tests. Confirming an acute clinical diagnosis using a serology test requires detectable virus-specific IgM and IgG in serum, or detectable virus-specific IgG, or a 4-fold or greater increase in titration to be observed during convalescence compared with the acute phase.

For 2, this is largely a question of monitoring patients, and we will not cover this in this review. Assessment of the accuracy of a test used for assessment of immune response would involve comparison with a reference standard test of antibody response, rather than evidence of infection.

Use 3 involves testing individuals during periods of convalescence (after symptoms have resolved) whereas 4 will involve testing people at a mixture of time points, including long follow-up. A key difference between 3 and 4 is the likelihood of disease, which is expected to be much higher for 3 than 4.

An extended version of use case scenarios is available in Appendix 2.

Prior test(s)

Prior testing depends on the purpose of the test. For 1 we would anticipate that patients were symptomatic and had most likely undergone RT-PCR testing and possible computed tomography (CT) imaging. Uses 3 and 4 will most likely include people who have not been tested, and may include people who are asymptomatic as well as symptomatic.

Alternative test(s)

This review is one of six planned reviews that cover the range of tests and characteristics being considered in the management of COVID-19 (Deeks 2020; McInnes 2020). Full details of the alternative tests and evidence of their accuracy will be summarised in these reviews.

Laboratory-based molecular tests

Testing for presence of the SARS-CoV-2 virus has been undertaken using quantitative RT-PCR (qRT-PCR). RT-PCR tests for SARS-CoV-2 identify viral ribonucleic acid (RNA). Reagents for the assay were rapidly produced once the viral RNA sequence was published. Testing is undertaken in central laboratories and can be very labour-intensive, with several points along the path of performing a single test where errors may occur, although some automation of parts of the process is possible. Although the actual qRT-PCR test does not take long, the stages of extraction, sample processing and data management mean that test results are typically available in 24 to 48 hours, although faster processes are being implemented. Other nucleic acid amplification methods such as loop-mediated isothermal amplification (LAMP), or CRISPR-based nucleic acid detection methods are also being developed, with the potential to reduce the time to produce test results to minutes, but the time for the whole process may still be significant. RT-PCR tests use upper and lower respiratory samples. Sputum is currently considered better than oropharynx swabs or nasopharynx swabs but is more difficult (and hazardous) to obtain and will only ever be available in a subset of patients.

Laboratory-independent point-of-care and near-patient molecular and antigen tests

Laboratory-independent RT-PCR devices can also be used for identification of infection near patients and even at the bedside. These are small platforms for testing which use matching test cartridges. Several companies have suitable existing technology systems and are producing the required new cartridges for diagnosis of SARS-CoV-2 infection. Test results are based on the same samples as those for qRT-PCR, with results available within minutes or hours. Antigen tests are based on the direct detection of the virus, indicating active infection (i.e. replication of the virus) similar to the detection of RNA. Antigen tests are mainly in the form of lateral flow assays. They will capture the relevant viral antigen using dedicated antibodies, and visualisation is either manual or using a reader device.

Signs and symptoms

Signs and symptoms are used in the initial diagnosis of suspected COVID-19, and in identifying people with COVID-19 pneumonia. Key symptoms that have been associated with mild to moderate COVID-19 include: troublesome dry cough (for example, coughing more than usual over a one-hour period, or three or more coughing episodes in 24 hours), fever greater than 37.8°C, diarrhoea, headache, breathlessness on light exertion, muscle pain, fatigue, and loss of sense of smell and taste. Red flags indicating possible pneumonia include: breathlessness at rest, increased respiratory rate (above 20 breaths per minute), increased heart rate (above 100 beats per minute), chest tightness, loss of appetite, confusion, pain or pressure in the chest, blue lips or face, and temperature above 38°C. Hypoxia based on measuring pulse oximetry is often used, with various arbitrary thresholds (for example, 93%).

Routinely available biomarkers

Routinely available biomarkers for infection and inflammation may be considered in the investigation of people with possible COVID-19. For example, many healthcare facilities have access to standard laboratory tests for infection, such as C-reactive protein (CRP), procalcitonin, measures of anticoagulation, and white blood cell count with different lymphocyte subsets. Evaluation of these commonly available tests, particularly in low-resource settings, may be helpful for the triage of people with potential COVID-19.

Imaging tests

Chest X-ray, ultrasound, and CT are widely used diagnostic imaging tests to identify COVID-19 pneumonia. Availability and usage varies between settings.

Rationale

It is essential to understand the clinical accuracy of tests and diagnostic features to identify the best way they can be used in different settings to develop effective diagnostic and management pathways. The suite of Cochrane 'living systematic reviews' summarises evidence on the clinical accuracy of different tests and diagnostic features, grouped according to the research questions and settings that we are aware of. Estimates of accuracy from these reviews will help inform diagnosis, screening, isolation, and patient management decisions.

Particularly for antibody tests, new tests are being developed and evidence is emerging at an unprecedented rate during the COVID-19 pandemic. Tests are being purchased in bulk for seroprevalence studies, and made available for personal purchase online. This review will be updated as often as is feasible to ensure that it provides current evidence about the accuracy of antibody tests.

OBJECTIVES

To assess the diagnostic accuracy of antibody tests to determine if a person presenting in the community or in primary or secondary care has SARS-CoV-2 infection, or has previously had SARS-CoV-2 infection, and the accuracy of antibody tests for use in seroprevalence surveys.

Secondary objectives

Where data are available, we will investigate the accuracy (either by stratified analysis or meta-regression) according to:

- current infection or past infection;
- test method and brand;
- days since onset of symptoms;
- reference standard;
- study design;
- setting.

METHODS

Criteria for considering studies for this review

Types of studies

We applied broad eligibility criteria in order to include all patient groups and all variations of a test (that is, if patient population was unclear, we included the study).

We included studies of all designs that produce estimates of test accuracy or provide data from which estimates can be computed, including the following.

- Studies restricted to participants confirmed to have (or to have had) the target condition (to estimate sensitivity) or confirmed not to have (or have had) the target condition (to estimate specificity). These types of studies may be excluded in later review updates.
- Single-group studies, which recruit participants before disease status has been ascertained
- Multi-group studies, where people with and without the target condition are recruited separately (often referred to as two-gate or diagnostic case-control studies)
- Studies based on either patients or samples

We excluded studies from which we could not extract data to compute either sensitivity or specificity.

We carefully considered the limitations of different study designs in the quality assessment and analyses.

We included studies reported in published articles and as preprints.

Participants

We included studies recruiting people presenting with suspicion of current or prior SARS-CoV-2 infection or those recruiting populations where tests were used to screen for disease (for example, contact tracing or community screening).

We also included studies that recruited people either known to have SARS-CoV-2 infection or known not to have SARS-CoV-2 infection (multi-group studies).

We excluded small studies with fewer than 10 samples or participants. Although the size threshold of 10 is arbitrary, such small studies are likely to give unreliable estimates of sensitivity or specificity and may be biased.

Index tests

We included studies evaluating any test for detecting antibodies to SARS-CoV-2, including laboratory-based methods and tests designed to be used at point-of-care. Test methods include the following.

Laboratory-based:

- enzyme-linked immunosorbent assays (ELISA)
- chemiluminescence immunoassays (CLIA)
- other laboratory-based methods (e.g. indirect immunofluorescence tests (IIFT), luciferase immunoprecipitation system (LIPS)

Rapid diagnostic tests:

- lateral flow assays, including both colloidal gold or fluorescence-labelled immunochromatographic assays (CGIA or FIA).

In this first version of the review we have included both commercially available tests, which have regulatory approval, with in-house assays and assays in development. Future versions of the review are likely to be restricted to only commercially available assays.

We identified the regulatory status of index tests using two main resources:

- WHO: COVID-19 listing in International Medical Device Regulators Forum (IMDRF) jurisdictions (www.who.int/diagnostics_laboratory/EUL/en/), which includes listings of FDA, Health Canada, Japan, Australia (Therapeutic Goods Administration), Singapore (Health Sciences Authority), Brazil (Agência Nacional de Vigilância Sanitária), South Korea (Ministry of Food and Drug Safety), China (National Medical Products Administration), and Russia (Roszdravnadzor);
- FIND: SARS-COV-2 Diagnostic Pipeline (www.finddx.org/covid-19/pipeline/), which overlaps with the WHO list, but in addition includes CE-IVD and IVD India.

In addition, we checked key national websites, including US FDA (www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#coronavirus2019) and China FDA (subsites.chinadaily.com.cn/nmpa/2020 03/27/c_465663.htm?bsh_bid=5496527208).

Target conditions

The target conditions were the identification of:

- current SARS-CoV-2 infection (in symptomatic cases);
- past SARS-CoV-2 infection (in convalescent (post-symptomatic) or asymptomatic cases).

Reference standards

We anticipated that studies would use a range of reference standards to define both the presence and absence of SARS-CoV-2 infection but were unclear at the start of the review exactly what methods would be encountered. For the QUADAS-2 (Quality Assessment tool for Diagnostic Accuracy Studies; Whiting 2011), assessment we categorised each method of defining COVID-19 cases according to the risk of bias (the chances that it would misclassify COVID-19 participants as non-COVID-19) and whether it defined COVID-19 in an appropriate way that reflected cases encountered in practice. Likewise, we considered the risk of bias in definitions of non-COVID-19, and whether the definition reflected those who, in practice, would be tested.

Search methods for identification of studies

Electronic searches

We conducted a single literature search to cover our suite of Cochrane COVID-19 diagnostic test accuracy (DTA) reviews (Deeks 2020; McInnes 2020).

We conducted electronic searches using two primary sources. Both of these searches aimed to identify all published articles and preprints related to COVID-19, and were not restricted to those evaluating biomarkers or tests. Thus, there are no test terms, diagnosis terms, or methodological terms in the searches. Searches were limited to 2019 and 2020, and for this version of the review have been conducted to 27 April 2020.

Cochrane COVID-19 Study Register searches

We used the Cochrane COVID-19 Study Register (covid-19.cochrane.org/), for searches conducted to 28 March 2020. At that time, the register was populated by searches of PubMed, as well as trials registers at ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP).

Search strategies were designed for maximum sensitivity, to retrieve all human studies on COVID-19 and with no language limits. See Appendix 3.

COVID-19 Living Evidence Database from the University of Bern

From 28 March 2020, we used the COVID-19 Living Evidence database from the Institute of Social and Preventive Medicine (ISPM) at the University of Bern (www.ispm.unibe.ch), as the primary source of records for the Cochrane COVID-19 DTA reviews. This search includes PubMed, Embase, and preprints indexed in bioRxiv and medRxiv databases. The strategies as described on the ISPM website are described here (ispmbern.github.io/covid-19/). See Appendix 4.

The decision to focus primarily on the 'Bern' feed was due to the exceptionally large numbers of COVID-19 studies available only as preprints. The Cochrane COVID-19 Study Register has undergone a number of iterations since the end of March and we anticipate moving back to the Register as the primary source of records for subsequent review updates.

Searching other resources

We identified Embase records obtained through Martha Knuth for the Centers for Disease Control and Prevention (CDC), Stephen B Thacker CDC Library, COVID-19 Research Articles Downloadable Database (www.cdc.gov/library/researchguides/2019novelcoronavirus/researcharticles.html), and de-duplicated them against the Cochrane COVID-19 Study Register up to 1 April 2020. See Appendix 5.

We also checked our search results against two additional repositories of COVID-19 publications including:

- the Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre) 'COVID-19: Living map of the evidence' (eppi.ioe.ac.uk/COVID19_MAP/covid_map_v4.html);
- the Norwegian Institute of Public Health 'NIPH systematic and living map on COVID-19 evidence' (www.nornesk.no/forskningskart/NIPH_diagnosisMap.html)

Both of these repositories allow their contents to be filtered according to studies potentially relating to diagnosis, and both have agreed to provide us with updates of new diagnosis studies added. For this iteration of the review, we examined all diagnosis studies from either source up to 16 April 2020.

In addition we have used the list of potentially eligible index tests (documented in Criteria for considering studies for this review), to search company and product websites for studies about test accuracy and to contact companies to request further information or studies using their tests. We will include the result of this process in a future iteration of this review.

We have also contacted research groups undertaking test evaluations (for example, UK Public Health England-funded studies, and FIND studies (www.finddx.org/). We appeal to researchers to supply details of additional published or unpublished studies at the following email address, which we will consider for inclusion in future updates (coviddta@contacts.bham.ac.uk).

We did not apply any language restrictions.

Data collection and analysis

Selection of studies

A team of experienced systematic reviewers from the University of Birmingham screened the titles and abstracts of all records retrieved from the literature searches. Two review authors independently screened studies in Covidence. A third, senior review author resolved any disagreements. We tagged all records selected as potentially eligible according to the Cochrane COVID-19 DTA review(s) that they might be eligible for and we then exported them to separate Covidence reviews for each review title.

We obtained the full texts for all studies flagged as potentially eligible. Two review authors independently screened the full texts for one of the COVID-19 molecular or antibody test reviews. We resolved any disagreements on study inclusion through discussion with a third review author.

Data extraction and management

One review author carried out data extraction, which was checked by a second review author. Items that we extracted are listed in Appendix 6. Both review authors independently performed data extraction of 2x2 contingency tables of the number of true positives, false positives, false negatives and true negatives. They resolved disagreements by discussion.

We encourage study authors to contact us regarding missing details on the included studies (coviddta@contacts.bham.ac.uk).

Where possible we extracted 2x2 tables according to time since onset of symptoms. We predefined groups of interest as 1-7, 8-14, 15-21, 22-35 and over 35 days since onset of symptoms. Where the data presented did not exactly match these categorisations we entered data in the time group that had the greatest overlap with our groupings. Where a study presented data for a group without stating an upper time limit (e.g. more than 21 days) we placed the data in the first category above the stated value (e.g. 22-35 days).

Where possible, we separately extracted data related to each class of antibody (IgA, IgG and IgM), and combinations of classes (IgA/

IgM, IgA/IgG, IgG/IgM, where a positive is defined as either or both classes of antibody being detected). We also extracted data on total antibodies where this was reported.

Assessment of methodological quality

Two review authors independently assessed risk of bias and applicability concerns using the QUADAS-2 checklist tailored to this review (Appendix 7; Whiting 2011). The two review authors resolved any disagreements by discussion.

Ideally, studies should prospectively recruit a representative sample of participants presenting with signs and symptoms of COVID-19, either in community or primary care settings or to a hospital setting, and they should clearly record the time of testing after the onset of symptoms. Studies should perform antibody tests in their intended use setting, using appropriate sample types as described in the 'Instructions for use' sheet (e.g. fingerprick blood for tests being evaluated for use as point-of-care tests), and tests should be performed by relevant personnel (e.g. healthcare workers), and should be interpreted blinded to the final diagnosis (COVID-19 or not). Serology samples should be taken at time points that reflect the intended use (either whilst symptomatic for diagnosis of infection, or during a convalescent period (after resolution of symptoms) for diagnosis of previous infection). The reference standard diagnosis should be blinded to the result of the antibody test, and should not incorporate the result of the index test or any other serology test. If the reference standard includes clinical diagnosis of COVID-19, then established criteria should be used. Studies including samples from participants known not to have COVID-19 should use pre-pandemic sources or contemporaneous samples with at least one RT-PCR-negative test result. Data should be reported for all study participants, including those where the result of the antibody test was inconclusive, or participants in whom the final diagnosis of COVID-19 was uncertain. If studies obtained multiple samples for testing over time from the same study participants, then they should disaggregate results by time post-symptom onset.

Statistical analysis and data synthesis

We grouped data by study and test. Thus studies that evaluated multiple tests in the same participants were included multiple times. We present estimates of sensitivity and specificity for each antibody (or combination of antibodies) using paired forest plots in tables, and also summarise them in tables as appropriate.

For analysis purposes, unlike in most DTA reviews we considered estimates of sensitivity and specificity separately, because many of the included studies presented only estimates of sensitivity. Estimates of specificity were typically exceptionally high, thus the correlation between sensitivity and specificity across studies was unlikely to be high (Macaskill 2010; Takwoingi 2017). We considered the heterogeneity in the study findings through visual inspection of forest plots when deciding to meta-analyse study estimates, and have not computed summary estimates where they were likely to be regarded as misleading.

Where we pooled results, we fitted random-effects logistic regression models using the meqrlogit command in Stata v15.1 (Stata). In a small number of instances, the random-effects logistic regression analyses failed to converge (usually when there were very small numbers of studies), and we have computed estimates and confidence intervals by summing the counts of true positive, false positive, false negative and true negative across 2x2 tables. These analyses are clearly marked in the tables. We present all estimates with 95% confidence intervals.

Investigations of heterogeneity

We investigated sources of heterogeneity in two ways. First, for analysis of sensitivity for time since onset of symptoms, we extracted data by week and extended the random-effects logistic regression model to include indicator variables for each week. There was a strong relationship between time since onset of symptoms and sensitivity, thus we elected to fit all subsequent models for investigation of heterogeneity in sensitivity stratifying by week. We excluded studies for which stratified data were not available at this stage. For analysis of sensitivity according to the RT-PCR status of patients (RT-PCR positive ‘confirmed’ and RT-PCR negative ‘suspect’), we extracted 2x2 tables stratified by RT-PCR result (as well as week) and extended the random-effects logistic regression to include terms for week and RT-PCR status.

We investigated heterogeneity related to study design, reference standard and test technology by including indicator variables in the random-effects logistic regression model alongside the variables for week since onset of symptoms. We present estimates from these models by test or reference standard type for the sensitivity of the test in the third week since onset of symptoms (since this is the time point most commonly recommended for post-infection testing to start to be undertaken).

We did not fit models to compare test brands due to the small number of studies available, but we do report estimates with confidence intervals for each brand.

Sensitivity analyses

We planned to undertake sensitivity analyses by excluding:

- unpublished studies;
- studies identified only from industry 'Instructions for use' documentation;
- studies using sample banks or spiked samples;
- studies with inadequate reference standards;
- for previous infection, we also planned to assess increasing lengths of time since symptoms cleared.

In this version of the review we did not undertake any of these analyses because the majority of studies were preprints, we did not include any company documents, and no study used spiked samples. We investigated issues with reference standards and time as part of the investigations of heterogeneity.

Assessment of reporting bias

We made no formal assessment of reporting bias. However we were aware of the manner in which results in studies could be suppressed by test developers or manufacturers, and detail where we believe this may have happened.

Summary of findings

We summarised key findings in a 'Summary of findings' table indicating the strength of evidence for each test and findings, and highlighted important gaps in the evidence.

Updating

We are aware that a substantial number of studies have been published since the search date of 27 April 2020 and plan to update this review imminently. We have already completed searches for the update up until 25 May 2020, and report the number of studies that we anticipate will be added to this review in the first update.

RESULTS

Results of the search

We screened 10,965 unique references (published or preprints) for inclusion in the complete suite of reviews to assist in the diagnosis of COVID-19 (Deeks 2020; McInnes 2020). Of 1430 records selected for further assessment for inclusion in any of the six reviews, we assessed 267 full-text reports for inclusion in this review. See Figure 1 for the PRISMA flow diagram of search and eligibility results (McInnes 2018; Moher 2009). We included 54 studies from 57 reports in this review, three studies are awaiting assessment including two foreign language papers and one study of neutralising antibodies (Characteristics of studies awaiting classification), 34 are ongoing studies (Characteristics of ongoing studies), and we excluded 172 publications. Exclusions were mainly due to ineligible study designs (n = 84) or index tests (n = 40), or because we could not extract or reconstruct 2x2 data (n = 21). The reasons for exclusion of all 172 publications are provided in Characteristics of excluded studies.

Figure 1. Study flow diagram

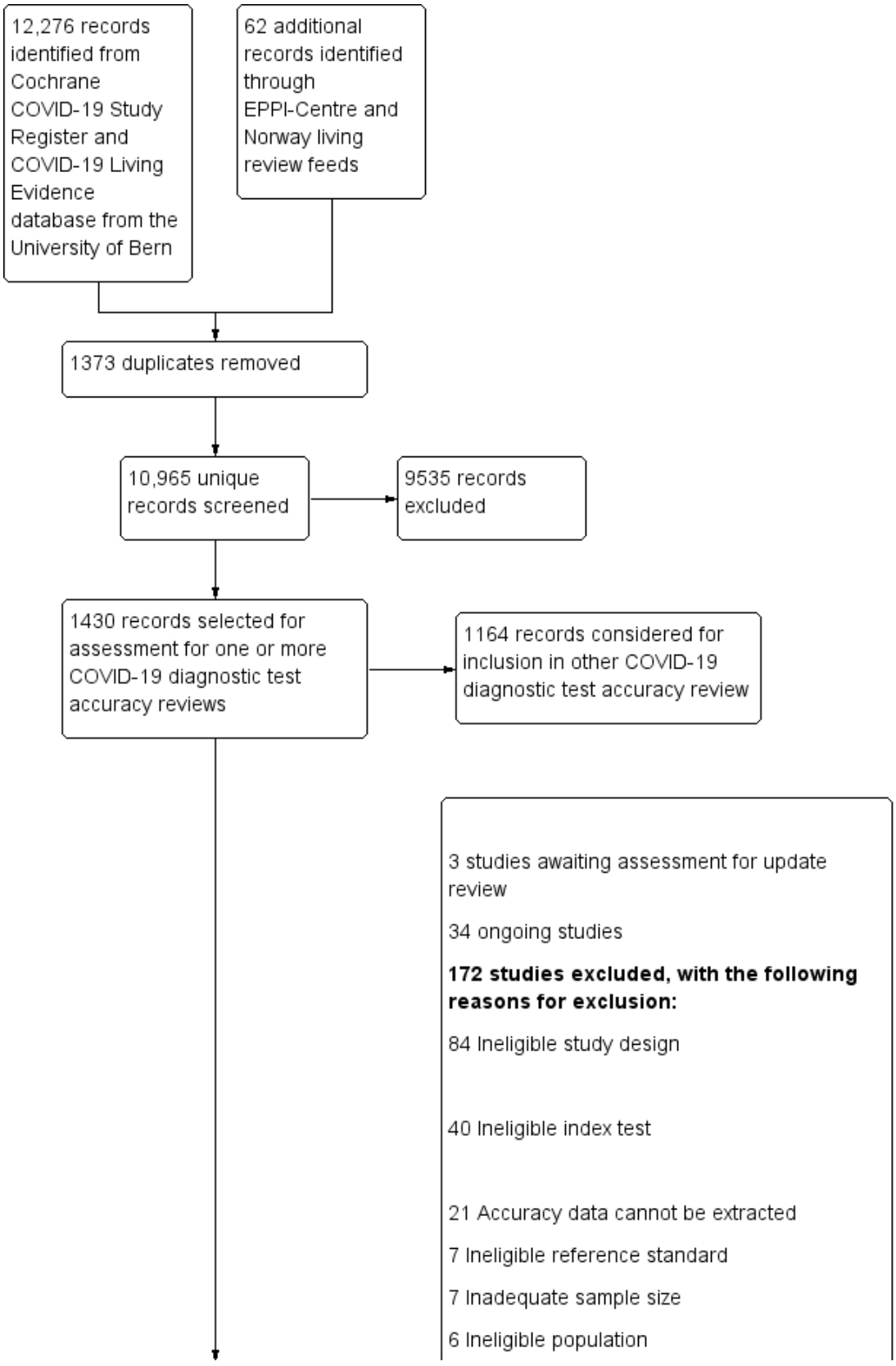
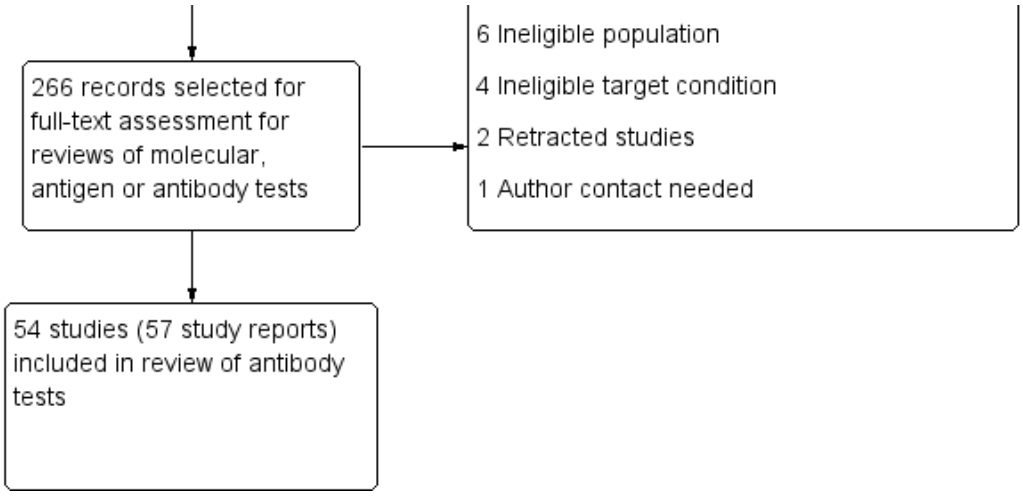


Figure 1. (Continued)



The 57 included study reports relate to 54 separate studies, six studies (Gao 2020a; Liu 2020d [A]; Pan 2020a; Okba 2020a; Wang 2020a [A]; Zhao 2020a), having two publications each, and three studies providing data for two separate cohorts of participants (Cassaniti 2020 (A); Cassaniti 2020 (B); Garcia 2020 (A); Garcia 2020 (B); Long 2020 (A); Long 2020 (B)). Of the 57 study reports, 28 studies are available only as preprints and four as preprints with subsequent journal publications. (Please note when naming studies, we use the letters (A), (B), (C) in standard brackets to indicate multiple studies from the same publication, and the letters [A], [B], [C] etc. in square brackets to indicate data on different tests evaluated in the same study).

Description of included studies

The 54 studies include a total of 15,976 samples, with 8526 samples from cases of COVID-19. Summary study characteristics are presented in Table 1 with further details of study design and index test details in Appendix 8 and Appendix 9. The median sample size across the included studies is 129.5 (interquartile range (IQR) 57 to 347) and median number of COVID-19 cases included is 62 (IQR 31 to 151). Thirty-eight studies were conducted in Asia: China (n = 36); Hong Kong (n = 1); or Singapore (n = 1). Fifteen studies were conducted in Europe, and the remaining study included samples from more than one country (Bendavid 2020). Forty-four studies included only hospital inpatient cases, one included hospital outpatients, two included participants attending emergency departments, two, community screening (including one study of close contacts). Five studies were conducted in mixed or unclear settings.

Participant characteristics

Twenty-three studies included cases during the early phase of illness only (< 21 days post-symptom onset), two only included cases 21 days or more post-symptom onset, 23 included mixed groups and six did not report days post-symptom onset. Few studies were clear whether participants were symptomatic or convalescent (i.e. symptoms had resolved) at the time of testing. It is therefore difficult to clearly separate out studies that detected current infection from studies that detected past infection. Thus the two target conditions we defined cannot clearly be distinguished. There were no studies exclusively in asymptomatic participants.

The mean or median age of included COVID-19 cases ranges from 37 to 76 years (reported in 31 studies), and 26% to 87% of participants were male (reported in 31 studies). Full details are in the Characteristics of included studies table.

Study designs

We identified six studies that recruited suspected COVID-19 cases before it was ascertained whether the patients did or did not have COVID-19. These six studies identified people with suspected COVID-19 based on symptoms or as close contacts of confirmed cases (symptomatic and asymptomatic). Sample sizes of these studies ranged from 50 to 814 with between 3 and 154 COVID-19 cases. Four of these studies defined the presence or absence of COVID-19 based on RT-PCR alone, and two also included clinically confirmed RT-PCR-negative cases based on undefined clinical suspicion or CT findings. The absence of SARS-CoV-2 infection was confirmed by a single RT-PCR-negative result in five of the six and by two or more negative RT-PCR results in one study.

The other forty-eight studies retrospectively recruited patients when it was already known whether or not they had COVID-19.

Twenty-nine studies used two- or multi-group study designs with separate selection of COVID-19 cases and healthy participants or non-COVID-19 participants with another disease. Sample sizes ranged from 17 to 3481 with between 7 and 276 COVID-19 cases. Nineteen of these studies defined COVID-19 cases based on a positive RT-PCR test, six included clinically defined RT-PCR-negative cases in addition to RT-PCR-positive cases and the remaining four studies used mixed or unclear criteria to define the presence of COVID-19. Four of the 29 studies included participants with suspected COVID-19 but who had subsequently been ruled out on the basis of one (2 studies) or more (2 studies) negative RT-PCR tests. Ten included contemporaneous non-COVID-19 groups, including samples from healthy participants (5 studies), patients with other diseases (one study) or both (4 studies), only two of which used RT-PCR testing to exclude the presence of SARS-CoV-2. Twelve studies included pre-pandemic non-COVID 19 groups, using samples from either healthy people (n = 5), participants with other diseases (n = 3), or both (n = 4). The remaining three studies included control samples from mixed sources including pre-

pandemic and contemporaneous samples, with or without RT-PCR testing.

Nineteen studies included only a single group of only COVID-19 cases, thus only allowing estimation of sensitivity. They determined COVID-19 cases based on positive RT-PCR alone (n = 9), clinically defined criteria including RT-PCR-negative cases (n = 8, 7 of which used Chinese government-issued COVID-19 guidelines to define cases), one using undefined clinical criteria, and one study that did not report how COVID-19 cases were defined.

Index tests

Forty-three studies evaluated only one test, five compared two tests, three compared 3 tests, one 5 tests, one 9 and one 10 tests. In total the 54 studies reported on a total of 89 test evaluations.

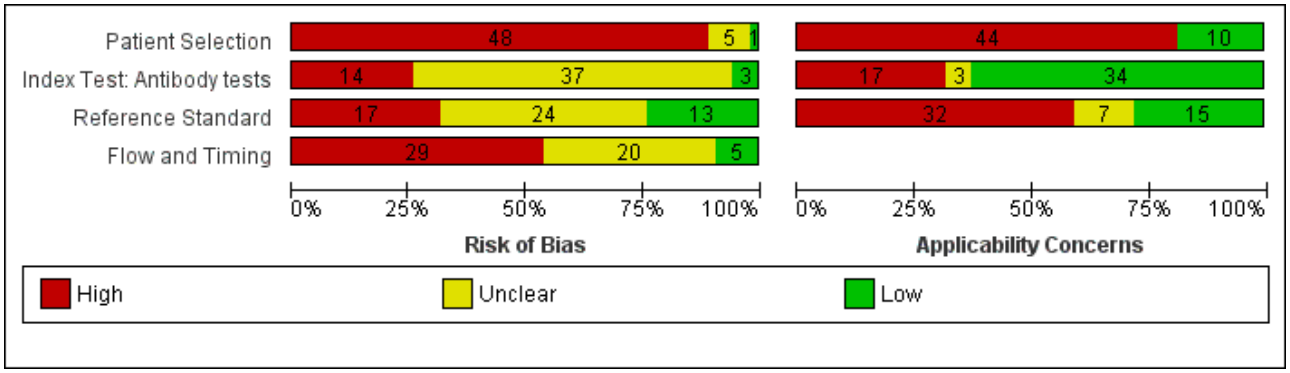
There were 52 evaluations of laboratory-based methods (27 ELISA, 19 CLIA, 6 other methods), including 32 using commercially available laboratory-based kits produced by 11 different commercial companies (16 ELISAs, 15 CLIAs and 1 IIFT), two where the manufacturer name was withheld, and 20 classified as using in-house methods (11 ELISA, 4 CLIA and 5 other approaches).

There were 34 evaluations of lateral flow assays, 23 were described as or discovered to be CGIA, two were FIAs and nine were not described. Thirty-one of the 34 evaluations used commercially available lateral flow assays and three were in-house (including two CGIA and one FIA). Of the 34 evaluations, only three used whole blood (two using the Vivadiag test), and only two used the assays as point-of-care tests rather than in a laboratory setting.

Methodological quality of included studies

We report the overall methodological quality assessed using the QUADAS-2 tool for all included studies (n = 54) in Figure 2 (Whiting 2011). See Appendix 10 for study-level ratings by quality.

Figure 2. Risk of bias and applicability concerns graph: review authors' judgements about each domain presented as percentages across included studies



Overall, we judged risk of bias to be high in 48 (89%) studies concerning how participants were selected, 14 (26%) studies related to application of the index test, 17 (31%) through concerns about the reference standard and 29 (54%) for issues related to participant flow and timing. No study had low risk in all domains. We judged that there were high concerns about the applicability of the evidence related to participants in 44 (81%) studies, 17 (31%) related to the index test and 32 (59%) related to the reference standard. Explanations of how we have reached these judgements are given below and in the Characteristics of included studies table.

Participant selection

For participant selection, we judged only one study to be at low risk of bias and five to be of unclear risk. The remaining 48 (89%) we judged to be at high risk of bias (n = 44) either due to the use of a multi-group design with healthy or other disease controls (n = 26) or recruitment of only COVID-19 cases (n = 19), inappropriate exclusions (n = 2) or inappropriate inclusions (n = 15). Numbers per group are not mutually exclusive. Eleven studies (20%) reported consecutive or random recruitment of participants.

We had high concerns about the applicability of the selection of participants in 44 studies (81%) meaning that the participants who were recruited were unlikely to be similar to those in whom the test would be used in clinical practice. This was largely because studies only recruited hospitalised, confirmed cases of COVID-19, often with severe symptoms (18 studies) or recruited healthy or other disease non-COVID-19 groups (26 studies). We judged 10 (19%) studies likely to have selected an appropriate patient group, including the six studies that recruited participants suspected of COVID-19 prior to definitive testing and four multi-group studies that separately recruited COVID-19 cases and suspected COVID-19 control groups.

Index tests

Eight studies explicitly reported that they had undertaken the index test with knowledge of whether individuals did or did not have COVID-19, and eight studies determined the threshold to define test positivity by analysing the data, rather than it being pre-determined. In 37 studies, reporting of one or both of these issues was too unclear to be able to rule out the possibility of bias. These issues led to the index test performance in 14 studies being rated as at high risk of bias. We judged only three studies to have implemented the index test in a way that protected against the risk of bias.

In 34 studies (63%) we judged the test to be implemented as it would be in practice. Twenty-two of these were evaluations of laboratory-based, commercially available tests, and 12 were evaluations of lateral flow assays associated with commercial test manufacturers, primarily evaluated in an inpatient setting. Two of the 12 evaluated the assays as point-of-care tests in an emergency

room setting. Sixteen studies raised concerns that the tests could not be purchased (high concerns for applicability). The remaining four studies provided inadequate information to make a judgement due to withholding of the names of the commercial tests (one additional study also withheld the names of the lateral flow assays evaluated but scored high concerns as it also reported results for an in-house ELISA test).

Reference standards

We judged 13 studies (24%) to have used an appropriate reference standard and implemented it in ways that prevented bias. In six studies there was a risk of misclassification, as they had used a single, negative RT-PCR result to define the absence of disease in people with suspected COVID-19; eight studies did not report any RT-PCR testing to confirm COVID-19 status for contemporaneous healthy or other disease non-COVID-19 groups; and one study used serology results in part to determine the reference standard diagnosis, thus risking incorporation bias. We judged 24 studies as having unclear risk of bias due to lack of information about blinding of the reference standard to the index test (19/24) or unclear descriptions of the reference standards used (6/24).

We judged the reference standard to be equivalent to WHO or China CDC definitions of COVID-19 in 15 studies (28%). We judged studies that used a definition based only on RT-PCR-positive results as high concern (32 (59%) of studies), and seven studies reported inadequate detail to assess the reference standard.

Flow and timing

Twenty-nine (54%) studies were at high risk of bias due to using different reference standards to verify COVID-19 and non-COVID-19 cases (n = 19), participants being excluded from the analysis (n = 15), or the inclusion of multiple samples per participant (n = 7). In 20 (37%) studies we could not make judgements on one or more of these issues, primarily due to lack of clarity around participant inclusion and exclusion from analyses. Five studies reported adequate detail to rule out these risks of bias. None of the included studies reported a Standards of Reporting Diagnostic Accuracy Studies (STARD)-style participant flow diagram (Bossuyt 2015), and none mentioned that they aimed to report in line with STARD reporting recommendations for test accuracy studies.

In 39 studies all authors declared no conflicts of interest although four included co-authors affiliated to test manufacturers. Ten studies did not provide a conflict of interest statement (two of these included co-authors affiliated to test manufacturers or biotechnology companies); and in the five remaining studies at least one author declared conflicts of interest in relation to test manufacturers (four studies) or vaccine companies (one study).

Nine studies provided no funding statement, six reported no funding sources to declare, and 39 studies reported one or more funding sources. The reported funding sources were primarily public funding sources. Two studies reported receipt of equipment ‘in kind’ from test manufacturers and two studies reported private donors.

Findings

We included 54 different studies, which were reported in 57 publications. Fourteen of the 54 studies evaluated more than one test (Table 1), up to a maximum of 10 tests per study. To incorporate all results from all tests, in these analyses we have treated results from different tests of the same samples within a study as separate data points, such that data are available on 89 test-study combinations. This leads to individual samples being included in some analyses multiple times where they have been evaluated using different tests. To identify where estimates are based on multiple assessments of the same sample sets, the tables include both the number of test-study combinations and the number of studies. The numbers of true positives, false positives, COVID-19 samples and non-COVID samples are based on test result counts.

Overall analyses

We are unable to distinguish between studies that evaluated the accuracy of antibody tests to identify current infection from past infection. Whilst time since onset of symptoms is strongly related to whether an infection was current or past, few studies reported whether participants' symptoms had resolved (and thus they were in a convalescent state) when serology samples were taken. Whilst 21 days post-symptom onset is assumed to be a point where COVID-19 cases are likely to be convalescent, many participants in these studies were hospitalised for prolonged periods and likely to reflect those with more severe and long-lasting symptoms.

A key aspect of interpreting the sensitivity of the tests is the relationship between accuracy and days since onset of symptoms. Sixteen (30%) studies only presented results aggregated over 0 to more than 35 days since onset, and did not present data (or provide datasets) that disaggregated data by week. The figures in Appendix 11 show forest plots of sensitivity and specificity estimates including these studies for IgG, IgM, and IgG/IgM (either positive), which clearly depict substantial heterogeneity in sensitivity, with estimates ranging from 0% to 100% for all three markers. Forest plots of results for IgA, total antibodies, IgA/IgG, IgA/IgM (Appendix 11), show similar heterogeneity with smaller numbers of studies. Given the heterogeneity and the known strong relationship of sensitivity with time, computation of an average estimate of sensitivity from these studies would be misleading and serves no purpose.

Sensitivity by time since onset of symptoms

Table 2 and Figure 3 present the results disaggregated by week of testing since onset of symptoms for IgG (from 23 studies), IgA (from 4 studies), IgM (from 24 studies), total antibodies (from 5 studies), combination of IgG/IgM (from 21 studies), and IgA/IgG (from 1 study; these results are based on a maximum of 12 participants per time period and we will not comment on them further). We did not find any data disaggregated by week for IgA/IgM. Forest plots of these data are given in Figure 4, Figure 5 and Figure 6. We have undertaken meta-analyses of data stratified by week as heterogeneity, whilst still present, is substantially less. As indicated in Table 2, the strength of the relationship of time with sensitivity shows exceptionally high levels of statistical significance ($P < 0.0005$). All further analyses of sensitivity in this report are thus stratified by week since symptom onset.

Figure 3. Meta-analytical estimates of sensitivity (with 95% CI) by antibody class and time since onset of symptoms

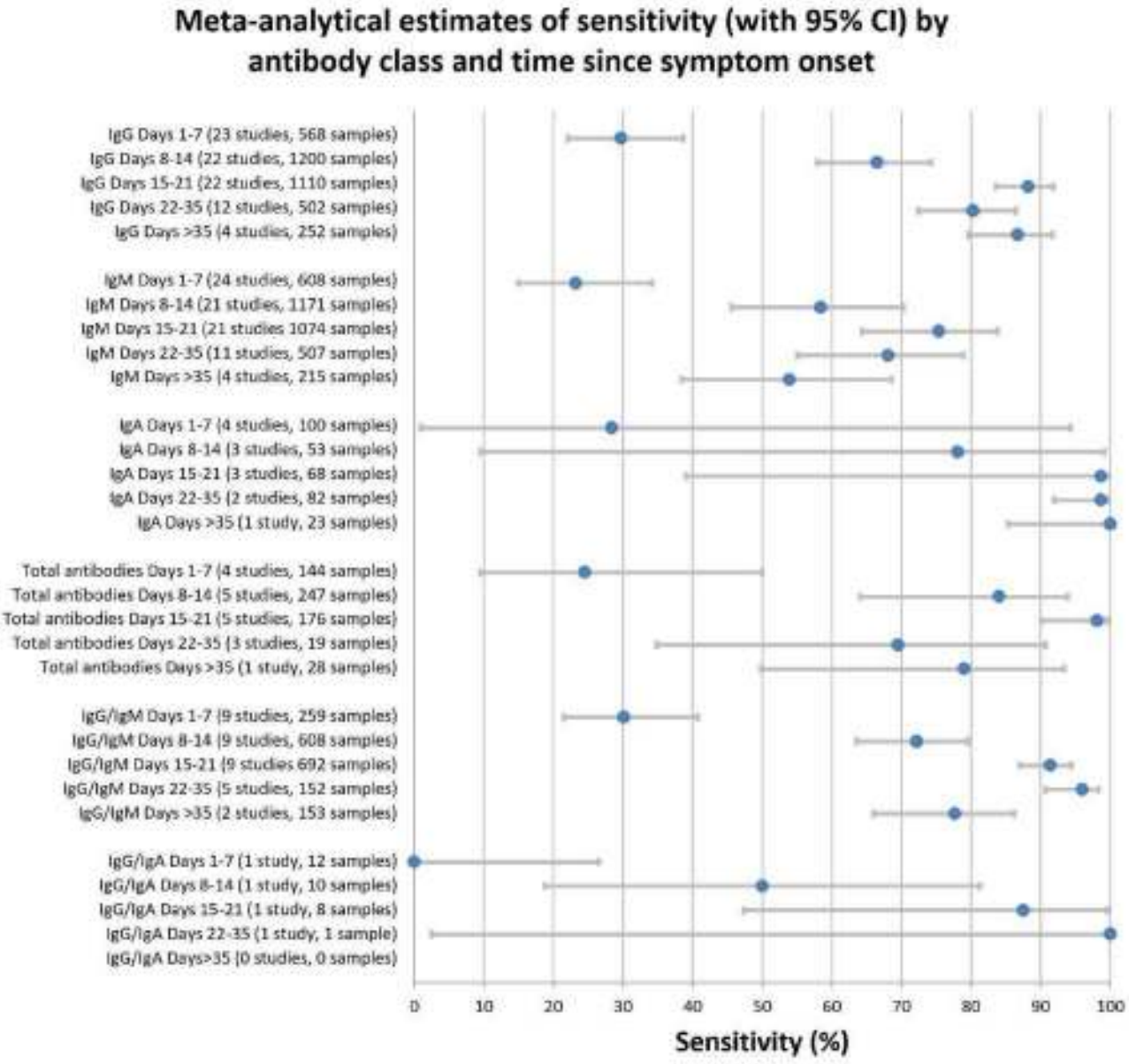


Figure 4. Forest plot of studies evaluating tests for detection of IgG according to week post-symptom onset and type of test

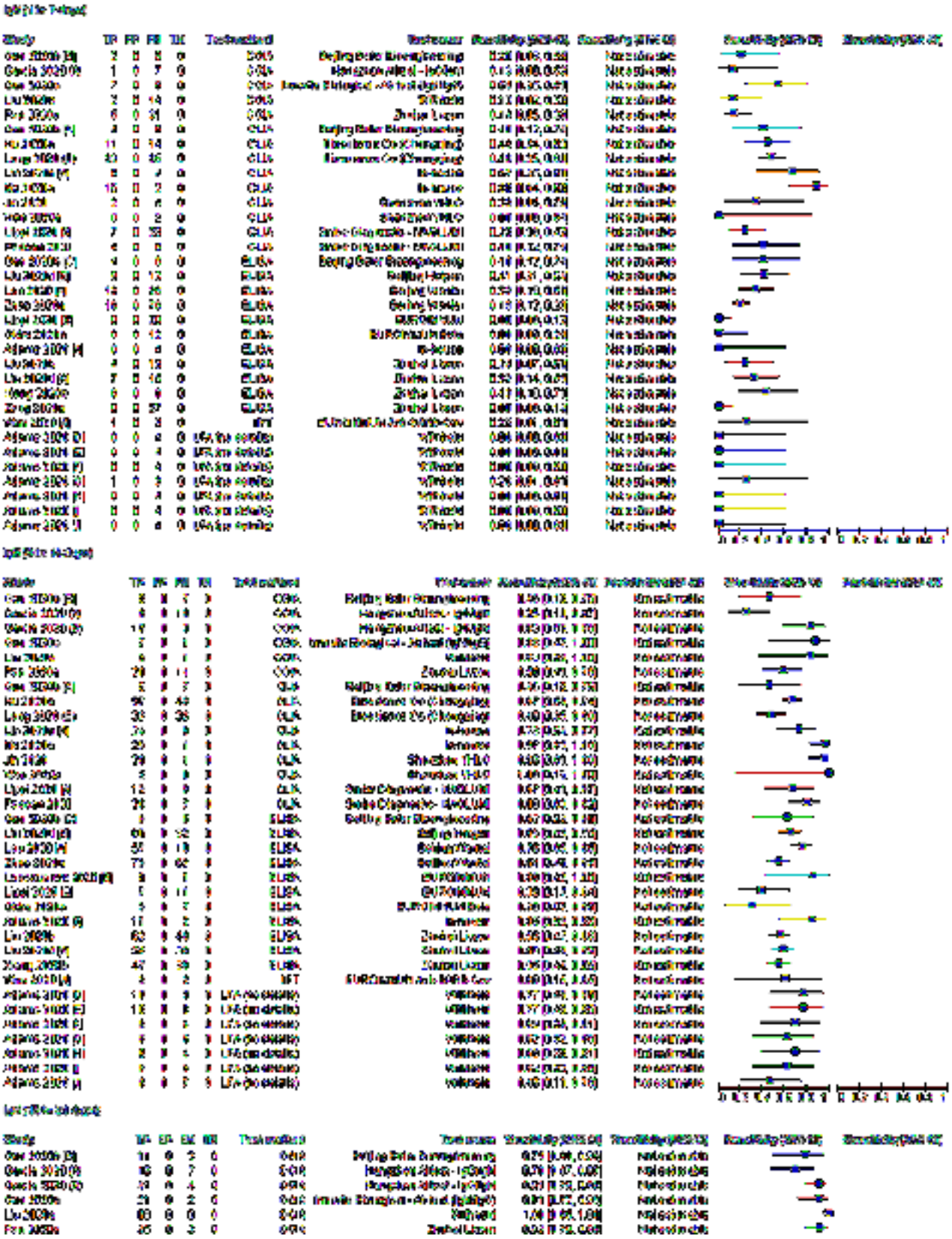


Figure 4. (Continued)

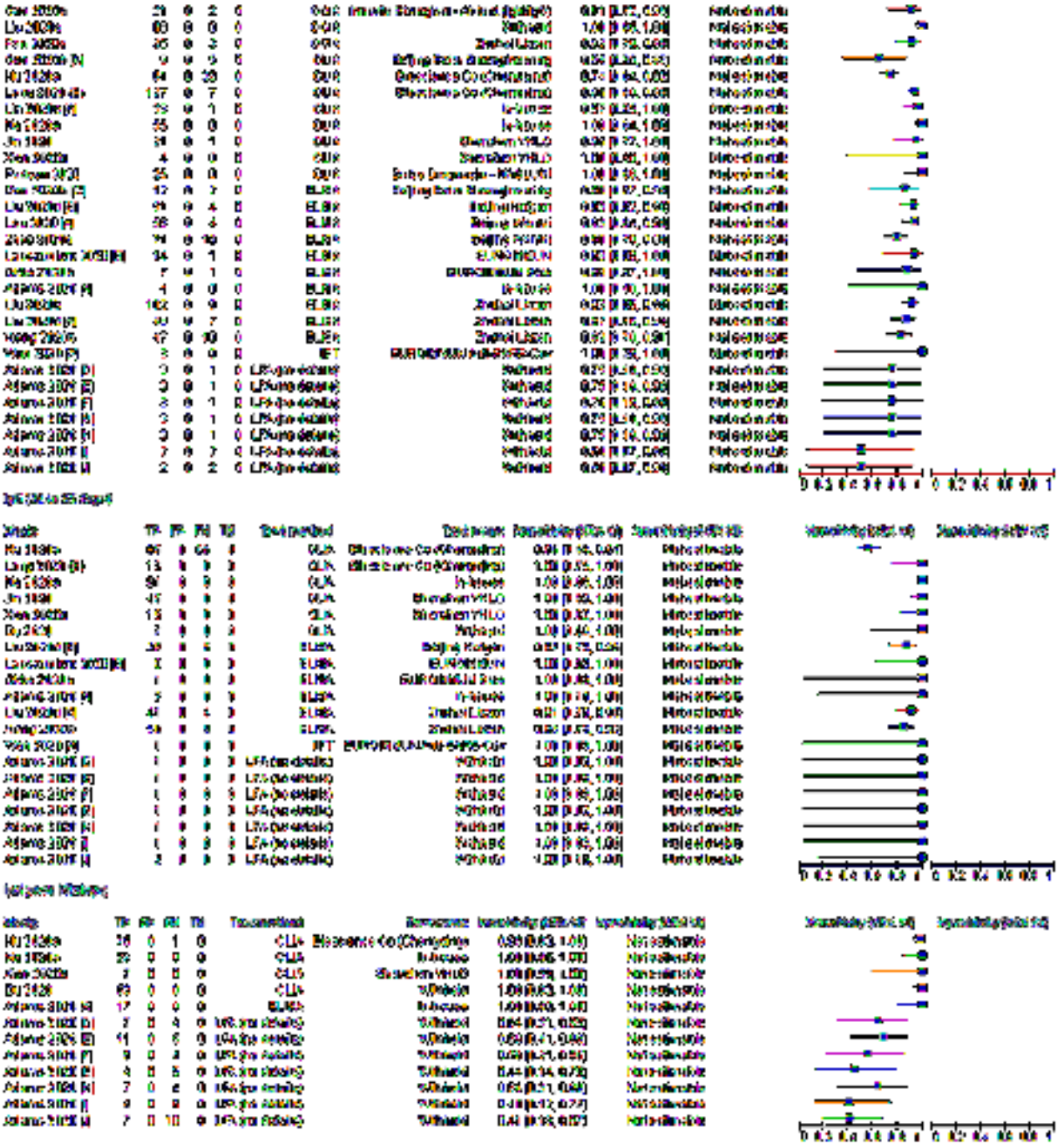
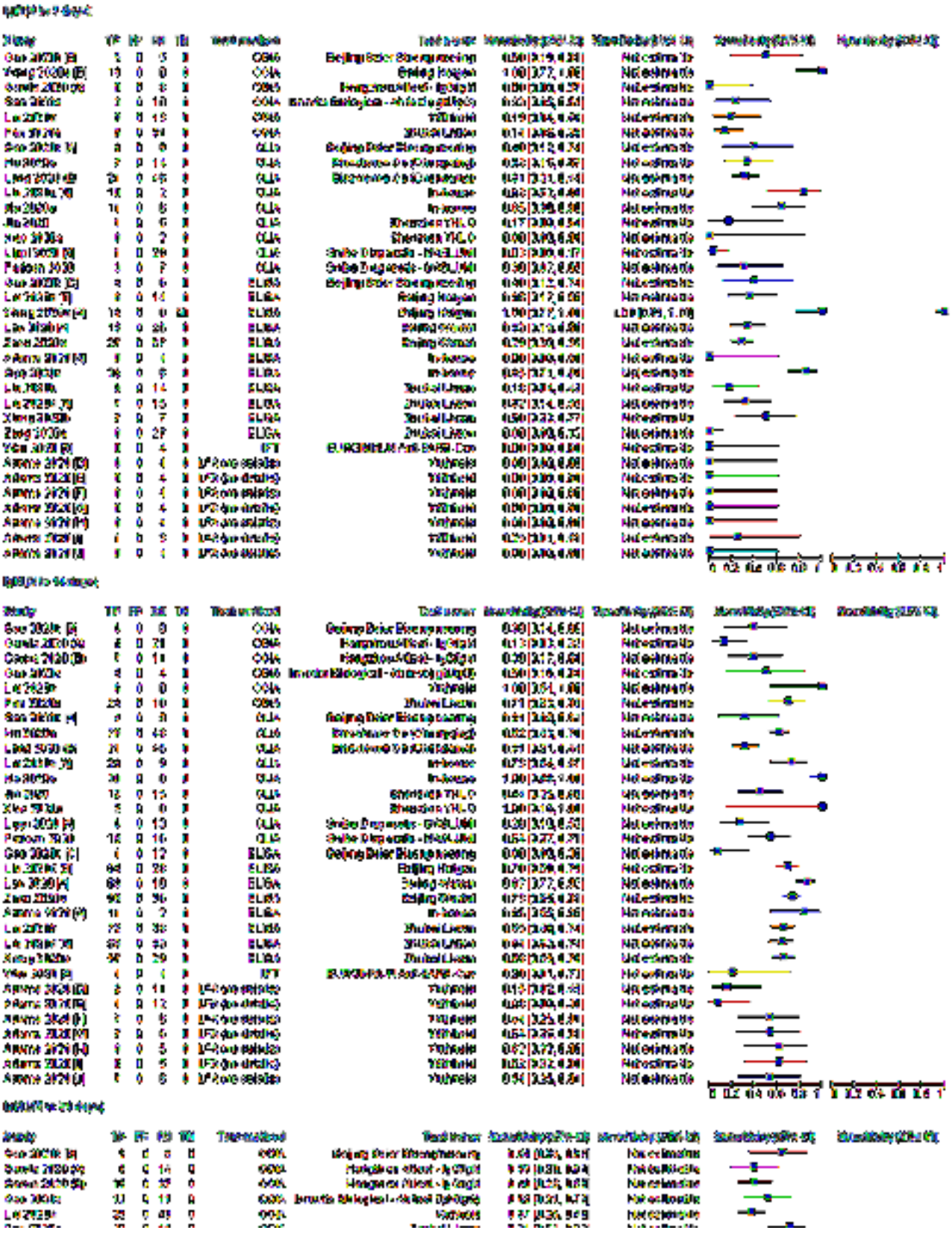


Figure 5. Forest plot of studies evaluating tests for detection of IgM according to week post-symptom onset and type of test



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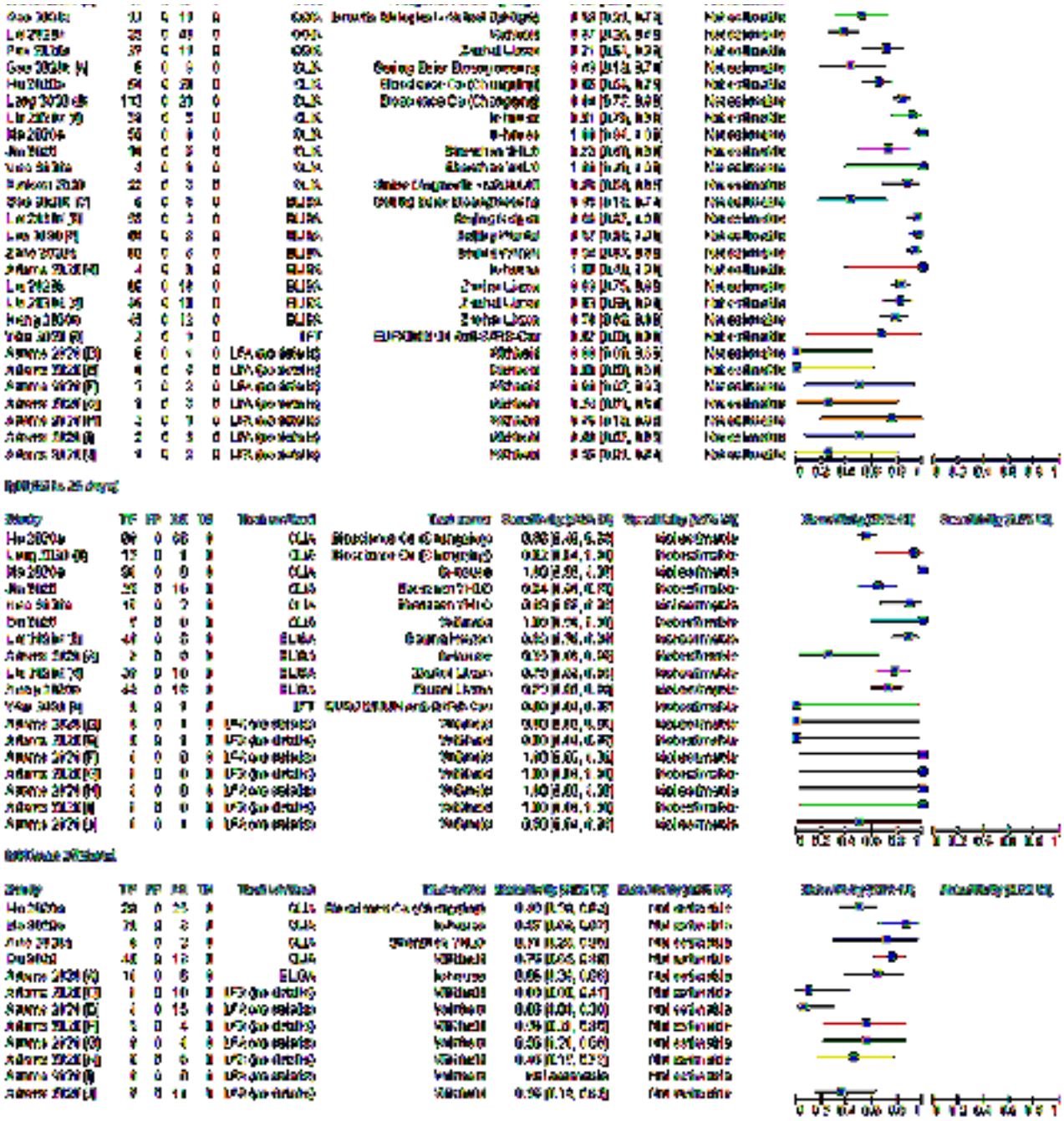


Figure 6. Forest plot of studies evaluating tests for detection of IgG/IgM according to week post-symptom onset and type of test

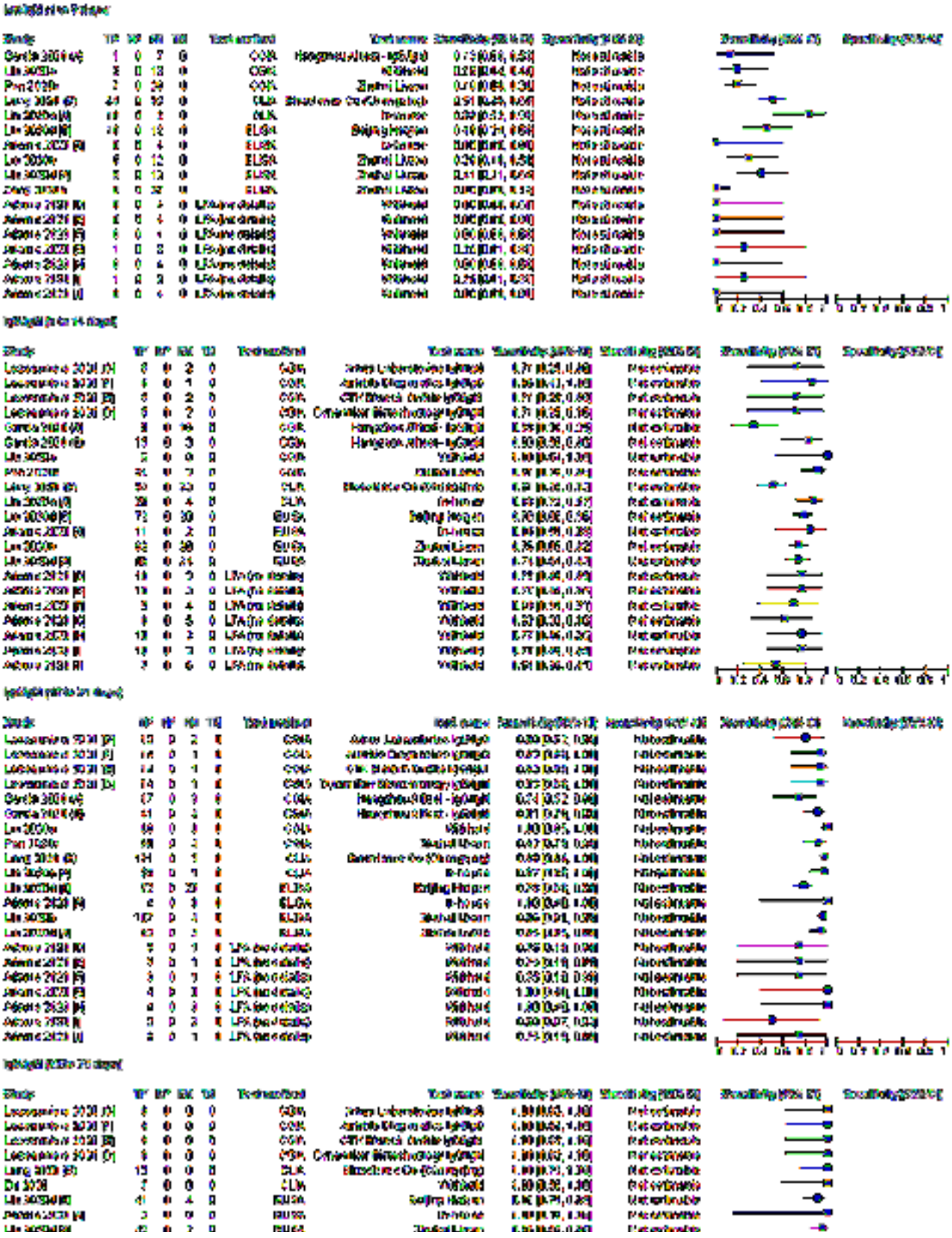
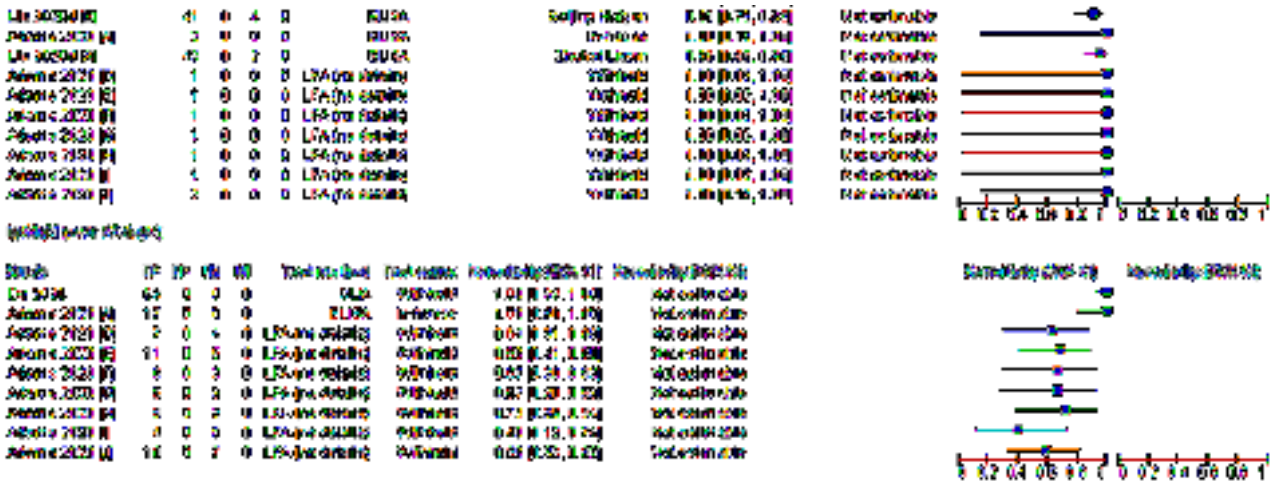


Figure 6. (Continued)



The numbers of individuals contributing data within each study within each week are very small, thus by pooling these data across studies these meta-analyses contribute clarity to the relationship between sensitivity and time, although the important limitations of these studies as described above should be considered when interpreting all findings.

Pooled results for IgG, IgM, IgA, total antibodies and IgG/IgM all show the same general pattern over the first three weeks, with sensitivity being low when tests were used in the first week since onset of symptoms, rising in the second week, and reaching their highest values in the third week. For IgG, sensitivity across the three weeks were 29.7% (95% confidence interval (CI) 22.1 to 38.6), 66.5% (95% CI 57.9 to 74.2) and 88.2% (95% CI 83.5 to 91.8); for IgM they were 23.2% (95% CI 14.9 to 34.2), 58.4% (95% CI 45.5 to 70.3) and 75.4% (95% CI 64.3 to 83.8); and for IgG/IgM they were 30.1% (95% CI 21.4 to 40.7), 72.2% (95% CI 63.5 to 79.5) and 91.4% (95% CI 87.0 to 94.4). Values for total antibodies and IgA are also given in Table 2.

It is important to note that these estimates are based on pooling multiple cross-sectional studies, and are not based on tracking the same groups of participants over time or even using the same tests. The reasons why individuals are included at some particular time points and not at others is mostly not reported.

Estimates of sensitivity beyond three weeks are based on smaller sample sizes, with a maximum of 12 studies contributing data in weeks 4 and 5, and only four studies providing any follow-up information beyond week 5. Estimates for IgA and total antibodies are based on fewer than 100 samples/participants and we will not comment upon them further. In weeks 4 and 5, pooled sensitivities of IgG were 80.3% (95% CI 72.4 to 86.4); IgM were 68.1% (95% CI 55.0 to 78.9); and for IgG/IgM were 96.0% (95% CI 90.6 to 98.3).

The data beyond week 5 gave sensitivity estimates of 86.7% (95% CI 79.6 to 91.7; IgG), 53.9% (95% CI 38.4 to 68.6; IgM) and 77.7% (95% CI 66.0 to 86.2; IgG/IgM). The expected decline in the sensitivity of IgM is evident.

Overall specificity

We estimated antibody test specificity from 35 studies. Specificity estimates for all studies are presented in Appendix 11 for IgG, IgM, IgG/IgM, IgA, total antibodies, and IgA/IgG. Results pooled across all studies are in Table 3 and show specificity exceeding 98% for all antibody types, with precise estimates (confidence intervals up to 2 percentage points wide), particularly for IgG, IgM, total antibodies and IgG/IgM, where estimates are based on several thousand non-COVID samples. Inspection of the figures shows low heterogeneity in study estimates of specificity across studies. Nine studies provided some information on the cross-reactivity of other infections, including other coronaviruses, with the SARS-CoV-2 antigens used in the assays (Table 4).

Impact of reference standard for COVID-19 cases on sensitivity

The majority of studies only included participants who were diagnosed with COVID-19 based upon observing a positive RT-PCR test. However, in clinical practice it is common to encounter patients from whom positive RT-PCR results are never obtained, but who demonstrate clinical and imaging features of COVID-19. Diagnostic criteria for COVID-19 produced by WHO and the China CDC include definitions for suspected COVID-19 in RT-PCR-negative patients. Twelve studies defined the presence of COVID-19 using these criteria, thus including RT-PCR-negative patients in the COVID-19 group as well as RT-PCR-positive patients. We compared estimates of sensitivity between studies using a RT-PCR-positive reference standard definition with a criteria-based reference standard (including both RT-PCR-positives and RT-PCR-negatives; Table 5). We stratified the analysis for weeks since onset of symptoms. All the observed differences were within magnitudes expected by chance.

In a further analysis, we separated COVID-19 participants who were RT-PCR-positive from those who were RT-PCR-negative, where studies allowed, and subgrouped the results to investigate whether there is a difference in accuracy according to RT-PCR status. Data from only three studies could be included in this analysis (Figure 7; Figure 8; Figure 9). Differences in estimates of sensitivity (pooled stratifying for weeks since onset of symptoms), varied in direction

for IgG and IgM, and were very similar for IgG/IgM (Table 6). All differences were within magnitudes expected by chance. There was no consistent evidence that the accuracy of serology tests was lower in RT-PCR-positive patients, although there is high uncertainty in these findings.

Figure 7. Sensitivity of IgG in PCR+ve and PCR-ve COVID-19 cases by week since onset of symptoms.

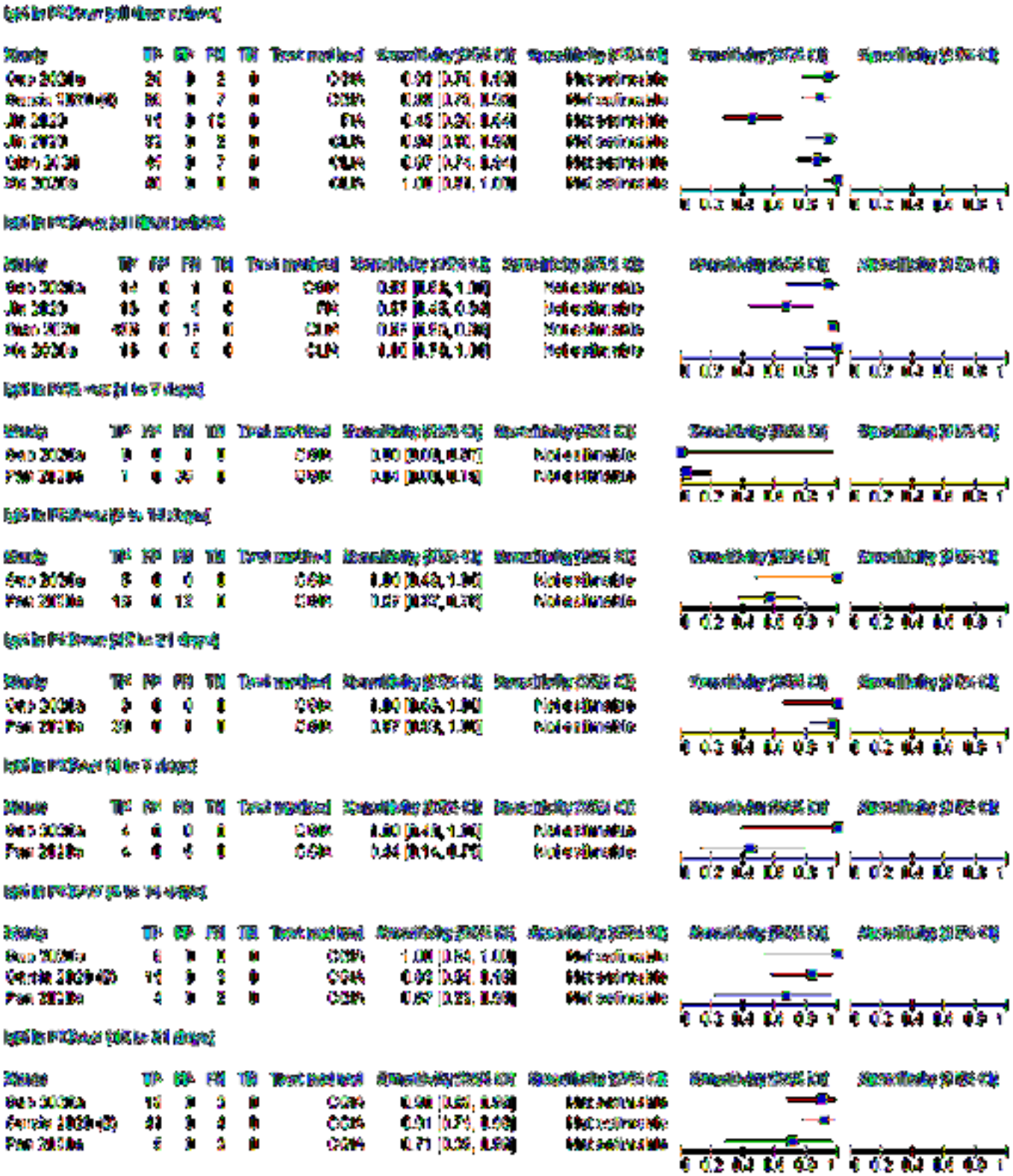


Figure 8. Sensitivity of IgM in PCR+ve and PCR-ve COVID-19 cases by week since onset of symptoms.

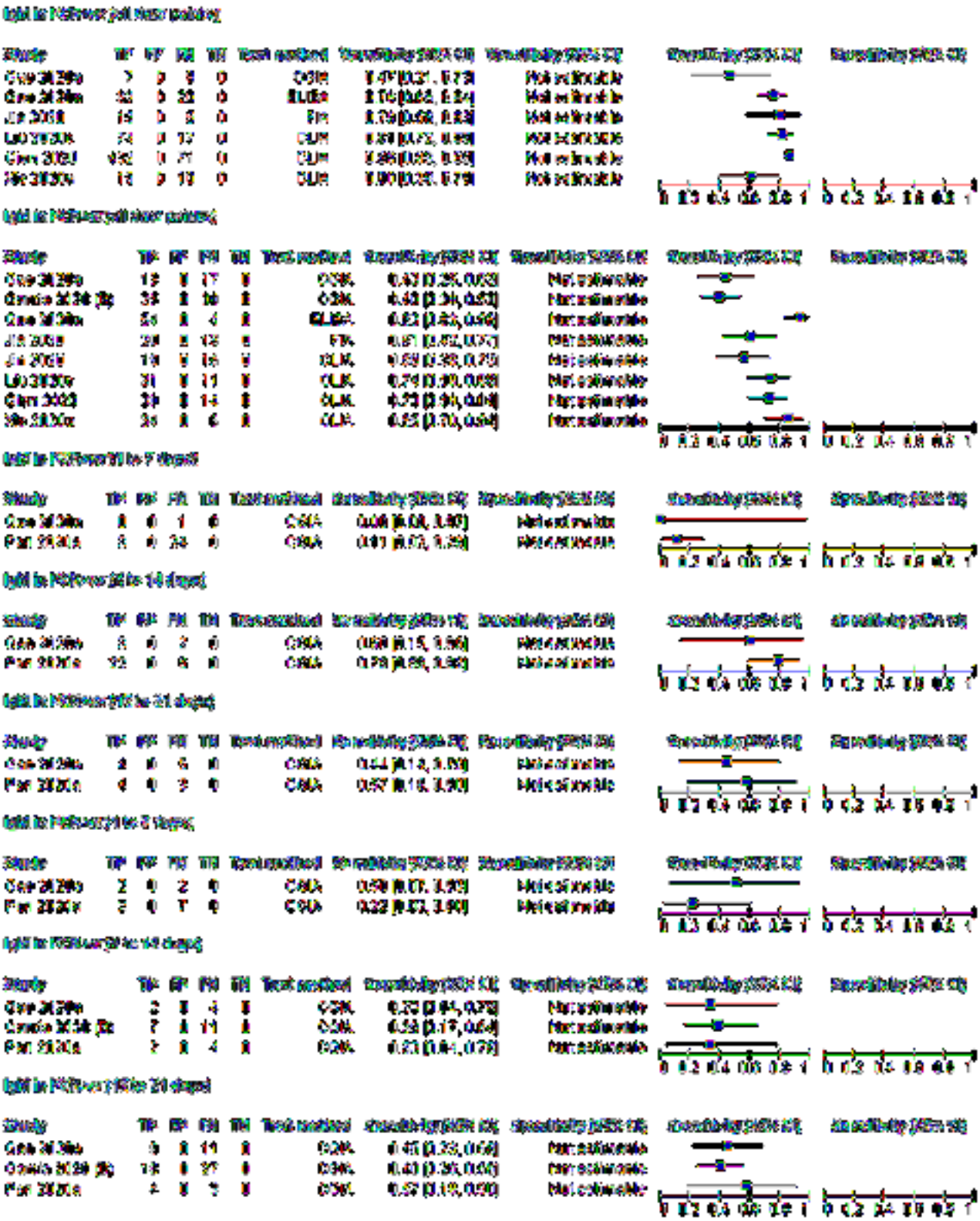


Figure 9. Sensitivity of IgG/IgM in PCR+ve and PCR-ve COVID-19 cases by week since onset of symptoms.

IgG/IgM in PCR+ve (all time points)

Study	TP	FP	FN	TN	Test method	Sensitivity (95% CI)	Specificity (95% CI)
Jia 2020	21	0	3	0	FIA	0.88 [0.68, 0.97]	Not estimable
Liu 2020b	127	0	26	0	ELISA	0.83 [0.76, 0.89]	Not estimable

IgG/IgM in PCR-ve (all time points)

Study	TP	FP	FN	TN	Test method	Sensitivity (95% CI)	Specificity (95% CI)
Garcia 2020 (B)	56	0	7	0	CGIA	0.89 [0.78, 0.95]	Not estimable
Jia 2020	24	0	9	0	FIA	0.73 [0.54, 0.87]	Not estimable
Jin 2020	32	0	2	0	CLIA	0.94 [0.80, 0.99]	Not estimable
Liu 2020b	67	0	18	0	ELISA	0.79 [0.69, 0.87]	Not estimable

IgG/IgM in PCR+ve (1 to 7 days)

Study	TP	FP	FN	TN	Test method	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020b	5	0	4	0	ELISA	0.56 [0.21, 0.86]	Not estimable
Pan 2020a	3	0	24	0	CGIA	0.11 [0.02, 0.29]	Not estimable

IgG/IgM in PCR+ve (8 to 14 days)

Study	TP	FP	FN	TN	Test method	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020b	11	0	14	0	ELISA	0.44 [0.24, 0.65]	Not estimable
Pan 2020a	26	0	2	0	CGIA	0.93 [0.76, 0.99]	Not estimable

IgG/IgM in PCR+ve (15 to 21 days)

Study	TP	FP	FN	TN	Test method	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020b	111	0	8	0	ELISA	0.93 [0.87, 0.97]	Not estimable
Pan 2020a	30	0	1	0	CGIA	0.97 [0.83, 1.00]	Not estimable

IgG/IgM in PCR-ve (1 to 7 days)

Study	TP	FP	FN	TN	Test method	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020b	0	0	8	0	ELISA	0.00 [0.00, 0.37]	Not estimable
Pan 2020a	4	0	5	0	CGIA	0.44 [0.14, 0.79]	Not estimable

IgG/IgM in PCR-ve (8 to 14 days)

Study	TP	FP	FN	TN	Test method	Sensitivity (95% CI)	Specificity (95% CI)
Garcia 2020 (B)	15	0	3	0	CGIA	0.83 [0.59, 0.96]	Not estimable
Liu 2020b	9	0	7	0	ELISA	0.56 [0.30, 0.80]	Not estimable
Pan 2020a	5	0	1	0	CGIA	0.83 [0.36, 1.00]	Not estimable

IgG/IgM in PCR-ve (15 to 21 days)

Study	TP	FP	FN	TN	Test method	Sensitivity (95% CI)	Specificity (95% CI)
Garcia 2020 (B)	41	0	4	0	CGIA	0.91 [0.79, 0.98]	Not estimable
Liu 2020b	58	0	3	0	ELISA	0.95 [0.86, 0.99]	Not estimable
Pan 2020a	5	0	2	0	CGIA	0.71 [0.29, 0.96]	Not estimable

Impact of reference standard for non-COVID-19 cases on specificity

We classified the reference standard used to verify non-COVID cases into three main groups: pre-pandemic controls (both healthy and with other diseases) who underwent no RT-PCR testing, current controls from healthy or other disease groups (typically who also did not undergo RT-PCR testing), and individuals who were investigated for COVID-19 but deemed non-COVID cases. Whilst results were similar for IgG and IgM, we noted more false positives for the IgG/IgM outcome in the studies using a COVID suspect group than in other studies (Table 3).

Sensitivity and specificity by assay type

We further investigated the heterogeneity in sensitivity estimates at any time point according to test technology type. We considered differences between CGIA, CLIAs, ELISAs and tests we can only describe as lateral flow assays due to lack of any names or detail (this group originate from the UK National COVID Testing Scientific Advisory Panel, which withheld names of the tests evaluated due to confidentiality clauses in the legal contracts with the manufacturers Adams 2020 [A]). There were inadequate numbers of studies evaluating FIAs and indirect immunofluorescence tests, luciferase immunoprecipitation assays and 'S-flow' assays to analyse, and we were only able to assess IgG, IgM and IgG/IgM targets. In a sensitivity analysis we restricted the included studies to those that used commercial (rather than in-house) tests.

We obtained estimates from a model that included all data stratified by weeks since onset of symptoms. The results presented in Table 7 and below correspond to estimates from the model of performance in week 3 post-symptom onset.

For IgG, there were clear differences in the sensitivity of assays, with CLIA (94.6%), CGIA (87.3%) and ELISA (85.8%) all outperforming the unknown lateral flow assay tests (76.0%). The differences between the groups was beyond that expected by chance (P = 0.004), but largely driven by the low value for lateral flow tests (all of the data coming from 40 COVID-19 patients in the UK National COVID Testing Scientific Advisory Panel study tested multiple times).

For IgM, although laboratory-based ELISA (84.5%) and CLIA (80.9%) outranked lateral flow CGIA (69.5%) and the unknown lateral flow assays (51.4%), the differences observed were in the realms of those expected by chance (P = 0.11).

In the smaller subset of studies that evaluated tests combining IgM/IgG, the performance of laboratory CLIA tests (97.3%) ranked above those of CGIA (91.4%), ELISA (90.5%) and unknown lateral flow tests (85.8%). These differences were beyond those expected by chance (P = 0.01)

Excluding the in-house tests, and thus restricting the analysis to only commercial tests, made little difference to estimates of sensitivity.

Analyses of specificity presented by assay type are also given in Table 7. Differences in specificity of IgG and IgM between assay types were small, CLIA and CGIA tests showed lower specificity for IgG/IgM tests than ELISA and LFIA, but confidence intervals on all estimates are wide.

Sensitivity and specificity by brand

We have tabulated the results by brand for the 27 commercial tests: 15 tests for IgG Table 8; 14 tests for IgM Table 9; and nine tests for IgG/IgM Table 10. The study data for these estimates are provided in Figure 4, Figure 5 and Figure 6. Appendix 12 tabulates the information that we have been able to derive regarding the current availability of these commercially produced tests. Data for sensitivity are stratified by week of onset of symptoms and we present the numbers of studies and samples from which data are available for each time interval. Caution is required in the interpretation of these data as many are based only on single studies with small sample sizes. We present confidence intervals to quantify the uncertainty in the estimates. We would advise focusing on estimates based on at least 100 samples/participants per week further. Three tests have estimates of sensitivity based on more than 100 samples (Beijing Wantai ELISA, Bioscience Co. (Chongqing) CLIA, Zuhai Livzon ELISA). We evaluated the studies that we pooled to create these estimates as having multiple domains at risk of bias and having concerns about the applicability of the findings (all studies having at most 2 of the 7 ratings in the QUADAS-2 assessment described as low risk or low concern).

Eight tests have estimates of specificity based on more than 100 samples, with estimates over 98% for five tests (Bejing Hotgen ELISA, Beijing Wantai ELISA, Beijing Wantai CGIA, Xiamen InnodDx Biotech ELISA, Zhuhai Livzon ELISA). Again please note the concerns in the risk of bias and applicability of these findings.

Other sources of heterogeneity

Our protocol included additional planned analyses by:

- current infection or past infection;
- study design; and
- setting.

We could not investigate these sources because of lack of variability across the studies in these features. Only two studies explicitly stated that they recruited only convalescent patients, and 48 (85%) studies recruited hospital inpatients. For study design only five out of 54 (11%) studies recruited a single group of suspected COVID-19 patients, and did not use a 'COVID-19 cases only' study, or a 'two-group' study design.

Investigation of publication bias

We observed direct evidence of selective reporting through the withholding of names of the nine lateral flow assay testing brands from the UK National COVID Testing Scientific Advisory Panel study (Adams 2020 [A]). The paper states, "Individual manufacturers did not approve release of device-level data, so device names are anonymised" (Adams 2020 [A]). The sensitivity estimates for the lateral flow assays in this study (which are most likely to be CGIA) were noted to be lower than estimates for CGIA tests from other studies. Four other studies also did not identify the test that they were evaluating.

DISCUSSION

This is the first version of a Cochrane living review summarising the accuracy of antibody tests for detecting current or previous SARS-CoV-2infection. This version of the review is based on published studies or studies available as preprints up until the 27 April 2020.

The speed of development and publication of studies for COVID-19 antibody tests is unprecedented, and the content of this review will always be out of date. We are continuously identifying new published studies, and plan to update this review several times during the next few months.

The studies included in this version are largely from China, evaluating tests from Chinese universities and manufacturers. Many of the studies are the first that have been published for each test, and thus are early-phase studies. Whilst there is no recognised stage classification of diagnostic studies, there are several common features of those undertaken during test development. These include multiple tests being described as 'in-house', that thresholds for tests are determined from the data collected during the study, that all tests are undertaken by technical experts in laboratories, that the samples used are from collections easily available to the research team, and that multiple samples are used from the same participants. These limitations explain much of the rating for high risk of bias and concerns about applicability in this review. Many of these issues make it likely that the accuracy of tests when used in clinical care will be lower than that observed here. We did locate six evaluations recruiting patients identified in clinical pathways before it was established whether they had COVID-19. This is more likely to produce results that reflect clinical practice, and we encourage future evaluations to consider this study design.

A concern with this review, and with its updates, is the high likelihood of selective reporting of results, particularly by manufacturers. We have already noted manufacturers being unwilling to be identified in the UK National COVID Testing Scientific Advisory Panel study (Adams 2020 [A]). Unlike randomised controlled trials of interventions, there are no requirements for test accuracy studies to be prospectively registered on study registers, nor to publish their findings. Many industry studies are only briefly described on 'Information for use' documents included with the tests, and study reports submitted to regulators are regarded as confidential. We are also aware that there are independent studies undertaken by National Public Health bodies, some of which have been submitted to FIND's data tracking tool for speedy data sharing. We plead for greater transparency and full publication in this field and continue to encourage laboratories to submit data and reports via FIND's portal. We request sharing of any unpublished reports for inclusion in future updates (please send to coviddta@contacts.bham.ac.uk). We have contacted test manufacturers to request full study reports which we will include in a future update of this review.

Summary of main results

We summarise 10 key findings from this review.

1. Evaluations of most antibody tests on the market are not available as publications or even as preprints. This review has evaluated data from 25 commercial tests and numerous in-house assays. These represent a small fraction of the antibody assays currently available. We have identified 66 additional studies of antibody tests published or available as preprints up until 25 May 2020, which we will appraise for inclusion in the review update, but there still remain no published data for the majority of tests on the current FIND list.
2. The design and execution of the current studies limits the strength of conclusions that we are currently able to draw. Nearly all studies sampled COVID-19 cases and non-COVID cases separately, and methods for selecting participants were not described. Only four studies reported blinding reference standard and index tests, and some reference standards may misclassify individuals.
3. Many studies only applied tests in laboratory settings on plasma or serum, whilst they are also approved for use as point-of-care tests using whole blood. From these data it is not possible to ascertain the clinical accuracy of these tests in lower resource and more accessible settings.
4. Sensitivity varies with the time since of onset of symptoms. Figures from the studies showed the ability of antibody tests to detect SARS-CoV-2infection is very low in the first week (average sensitivity 30.1%, 95% CI 21.4 to 40.7) and only moderate (average sensitivity 72.2%, 95% CI 63.5 to 79.5) in the second week post-symptom onset. These estimates are based on patients who have been hospitalised with COVID-19, and remain in hospital at the time of sampling, and thus are likely to represent the more severe end of the disease spectrum and are potentially individuals with higher antibody responses.
5. Tests have higher sensitivity when done later in the course of the disease. The average sensitivity across all the included studies for IgG/IgM tests was estimated from the included studies as 91.4% (95% CI 87.0 to 94.4) for 15 to 21 days, and 96.0% (95% CI 90.6 to 98.3) for 22 to 35 days. Too few studies had evaluated tests beyond 35 days to estimate accuracy. These findings are expected given the delayed rise of IgG antibodies.
6. Studies estimate the specificity of tests precisely, and it appears to be high. The average from the studies for IgG/IgM is 98.7% (95% CI 97.2% to 99.4%). However, estimates of specificity are mainly based on testing pre-pandemic, healthy people, or people known to have other disorders, and not those being investigated for possible COVID-19.
7. From the limited evaluations studied, some differences were noted by test technology, CLIA methods appearing more sensitive (97.5%, 95% CI 94.0 to 99.0) than ELISA (90.7%, 95% CI 83.3 to 95.0) or CGIA-based lateral flow assays (90.7%, 95% CI 82.7 to 95.2) for IgG/IgM, (there are also differences for IgG but no differences for IgM). There was little clear evidence of differences in specificity between technology types.
8. There is currently too little data on individual tests to be able to consider comparisons of their performance.
9. Study reports did not include many of the key items listed on the STARD reporting guideline for test accuracy studies (Bossuyt 2015), which has hindered assessment and data extraction. No study utilised a STARD participant flow diagram to enable identification of missing, indeterminate or unavailable test results.
10. We observed partial reporting (suppression of the identify of tests) in five studies, indicating the likelihood of publication bias.

Strengths and weaknesses of the review

Our review used a broad search screening all articles concerning COVID-19. We undertook all screening and eligibility assessments, QUADAS-2 assessments (Whiting 2011), and data extraction of study findings independently and in duplicate. Whilst we thus have reasonable confidence in the completeness and accuracy of the findings up until the search date, should errors be noted please inform us at coviddta@contacts.bham.ac.uk so that we can check and correct in our next update.

Weaknesses of the review primarily reflect the weaknesses in the primary studies and their reporting. Many studies omitted descriptions of sample recruitment, and key aspects of study design and execution. Some studies omit information that allows the tests to be identified. We have had to treat studies that describe their data as being based on 'samples' as if the samples were individual patients. We have been explicit about these issues where they arose.

More than half (28/54) of the studies we have included are currently only available as preprints, and as yet, have not undergone peer review. As published versions of these studies are identified in the future, we will double-check study descriptions, methods and findings, and update the review as required.

We also did not make within-study comparisons between tests. Two studies (Adams 2020 [A]; Lassauniere 2020 [A]), evaluated panels of nine or 10 tests, nine other studies evaluated two, three, or five tests. As we could not identify tests in Adams 2020 [A], and the sample of Lassauniere 2020 [A] was very small, it is not possible from the studies available at this time to make direct comparisons between alternative tests.

We identified only one study that included comparison of test results with a reference standard of a neutralisation assay in studies identified for inclusion in this first version of the review (Thompson 2020), but we did not include these data in this version of the review. We are aware of several more studies of these assays in more recent publications and will include this as a new target condition in the next update of the review.

In such a current and fast moving field searches will always be out of date. However we are committed to ongoing updates of this living review

Applicability of findings to the review question

In the background we outlined four main roles for antibody testing that would be addressed in this review.

1. In diagnosis of infection in patients presenting with symptoms of suspected COVID-19, particularly where molecular testing had failed to detect the virus. Most studies included in the review collected data from patients in the acute phase of disease in hospital settings and thus provide evidence to address this question amongst hospitalised patients. The review showed that antibody tests had very low sensitivity in the first week following onset of symptoms, but sensitivity rose in the second week, and only exceeded 90% in the third week. In addition we saw no difference in sensitivity of tests according to RT-PCR status. We had no data to inform the accuracy of the test in primary care and community settings for the purpose of diagnosis, where patients are likely to have milder symptoms.
2. In assessment of immune response in patients with severe disease. We stated in the Background that we would not cover this in this review. In any case, we found no studies that directly addressed this question. Assessment of the accuracy of a test used for assessment of immune response would involve comparison with a reference standard test of antibody response, rather than evidence of infection.
3. To assess whether individuals have had a SARS-CoV-2 infection. As above, we found no studies that directly addressed this question, and very few studies were undertaken in community settings in patients who had not undergone RT-PCR testing during their symptomatic period. Conclusions about the likely value of tests for this purpose rely on the sensitivity of the tests being no different in mild disease than in severe disease that requires hospital admission.
4. In seroprevalence surveys for public health management purposes. We also found no studies that directly addressed this question (although Bendavid 2020 is a seroprevalence study, it did not evaluate the accuracy of the test in the seroprevalence sample). High specificity of tests is essential in seroprevalence testing, which appears likely for many of the tests included in this review. However, the suitability of pre-pandemic samples to establish specificity requires further discussion. We found no difference in specificity between pre-pandemic and current non-COVID-19 samples, but lower specificity in those where COVID-19 was ruled out after initially being suspected. This either reflects misclassification, or a true lower specificity in those presenting with symptoms. As sensitivity of the tests was mainly evaluated in hospitalised patients it is also unclear whether the tests have the ability to detect lower antibody levels likely in non-hospitalised COVID-19 patients.

AUTHORS' CONCLUSIONS

Implications for practice

Diagnosis of acute suspected COVID-19 in symptomatic patients

Based on this analysis, in patients presenting with symptoms of acute suspected COVID-19, antibody tests have no role on their own as the primary test to use in the diagnosis of COVID-19 when patients present during the first week since onset of symptoms, as their sensitivity is too low.

A small number of studies showed that the sensitivity of antibody tests is no different in those who were reverse transcription polymerase chain reaction (RT-PCR)-negative rather than RT-PCR-positive. Thus in hospitalised patients where molecular tests have failed to detect virus, antibody tests have an increasing likelihood of detecting immune response to the infection as time since onset of symptoms progresses.

There may therefore be a role in using antibody tests in COVID-19 RT-PCR-negative but strongly suspected patients where patients are more than two weeks since the onset of symptoms. This is in line with the most recent version of the China CDC (National Health Commission of the People's Republic of China) COVID-19 case definition (Appendix 2).

Assessment of previous SARS-CoV-2 infection and immune response

The data analysed in the review suggest that antibody tests are likely to have a useful role for detecting previous SARS-CoV-2 infection if used at 15 days or more after the onset of symptoms. This conclusion needs to be cautioned by the poor study quality, the small sample sizes and restricted number of tests that have undergone evaluation. In addition, we have scant data to inform the accuracy of the test in non-hospitalised patients with milder disease, and too little data to comment on accuracy beyond 35 days.

Using, for illustration the overall IgG/IgM data at days 15 to 21 (sensitivity 91.4%, 95% CI 87.0 to 94.4 and specificity 98.7%, 93% CI 97.2 to 99.4), we have computed predictive values, and the numbers of true positives, false positives, false negatives and true negatives in a sample of 1000, at a prevalence of 50% (a value seen in healthcare worker populations who have suffered respiratory symptoms in the past months). In this scenario, the positive predictive value is estimated as 99% (95% CI 97 to 99), the negative predictive value as 92% (95% CI 88 to 95), and of 1000 people undergoing testing we would anticipate 7 (95% CI 3 to 14) false positives and 43 (95% CI 28 to 65) false negatives.

Please note that it is not certain whether a detectable immune response indicates that a patient is immune nor no longer infectious.

Seroprevalence surveys for public health management purposes

The duration of antibody rises is not yet known, and this review contains very little data beyond 35 days post-onset of symptoms. In the 'Summary of findings' table we present scenarios for the likely numbers of missed cases (false negatives) and false positive cases for prevalences of 2%, 5%, (likely values in national surveys), 10% and 20% (likely values in high-risk settings such as healthcare workers), presuming that the performance of an IgG/IgM test would continue at the same level as for 14-21 days. Again this conclusion needs to be cautioned by the poor study quality, the applicability of the study settings, the small sample sizes and restricted number of tests that have undergone evaluation. At a prevalence of 20%, a possible value in surveys in high-risk settings, 17 (95% CI 11 to 26) would be missed per 1000 people tested and 10 (95% CI 5 to 22) would be falsely positive. At a lower prevalence of 5%, a likely value in national surveys, 4 (95% CI 3 to 7) would be missed per 1000 tested, and 12 (95% CI 6 to 27) would be falsely positive.

Implications for research

Many more high-quality evaluation studies of COVID-19 antibody tests are needed in patients more than 21 days post-symptom onset, and in people in the community, particularly those who experience milder symptoms, or who are asymptomatic (but known to be infected).

Future studies must report data on sensitivity disaggregated by time since onset of symptoms. In future updates of this review we will not include studies for analysis of sensitivity where this has not been done. We would suggest that studies standardise how they define time since symptom onset (not, for example, using time since positive RT-PCR results since this has no biological basis) and present results using standard time groupings (we suggest initially by week up until 35 days and larger time intervals beyond). Studies that sample from the same patients at several time points over time are needed to fully understand how time since symptom onset directly affects performance – our current estimates are based on collation of multiple cross-sectional studies, which has limitations.

Primary studies need to be undertaken for the many tests that are on the market but as yet have no independent evaluations. Future studies should evaluate test performance in consecutive individuals who are recruited in clinical care with suspected COVID-19, to estimate both sensitivity and specificity, as this will estimate the likely performance of the tests in practice.

COVID-19-positive cases who are RT-PCR-negative should be included as well as those confirmed RT-PCR, in accordance with the World Health Organization (WHO) and China CDC case definitions.

Studies should ensure that the test is used as it is intended to be used in clinical practice (i.e. being undertaken at point-of-care rather than in laboratories (where appropriate) on the right specimens, by the intended healthcare worker). However, when validating people with suspected COVID-19 who do not have a positive identification of COVID-19 by RT-PCR, these studies need to take care to confirm or rule out COVID-19 by obtaining standardised evidence from other sources (e.g. repeat RT-PCR, CT scans, follow-up). Future studies need to recruit larger sample sizes and consider recruiting from multiple centres. We did not find any multicentre studies for this review.

We would also encourage investigators to utilise blinding in their study designs, such that index tests are undertaken without knowledge of the reference standard diagnosis, and likewise, reference standards are determined without knowledge of the index test findings.

We need good data upon which to compare tests. The strongest comparisons are made by testing the same participants multiple times with different tests. Whilst it is possible for this to be undertaken in prospective studies, it is easier to undertake in laboratory-based studies utilising serum banks, which will compromise on the applicability of the absolute estimates of test accuracy, but provide some information about comparability.

From these studies we can only draw limited conclusions about cross-reactivity of COVID-19 tests with other coronaviruses as these data are summarised in analytical accuracy studies. It would be of value for these results to be reviewed as well as clinical accuracy studies.

Study reporting requires substantial improvement. The STARD checklist outlines standard requirements for the reporting of a test accuracy study, which study investigators should take note of when planning their study to ensure the relevant information is collected and reported. No study was found that reported data using a STARD participant flow-diagram (Bossuyt 2015).

Due to the speed of new publications in this field, frequent updates of this review are required. Future updates will not include data on tests that are not (or not likely to become) commercially available (thus we will exclude all in-house assays).

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  * Signs and symptoms (Stuyf T, Domen J, Horn S)
  * Routine laboratory markers (Yang B, Langendam M, Ochodo E, Guleid F, Holtman G, Verbakel J, Wang J, Stegeman I)
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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Adams 2020 [A]

Study characteristics	
Patient Sampling	2-group study recruiting patients estimating sensitivity and specificity [1] Rt-PCR confirmed COVID-19 cases (n = 40) [2] Pre-pandemic controls (n = 142) Recruitment: unclear Prospective or retrospective recruitment of cases: retrospective Sample size (virus/COVID cases): 182 (40) Inclusion and exclusion criteria: none stated
Patient characteristics and setting	Setting [1] Acute hospital samples (n = 16), recovering healthcare workers (n = 6), convalescent patients (n = 18) [2] Health blood donors (n = 60); organ donor samples (n = 50); pertussis vaccine study (BERT) (n = 32) Location [1] Acute hospital patients from Oxford University Hospitals NHS Foundation Trust (location of other groups NR) [2] National Health Service Blood and Transplant, UK National Quality in Organ Donation (QUOD) study, the 'BERT' study (A Study Exploring Whooping Cough Protection in Children and Adults), UK Country: UK Dates: [1] NR; [2] before December 2019 Symptoms and severity: [1] asymptomatic (n = 1); mild (n = 26); severe (n = 4); critical (n = 9) Sex: NR Age: [1] Median (range): 57 (22-95) years; [2] NR Exposure history: NR
Index tests	Adams 2020 [A] is test [A] from the following entry: Test name: [A] ELISA test [B]-[J] LFIA names withheld Manufacturer: [A] in-house [B]-[J] manufacturer name withheld Ab targets: [A] IgG and IgM [B]-[C] total antibodies [D]-[J] IgG and IgM Antigens used: [A] SARS-CoV-2 trimeric S protein [B]-[J] details withheld Test method: [A] ELISA [B]-[J] LFIA further details withheld Timing of samples: 4-62 days after onset of symptoms Samples used: plasma Test operators: laboratory staff Definition of test positivity: [A]-[J] NR Blinded to reference standard: NR Threshold predefined: no for [A], unclear for [B] to [J]
Target condition and reference standard(s)	Reference standard for cases: RT-PCR Samples used: nose or throat swabs Timing of reference standard: NR Blinded to index test: yes Incorporated index test: no Reference standard for non-cases: pre-pandemic
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: computed from analysis of individual participant data

Adams 2020 [A] *(Continued)*

	All participants received the same reference standard: no Missing data: different tests were evaluted in different numbers of samples, no information on how sampling decisions were made Uninterpretable results: not mentioned Indeterminate results: not mentioned Unit of analysis: per patient
Comparative	
Notes	Funding: NIHR, Oxford Biomedical Research Centre, the UK Government Department of Health and Social Care and grants from NIHR and the Medical Research Council Publication status: preprint (not peer reviewed) Source: medRxiv Study author COI: several authors declared relationships with companies for other work; funders were co-authors

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			

Adams 2020 [A] *(Continued)*

Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Adams 2020 [B]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Index tests	Adams 2020 [B] is test [B] from the following entry: Test name: [A] ELISA test [B]-[J] LFIA names withheld Manufacturer: [A] in-house [B]-[J] manufacturer name withheld Ab targets: [A] IgG and IgM [B]-[C] total antibodies [D]-[J] IgG and IgM Antigens used: [A] SARS-CoV-2 trimeric S protein [B]-[J] details withheld Test method: [A] ELISA [B]-[J] LFIA further details withheld Timing of samples: 4-62 days after onset of symptoms Samples used: plasma

Adams 2020 [B] *(Continued)*

	Test operators: laboratory staff Definition of test positivity: [A]-[J] NR Blinded to reference standard: NR Threshold predefined: no for [A], unclear for [B] to [J]
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Comparative	
Notes	

Adams 2020 [C]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Index tests	Adams 2020 [C] is test [C] from the following entry: Test name: [A] ELISA test [B]-[J] LFIA names withheld Manufacturer: [A] in-house [B]-[J] manufacturer name withheld Ab targets: [A] IgG and IgM [B]-[C] total antibodies [D]-[J] IgG and IgM Antigens used: [A] SARS-CoV-2 trimeric S protein [B]-[J] details withheld Test method: [A] ELISA [B]-[J] LFIA further details withheld Timing of samples: 4-62 days after onset of symptoms Samples used: plasma Test operators: laboratory staff Definition of test positivity: [A]-[J] NR Blinded to reference standard: NR Threshold predefined: no for [A], unclear for [B] to [J]
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Comparative	
Notes	

Adams 2020 [D]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Index tests	Adams 2020 [D] is test [D] from the following entry: Test name: [A] ELISA test [B]-[J] LFIA names withheld Manufacturer: [A] in-house [B]-[J] manufacturer name withheld Ab targets: [A] IgG and IgM [B]-[C] total antibodies [D]-[J] IgG and IgM Antigens used: [A] SARS-CoV-2 trimeric S protein [B]-[J] details withheld Test method: [A] ELISA [B]-[J] LFIA further details withheld Timing of samples: 4-62 days after onset of symptoms Samples used: plasma Test operators: laboratory staff Definition of test positivity: [A]-[J] NR Blinded to reference standard: NR Threshold predefined: no for [A], unclear for [B] to [J]
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Comparative	
Notes	

Adams 2020 [E]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Index tests	Adams 2020 [E] is test [E] from the following entry: Test name: [A] ELISA test [B]-[J] LFIA names withheld Manufacturer: [A] in-house [B]-[J] manufacturer name withheld Ab targets: [A] IgG and IgM [B]-[C] total antibodies [D]-[J] IgG and IgM Antigens used: [A] SARS-CoV-2 trimeric S protein [B]-[J] details withheld Test method: [A] ELISA [B]-[J] LFIA further details withheld Timing of samples: 4-62 days after onset of symptoms Samples used: plasma Test operators: laboratory staff Definition of test positivity: [A]-[J] NR

Adams 2020 [E] *(Continued)*

	Blinded to reference standard: NR Threshold predefined: no for [A], unclear for [B] to [J]
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Comparative	
Notes	

Adams 2020 [F]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Index tests	Adams 2020 [F] is test [F] from the following entry: Test name: [A] ELISA test [B]-[J] LFIA names withheld Manufacturer: [A] in-house [B]-[J] manufacturer name withheld Ab targets: [A] IgG and IgM [B]-[C] total antibodies [D]-[J] IgG and IgM Antigens used: [A] SARS-CoV-2 trimeric S protein [B]-[J] details withheld Test method: [A] ELISA [B]-[J] LFIA further details withheld Timing of samples: 4-62 days after onset of symptoms Samples used: plasma Test operators: laboratory staff Definition of test positivity: [A]-[J] NR Blinded to reference standard: NR Threshold predefined: no for [A], unclear for [B] to [J]
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Comparative	
Notes	

Adams 2020 [G]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Index tests	Adams 2020 [G] is test [G] from the following entry: Test name: [A] ELISA test [B]-[J] LFIA names withheld Manufacturer: [A] in-house [B]-[J] manufacturer name withheld Ab targets: [A] IgG and IgM [B]-[C] total antibodies [D]-[J] IgG and IgM Antigens used: [A] SARS-CoV-2 trimeric S protein [B]-[J] details withheld Test method: [A] ELISA [B]-[J] LFIA further details withheld Timing of samples: 4-62 days after onset of symptoms Samples used: plasma Test operators: laboratory staff Definition of test positivity: [A]-[J] NR Blinded to reference standard: NR Threshold predefined: no for [A], unclear for [B] to [J]
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Comparative	
Notes	

Adams 2020 [H]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Index tests	Adams 2020 [H] is test [H] from the following entry: Test name: [A] ELISA test [B]-[J] LFIA names withheld Manufacturer: [A] in-house [B]-[J] manufacturer name withheld Ab targets: [A] IgG and IgM [B]-[C] total antibodies [D]-[J] IgG and IgM Antigens used: [A] SARS-CoV-2 trimeric S protein [B]-[J] details withheld Test method: [A] ELISA [B]-[J] LFIA further details withheld Timing of samples: 4-62 days after onset of symptoms Samples used: plasma Test operators: laboratory staff Definition of test positivity: [A]-[J] NR

Adams 2020 [H] *(Continued)*

	Blinded to reference standard: NR Threshold predefined: no for [A], unclear for [B] to [J]
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Comparative	
Notes	

Adams 2020 [I]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Index tests	Adams 2020 [I] is test [I] from the following entry: Test name: [A] ELISA test [B]-[J] LFIA names withheld Manufacturer: [A] in-house [B]-[J] manufacturer name withheld Ab targets: [A] IgG and IgM [B]-[C] total antibodies [D]-[J] IgG and IgM Antigens used: [A] SARS-CoV-2 trimeric S protein [B]-[J] details withheld Test method: [A] ELISA [B]-[J] LFIA further details withheld Timing of samples: 4-62 days after onset of symptoms Samples used: plasma Test operators: laboratory staff Definition of test positivity: [A]-[J] NR Blinded to reference standard: NR Threshold predefined: no for [A], unclear for [B] to [J]
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Comparative	
Notes	

Adams 2020 [J]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Index tests	Adams 2020 [J] is test [J] from the following entry: Test name: [A] ELISA test [B]-[J] LFIA names withheld Manufacturer: [A] in-house [B]-[J] manufacturer name withheld Ab targets: [A] IgG and IgM [B]-[C] total antibodies [D]-[J] IgG and IgM Antigens used: [A] SARS-CoV-2 trimeric S protein [B]-[J] details withheld Test method: [A] ELISA [B]-[J] LFIA further details withheld Timing of samples: 4-62 days after onset of symptoms Samples used: plasma Test operators: laboratory staff Definition of test positivity: [A]-[J] NR Blinded to reference standard: NR Threshold predefined: no for [A], unclear for [B] to [J]
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Adams 2020 [A])
Comparative	
Notes	

Bendavid 2020

Study characteristics	
Patient Sampling	Multiple-group study recruiting patients estimating sensitivity and specificity [1] Specimens from COVID-19 cases recruited from 3 different sources (n = 157 specimens) [2] Specimens from non-cases recruited from 13 different sources (n = 3308 specimens) Recruitment: unclear Prospective or retrospective recruitment of cases: unclear Sample size (virus/COVID cases): 3481 (3324) specimens Inclusion and exclusion criteria: none stated
Patient characteristics and setting	Setting: not described for most sample sets Location: not described for most sample sets Country: USA, China, but not described for most sample sets Dates: not described Symptoms and severity: not described Sex: not described Age: not described

Bendavid 2020 *(Continued)*

	Exposure history: not described
Index tests	Test name: unnamed test Manufacturer: Premier Biotech, Minneapolis, USA (may be Hangzhou All-test) Ab targets: IgG, IgM Antigens used: NR Test method: NR Timing of samples: NR Samples used: serum, plasma, fingerstick blood, venous whole blood (may be blood for majority of cases) Test operators: NR Definition of test positivity: NR Blinded to reference standard: no Threshold predefined: NR
Target condition and reference standard(s)	Reference standard for cases: various unclear, includes RT-PCR-pos Samples used: NR Timing of reference standard: NR Blinded to index test: yes Incorporated index test: serology tests were included in 1 cohort Reference standard for non-cases: pre-pandemic, RT-PCR-neg, healthy volunteers
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: no All participants received the same reference standard: no Missing data: none mentioned Uninterpretable results: none mentioned Indeterminate results: none mentioned Unit of analysis: specimens
Comparative	
Notes	Funding: individual donors Publication status: preprint (not peer reviewed) Source: medRxiv Study author COI: none declared

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	

Bendavid 2020 *(Continued)*

Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	No		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Unclear		
Were results presented per patient?	No		
Could the patient flow have introduced bias?		High risk	

Burbelo 2020 [A]

Study characteristics			

Burbelo 2020 [A] *(Continued)*

Patient Sampling	2-group study recruiting patients estimating sensitivity and specificity [1] 35 patients with COVID-19 symptoms and RT-PCR-positive [2] 32 pre-pandemic blood donors Recruitment: unclear Prospective or retrospective recruitment of cases: retrospective Sample size (virus/COVID cases): 67 (35) Inclusion and exclusion criteria: nothing additional The study included a 3rd group on COVID-19 suspects (n = 10) who were not included as they had no reference standard diagnosis
Patient characteristics and setting	Setting [1] Hospital patients [2] Blood donors Location [1] University of California, San Diego; University of Washington, Seattle; EvergreenHealth, Kirkland, Washington; NIH Clinical Center, NIH [2] NIH Clinical Center, NIH Country: USA Dates: NR Symptoms and severity: [1] 37% (13/35) were on a ventilator Sex: [1] 87% (30/35) male [2] NR Age: [1] median age 44 years (range 32-50 years) [2] NR Exposure history: NR
Index tests	This entry (Burbelo 2020 [A]) refers to the LIPS assay to detect antibodies to the nucleocapsid (N) protein Test name: LIPS Manufacturer: in-house Ab targets: antibodies for the nucleocapsid and S proteins Antigens used: nucleocapsid and S proteins Test method: LIPS Timing of samples: 2-50 days pso Samples used: plasma or serum Test operators: presumed laboratory researchers Definition of test positivity: 125,000 LU for nucleocapsid and 45,000 LU for S proteins Blinded to reference standard: unclear Threshold predefined: no, derived from analysis of group [2] to achieve 100% specificity
Target condition and reference standard(s)	Reference standard for cases: RT-PCR Samples used: nasal or throat swabs Timing of reference standard: unclear Blinded to index test: yes Incorporated index test: no Reference standard for non-cases: pre-pandemic controls (no testing)
Flow and timing	Time interval between index and reference tests: unclear Results presented by time period: ≤ 14 days; > 14 days All participants received the same reference standard: no Missing data: yes - unclear why there are different numbers for spike and nucleocapsid tests Uninterpretable results: not mentioned Indeterminate results: not mentioned

Burbelo 2020 [A] *(Continued)*

Comparative	
Notes	Funding: intramural research programmes of the National Institute of Dental and Craniofacial Research, the National Institute of Allergy and Infectious Diseases, and the National Institute of Health Clinical Center Publication status: preprint (not peer reviewed) Source: medRxiv Study author COI: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		

Burbelo 2020 [A] *(Continued)*

The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Unclear		
Were results presented per patient?	No		
Could the patient flow have introduced bias?		High risk	

Burbelo 2020 [B]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Burbelo 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Burbelo 2020 [A])
Index tests	This entry (Burbelo 2020 [B]) refers to the LIPS assay to detect antibodies to the spike (S) protein; see (Burbelo 2020 [A] for further study characteristics and QUADAS-2 assessments) Test name: LIPS Manufacturer: in-house Ab targets: antibodies for the nucleocapsid and S proteins Antigens used: nucleocapsid and S proteins Test method: LIPS Timing of samples: 2-50 days pso Samples used: plasma or serum Test operators: presumed laboratory researchers Definition of test positivity: 125,000 LU for nucleocapsid and 45,000 LU for S proteins Blinded to reference standard: unclear Threshold predefined: no - derived from analysis of group [2] to achieve 100% specificity
Target condition and ref-	See main entry for this study for characteristics and QUADAS-2 assessment (Burbelo 2020 [A])

Burbelo 2020 [B] *(Continued)*

erence standard(s)	
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Burbelo 2020 [A])
Comparative	
Notes	

Cai 2020a

Study characteristics	
Patient Sampling	2-group study to estimate sensitivity and specificity for detection of active disease [1] Laboratory-confirmed COVID-19 patients (n = 276) [2] Controls with other infections (n = 167). A third group of healthy controls was used to set thresholds (n = 200) but not estimate accuracy. Recruitment method: NR if patients were consecutive Sample size (viral/COVID cases): 443 (276) Exclusion criteria: none stated
Patient characteristics and setting	[1] Hospital (inpatients); Chongqing Three Gorges Central Hospital, Yongchuan Hospital Affiliated to Chongqing Medical University (CQMU), and The Public Health Center, in Chongqing, China (recruitment dates NR). 168/276 (61%) had fever. Median age 48 (IQR 37-56; range 0-84) years, 151/276 (55%) male. 99/276 (36%) reported known exposure [2] Controls with other infection (n = 167); Second Hospital Affiliated to CQMU and Children's Hospital Affiliated to CQMU; time NR. Other infections included: influenza A virus (25), respiratory syncytial virus (7), parainfluenza 111 virus (8), influenza B virus (5), adenovirus (6), *Klebsiella pneumoniae* (8), *Streptococcus pneumoniae* (3), Mycoplasma (5), *Acinetobacter baumannii* (10), *Candida albicans* (2), *Staphylococcus aureus* (3), *Mycobacterium tuberculosis* (4), Hepatitis B virus (33), Hepatitis C virus (22), Syphilis (23) and Saccharomycopsis (3) [3] Healthy controls (n = 200), source NR; recruited > 1 year before the outbreak. No further details
Index tests	1 Ab test, blinding NR Laboratory-based in-house luminescent immunoassay (CLIA) using serum samples Measured IgM +IgG. Antigen: peptide from SARS-CoV-2 S protein Test threshold: determined as the mean luminescence (CL) value of the 200 normal sera plus 5 folds of SD; cut-off used ≥ 0.7 CL (for both IgG and IgM). (Determined in the healthy control group) Samples acquired day 2-day 27 after symptoms. Person applying the test NR.
Target condition and reference standard(s)	1. Real time RT-PCR detection of virus RNA, samples not described. Reference threshold and timing NR. Blinded to index test 2. Healthy controls, pre-December 2019
Flow and timing	Time interval between index and reference: NR. Accuracy results were not disaggregated by time period since point of symptom onset. No missing data, uninterpretable or indeterminate results described Analysis participant-based

Cai 2020a *(Continued)*

Comparative	
Notes	Funded by Emergency Project from the Science & Technology Commission of Chongqing; Major National S&T program grant from Science & Technology Commission of China; Grant from the National Natural Science Foundation of China, Grant from the Science & Technology Commission of Yuzhong district, Chongqing. COI (reported or derived): study author employed by BioScience Co. LTD, Tianjin, China Publication status (source): preprint (not peer reviewed) (medRxiv) NOTE: Study author institution reported as BioScience Co. LTD, Tianjin, China (www.bio-science-tj.com/en/about.php)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		

Cai 2020a *(Continued)*

Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Cassaniti 2020 (A)

Study characteristics	
Patient Sampling	The report contains 3 different groups that fit with 2 different comparisons. 2-group design with separate estimates of sensitivity and specificity [1] COVID-19-positive patients in ICU (n = 30) [2] Healthy volunteers with negative RT-PCR results (n = 30) Recruitment: unclear Sample size (virus/COVID cases): 60 (30) Inclusion and exclusion criteria: not further described (Single group recruiting individuals presenting with symptoms extracted as Cassaniti 2020 (B))
Patient characteristics and setting	Setting: hospital inpatients (Infectious Diseases Unit or ICU, Tertiary hospital) Location: Fondazione IRCCS Policlinico San Matteo, Pavia Country: Italy Dates: NR Symptoms and severity: [1] NR [2] NR Sex: [1] 83% male (25/30); [2] 55% Male (11/30)

Cassaniti 2020 (A) *(Continued)*

	Age: [1] median age, 73.5; range 38-86 years; [2] median age, 38.5; range 25-69 years) Exposure history: [1] NR; [2] 10 (33.3%) previously infected with common OC43, 229E, HKU1, and NL63 coronavirus
Index tests	Test name: VivaDiag COVID-19 IgM/IgG Manufacturer: VivaChek Ab targets: IgM, IgG Antigens used: NR Test method: LFIA Timing of samples: [1] median 7 days (IQR 4-11) after first test; [2] NR Samples used: serum or blood Test operators: NR Definition of test positivity: visible line Blinded to reference standard: unclear Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: RT-PCR targeting RNA-dependent RNA polymerase and E genes were used to detect the presence of SARS-CoV-2 according to the WHO guidelines (2 negatives required for non-cases) Samples used: respiratory samples Timing of reference standard: [1] during patient care [2] unclear Blinded to index test: yes Incorporated index test: no
Flow and timing	Time interval between index and reference tests: no information Results presented by time period: no information All participants received the same reference standard: yes Missing data: none mentioned Uninterpretable results: none mentioned Indeterminate results: none mentioned Unit of analysis: participants
Comparative	
Notes	Funding: VivaDiag COVID-19 IgM/IgG Rapid Test provided free of charge by the Italian Chinese community. Regional Health Authority of Lombardy, Milan, Italy and Italian Ministry of Health, Ricerca Finalizzata Publication status: published letter Source: academic journal Study author COI: none mentioned

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		

Cassaniti 2020 (A) *(Continued)*

Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Cassaniti 2020 (B)

Study characteristics	
Patient Sampling	Single-group study estimating sensitivity and specificity Patients presenting to A&E with fever and respiratory symptoms indicative of COVID-19 infection. 2 additional cohorts extracted as separate 2-group study (Cassaniti 2020 (A)) Recruitment: unclear Sample size (virus/COVID cases): 50 (38) Inclusion and exclusion criteria: NR
Patient characteristics and setting	Setting: A&E Location: Fondazione IRCCS Policlinico San Matteo, Pavia Country: Italy Dates: NR Symptoms and severity: NR Sex: 68% male 34 male/16 female Age: median age, 61.50; range 33-97 years Exposure history: NR
Index tests	Test name: VivaDiag COVID-19 IgM/IgG Manufacturer: VivaChek Ab targets: IgM, IgG Antigens used: NR Test method: LFIA Timing of samples: on presentation at A&E Samples used: serum or blood Test operators: NR Definition of test positivity: visible line Blinded to reference standard: yes on presentation Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: RT-PCR targeting RNA-dependent RNA polymerase and E genes were used to detect the presence of SARS-CoV-2 according to the WHO guidelines Samples used: nasal swab Timing of reference standard: on presentation Blinded to index test: yes Incorporated index test: no Reference standard for non-cases: single negative RT-PCR result
Flow and timing	Time interval between index and reference tests: done at the same time Results presented by time period: no (likely to be short as on admission) All participants received the same reference standard: yes Missing data: none mentioned Uninterpretable results: none mentioned Indeterminate results: not mentioned Unit of analysis: participants
Comparative	
Notes	Funding: VivaDiag COVID-19 IgM/IgG Rapid Test provided free of charge by the Italian Chinese community. Regional Health Authority of Lombardy, Milan, Italy and Italian Ministry of Health, Ricerca Finalizzata Publication status: published letter Source:Academic journal

Cassaniti 2020 (B) *(Continued)*

Study author COI: none mentioned

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High

Cassaniti 2020 (B) *(Continued)*

DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Were results presented per patient?	Yes
Could the patient flow have introduced bias?	Unclear risk

Chen 2020a

Study characteristics	
Patient Sampling	Unclear whether study recruited as 1 or 2 groups (we describe it as a 2-group study), estimating sensitivity and specificity [1] RT–PCR-positive samples, n = 7 samples [2] RT–PCR-negative samples, but clinically suspicious for COVID-19, n = 12 samples A 3rd group of 'normal' samples (n = 51), were used to derive test threshold and not included in the accuracy evaluation. Recruitment: unclear Prospective or retrospective recruitment of cases: unclear Sample size (virus/COVID cases): 19 (7) Inclusion and exclusion criteria: NR
Patient characteristics and setting	Setting: hospital samples Location: Guangzhou Eighth People's Hospital and Nanfang Hospital, Guangzhou province Country: China Dates: NR Symptoms and severity: [1] NR; [2] fever: 12/12 (100%) Sex: NR Age: NR Exposure history: NR
Index tests	Test name: no name. LFIA that uses lanthanide-doped polystyrene nanoparticles (LNPs) Manufacturer: in–house Ab targets: IgG Antigens used: recombinant nucleocapsid phosphoprotein of SARS-CoV-2 Test method: LFIA that uses lanthanide-doped polystyrene nanoparticles (LNPs) Timing of samples: NR Samples used: serum Test operators: NR Definition of test positivity: At/Ac ratio (R) > 0.0666 Blinded to reference standard: NR Threshold predefined: defined from control samples
Target condition and reference standard(s)	Reference standard for cases: RT–PCR

Chen 2020a *(Continued)*

	Samples used: NR Timing of reference standard: NR Blinded to index test: yes Incorporated index test: no Reference standard for non-cases: RT–PCR single negative
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: NR All participants received the same reference standard: yes Missing data: none reported Uninterpretable results: none reported Indeterminate results: none reported Unit of analysis: sample
Comparative	
Notes	Funding: National Natural Science Foundation of China and China Postdoctoral Science Foundation Publication status: peer–reviewed early online Source: academic journal Study author COI: study authors state no competing financial interests

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High

Chen 2020a *(Continued)*

DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	No		
Could the patient flow have introduced bias?		High risk	

Dohla 2020

Study characteristics	
Patient Sampling	2-group study recruiting patients estimating sensitivity and specificity [1] COVID-19 suspects attending community screening (n = 39) [2] Confirmed COVID-19 cases (n = 10) Recruitment: [1] random selection (no random sampling method stated); [2] unclear Prospective or retrospective recruitment of cases: [1] prospective; [2]retrospective Sample size (virus/COVID cases): 49 (22) Inclusion and exclusion criteria: NR
Patient characteristics and setting	Setting: [1] community screening centre; [2] NR Location: [1] German Red Cross COVID-19 testing centre; [2] NR Country: Germany Dates: NR Symptoms and severity: (71%) with dry cough; (65%) with fatigue; (46%) with runny nose (only %s reported). 5/49 (10%) were asymptomatic Sex: 25/49 (51%) male Age: median 46 (IQR 28–72) years

Dohla 2020 *(Continued)*

	Exposure history: identified in 22/49 (45%): median time exposure–to–test of 18.5 days (IQR 15–24)
Index tests	Test name: NR Manufacturer: NR Ab targets: IgM and IgG Antigens used: SARS-CoV-2 antigen (not further described) Test method: CGIA Threshold: visible line - weak and strong responses counted as positive Timing of median time exposure–to–test = 18.5 days (IQR 15–24) known (45%) for samples Samples used: [1] fingerprick blood [2] stored serum Test operators: NR Definition of test positivity: weakly clearly visible line Blinded to reference standard: unclear Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: [1] RT–qPCR (Altona Diagnostics), threshold NR; [2] RT–qPCR (unknown if same kit), threshold NR Samples used: [1] throat swab; [2] NR Timing of reference standard: [1] same time as index test. [2] NR. For 22 participants (unclear how many in group 1 or 2): median time exposure–to–test of 18.5 days (IQR 15–24) Blinded to index test: NR - presumed Incorporated index test: no Reference standard for non-cases: single negative RT-qPCR
Flow and timing	Time interval between index and reference tests: simultaneous Results presented by time period: no All participants received the same reference standard: yes Missing data: none reported Uninterpretable results: reporting that there were none Indeterminate results: weak lines considered as test positive Unit of analysis: participant
Comparative	
Notes	Funding: none declared Publication status: published paper (proof) Source: academic journal Study author COI: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		

Dohla 2020 *(Continued)*

Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Low risk	

Du 2020

Study characteristics	
Patient Sampling	Single group estimating sensitivity in convalescent patients [1] Hospital COVID-19 convalescent patients (n = 60) Recruitment: unclear Sample size (virus/COVID cases): 60 (60) Inclusion and exclusion criteria: NR
Patient characteristics and setting	Setting: hospital inpatients (convalescent) Location: Wuhan Tongji Hospital Country: China Dates: admitted 12 January 2020-5 February 2020 Symptoms and severity: no information Sex: no information Age: no information Exposure history: no information
Index tests	Test name: NR Manufacturer: NR Ab targets: IgM, IgG Antigens used: NR Test method: NR but presumed to be CLIA based on reported threshold in AU/mL Timing of samples: during hospital stay (between 3 March 2020 and 14 March 2020) Samples used: NR Test operators: unclear Definition of test positivity: > 10 AU/mL Blinded to reference standard: unclear Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases (including threshold): method NR Samples used: NR Timing of reference standard: diagnosed during initial hospital stay (6-7 weeks previously) Blinded to index test: yes Incorporated index test: no
Flow and timing	Time interval between index and reference tests: 6-7 weeks Results presented by time period: results presented by day since onset All participants received the same reference standard: presumed Missing data: none mentioned Uninterpretable results: none mentioned Indeterminate results: none mentioned Unit of analysis: participant
Comparative	
Notes	Funding: Beijing Natural Science Foundation Publication status: published letter Source: academic journal Study author COI: none mentioned
Methodological quality	

Du 2020 *(Continued)*

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	No		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Unclear
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		

Du 2020 *(Continued)*

Did all participants receive a reference standard?	Yes	
Were results presented per patient?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Freeman 2020

Study characteristics	
Patient Sampling	2-group study recruiting patients estimating sensitivity and specificity [1] confirmed COVID-19 cases (n = 99) [2] Healthy adults (n = 377) or with other infections (n = 142) Additionally reports a separate cross-reactivity study using acute and convalescent paired sera from PCR confirmed commonly circulating coronavirus (229E, NL63, OC43, and HKU1)- infected patients Recruitment: unclear Prospective or retrospective recruitment of cases: unclear Sample size (virus/COVID cases): 618 (99) Inclusion and exclusion criteria: [1] convalescent PCR+ COVID-19 cases sera collected at day 10 pso or later
Patient characteristics and setting	Setting: NR Location: NR Country: USA Dates: NR Symptoms and severity: [1] NR [2] healthy controls (n = 377); suspected hantavirus (n = 101); HIV (n = 21); hepatitis B virus (n = 10); hepatitis C virus-positive (n = 10) Sex: NR Age: NR Exposure history: NR
Index tests	Test name: SARS-CoV-2 S protein ELISA Manufacturer: in-house Ab targets: IgG, IGM and total antibodies Antigens used: pre-fusion stabilised ectodomain of SARS-CoV-2 spike (S) Test method: ELISA Timing of samples: at day 10 pso or later Samples used: serum Test operators: laboratory staff Definition of test positivity: based on optical density signal Blinded to reference standard: NR Threshold predefined: NR
Target condition and reference standard(s)	Reference standard for cases: PCR Samples used: NR Timing of reference standard: NR Blinded to index test: yes, PCR was performed before index test (inferred) Incorporated index test: no Reference standard for non-cases: pre-pandemic (healthy controls or with other diseases)
Flow and timing	Time interval between index and reference tests: not clear Results presented by time period: no

Freeman 2020 *(Continued)*

	All participants received the same reference standard: no Missing data: not mentioned Uninterpretable results: not mentioned Indeterminate results: not mentioned Unit of analysis: per participant
Comparative	
Notes	Funding: intramural funding from the National Institute of Allergy and Infectious Diseases Publication status: preprint (not peer-reviewed) Source: bioRxiv Study author COI: NR

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		

Freeman 2020 *(Continued)*

Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Gao 2020a

Study characteristics	
Patient Sampling	Single-group study estimating sensitivity [1] Patients with confirmed COVID-19 (n = 38) Recruitment: unclear Sample size (virus/COVID cases): 38 (38) Inclusion and exclusion criteria: COVID-19 confirmed by New Coronavirus Pneumonia Prevention and Control Program (5th edition) published by the National Health Commission of China.
Patient characteristics and setting	Setting: hospital inpatient Location: Second People's Hospital of Fuyang Country: China Dates: 22 January 2020-28 February 2020 Symptoms and severity: 3/38 described as in severe or critical conditions; 35/38 described as mild cases Sex: 55.3% (21/38) male Age: median age 40.5 years (IQR 31.0-49.5years), range 15-75 years Exposure history: NR
Index tests	Test name: Colloidal Gold Antibodies Test Manufacturer: Innovita Biological Technology Co., Ltd Ab targets: IgM, IgG Antigens used: NR Test method: CGIA

Gao 2020a *(Continued)*

	Timing of samples: days 0-15+ Samples used: serum Test operators: NR Definition of test positivity: visible line Blinded to reference standard: NR Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: participants met the criteria of the New Coronavirus Pneumonia Prevention and Control Program (5th edition) published by the National Health Commission of China Samples used: NR Timing of reference standard: NR Blinded to index test: yes Incorporated index test: no
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: yes: 0-7 days (n = 13), 8-14 days (n = 8) and ≥ 15 days (n = 23) after onset of symptoms All participants received the same reference standard: yes Missing data: NR Uninterpretable results: NR Indeterminate results: NR Unit of analysis: results reported for participants. 38 participants included and 76 serum samples collected in total from these 38 participants. Median number of samples collected from each participant was 8
Comparative	
Notes	Funding: The Science and Technology Bureau of Fuyang Publication status: accepted manuscript (peer reviewed) Source: Journal of Medical Virology Study author COI: none reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			

Gao 2020a *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Gao 2020b [A]

Study characteristics	
Patient Sampling	Single-group study recruiting patients estimating sensitivity [1] confirmed COVID-19 cases Recruitment: consecutive (inferred). From all confirmed cases admitted to hospital Prospective or retrospective recruitment of cases: retrospectively (appears) Sample size (virus/COVID cases): 22 participants (corresponding to 37 samples) Inclusion and exclusion criteria: not clearly defined; describes all participants having typical ground-glass opacity of the lung on CT but not clear if this was part of eligibility

Gao 2020b [A] *(Continued)*

Patient characteristics and setting	Setting: hospital inpatient Location: Fifth Hospital of Shijiazhuang Country: China Dates: from 21 January-24 February 2020 Symptoms and severity: typical ground-glass opacity in lung was observed in CT scan results of all participants. At the time the paper was written all participants had recovered and been discharged from hospital. Sex: 14/22 male (64%) Age: 40 (4-72) years Exposure history: 11 participants had recent history of travel to epidemic areas, and the remaining 10 had close contacts with their family members, who were confirmed to be infected by 2019-nCoV
Index tests	Gao 2020b [A] is test [A] from the following entry: Test name: [A] CLIA; [B] GICA; [C] ELISA Manufacturer: Beier Bioengineering Company (Beijing, China) Ab targets: IgG and IgM Antigens used: spike (S) and nucleocapsid (N) proteins of 2019-nCoV Test method: [A] CLIA; [B] GICA; [C] ELISA Timing of samples: [1] early stage (1-7 days pso) 10/37 samples (27%), [2] middle stage (8-14 days pso) 13/37 samples (35%); [3] late stage (14-24 days pso) 14/37 samples (38%) Samples used: serum Test operators: laboratory staff Definition of test positivity: [A] samples with an concentration ≥ 8 arbitrary unit (AU)/mL were considered positive. [B] Visible line. [C] The absorbance at 450 nm (A450 nm) of each well was determined and the cut-off value was 0.10+Anegative control. A value > cut-off value was considered a positive result. Blinded to reference standard: NR Threshold predefined: [A] samples with an concentration ≥ 8 arbitrary unit (AU)/mL were considered positive. [B] Positive results showed the appearance of both control line and testing line. [C] The absorbance at 450 nm (A450 nm) of each well was determined and the cut-off value was 0.10+Anegative control. A value > cut-off value was considered a positive result.
Target condition and reference standard(s)	Reference standard for cases: RT-PCR assay (2019-nCoV RNA Test Kit, Daan Gene Company, China) Samples used: nasal and pharyngeal swab specimens Timing of reference standard: on admission (most likely) Blinded to index test: yes, index tests performed on already-confirmed cases (inferred) Incorporated index test: no Reference standard for non-cases: N/A
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: yes All participants received the same reference standard: yes Missing data: timing of reference standard test Uninterpretable results: Indeterminate results: Unit of analysis: samples
Comparative	
Notes	Funding: NR Publication status: published letter Source: Chinese Medical Journal Study author COI: none
Methodological quality	

Gao 2020b [A] *(Continued)*

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference			High

Gao 2020b [A] *(Continued)*

standard does not match the question?	
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Were results presented per patient?	No
Could the patient flow have introduced bias?	High risk

Gao 2020b [B]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Gao 2020b [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Gao 2020b [A])
Index tests	Gao 2020b [B] is test [B] from the following entry: Test name: [A] CLIA; [B] GICA; [C] ELISA Manufacturer: Beier Bioengineering Company (Beijing, China) Ab targets: IgG and IgM Antigens used: spike (S) and nucleocapsid (N) proteins of 2019-nCoV Test method: [A] CLIA; [B] GICA; [C] ELISA Timing of samples: [1] early stage (1-7 days pso) 10/37 samples (27%), [2] middle stage (8-14 days pso) 13/37 samples (35%); [3] late stage (14-24 days pso) 14/37 samples (38%) Samples used: serum Test operators: laboratory staff Definition of test positivity: [A] samples with an concentration ≥ 8 arbitrary unit (AU)/mL were considered positive. [B] Visible line. [C] The absorbance at 450 nm (A450 nm) of each well was determined and the cut-off value was 0.10+Anegative control. A value > cut-off value was considered a positive result. Blinded to reference standard: NR Threshold predefined: [A] samples with an concentration ≥ 8 arbitrary unit (AU)/mL were considered positive. [B] Positive results showed the appearance of both control line and testing line. [C] The absorbance at 450 nm (A450 nm) of each well was determined and the cut-off value was 0.10+Anegative control. A value > cut-off value was considered a positive result.
Target condition and ref-	See main entry for this study for characteristics and QUADAS-2 assessment (Gao 2020b [A])

Gao 2020b [B] *(Continued)*

erence standard(s)	
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Gao 2020b [A])
Comparative	
Notes	

Gao 2020b [C]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Gao 2020b [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Gao 2020b [A])
Index tests	Gao 2020b [C] is test [C] from the following entry: Test name: [A] CLIA; [B] GICA; [C] ELISA Manufacturer: Beier Bioengineering Company (Beijing, China) Ab targets: IgG and IgM Antigens used: spike (S) and nucleocapsid (N) proteins of 2019-nCoV Test method: [A] CLIA; [B] GICA; [C] ELISA Timing of samples: [1] early stage (1-7 days pso) 10/37 samples (27%), [2] middle stage (8-14 days pso) 13/37 samples (35%); [3] late stage (14-24 days pso) 14/37 samples (38%) Samples used: serum Test operators: laboratory staff Definition of test positivity: [A] samples with an concentration ≥ 8 arbitrary unit (AU)/mL were considered positive. [B] Visible line. [C] The absorbance at 450 nm (A450 nm) of each well was determined and the cut-off value was 0.10+Anegative control. A value > cut-off value was considered a positive result. Blinded to reference standard: NR Threshold predefined: [A] samples with an concentration ≥ 8 arbitrary unit (AU)/mL were considered positive. [B] Positive results showed the appearance of both control line and testing line. [C] The absorbance at 450 nm (A450 nm) of each well was determined and the cut-off value was 0.10+Anegative control. A value > cut-off value was considered a positive result.
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Gao 2020b [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Gao 2020b [A])
Comparative	
Notes	

Garcia 2020 (A)

Study characteristics	
Patient Sampling	3-group study estimating sensitivity and specificity [1] COVID-19 patients (n = 55) [2] Pre-pandemic healthy controls (n = 45) Third group of patients admitted with a clinical and radiological diagnosis of pneumonia of unknown etiology but RT-PCR-negative reported as Garcia 2020 (B) Recruitment: NR Sample size (virus/COVID cases): 100 (55) Inclusion and exclusion criteria: NR
Patient characteristics and setting	Setting: [1] hospital inpatient [2] pre-pandemic controls Location: [1] Hospital Universitario Príncipe de Asturias, Madrid [2] Hospital Universitario Príncipe de Asturias Country: Spain Dates: [1] 1 March-6 April 2020 [2] 1 October-30 November 2019 Symptoms and severity: NR Sex: [1] male n = 33, 60% [2] male n = 27, 60% Age: [1] median age 63, IQR 50-79 [2] median age 55, IQR 34-66 Exposure history: NR
Index tests	Test name: AllTest COV-19 IgG / IgM kit Manufacturer: AllTest Biotech, Hangzhou, China Ab targets: IgM, IgG Antigens used: NR Test method: immunochromatography Timing of samples: days 0-14+ pso Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: RT-PCR Samples used: NR Timing of reference standard: NR Blinded to index test: yes Incorporated index test: no
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: yes: < 7 days 15% (n = 8); 7-13 days 44% (n = 24); ≥ 14 days 42% (n = 23) All participants received the same reference standard: no Missing data: NR Uninterpretable results: NR Indeterminate results: NR Unit of analysis: participants
Comparative	
Notes	Funding: no funding received Publication status: preprint (not peer reviewed) Source: medRxiv Study author COI: none declared
Methodological quality	

Garcia 2020 (A) *(Continued)*

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		

Garcia 2020 (A) *(Continued)*

Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Did all participants receive a reference standard?	Yes	
Were results presented per patient?	Yes	
Could the patient flow have introduced bias?		Low risk

Garcia 2020 (B)

Study characteristics	
Patient Sampling	3-group study estimating sensitivity and specificity [3] Patients admitted with a clinical and radiological diagnosis of pneumonia of unknown etiology but RT-PCR-negative (n = 63) 2 additional cohorts extracted as separate 2-group study (Garcia 2020 (A)) Recruitment: NR Sample size (virus/COVID cases): 100 (55) Inclusion and exclusion criteria: NR
Patient characteristics and setting	Setting: hospital inpatient Location: Hospital Universitario Príncipe de Asturias, Madrid Country: Spain Dates: 9 February-2 April 2020 Symptoms and severity: NR Sex: male n = 47, 74% Age: median age 67, IQR 57-74 Exposure history: NR
Index tests	Test name: AllTest COV-19 IgG / IgM kit Manufacturer: AllTest Biotech, Hangzhou, China Ab targets: IgM, IgG. Antigens used: NR Test method: immunochromatography Timing of samples: days 0-14+ pso Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: clinical diagnosis of COVID-19 Criteria NR Timing of reference standard: NR Blinded to index test: yes Incorporated index test: no
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: yes: 7-13 days 29% (n = 18); ≥ 14 days 71% (n = 45) All participants received the same reference standard: yes Missing data: NR

Garcia 2020 (B) *(Continued)*

	Uninterpretable results: NR Indeterminate results: NR Unit of analysis: participants
Comparative	
Notes	Funding: no funding received Publication status: preprint (not peer reviewed) Source: medRxiv Study author COI: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Unclear		

Garcia 2020 (B) *(Continued)*

Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		Unclear
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Were results presented per patient?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Grzelak 2020 [A]

Study characteristics	
Patient Sampling	4-group study to estimate sensitivity and specificity for diagnosing active disease. [1] Hospitalised COVID-19 patients (51; 161 samples) [2] Pre-pandemic sera (491) Recruitment: NR (appears retrospective); consecutive or otherwise NR Review team excluded: [3] Blood donors during pandemic (200) [4] Cohort of 209 pauci-symptomatic suspected cases (mild signs compatible with COVID-19 -fever, cough or dyspnea) who had been in contact with a confirmed case as no reference standard reported
Patient characteristics and setting	Setting: inpatient Location: Hôpital Bichat, Paris Country: France Dates: NR
Index tests	This entry (Grzelak 2020 [A]) refers to test [A] in the list below: 5 tests evaluated: A. LIPS (S1 protein) B. LIPS (N protein) C. ELISA (N protein) D. S-Flow (unknown) E. ELISA tri-S (S protein) Manufacturer: in-house Ab targets: A. total Ab; B. total Ab; C. IgG; D IgM or IgG; E. total Ab

Grzelak 2020 [A] *(Continued)*

	Antigens used: A. S1; B. N-based; C. full-length SARS-CoV-2 N protein; D. S at the cell surface; E. trimeric S (recombinant S glycoprotein ectodomain)
Target condition and reference standard(s)	Reference standard for cases: NR. Described as confirmed COVID-19 hospitalised cases only Samples used: not described Timing of reference standard: not described Was it blind to index test: not described
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: no All participants received the same reference standard: no Missing data: pre-pandemic sera are missing from the evaluations of ELISA tri-S (n = 391), S-flow (n = 357) and LIPS S1 and N (n = 2) Sample-based analysis
Comparative	
Notes	Funding: OS lab is funded by Institut Pasteur, ANRS, Sidaction, the Vaccine Research Institute (ANR- 10-LABX-77), Labex IBEID (ANR-10-LABX-62 IBEID), "TIMTAMDEN" ANR-14-CE14-0029, "CHIKV-Viro- Immuno" ANR-14-CE14-0015-01 and the Gilead HIV cure program. LG is supported by the French Ministry of Higher Education, Research and Innovation.ME lab is funded by Institut Pasteur, Labex IBEID (ANR-10-LABX-62-IBEID), Reacting, EU grant Recover, ANR Oh'ticks. HM received core grants from the G5 Institut Pasteur Program, the Milieu Intérieur Program (ANR-10-LABX-69-01) and INSERM. C.P. is supported by a fellowship from the Agence Nationale de Recherches sur le Sida et les Hépatites Virales (ANRS). SVDW lab is funded by Institut Pasteur, CNRS, Université de Paris, Santé publique France, Labex IBEID (ANR-10-LABX-62-IBEID), REACTing, EU grant Recover. Publication status: preprint Source: medRxiv Study author COI: PC is the founder and CSO of TheraVectys

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			

Grzelak 2020 [A] *(Continued)*

DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Unclear
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	No		
Could the patient flow have introduced bias?		High risk	

Grzelak 2020 [B]

Study characteristics			

Grzelak 2020 [B] *(Continued)*

Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Index tests	This entry (Grzelak 2020 [B]) refers to test [B] in the list below; see Grzelak 2020 [A] for further study characteristics and QUADAS-2 assessments) 5 tests evaluated: A. LIPS (S1 protein) B. LIPS (N protein) C. ELISA (N protein) D. S-Flow (unknown) E. ELISA tri-S (S protein) Manufacturer: in-house Ab targets: A. total Ab; B. total Ab; C. IgG; D IgM or IgG; E. total Ab Antigens used: A. S1; B. N-based; C. full-length SARS-CoV-2 N protein; D. S at the cell surface; E. trimeric S (recombinant S glycoprotein ectodomain)
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Comparative	
Notes	

Grzelak 2020 [C]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Index tests	This entry (Grzelak 2020 [C]) refers to test [C] in the list below; see Grzelak 2020 [A] for further study characteristics and QUADAS-2 assessments) 5 tests evaluated: A. LIPS (S1 protein) B. LIPS (N protein) C. ELISA (N protein)

Grzelak 2020 [C] *(Continued)*

	D. S-Flow (unknown) E. ELISA tri-S (S protein) Manufacturer: in-house Ab targets: A. total Ab; B. total Ab; C. IgG; D IgM or IgG; E. total Ab Antigens used: A. S1; B. N-based; C. full-length SARS-CoV-2 N protein; D. S at the cell surface; E. trimeric S (recombinant S glycoprotein ectodomain)
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Comparative	
Notes	

Grzelak 2020 [D]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Index tests	This entry (Grzelak 2020 [D]) refers to test [D] in the list below; see Grzelak 2020 [A] for further study characteristics and QUADAS-2 assessments) 5 tests evaluated: A. LIPS (S1 protein) B. LIPS (N protein) C. ELISA (N protein) D. S-Flow (unknown) E. ELISA tri-S (S protein) Manufacturer: in-house Ab targets: A. total Ab; B. total Ab; C. IgG; D IgM or IgG; E. total Ab Antigens used: A. S1; B. N-based; C. full-length SARS-CoV-2 N protein; D. S at the cell surface; E. trimeric S (recombinant S glycoprotein ectodomain)
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Comparative	

Grzelak 2020 [D] *(Continued)*

Notes	

Grzelak 2020 [E]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Index tests	This entry (Grzelak 2020 [E]) refers to test [E] in the list below; see Grzelak 2020 [A] for further study characteristics and QUADAS-2 assessments) 5 tests evaluated: A. LIPS (S1 protein) B. LIPS (N protein) C. ELISA (N protein) D. S-Flow (unknown) E. ELISA tri-S (S protein) Manufacturer: in-house Ab targets: A. total Ab; B. total Ab; C. IgG; D IgM or IgG; E. total Ab Antigens used: A. S1; B. N-based; C. full-length SARS-CoV-2 N protein; D. S at the cell surface; E. trimeric S (recombinant S glycoprotein ectodomain)
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Grzelak 2020 [A])
Comparative	
Notes	

Guo 2020a

Study characteristics	
Patient Sampling	2-group study estimating sensitivity and specificity for detection of active disease in people with suspected or confirmed SARS-Cov-2 infection and other infection controls. 1. Cases - 101 inpatients from Wuhan (43 PCR confirmed and 58 probable) provided 169 paired throat and blood samples (69 from confirmed and 100 from probable) 2. Cases - 39 inpatient confirmed cases from Beijing provided 39 samples (total of 208 samples) 3. Control samples provided by people with acute LRTI (135)

Guo 2020a *(Continued)*

	Family cluster also recruited but does not contribute data. Healthy individuals (150) used to define threshold. Additional plasma samples positive for human CoV-229E, -NL63, -OC43, -HKU1, and SARS-CoV previously obtained were included for Western Blot cross-reactivity analysis. Recruitment method NR
Patient characteristics and setting	1. Inpatients at Wuhan hospitals. 43 confirmed cases (PCR or deep sequencing): 20 severe; 23 mild to moderate; 58 possible cases (test-negative but with clinical signs, X-ray evidence): 5 severe, 53 mild to moderate. Exposure history NR 2. Beijing hospitals, China (recruitment dates January 2020); 8 severe and 31 mild to moderate. No further details 3. Acute LRTI infection controls: 135 samples from adult patients. No further detail (Family cluster of 6; aged 2-64, 3 male 3 female. Healthy control samples from Wuhan City adult health check-ups, 2018-19)
Index tests	3 ELISA assays, blinding NR In-house ELISA (indirect, laboratory-based, using blood/plasma samples. Measured IgM, IgA, IgG. Antigen: rNPs (recombinant N protein) from SARS-CoV-2 virus Test threshold determined from mean values and SD of healthy individual plasma (calculated the mean absorbance at 450 nm (A450) of the negative sera plus 3 folds of the SD values which were 0.13, 0.1 and 0.30 for IgM, IgA, and IgG, respectively. Samples acquired 1-39 days after disease onset (41/208 at 1-7 days; 84/208 at 8-14 days; 83 > 14 days pso). Person applying the test not described
Target condition and reference standard(s)	1. and 2. Confirmed cases - deep sequencing or a qPCR assay with a detection limit of 1 copy/µL, using throat swabs samples. Positivity threshold: NR. Probable cases - clinical manifestation, chest radiography imaging and epidemiology but no virus detected by deep sequencing or qPCR. Timing NR. Not blinded to index test. 3. LRTI controls: pre-pandemic samples (2018-2019)
Flow and timing	Differential verification: all cases had RT-PCR but some were negative, plus controls did not have RT-PCR. Time interval between index and reference: presumed short. There are multiple samples for some participants (cases) but others contribute only sample with a range of days pso; only data for 1-7 days pso can be disaggregated from the rest. Missing data, uninterpretable and indeterminate results not described Per participant and per sample data can be extracted
Comparative	
Notes	Funded by Chinese Academy of Medical Sciences (CAMS) Innovation Fund for Medical Sciences, Non-profit Central Research Institute Fund of CAMS, National Major Science & Technology Project for Control and Prevention of Major Infectious Diseases in China. No conflicts of interest reported Publication status: preprint

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		

Guo 2020a *(Continued)*

Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		

Guo 2020a *(Continued)*

Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Were results presented per patient?	Yes
Could the patient flow have introduced bias?	Unclear risk

Hu 2020a

Study characteristics	
Patient Sampling	Single-group study to estimate sensitivity for detecting active or prior infection Confirmed COVID-19 patients (211) Recruitment: NR; likely retrospective. Consecutive or otherwise NR
Patient characteristics and setting	Setting: inpatient Location: Chongqing Three Gorges Central Hospital, Chongqing. Country: China Dates: 23 January-3 March
Index tests	Test name: Magnetic Chemiluminescence Enzyme Immunoassay (MCLIA) kit Manufacturer: Bioscience Co., Ltd (Chongqing, China) Ab targets: IgM, IgG Antigens used: N and S (nucleoprotein and a peptide from the SARS SARS-CoVCoV-2 S protein)
Target condition and reference standard(s)	Reference standard for cases: Chinese CDC guidelines (Trial Version 6); included RT-PCR Samples used: NR Timing of reference standard: unclear; appears that repeat PCR undertaken during hospitalisation; 74/211 met discharge criteria during study period (normal temperature, significantly improving respiratory symptoms and chest radiology plus 2 repeat negative PCRs with ≥ 1-day interval) Was it blind to index test: unclear
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: yes All participants received the same reference standard: yes Missing data: none described; however text states 993 samples but only 409 reported for IgM and 507 for IgG Uninterpretable results: none described
Comparative	
Notes	Funding: funded by Chongqing Education Board “new coronavirus infection and prevention” emergency scientific research project

Hu 2020a *(Continued)*

(KYYJ202006YYJ202006). Chongqing Science and Technology Bureau "new crown pneumonia epidemic emergency science and technology special" the fourth batch of projects. Famous teacher project of Chongqing talent plan
Publication status: preprint
Source: medRxiv
Study author COI: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	

Hu 2020a *(Continued)*

Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Were results presented per patient?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Infantino 2020

Study characteristics	
Patient Sampling	3-group study recruiting patients estimating sensitivity and specificity [1] COVID-19 confirmed [2] Rheumatic disease or infectious disease control group (2018-19; pre COVID-19 era) [3] Blood donor control group (November/December 2019) Recruitment: unclear Prospective or retrospective recruitment of cases: prospective Sample size (virus/COVID cases): 125 (51 COVID cases) Inclusion and exclusion criteria: COVID-19 cases were confirmed by RT-PCR
Patient characteristics and setting	Setting: hospital inpatient Location: San Giovanni di Dio Hospital, Florence Country: Italy Dates: NR Symptoms and severity: 30/61 (49%) mild to moderate symptoms 31/61 (51%) with severe pneumonia required admission to the ICU Sex: [1] 26/61 (43%) male [2] 26/61 (43%) male [3] 12/20 (60%) male Age: [1] mean 59 ± 23 years; [2] mean 49 ± 17 years; [3] 44 ± 11 years Exposure history: NR
Index tests	Test name: SARS CoV-2 antibodies IgM and IgG CLIA kits (analysed with iFlash1800 fully automatic CLIA) Manufacturer: Shenzhen YHLO Biotech Co., Ltd (China) Ab targets: IgM or IgG Antigens used: N protein and S protein Test method: CLIA Timing of samples: NR Samples used: blood (discussion mentions serum) Test operators: NR Definition of test positivity: ≥ 10 AU/mL Blinded to reference standard: NR Threshold predefined: yes

Infantino 2020 *(Continued)*

Target condition and reference standard(s)	Reference standard for cases: RT-PCR Samples used: OP and NP swabs Timing of reference standard: NR Blinded to index test: NR Incorporated index test: no Reference standard for non-cases: [2] pre-pandemic; [2] NR (contemporaneous blood donors)
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: no All participants received the same reference standard: no Missing data: no Uninterpretable results: no Indeterminate results: no Unit of analysis: participant
Comparative	
Notes	Funding: NR Publication status: accepted Source: Journal of Medical Virology Study author COI: NR

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	

Infantino 2020 *(Continued)*

Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Unclear		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Jia 2020

Study characteristics	
Patient Sampling	Single-group study estimating sensitivity for detection of active or recent infection in people with suspected COVID-19. Patients with highly suspected COVID-19 (n = 57; 24 PCR-positive) defined by exposure history, one of: 1. the patient has a history of travel or resident in Wuhan or surrounding area, or communities with COVID-19 patients within 14 days before onset; 2. has a contact history with people infected with COVID-19 (positive NAAT) within 14 days before onset; 3. has a contact history with patients from Wuhan and surrounding areas, or has a contact history with patients who have fever or respiratory symptoms from communities with COVID-19; 4. cluster onset; and by clinical manifestations, 2 of:

Jia 2020 *(Continued)*

	1. fever and (or) respiratory symptoms; 2. conforming to the imaging features; 3. white blood cells are normal or reduced in early stage of disease, and lymphocyte count is reduced. Second, if there is no clear epidemiological history, it meets the above 3 clinical manifestations
Patient characteristics and setting	Inpatients at > 20 hospitals of ShenZhen, China (recruitment dates NR). Sample characteristics and exposure history not described
Index tests	1 Ab test, blinding NR LFA. Time-Resolved Immunofluorescence assay (needs fluorescence analyser); Beijing Diagreat Biotechnologies Co., Ltd, Lot: 20200214). Samples and timing of sampling not described. Measured IgM and IgG; antigen not described. Threshold (Flu) for IgM ≥ 0.88 Flu and IgG ≥ 1.02 Flu. Estimated from 242 healthy people without related diseases (95% of the values were negative) Person applying the test not described
Target condition and reference standard(s)	RT-PCR using 2 kits from one of 6 companies (DAAN, Sansure Biotech, BGI, ShangHai ZJ Biotech, Geneodx, Biogerm) across 20 different hospitals. Each participant tested 3 times at different time points (24 positive on first test, all negative on 2nd and 3rd tests), using pharyngeal swabs (acquired 1-34 days from exposure to first test). Negative on all PCR tests classed as D- for purposes of this review For PCR-negative, clinical diagnosis criteria required exposure history plus 2 (1) fever and (or) respiratory symptoms; (2) conforming to the imaging features; (3) white blood cells are normal or reduced in early stage of disease, and lymphocyte count is reduced. If there was no clear epidemiological history, 3 clinical manifestations required. No guideline cited but criteria clearly defined. Blinding to index test NR
Flow and timing	All received same reference standard but not all PCR-positive; Time interval between index and reference not described. (Serology sample timing NR; PCR was 1-34 days from exposure to confirmed case. Time pso NR) No missing data, uninterpretable or indeterminate results reported Participant-based analysis
Comparative	
Notes	No funding sources described COI: none described Publication status: preprint (not peer reviewed)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		

Jia 2020 *(Continued)*

Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		

Jia 2020 *(Continued)*

Were results presented per patient?	Yes
Could the patient flow have introduced bias?	Unclear risk

Jin 2020

Study characteristics	
Patient Sampling	2-group study recruiting patients estimating sensitivity and specificity [1] Laboratory-confirmed COVID-19 patients (n = 43); reported separately for 27 patients while still PCR-positive and for 34 patients after becoming PCR-negative (excluded from review) [2] Patients admitted with suspected SARS-CoV-2 infection, in whom the disease was eventually excluded in the hospital and who quarantined at home, were included as a control group (n = 33) Recruitment: unclear Sample size (virus/COVID cases): 76 (43) Inclusion and exclusion criteria: suspected SARS-CoV-2 infection (fever or any respiratory symptoms, especially in those with a history of travel to Wuhan or exposure to an infected case within 2 weeks)
Patient characteristics and setting	Setting: hospital inpatients Location: Xixi Hospital of Hangzhou, Zhejiang Province Country: China Dates: January 2020-4 March 2020 Symptoms and severity: [1] COVID-19 patients: 27/43 (63%) fever; 26/43 (61%) cough; [2] non-COVID-19 patients: 24/43 (73%) fever; 15/33 (46%) cough Sex: [1] COVID-19 patients: 17/43 (40%) male. [2] Non-COVID-19 patients: 22/33 (67%) male Age: [1] COVID-19 patients: median age 47 (IQR 34–59) years; [2] non-COVID-19 patients: median age 31 (IQR 26–38) years Exposure history: [1] NR; [2] NR
Index tests	Test name: The SARS-CoV-2 IgM and IgG CLIA kits Manufacturer: Shenzhen YHLO Biotech Co., Ltd (China) Ab targets: IgM, IgG Antigens used: N protein, S protein Test method: CLIA Timing of samples: 1-55 days pso whilst still in hospital Samples used: serum Test operators: laboratory Definition of test positivity: > 10 AU/mL Blinded to reference standard: unclear Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: RT-PCR testing at the Center for Disease Control of Hangzhou Samples used: oral swab or sputum Timing of reference standard: during patient care Blinded to index test: unclear Incorporated index test: no Reference standard for non-cases: 2 consecutive negative RT-PCR 24 h apart
Flow and timing	Time interval between index and reference tests: between 1 and 32 days

Jin 2020 *(Continued)*

	Results presented by time period: days pso: 0-5 6% (n = 6); 6-10 12% (n = 12); 11-15 15% (n = 15); 16-20 22% (n = 22); 21-25 22% (n = 22); 26-30 15% (n = 15); 31-55 8% (n = 8) All participants received the same reference standard: yes Missing data: review team excluded serology data for 34 participants after becoming PCR-negative; no data reported for 16 participants while PCR-positive Uninterpretable results: none mentioned Indeterminate results: none mentioned Unit of analysis: participants overall; samples by time period
Comparative	
Notes	Funding: research Project on the Prevention and Treatment of COVID-19 in Hangzhou (establishment of a clinical diagnosis and treatment system for COVID-19 with treatment evaluation) Publication status: published paper Source: academic journal Study author COI: none mentioned

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	

Jin 2020 *(Continued)*

Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Lassauniere 2020 [A]

Study characteristics	
Patient Sampling	2-group design estimating sensitivity and specificity for 9 tests Groups: [1] COVID-19-positive group (n = 30) admitted to ICU; [2] non-COVID-19 group (n = 82) including pre-pandemic (2017) blood donors (n = 10); acute viral respiratory tract infections with other coronaviruses (n = 5) or non-coronaviruses (n = 45); dengue virus (n = 9), CMV; n = 2 and Epstein Barr virus (n = 10). 1 additional patient positive for both CMV and Epstein Barr virus Recruitment: [1] recruited consecutively (all cases in ICU on a single day); [2] unclear Sample size (virus/COVID cases): 112 (30) Inclusion and exclusion criteria: none stated

Lassauniere 2020 [A] *(Continued)*

Patient characteristics and setting	Setting: [1] ICU; [2] biobank samples Location: [1] Hillerød Hospital Country: Denmark Dates: NR Symptoms and severity: NR Sex: 75% (24/32) male Age: median 67 years (IQR 52-76) Exposure history: NR
Index tests	9 tests evaluated, 3 ELISA and 6 LFIA; this entry (Lassauniere 2020 [A]), refers to test [A] in the list below: [A] test name: Wantai SARS-CoV-2 Ab ELISA Manufacturer: Beijing Wantai Biological Pharmacy Enterprise, Beijing, China; Cat # WS-1096 Ab targets: total Ab Antigens used: SARS-CoV-2 S protein RBD Test method: ELISA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: calculated negative control value to 0.160 Blinded to reference standard: no Threshold predefined: yes [B] test name: Anti-SARS-CoV-2 IgG ELISA Manufacturer: Euroimmun Medizinische Labordiagnostika, Lübeck, Germany; Cat # EI 2668-9601 G Ab targets: IgG Antigens used: SARS-CoV-2 S protein subunit 1 (S1) Test method: ELISA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: ratio < 0.8 is considered negative, ≥ 0.8 and < 1.1 borderline, and ≥ 1.1 positive. For analysis 1.1 a more stringent cut-off was used, and all values < 1.1 were considered negative. Blinded to reference standard: no Threshold predefined: yes [C] test name: Anti-SARS-CoV-2 IgA ELISA Manufacturer: Euroimmun Medizinische Labordiagnostika, Lübeck, Germany; Cat # EI 2606-9601 A Ab targets: IgA Antigens used: SARS-CoV-2 S protein subunit 1 (S1) Test method: ELISA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: ratio < 0.8 is considered negative, ≥ 0.8 and < 1.1 borderline, and ≥ 1.1 positive. For analysis 1.1 a more stringent cut-off was used, and all values < 1.1 were considered negative. Blinded to reference standard: no Threshold predefined: yes [D] Test name: 2019-nCOV IgG/IgM Rapid Test Manufacturer: Dynamiker Biotechnology, Tianjin, China Cat # DNK-1419-1 Ab targets: IgM, IgG Antigens used: NR Test method: CGIA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes [E] Test name: OnSiteTM COVID-19 IgG/IgM Rapid Test Manufacturer: CTK Biotech, Poway, CA, USA; Cat # R0180C Ab targets: IgM, IgG Antigens used: NR

Lassauniere 2020 [A] *(Continued)*

	Test method: CGIA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes [F] Test name: Anti-SARS-CoV-2 Rapid Test Manufacturer: AutoBio Diagnostics, Zhengzhou, China; Cat # RTA0204 Ab targets: IgM, IgG Antigens used: NR Test method: CGIA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes [G] Test name: Coronavirus Diseases 2019 (COVID-19) IgM/IgG Ab Test Manufacturer: Artron Laboratories, Burnaby, Canada; Cat # A03-51-322 Ab targets: IgM, IgG. Antigens used: NR Test method: CGIA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes [H] Test name: 2019-nCoV IgG/IgM Rapid Test Cassette Manufacturer: Acro Biotech, Rancho Cucamonga, CA, USA; Cat # INCP-402 Ab targets: IgM, IgG Antigens used: NR Test method: CGIA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes [I] Test name: 2019-nCoV IgG/IgM Rapid Test Cassette Manufacturer: Hangzhou Alltest Biotech, Hangzhou, China; Cat # INCP-402 Ab targets: IgM, IgG Antigens used: NR Test method: CGIA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases (including threshold): viral nucleic acid detection (no further detail) in hospital patients Samples used: respiratory Timing of reference standard: during hospital stay Blinded to index test: yes Incorporated index test: no Reference standard for non-cases: pre-pandemic (2017)

Lassauniere 2020 [A] *(Continued)*

Flow and timing	Time interval between index and reference tests: unclear Results presented by time period: days since onset: 7-13 (n = 7); 14-20 (n = 15); ≥ 21 (n = 8) All participants received the same reference standard: no Missing data: some participant samples were not tested with all assays. Only 32 of the 80 control participants were tested with POC assays. Unclear how the 32 were selected Uninterpretable results: not mentioned Indeterminate results: borderline results for [2] and [3] were considered test-negative. For POC tests, weak signals for IgM and IgG were considered positive. Unit of analysis: participants
Comparative	
Notes	Funding: Danish National Biobank resource, supported by the Novo Nordisk Foundation Publication status: preprint (not peer reviewed) Source: medRxiv Study author COI: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		

Lassauniere 2020 [A] *(Continued)*

Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Yes		

Lassauniere 2020 [A] *(Continued)*

Were results presented per patient?	Yes
Could the patient flow have introduced bias?	High risk

Lassauniere 2020 [B]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Index tests	9 tests evaluated, 3 ELISA and 6 LFIA; this entry (Lassauniere 2020 [B]) refers to test [B] [B] test name: Anti-SARS-CoV-2 IgG ELISA Manufacturer: Euroimmun Medizinische Labordiagnostika, Lübeck, Germany; Cat # EI 2668-9601 G Ab targets: IgG. Antigens used: SARS-CoV-2 S protein subunit 1 (S1) Test method: ELISA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: ratio < 0.8 is considered negative, ≥ 0.8 and < 1.1 borderline, and ≥ 1.1 positive. For analysis 1.1 a more stringent cut-off was used, and all values < 1.1 were considered negative. Blinded to reference standard: no Threshold predefined: yes
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Comparative	
Notes	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])

Lassauniere 2020 [C]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])

Lassauniere 2020 [C] *(Continued)*

Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Index tests	Nine tests evaluated, 3 ELISA and six LFIA; this entry (Lassauniere 2020 [C]) refers to test [C] [C] test name: Anti-SARS-CoV-2 IgA ELISA Manufacturer: Euroimmun Medizinische Labordiagnostika, Lübeck, Germany; Cat # EI 2606-9601 A Ab targets: IgA Antigens used: SARS-CoV-2 S protein subunit 1 (S1) Test method: ELISA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: ratio < 0.8 is considered negative, ≥ 0.8 and < 1.1 borderline, and ≥ 1.1 positive. For analysis 1.1 a more stringent cut-off was used, and all values < 1.1 were considered negative. Blinded to reference standard: no Threshold predefined: yes
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Comparative	
Notes	

Lassauniere 2020 [D]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Index tests	9 tests evaluated, 3 ELISA and 6 LFIA; this entry (Lassauniere 2020 [D]) refers to test [D] [D] Test name: 2019-nCOV IgG/IgM Rapid Test Manufacturer: Dynamiker Biotechnology, Tianjin, China Cat # DNK-1419-1 Ab targets: IgM, IgG Antigens used: NR Test method: CGIA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes

Lassauniere 2020 [D] *(Continued)*

Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Comparative	
Notes	

Lassauniere 2020 [E]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Index tests	9 tests evaluated, 3 ELISA and 6 LFIA; this entry (Lassauniere 2020 [E]) refers to test [E] [E] Test name: OnSiteTM COVID-19 IgG/IgM Rapid Test Manufacturer: CTK Biotech, Poway, CA, USA; Cat # R0180C Ab targets: IgM, IgG Antigens used: NR Test method: CGIA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Comparative	
Notes	

Lassauniere 2020 [F]

Study characteristics	

Lassauniere 2020 [F] *(Continued)*

Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Index tests	9 tests evaluated, 3 ELISA and 6 LFIA; this entry (Lassauniere 2020 [F]) refers to test [F] [F] Test name: Anti-SARS-CoV-2 Rapid Test Manufacturer: AutoBio Diagnostics, Zhengzhou, China; Cat # RTA0204 Ab targets: IgM, IgG Antigens used: NR Test method: CGIA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Comparative	
Notes	

Lassauniere 2020 [G]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Index tests	9 tests evaluated, 3 ELISA and 6 LFIA; this entry (Lassauniere 2020 [G]) refers to test [G] [G] Test name: Coronavirus Diseases 2019 (COVID-19) IgM/IgG Ab Test Manufacturer: Artron Laboratories, Burnaby, Canada; Cat # A03-51-322 Ab targets: IgM, IgG. Antigens used: NR Test method: CGIA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes

Lassauniere 2020 [G] *(Continued)*

Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Comparative	
Notes	

Lassauniere 2020 [H]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Index tests	9 tests evaluated, 3 ELISA and 6 LFIA; this entry (Lassauniere 2020 [H]) refers to test [H] [H] Test name: 2019-nCoV IgG/IgM Rapid Test Cassette Manufacturer: Acro Biotech, Rancho Cucamonga, CA, USA; Cat # INCP-402 Ab targets: IgM, IgG Antigens used: NR Test method: CGIA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Comparative	
Notes	

Lassauniere 2020 [I]

Study characteristics	

Lassauniere 2020 [I] *(Continued)*

Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Index tests	9 tests evaluated, 3 ELISA and 6 LFIA; this entry (Lassauniere 2020 [I]) refers to test [I] [I] Test name: 2019-nCoV IgG/IgM Rapid Test Cassette Manufacturer: Hangzhou Alltest Biotech, Hangzhou, China; Cat # INCP-402 Ab targets: IgM, IgG Antigens used: NR Test method: CGIA Timing of samples: Samples used: serum Test operators: laboratory staff Definition of test positivity: visible line Blinded to reference standard: no Threshold predefined: yes
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Lassauniere 2020 [A])
Comparative	
Notes	

Li 2020a

Study characteristics	
Patient Sampling	Single-group study estimating sensitivity for detection of active or recent infection Particpants with COVID-19 according to guideline of diagnosis and treatment of COVID-19 (9 Feb), 525 participants (397 PCR-positive) Data comparing results using fingerstick blood, serum and plasma for COVID-19 patients (7) and healthy volunteers (3) not extracted
Patient characteristics and setting	Samples from various hospitals and CDC testing laboratories (total 8) at 6 different provinces, China Recruitment dates NR Sample characteristics and exposure history not described
Index tests	1 Ab test, blinding not described LFIA (colloidal gold). SARS-CoV-2 rapid IgG-IgM combined Ab test kit, from Jiangsu Medomics Medical Technologies, Nanjing, China. Target: IgM and IgG, using recombinant antigen from SARS-CoV-2 S protein (MK201027) Threshold predefined, as per manufacturer Tests conducted using serum and plasma from venous blood. Samples acquired by clinical staff at each site. Timing not clearly described (dur-

Li 2020a *(Continued)*

	ing hospital stay for inpatients); detail provided for 1 site (n = 58), sampling between day 8 and 33 pso
Target condition and reference standard(s)	COVID-19 clinically confirmed, according to guideline. (Prevention CCfDCa. The guideline of diagnosis and treatment of COVID-19. 9 February 2020). PCR test using pharyngeal (throat) swab samples and sputum (threshold NR). Timing not described Presume blinded to index test
Flow and timing	Time interval between index and reference not described. No disaggregation of results by time pso No missing data, uninterpretable or indeterminate results reported Participant-based analysis
Comparative	
Notes	Funding not described Conflicts of interest: 4 co-authors employed by Jiangsu Medomics Medical Technology Accepted for publication with full peer review

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			

Li 2020a *(Continued)*

Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Lin 2020a [A]

Study characteristics	
Patient Sampling	3-group study estimating sensitivity and specificity [1] COVID-19 cases (n = 79) [2] Healthy volunteers (n = 29) [3] TB patients (n = 51) Recruitment: 'Random' for [1] (method not stated), no details given for [2] and [3] Sample size (virus/COVID cases): 159 (79) Inclusion and exclusion criteria: for [1]: "combinations of epidemiological risk, clinical features and RT-PCR respiratory specimen positive"
Patient characteristics and setting	Setting: [1] specialist COVID hospital (inpatients); [2] university; [3] TB inpatient clinic Location: [1] Third People's Hospital, Shenzhen; [2] Shenzhen University; [3] Shenzhen Baoan Hospital Country: China Dates: NR Symptoms and severity: NR Sex: NR Age: [1] and [3] NR; [2] range 19-72 Exposure history: NR
Index tests	2 tests were evaluated; this entry (Lin 2020a [A]) refers to test [A] in the list below

Lin 2020a [A] *(Continued)*

	Test name: [A] not named; [B] commercial ELISA kit Manufacturer: [A] in-house; [B] Darui Biotech, China Ab targets: [A] and [B]: IgM, IgG Antigens used: [A] recombinant nucleocapsid (YP_009724397.2); [B] SARS-CoV-2 N protein Test method: [A] CLIA; [B] ELISA Timing of samples: 0 to > 14 days (maximum NR) pso Samples used: serum Test operators: NR (assume laboratory staff) Definition of test positivity: [A] IgM (RLU 162296); IgG (RLU 336697) [B] manufacturer's recommendation Blinded to reference standard: not mentioned Threshold predefined: [A] threshold derived from ROC curve; [B] yes (QUADAS ratings are for ELISA test)
Target condition and reference standard(s)	Reference standard: RT-PCR: GeneoDX kit (Taqman RT-PCR method, targeting the ORF1ab 101 and N genes) [2] and [3] were persistently negative in at least 3 tests. Samples used: respiratory Timing of reference standard: presume on presentation Blinded to index test: NR Incorporated index test: no
Flow and timing	Time interval between index and reference tests: unclear Results presented by time period:days 1-7 (15%); 8-13 (42%); 14+ (43%) All participants received the same reference standard: yes Missing data: 65/79 D+ serum samples available for ELISA; 64/80 D- serum samples available for ELISA; reason not given Uninterpretable results: NR Indeterminate results: NR Unit of analysis: participants
Comparative	
Notes	Funding: Guangdong Provincial Science and Technology Program, National Natural Science Funds of China, Shenzhen University and the National Science and Technology Major Project Publication status: preprint (not peer reviewed) Source: medRxiv Study author COI: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		

Lin 2020a [A] *(Continued)*

Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		

Lin 2020a [A] *(Continued)*

Could the patient flow have introduced bias?	High risk

Lin 2020a [B]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Lin 2020a [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Lin 2020a [A])
Index tests	2 tests were evaluated; this entry (Lin 2020a [B]) refers to test [B] in the list below Test name: [A] not named (CLIA); [B] commercial ELISA kit Manufacturer: [A] in-house; [B] Darui Biotech, China Ab targets: [A] and [B]: IgM, IgG Antigens used: [A] recombinant nucleocapsid (YP_009724397.2); [B] SARS-CoV-2 N protein Test method: [A] CLIA; [B] ELISA Timing of samples: 0 to > 14 days (maximum NR) pso Samples used: serum Test operators: NR (assume laboratory staff) Definition of test positivity: [A] IgM (RLU 162296); IgG (RLU 336697) [B] manufacturer's recommendation Blinded to reference standard: not mentioned Threshold predefined: [A] threshold derived from ROC curve; [B] yes (QUADAS ratings are for ELISA test)
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Lin 2020a [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Lin 2020a [A])
Comparative	
Notes	See main entry for this study for characteristics and QUADAS-2 assessment (Lin 2020a [A])

Lippi 2020 [A]

Study characteristics	
Patient Sampling	1-group study recruiting patients estimating sensitivity and specificity [1] Suspected COVID-19; subgroup of confirmed cases included Recruitment: consecutive patients Prospective or retrospective recruitment of cases: prospective Sample size (virus/COVID cases): 131 (NR); subgroup of 48 confirmed cases included Inclusion and exclusion criteria: suspected COVID-19 patients hospitalised, in whom NP and OP swabs were collected along with blood samples during hospital stay, for purposes of COVID-19 diagnosis and/or monitoring

Lippi 2020 [A] *(Continued)*

Patient characteristics and setting	Setting: hospital inpatients Location: University Hospital of Verona Country: Italy Dates: NR Symptoms and severity: NR Sex: 60/131 (46%) male Age: mean 56 ± 21 years Exposure history: NR
Index tests	2 tests were evaluated; this entry (Lippi 2020 [A]) refers to test [A] in the list below Test name: [A] MAGLUMI 2019-nCoV IgG and IgM (2 indirect tests) [B] Anti-SARS-CoV-2 IgA and IgG ELISA Manufacturer: [A] SNIBE – Shenzhen New Industries Biomedical Engineering Co., Ltd, Shenzhen, China [B] Euroimmun AG, Lübeck, Germany Ab targets: [A] IgM or IgG ; [B] IgA or IgG Antigens used: [A] CoV-S (spike) and e CoV-N (nucleocapsid); [B] NR Test method: [A] CLIA; [B] ELISAs Timing of samples: NR Samples used: blood, serum or plasma Test operators: NR Definition of test positivity: [A] ≥ 1.10 AU/mL [B] ≥ 1.1 (absorbance of patient sample/absorbance of calibrator) Blinded to reference standard: NR Threshold predefined: yes by manufacturer
Target condition and reference standard(s)	Reference standard for cases: RT-PCR (commercial RT-PCR method, Seegene AllplexTM2019-nCoV Assay) Samples used: venous blood Timing of reference standard: during hospital stay Blinded to index test: NR Incorporated index test: no Reference standard for non-cases: same reference standard, single-group
Flow and timing	Time interval between index and reference tests: both during hospital stay Results presented by time period: no All participants received the same reference standard: yes Missing data: NR Uninterpretable results: NR Indeterminate results: 36 Inconclusive results Unit of analysis: per patient
Comparative	
Notes	Funding: none declared Publication status: published letter Source: Clinical Chemistry and Laboratory Medicine Study author COI: study authors state no conflict of interest

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Lippi 2020 [A] *(Continued)*

Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		

Lippi 2020 [A] *(Continued)*

Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Did all participants receive a reference standard?	Yes	
Were results presented per patient?	Yes	
Could the patient flow have introduced bias?		Low risk

Lippi 2020 [B]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Lippi 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Lippi 2020 [A])
Index tests	2 tests were evaluated; this entry (Lippi 2020 [B]) refers to test [B] in the list below Test name: [A] MAGLUMI 2019-nCoV IgG and IgM (2 indirect tests) [B] Anti-SARS-CoV-2 IgA and IgG ELISA Manufacturer: [A] SNIBE – Shenzhen New Industries Biomedical Engineering Co., Ltd, Shenzhen, China [B] Euroimmun AG, Lübeck, Germany Ab targets: [A] IgM or IgG ; [B] IgA or IgG Antigens used: [A] CoV-S (spike) and e CoV-N (nucleocapsid); [B] NR Test method: [A] CLIA (CLIAs); [B] ELISA Timing of samples: NR Samples used: blood, serum or plasma Test operators: NR Definition of test positivity: [A] ≥1.10 AU/mL [B] ≥1.1 (absorbance of patient sample/absorbance of calibrator Blinded to reference standard: NR Threshold predefined: yes by manufacturer
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Lippi 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Lippi 2020 [A])
Comparative	
Notes	

Liu 2020a

Study characteristics	
Patient Sampling	Described as one group to estimate sensitivity and specificity (but unclear whether actually recruited as 2 groups) [1]. RT-PCR confirmed COVID-19 patients (n = 90) [2]. (a) COVID-19 suspects with RT-PCR-negative results (n = 25) and [2]. (b) inpatients with 'other disease' with RT-PCR-negative results (n = 64) Recruitment: unclear Sample size (virus/COVID cases): 179 (90 confirmed; data for 5 clinically confirmed included as D+) Inclusion and exclusion criteria:
Patient characteristics and setting	All participants considered COVID-19 suspects (criteria NR) Setting: hospital (inpatients and outpatients) Location: General Hospital of Central Theatre Command, Hubei Province Country: China Dates: 1 January to 12 March 2020 Group [1] Symptoms and severity: 46 mild/common cases; 44 severe/critical cases Sex: M/F: 60:30 (67%) Age: Age: mean 76 (SD 15) years Exposure history: NR. Group [2] [2a] Diagnoses: COVID-19 diagnoses: 5 confirmed; 20 suspected. [2b] Non-COVID-19 diagnosis: n = 64 (10 cases of Sjogren's syndrome, 8 cases of diabetes, 6 cases of systemic lupus erythematosus, 5 cases of rheumatoid arthritis, 2 cases of dermatomyositis, 2 cases of connective tissue disease, 1 case of scleroderma, and 30 cases of common injuries with no underlying diseases) Sex: M/F: 38:51 (35%) Age: mean 56 (SD 21) years Exposure history: NR
Index tests	Test name: SARS-CoV-2 IgG/IgM Ab test kit Manufacturer: A 'Chinese biotechnology company" Ab targets: IgM, IgG Antigens used: NR Test method: LFA (CGIA) Timing of samples: time pso to sample collection mean (SD) (days): PCR-postiive 30 (17), PCR-negative 18 (14) Samples used: serum Test operators: NR, but suspect in laboratory (as serum was used) Definition of test positivity: visible line Blinded to reference standard: unclear Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases (including threshold): RT-PCR test positive or 'clinically confirmed' Samples used: nasal and pharyngeal swabs Timing of reference standard: NR Blinded to index test: NR Incorporated index test: NR Reference standard for non-cases [2b]: RT-PCR test negative and diagnosis of alternative condition
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: known for 115 cases: 0-7 days: n = 25 (22%); 8-15 days n = 8 (7%); ≥ 16 days n = 82 (71%) All participants received the same reference standard: no

Liu 2020a *(Continued)*

	Missing data: none mentioned Uninterpretable results: none mentioned Indeterminate results: none mentioned Unit of analysis: participants
Comparative	
Notes	Funding: none reported Publication status: preprint (not peer reviewed) Source: medRxiv Study author COI: none reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		

Liu 2020a *(Continued)*

Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Unclear
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Liu 2020b

Study characteristics	
Patient Sampling	2-group study estimating sensitivity and specificity for diagnosing active disease. [1]. Consecutively recruited cohort of patients with confirmed or suspected COVID-19 (n = 238; 153 PCR confirmed) [2]. Cohort of ordinary patients (n = 70); [3]. Cohort of randomly sampled healthy blood donors (n = 50) randomly sampled No further details
Patient characteristics and setting	[1]. Inpatients at General Hospital of Central Theater Command of People's Liberation Army (PLA), China (recruitment dates 6-14 February 2020). Symptoms included fever (87%); dry cough (54%); fatigue (33%). 235/238 (99%) had CT ground glass opacity/patchy shadowing. Exposure history not described. Median age 55 [IQR 38.3-65] years; 58% male [2]. Ordinary patients, characteristics not described. [3]. Healthy blood donors (n = 50), characteristics not described
Index tests	2 Ab tests, blinding NR Both laboratory-based a. ELISA kit (Lizhu, Zhuhai, China). Measured IgG and IgM detected using recombinant (rN) protein of SARS-CoV-2. Test threshold: NR, presumed as per manufacturer

Liu 2020b *(Continued)*

	b. In-house CLIA Serum samples acquired 17 (7%) day 0-5; 41 (17%) day 6-10; 21 (9%) day 11-12; 48 (20%) day 13-15; 111 (47%) day ≥ 16
Target condition and reference standard(s)	1. RT-PCR (Daan Gene) targeting ORF1ab and N gene; Ct-value ≤ 40 was defined as a positive test result. Pharyngeal swab specimens used Clinical diagnosis of highly-suspected cases according to General Office of National Health Committee notice (General Office of National Health Committee. Office of State Administration of Traditional Chinese Medicine. Notice on the issuance of strategic guidelines for diagnosis and treatment of novel coronavirus (2019-nCoV) infected pneumonia (Fifth edition draft) (2020-02-09) [EB/OL]) Timing: clinical diagnosis presumed on admission. RT-PCR sampling - 54 (23%) day 0-5; 71 (30%) day 6-10; 28 (12%) day 11-12; 35 (15%) day 13-15; 50 (21%) day ≥ 16 2. No reference standard described for 'ordinary' patients or healthy controls
Flow and timing	Time interval between index and reference NR, but within hospital stay. Data are disaggregated by time pso but different participants contributed samples at each time. No missing data, uninterpretable or indeterminate results described. Basis for analysis: participants
Comparative	
Notes	Funded by National Natural Science Foundation of China; National Key Research and Development Program of China; and the China Postdoctoral Science Foundation. Wuhan Institute of Virology of Chinese Academy of Sciences and Zhuhai Lizhu Diagnostics Inc. for providing assistance in ELISA detection. Conflicts of interest: Zhuhai Lizhu Diagnostics Inc. acknowledged in Funding statement. Preprint (not peer reviewed): medRxiv

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			

Liu 2020b *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Liu 2020c

Study characteristics	
Patient Sampling	Single-group study to determine sensitivity in acute phase sera.

Liu 2020c *(Continued)*

	Cohort of 133 patients diagnosed with SARS-Cov-2 according to the "pneumonia diagnosis protocol for novel coronavirus infection (trial version 5)". Inclusion and exclusion criteria not further described
Patient characteristics and setting	Inpatients at Renmin Hospital (Wuhan University), China (recruitment dates 17 February-1 March 2020). Severity of condition classified as moderate 44, 33%; severe 52, 39%; critical 37, 29%. Median age (range) per group: moderate 67.5 years (64 to 71.5 years); severe 68 years (61.25 to 74); critical 70 years (60 to 76.5). Male 70, 53% Exposure history not described
Index tests	One Ab test, blinding NR Laboratory-based evaluation of CLIA (details as per company contact) to measure IgG and IgM - SARS-CoV-2 Ab detection kit (iFLash-SARS-CoV-2 IgG/IgM CLIA) (YHLO Biotech, Shenzhen), using serum samples. Antigen used NR Sample timing not described
Target condition and reference standard(s)	1. Clinical diagnosis according to established protocol (not cited but appears to be Chinese Government-issued - National Health Commission of the People's Republic of China, pneumonia diagnosis protocol for novel coronavirus detection (trial version 5)) 2. RT-PCR (ORF1ab/N qPCR detection kit from GeneoDx Biotech, Shanghai, China). 2 tests per participant but number of positive tests required NR. Samples not described, but Table 2 refers to 'NP', which could be NP samples. Positivity threshold not described
Flow and timing	Time interval between index and reference standard not described; time pso not described No missing data, uninterpretable or indeterminate results described Basis for analysis: participants
Comparative	
Notes	Funded by National Natural Science Foundation of China (81672079 to CZ and 31800147 to ZL), the Open Research Fund Program of the State Key Laboratory of Virology of China (2019KF001 to ZL), the Outstanding Leaders Training Program of Pudong Health Bureau of Shanghai (PWR12018-05 to XL), and the Key Disciplines Group Construction Project of Pudong Health Bureau of Shanghai (PWZxq2017-15 to XL) No conflicts of interest declared Preprint (not peer reviewed): medRxiv

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		

Liu 2020c *(Continued)*

Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Liu 2020d [A]

Study characteristics	
Patient Sampling	2-group study to estimate sensitivity and specificity in acute and convalescent phase sera 1. RT-PCR confirmed COVID-19 cases (n = 214) 2. Healthy blood donors (n = 100) Retrospective design; recruitment method NR. No further detail
Patient characteristics and setting	[1] Inpatients at General Hospital of the Central Theater Command of the People's Liberation Army (PLA), China (recruitment dates 18 January-26 February). Exposure history and participant characteristics not described [2] Healthy blood donors; not further described
Index tests	2 Ab tests, blinding NR; this entry (Liu 2020d [A]) refers to test [A] in the list below Laboratory-based evaluations of ELISA assays measuring IgM and IgG using serum samples: A. rN-based ELISA (Lizhu, Zhuhai, China), using recombinant N protein B. rS-based ELISA (Hotgen, Beijing, China), using receptor-binding domain of the recombinant S polypeptide (rS) Test thresholds: A. cut-off calculated by summing 0.100 (IgM) or 0.130 (IgG) and the average A450 of negative control replicates. When A450 < cut-off value, the test was considered negative, and when A450 was ≥ cut-off value, the test was considered positive. B. cut-off values (IgM and IgG) calculated by summing 0.250 and the average A450 of negative control replicates. When A450 < cut-off value, the test was considered negative, and when A450 was ≥ cut-off value, the test was considered positive. Samples acquired 0-5 d 22, 10%; 6-10 d 38, 18%; 11-15 d 54, 25%; 16-20 d 55, 26%; ≥ 21 d 45, 21% (32/45 are d 21-30). Person applying the test not described
Target condition and reference standard(s)	[1] RT-PCR (no further detail), using pharyngeal swabs samples. Positivity threshold NR. Samples acquired at a median of 15 d pso (range 0–55 days) 2. Healthy blood donors; no description of timing of serum sample collection
Flow and timing	Sampling for index and reference for cases was conducted within same time frame. No missing data, uninterpretable or indeterminate results described Basis for analysis: participants. Includes a single sample per participant with results disaggregated by time pso, but different participants contributed data to each time period.
Comparative	
Notes	Supported by the National Natural Science Foundation, the China Postdoctoral Science Foundation (2019M664008), and the Wuhan Young and Middle-aged Medical Backbone Talents Training Project (Wuweitong [2019] 87th266) Accepted manuscript (Journal of Clinical Microbiology) No conflicts of interest declared

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			

Liu 2020d [A] *(Continued)*

Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		

Liu 2020d [A] *(Continued)*

Did all patients receive the same reference standard?	No	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Were results presented per patient?	Yes	
Could the patient flow have introduced bias?		High risk

Liu 2020d [B]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Liu 2020d [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Liu 2020d [A])
Index tests	2 Ab tests, blinding NR; this entry (Liu 2020d [B]) refers to test [B] in the list below Laboratory-based evaluations of ELISA assays measuring IgM and IgG using serum samples A. rN-based ELISA (Lizhu, Zhuhai, China), using recombinant N protein B. rS-based ELISA (Hotgen, Beijing, China), using receptor-binding domain of the recombinant S polypeptide (rS) Test thresholds: A. cut-off calculated by summing 0.100 (IgM) or 0.130 (IgG) and the average A450 of negative control replicates. When A450 < cut-off value, the test was considered negative, and when A450 was ≥ cut-off value, the test was considered positive. B. cut-off values (IgM and IgG) calculated by summing 0.250 and the average A450 of negative control replicates. When A450 < cut-off value, the test was considered negative, and when A450 was ≥ cut-off value, the test was considered positive. Samples acquired 0-5 d 22, 10%; 6-10 d 38, 18%; 11-15 d 54, 25%; 16-20 d 55, 26%; ≥ 21 d 45, 21% (32/45 are d 21-30). Person applying the test not described
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Liu 2020d [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Liu 2020d [A])
Comparative	
Notes	

Long 2020 (A)

Study characteristics

Long 2020 (A) *(Continued)*

Patient Sampling	Single-group study to estimate sensitivity and specificity for detection of active or prior infection Cohort of close contacts (n = 164, 23 cases) of 2 index cases (diagnosis confirmed 4 February 2020; contacts between 20 January-6 February 2020 identified and PCR tested) Additional cohorts reported but not extracted included: a. follow-up cohort in RT-PCR-positive confirmed cases sampling every 3 days (n = 63 subset of cross-sectional study); does not provide accuracy data b. cohort of RT-PCR-negative suspects (n = 52); did not provide full accuracy data (specificity only could be extracted) c. extracted as Long 2020 (B)
Patient characteristics and setting	Close contacts identified by Chongqing CDC in Wanzhou (n = 164), China PCR testing conducted 31 January-9 February; serum samples collected 2 March 2020 13 (8%) symptomatic, 151 asymptomatic; no further details
Index tests	One Ab test, blinding NR Laboratory-based evaluated of magnetic CLIA kit (Bioscience (Chongqing) Co., Ltd), measuring IgM and IgG in serum samples, using recombinant antigen containing nucleoprotein and a peptide from S protein. Test threshold not described; presume interpretation according to manufacturer's instructions. Sample timing: 21-31 days after PCR test
Target condition and reference standard(s)	RT-PCR using nasal and pharyngeal swab specimens during hospital stay. No further detail. Theshold for positivity NR Timing of reference standard sampling: within 17-day period after contact with confirmed cases
Flow and timing	Time interval between index and reference: index 21-30 days after PCR test, potential for repeat exposure during this time. No missing data, uninterpretable or indeterminate results reported Participant-based analysis
Comparative	
Notes	Funded by Emergency Project from the Science & Technology Commission of Chongqing; The Major National S&T programme grant from Science & Technology Commission of China. No conflicts of interest reported; 1 author from BioScience Co. Ltd, Chongqing, China Preprint (not peer reviewed)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		

Long 2020 (A) *(Continued)*

Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	No		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Low risk	

Long 2020 (B)

Study characteristics	
Patient Sampling	Single-group study to estimate sensitivity for diagnosing acute phase infection RT-PCR-positive confirmed cases (n = 285). No further detail of inclusion or exclusion criteria. Additional cohorts reported but not extracted included: a. follow-up cohort in RT-PCR-positive confirmed cases sampling every 3 days (n = 63 subset of cross-sectional study); does not provide accuracy data b. cohort of RT-PCR-negative suspects (n = 52); did not provide full accuracy data (specificity only could be extracted) c. cohort of asymptomatic contacts of 2 confirmed cases extracted as Long 2020 (A)
Patient characteristics and setting	Inpatients at 3 hospitals, Chongqing Three Gorges Central Hospital (TGH) (n = 158), Yongchuan Hospital Affiliated to Chongqing Medical University (YCH) (n = 75), and The Public Health Center of Chongqing (PHCC), China (n = 52), recruited 5 February 2020 Median age 47 years (IQR 34-56 years); 55.4% male. 39/285 (14%) severe or critical in ICU. 103/285 (36%) patients had an history of exposure to transmission sources
Index tests	One Ab test, blinding NR Laboratory-based evaluated of magnetic CLIA kit (Bioscience (Chongqing) Co., Ltd), measuring IgM and IgG in serum samples, using recombinant antigen containing nucleoprotein and a peptide from S protein. Test threshold not described; presume interpretation according to manufacturer's instructions Sample timing: 67/363 (18%) day 2-7 from symptom onset; 149 (41%) day 8-13; and 147 (40%) day 14+
Target condition and reference standard(s)	RT-PCR using nasal and pharyngeal swab specimens during hospital stay. No further detail. Theshold for positivity NR Timing of reference standard sampling NR
Flow and timing	Time interval between index and reference NR. Data are disaggregated by time period but different participants contributed samples at each time pso Missing data: 23 participants with no information on time pso were excluded leaving 363 samples from 262 participants No uninterpretable or indeterminate results reported Basis for analysis: samples
Comparative	
Notes	Funded by Emergency Project from the Science & Technology Commission of Chongqing; The Major National S&T programme grant from Science & Technology Commission of China No conflicts of interest declared; 1 study author from BioScience Co. Ltd, Chongqing, China Preprint paper (not peer reviewed)

Methodological quality			
Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			

Long 2020 (B) *(Continued)*

Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		

Long 2020 (B) *(Continued)*

Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Were results presented per patient?	Yes
Could the patient flow have introduced bias?	High risk

Lou 2020 [A]

Study characteristics	
Patient Sampling	2-group study recruiting patients estimating sensitivity and specificity [1] n = 80 confirmed COVID cases [2] n = 300 healthy people enrolled from the community Recruitment: Prospective or retrospective recruitment of cases: Sample size (virus/COVID cases): 380 (80) Inclusion and exclusion criteria: willing to donate blood
Patient characteristics and setting	Setting: inpatient Location: First affiliated hospital of Zhejiang University Country: China Dates: 19 January-9 February 2020 Symptoms and severity: n = 26. Critical case = any one of a) ARDS or oxygen saturation < 93% and needing mechanical ventilation invasively or non-invasively; b) shock; c) complication of organ failure requiring ICU support N= 54 non-critical case (not meeting criteria a) or b) or c) above Sex: 38.7% female Age: 55 years (IQR 45-64) Exposure history: for 45/80: incubation period (defined as interval between earliest date of SARS-Cov-2 exposure (unambiguous close contact with confirmed COVID-19 case) and earliest date of symptom onset) range 0-23 days, median 5 (IQR 2–10)
Index tests	3 tests evaluated, this entry (Lou 2020 [A]) refers to test [A] Test name: [A] ELISA; [B] CGIA; [C] CLIA Manufacturer: NR Ab targets: Ab; IgM; IgG Antigens used: IgM and Ab: RBD of the SARS-CoV-2 S protein IgG: indirect immunoassays using recombinant nucleoprotein of SARS-CoV-2 Test method: ELISA, CLIA; LFIA Timing of samples: between 0 and 29 days pso Samples used: serum Test operators: NR Definition of test positivity: NR Blinded to reference standard: unclear Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: confirmed case should meet 3 criteria: 1) fever and/or respiratory symptoms; 2) abnormal lung imaging findings; and 3) positive result of the nucleic acid of SARS-CoV-2

Lou 2020 [A] *(Continued)*

	Samples used: deep sputum Timing of reference standard: on admission Blinded to index test: unclear Incorporated index test: unclear Reference standard for non-cases: NR
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: yes All participants received the same reference standard: unclear Missing data: [1] 36, 71 and 58/80 contributed to 0-7, 8-14 and 15-29 days pso estimates of sensitivity for tests [A], [B] and [C] only [2] Not all control group participants were tested by all index tests (range 100-300/300) Uninterpretable results: NR Indeterminate results: NR Unit of analysis: participant
Comparative	
Notes	Funding: China National Mega-Projects for Infectious Diseases and the Science and Technology Major Project of Xiamen Publication status: preprint Source:Pre print server (medRxiv) Study author COI: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		

Lou 2020 [A] *(Continued)*

Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Unclear		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Unclear		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Lou 2020 [B]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Lou 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Lou 2020 [A])

Lou 2020 [B] *(Continued)*

Index tests	3 tests evaluated, this entry (Lou 2020 [B]) refers to test [B] Test name: [A] ELISA; [B] CGIA; [C] CLIA Manufacturer: NR Ab targets: Ab; IgM; IgG Antigens used: IgM and Ab: RBD of the SARS-CoV-2 S protein IgG: indirect immunoassays using recombinant nucleoprotein of SARS-CoV-2 Test method: ELISA, CLIA; LFIA Timing of samples: between 0 and 29 days pso Samples used: serum Test operators: NR Definition of test positivity: NR Blinded to reference standard: unclear Threshold predefined: yes
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Lou 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Lou 2020 [A])
Comparative	
Notes	

Lou 2020 [C]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Lou 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Lou 2020 [A])
Index tests	3 tests evaluated, this entry (Lou 2020 [C]) refers to test [C] Test name: [A] ELISA; [B] CGIA; [C] CLIA Manufacturer: NR Ab targets: Ab; IgM; IgG Antigens used: IgM and Ab: RBD of the SARS-CoV-2 S protein IgG: indirect immunoassays using recombinant nucleoprotein of SARS-CoV-2 Test method: ELISA, CLIA; LFIA Timing of samples: between 0 and 29 days pso Samples used: serum Test operators: NR Definition of test positivity: NR Blinded to reference standard: unclear Threshold predefined: yes
Target condition and ref-	See main entry for this study for characteristics and QUADAS-2 assessment (Lou 2020 [A])

Lou 2020 [C] *(Continued)*

erence standard(s)	
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Lou 2020 [A])
Comparative	
Notes	

Ma 2020a

Study characteristics	
Patient Sampling	4-group study recruiting patients estimating sensitivity and specificity [1] n = 87 confirmed COVID-19 (216 samples) [2] n = 330 healthy donors pre-October 2019 [3] n = 138 'other diseases' (no mention of PCR) [4] n = 15 suspected COVID pneumonia but negative PCR Recruitment: cases admitted between 26 January-5 March 2020 Prospective or retrospective recruitment of cases: retrospective Sample size (virus/COVID cases): 570 (87) Inclusion and exclusion criteria: NR
Patient characteristics and setting	Setting: inpatient Location: First Affiliated Hospital of USTC Hospital and the First Affiliated Hospital of Anhui Medical University Country: China Dates: 26 January-5 March 2020 Symptoms and severity: 56/87 clinically moderate, 17 severe, 5 critical, "few mild" Sex: NR Age: NR Exposure history: NR
Index tests	Test name: CLIA RBD Manufacturer: in-house Ab targets: IgM;IgG;IgA Antigens used: SARS CoV-2 RBD protein (S-based) Test method: CLIA Timing of samples: during 'routine inpatient testing' Samples used: serum Test operators: NR Definition of test positivity: NR Blinded to reference standard: unclear Threshold predefined: no
Target condition and reference standard(s)	Reference standard for cases: New Coronavirus Pneumonia Prevention and Control Program (7th edition) published by the National Health Commission of China, RT-qPCR was used to confirm COVID-19 (all cases were RT-PCR-positive) Samples used: serum Timing of reference standard: during 'routine inpatient testing' Blinded to index test: unclear Incorporated index test: no Reference standard for non-cases: [2] Pre-pandemic [3] NR [4] NR

Ma 2020a *(Continued)*

Flow and timing	Time interval between index and reference tests: NR Results presented by time period: yes All participants received the same reference standard: no Missing data: for comparison of sensitivity and specificity of 2 antigens only 20/total of 479 control sera were used (20/138 from 'other disease' group Uninterpretable results: NR Indeterminate results: NR Unit of analysis: samples
Comparative	
Notes	Funding: T.J. is supported by the Strategic Priority Research Program of the Chinese Academy of Sciences (XDB29030104), National Natural Science Fund (Grant No.: 31870731 and U1732109), the Fundamental Research Funds for the Central Universities (WK2070000108). TJ and XLM is supported by a COVID-19 special task grant supported by Chinese Academy of Science Clinical Research Hospital (Hefei) with Grant No. YD2070002017 and YD2070002001, respectively. M.H. is supported by the new medical science fund of USTC (WK2070000130). Publication status: preprint Source: preprint server: medRxiv Study author COI: 3 study authors are employees of Kangrun Biotech LTD (Guangzhou, 308 China). 4 study authors have jointly applied for a patent related to the Ab detecting kits.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		

Ma 2020a *(Continued)*

Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Yes		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	No		
Could the patient flow have introduced bias?		High risk	

Okba 2020a

Study characteristics	
Patient Sampling	2-group design estimating sensitivity and specificity in acute disease [1] SARS-CoV-2 cases confirmed by RT-PCR (n = 9, 31 samples) [2] Healthy blood donors (n = 45) date NR Recruitment method and exclusion criteria NR Third group of RT-PCR confirmed cases from France (n = 3, 10 samples excluded by review author team)

Okba 2020a *(Continued)*

Patient characteristics and setting	[1] Inpatient (plus initial testing prior to admission) at hospital in Munich, Germany. Cases are epidemiologically linked, identified through exposure to known cases, and occurred after 23 January 2020, discovered on 27 January (Woelfel 2020). Symptoms and severity, and demographics NR [2] Sanquin Blood Bank, Netherlands, date not specified
Index tests	Beta version of commercial EuroImmun IgA and IgG ELISA Ab test, from EUROIMMUN Medizinische Labordiagnostika AG. Targets IgA and IgG. Threshold not pre-defined: in-house threshold of mean background reactivity of all SARS-CoV-2–negative serum samples in the study multiplied by 3. Blinding NR
Target condition and reference standard(s)	[1] All positive on RT-PCR between days 1-5 of symptom onset, using OP or NP swab. Blind to index test [2] Blood bank samples, reported as negative but date of sampling NR
Flow and timing	Different reference standard for cases and controls, and cases were from 2 separate cohorts. Limited details available for each cohort. Results available by case, but only in graph format Indeterminate or unclear index results on graphs considered negative by review team
Comparative	
Notes	No information provided on study author conflicts. Published as early release (not final). Report the following funding "Zoonoses Anticipation and Preparedness Initiative (project Innovative Medicines Initiative grant no. 115760), the Innovative Medicines Initiative; the European Commission, and partners of the European Federation of Pharmaceutical Industries and Associations"

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			

Okba 2020a *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	No		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Padoan 2020

Study characteristics	
Patient Sampling	1-group study recruiting patients estimating sensitivity [1] Hospitalised patients with confirmed COVID-19 Recruitment: cases with residual serum samples collected between 18 March-26 March 2020 Prospective or retrospective recruitment of cases: retrospective Sample size (virus/COVID cases): 37 (37) Inclusion and exclusion criteria:

Padoan 2020 *(Continued)*

Patient characteristics and setting	Setting: inpatient Location: University Hospital of Padova Country: Italy Dates: 18 March-26 March 2020 Symptoms and severity: NR Sex: NR Age: NR Exposure history: NR
Index tests	Test name: MAGLUMI 2000 Plus nCoV IgM and IgG Manufacturer: New Industries Biomedical Engineering Co., Ltd [Snibe], Shenzhen, China Ab targets: IgM; IgG Antigens used: NR Test method: CLIA Timing of samples: days since symptom onset: ≤ 5 days 4/37 (11%) 6-7 days 6/37 (16%) 0-7 days: 10/37 (27%) 8-9 days 12/37 (32%) 10-11 days 14/37 (38%) 12-13 days 9/37 (24%) 8-13 days: 35/37 (95%) > 13 days 25/37 (68%) Samples used: serum Test operators: NR Definition of test positivity: [A] IgM 1.0 AU/mL [B] IgG 1.1 AU/mL Blinded to reference standard: no Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: PCR Samples used: NP Timing of reference standard: NR Blinded to index test: yes Incorporated index test: no Reference standard for non-cases: N/A
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: yes All participants received the same reference standard: yes Missing data: text describes 87 samples from 37 participants but only 70 samples reported per time period and no per participant data are reported Uninterpretable results: NR Indeterminate results: NR Unit of analysis: sample
Comparative	
Notes	Funding: none declared Publication status: published Source: academic journal Study author COI: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns

Padoan 2020 *(Continued)*

DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	No		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		

Padoan 2020 *(Continued)*

Did all participants receive a reference standard?	Yes
Were results presented per patient?	No
Could the patient flow have introduced bias?	High risk

Pan 2020a

Study characteristics	
Patient Sampling	Single group of cases to estimate sensitivity in acute disease SARS-CoV-2-positive cases (n = 105, 134 samples) of which 67 cases (86 samples) confirmed by RT-PCR, and 37 patients (39 samples) clinically diagnosed (RT-PCR-negative, radiography-positive) Recruitment method NR Exclusion criteria NR
Patient characteristics and setting	Inpatients in Zhongnan hospital (Wuhan University, China). Testing 6 February-23 February 2020, symptom onset 7 January-18 February 2020 (for subgroup of 108) 48 male, 57 female, median age 58 years (range 20-96). Symptoms and severity and exposure status NR
Index tests	Commercial Ab test LFA (conducted in laboratory setting). Colloidal gold-based immunochromatographic strip assay (Zhuhai Livzon Diagnositic Inc) to detect IgM, IgG. Antigen used NR (as per manufacturer) Presence of T line indicating positive Serum or plasma samples used (includes comparison with whole blood for subgroup; not extracted). No information on timing or who read the test results.
Target condition and reference standard(s)	1. RT-PCR following WHO guidelines for qRT-PCR, using throat swabs (Chinese CDC recommended kit used, BioGerm, Shanghai, China) 2. clinically diagnosed as SARS-CoV-2 infection according to the 5th edition of guideline on diagnosis and treatment of the novel coronavirus pneumonia. Specifically, the clinical diagnosis means the suspected cases were negative to the real-time RT-PCR test but presented viral pneumonia by radiography Samples taken during inpatient stay but no details about timing or personnel for test interpretation
Flow and timing	All participants received a reference standard, but there was differential verification with some patients confirmed by RT-PCR and others RT-PCR-negative but confirmed by radiography. Subset who were RT-PCR-positive are reported separately. Timing of index tests and reference standard unclear. Data reported only for those with symptom onset information; 26 samples excluded. No reporting of test failures or indeterminate results. Per-sample analysis; multiple samples (2 or 3) per participant disaggregated over time
Comparative	
Notes	Funding from the National Key Research and Development Program of China (2018YFE0204500) Declared no conflict of interest Published in the Journal of Infection

Pan 2020a *(Continued)*

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern

Pan 2020a *(Continued)*

DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Were results presented per patient?	Yes
Could the patient flow have introduced bias?	Unclear risk

Paradiso 2020a

Study characteristics	
Patient Sampling	Single-group study to estimate sensitivity and specificity for diagnosing SARS-Cov-2 [1] Cohort of patients attending A&E with COVID-19-like symptoms Recruitment: consecutive Sample size (virus/COVID cases): 191 (70) Inclusion and exclusion criteria: no further details
Patient characteristics and setting	Setting: A&E Location: Ospedale Policlinico Consorziale of Bari Country: Italy Dates: 23-29 March 2020 Symptoms and severity: 14/160 (9%) asymptomatic; symptoms not available for 31/191 Sex: 116, 60.6% male Age: median 58.5 years Exposure history: NR
Index tests	Test name: VivaDiag Manufacturer: Jiangsu Medomics Medical Technologies Ab targets: IgM, IgG Antigens used: surface antigen from SARSCoV-2 POC or laboratory: POC Test method: LFA (CGIA) Timing of samples: on presentation; time from symptom onset varied from asymptomatic 14, 9%; d 0-5 97, 61%; d 6-8 17, 11%; d 9-10 21, 13%; d 11-15 5, 3%, > 15 d 6, 5%; NR 31, 19%) Samples used: venous blood Test operators: 2 operators in the laboratory (operators obtained images of the device and disagreements evaluated by a third party) Definition of test positivity: presence of red/purple line in the specific region indicated on the device Blinded to reference standard: yes Threshold predefined: as per manufacturer

Paradiso 2020a *(Continued)*

Target condition and reference standard(s)	Reference standard for cases including threshold: RT-PCR (Allplex2019-nCoV Assay; Seegene, Seoul, Republic of Korea); target genes E gene, RdRP gene and N gene; threshold NR Single PCR-negative for D- presumed (NR) Samples used: NP/OP swabs Timing of reference standard: obtained simultaneously with blood samples (on presentation) Blinded to index test: yes Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous testing All participants received the same reference standard: yes Missing data: 1 participant missing from 2x2 table with no explanation although all participants had the reference standard and index test. No data on time pso for 31/191 Uninterpretable results: none stated Indeterminate results: none stated Unit of analysis: participant. A considerable range in time pso was reported however, and results were not disaggregated by time pso.
Comparative	
Notes	Funding: none stated Publication status: preprint (not peer reviewed) Source: medRxiv Study author COI: none stated

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		

Paradiso 2020a *(Continued)*

If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Qian 2020

Study characteristics	
Patient Sampling	4-group study recruiting patients estimating sensitivity and specificity [1] Confirmed COVID-19 cases (RT-PCR-positive) (n = 503) and [2] suspected COVID-19 cases based on epidemiological history, clinical symptoms and chest X-ray but 3 x PCR-negative (n = 52) Apparently contemporaneous controls, including:

Qian 2020 *(Continued)*

	[3] hospitalised with non-COVID-19 conditions (PCR testing not described) (n = 972) [4] healthy controls (n = 586) Recruitment: unclear Prospective or retrospective recruitment of cases: prospective Sample size (virus/COVID cases): 2113 (555) Inclusion and exclusion criteria: NR
Patient characteristics and setting	Setting: hospital inpatients (cases) Location: 10 hospitals Country: China Dates: unclear Symptoms and severity: NR Sex: NR Age: NR Exposure history: NR
Index tests	Test name: NR Manufacturer: in-house Ab targets: IgG, IgM Antigens used: recombinant antigen from viral N protein and S protein Test method: CLIA Timing of samples: NR Samples used: serum Test operators: unclear Definition of test positivity: ≥ 10 AU/mL Blinded to reference standard: unclear Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: RT-PCR for confirmed cases; suspected cases according to National Health Commission guideline (version 5) Samples used: unclear Timing of reference standard: during hospitalisation Blinded to index test: yes Incorporated index test: no Reference standard for non-cases: unclear
Flow and timing	Time interval between index and reference tests: unclear Results presented by time period: no All participants received the same reference standard: unclear Missing data: NR Uninterpretable results: NR Indeterminate results: NR Unit of analysis: participant
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Qian 2020 *(Continued)*

Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Yes		
Did all participants receive a reference standard?	Unclear		

Qian 2020 *(Continued)*

Were results presented per patient?	Yes
Could the patient flow have introduced bias?	High risk

To 2020a [A]

Study characteristics	
Patient Sampling	Single-group study recruiting patients estimating sensitivity and specificity [1] Confirmed COVID-19 patients from 2 hospitals (n = 23) Recruitment: consecutive cases between 22 January-12 February, but excluding people with insufficient stored material Prospective or retrospective recruitment of cases: retrospective Sample size (virus/COVID cases): 108 serum samples from 23 participants (23 cases). Only extractable > 14-day subset of 16 cases Inclusion and exclusion criteria: confirmed cases
Patient characteristics and setting	Setting: hospital inpatients Location: Princess Margaret Hospital and Queen Mary Hospital, Hong Kong Country: Hong Kong, China Dates: 22 January-12 February Symptoms and severity: 10/23 (43%) severe Sex: 13/23 (57%) male Age: median 62 years (range 37-75) Exposure history: NR
Index tests	2 tests evaluated, this entry (To 2020a [A]) refers to test [A] Test name: EIAs for [A] SARS-CoV-2 nucleoprotein and [B] S protein RBD Manufacturer: in-house Ab targets: IgG IgM Antigens used: [A] nucleoprotein and [B] S protein RBD Test method: EIA (considered with ELISA tests for analysis purposes) Timing of samples: 3-30 days pso Samples used: serum remnant from blood samples Test operators: NR Definition of test positivity: mean of 93 archived serum samples plus 3 x SD Blinded to reference standard: NR Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: laboratory confirmed - exact test unclear Samples used: NP or sputum specimens Timing of reference standard: NR Blinded to index test: yes Incorporated index test: no Reference standard for non-cases: n/a
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: no, not extractable All participants received the same reference standard: yes Missing data: 7/23 (30%) were not tested between days 14 and 30 Uninterpretable results: NR Indeterminate results: NR Unit of analysis: unclear

To 2020a [A] *(Continued)*

Comparative	
Notes	Funding: this study was partly supported by the Consultancy Service for Enhancing Laboratory Surveillance of Emerging Infectious Diseases and Research Capability on Antimicrobial Resistance for the Department of Health of Hong Kong; the Theme-Based Research Scheme (T11/707/15) of the Research Grants Council, Hong Kong Special Administrative Region; Sanming Project of Medicine in Shenzhen, China (SZSM201911014); the High Level-Hospital Program, Health Commission of Guangdong Province, China; and donations from the Shaw Foundation Hong Kong, Richard Yu and Carol Yu, May Tam Mak Mei Yin, Michael Seak-Kan Tong, Respiratory Viral Research Foundation, Hui Ming, Hui Hoy and Chow Sin Lan Charity Fund Limited, Chan Yin Chuen Memorial Charitable Foundation, Marina Man-Wai Lee, and the Hong Kong Hainan Commercial Association South China Microbiology Research Fund Publication status: published paper Source: Lancet Infectious Diseases Study author COI: declare they have none

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	No		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High

To 2020a [A] *(Continued)*

DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Unclear		
Could the patient flow have introduced bias?		High risk	

To 2020a [B]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (To 2020a [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (To 2020a [A])
Index tests	2 tests evaluated, this entry (To 2020a [B]) refers to test [B] Test name: EIAs for [A] SARS-CoV-2 nucleoprotein and [B] S protein RBD Manufacturer: in-house Ab targets: IgG IgM Antigens used: [A] nucleoprotein and [B] S protein RBD Test method: EIA (considered with ELISA tests for analysis purposes)

To 2020a [B] *(Continued)*

	Timing of samples: 3-30 days pso Samples used: serum remnant from blood samples Test operators: NR Definition of test positivity: mean of 93 archived serum samples plus 3 x SD Blinded to reference standard: NR Threshold predefined: yes
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (To 2020a [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (To 2020a [A])
Comparative	
Notes	

Wan 2020 [A]

Study characteristics	
Patient Sampling	2-group design estimating sensitivity and specificity in acute disease [1] SARS-Cov-2-positive cases confirmed by RT-PCR (n = 7, 26 samples) [2] prepandemic sera (n = 5) and controls SARS-Cov-2 negative on 2 occasions (n = 5) Recruitment method NR Exclusion criteria NR
Patient characteristics and setting	[1] Inpatients at Singapore General Hospital, Singapore. Recruitment dates NR. Symptoms and severity, demographics and exposure history NR [2] Archived controls (n = 5) from Singapore General Hospital from 2015; recent patients with pneumonia investigated for COVID-19 but RT-PCR-negative twice and not meeting the criteria for suspected SARS-Cov-2 (n = 5)
Index tests	2 Ab tests used on serology samples, this entry (Wan 2020 [A]) refers to test [A] [A] in-house SARS-CoV total Ab ELISA laboratory assay (not a SARS-CoV-2-specific test). Measured total Ab; antigens NR. Positive defined as ≥ 400 [B] anti-SARS CoV IIFT laboratory assay from Euroimmun (Germany) (not a SARS-CoV-2-specific test). Measured IgM and IgG; antigens NR. Threshold NR Samples anonymised and blinded
Target condition and reference standard(s)	[1] Confirmed COVID-19 determined by RT-PCR; samples and methods NR. Tests undertaken during inpatient stay; blind to the index test [2] Confirmed not COVID-19 by chronology in n = 5, and by 2 repeated RT-PCR-negative results and not fulfilling criteria for suspected COVID-19 in n = 5; samples and methods NR. Tests undertaken during inpatient stay; blind to the index test
Flow and timing	All participants received a reference standard, but different reference standards were used in [1] and [2]. Multiple samples were included per participant; however these were disaggregated by time pso. Timing of reference standard and index tests NR

Wan 2020 [A] *(Continued)*

	Uninterpretable results not mentioned; 1/10 samples in group [2] indeterminate due to non-specific fluorescence. 5/26 samples in group [1] excluded due to narrow interval between tests or close proximity to the date of onset of illness. In group [1] between 1 and 9 samples per participant (mean = 3.7). Results for all samples per participant are presented allowing participant- and sample-based analyses.
Comparative	
Notes	No funding declared No conflicts of interest noted Report from a medRxiv preprint (not peer reviewed)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		

Wan 2020 [A] *(Continued)*

Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Wan 2020 [B]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Wan 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Wan 2020 [A])
Index tests	2 Ab tests used on serology samples, this entry (Wan 2020 [B]) refers to test [B] [A) in-house SARS-CoV total Ab ELISA laboratory assay (not a SARS-CoV-2-specific test). Measured total Ab; antigens NR. Positive defined as ≥ 400 [B] anti-SARS CoV IIFT laboratory assay from Euroimmun (Germany) (not a SARS-CoV-2 specific test). Measured IgM and IgG; antigens NR. Threshold NR Samples anonymised and blinded
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Wan 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Wan 2020 [A])

Wan 2020 [B] *(Continued)*

Comparative	
Notes	

Wang 2020a [A]

Study characteristics	
Patient Sampling	Purpose: diagnosis of active infection Design: 2-group study to estimate sensitivity and specificity for diagnosis of acute infection [1] COVID-19 patients, meeting diagnostic criteria a to Chinese Government guidelines (fifth edition) (n = 14) [2] Sera from patients with different pathogen infections and related chronic diseases with no clinical symptoms or imaging evidence of COVID-19 (n = 72), (with deliberate selection of rheumatoid factor IgM-positive sera) Recruitment: NR Sample size (virus/COVID cases): 86 (14) Inclusion and exclusion criteria: not described
Patient characteristics and setting	Setting: inpatient Location: affiliated Hospital of North Sichu, Chinaan Medical College and Nanchong Central Hospital Country: China Dates: 25 January -15 February 2020 Symptoms and severity: NR Demographics: NR Exposure history: NR Non-COVID patients group: other infection/chronic disease controls Source and time: 25 January-15 February 2020 Characteristics: IgM-positive sera from patients with different pathogen infections and related chronic diseases with no clinical symptoms or imaging evidence of COVID-19 (n = 72); flu A (n = 5), flu B (n = 5), *Mycoplasma pneumoniae* (n = 5), *Legionella pneumophila* (n = 5), positive rheumatoid factor (n = 36), HIV infection (n = 6), hypertension (n = 5) and diabetes mellitus (n = 5)
Index tests	2 tests evaluated, this entry (Wang 2020a [A]) refers to test [A] A. SARS-CoV-2 IgM detection kit CGIA (Beijing Hotgen Biotechnology Co., Beijing, China) (POC test, evaluation appears to be laboratory-based) B. ELISA (Beijing Hotgen Biotechnology Co., Beijing, China) (laboratory test) Ab targets: IgM Antigens used: NR Timing of samples: within 3-7 days after the beginning of the clinical symptoms for COVID-19 cases Samples used: serum Test operators: NR Definition of test positivity: A. as per manufacturer, colloidal gold colour reaction occurs at both T-line and C-line positions B. not described Blinded to reference standard: NR Threshold predefined: yes, as per manufacturer

Wang 2020a [A] *(Continued)*

Target condition and reference standard(s)	Reference standard for cases including threshold: diagnostic criteria from "Notice on the Issuance of Strategic Guidelines for Diagnosis and Treatment of Novel Coronavirus (SARS-CoV-2) Infected Pneumonia (Fifth Edition Version) Samples used: NR/ N/A Timing of reference standard: during hospital stay Blinded to index test: NR Incorporated index test: no Reference standard for controls: no clinical symptoms or imaging evidence of COVID-19 Samples used: NR Timing of reference standard: NR Blinded to index test: NR Incorporated index test: no
Flow and timing	Time interval between index and reference tests: NR, but all serology samples acquired within first week pso All participants received the same reference standard: yes Missing data: none stated Uninterpretable results: none stated Indeterminate results: none stated Unit of analysis: participant
Comparative	
Notes	Funding: none declared Publication status: accepted manuscript Source: Journal of Clinical Microbiology Study author COI: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			

Wang 2020a [A] *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Wang 2020a [B]

Study characteristics

Wang 2020a [B] *(Continued)*

Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Wang 2020a [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Wang 2020a [A])
Index tests	2 tests evaluated, this entry(Wang 2020a [B]) refers to test [B] A. SARS-CoV-2 IgM detection kit CGIA (Beijing Hotgen Biotechnology Co., Beijing, China) (POC test, evaluation appears to be laboratory-based) B. ELISA (Beijing Hotgen Biotechnology Co., Beijing, China) (laboratory test) Ab targets: IgM Antigens used: NR Timing of samples: within 3-7 days after the beginning of the clinical symptoms for COVID-19 cases Samples used: serum Test operators: NR Definition of test positivity: A. as per manufacturer, colloidal gold colour reaction occurs at both T-line and C-line positions B. not described Blinded to reference standard: NR Threshold predefined: yes, as per manufacturer
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Wang 2020a [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Wang 2020a [A])
Comparative	
Notes	

Xiang 2020a [A]

Study characteristics	
Patient Sampling	2-group design estimating sensitivity and specificity in acute disease [1] SARS-Cov-2 diagnosed patients (n = 63 for ELISA, n = 91 for GICA, some overlap of cases) [2] Healthy individuals (n = 35) Group [1] were recruited as a consecutive series and were inpatients with confirmed COVID-19 diagnosed according to WHO interim guidance
Patient characteristics and setting	[1] Inpatients at Wuhan Jinyintan Hospital, China, admitted 1-28 January 2020. Samples taken 2-4 February 2020. For ELISA 4/63 (6%) and GICA 4/91 (4%) classified as severe; 35/63 (56%) and 49/91 (54%) male. Median (IQR) age 65 (55-74) (n = 63) and 61 (48.5-67) years. Exposure NR [2] Healthy controls (n = 35). 17/35 (49%) male. Median (IQR) age 44 (39-49.5) years. No other detail given
Index tests	2 tests evaluated, this entry (Xiang 2020a [A]) refers to test [A]

Xiang 2020a [A] *(Continued)*

	[A] novel coronavirus IgG/IgM Ab ELISA kits (laboratory kit manufactured by Zhu Hai Livzon Diagnostics). Measured IgM and IgG; antigen reported as "Enzyme-labelled antibody-linked antigen" for IgM and "recombinant antigen of new coronavirus" for IgG. Threshold NR [B] novel coronavirus IgG/IgM Ab GICA kits (POC test strips manufactured by Zhu Hai Livzon Diagnostics). Measured IgM and IgG; antigens NR. Threshold based on observing a coloured band turning red. A subset of participants who provided throat swab samples were also re-tested with a qRT-PCR test. Discussion states "that the new type of coronavirus antibody of the kit (doesn't specify which kit though) is against the severe acute respiratory syndrome (SARS)-like coronavirus, not only against SARS-CoV-2"
Target condition and reference standard(s)	[1] Confirmed COVID-19 determined according to WHO interim guidance; tests, samples and methods NR. Diagnosis made during inpatient stay; prior to the index test [2] No description given
Flow and timing	Unclear which participants received a reference standard, and the form of the reference standard Timing of reference standard and index tests NR Uninterpretable, indeterminate and missing results not mentioned One sample tested by each test per participant, unstated overlap of participants
Comparative	
Notes	Supported by the Zhongnan Hospital of Wuhan University Science, Technology and Innovation Seed Fund. No conflicts of interest noted. Report from a medRxiv preprint (not peer reviewed)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	No		

Xiang 2020a [A] *(Continued)*

If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Xiang 2020a [B]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Xiang 2020a [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Xiang 2020a [A])

Xiang 2020a [B] *(Continued)*

Index tests	2 tests evaluated, this entry (Xiang 2020a [B] refers to test [B] [A] novel coronavirus IgG/IgM Ab ELISA kits (laboratory kit manufactured by Zhu Hai Livzon Diagnostics) Measured IgM and IgG; antigen reported as "Enzyme-labelled antibody-linked antigen" for IgM and "recombinant antigen of new coronavirus" for IgG. Threshold NR [B] novel coronavirus IgG/IgM Ab GICA kits (POC test strips manufactured by Zhu Hai Livzon Diagnostics) Measured IgM and IgG; antigens NR. Threshold based on observing a coloured band turning red. A subset of participants who provided throat swab samples were also re-tested with a qRT-PCR test. Discussion states "that the new type of coronavirus antibody of the kit (doesn't specify which kit though) is against the severe acute respiratory syndrome (SARS)-like coronavirus, not only against SARS-CoV-2"
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Xiang 2020a [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Xiang 2020a [A])
Comparative	
Notes	

Xiang 2020b

Study characteristics	
Patient Sampling	2-group study recruiting patients estimating sensitivity and specificity PCR conducted for patients presenting with a history of travel to or residence in Wuhan or local endemic areas; contact history with confirmed or suspected COVID-19 patients or part of a clustering outbreak, combined with clinical manifestation of 1) fever and/or respiratory symptoms, or 2) positive findings similar to COVID-19 pneumonia on chest CT scan, or 3) laboratory tests showing reduced lymphocytes and white blood cell counts in the early stage. Resulted in inclusion of [1] 85 RT-PCR-confirmed cases [2] 24 suspected cases with ≥ 2 negative RT-PCR and none positive (and protocol is to retest RT-PCR negatives every 1-2 days) [3] 60 control group of healthy blood donors (hospital staff) or from patients with other lung diseases in the same hospital (all PCR-negative) Recruitment: NR Prospective or retrospective recruitment of cases: unclear Sample size (virus/COVID cases): 169 (109; data for 66 lab-confirmed and 24 suspected cases extracted as D+ group) Inclusion and exclusion criteria: unclear
Patient characteristics and setting	Setting: hospital inpatients Location: Wuhan Country: China Dates: 19 January-2 March 2020 Symptoms and severity: [1] severe 18/85 (21%) [2] 2/24 (8%) severe Sex: [1] female 54/85 (64%) [2] female 12/24 (50%) [3] 35/60 (58%) female Age: [1] median 51 (IQR 32-65) [2] median 44 (IQR 36-61) [3] median 34 (IQR 29-51) Exposure history: NR
Index tests	Test name: ELISA Livzon Manufacturer: ELISA kits, Livzon Inc, Zhuhai, P.R.China, lot number of IgM: 20200308, IgG: 20200308

Xiang 2020b *(Continued)*

	Ab targets: IgG IgM Antigens used: N protein? Test method: ELISA Timing of samples: NR Samples used: serum Test operators: NR Definition of test positivity: unclear "The optical density of each well was determined by a microplate reader set to 450 nm within 30 min. The ratio of optical density to the cut off value (optical density of the blank well + 0.1) was reported as the Ab concentration. For detection of IgG, the dilution factor was changed (1:20) and the cut off value was modified (optical density of the blank well + 0.13)." Blinded to reference standard: no Threshold predefined: unclear
Target condition and reference standard(s)	Reference standard for cases: [1] RT-PCR [2] Symptoms and PCR-negative (no guideline cited but criteria clearly elaborated) Samples used: NP and/or OP swabs Timing of reference standard: NR Blinded to index test: yes Incorporated index test: no Reference standard for non-cases: (no exposure or symptoms) and RT-PCR-negative
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: no All participants received the same reference standard: Missing data: data per sample are provided for the 85 confirmed cases, however per participant data are available only for 66/85 confirmed cases plus 24/24 suspected cases (total number of cases reported = 90) Uninterpretable results: NR Indeterminate results: NR Unit of analysis: reports both samples and participants
Comparative	
Notes	Funding: this work is funded by National Natural Science Foundation of China (No. 81973990, 91643101), and Science Foundation of Huazhong University of Science and Technology (No. 2020kfyXGYJ100) Publication status: published in journal Source:Infectious Disease Society of America Study author COI: declare that they have none

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		

Xiang 2020b *(Continued)*

Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	No		
If a threshold was used, was it prespecified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		

Xiang 2020b *(Continued)*

Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Were results presented per patient?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Xiao 2020a

Study characteristics	
Patient Sampling	Single-group study to estimate sensitivity for diagnosing active or prior infection Confirmed cases of COVID-19 (n = 34) according to the diagnosis and treatment guideline for SARS-CoV-2 from Chinese National Health Committee (Version 5) and the interim guidance from Centers for Disease Control and Prevention Recruitment method not clearly reported, likely convenience sample
Patient characteristics and setting	Inpatients, presumably at study authors' institution (Tongji Hospital) Wuhan, China. Admission date: 1-29 February 2020; final follow-up date 3 March 2020 NR Exposure history Sex: 12 female, 22 male Median age (review team estimated) 49 years (range 26-87), 22 (65%) male. Exposure history not described
Index tests	1 Ab test, blinding NR Laboratory-based CLIA (Shenzhen Yahuilong Biotechnology Co. Ltd.) measuring IgM and IgG. Antigen used not described. Threshold ≤ 10 AU/mL (describes following manufacturer protocol, but unclear if this includes threshold setting) Blood samples acquired ≥ 2 weeks after symptoms onset for 32/34 participants; and on day 2 and day 3 for remaining 2 participants
Target condition and reference standard(s)	COVID-19 according to diagnosis and treatment guideline for SARS-CoV-2 from Chinese National Health Committee (Version 5) and the interim guidance from Centers for Disease Control and Prevention; no further detail Timing and blinding to index test not described
Flow and timing	Time interval between index and reference not described. Study provides a breakdown in results by time pso but is different participants in each time period rather than multiple samplings for same participants No missing data, uninterpretable or indeterminate results described
Comparative	
Notes	No funding sources declared No conflicts of interest declared Pre-proof paper accepted for publication (Journal of Infection)

Xiao 2020a *(Continued)*

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			

Xiao 2020a *(Continued)*

Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Unclear	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Were results presented per patient?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Xie 2020a

Study characteristics	
Patient Sampling	Single-group study recruiting patients estimating sensitivity to detect active disease [1] 16 confirmed COVID-19 using RT-PCR [2] 40 suspected cases using Chinese criteria but PCR-negative Recruitment: upon admission between 15-25 February 2020, unclear if consecutive Prospective or retrospective recruitment of cases: prospective Sample size (virus/COVID cases): 56 (56) of which 16 confirmed by RT-PCR Inclusion and exclusion criteria: unclear
Patient characteristics and setting	Setting: hospital inpatient Location: Unit Z6 at the Cancer Center of Wuhan Union Hospital Country: China Dates: enrolled 15-25 February 2020 Symptoms and severity: 34 severe, 22 not severe (more details on data extraction) Sex: 32/56 (57% female) Age: median age was 56.5 years (IQR 49.25-64.75) Exposure history: NR
Index tests	Test name: CLIA Manufacturer: YHLO Biological Technology Co., Ltd., Shenzhen, China Ab targets: IgG IgM Antigens used: envelope (E) protein and N protein Test method: CLIA Timing of samples: upon admission to hospital (with questionnaire to determine how many days prior to this symptom onset) Samples used: serum Test operators: NR Definition of test positivity: ≥ 10 AU/mL Blinded to reference standard: yes (upon admission) Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: [1] RT-PCR QIAamp RNA virus kit (Qiagen, Heiden, Germany), 1ab (ORF1ab) and N protein [2] diagnosed according to the 5th edition of the Guideline on diagnosis and treatment of COVID-19 established by China's National Health Commission, in-

Xie 2020a *(Continued)*

	cluding patient's epidemic history, clinical characteristics, chest CT scan and laboratory findings - RT-PCR-negative Samples used: NP and throat swabs Timing of reference standard: NR Blinded to index test: NR Incorporated index test: no Reference standard for non-cases: N/A
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: no All participants received the same reference standard: yes Missing data: NR Uninterpretable results: NR Indeterminate results: NR Unit of analysis: participant
Comparative	
Notes	Funding: this work was funded by the Special Project for Emergency Scientific and Technological Research on New Coronavirus Infection

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern

Xie 2020a *(Continued)*

DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Xu 2020a

Study characteristics	
Patient Sampling	Single-group study recruiting patients estimating sensitivity [1] confirmed COVID-19 cases Recruitment: unclear Prospective or retrospective recruitment of cases: retrospective Sample size (virus/COVID cases): 10 (10) patients Inclusion and exclusion criteria: unclear
Patient characteristics and setting	Setting: hospital inpatients Location: Affiliated hospitals of Shanghai University of Medicine & Health Sciences Country: China Dates: NR Symptoms and severity: 2/10 died, 10/10 required oxygen Sex: 6/10 (60%) male Age: NR Exposure history: NR

Xu 2020a *(Continued)*

Index tests	Test name: COVID-19 IgG and IgM LFA Manufacturer: in-house Ab targets: IgG and IgM Antigens used: recombinant antigen (R18850) Test method: NR, lateral flow type Timing of samples: day 15-30 of observation Samples used: NR Test operators: NR Definition of test positivity: NR Blinded to reference standard: NR Threshold predefined: NR
Target condition and reference standard(s)	Reference standard for cases: RT-PCR Samples used: NR Timing of reference standard: NR Blinded to index test: NR Incorporated index test: no Reference standard for non-cases: N/A
Flow and timing	Time interval between index and reference tests: unclear Results presented by time period: no All participants received the same reference standard: yes Missing data: NR Uninterpretable results: NR Indeterminate results: NR Unit of analysis: participant
Comparative	
Notes	Funding: NR Publication status: preprint Source: medRxiv Study author COI: NR

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			

Xu 2020a *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Yongchen 2020

Study characteristics	
Patient Sampling	1-group study recruiting patients estimating sensitivity [1] 11 non-severe COVID-19 patients [2] 5 severe COVID-19 patients [3] 5 asymptomatic carriers Recruitment: Prospective or retrospective recruitment of cases: retrospective Sample size (virus/COVID cases): 21 (21) Inclusion and exclusion criteria: no more details available

Yongchen 2020 *(Continued)*

Patient characteristics and setting	Setting: hospital Location: 2 medical centres - Second Hospital of Nanjing and the Affiliated Hospital of Xuzhou Medical University in Jiangsu Province Country: China Dates: 25 January-18 March 2020 Symptoms and severity: 5 severe, 11 non-severe and 5 asymptomatic cases. Illness severity defined according to the Chinese management guideline for COVID-19 (version 6.0). Severe cases defined as having any of the following: (a) respiratory distress; (b) hypoxia (SpO2 ≤ 93%); (c) abnormal blood gas analysis (PaO2/FiO2 ≤ 300 mm Hg); or (d) severe disease complications including respiratory failure, which requires mechanical ventilation, septic shock, or non-respiratory organ failure. Asymptomatic carriers were defined as individuals who were positive for COVID-19 nucleic acid but without any symptoms during screening of close contacts. Sex: 13/21 (62%) male Age: median (range) = 37 (10-73) Exposure history: NR
Index tests	Test name: no commercial name stated Manufacturer: Innovita Co., Ltd, China Ab targets: IgG and IgM Antigens used: SARS-CoV-2 S protein and N protein Test method: GICA Timing of samples: NR Samples used: serum Test operators: NR Definition of test positivity: NR Blinded to reference standard: NR and no assumptions made based on timing of the test Threshold predefined: NR
Target condition and reference standard(s)	Reference standard for cases: RT-PCR - confirmed after 2 sequential positive respiratory tract sample results Samples used: throat swabs Timing of reference standard: throat swab samples collected every 1-2 days Blinded to index test: yes (serum samples for serological evaluation were stored for later evaluation) Incorporated index test: no Reference standard for non-cases: N/A
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: yes All participants received the same reference standard: yes Missing data: NR Uninterpretable results: NR Indeterminate results: NR Unit of analysis: participant
Comparative	
Notes	Funding: supported by the National Natural Science Foundation of China, Jiangsu Provincial Medical Talent, Six talent peaks project of Jiangsu Province, Advanced health talent of six-one project of Jiangsu Province, Nanjing Medical Science and Technique Development Foundation Publication status: published paper Source: Emerging Microbes & Infections Study author COI: none was declared
Methodological quality	

Yongchen 2020 *(Continued)*

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	

Yongchen 2020 *(Continued)*

Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?			Unclear risk

Zeng 2020a

Study characteristics	
Patient Sampling	2-group study recruiting patients estimating sensitivity and specificity [1] COVID-19 cases [2] Healthy controls Recruitment: NR Prospective or retrospective recruitment of cases: prospective Sample size (virus/COVID cases): 63 (27) Inclusion and exclusion criteria: no details available
Patient characteristics and setting	Setting: hospital inpatient Location: Zhongnan Hospital, Wuhan Country: China Dates: NR Symptoms and severity: 17 severe cases. No further details Sex: 14/27 (52%) male Age: cases only - median (range) 62 (29-87) years; IQR 46-67 years Exposure history: NR
Index tests	Test name: none Manufacturer: Zhuhai Livzon Diagnostics INC Ab targets: IgG and IgM Antigens used: NR Test method: ELISA Timing of samples: 3-39 days for cases Samples used: serum Test operators: NR Definition of test positivity: OD = 0.105 Blinded to reference standard: NR Threshold predefined: unclear
Target condition and reference standard(s)	Reference standard for cases: NR

Zeng 2020a *(Continued)*

	Samples used: NR Timing of reference standard: NR Blinded to index test: NR Incorporated index test: NR Reference standard for non-cases: healthy controls; no indication of timing, PCR testing
Flow and timing	Time interval between index and reference tests: NR Results presented by time period: yes but only average Ab levels All participants received the same reference standard: NR Missing data: NR Uninterpretable results: NR Indeterminate results: NR Unit of analysis: participant
Comparative	
Notes	Funding: supported by National Key Research and Development Program of China and Emergency Science and Technology Project of Hubei Province Publication status: Journal pre-proof Source: Journal of Infection Study author COI: none

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern

Zeng 2020a *(Continued)*

DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Unclear
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Unclear		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Unclear		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Zhang 2020a

Study characteristics	
Patient Sampling	Single-group design estimating sensitivity in acute and convalescent phase sera SARS-Cov-2 laboratory (RT-PCR detection or Ab assay) confirmed patients (n = 222) Participants were identified retrospectively, likely as a consecutive series
Patient characteristics and setting	Inpatients at Renmin Hospital of Wuhan University, China, admitted 13 January-1 March 2020. Samples dates not known. 87/222 (39%) classified as severe; 35/63 (56%) male. Median (IQR) age 62 (52-69) years. Exposure NR
Index tests	2 Ab tests used on serology samples iFlash-SARS-CoV-2 IgG and iFlash-SARS-CoV-2 IgM (laboratory tests manufactured by Shenzhen YHLO Biotech Co., Ltd.,). Measured IgM and IgG; antigens NR. Thresholds NR. Serum taken between day 1 and 35, 148/222 (67%) from day 21 onwards.
Target condition and reference standard(s)	COVID-19 determined with laboratory RT-PCR or anti-SARS-CoV-2 assay from nasal or pharyngeal swabs. No further detail given (cod-

Zhang 2020a *(Continued)*

	ed as Chinese government guideline, 7th Ed) guideline. Diagnosis made during inpatient stay; prior to the index test
Flow and timing	Unclear which participants received which test (RT-PCR or Ab test as the reference standard). Samples acquired over considerable period pso; only disaggregation is for day 21 and over Timing of reference standard and index tests NR Uninterpretable, indeterminate and missing results not mentioned One sample tested by each test per participant
Comparative	
Notes	No funding declared. No conflicts of interest noted Report from a medRxiv preprint (not peer reviewed)

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		

Zhang 2020a *(Continued)*

The reference standard does not incorporate the index test	No		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Zhang 2020b

Study characteristics	
Patient Sampling	Multi-group design estimating sensitivity and specificity in acute phase sera First group included as single cohort to estimate sensitivity and specificity [1] Suspected COVID-19 cases (n = 228) admitted to fever clinic with RT-PCR testing for COVID-19 Other groups recruited but not analysed as part of this review: [2] Controls - outpatients with other diseases (n = 222) [3] Controls - medical staff working for the fever clinic (n = 63) [4] Controls - pre-pandemic healthy physical examinees (n = 223) No information about recruitment
Patient characteristics and setting	[1] Inpatients at Fever Clinic, Shengjing Hospital of China Medical University, China, admitted between 21 January-16 February 2020, samples dates not known. Median (range) age 35 (1-86). 124/225 (55%) male. Exposure NR [2] Outpatients at Shengjing Hospital of China Medical University, China, admitted between 21 January-16 February 2020, samples dates not known. Median (range) age 50 (27-85). 62/222 (28%) male [3] Medical staff at Fever Clinic, Shengjing Hospital of China Medical University, China, samples dates not known. Median (range) age 40 (25-61). 7/63 (11%) male [4] Healthy controls. Physical examinees in 2018. No setting stated. Median (range) age 59 (29-95). 77/223 (35%) male
Index tests	1 Ab test, no mention of blinding Unnamed IgG and IgM CLIA assay (laboratory tests manufactured by Shenzhen YHLO Biotech Co., Ltd). Measured IgM and IgG in sera; 2019-nCoV S protein S and N protein N antigen. Thresholds > 10.0 AU/mL (Ab concentration per mL. Sample timing only described for 3 cases (tests repeated every 1-3 days until between day 11 and day 17 (from Figure 1)

Zhang 2020b *(Continued)*

Target condition and reference standard(s)	[1] Virus detected with RT-PCR from NP/OP swabs. Ct value according to manufacturers instructions (NR); one of ORF1ab and N gene were required to be positive in same sample. Tests repeated once in negatives. Timing of swabs unclear Excluded cohorts: [2] No reference standard stated [3] No reference standard stated [4] Reference standard based on being pre-pandemic samples
Flow and timing	Timing of reference standard NR. Time pso reported only for the 3 confirmed cases Uninterpretable, indeterminate and missing results not mentioned 1 sample tested per participant
Comparative	
Notes	Funded by National Science and Technology Major Project of China, Liaoning Province Natural Science Foundation Project, Liaoning Province Central Government's special project to guide local scientific and technological development, Guangdong Province Major key projects of indusTentative technology, Major Special Project of Construction Program of China Medical University in 2018 and 345 talent project of Shengjing Hospital of China Medical University No conflicts of interest noted Report from a preprint (not peer reviewed)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Unclear		

Zhang 2020b *(Continued)*

Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Low risk	

Zhang 2020c

Study characteristics	
Patient Sampling	Single-group design estimating sensitivity in acute phase sera. RT-PCR positive confirmed patients (n = 139) who received around 10 days of medical treatment after admission (n = 16) were identified. No information about recruitment

Zhang 2020c *(Continued)*

	The study includes a separate group of patients reporting multiple RT-PCR results
Patient characteristics and setting	Inpatients at Wuhan pulmonary hospital, China, admission dates NR, samples dates not known. No demographic or clinical information. Exposure NR
Index tests	One Ab test, blinding not described Anti-SARSr-CoV IgG and IgM ELISA kits (in-house laboratory method). Measured IgM and IgG in serum from samples on day 0 and day 5; antigen: SARSr-CoV Rp3 nucleoprotein. Threshold NR
Target condition and reference standard(s)	COVID-19 confirmed with laboratory RT-PCR. No further detail given. Diagnosis made during inpatient stay; prior to the index test
Flow and timing	Timing of reference standard NR Excluded if < 10 days medical treatment (n = 123) Uninterpretable, indeterminate results not mentioned One sample tested per participant at each time point; samples obtained on same days pso and all participants had ≥ 10 days medical Rx post admission
Comparative	
Notes	Supported by the Mega-Project for Infectious Disease from Minister of Science and Technology of the People's Republic of China, China Natural Science Foundation for excellent scholars, Strategic Priority Research Program of the CAS, Youth innovation promotion association of CAS No conflicts of interest noted Report from a published peer reviewed paper

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			

Zhang 2020c *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Zhang 2020d

Study characteristics	
Patient Sampling	Single-group study recruiting patients estimating sensitivity and specificity [1] Patients with suspected COVID-19 (n = 824, 154 cases) Recruitment: unclear
Patient characteristics and setting	Setting: hospital Location: 5 hospitals - Huoshenshan Hospital (Wuhan), General Hospital of Central 19 Threater Command of the PLA (Wuhan), the Sixth People's Hospital of Shenyang, Peking Union Medical College Hospital, and Shijiazhuang Fifth Hospital.

Zhang 2020d *(Continued)*

	Country: China Dates: no details Symptoms and severity: no details Sex: no details Age: no details Exposure history: no details
Index tests	Test name: colloidal GICA Manufacturer: in-house Ab targets: total Abs (IgG and IgM) Antigens used: rS1 and rS-RBD-mFc S proteins Test method: CGIA Timing of samples: NR Samples used: serum Test operators: NR Definition of test positivity: visible line Blinded to reference standard: unclear Threshold predefined: yes
Target condition and reference standard(s)	Reference standard for cases: real-time PCR kit, included patients PCR-negative but clinically diagnosed by CT as D+; D- are RT-PCR negative but unclear if all had CT to confirm absence Samples used: nasal/pharyngeal swab Timing of reference standard: unclear Blinded to index test: unclear Incorporated index test: no Reference standard for non-cases: single PCR-negative
Flow and timing	Time interval between index and reference tests: no information Results presented by time period: no All participants received the same reference standard: yes Missing data: no information Uninterpretable results: no information Indeterminate results: no information Unit of analysis: participant
Comparative	
Notes	Funding: The National Key Research and Development Program of China, and The National Science and Technology Major Project Publication status: preprint Source:preprint server (medRxiv) Study author COI: report no COI but 1 author from a company (Beijing Hotgen Biotechnology Inc., Beijing)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		

Zhang 2020d *(Continued)*

Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Unclear
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Zhao 2020a

Study characteristics	
Patient Sampling	2-group design estimating sensitivity and specificity in acute phase sera [1] Confirmed COVID-19 cases (n = 173) with positive RT-PCR testing for COVID-19 [2] Controls - pre-pandemic healthy individuals (n = 213) No information about recruitment
Patient characteristics and setting	[1] Inpatients at Shenzhen Third People's Hospital, Shenzhen, China, admitted between 11 January-9 February 2020, samples between day 1 and day 39. Median (IQR) age 48 (35-61). 84/173 (49%) male. 126/173 (73%) clear exposure identified. 32/173 (18%) considered critical (presence of ARDS or oxygen saturation < 93%, requiring mechanical ventilation) [2] No information given
Index tests	One Ab test, no mention of blinding ELISA double antigen sandwich immunoassay (laboratory tests manufactured by Shenzhen YHLO Biotech Co.,Ltd). Measured total Ab, IgM and IgG in plasma; Ab and IgM - RBD of the S protein of SARS-CoV-2; IgG - recombinant nucleoprotein antigen. Thresholds NR. Sample timing described for all participants Results from repeat RT-PCR test mentioned, but no details given
Target condition and reference standard(s)	[1] Virus detected with RT-PCR from respiratory swabs. Timing of swabs unclear but precedes serology tests [2] Reference standard based on being pre-pandemic samples
Flow and timing	Timing of reference standard NR, all within hospital stay Inadequate plasma samples for 2 IgM tests and 1 IgG test Uninterpretable and indeterminate results not mentioned 535 samples tested from 173 participants; data disaggregated over time. Overall sensitivity and specificity defined as positive at any time point. Accuracy in different time periods based on fewer repeat samples (numbers not known)
Comparative	
Notes	Supported by Bill & Melinda Gates Foundation No conflicts of interest noted Report from a preprint (not peer reviewed)

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		

Zhao 2020a *(Continued)*

Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	No		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	No		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Zhao 2020b

Study characteristics	
Patient Sampling	3-group study recruiting patients estimating sensitivity and specificity [1] Pre-pandemic controls (n = 257) [2] Controls selected during pandemic (n = 155) [3] Cases from hospitalised or recovered patients (n = 69) Recruitment: various sources and locations Prospective or retrospective recruitment of cases: prospective Sample size (virus/COVID cases): 481 (69) Inclusion and exclusion criteria: no details
Patient characteristics and setting	Setting: hospital inpatient (cases), community/hospital/clinical lab (controls) Location: for cases various hospitals (including 2 in Beijing and one in Wuhan); group 2 controls from Beijing (N = 15) and Zheiiang province (N = 140) Country: China Dates: NR Symptoms and severity: cases-at different clinic stages. No more detail Sex: no overall details Age: no details Exposure history: no details
Index tests	Test name: SARS-CoV-2 virus serology ELISA kit Manufacturer: in-house Ab targets: total Ab (IgG + IgM) Antigens used: SARS-CoV-2-S1 protein Test method: ELISA Timing of samples: during hospitalisation Samples used: plasma Test operators: NR Definition of test positivity: standard ELISA method Blinded to reference standard: unclear Threshold predefined: as per controls supplied with ELISA
Target condition and reference standard(s)	Reference standard for cases: unclear Samples used: unclear Timing of reference standard: unclear Blinded to index test: yes Incorporated index test: unclear Reference standard for non-cases: group 1-pre-pandemic, group 2-unclear
Flow and timing	Time interval between index and reference tests: unclear Results presented by time period: no but possible for a subset of the cases All participants received the same reference standard: no Missing data: no details Uninterpretable results: no details Indeterminate results: no details Unit of analysis: unclear
Comparative	
Notes	Funding: research Grants from Beijing Science and Technology Commission, Bill & Melinda Gates Foundation, National Natural Science Foundation of China (NSFC) and the National Science and Technology Major Project Publication status: preprint Source: preprint server medRxiv Study author COI: no details but 3 authors are from 3 different companies (Any-Go Technology Co., Ltd, Beijing; AbMax Biotechnology Co., LTD, Beijing; Zhenge Biotechnology Co., LTD, Shanghai)

Zhao 2020b *(Continued)*

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
The reference standard does not incorporate the index test	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Unclear

Zhao 2020b *(Continued)*

DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	No
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Were results presented per patient?	Yes
Could the patient flow have introduced bias?	High risk

Zhong 2020 [A]

Study characteristics	
Patient Sampling	2-group study to estimate sensitivity and specificity for diagnosis of active infection [1] PCR-positive COVID-19 patients (n = 47) [2] Healthy controls (n = 300) No further details of inclusion or exclusion criteria
Patient characteristics and setting	[1] Source of cases not described. Study conducted in China. Recruitment period not described (symptom onset for cases dates from 15 January-13 February 2020; sampling dates from 28 January-21 February 2020) Severity (cases only): mild = 22 (47%); moderate = 14 (30%); severe = 6 (13%); critical 5 (11%) Sex: 34% male Age: median 48 (range 18-82) years. Exposure history not described [2] Healthy controls not described in regard to timing of sampling or characteristics
Index tests	3 tests evaluated, this entry (Zhong 2020 [A]) refers to test [A] Both laboratory-based evaluations to detect IgM and IgG A. ELISA using N gene of the SARS-CoV-2 cloned into a pET28a vector (rN-based assay) B ELISA using S gene cloned into a pMFcIg vector-based (rS-based assay) C. CLIA (not clearly described; potentially uses both of above described antigens) Thesholds defined retrospectively in regard to optimal cut-off on ROC curve
Target condition and reference standard(s)	[1] PCR (no further details); positivity threshold not described. Symptom onset 15 January-13 February, with serology sampling up to 21 February 2020. RT-PCR probably SARS-Cov-2 specific, but not certain [2] No description of healthy controls provided
Flow and timing	Time interval between index and reference not described. Results not disaggregated by time period pso No missing data, uninterpretable or indeterminate results described

Zhong 2020 [A] *(Continued)*

	Patient-based analysis
Comparative	
Notes	Work was supported by the grants from Sichuan Science and Technology Program (2020YFS0014 and 2020YFS0558), the Chinese Academy of Medical Sciences (2019-I2M-5-032) and Technology & Science & Technology Bureau of Chengdu (2020-YF05-00060-SN and 2020-YF05-00075-SN) Authors declare no COI present; 3 co-authors employed by Maccura Biotech Published letter to Editor (Sci China Life Sci)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
DOMAIN 2: Index Test (Antibody tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		

Zhong 2020 [A] *(Continued)*

The reference standard does not incorporate the index test	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Unclear		
Did all participants receive a reference standard?	Yes		
Were results presented per patient?	Yes		
Could the patient flow have introduced bias?		High risk	

Zhong 2020 [B]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Zhong 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Zhong 2020 [A])
Index tests	3 tests evaluated, this entry (Zhong 2020 [B]) refers to test [B] Both laboratory-based evaluations to detect IgM and IgG A. ELISA using N gene of the SARS-CoV-2 cloned into a pET28a vector (rN-based assay) B ELISA using S gene cloned into a pMFcIg vector-based (rS-based assay) C. CLIA (not clearly described; potentially uses both of above described antigens) Thesholds defined retrospectively in regard to optimal cut-off on ROC curve
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Zhong 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Zhong 2020 [A])
Comparative	
Notes	

Zhong 2020 [C]

Study characteristics	
Patient Sampling	See main entry for this study for characteristics and QUADAS-2 assessment (Zhong 2020 [A])
Patient characteristics and setting	See main entry for this study for characteristics and QUADAS-2 assessment (Zhong 2020 [A])
Index tests	3 tests evaluated, this entry (Zhong 2020 [C]) refers to test [C] Both laboratory-based evaluations to detect IgM and IgG A. ELISA using N gene of the SARS-CoV-2 cloned into a pET28a vector (rN-based assay) B ELISA using S gene cloned into a pMFcIg vector-based (rS-based assay) C. CLIA (not clearly described; potentially uses both of above described antigens) Thesholds defined retrospectively in regard to optimal cut-off on ROC curve
Target condition and reference standard(s)	See main entry for this study for characteristics and QUADAS-2 assessment (Zhong 2020 [A])
Flow and timing	See main entry for this study for characteristics and QUADAS-2 assessment (Zhong 2020 [A])
Comparative	
Notes	

A&E: Accident and Emergency Department; **Ab:** antibody; **ARDS:** acute respiratory distress syndrome; **AU:** arbitrary unit; **CDC:** Center for Disease Control; **CMV:** cytomegalovirus; **CT:** computed tomography; **CGIA:** colloidal gold immunoassay; **CLIA:** chemiluminescence immunoassay; **COI:** conflict of interest; **D-:** disease negative; **D+:** disease positive; **EIA:** enzyme immunoassay; **ELISA:** enzyme-linked immunosorbent assay; **Flu:** fluorescence intensity; **GICA:** gold immunochromatography assay; **HCW:** healthcare worker; **ICU:** intensive care unit; **IIFT:** indirect Immunofluorescence test; **LFA:** lateral flow assay; **LFIA:** lateral flow immunoassay; **LIPS:** luciferase immunoprecipitation system; **LRTI:** lower respiratory tract infection; **N protein:** nucleocapsid protein; **N/A:** not applicable; **NAAT:** nucleic acid amplification test; **NIH:** National Institues of Health; **NIHR:** National Institute for Health Research; **NP:** nasopharyngeal; **NR:** not reported; **OP:** oropharyngeal; **PCR:** polymerase chain reaction; **POC:** point-of-care; **pso:** post-symptom onset; **RBD:** receptor binding domain; **RNA:** ribonucleic acid; **ROC:** receiver operating characteristic; **RT-PCR:** reverse transcriptase polymerase chain reaction; **RT-qPCR:** reverse transcriptase quantitative polymerase chain reaction; **SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2; **S-flow:** flow-cytometry based test; **S protein:** spike protein; **SD:** standard deviation; **TB:** tuberculosis; **WHO:** World Health Organization

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ai 2020	Ineligible reference standard
Aitken 2020	Ineligible study design
Amanat 2020	Accuracy data cannot be extracted
Annamalai 2020	Ineligible study design
Argenziano 2020	Ineligible index test
Arons 2020	Ineligible index test
Arumugam 2020	Ineligible study design

Study	Reason for exclusion
Baggett 2020	Ineligible study design
Bai 2020	Inadequate sample size
Bajema 2020	Ineligible study design
Barra 2020	Ineligible study design
Batista 2020	Ineligible index test
Beltran Corbellini 2020	Ineligible index test
Beltran Pavez 2020	Inadequate sample size
Ben Ami 2020	Ineligible index test
Bhadra 2020	Ineligible study design
Bordi 2020	Ineligible study design
Burhan 2020	Ineligible study design
Cai 2020	Ineligible study design
Callahan 2020	Accuracy data cannot be extracted
Chan 2020	Ineligible study design
Chandler Brown 2020	Ineligible study design
Chen 2020b	Ineligible target condition
Chen 2020c	Ineligible study design
Cheng 2020a	Ineligible reference standard
Chu 2020	Ineligible study design
Colson 2020	Inadequate sample size
Comar 2020	Ineligible reference standard
Corman 2020	Ineligible study design
Cui 2020	Ineligible study design
Curti 2020	Ineligible study design
Dahlke 2020	Inadequate sample size
Ding 2020	Ineligible study design
Fang 2020z	Ineligible index test
Farfan 2020	Ineligible study design

Study	Reason for exclusion
Feng 2020	Ineligible index test
Fontanet 2020	Ineligible study design
Fu 2020a	Ineligible population
Fu 2020b	Accuracy data cannot be extracted
Fumeaux 2020	Ineligible study design
Gao 2020	Ineligible index test
Giamarellos Bourboulis 2020	Ineligible study design
Gietema 2020	Ineligible index test
Gonzalez Gonzalez 2020a	Ineligible study design
Gonzalez Gonzalez 2020b	Ineligible study design
Guan 2020	Ineligible study design
Guo 2020b	Ineligible study design
Guo 2020c	Ineligible population
Han 2020	Ineligible index test
Hao 2020	Ineligible study design
Hass 2020	Ineligible target condition
Hirotsu 2020	Ineligible study design
Hogan 2020	Ineligible index test
Holland 2020	Ineligible study design
Hu 2020b	Ineligible study design
Hu 2020c	Author contact needed
Hu 2020d	Ineligible index test
Huang 2020a	Ineligible study design
Jenkins 2020	Ineligible study design
Jiang 2020a	Ineligible study design
Jiang 2020b	Accuracy data cannot be extracted
Jung 2020	Ineligible study design
Khan 2020	Ineligible study design

Study	Reason for exclusion
Kim 2019	Ineligible study design
Kong 2020	Ineligible study design
Konrad 2020	Ineligible study design
Kurstjens 2020	Ineligible index test
Lamb 2020	Ineligible study design
Lan 2020	Ineligible population
Lechien 2020	Ineligible index test
Lei 2020	Ineligible study design
Li 2020c	Inadequate sample size
Li 2020d	Ineligible study design
Li 2020e	Ineligible index test
Li 2020f	Ineligible population
Li 2020g	Ineligible index test
Liang 2020a	Ineligible index test
Liang 2020b	Ineligible study design
Ling 2020	Ineligible target condition
Liu 2020e	Ineligible index test
Liu 2020f	Ineligible index test
Liu 2020g	Ineligible index test
Liu 2020h	Ineligible study design
Lo 2020	Ineligible index test
Lopez-Rincon 2020	Ineligible study design
Lu 2020	Ineligible study design
Ma 2020b	Ineligible study design
Mahari 2020	Ineligible study design
Mardani 2020	Ineligible index test
Marzinotto 2020	Accuracy data cannot be extracted
McKay 2020	Ineligible study design

Study	Reason for exclusion
McRae 2020	Ineligible index test
Mei 2020	Ineligible index test
Meng 2020	Ineligible index test
Mercurio 2020	Ineligible study design
Metsky 2020	Ineligible study design
Nelson 2020	Ineligible study design
Nemati 2020	Ineligible study design
Nie 2020	Ineligible study design
Nunez Bajo 2020	Ineligible study design
Okba 2020b	Ineligible study design
Paden 2020	Ineligible study design
Pan 2020b	Ineligible index test
Pan 2020c	Ineligible study design
Pan 2020d	Ineligible index test
Pan 2020e	Ineligible study design
Paradiso 2020b	Accuracy data cannot be extracted
Park 2020	Ineligible study design
Peng 2020	Ineligible index test
Pfefferle 2020	Ineligible study design
Rauch 2020	Ineligible study design
Scallan 2020	Accuracy data cannot be extracted
Seo 2020	Accuracy data cannot be extracted
Shental 2020	Ineligible study design
Shi 2020	Ineligible index test
Shirato 2020	Ineligible study design
Song 2020	Ineligible index test
Su 2020	Ineligible index test
Sun 2020a	Ineligible index test

Study	Reason for exclusion
Sun 2020b	Ineligible index test
Sun 2020c	Ineligible study design
Tagarro 2020	Ineligible index test
Tan 2020a	Ineligible study design
Tan 2020b	Ineligible index test
Tan 2020c	Ineligible study design
Toptan 2020	Ineligible study design
Tsang 2003	Ineligible target condition
Vermeiren 2020	Accuracy data cannot be extracted
Viehweger 2020	Ineligible study design
Vogels 2020	Ineligible study design
Waghmare 2020	Ineligible population
Wang 2020b	Ineligible index test
Wang 2020c	Accuracy data cannot be extracted
Wang 2020d	Accuracy data cannot be extracted
Wang 2020e	Accuracy data cannot be extracted
Wang 2020f	Ineligible study design
Wang 2020g	Retracted study
Wang 2020h	Accuracy data cannot be extracted
Wang 2020i	Ineligible index test
Wee 2020	Ineligible study design
Weiss 2020	Accuracy data cannot be extracted
Woelfel 2020	Ineligible reference standard
Won 2020	Ineligible study design
Woo 2020	Ineligible study design
Wu 2020a	Ineligible index test
Wu 2020b	Ineligible study design
Wu 2020c	Accuracy data cannot be extracted

Study	Reason for exclusion
Xia 2020a	Ineligible index test
Xia 2020b	Ineligible study design
Xie 2020b	Ineligible population
Xie 2020c	Accuracy data cannot be extracted
Xing 2020a	Inadequate sample size
Xing 2020b	Ineligible reference standard
Xu 2020b	Ineligible study design
Xu 2020c	Inadequate sample size
Xu 2020d	Ineligible index test
Yan 2020	Ineligible study design
Yang 2020a	Ineligible reference standard
Yang 2020b	Ineligible study design
Yelin 2020	Ineligible study design
Yuan 2020	Accuracy data cannot be extracted
Yun 2020	Ineligible study design
Zeng 2020b	Accuracy data cannot be extracted
Zhang 2020e	Ineligible study design
Zhang 2020f	Ineligible study design
Zhang 2020g	Accuracy data cannot be extracted
Zhang 2020h	Accuracy data cannot be extracted
Zhao 2020c	Ineligible study design
Zhao 2020d	Ineligible study design
Zhifeng 2020	Ineligible reference standard
Zhou 2020	Accuracy data cannot be extracted
Zhuang 2020	Retracted study

Characteristics of studies awaiting classification *[ordered by study ID]*

Li 2020b

Patient Sampling	Foreign language study awaiting translation
Patient characteristics and setting	
Index tests	
Target condition and reference standard(s)	
Flow and timing	
Comparative	
Notes	

Thompson 2020

Patient Sampling	Study of neutralising antibodies; to be assessed for inclusion in review update
Patient characteristics and setting	
Index tests	
Target condition and reference standard(s)	
Flow and timing	
Comparative	
Notes	

Xiong 2020

Patient Sampling	Foreign language study awaiting translation
Patient characteristics and setting	
Index tests	
Target condition and reference standard(s)	
Flow and timing	
Comparative	
Notes	

Characteristics of ongoing studies *[ordered by study ID]*

ChiCTR2000029625	
Study name	Construction of early warning and prediction system for patients with severe / critical novel coronavirus pneumonia (COVID-19)
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000029695	
Study name	Early detection of novel coronavirus pneumonia (COVID-19) based on a novel high-throughput mass spectrometry analysis with exhaled breath
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000029810	
Study name	Clinical study of a novel high sensitivity nucleic acid assay for novel coronavirus pneumonia (COVID-19) based on CRISPR-cas protein
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000029870	
Study name	Evaluation of rapid diagnostic kit (IgM/IgG) for novel coronavirus pneumonia (COVID-19)
Target condition and reference standard(s)	

ChiCTR2000029870 *(Continued)*

Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000029883

Study name	A comparative study on the sensitivity of nasopharyngeal and oropharyngeal swabbing for the detection of SARS-CoV-2 by re-al-time PCR
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000029982

Study name	Study for using multiomics in the diagnosis and treatment of novel coronavirus pneumonia (COVID-19
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030005

Study name	Nucleic acid analysis of novel coronavirus pneumonia (COVID-19) in morning sputum samples and pharyngeal swabs-a prospectively diag-nostic test
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	

ChiCTR2000030005 *(Continued)*

Contact information	
Notes	

ChiCTR2000030085

Study name	Cancelled by the investigator Study for the false positive rate of IgM / IgG antibody test kit for novel coronavirus pneumonia (COVID-19) in different inpatients
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030185

Study name	The value of critical care ultrasound in rapid screening, diagnosis, evaluation of effectiveness and intensive prevention of novel coronavirus pneumonia (COVID-19)
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030253

Study name	Exploration and research for a new method for detection of novel coronavirus (COVID-19) nucleic acid
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030334

Study name	MicroRNA as a marker for early diagnosis of novel coronavirus infection (COVID-19)
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030542

Study name	A clinical study about the diagnosis and prognosis evaluation of novel coronavirus pneumonia (COVID-19) based on viral genome, host genomic sequencing, relative cytokines and other laboratory indexes
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030543

Study name	Detection of coronavirus in simultaneously collecting tears and throat swab samples collected from the patients with novel coronavirus pneumonia (COVID-19)
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030558

Study name	Cancelled by the investigator Epidemiological research of novel coronavirus pneumonia (COVID-19) suspected cases based on virus nucleic acid test combined with low-dose chest CT screening in primary hospital
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030706

Study name	Cancelled by the investigator Application of cas13a-mediated RNA detection in the assay of novel coronavirus nucleic acid (COVID-19)
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030721

Study name	A comparative study for the sensitivity of induced sputum and throat swabs for the detection of SARS-CoV-2 by real-time PCR in patients with novel coronavirus pneumonia (COVID-19)
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030754

Study name	Medical records based study for the accuracy of SARS-CoV-2 IgM antibody screening for diagnosis of novel coronavirus pneumonia (COVID-19)

ChiCTR2000030754 *(Continued)*

Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030833

Study name	Clinical validation and application of high-throughput novel coronavirus (2019-nCoV) screening detection kit
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030834

Study name	Epidemiological characteristics and antibody levels of novel coronavirus pneumonia (COVID-19) of pediatric medical staff working in quarantine area
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030838

Study name	Development of warning system with clinical differential diagnosis and prediction for severe type of novel coronavirus pneumonia (COVID-19) patients based on artificial intelligence and CT images
Target condition and reference standard(s)	
Index and comparator tests	

ChiCTR2000030838 *(Continued)*

Starting date	
Contact information	
Notes	

ChiCTR2000030856

Study name	An artificial intelligence assistant system for suspected novel coronavirus pneumonia (COVID-19) based on chest CT
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030859

Study name	A medical based analysis for influencing factors of death of novel coronavirus pneumonia (COVID-19) patients in Wuhan Third Hospital
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

ChiCTR2000030860

Study name	A medical records based study for investigation of dynamic profile of RT-PCR test for SARS-CoV-2 nucleic acid of novel coronavirus pneumonia (COVID-19) patients
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	

ChiCTR2000030860 *(Continued)*

Notes	

ChiCTR2000030862

Study name	Correlation analysis of blood eosinophil cell levels and clinical type category of novel coronavirus pneumonia (COVID-19): a medical records based retrospective study
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

NCT04245631

Study name	Development of a simple, fast and portable recombinase aided amplification assay for 2019-nCoV
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

NCT04259892

Study name	Viral excretion in contact subjects at high/moderate risk of coronavirus 2019-nCoV infection
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

NCT04279795

Study name	Detection of 2019 novel coronavirus in multiple organ system and its relationship with clinical manifestations
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

NCT04304690

Study name	SARS-CoV2 seroconversion among front line medical and paramedical staff in emergency, intensive care units and infectious disease departments during the 2020 epidemic
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

NCT04311398

Study name	Development and verification of a new coronavirus multiplex nucleic acid detection system
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

NCT04316728

Study name	Clinical performance of the VivaDiag ™ COVID-19 IgM IgG rapid test in early detecting the infection of COVID-19
Target condition and reference standard(s)	

NCT04316728 *(Continued)*

Index and comparator tests	
Starting date	
Contact information	
Notes	

NCT04321369

Study name	Impact of swab site and sample collector on testing sensitivity for SARS-CoV-2 virus in symptomatic individuals
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

NCT04322279

Study name	Factors associated with a positive SARS-CoV-2 serology in contact subjects at high/moderate risk of coronavirus SARS-CoV-2 infection (CoV-CONTACT-SERO)
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

NCT04322513

Study name	Biomarkers for identification of SARS-COV-2 infection
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	

NCT04322513 *(Continued)*

Contact information	
Notes	

Sullivan 2020

Study name	Detection of SARS-CoV-2 RNA and antibodies in diverse samples: protocol to validate the sufficiency of provider-observed home-collected blood, saliva and oropharyngeal samples
Target condition and reference standard(s)	
Index and comparator tests	
Starting date	
Contact information	
Notes	

DATA

Presented below are all the data for all of the tests entered into the review.

Table Tests. Data tables by test

Test	No. of studies	No. of participants
1 IgG (all time points)	62	11748
2 IgG (1 to 7 days)	33	585
3 IgG (8 to 14 days)	34	1220
4 IgG (15 to 21 days)	32	1108
5 IgG (22 to 35 days)	20	495
6 IgG (over 35 days)	12	259
7 IgM (all time points)	58	11436
8 IgM (8 to 14 days)	31	1166
9 IgM (1 to 7 days)	34	658
10 IgM (15 to 21 days)	30	1057
11 IgM (22 to 35 days)	18	492

Test	No. of studies	No. of participants
12 IgM (over 35 days)	12	222
13 IgG/IgM (all time points)	44	9496
14 IgG/IgM (1 to 7 days)	17	259
15 IgG/IgM (8 to 14 days)	21	608
16 IgG/IgM (15 to 21 days)	21	692
17 IgG/IgM (22 to 35 days)	16	152
18 IgG/IgM (over 35 days)	9	153
19 IgA (all time points)	5	1278
20 IgA (1 to 7 days)	4	100
21 IgA (8 to 14 days)	4	65
22 IgA (15 to 21 days)	3	78
23 IgA (22 to 35 days)	3	90
24 IgA (over 35 days)	1	23
25 Total antibodies (Ab) (all time points)	17	5339
27 Total antibodies (Ab) (1 to 7 days)	5	144
29 Total antibodies (Ab) (8 to 14 days)	6	247
30 Total antibodies (Ab) (15 to 21 days)	6	176
31 Total antibodies (Ab) (21 to 35 days)	4	19
32 Total antibodies (Ab) (over 35 days)	2	28
33 IgA/IgG (all time points)	2	775
34 IgA/IgG (1 to 7 days)	1	12
35 IgA/IgG (8 to 14 days)	1	10
36 IgA/IgG (15 to 21 days)	1	8
37 IgA/IgG (22 to 35 days)	1	1
38 IgA/IgM (all time points)	1	699
39 IgG in PCR+ve (all time points)	4	558
40 IgG in PCR +ve (1 to 7 days)	2	28
41 IgG in PCR+ve (8 to 14 days)	2	33

Test	No. of studies	No. of participants
42 IgG in PCR+ve (15 to 21 days)	2	40
43 IgG in PCR-ve (all time points)	6	252
44 IgG in PCR-ve (1 to 7 days)	2	13
45 IgG in PCR-ve (8 to 14 days)	3	30
46 IgG in PCR-ve (15 to 21 days)	3	72
47 IgM in PCR+ve (all time points)	6	740
48 IgM in PCR+ve (1 to 7 days)	2	28
49 IgM in PCR+ve (8 to 14 days)	2	33
50 IgM in PCR+ve (15 to 21 days)	2	16
51 IgM in PCR-ve (all time points)	8	352
52 IgM in PCR-ve (1 to 7 days)	2	13
53 IgM in PCR-ve (8 to 14 days)	3	30
54 IgM in PCR-ve (15 to 21 days)	3	72
55 IgG/IgM in PCR+ve (all time points)	2	177
56 IgG/IgM in PCR+ve (1 to 7 days)	2	36
57 IgG/IgM in PCR+ve (8 to 14 days)	2	53
58 IgG/IgM in PCR+ve (15 to 21 days)	2	150
59 IgG/IgM in PCR-ve (all time points)	4	215
60 IgG/IgM in PCR-ve (1 to 7 days)	2	17
61 IgG/IgM in PCR-ve (8 to 14 days)	3	40
62 IgG/IgM in PCR-ve (15 to 21 days)	3	113
63 IgG (moderate)	1	44
64 IgG (severe)	1	52
65 IgG (critical)	1	37
66 IgM (moderate)	1	44
67 IgM (severe)	1	52
68 IgM (critical)	1	37
69 RT-PCR (all time points - throat)	2	276

Test	No. of studies	No. of participants
70 RT-PCR (1 to 7 days throat)	2	67
71 RT-PCR (8 to 14 days - throat)	2	142
72 RT-PCR (15 to 21 days - throat)	2	73
73 RT-PCR (all time points - sputum)	1	53
74 RT-PCR (1 to 7 days - sputum)	1	13
75 RT-PCR (8 to 14 days - sputum)	1	8
76 RT-PCR (15 to 21 days - sputum)	1	23

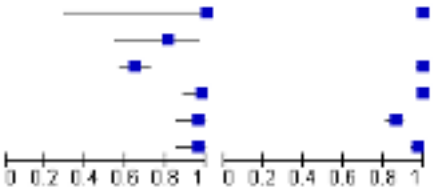
Test 1. IgG (all time points)

IgG (all time points)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	34	0	6	50	0.85 [0.70, 0.94]	1.00 [0.93, 1.00]
Adams 2020 [D]	21	2	12	58	0.64 [0.45, 0.80]	0.97 [0.88, 1.00]
Adams 2020 [E]	25	1	13	59	0.66 [0.49, 0.80]	0.98 [0.91, 1.00]
Adams 2020 [F]	18	1	13	59	0.58 [0.39, 0.75]	0.98 [0.91, 1.00]
Adams 2020 [G]	17	0	14	60	0.55 [0.36, 0.73]	1.00 [0.94, 1.00]
Adams 2020 [H]	20	2	13	58	0.61 [0.42, 0.77]	0.97 [0.88, 1.00]
Adams 2020 [I]	15	0	17	60	0.47 [0.29, 0.65]	1.00 [0.94, 1.00]
Adams 2020 [J]	17	0	23	142	0.42 [0.27, 0.59]	1.00 [0.97, 1.00]
Cai 2020a	197	0	79	167	0.71 [0.66, 0.77]	1.00 [0.98, 1.00]
Cassaniti 2020 (A)	24	0	6	30	0.80 [0.61, 0.92]	1.00 [0.88, 1.00]
Cassaniti 2020 (B)	5	0	33	12	0.13 [0.04, 0.28]	1.00 [0.74, 1.00]
Chen 2020a	7	1	0	11	1.00 [0.59, 1.00]	0.92 [0.62, 1.00]
Du 2020	60	0	0	0	1.00 [0.94, 1.00]	Not estimable
Freeman 2020	84	0	5	0	0.95 [0.89, 0.98]	Not estimable
Gao 2020a	35	0	3	0	0.92 [0.78, 0.98]	Not estimable
Gao 2020b [A]	19	0	18	0	0.51 [0.34, 0.68]	Not estimable
Gao 2020b [B]	19	0	18	0	0.51 [0.34, 0.68]	Not estimable
Gao 2020b [C]	24	0	13	0	0.65 [0.47, 0.80]	Not estimable
Garcia 2020 (A)	23	0	32	45	0.42 [0.29, 0.55]	1.00 [0.92, 1.00]
Garcia 2020 (B)	66	0	7	0	0.90 [0.70, 0.95]	Not estimable
Grzelak 2020 [C]	127	23	34	460	0.79 [0.72, 0.85]	0.95 [0.93, 0.97]
Guo 2020a	162	0	46	135	0.78 [0.72, 0.83]	1.00 [0.97, 1.00]
Infantino 2020	44	0	17	64	0.72 [0.59, 0.83]	1.00 [0.94, 1.00]
Jia 2020	31	0	26	0	0.54 [0.41, 0.68]	Not estimable
Jin 2020	24	3	3	30	0.89 [0.71, 0.98]	0.91 [0.76, 0.98]
Lassauniere 2020 [B]	20	3	10	79	0.67 [0.47, 0.83]	0.96 [0.90, 0.99]
Li 2020a	260	0	117	0	0.71 [0.66, 0.75]	Not estimable
Lin 2020a [A]	65	2	14	78	0.82 [0.72, 0.90]	0.97 [0.91, 1.00]
Lin 2020a [B]	15	0	50	64	0.23 [0.14, 0.35]	1.00 [0.94, 1.00]
Lippi 2020 [A]	19	0	29	0	0.40 [0.26, 0.55]	Not estimable
Lippi 2020 [B]	7	0	41	0	0.15 [0.06, 0.28]	Not estimable
Liu 2020a	77	5	18	79	0.81 [0.72, 0.88]	0.94 [0.87, 0.98]
Liu 2020b	188	2	70	118	0.71 [0.64, 0.76]	0.98 [0.94, 1.00]
Liu 2020c	129	0	4	0	0.97 [0.92, 0.99]	Not estimable
Liu 2020d [A]	150	0	64	100	0.70 [0.63, 0.76]	1.00 [0.96, 1.00]
Liu 2020d [B]	159	0	55	100	0.74 [0.68, 0.80]	1.00 [0.96, 1.00]
Long 2020 (B)	287	0	76	0	0.79 [0.75, 0.83]	Not estimable
Lou 2020 [A]	71	0	9	100	0.89 [0.80, 0.95]	1.00 [0.96, 1.00]
Lou 2020 [B]	69	1	11	208	0.86 [0.77, 0.93]	1.00 [0.97, 1.00]
Ma 2020a	209	1	7	482	0.97 [0.93, 0.99]	1.00 [0.99, 1.00]
Okba 2020a	11	0	20	45	0.35 [0.19, 0.55]	1.00 [0.92, 1.00]
Padoan 2020	57	0	13	0	0.81 [0.70, 0.90]	Not estimable
Pan 2020a	60	0	48	0	0.56 [0.46, 0.65]	Not estimable
Qian 2020	531	30	24	1528	0.96 [0.94, 0.97]	0.98 [0.97, 0.99]
To 2020a [A]	15	0	1	0	0.94 [0.70, 1.00]	Not estimable
To 2020a [B]	16	0	0	0	1.00 [0.79, 1.00]	Not estimable
Wan 2020 [A]	6	0	1	10	0.86 [0.42, 1.00]	1.00 [0.69, 1.00]
Wang 2020a [A]	14	22	0	50	1.00 [0.77, 1.00]	0.69 [0.57, 0.80]
Xiang 2020a [A]	52	0	11	35	0.83 [0.71, 0.91]	1.00 [0.90, 1.00]
Xiang 2020a [B]	74	0	17	35	0.81 [0.72, 0.89]	1.00 [0.90, 1.00]
Xiang 2020b	72	3	18	57	0.80 [0.70, 0.89]	0.95 [0.86, 0.99]
Xiao 2020a	32	0	2	0	0.94 [0.80, 0.99]	Not estimable
Xie 2020a	66	0	0	0	1.00 [0.94, 1.00]	Not estimable
Xu 2020a	3	0	7	0	0.30 [0.07, 0.65]	Not estimable
Zeng 2020a	0	0	27	38	0.00 [0.00, 0.13]	1.00 [0.90, 1.00]
Zhang 2020a	219	0	3	0	0.99 [0.96, 1.00]	Not estimable
Zhang 2020b	3	1	0	224	1.00 [0.29, 1.00]	1.00 [0.98, 1.00]
Zhang 2020c	13	0	3	0	0.81 [0.54, 0.96]	Not estimable

Test 1. (Continued)

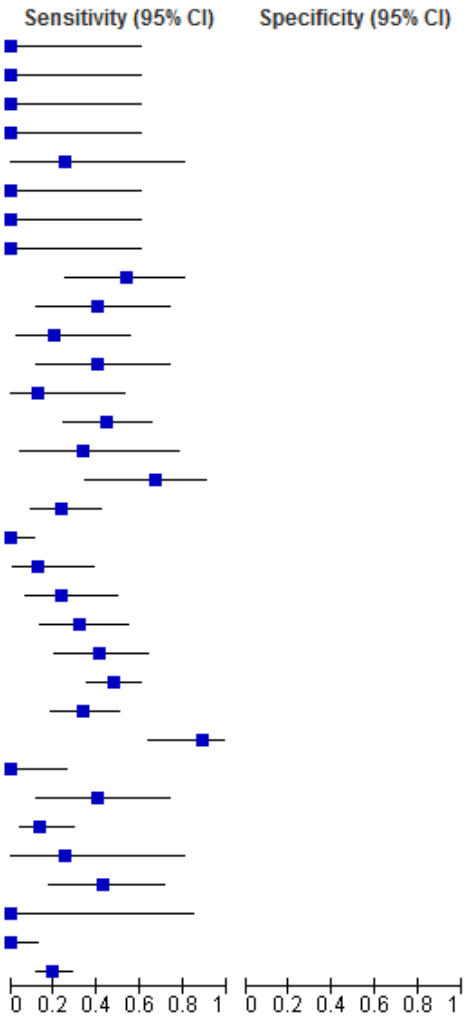
Zhang 2020b	3	1	0	224	1.00 [0.29, 1.00]	1.00 [0.98, 1.00]
Zhang 2020c	13	0	3	0	0.81 [0.54, 0.96]	Not estimable
Zhao 2020a	112	2	81	195	0.65 [0.57, 0.72]	0.99 [0.96, 1.00]
Zhong 2020 [A]	46	1	1	289	0.98 [0.89, 1.00]	1.00 [0.98, 1.00]
Zhong 2020 [B]	45	43	2	257	0.96 [0.85, 0.99]	0.86 [0.81, 0.89]
Zhong 2020 [C]	45	10	2	290	0.96 [0.85, 0.99]	0.97 [0.94, 0.98]



Test 2. IgG (1 to 7 days)

IgG (1 to 7 days)

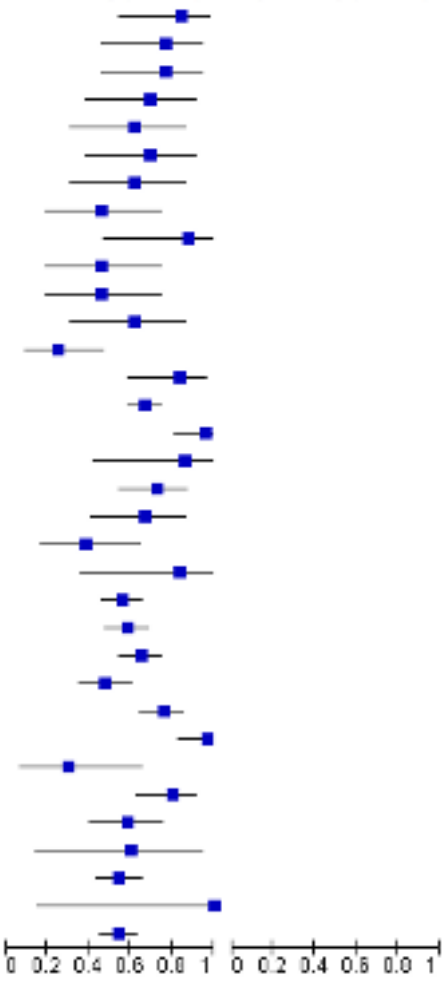
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [D]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [E]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [F]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [G]	1	0	3	0	0.25 [0.01, 0.81]	Not estimable
Adams 2020 [H]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [I]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [J]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Gao 2020a	7	0	6	0	0.54 [0.25, 0.81]	Not estimable
Gao 2020b [A]	4	0	6	0	0.40 [0.12, 0.74]	Not estimable
Gao 2020b [B]	2	0	8	0	0.20 [0.03, 0.56]	Not estimable
Gao 2020b [C]	4	0	6	0	0.40 [0.12, 0.74]	Not estimable
Garcia 2020 (A)	1	0	7	0	0.13 [0.00, 0.53]	Not estimable
Hu 2020a	11	0	14	0	0.44 [0.24, 0.65]	Not estimable
Jin 2020	2	0	4	0	0.33 [0.04, 0.78]	Not estimable
Lin 2020a [A]	8	0	4	0	0.67 [0.35, 0.90]	Not estimable
Lippi 2020 [A]	7	0	23	0	0.23 [0.10, 0.42]	Not estimable
Lippi 2020 [B]	0	0	30	0	0.00 [0.00, 0.12]	Not estimable
Liu 2020a	2	0	14	0	0.13 [0.02, 0.38]	Not estimable
Liu 2020b	4	0	13	0	0.24 [0.07, 0.50]	Not estimable
Liu 2020d [A]	7	0	15	0	0.32 [0.14, 0.55]	Not estimable
Liu 2020d [B]	9	0	13	0	0.41 [0.21, 0.64]	Not estimable
Long 2020 (B)	32	0	35	0	0.48 [0.35, 0.60]	Not estimable
Lou 2020 [A]	13	0	26	0	0.33 [0.19, 0.50]	Not estimable
Ma 2020a	15	0	2	0	0.88 [0.64, 0.99]	Not estimable
Okba 2020a	0	0	12	0	0.00 [0.00, 0.26]	Not estimable
Padoan 2020	4	0	6	0	0.40 [0.12, 0.74]	Not estimable
Pan 2020a	5	0	31	0	0.14 [0.05, 0.29]	Not estimable
Wan 2020 [A]	1	0	3	0	0.25 [0.01, 0.81]	Not estimable
Xiang 2020b	6	0	8	0	0.43 [0.18, 0.71]	Not estimable
Xiao 2020a	0	0	2	0	0.00 [0.00, 0.84]	Not estimable
Zeng 2020a	0	0	27	0	0.00 [0.00, 0.13]	Not estimable
Zhao 2020a	18	0	76	0	0.19 [0.12, 0.29]	Not estimable



Test 3. IgG (8 to 14 days)

IgG (8 to 14 days)

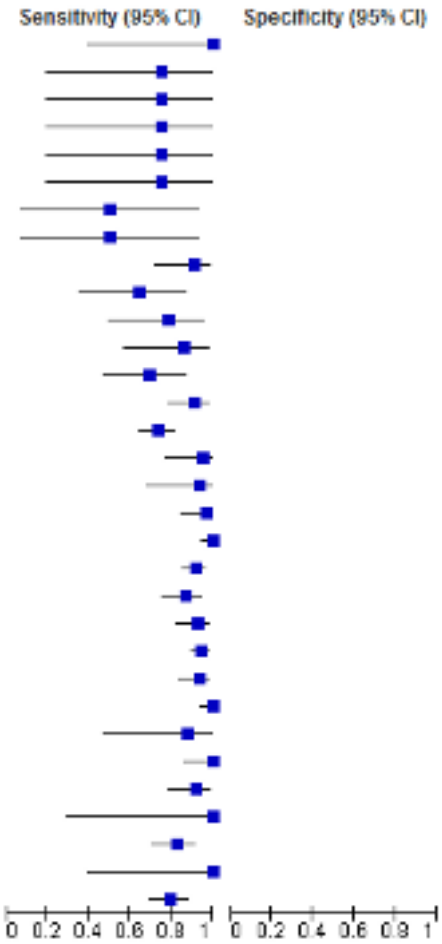
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	11	0	2	0	0.85 [0.55, 0.98]	Not estimable
Adams 2020 [D]	10	0	3	0	0.77 [0.46, 0.95]	Not estimable
Adams 2020 [E]	10	0	3	0	0.77 [0.46, 0.95]	Not estimable
Adams 2020 [F]	9	0	4	0	0.69 [0.39, 0.91]	Not estimable
Adams 2020 [G]	8	0	5	0	0.62 [0.32, 0.86]	Not estimable
Adams 2020 [H]	9	0	4	0	0.69 [0.39, 0.91]	Not estimable
Adams 2020 [I]	8	0	5	0	0.62 [0.32, 0.86]	Not estimable
Adams 2020 [J]	6	0	7	0	0.46 [0.19, 0.75]	Not estimable
Gao 2020a	7	0	1	0	0.88 [0.47, 1.00]	Not estimable
Gao 2020b [A]	6	0	7	0	0.46 [0.19, 0.75]	Not estimable
Gao 2020b [B]	6	0	7	0	0.46 [0.19, 0.75]	Not estimable
Gao 2020b [C]	8	0	5	0	0.62 [0.32, 0.86]	Not estimable
Garcia 2020 (A)	6	0	18	0	0.25 [0.10, 0.47]	Not estimable
Garcia 2020 (B)	15	0	3	0	0.83 [0.59, 0.96]	Not estimable
Hu 2020a	97	0	48	0	0.67 [0.59, 0.74]	Not estimable
Jin 2020	26	0	1	0	0.96 [0.81, 1.00]	Not estimable
Lassaunière 2020 [B]	6	0	1	0	0.86 [0.42, 1.00]	Not estimable
Lin 2020a [A]	24	0	9	0	0.73 [0.54, 0.87]	Not estimable
Lippi 2020 [A]	12	0	6	0	0.67 [0.41, 0.87]	Not estimable
Lippi 2020 [B]	7	0	11	0	0.39 [0.17, 0.64]	Not estimable
Liu 2020a	5	0	1	0	0.83 [0.36, 1.00]	Not estimable
Liu 2020b	62	0	48	0	0.56 [0.47, 0.66]	Not estimable
Liu 2020d [A]	54	0	38	0	0.59 [0.48, 0.69]	Not estimable
Liu 2020d [B]	60	0	32	0	0.65 [0.55, 0.75]	Not estimable
Long 2020 (B)	32	0	35	0	0.48 [0.35, 0.60]	Not estimable
Lou 2020 [A]	57	0	18	0	0.76 [0.65, 0.85]	Not estimable
Ma 2020a	29	0	1	0	0.97 [0.83, 1.00]	Not estimable
Okba 2020a	3	0	7	0	0.30 [0.07, 0.65]	Not estimable
Padoan 2020	28	0	7	0	0.80 [0.63, 0.92]	Not estimable
Pan 2020a	20	0	14	0	0.59 [0.41, 0.75]	Not estimable
Wan 2020 [A]	3	0	2	0	0.60 [0.15, 0.95]	Not estimable
Xiang 2020b	47	0	39	0	0.55 [0.44, 0.65]	Not estimable
Xiao 2020a	2	0	0	0	1.00 [0.16, 1.00]	Not estimable
Zhao 2020a	73	0	62	0	0.54 [0.45, 0.63]	Not estimable



Test 4. IgG (15 to 21 days)

IgG (15 to 21 days)

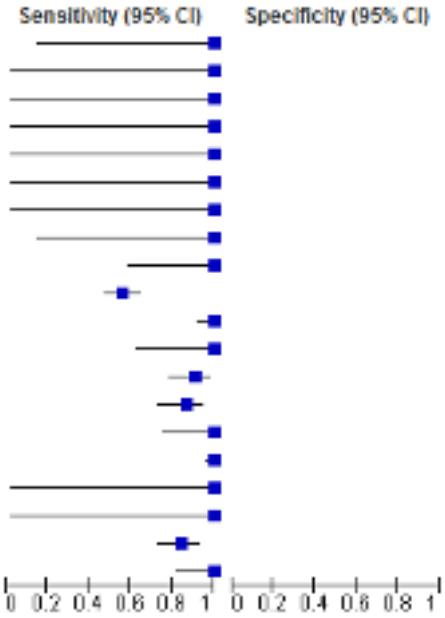
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	4	0	0	0	1.00 [0.40, 1.00]	Not estimable
Adams 2020 [D]	3	0	1	0	0.75 [0.19, 0.99]	Not estimable
Adams 2020 [E]	3	0	1	0	0.75 [0.19, 0.99]	Not estimable
Adams 2020 [F]	3	0	1	0	0.75 [0.19, 0.99]	Not estimable
Adams 2020 [G]	3	0	1	0	0.75 [0.19, 0.99]	Not estimable
Adams 2020 [H]	3	0	1	0	0.75 [0.19, 0.99]	Not estimable
Adams 2020 [I]	2	0	2	0	0.50 [0.07, 0.93]	Not estimable
Adams 2020 [J]	2	0	2	0	0.50 [0.07, 0.93]	Not estimable
Gao 2020a	21	0	2	0	0.91 [0.72, 0.98]	Not estimable
Gao 2020b [A]	9	0	5	0	0.64 [0.35, 0.87]	Not estimable
Gao 2020b [B]	11	0	3	0	0.79 [0.49, 0.95]	Not estimable
Gao 2020b [C]	12	0	2	0	0.86 [0.57, 0.98]	Not estimable
Garcia 2020 (A)	16	0	7	0	0.70 [0.47, 0.87]	Not estimable
Garcia 2020 (B)	41	0	4	0	0.91 [0.79, 0.98]	Not estimable
Hu 2020a	81	0	28	0	0.74 [0.64, 0.82]	Not estimable
Jin 2020	21	0	1	0	0.95 [0.77, 1.00]	Not estimable
Lassauniere 2020 [B]	14	0	1	0	0.93 [0.68, 1.00]	Not estimable
Lin 2020a [A]	33	0	1	0	0.97 [0.85, 1.00]	Not estimable
Liu 2020a	56	0	0	0	1.00 [0.95, 1.00]	Not estimable
Liu 2020b	102	0	9	0	0.92 [0.85, 0.96]	Not estimable
Liu 2020d [A]	48	0	7	0	0.87 [0.76, 0.95]	Not estimable
Liu 2020d [B]	51	0	4	0	0.93 [0.82, 0.98]	Not estimable
Long 2020 (B)	127	0	7	0	0.95 [0.90, 0.98]	Not estimable
Lou 2020 [A]	56	0	4	0	0.93 [0.84, 0.98]	Not estimable
Ma 2020a	55	0	0	0	1.00 [0.94, 1.00]	Not estimable
Okba 2020a	7	0	1	0	0.88 [0.47, 1.00]	Not estimable
Padoan 2020	25	0	0	0	1.00 [0.88, 1.00]	Not estimable
Pan 2020a	35	0	3	0	0.92 [0.79, 0.98]	Not estimable
Wan 2020 [A]	3	0	0	0	1.00 [0.29, 1.00]	Not estimable
Xiang 2020b	47	0	10	0	0.82 [0.70, 0.91]	Not estimable
Xiao 2020a	4	0	0	0	1.00 [0.40, 1.00]	Not estimable
Zhao 2020a	71	0	16	0	0.80 [0.70, 0.88]	Not estimable



Test 5. IgG (22 to 35 days)

IgG (22 to 35 days)

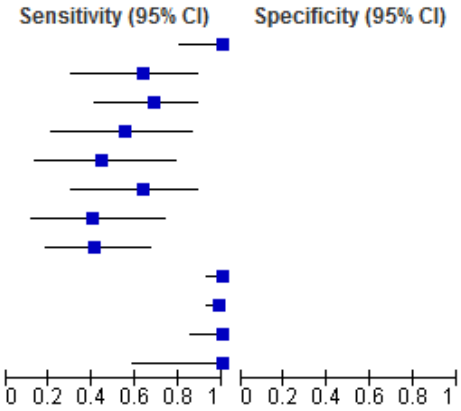
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	2	0	0	0	1.00 [0.16, 1.00]	Not estimable
Adams 2020 [D]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [E]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [F]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [G]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [H]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [I]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [J]	2	0	0	0	1.00 [0.16, 1.00]	Not estimable
Du 2020	7	0	0	0	1.00 [0.59, 1.00]	Not estimable
Hu 2020a	85	0	86	0	0.56 [0.48, 0.64]	Not estimable
Jin 2020	45	0	0	0	1.00 [0.92, 1.00]	Not estimable
Lassaunière 2020 [D]	6	0	0	0	1.00 [0.63, 1.00]	Not estimable
Liu 2020d [A]	41	0	4	0	0.91 [0.79, 0.98]	Not estimable
Liu 2020d [B]	39	0	6	0	0.87 [0.73, 0.95]	Not estimable
Long 2020 (B)	13	0	0	0	1.00 [0.75, 1.00]	Not estimable
Ma 2020a	91	0	0	0	1.00 [0.96, 1.00]	Not estimable
Okba 2020a	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Wan 2020 [A]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Xiang 2020b	50	0	9	0	0.85 [0.73, 0.93]	Not estimable
Xiao 2020a	19	0	0	0	1.00 [0.82, 1.00]	Not estimable



Test 6. IgG (over 35 days)

IgG (over 35 days)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	17	0	0	0	1.00 [0.80, 1.00]	Not estimable
Adams 2020 [D]	7	0	4	0	0.64 [0.31, 0.89]	Not estimable
Adams 2020 [E]	11	0	5	0	0.69 [0.41, 0.89]	Not estimable
Adams 2020 [F]	5	0	4	0	0.56 [0.21, 0.86]	Not estimable
Adams 2020 [G]	4	0	5	0	0.44 [0.14, 0.79]	Not estimable
Adams 2020 [H]	7	0	4	0	0.64 [0.31, 0.89]	Not estimable
Adams 2020 [I]	4	0	6	0	0.40 [0.12, 0.74]	Not estimable
Adams 2020 [J]	7	0	10	0	0.41 [0.18, 0.67]	Not estimable
Du 2020	53	0	0	0	1.00 [0.93, 1.00]	Not estimable
Hu 2020a	75	0	1	0	0.99 [0.93, 1.00]	Not estimable
Ma 2020a	23	0	0	0	1.00 [0.85, 1.00]	Not estimable
Xiao 2020a	7	0	0	0	1.00 [0.59, 1.00]	Not estimable



Test 7. IgM (all time points)

IgM (all time points)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	28	0	12	50	0.70 [0.53, 0.83]	1.00 [0.93, 1.00]
Adams 2020 [D]	3	0	30	80	0.09 [0.02, 0.24]	1.00 [0.94, 1.00]
Adams 2020 [E]	2	0	36	60	0.05 [0.01, 0.18]	1.00 [0.94, 1.00]
Adams 2020 [F]	15	1	16	59	0.48 [0.30, 0.67]	0.98 [0.91, 1.00]
Adams 2020 [G]	14	1	17	59	0.45 [0.27, 0.64]	0.98 [0.91, 1.00]
Adams 2020 [H]	17	1	16	59	0.52 [0.34, 0.69]	0.98 [0.91, 1.00]
Adams 2020 [I]	14	0	18	60	0.44 [0.26, 0.62]	1.00 [0.94, 1.00]
Adams 2020 [J]	15	4	25	138	0.38 [0.23, 0.54]	0.97 [0.93, 0.99]
Cai 2020a	158	0	116	167	0.57 [0.51, 0.63]	1.00 [0.98, 1.00]
Cassaniti 2020 (A)	25	0	5	30	0.83 [0.65, 0.94]	1.00 [0.88, 1.00]
Cassaniti 2020 (B)	6	1	32	11	0.16 [0.06, 0.31]	0.92 [0.62, 1.00]
Du 2020	47	0	13	0	0.78 [0.66, 0.88]	Not estimable
Freeman 2020	75	0	24	0	0.76 [0.66, 0.84]	Not estimable
Gao 2020a	19	0	19	0	0.50 [0.33, 0.67]	Not estimable
Gao 2020b [A]	14	0	23	0	0.38 [0.22, 0.55]	Not estimable
Gao 2020b [B]	18	0	18	0	0.51 [0.34, 0.68]	Not estimable
Gao 2020b [C]	11	0	26	0	0.30 [0.16, 0.47]	Not estimable
Garcia 2020 (A)	12	0	43	45	0.22 [0.12, 0.35]	1.00 [0.92, 1.00]
Garcia 2020 (B)	25	0	38	0	0.40 [0.28, 0.53]	Not estimable
Guo 2020a	188	0	20	135	0.90 [0.86, 0.94]	1.00 [0.97, 1.00]
Infantino 2020	46	4	15	59	0.75 [0.63, 0.85]	0.94 [0.85, 0.98]
Jia 2020	39	0	10	0	0.80 [0.65, 0.90]	Not estimable
Jin 2020	13	0	14	33	0.48 [0.29, 0.68]	1.00 [0.89, 1.00]
Li 2020a	328	0	69	0	0.83 [0.79, 0.86]	Not estimable
Lin 2020a [A]	65	15	14	65	0.82 [0.72, 0.90]	0.81 [0.71, 0.89]
Lin 2020a [B]	30	14	35	50	0.46 [0.34, 0.59]	0.78 [0.66, 0.87]
Lippi 2020 [A]	6	0	42	0	0.13 [0.05, 0.25]	Not estimable
Liu 2020a	35	5	60	79	0.37 [0.27, 0.47]	0.94 [0.87, 0.98]
Liu 2020b	167	3	71	117	0.70 [0.64, 0.75]	0.97 [0.93, 0.99]
Liu 2020c	105	0	20	0	0.79 [0.71, 0.86]	Not estimable
Liu 2020d [A]	148	0	88	100	0.88 [0.82, 0.74]	1.00 [0.96, 1.00]
Liu 2020d [B]	165	0	49	100	0.77 [0.71, 0.83]	1.00 [0.96, 1.00]
Long 2020 (B)	243	0	120	0	0.67 [0.62, 0.72]	Not estimable
Lou 2020 [A]	74	0	6	300	0.93 [0.84, 0.97]	1.00 [0.99, 1.00]
Lou 2020 [B]	71	4	9	205	0.89 [0.80, 0.95]	0.98 [0.95, 0.99]
Lou 2020 [C]	69	2	11	298	0.86 [0.77, 0.93]	0.99 [0.98, 1.00]
Ma 2020a	209	37	7	446	0.97 [0.93, 0.99]	0.92 [0.90, 0.95]
Padoan 2020	44	0	26	0	0.63 [0.50, 0.74]	Not estimable
Pan 2020a	56	0	52	0	0.52 [0.42, 0.62]	Not estimable
Qian 2020	470	29	86	1529	0.85 [0.81, 0.88]	0.98 [0.97, 0.99]
To 2020a [A]	14	0	2	0	0.88 [0.62, 0.98]	Not estimable
To 2020a [B]	15	0	1	0	0.94 [0.70, 1.00]	Not estimable
Wan 2020 [A]	2	1	5	9	0.29 [0.04, 0.71]	0.90 [0.55, 1.00]
Wang 2020a [B]	14	22	0	50	1.00 [0.77, 1.00]	0.69 [0.57, 0.80]
Xiang 2020a [A]	35	0	28	35	0.56 [0.42, 0.68]	1.00 [0.90, 1.00]
Xiang 2020a [B]	52	0	39	35	0.57 [0.46, 0.67]	1.00 [0.90, 1.00]
Xiang 2020b	72	0	10	60	0.80 [0.70, 0.89]	1.00 [0.94, 1.00]
Xiao 2020a	28	0	6	0	0.82 [0.65, 0.93]	Not estimable
Xie 2020a	49	0	7	0	0.88 [0.76, 0.95]	Not estimable
Xu 2020a	4	0	6	0	0.40 [0.12, 0.74]	Not estimable
Zeng 2020a	0	0	27	36	0.00 [0.00, 0.13]	1.00 [0.90, 1.00]
Zhang 2020a	182	0	40	0	0.82 [0.76, 0.87]	Not estimable
Zhang 2020b	3	6	0	219	1.00 [0.29, 1.00]	0.97 [0.94, 0.99]
Zhang 2020c	16	0	0	0	1.00 [0.79, 1.00]	Not estimable
Zhao 2020a	143	3	30	210	0.83 [0.76, 0.89]	0.99 [0.96, 1.00]
Zhong 2020 [A]	48	1	1	299	0.98 [0.89, 1.00]	1.00 [0.98, 1.00]
Zhong 2020 [B]	42	9	6	291	0.89 [0.77, 0.96]	0.97 [0.94, 0.99]

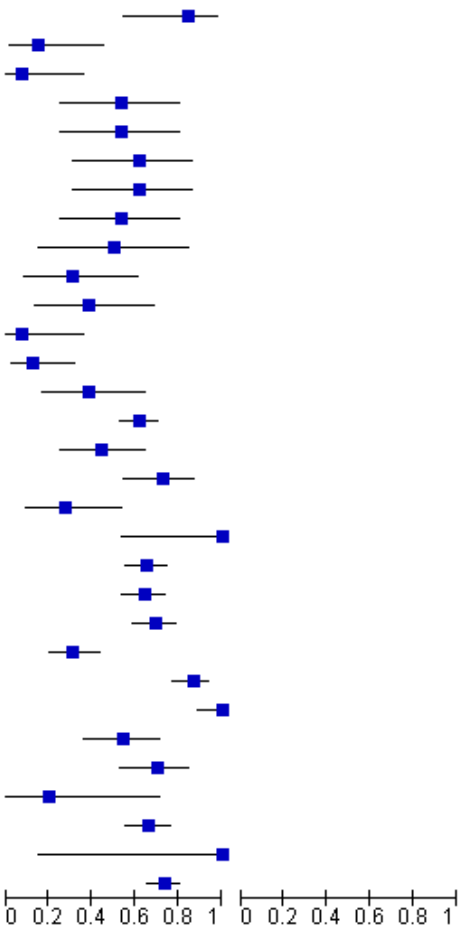
Test 7. (Continued)

Zhong 2020 [A]	48	1	1	299	0.98 [0.89, 1.00]	1.00 [0.98, 1.00]
Zhong 2020 [B]	42	8	5	291	0.89 [0.77, 0.96]	0.97 [0.94, 0.99]
Zhong 2020 [C]	46	14	1	286	0.98 [0.89, 1.00]	0.95 [0.92, 0.97]

Test 8. IgM (8 to 14 days)

IgM (8 to 14 days)

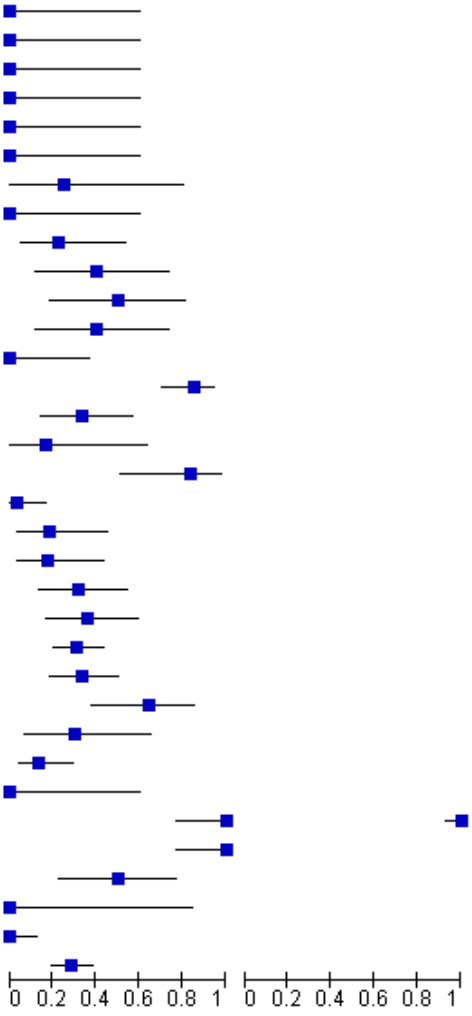
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	11	0	2	0	0.85 [0.55, 0.98]	Not estimable
Adams 2020 [D]	2	0	11	0	0.15 [0.02, 0.45]	Not estimable
Adams 2020 [E]	1	0	12	0	0.08 [0.00, 0.36]	Not estimable
Adams 2020 [F]	7	0	6	0	0.54 [0.25, 0.81]	Not estimable
Adams 2020 [G]	7	0	6	0	0.54 [0.25, 0.81]	Not estimable
Adams 2020 [H]	8	0	5	0	0.62 [0.32, 0.86]	Not estimable
Adams 2020 [I]	8	0	5	0	0.62 [0.32, 0.86]	Not estimable
Adams 2020 [J]	7	0	6	0	0.54 [0.25, 0.81]	Not estimable
Gao 2020a	4	0	4	0	0.50 [0.16, 0.84]	Not estimable
Gao 2020b [A]	4	0	9	0	0.31 [0.09, 0.61]	Not estimable
Gao 2020b [B]	5	0	8	0	0.38 [0.14, 0.68]	Not estimable
Gao 2020b [C]	1	0	12	0	0.08 [0.00, 0.36]	Not estimable
Garcia 2020 (A)	3	0	21	0	0.13 [0.03, 0.32]	Not estimable
Garcia 2020 (B)	7	0	11	0	0.39 [0.17, 0.64]	Not estimable
Hu 2020a	78	0	48	0	0.62 [0.53, 0.70]	Not estimable
Jin 2020	12	0	15	0	0.44 [0.25, 0.65]	Not estimable
Lin 2020a [A]	24	0	9	0	0.73 [0.54, 0.87]	Not estimable
Lippi 2020 [A]	5	0	13	0	0.28 [0.10, 0.53]	Not estimable
Liu 2020a	6	0	0	0	1.00 [0.54, 1.00]	Not estimable
Liu 2020b	72	0	38	0	0.65 [0.56, 0.74]	Not estimable
Liu 2020d [A]	59	0	33	0	0.64 [0.53, 0.74]	Not estimable
Liu 2020d [B]	64	0	28	0	0.70 [0.59, 0.79]	Not estimable
Long 2020 (B)	21	0	46	0	0.31 [0.21, 0.44]	Not estimable
Lou 2020 [A]	65	0	10	0	0.87 [0.77, 0.93]	Not estimable
Ma 2020a	30	0	0	0	1.00 [0.88, 1.00]	Not estimable
Padoan 2020	19	0	16	0	0.54 [0.37, 0.71]	Not estimable
Pan 2020a	24	0	10	0	0.71 [0.53, 0.85]	Not estimable
Wan 2020 [A]	1	0	4	0	0.20 [0.01, 0.72]	Not estimable
Xiang 2020b	57	0	29	0	0.66 [0.55, 0.76]	Not estimable
Xiao 2020a	2	0	0	0	1.00 [0.16, 1.00]	Not estimable
Zhao 2020a	99	0	36	0	0.73 [0.65, 0.81]	Not estimable



Test 9. IgM (1 to 7 days)

IgM (1 to 7 days)

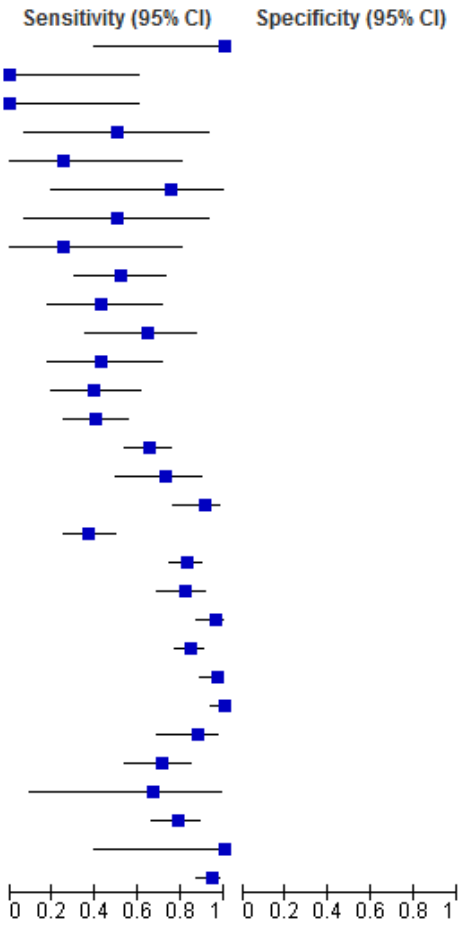
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [D]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [E]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [F]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [G]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [H]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [I]	1	0	3	0	0.25 [0.01, 0.81]	Not estimable
Adams 2020 [J]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Gao 2020a	3	0	10	0	0.23 [0.05, 0.54]	Not estimable
Gao 2020b [A]	4	0	6	0	0.40 [0.12, 0.74]	Not estimable
Gao 2020b [B]	5	0	5	0	0.50 [0.19, 0.81]	Not estimable
Gao 2020b [C]	4	0	6	0	0.40 [0.12, 0.74]	Not estimable
Garcia 2020 (A)	0	0	8	0	0.00 [0.00, 0.37]	Not estimable
Guo 2020a	35	0	6	0	0.85 [0.71, 0.94]	Not estimable
Hu 2020a	7	0	14	0	0.33 [0.15, 0.57]	Not estimable
Jin 2020	1	0	5	0	0.17 [0.00, 0.64]	Not estimable
Lin 2020a [A]	10	0	2	0	0.83 [0.52, 0.98]	Not estimable
Lippi 2020 [A]	1	0	29	0	0.03 [0.00, 0.17]	Not estimable
Liu 2020a	3	0	13	0	0.19 [0.04, 0.46]	Not estimable
Liu 2020b	3	0	14	0	0.18 [0.04, 0.43]	Not estimable
Liu 2020d [A]	7	0	15	0	0.32 [0.14, 0.55]	Not estimable
Liu 2020d [B]	8	0	14	0	0.36 [0.17, 0.59]	Not estimable
Long 2020 (B)	21	0	46	0	0.31 [0.21, 0.44]	Not estimable
Lou 2020 [A]	13	0	26	0	0.33 [0.19, 0.50]	Not estimable
Ma 2020a	11	0	6	0	0.65 [0.38, 0.86]	Not estimable
Padoan 2020	3	0	7	0	0.30 [0.07, 0.65]	Not estimable
Pan 2020a	5	0	31	0	0.14 [0.05, 0.29]	Not estimable
Wan 2020 [A]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Wang 2020a [A]	14	0	0	50	1.00 [0.77, 1.00]	1.00 [0.93, 1.00]
Wang 2020a [B]	14	0	0	0	1.00 [0.77, 1.00]	Not estimable
Xiang 2020b	7	0	7	0	0.50 [0.23, 0.77]	Not estimable
Xiao 2020a	0	0	2	0	0.00 [0.00, 0.84]	Not estimable
Zeng 2020a	0	0	27	0	0.00 [0.00, 0.13]	Not estimable
Zhao 2020a	27	0	67	0	0.29 [0.20, 0.39]	Not estimable



Test 10. IgM (15 to 21 days)

IgM (15 to 21 days)

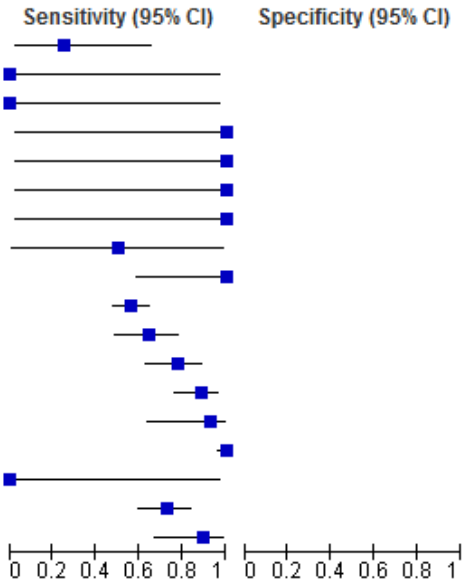
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	4	0	0	0	1.00 [0.40, 1.00]	Not estimable
Adams 2020 [D]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [E]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [F]	2	0	2	0	0.50 [0.07, 0.93]	Not estimable
Adams 2020 [G]	1	0	3	0	0.25 [0.01, 0.81]	Not estimable
Adams 2020 [H]	3	0	1	0	0.75 [0.19, 0.99]	Not estimable
Adams 2020 [I]	2	0	2	0	0.50 [0.07, 0.93]	Not estimable
Adams 2020 [J]	1	0	3	0	0.25 [0.01, 0.81]	Not estimable
Gao 2020a	12	0	11	0	0.52 [0.31, 0.73]	Not estimable
Gao 2020b [A]	6	0	8	0	0.43 [0.18, 0.71]	Not estimable
Gao 2020b [B]	9	0	5	0	0.64 [0.35, 0.87]	Not estimable
Gao 2020b [C]	6	0	8	0	0.43 [0.18, 0.71]	Not estimable
Garcia 2020 (A)	9	0	14	0	0.39 [0.20, 0.61]	Not estimable
Garcia 2020 (B)	18	0	27	0	0.40 [0.26, 0.56]	Not estimable
Hu 2020a	54	0	29	0	0.65 [0.54, 0.75]	Not estimable
Jin 2020	16	0	6	0	0.73 [0.50, 0.89]	Not estimable
Lin 2020a [A]	31	0	3	0	0.91 [0.76, 0.98]	Not estimable
Liu 2020a	25	0	43	0	0.37 [0.25, 0.49]	Not estimable
Liu 2020b	92	0	19	0	0.83 [0.75, 0.89]	Not estimable
Liu 2020d [A]	45	0	10	0	0.82 [0.69, 0.91]	Not estimable
Liu 2020d [B]	53	0	2	0	0.96 [0.87, 1.00]	Not estimable
Long 2020 (B)	113	0	21	0	0.84 [0.77, 0.90]	Not estimable
Lou 2020 [A]	58	0	2	0	0.97 [0.88, 1.00]	Not estimable
Ma 2020a	55	0	0	0	1.00 [0.94, 1.00]	Not estimable
Padoan 2020	22	0	3	0	0.88 [0.69, 0.97]	Not estimable
Pan 2020a	27	0	11	0	0.71 [0.54, 0.85]	Not estimable
Wan 2020 [A]	2	0	1	0	0.67 [0.09, 0.99]	Not estimable
Xiang 2020b	45	0	12	0	0.79 [0.66, 0.89]	Not estimable
Xiao 2020a	4	0	0	0	1.00 [0.40, 1.00]	Not estimable
Zhao 2020a	83	0	5	0	0.94 [0.87, 0.98]	Not estimable



Test 11. IgM (22 to 35 days)

IgM (22 to 35 days)

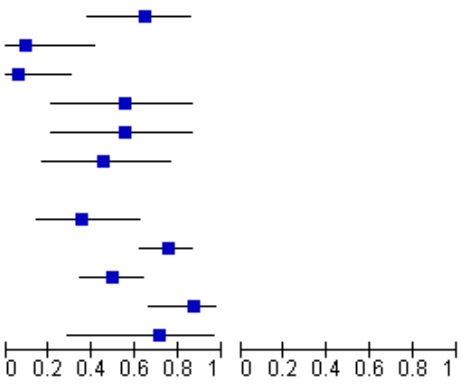
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	2	0	6	0	0.25 [0.03, 0.65]	Not estimable
Adams 2020 [D]	0	0	1	0	0.00 [0.00, 0.97]	Not estimable
Adams 2020 [E]	0	0	1	0	0.00 [0.00, 0.97]	Not estimable
Adams 2020 [F]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [G]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [H]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [I]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [J]	1	0	1	0	0.50 [0.01, 0.99]	Not estimable
Du 2020	7	0	0	0	1.00 [0.59, 1.00]	Not estimable
Hu 2020a	85	0	66	0	0.56 [0.48, 0.64]	Not estimable
Jin 2020	29	0	16	0	0.64 [0.49, 0.78]	Not estimable
Liu 2020d [A]	35	0	10	0	0.78 [0.63, 0.89]	Not estimable
Liu 2020d [B]	40	0	5	0	0.89 [0.76, 0.96]	Not estimable
Long 2020 (B)	12	0	1	0	0.92 [0.64, 1.00]	Not estimable
Ma 2020a	91	0	0	0	1.00 [0.96, 1.00]	Not estimable
Wan 2020 [A]	0	0	1	0	0.00 [0.00, 0.97]	Not estimable
Xiang 2020b	43	0	16	0	0.73 [0.60, 0.84]	Not estimable
Xiao 2020a	17	0	2	0	0.89 [0.67, 0.99]	Not estimable



Test 12. IgM (over 35 days)

IgM (over 35 days)

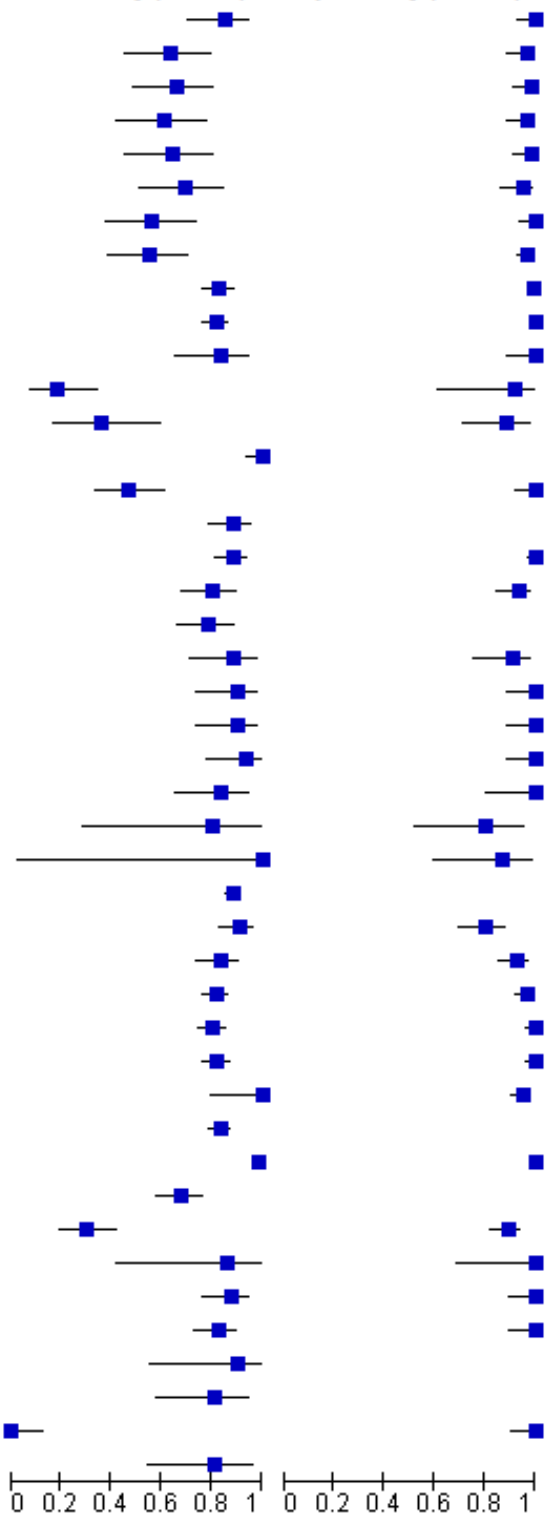
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	11	0	6	0	0.65 [0.38, 0.86]	Not estimable
Adams 2020 [D]	1	0	10	0	0.09 [0.00, 0.41]	Not estimable
Adams 2020 [E]	1	0	15	0	0.06 [0.00, 0.30]	Not estimable
Adams 2020 [F]	5	0	4	0	0.56 [0.21, 0.86]	Not estimable
Adams 2020 [G]	5	0	4	0	0.56 [0.21, 0.86]	Not estimable
Adams 2020 [H]	5	0	6	0	0.45 [0.17, 0.77]	Not estimable
Adams 2020 [I]	0	0	0	0	Not estimable	Not estimable
Adams 2020 [J]	6	0	11	0	0.35 [0.14, 0.62]	Not estimable
Du 2020	40	0	13	0	0.75 [0.62, 0.86]	Not estimable
Hu 2020a	24	0	25	0	0.49 [0.34, 0.64]	Not estimable
Ma 2020a	20	0	3	0	0.87 [0.66, 0.97]	Not estimable
Xiao 2020a	5	0	2	0	0.71 [0.29, 0.96]	Not estimable



Test 13. IgG/IgM (all time points)

IgG/IgM (all time points)

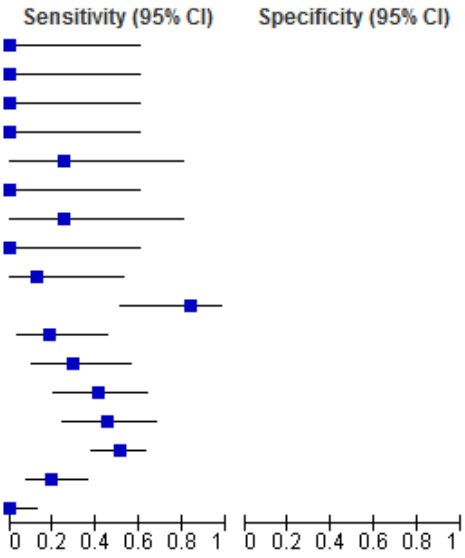
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	34	0	6	50	0.85 [0.70, 0.94]	1.00 [0.93, 1.00]
Adams 2020 [D]	21	2	12	58	0.64 [0.45, 0.80]	0.97 [0.88, 1.00]
Adams 2020 [E]	25	1	13	59	0.66 [0.49, 0.80]	0.98 [0.91, 1.00]
Adams 2020 [F]	19	2	12	58	0.61 [0.42, 0.78]	0.97 [0.88, 1.00]
Adams 2020 [G]	20	1	11	59	0.65 [0.45, 0.81]	0.98 [0.91, 1.00]
Adams 2020 [H]	23	3	10	57	0.70 [0.51, 0.84]	0.95 [0.86, 0.99]
Adams 2020 [I]	18	0	14	60	0.56 [0.38, 0.74]	1.00 [0.94, 1.00]
Adams 2020 [J]	22	4	18	138	0.55 [0.38, 0.71]	0.97 [0.93, 0.99]
Bendavid 2020	130	16	27	3308	0.83 [0.76, 0.88]	1.00 [0.99, 1.00]
Cai 2020a	225	0	51	167	0.82 [0.76, 0.86]	1.00 [0.98, 1.00]
Cassaniti 2020 (A)	25	0	5	30	0.83 [0.65, 0.94]	1.00 [0.88, 1.00]
Cassaniti 2020 (B)	7	1	31	11	0.18 [0.08, 0.34]	0.92 [0.62, 1.00]
Dohla 2020	8	3	14	24	0.36 [0.17, 0.59]	0.89 [0.71, 0.98]
Du 2020	60	0	0	0	1.00 [0.94, 1.00]	Not estimable
Garcia 2020 (A)	26	0	29	45	0.47 [0.34, 0.61]	1.00 [0.92, 1.00]
Garcia 2020 (B)	56	0	7	0	0.89 [0.78, 0.95]	Not estimable
Grzelak 2020 [D]	106	0	14	134	0.88 [0.81, 0.93]	1.00 [0.97, 1.00]
Infantino 2020	49	4	12	59	0.80 [0.68, 0.89]	0.94 [0.85, 0.98]
Jia 2020	45	0	12	0	0.79 [0.66, 0.89]	Not estimable
Jin 2020	24	3	3	30	0.89 [0.71, 0.98]	0.91 [0.76, 0.98]
Lassauniere 2020 [D]	27	0	3	32	0.90 [0.73, 0.98]	1.00 [0.89, 1.00]
Lassauniere 2020 [E]	27	0	3	32	0.90 [0.73, 0.98]	1.00 [0.89, 1.00]
Lassauniere 2020 [F]	28	0	2	32	0.93 [0.78, 0.99]	1.00 [0.89, 1.00]
Lassauniere 2020 [G]	25	0	5	17	0.83 [0.65, 0.94]	1.00 [0.80, 1.00]
Lassauniere 2020 [H]	4	3	1	12	0.80 [0.28, 0.99]	0.80 [0.52, 0.96]
Lassauniere 2020 [I]	1	2	0	13	1.00 [0.03, 1.00]	0.87 [0.60, 0.98]
Li 2020a	352	0	45	0	0.89 [0.85, 0.92]	Not estimable
Lin 2020a [A]	72	16	7	64	0.91 [0.83, 0.96]	0.80 [0.70, 0.88]
Liu 2020a	79	6	16	78	0.83 [0.74, 0.90]	0.93 [0.85, 0.97]
Liu 2020b	194	4	44	116	0.82 [0.76, 0.86]	0.97 [0.92, 0.99]
Liu 2020d [A]	172	0	42	100	0.80 [0.74, 0.85]	1.00 [0.96, 1.00]
Liu 2020d [B]	176	0	38	100	0.82 [0.76, 0.87]	1.00 [0.96, 1.00]
Long 2020 (A)	16	7	0	141	1.00 [0.79, 1.00]	0.95 [0.90, 0.98]
Long 2020 (B)	302	0	61	0	0.83 [0.79, 0.87]	Not estimable
Ma 2020a	213	0	3	483	0.99 [0.96, 1.00]	1.00 [0.99, 1.00]
Pan 2020a	73	0	35	0	0.68 [0.58, 0.76]	Not estimable
Paradiso 2020a	21	13	49	107	0.30 [0.20, 0.42]	0.89 [0.82, 0.94]
Wan 2020 [A]	6	0	1	10	0.86 [0.42, 1.00]	1.00 [0.69, 1.00]
Xiang 2020a [A]	55	0	8	35	0.87 [0.77, 0.94]	1.00 [0.90, 1.00]
Xiang 2020a [B]	75	0	16	35	0.82 [0.73, 0.90]	1.00 [0.90, 1.00]
Xu 2020a	9	0	1	0	0.90 [0.55, 1.00]	Not estimable
Yongchen 2020	17	0	4	0	0.81 [0.58, 0.95]	Not estimable
Zeng 2020a	0	0	27	36	0.00 [0.00, 0.13]	1.00 [0.90, 1.00]
Zhang 2020c	13	0	3	0	0.81 [0.54, 0.96]	Not estimable



Test 14. IgG/IgM (1 to 7 days)

IgG/IgM (1 to 7 days)

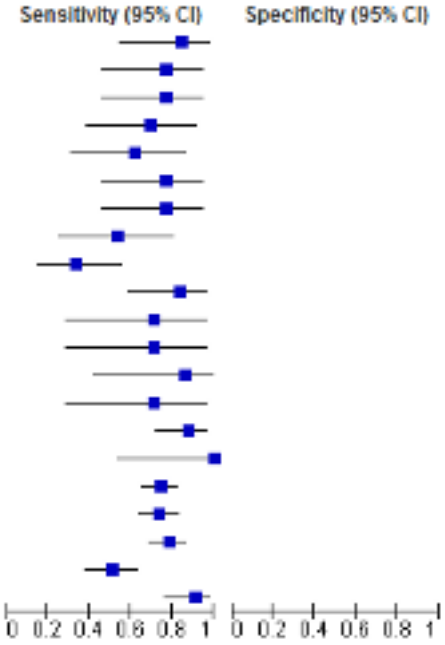
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [D]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [E]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [F]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [G]	1	0	3	0	0.25 [0.01, 0.81]	Not estimable
Adams 2020 [H]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [I]	1	0	3	0	0.25 [0.01, 0.81]	Not estimable
Adams 2020 [J]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Garcia 2020 (A)	1	0	7	0	0.13 [0.00, 0.53]	Not estimable
Lin 2020a [A]	10	0	2	0	0.83 [0.52, 0.98]	Not estimable
Liu 2020a	3	0	13	0	0.19 [0.04, 0.46]	Not estimable
Liu 2020b	5	0	12	0	0.29 [0.10, 0.56]	Not estimable
Liu 2020d [A]	9	0	13	0	0.41 [0.21, 0.64]	Not estimable
Liu 2020d [B]	10	0	12	0	0.45 [0.24, 0.68]	Not estimable
Long 2020 (B)	34	0	33	0	0.51 [0.38, 0.63]	Not estimable
Pan 2020a	7	0	29	0	0.19 [0.08, 0.36]	Not estimable
Zeng 2020a	0	0	27	0	0.00 [0.00, 0.13]	Not estimable



Test 15. IgG/IgM (8 to 14 days)

IgG/IgM (8 to 14 days)

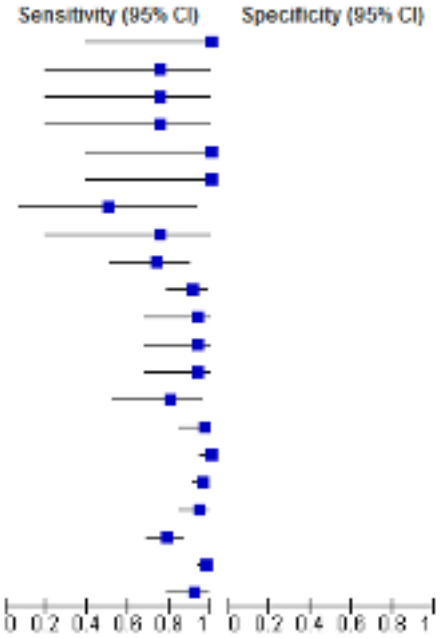
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	11	0	2	0	0.85 [0.55, 0.98]	Not estimable
Adams 2020 [D]	10	0	3	0	0.77 [0.46, 0.95]	Not estimable
Adams 2020 [E]	10	0	3	0	0.77 [0.46, 0.95]	Not estimable
Adams 2020 [F]	9	0	4	0	0.69 [0.39, 0.91]	Not estimable
Adams 2020 [G]	9	0	5	0	0.62 [0.32, 0.86]	Not estimable
Adams 2020 [H]	10	0	3	0	0.77 [0.46, 0.95]	Not estimable
Adams 2020 [I]	10	0	3	0	0.77 [0.46, 0.95]	Not estimable
Adams 2020 [J]	7	0	8	0	0.54 [0.25, 0.81]	Not estimable
Garcia 2020 (A)	8	0	16	0	0.33 [0.16, 0.55]	Not estimable
Garcia 2020 (B)	15	0	3	0	0.83 [0.59, 0.96]	Not estimable
Lassauniere 2020 [D]	5	0	2	0	0.71 [0.29, 0.96]	Not estimable
Lassauniere 2020 [E]	5	0	2	0	0.71 [0.29, 0.96]	Not estimable
Lassauniere 2020 [F]	6	0	1	0	0.86 [0.42, 1.00]	Not estimable
Lassauniere 2020 [G]	5	0	2	0	0.71 [0.29, 0.96]	Not estimable
Lin 2020a [A]	29	0	4	0	0.88 [0.72, 0.97]	Not estimable
Liu 2020a	8	0	0	0	1.00 [0.54, 1.00]	Not estimable
Liu 2020b	82	0	28	0	0.75 [0.65, 0.82]	Not estimable
Liu 2020d [A]	69	0	24	0	0.74 [0.64, 0.83]	Not estimable
Liu 2020d [B]	72	0	20	0	0.78 [0.68, 0.86]	Not estimable
Long 2020 (B)	34	0	33	0	0.51 [0.38, 0.63]	Not estimable
Pan 2020a	31	0	3	0	0.91 [0.76, 0.98]	Not estimable



Test 16. IgG/IgM (15 to 21 days)

IgG/IgM (15 to 21 days)

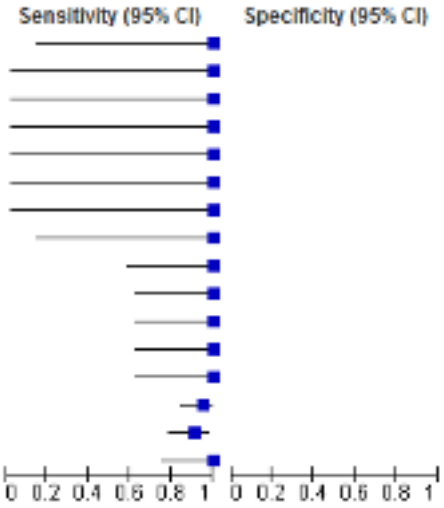
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	4	0	0	0	1.00 [0.40, 1.00]	Not estimable
Adams 2020 [D]	3	0	1	0	0.75 [0.19, 0.99]	Not estimable
Adams 2020 [E]	3	0	1	0	0.75 [0.19, 0.99]	Not estimable
Adams 2020 [F]	3	0	1	0	0.75 [0.19, 0.99]	Not estimable
Adams 2020 [G]	4	0	0	0	1.00 [0.40, 1.00]	Not estimable
Adams 2020 [H]	4	0	0	0	1.00 [0.40, 1.00]	Not estimable
Adams 2020 [I]	2	0	2	0	0.50 [0.07, 0.93]	Not estimable
Adams 2020 [J]	3	0	1	0	0.75 [0.19, 0.99]	Not estimable
Garcia 2020 (A)	17	0	6	0	0.74 [0.52, 0.90]	Not estimable
Garcia 2020 (B)	41	0	4	0	0.91 [0.79, 0.96]	Not estimable
Lassauniere 2020 [D]	14	0	1	0	0.93 [0.68, 1.00]	Not estimable
Lassauniere 2020 [E]	14	0	1	0	0.93 [0.68, 1.00]	Not estimable
Lassauniere 2020 [F]	14	0	1	0	0.93 [0.68, 1.00]	Not estimable
Lassauniere 2020 [G]	12	0	3	0	0.80 [0.52, 0.96]	Not estimable
Lin 2020a (A)	33	0	1	0	0.97 [0.85, 1.00]	Not estimable
Liu 2020a	68	0	0	0	1.00 [0.95, 1.00]	Not estimable
Liu 2020b	107	0	4	0	0.96 [0.91, 0.99]	Not estimable
Liu 2020c (A)	52	0	3	0	0.95 [0.85, 0.99]	Not estimable
Liu 2020c (B)	72	0	20	0	0.78 [0.68, 0.86]	Not estimable
Long 2020 (B)	131	0	3	0	0.98 [0.94, 1.00]	Not estimable
Pan 2020a	35	0	3	0	0.92 [0.79, 0.99]	Not estimable



Test 17. IgG/IgM (22 to 35 days)

IgG/IgM (22 to 35 days)

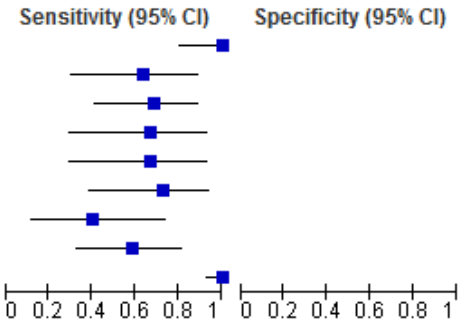
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	2	0	0	0	1.00 [0.16, 1.00]	Not estimable
Adams 2020 [D]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [E]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [F]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [G]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [H]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [I]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [J]	2	0	0	0	1.00 [0.16, 1.00]	Not estimable
Du 2020	7	0	0	0	1.00 [0.59, 1.00]	Not estimable
Lassauniere 2020 [D]	9	0	0	0	1.00 [0.63, 1.00]	Not estimable
Lassauniere 2020 [E]	9	0	0	0	1.00 [0.63, 1.00]	Not estimable
Lassauniere 2020 [F]	9	0	0	0	1.00 [0.63, 1.00]	Not estimable
Lassauniere 2020 [G]	9	0	0	0	1.00 [0.63, 1.00]	Not estimable
Liu 2020d [A]	43	0	2	0	0.96 [0.85, 0.99]	Not estimable
Liu 2020d [B]	41	0	4	0	0.91 [0.79, 0.96]	Not estimable
Long 2020 (B)	13	0	0	0	1.00 [0.75, 1.00]	Not estimable



Test 18. IgG/IgM (over 35 days)

IgG/IgM (over 35 days)

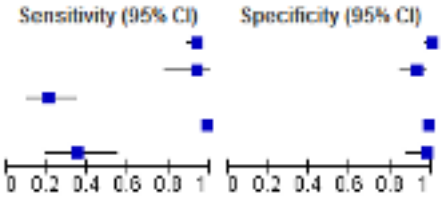
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [A]	17	0	0	0	1.00 [0.80, 1.00]	Not estimable
Adams 2020 [D]	7	0	4	0	0.64 [0.31, 0.89]	Not estimable
Adams 2020 [E]	11	0	5	0	0.69 [0.41, 0.89]	Not estimable
Adams 2020 [F]	6	0	3	0	0.67 [0.30, 0.93]	Not estimable
Adams 2020 [G]	6	0	3	0	0.67 [0.30, 0.93]	Not estimable
Adams 2020 [H]	8	0	3	0	0.73 [0.39, 0.94]	Not estimable
Adams 2020 [I]	4	0	6	0	0.40 [0.12, 0.74]	Not estimable
Adams 2020 [J]	10	0	7	0	0.59 [0.33, 0.82]	Not estimable
Du 2020	53	0	0	0	1.00 [0.93, 1.00]	Not estimable



Test 19. IgA (all time points)

IgA (all time points)

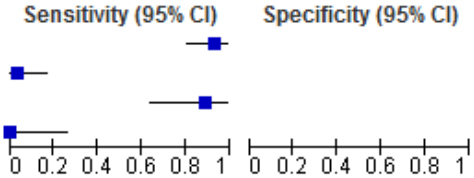
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Guo 2020a	194	0	14	135	0.93 [0.89, 0.96]	1.00 [0.97, 1.00]
Lassauniere 2020 [C]	28	6	2	76	0.93 [0.78, 0.99]	0.93 [0.85, 0.97]
Lippi 2020 [B]	10	0	38	0	0.21 [0.10, 0.35]	Not estimable
Ma 2020a	213	9	3	474	0.99 [0.96, 1.00]	0.98 [0.96, 0.99]
Okba 2020a	11	1	20	44	0.35 [0.18, 0.55]	0.98 [0.88, 1.00]



Test 20. IgA (1 to 7 days)

IgA (1 to 7 days)

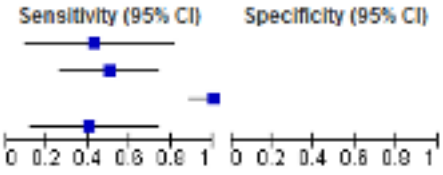
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Guo 2020a	38	0	3	0	0.93 [0.80, 0.98]	Not estimable
Lippi 2020 [B]	1	0	29	0	0.03 [0.00, 0.17]	Not estimable
Ma 2020a	15	0	2	0	0.88 [0.64, 0.99]	Not estimable
Okba 2020a	0	0	12	0	0.00 [0.00, 0.26]	Not estimable



Test 21. IgA (8 to 14 days)

IgA (8 to 14 days)

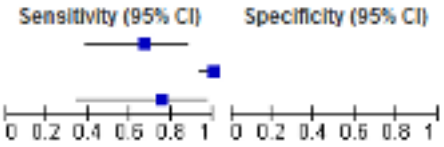
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Lassauniere 2020 [C]	3	0	4	0	0.43 [0.10, 0.82]	Not estimable
Lippi 2020 [D]	9	0	9	0	0.50 [0.26, 0.74]	Not estimable
Ma 2020a	30	0	0	0	1.00 [0.88, 1.00]	Not estimable
Okba 2020a	4	0	5	0	0.40 [0.12, 0.74]	Not estimable



Test 22. IgA (15 to 21 days)

IgA (15 to 21 days)

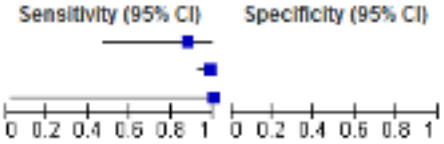
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Lassauniere 2020 [C]	10	0	5	0	0.67 [0.38, 0.88]	Not estimable
Ma 2020a	65	0	0	0	1.00 [0.94, 1.00]	Not estimable
Okba 2020a	6	0	2	0	0.75 [0.35, 0.97]	Not estimable



Test 23. IgA (22 to 35 days)

IgA (22 to 35 days)

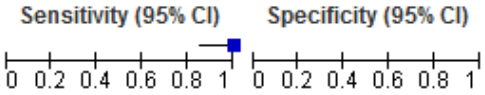
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Lassauniere 2020 [C]	7	0	1	0	0.88 [0.47, 1.00]	Not estimable
Ma 2020a	60	0	1	0	0.99 [0.93, 1.00]	Not estimable
Okba 2020a	1	0	0	0	1.00 [0.03, 1.00]	Not estimable



Test 24. IgA (over 35 days)

IgA (over 35 days)

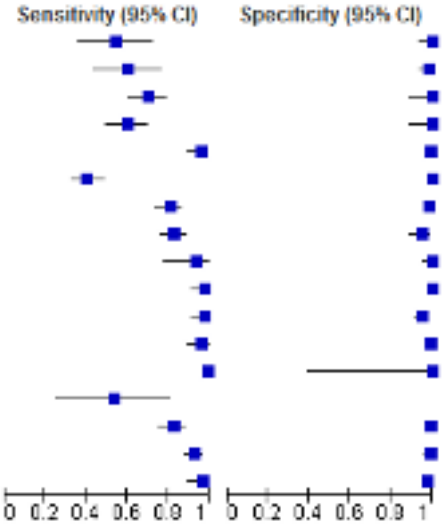
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ma 2020a	23	0	0	0	1.00 [0.85, 1.00]	Not estimable



Test 25. Total antibodies (Ab) (all time points)

Total antibodies (Ab) (all time points)

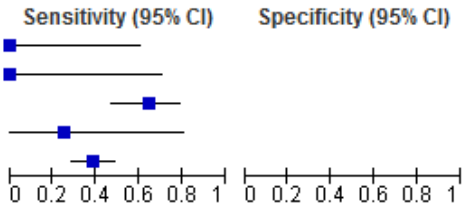
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [D]	10	0	15	60	0.55 [0.36, 0.72]	1.00 [0.94, 1.00]
Adams 2020 [C]	23	1	15	90	0.61 [0.43, 0.78]	0.99 [0.94, 1.00]
Burbelo 2020 [A]	76	0	32	32	0.70 [0.61, 0.78]	1.00 [0.89, 1.00]
Burbelo 2020 [E]	60	0	40	32	0.60 [0.50, 0.70]	1.00 [0.89, 1.00]
Freeman 2020	95	4	4	515	0.96 [0.90, 0.99]	0.99 [0.90, 1.00]
Grzelak 2020 [A]	65	0	98	280	0.40 [0.33, 0.48]	1.00 [0.99, 1.00]
Grzelak 2020 [B]	130	3	31	277	0.81 [0.74, 0.87]	0.99 [0.97, 1.00]
Grzelak 2020 [E]	132	5	27	95	0.83 [0.76, 0.89]	0.95 [0.89, 0.98]
Lassauniere 2020 [A]	20	0	2	82	0.93 [0.76, 0.99]	1.00 [0.96, 1.00]
Lou 2020 [A]	78	0	2	300	0.97 [0.91, 1.00]	1.00 [0.99, 1.00]
Lou 2020 [B]	78	10	2	199	0.97 [0.91, 1.00]	0.95 [0.91, 0.98]
Lou 2020 [C]	77	2	3	298	0.96 [0.89, 0.99]	0.98 [0.96, 1.00]
Ma 2020a	215	0	1	4	1.00 [0.97, 1.00]	1.00 [0.40, 1.00]
Wan 2020 [B]	7	0	6	0	0.54 [0.25, 0.81]	Not estimable
Zhang 2020d	127	4	27	887	0.82 [0.76, 0.88]	0.99 [0.98, 1.00]
Zhao 2020a	161	2	12	211	0.93 [0.88, 0.96]	0.98 [0.97, 1.00]
Zhao 2020b	67	10	2	402	0.97 [0.90, 1.00]	0.96 [0.96, 0.99]



Test 27. Total antibodies (Ab) (1 to 7 days)

Total antibodies (Ab) (1 to 7 days)

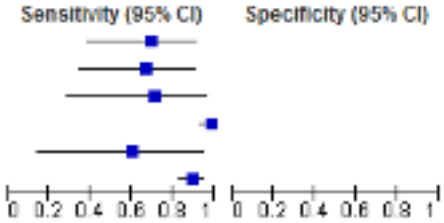
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [B]	0	0	4	0	0.00 [0.00, 0.60]	Not estimable
Adams 2020 [C]	0	0	3	0	0.00 [0.00, 0.71]	Not estimable
Lou 2020 [A]	25	0	14	0	0.64 [0.47, 0.79]	Not estimable
Wan 2020 [B]	1	0	3	0	0.25 [0.01, 0.81]	Not estimable
Zhao 2020a	36	0	58	0	0.38 [0.28, 0.49]	Not estimable



Test 29. Total antibodies (Ab) (8 to 14 days)

Total antibodies (Ab) (8 to 14 days)

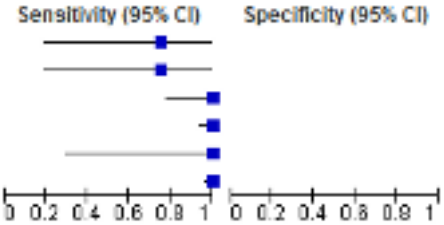
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [B]	9	0	4	0	0.69 [0.39, 0.91]	Not estimable
Adams 2020 [C]	8	0	4	0	0.67 [0.35, 0.90]	Not estimable
Lassauniere 2020 [A]	5	0	2	0	0.71 [0.29, 0.96]	Not estimable
Lou 2020 [A]	74	0	1	0	0.99 [0.93, 1.00]	Not estimable
Wan 2020 [B]	3	0	2	0	0.60 [0.15, 0.95]	Not estimable
Zhao 2020a	121	0	14	0	0.90 [0.83, 0.94]	Not estimable



Test 30. Total antibodies (Ab) (15 to 21 days)

Total antibodies (Ab) (15 to 21 days)

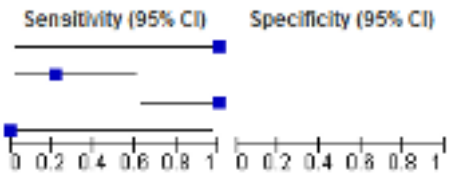
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [B]	3	0	1	0	0.75 [0.19, 0.99]	Not estimable
Adams 2020 [C]	3	0	1	0	0.75 [0.19, 0.99]	Not estimable
Lassauniere 2020 [A]	15	0	0	0	1.00 [0.78, 1.00]	Not estimable
Lou 2020 [A]	60	0	0	0	1.00 [0.94, 1.00]	Not estimable
Wan 2020 [B]	3	0	0	0	1.00 [0.29, 1.00]	Not estimable
Zhao 2020a	80	0	0	0	1.00 [0.96, 1.00]	Not estimable



Test 31. Total antibodies (Ab) (21 to 35 days)

Total antibodies (Ab) (21 to 35 days)

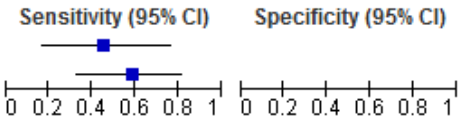
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [B]	1	0	0	0	1.00 [0.03, 1.00]	Not estimable
Adams 2020 [C]	2	0	7	0	0.22 [0.03, 0.60]	Not estimable
Lassauniere 2020 [A]	8	0	0	0	1.00 [0.63, 1.00]	Not estimable
Wan 2020 [B]	0	0	1	0	0.00 [0.00, 0.97]	Not estimable



Test 32. Total antibodies (Ab) (over 35 days)

Total antibodies (Ab) (over 35 days)

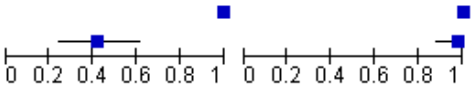
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Adams 2020 [B]	5	0	6	0	0.45 [0.17, 0.77]	Not estimable		
Adams 2020 [C]	10	0	7	0	0.59 [0.33, 0.82]	Not estimable		



Test 33. IgA/IgG (all time points)

IgA/IgG (all time points)

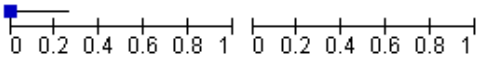
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Ma 2020a	214	0	2	483	0.99 [0.97, 1.00]	1.00 [0.99, 1.00]		
Okba 2020a	13	1	18	44	0.42 [0.25, 0.61]	0.98 [0.88, 1.00]		



Test 34. IgA/IgG (1 to 7 days)

IgA/IgG (1 to 7 days)

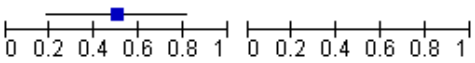
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Okba 2020a	0	0	12	0	0.00 [0.00, 0.26]	Not estimable		



Test 35. IgA/IgG (8 to 14 days)

IgA/IgG (8 to 14 days)

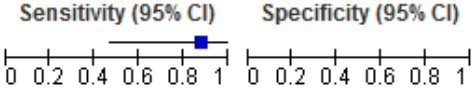
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Okba 2020a	5	0	5	0	0.50 [0.19, 0.81]	Not estimable		



Test 36. IgA/IgG (15 to 21 days)

IgA/IgG (15 to 21 days)

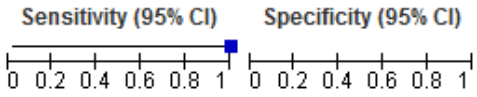
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Okba 2020a	7	0	1	0	0.88 [0.47, 1.00]	Not estimable		



Test 37. IgA/IgG (22 to 35 days)

IgA/IgG (22 to 35 days)

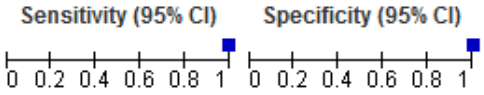
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Okba 2020a	1	0	0	0	1.00 [0.03, 1.00]	Not estimable



Test 38. IgA/IgM (all time points)

IgA/IgM (all time points)

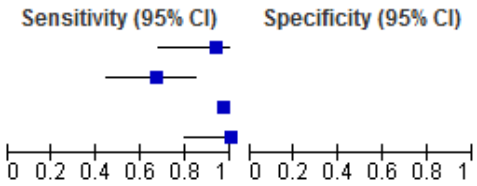
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ma 2020a	215	1	1	482	1.00 [0.97, 1.00]	1.00 [0.99, 1.00]



Test 39. IgG in PCR+ve (all time points)

IgG in PCR+ve (all time points)

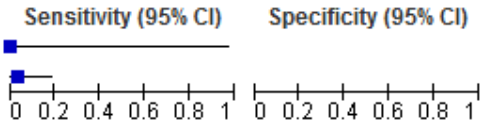
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	14	0	1	0	0.93 [0.68, 1.00]	Not estimable
Jia 2020	16	0	8	0	0.67 [0.45, 0.84]	Not estimable
Qian 2020	486	0	17	0	0.97 [0.95, 0.98]	Not estimable
Xie 2020a	16	0	0	0	1.00 [0.79, 1.00]	Not estimable



Test 40. IgG in PCR +ve (1 to 7 days)

IgG in PCR +ve (1 to 7 days)

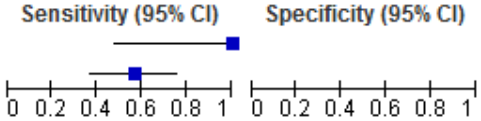
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	0	0	1	0	0.00 [0.00, 0.97]	Not estimable
Pan 2020a	1	0	26	0	0.04 [0.00, 0.19]	Not estimable



Test 41. IgG in PCR+ve (8 to 14 days)

IgG in PCR+ve (8 to 14 days)

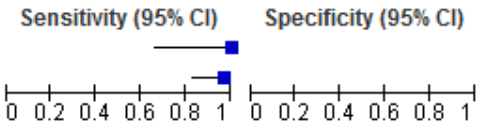
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	5	0	0	0	1.00 [0.48, 1.00]	Not estimable
Pan 2020a	16	0	12	0	0.57 [0.37, 0.76]	Not estimable



Test 42. IgG in PCR+ve (15 to 21 days)

IgG in PCR+ve (15 to 21 days)

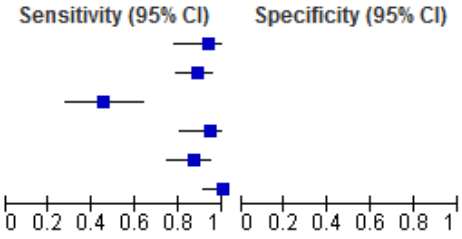
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	9	0	0	0	1.00 [0.66, 1.00]	Not estimable
Pan 2020a	30	0	1	0	0.97 [0.83, 1.00]	Not estimable



Test 43. IgG in PCR-ve (all time points)

IgG in PCR-ve (all time points)

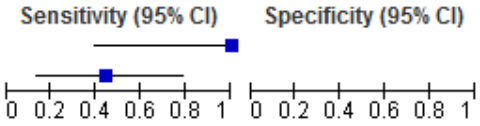
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	28	0	2	0	0.93 [0.78, 0.99]	Not estimable
Garcia 2020 (B)	56	0	7	0	0.89 [0.78, 0.95]	Not estimable
Jia 2020	15	0	18	0	0.45 [0.28, 0.64]	Not estimable
Jin 2020	32	0	2	0	0.94 [0.80, 0.99]	Not estimable
Qian 2020	45	0	7	0	0.87 [0.74, 0.94]	Not estimable
Xie 2020a	40	0	0	0	1.00 [0.91, 1.00]	Not estimable



Test 44. IgG in PCR-ve (1 to 7 days)

IgG in PCR-ve (1 to 7 days)

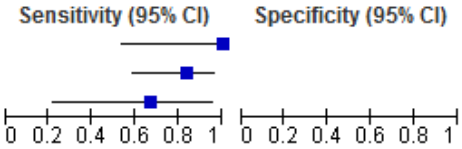
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	4	0	0	0	1.00 [0.40, 1.00]	Not estimable
Pan 2020a	4	0	5	0	0.44 [0.14, 0.79]	Not estimable



Test 45. IgG in PCR-ve (8 to 14 days)

IgG in PCR-ve (8 to 14 days)

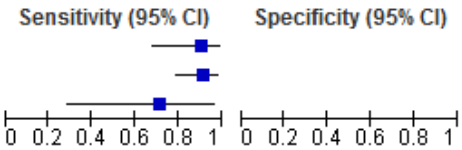
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	6	0	0	0	1.00 [0.54, 1.00]	Not estimable
Garcia 2020 (B)	15	0	3	0	0.83 [0.59, 0.96]	Not estimable
Pan 2020a	4	0	2	0	0.67 [0.22, 0.96]	Not estimable



Test 46. IgG in PCR-ve (15 to 21 days)

IgG in PCR-ve (15 to 21 days)

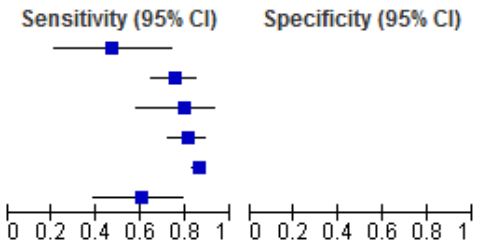
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	18	0	2	0	0.90 [0.68, 0.99]	Not estimable
Garcia 2020 (B)	41	0	4	0	0.91 [0.79, 0.98]	Not estimable
Pan 2020a	5	0	2	0	0.71 [0.29, 0.96]	Not estimable



Test 47. IgM in PCR+ve (all time points)

IgM in PCR+ve (all time points)

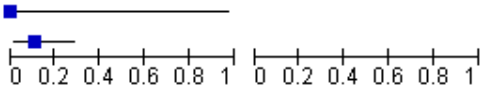
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	7	0	8	0	0.47 [0.21, 0.73]	Not estimable
Guo 2020a	62	0	20	0	0.76 [0.65, 0.84]	Not estimable
Jia 2020	19	0	5	0	0.79 [0.58, 0.93]	Not estimable
Liu 2020c	74	0	17	0	0.81 [0.72, 0.89]	Not estimable
Qian 2020	432	0	71	0	0.86 [0.83, 0.89]	Not estimable
Xie 2020a	15	0	10	0	0.60 [0.39, 0.79]	Not estimable



Test 48. IgM in PCR+ve (1 to 7 days)

IgM in PCR+ve (1 to 7 days)

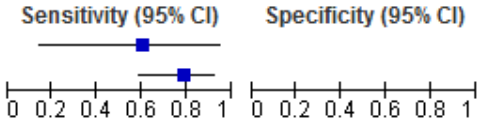
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	0	0	1	0	0.00 [0.00, 0.97]	Not estimable
Pan 2020a	3	0	24	0	0.11 [0.02, 0.29]	Not estimable



Test 49. IgM in PCR+ve (8 to 14 days)

IgM in PCR+ve (8 to 14 days)

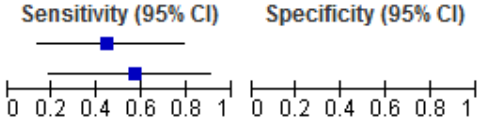
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	3	0	2	0	0.60 [0.15, 0.95]	Not estimable
Pan 2020a	22	0	6	0	0.79 [0.59, 0.92]	Not estimable



Test 50. IgM in PCR+ve (15 to 21 days)

IgM in PCR+ve (15 to 21 days)

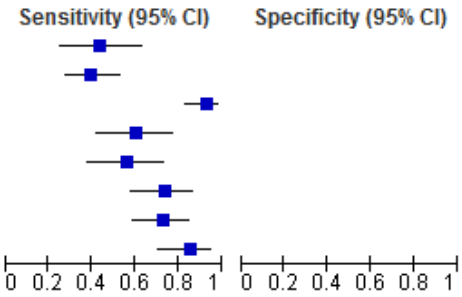
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	4	0	5	0	0.44 [0.14, 0.79]	Not estimable
Pan 2020a	4	0	3	0	0.57 [0.18, 0.90]	Not estimable



Test 51. IgM in PCR-ve (all time points)

IgM in PCR-ve (all time points)

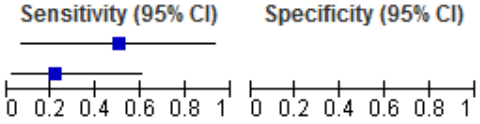
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	13	0	17	0	0.43 [0.25, 0.63]	Not estimable
Garcia 2020 (B)	25	0	38	0	0.40 [0.28, 0.53]	Not estimable
Guo 2020a	54	0	4	0	0.93 [0.83, 0.98]	Not estimable
Jia 2020	20	0	13	0	0.61 [0.42, 0.77]	Not estimable
Jin 2020	19	0	15	0	0.56 [0.38, 0.73]	Not estimable
Liu 2020c	31	0	11	0	0.74 [0.58, 0.86]	Not estimable
Qian 2020	38	0	14	0	0.73 [0.59, 0.84]	Not estimable
Xie 2020a	34	0	6	0	0.85 [0.70, 0.94]	Not estimable



Test 52. IgM in PCR-ve (1 to 7 days)

IgM in PCR-ve (1 to 7 days)

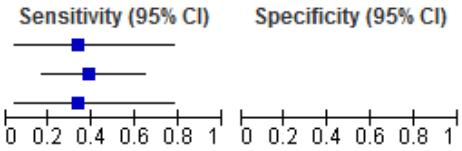
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	2	0	2	0	0.50 [0.07, 0.93]	Not estimable
Pan 2020a	2	0	7	0	0.22 [0.03, 0.60]	Not estimable



Test 53. IgM in PCR-ve (8 to 14 days)

IgM in PCR-ve (8 to 14 days)

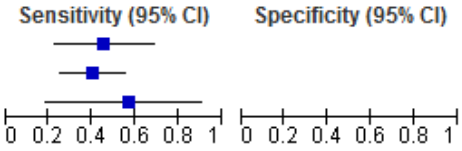
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	2	0	4	0	0.33 [0.04, 0.78]	Not estimable
Garcia 2020 (B)	7	0	11	0	0.39 [0.17, 0.64]	Not estimable
Pan 2020a	2	0	4	0	0.33 [0.04, 0.78]	Not estimable



Test 54. IgM in PCR-ve (15 to 21 days)

IgM in PCR-ve (15 to 21 days)

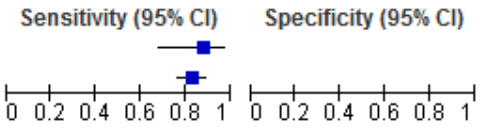
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	9	0	11	0	0.45 [0.23, 0.68]	Not estimable
Garcia 2020 (B)	18	0	27	0	0.40 [0.26, 0.56]	Not estimable
Pan 2020a	4	0	3	0	0.57 [0.18, 0.90]	Not estimable



Test 55. IgG/IgM in PCR+ve (all time points)

IgG/IgM in PCR+ve (all time points)

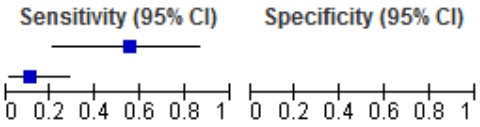
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jia 2020	21	0	3	0	0.88 [0.68, 0.97]	Not estimable
Liu 2020b	127	0	26	0	0.83 [0.76, 0.89]	Not estimable



Test 56. IgG/IgM in PCR+ve (1 to 7 days)

IgG/IgM in PCR+ve (1 to 7 days)

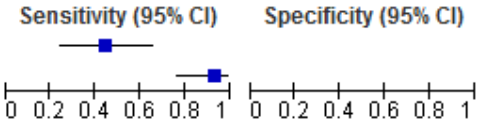
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020b	5	0	4	0	0.56 [0.21, 0.86]	Not estimable
Pan 2020a	3	0	24	0	0.11 [0.02, 0.29]	Not estimable



Test 57. IgG/IgM in PCR+ve (8 to 14 days)

IgG/IgM in PCR+ve (8 to 14 days)

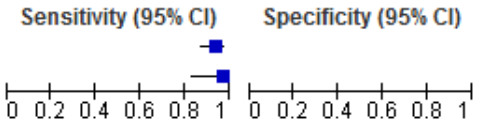
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020b	11	0	14	0	0.44 [0.24, 0.65]	Not estimable
Pan 2020a	26	0	2	0	0.93 [0.76, 0.99]	Not estimable



Test 58. IgG/IgM in PCR+ve (15 to 21 days)

IgG/IgM in PCR+ve (15 to 21 days)

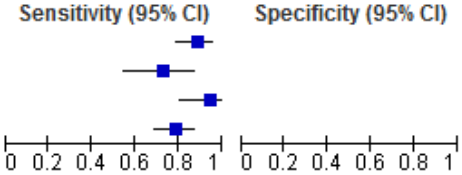
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020b	111	0	8	0	0.93 [0.87, 0.97]	Not estimable
Pan 2020a	30	0	1	0	0.97 [0.83, 1.00]	Not estimable



Test 59. IgG/IgM in PCR-ve (all time points)

IgG/IgM in PCR-ve (all time points)

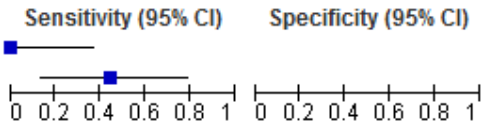
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Garcia 2020 (B)	56	0	7	0	0.89 [0.78, 0.95]	Not estimable
Jia 2020	24	0	9	0	0.73 [0.54, 0.87]	Not estimable
Jin 2020	32	0	2	0	0.94 [0.80, 0.99]	Not estimable
Liu 2020b	67	0	18	0	0.79 [0.69, 0.87]	Not estimable



Test 60. IgG/IgM in PCR-ve (1 to 7 days)

IgG/IgM in PCR-ve (1 to 7 days)

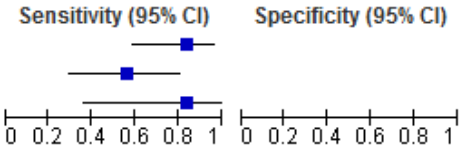
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020b	0	0	8	0	0.00 [0.00, 0.37]	Not estimable
Pan 2020a	4	0	5	0	0.44 [0.14, 0.79]	Not estimable



Test 61. IgG/IgM in PCR-ve (8 to 14 days)

IgG/IgM in PCR-ve (8 to 14 days)

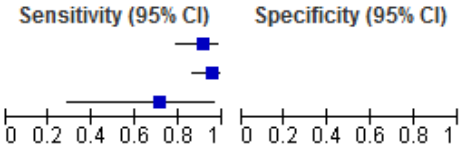
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Garcia 2020 (B)	15	0	3	0	0.83 [0.59, 0.96]	Not estimable
Liu 2020b	9	0	7	0	0.56 [0.30, 0.80]	Not estimable
Pan 2020a	5	0	1	0	0.83 [0.36, 1.00]	Not estimable



Test 62. IgG/IgM in PCR-ve (15 to 21 days)

IgG/IgM in PCR-ve (15 to 21 days)

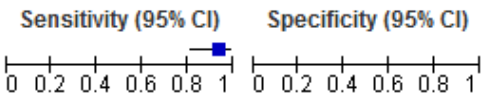
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Garcia 2020 (B)	41	0	4	0	0.91 [0.79, 0.98]	Not estimable
Liu 2020b	58	0	3	0	0.95 [0.86, 0.99]	Not estimable
Pan 2020a	5	0	2	0	0.71 [0.29, 0.96]	Not estimable



Test 63. IgG (moderate)

IgG (moderate)

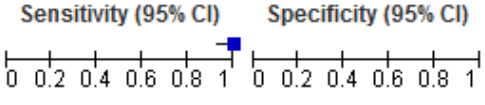
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020c	41	0	3	0	0.93 [0.81, 0.99]	Not estimable



Test 64. IgG (severe)

IgG (severe)

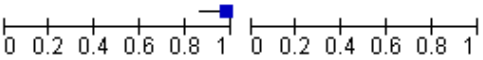
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020c	52	0	0	0	1.00 [0.93, 1.00]	Not estimable



Test 65. IgG (critical)

IgG (critical)

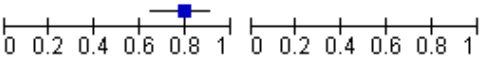
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020c	36	0	1	0	0.97 [0.86, 1.00]	Not estimable		



Test 66. IgM (moderate)

IgM (moderate)

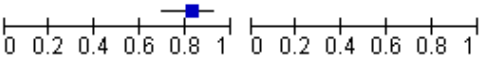
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020c	35	0	9	0	0.80 [0.65, 0.90]	Not estimable		



Test 67. IgM (severe)

IgM (severe)

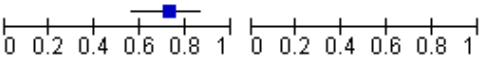
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020c	43	0	9	0	0.83 [0.70, 0.92]	Not estimable		



Test 68. IgM (critical)

IgM (critical)

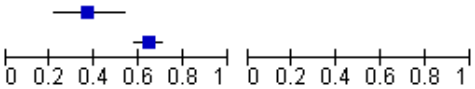
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Liu 2020c	27	0	10	0	0.73 [0.56, 0.86]	Not estimable		



Test 69. RT-PCR (all time points - throat)

RT-PCR (all time points - throat)

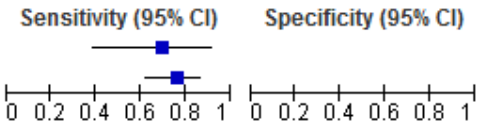
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	14	0	24	0	0.37 [0.22, 0.54]	Not estimable		
Liu 2020b	153	0	85	0	0.64 [0.58, 0.70]	Not estimable		



Test 70. RT-PCR (1 to 7 days throat)

RT-PCR (1 to 7 days throat)

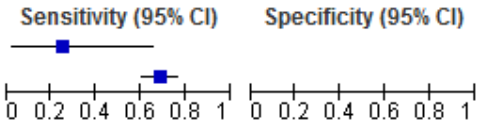
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	9	0	4	0	0.69 [0.39, 0.91]	Not estimable
Liu 2020b	41	0	13	0	0.76 [0.62, 0.87]	Not estimable



Test 71. RT-PCR (8 to 14 days - throat)

RT-PCR (8 to 14 days - throat)

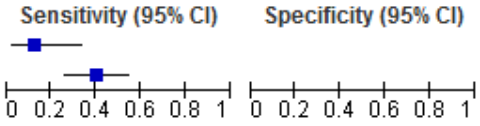
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	2	0	6	0	0.25 [0.03, 0.65]	Not estimable
Liu 2020b	92	0	42	0	0.69 [0.60, 0.76]	Not estimable



Test 72. RT-PCR (15 to 21 days - throat)

RT-PCR (15 to 21 days - throat)

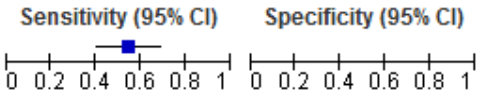
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	3	0	20	0	0.13 [0.03, 0.34]	Not estimable
Liu 2020b	20	0	30	0	0.40 [0.26, 0.55]	Not estimable



Test 73. RT-PCR (all time points - sputum)

RT-PCR (all time points - sputum)

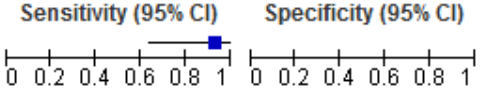
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	29	0	24	0	0.55 [0.40, 0.68]	Not estimable



Test 74. RT-PCR (1 to 7 days - sputum)

RT-PCR (1 to 7 days - sputum)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	12	0	1	0	0.92 [0.64, 1.00]	Not estimable



Test 75. RT-PCR (8 to 14 days - sputum)

RT-PCR (8 to 14 days - sputum)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	3	0	5	0	0.38 [0.09, 0.76]	Not estimable	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test 76. RT-PCR (15 to 21 days - sputum)

RT-PCR (15 to 21 days - sputum)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gao 2020a	14	0	9	0	0.61 [0.39, 0.80]	Not estimable	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

ADDITIONAL TABLES

Table 1. Description of studies

Participants		**Studies (percentage) (n=54 studies)**
Sample size	Median (IQR) 129.5 (57 to 347)	Min 10, max 3481
Number of COVID-19 cases	Median (IQR) 62 (31 to 151)	Min 3, max 555
Setting	Hospital inpatient	44 (81%)
	Hospital outpatient	1 (2%)
	Hospital accident and emergency	2 (4%)
	Community	2 (4%)
	Mixed or unclear	5 (9%)
Patient group	Asymptomatic	0 (0%)
	Asymptomatic and acute	1 (2%)
	Acute	23 (43%)
	Acute and convalescent	22 (41%)
	Convalescent	2 (4%)
	Mixed or unclear	6 (11%)
Study design		

Table 1. Description of studies *(Continued)*

Recruitment structure	Single group, both COVID-19 and non-COVID-19 cases	6 (11%)
	Single group, only COVID-19 cases	19 (35%)
	Two or more groups with COVID-19 and non-COVID-19 cases	29 (54%)
Reference standard for COVID-19 cases	All RT-PCR-positive	32 (59%)
	China CDC criteria including RT-PCR-negative patients	11 (20%)
	WHO criteria including RT-PCR-negative patients	1 (2%)
	Other criteria including RT-PCR-negative patients	3 (6%)
	Other	2 (4%)
	Mixed or unclear	5 (9%)
Reference standard for non-COVID-19	Pre-pandemic healthy	4 (7%)
	Pre-pandemic other disease	3 (6%)
	Pre-pandemic healthy + other disease	4 (7%)
	Current healthy (untested)	5 (9%)
	Current other disease (untested)	1 (2%)
	Current healthy + other disease (untested)	2 (4%)
	Current healthy + other disease (RT-PCR-negative)	2 (4%)
	COVID suspects, single RT-PCR-negative	8 (15%)
	COVID suspects, two or more RT-PCR–negative results	3 (6%)
	Mixed/other	3 (6%)
Tests		
Number of tests per study	1	40 (74%)
	2	8 (15%)
	3-5	4 (8%)
	6-10	2 (2%)
Test technology (n = 89)	CGIA	23 (26%)
	CLIA	20 (22%)

Table 1. Description of studies *(Continued)*

	ELISA	28 (31%)
	FIA	2 (2%)
	IIFT	1 (1%)
	LFA (no details)	10 (11%)
	LIPS	4 (4%)
	S-flow	1 (1%)
Test brand (n = 89)	Withheld	13 (%)
	Acro Biotech - IgG/IgM	1 (1%)
	Artron Laboratories IgM/IgG	1 (1%)
	Autobio Diagnostics IgM/IgG	1 (1%)
	Beijing Beier Bioengineering CGIA	1 (1%)
	Beijing Beier Bioengineering CLIA	1 (1%)
	Beijing Beier Bioengineering ELISA	1 (1%)
	Beijing Diagreat	1 (1%)
	Beijing Hotgen CGIA	1 (1%)
	Beijing Hotgen ELISA	2 (3%)
	Beijing Wantai CGIA	1 (1%)
	Beijing Wantai ELISA	3 (3%)
	Bioscience Co (Chongqing)	3 (3%)
	CTK Biotech OnSite IgG/IgM	1 (1%)
	Darui Biotech	1 (1%)
	Dynamiker Biotechnology IgG/IgM	1 (1%)
	EUROIMMUN	3 (3%)
	EUROIMMUN Anti-SARS-Cov	1 (1%)
	EUROIMMUN Beta	1 (1%)
	Hangzhou Alltest - IgG/IgM	3 (3%)
	Innovita Biological - Ab test (IgM/IgG)	2 (3%)
	Jiangsu Medomics IgG-IgM	1 (1%)

Table 1. Description of studies *(Continued)*

	Shenzhen YHLO	7 (8%)
	Snibe Diagnostic - MAGLUMI	2 (3%)
	Vivachek - VivaDiag IgM/IgG	3 (3%)
	Xiamen InnodDx Biotech	1 (1%)
	Zhuhai Livzon CGIA	2 (3%)
	Zhuhai Livzon ELISA	5 (6%)
	In-house, S-based ELISA	1 (1%)
	In-house, S-based LIPS	1 (1%)
	In-house, rN-based ELISA	1 (1%)
	In-house, rS-based ELISA	1 (1%)
	In-house CGIA	2 (2%)
	In-house CLIA	5 (6%)
	In-house ELISA	6 (7%)
	In-house FIA	1 (1%)
	In-house S-flow	1 (1%)
	In-house - N-based ELISA	1 (1%)
	In-house - N-based LIPS	2 (2%)
	In-house - S1-based LIPS	1 (1%)
	In-house - tri-S-based ELISA	1 (1%)
	In-house Anti-SARS-Cov ELISA	1 (1%)

Ab: antibody; **CDC:** Center for Disease Control and Prevention; **CGIA:** colloidal gold immunoassay; **CLIA:** chemiluminescence immunoassay; **ELISA:** enzyme-linked immunosorbent assay; **FIA:** fluorescence immunoassay; **IQR:** interquartile range; **IIFT:** indirect immunofluorescence assay; **LFA:** lateral flow assay; **LIPS:** luciferase immunoprecipitation system; **max:** maximum; **min:** minimum; **N-based:** nucleocapsid protein; **RT-PCR:** reverse transcription polymerase chain reaction; **S-based:** spike protein; **S-flow:** flow-cytometry assay; **WHO:** World Health Organization

Table 2. Test sensitivity by time since onset of symptoms

	Days 1-7	Days 8-14	Days 15-21	Days 22-35	Days > 35	Comparison
Test groups [studies] (true positives/COVID cases)						

Table 2. Test sensitivity by time since onset of symptoms *(Continued)*

	Sensitivity (95% CI)					
IgG	33 [23] (165/568)	34 [22] (766/1200)	34 [22] (974/1110)	20 [12] (417/502)	11 [4] (213/252)	
	29.7% (22.1 to 38.6)	66.5% (57.9 to 74.2)	88.2% (83.5 to 91.8)	80.3% (72.4 to 86.4)	86.7% (79.6 to 91.7)	P < 0.00005
IgM	34 [24] (207/608)	32 [21] (724/1171)	32 [21] (800/1074)	19 [11] (378/507)	11 [4] 118/215	
	23.2% (14.9 to 34.2)	58.4% (45.5 to 70.3)	75.4% (64.3 to 83.8)	68.1% (55.0 to 78.9)	53.9% (38.4 to 68.6)	P < 0.00005
IgA	4 [4] (54/100)	3 [3] (38/53)	3 [3] (66/68)	2 [2] (81/82)	1 [1] (23/23)	
	28.4% (0.9 to 94.3)	78.1% (9.5 to 99.2)	98.7% (39.0 to 100)	98.7% (91.9 to 99.8)	100% (85.2 to 100)	*
Total antibodies	5 [4] (62/144)	6 [5] (220/247)	6 [5] (174/176)	4 [3] (11/19)	2 [1] (15/28)	
	24.5% (9.5 to 50.0)	84.0% (64.1 to 93.9)	98.1% (90.1 to 99.6)	69.5% (34.8 to 90.7)	79.0% (49.8 to 93.4)	P < 0.00005
IgG/IgM	17 [9] (81/259)	21 [9] (441/608)	21 [9] (636/692)	16 [5] (146/152)	9 [2] (122/153)	
	30.1% (21.4 to 40.7)	72.2% (63.5 to 79.5)	91.4% (87.0 to 94.4)	96.0% (90.6 to 98.3)	77.7% (66.0 to 86.2)	P < 0.00005
IgA/IgG	1 [1] (0/12)	1 [1] (5/10)	1 [1] (7/8)	1 [1] (1/1)	0 [0]	
	0% (0 to 26.5)	50.0% (18.7 to 81.3)	87.5% (47.3 to 99.6)	100% (2.5 to 100)		*
IgA/IgM	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	

CI: confidence interval; * inadequate data to make a formal statistical comparison

Table 3. Specificity and impact of reference standard for non-COVID cases

	Overall specificity[a]	COVID suspects deemed negative	Current healthy or other disease	Pre-pandemic	Comparison of control groups
	Test groups [studies] (false positives/non-COVID cases) Specificity (95% CI)				
IgG	62 [44] (159/6136)	6 [6] (10/396)	14 [10] (60/2614)	19 [10] (88/2633)	

Table 3. Specificity and impact of reference standard for non-COVID cases *(Continued)*

	99.1% (98.3% to 99.6%)	98.0% (91.0% to 99.6%)	99.2% (97.6% to 99.8%)	99.2% (97.8% to 99.7%)	P = 0.56
IgM	59 [41] (183/6103)	5 [5] (12/384)	14 [10] (89/3069)	17 [9] (38/2075)	
	98.7% (97.4% to 99.3%)	98.1% (89.9% to 99.7%)	98.6% (96.0% to 99.5%)	99.3% (98.0% to 99.8%)	P = 0.50
IgG/IgM	34 [23] (78/5761)	7 [7] (33/454)	7 [5] (20/506)	18 [6] (22/1104)	No formal comparison possible
	98.7% (97.2% to 99.4%)	92.8% (89.7% to 95.0%)	99.9% (65.2% to 100%)	98.7% (96.6% to 99.5%)	
Total antibodies	16 [10] (41/3585)				
	99.2% (98.3% to 99.6%)				
IgA	4 [4] (10/663)				
	98.5% (97.2% to 99.2%)				
IgA/IgG [b]	2 [2] (1/528)				
	99.8% (98.9% to 100%)				
IgA/IgM [b]	1 [1] (1/483)				
	99.8% (99.2% to 100%)				

CI: confidence interval

[a]Includes studies that are categorised as mixed/other not included in the subgroups.
[b]Confidence intervals computed using binomial exact on totals.

Table 4. Reported cross-reactivity with SARS-CoV-2 antigens

Study	Test(s) evaluated	What the study says about cross-reactivity
Cai 2020	In-house CLIA	Reported no cross-reactivity in 167 sera from patients with infection with other pathogens (influenza A virus (25), respiratory syncytial virus (7), parainfluenza virus (8), influenza B virus (5), adenovirus (6), *Klebsiella pneumoniae* (8), *Streptococcus pneumoniae* (3), mycoplasma (5), *Acinetobacter baumannii* (10), *Candida albicans* (2), *Staphylococcus aureus* (3), *Mycobacterium tuberculosis* (4), hepatitis B virus (33), hepatitis C virus (22), syphilis (23) and saccharomycopsis (3)).
Freeman 2020	In-house ELISA	Reported cross-reactivity to SARS-CoV-2 spike protein in sera from patients with SARS-1 and MERS-CoV, and no cross-reactivity with NL63, OC43, HKU1, 229E

Table 4. Reported cross-reactivity with SARS-CoV-2 antigens *(Continued)*

Guo 2020a	In-house ELISA	Reported Western Blot cross-reactivity analysis in plasma samples positive for human CoV-229E, -NL63, -OC43, -HKU1, and SARS-CoV. Strong cross-reactivity was observed only for SARS-CoV.
Infantino 2020	Shenzhen YHLO CLIA	Observed no cross-reactivity in sample from blood donors from the COVID-19 era (winter 2019) but positive results in two samples from people with CMV infections and 2 with rheumatic disease.
Lassauniere 2020 [A]	[A] Beijing Wantai ELISA [B] EUROIMMUN IgG ELISA [C] EUROIMMUN IgA ELISA [D] Dynamiker Biotechnology LFA [E] CTK Biotech - OnSite LFA [F] Autobio Diagnostics LFA [G] Artron Laboratories LFA [H] Acro Biotech LFA [I] Hangzhou Alltest LFA	Included sera from patients with acute viral respiratory tract infections caused by other coronaviruses (n = 5) or non-coronaviruses (n = 45), and sera from patients positive for dengue virus (n = 9), CMV (n = 2) and Epstein Barr virus (n = 10). Cross reaction was observed for the EUROMIMMUN IgA ELISA (> 1 respiratory virus present, adenovirus, dengue virus) and for the EUROMIMMUN IgG ELISA (coronavirus HKU1 and adenovirus). Some cross-reactivity also observed for CGIA tests. Study authors suggest related to antigen target and ELISA format.
Ma 2020a	In-house CLIA	Limited detail but suggests limited cross-reaction
Wang 2020a [A]	A. Beijing Hotgen IgM CGIA B. Beijing Hotgen IgM ELISA	Demonstrated considerable cross-reaction with rheumatoid factor IgM (22/36 false positive results). Other pathogens included influenza A virus (n = 5), influenza B virus (n = 5), *Mycoplasma pneumoniae* (n = 5), *Legionella pneumophila* (n = 5), HIV infection (n = 6), hypertension (n = 5) and diabetes mellitus (n = 5)
Zhang 2020b	Shenzhen YHLO CLIA	Observed false positive results in influenza A and B (2 each), adenovirus (n = 4) and *Mycoplasma pneumoniae* (n = 17).
Zhang 2020d	In-house CGIA (co-author Beijing Hotgen)	Appears to report a separate cross-reactivity study for influenza A, influenza B, respiratory syncytial virus, *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*. No cross reactions were observed.

CGIA: colloidal gold immunoassay; **CLIA:** Chemiluminescence immunoassay; **CMV:** cytomegalovirus; **ELISA:** enzyme-linked immunosorbent assay; **LFA:** lateral flow assay; **MERS:** Middle East respiratory syndrome; **SARS:** severe acute respiratory syndrome

Table 5. Investigation of impact of reference standard on sensitivity

	RT-PCR-positive COVID-19 cases	RT-PCR-negative COVID-19 cases	Comparison
	Test groups [studies] (true positives/COVID cases)		

Table 5. Investigation of impact of reference standard on sensitivity *(Continued)*

	Sensitivity (95% CI)[a]		
IgG	26 [15] (1555/2280)	8 [8] (925/1300)	
	87.9% (82.7 to 91.7)	91.2% (83.9 to 95.4)	P = 0.36
IgM	23 [13] (1368/2166)	10 [9] (792/1292)	
	70.8% (56.3 to 82.0)	87.5% (73.7 to 94.6)	P = 0.06
IgG/IgM	17 [6] (966/1278)	4 [4] (400/499)	
	90.6% (86.6 to 93.5)	93.6% (88.9 to 96.4)	P = 0.22

CI: confidence interval; **RT-PCR:** reverse transcription polymerase chain reaction

[a]We obtained sensitivity estimates from a model of all data stratified by week, estimating the average difference in sensitivity across follow-up. The figures quoted correspond to the week 3 strata (15-21 days) in the model.

Table 6. Studies reporting sensitivity in both RT-PCR-positive and RT-PCR-negative subgroups

	RT-PCR-positive COVID-19 cases		RT-PCR-negative COVID-19 cases	
	Test groups [studies] (True positives/COVID-19 cases)	**Sensitivity (95% CI)**	**Test groups [studies] (True positives/COVID-19 cases)**	**Sensitivity (95% CI)**
IgG				
Days 1-7[b]	2 [2] (1/28)		2 [2] (8/13)	
Days 8-14[b]	2 [2] (21/33)		3 [3] (25/30)	
Days 15-21[b]	2 [2] (39/40)		3 [3] (64/72)	
Pooled[a] (stratified by time)		72.6% (46.2% to 89.1%)		84.0% (64.4% to 93.9%)
Test for difference in sensitivity between RT-PCR-positive and RT-PCR-negative groups: P = 0.18				
IgM				
Days 1-7[b]	2 [2] (3/28)		2 [2] (4/13)	
Days 8-14[b]	2 [2] (25/33)		3 [3] (11/30)	
Days 15-21[b]	2 [2] (8/16)		3 [3] (31/72)	
Pooled[a] (stratified by time)		64.6% (49.7% to 77.1%)		49.0% (34.2% to 63.9%)
Test for difference in sensitivity between RT-PCR-positive and RT-PCR-negative group: P = 0.07				
IgG/IgM				

Table 6. Studies reporting sensitivity in both RT-PCR-positive and RT-PCR-negative subgroups *(Continued)*

Days 1-7[b]	2 [2] (8/36)	2 [2] (4/17)	
Days 8-14[b]	2 [2] (37/53)	3 [3] (29/40)	
Days 15-21[b]	2 [2] (141/150)	3 [3] (104/113)	
Pooled[a] (stratified by time)		71.9% (58.7% to 82.2%)	71.1% (57.0% to 82.0%)
Test for difference in sensitivity between RT-PCR-positive and RT-PCR-negative group: P = 0.90			

CI: confidence interval; **RT-PCR:** reverse transcription polymerase chain reaction

[a]The sensitivity estimates are produced from a model that combines all data from both subgroups and time-groups, stratifying by time-group. The estimate corresponds to sensitivity in Days 15-21.
[b]RT-PCR-positive data have only been included here when the study includes a RT-PCR-negative subgroup as well.

Table 7. Sensitivity and specificity by test technology

		Test method				
	Test method	**CGIA**	**CLIA**	**ELISA**	**LFA**	**Comparison**
IgG						
	Test groups [studies] (True positives/COVID cases)	6 [5] (268/397)	10 [10] (1112/1432)	12 [11] (1014/1552)	7 [1] (133/238)	
	Sensitivity (95% CI)[a]	87.3% (77.0 to 93.4)	94.6% (90.7 to 97.0)	85.8% (78.0 to 91.1)	76.0% (61.0 to 86.5)	P = 0.004
	Test groups [studies] (True negatives/non-COVID cases)	11 [11] (409/415)	12 [12] (318/322)	18 [16] (2003/2102)	6 [1] (354/360)	
	Specificity (95% CI)[a]	99.5% (96.5 to 99.9)	99.0% (91.6 to 99.9)	98.8% (96.5 to 99.6)	99.0% (95.3 to 99.8)	P = 0.85
IgM						
	Test groups [studies] (True positives/COVID cases)	7 [6] (109/411)	10 [10] (884/1355)	12 [11] (1083/1568)	7 [1] (78/228)	
	Sensitivity (95% CI)[a]	69.5% (44.3 to 86.7)	80.9% (63.8 to 91.0)	84.5% (70.7 to 92.5)	51.4% (26.5 to 75.6)	P = 0.11
	Test groups [studies] (True negatives/non-COVID cases)	12 [11] (455/487)	13 [13] (609/621)	14 [12] (1674/1710)	6 [1] (357/360)	

Table 7. Sensitivity and specificity by test technology *(Continued)*

	Specificity (95% CI)[a]	97.3 (90.0 to 99.3)	98.5 (92.3 to 99.7)	99.1 (97.2 to 99.7)	99.6 (97.3 to 99.9)	P = 0.40
IgG/ IgM						
	Test groups [studies] **(True positives/COVID cases)**	4 [3] (232/316)	3 [3] (344/420)	5 [4] (595/770)	11 [2] (255/358)	
	Sensitivity (95% CI)[a]	90.7% (82.7 to 95.2)	97.5% (94.0 to 99.0)	90.7% (83.3 to 95.0)	88.6% (82.0 to 93.0)	P = 0.02
	Test groups [studies] **(True negatives/non-COVID cases)**	11 [11] (330/353)	5 [4] (230/244)	5 [4] (387/391)	13 [3] (3797/3827)	
	Specificity (95% CI)[a]	96.0 (90.1 to 98.5)	94.1 (82.7 to 98.2)	99.4 (97.4 to 99.9)	98.2 (96.3 to 99.1)	P = 0.05

CGIA: colloidal gold immunoassay; **CI:** confidence interval; **CLIA:** chemiluminescence immunoassay; **ELISA:** enzyme-linked immunosorbent assay; **LFA:** lateral flow assay (no further detail)

[a]We obtained sensitivity estimates from a model of all data stratified by week, estimating the average difference in sensitivity across follow-up. The figures quoted correspond to the Week 3 (15-21 days) strata in the model.

Table 8. Sensitivity and specificity by test brand (IgG)

Test name[a]	Test method	IgG sensitivity by time since onset of symptoms Studies (true positives/COVID-19 cases) Sensitivity (95% CI)					IgG specificity Studies (false positives/COVID-19 cases) Specificity (95% CI)
		1-7 days	8-14 days	15-21 days	22-35 days	> 35 days	
Beijing Beier Bioengineering	CGIA	1 (2/10)	1 (6/13)	1 (11/14)			
		20.0% (2.5 to 55.6)	46.2% (19.2 to 74.9)	78.6% (49.2 to 95.3)			
Beijing Beier Bioengineering	CLIA	1 (4/10)	1 (6/13)	1 (9/14)			
		40.0% (12.2 to 73.8)	46.2% (19.2 to 74.9)	64.3% (35.1 to 87.2)			
Beijing Beier Bioengineering	ELISA	1 (4/10)	1 (8/13)	1 (12/14)			
		40.0% (12.2 to 73.8)	61.5% (31.6 to 86.1)	85.7% (57.2 to 98.2)			
Beijing Hotgen	ELISA	1 (9/22)	1 (60/92)	1 (51/55)	1 (39/45)		2 (22/172)
		40.9% (20.7 to 63.6)	65.2% (54.6 to 74.9)	92.7% (82.4 to 98.0)	86.7% (73.2 to 94.9)		87.2% (81.3 to 91.8)
Beijing Wantai	ELISA	2 (31/133)	2 (130/210)	2 (127/149)			2 (2/297)
		23.3% (16.4 to 31.4)	61.9% (55.0 to 68.5)	85.2% (78.5 to 90.5)			99.3% (97.6 to 99.9)
Beijing Wantai	CGIA						1 (1/209)
							99.5% (97.4 to 100)
Bioscience Co (Chongqing)	CLIA	2 (43/92)	2 (129/212)	2 (208/244)	2 (98/164)	1 (75/76)	
		46.7% (36.3 to 57.4)	60.8% (53.9 to 67.5)	85.2% (80.2 to 89.4)	59.8% (51.8 to 67.3)	98.6% (92.9 to 100)	

Table 8. Sensitivity and specificity by test brand (IgG) *(Continued)*

Darui Biotech	ELISA						1 (0/64)
							100% (94.4 to 100)
EUROIMMUN	ELISA	1 (2/13)	2 (13/25)	2 (14/15)	2 (98/164)		2 (3/82)
		15.4% (1.9 to 45.4)	52.0% (31.3 to 72.2)	93.3% (68.1 to 99.8)	59.8% (51.8 to 67.3)		96.3% (89.7 to 99.2)
EUROIMMUN Anti-SARS-Cov	IIFT	1 (1/4)	1 (3/5)	1 (3/3)	1 (1/1)		1 (0/10)
		25.0% (0.6 to 80.6)	60.0% (14.7 to 94.7)	100% (29.2 to 100)	100% (2.5 to 100)		100% (69.2 to 100)
EUROIMMUN Beta	ELISA	1 (0/12)	1 (3/10)	1 (7/8)	1 (1/1)		1 (0/45)
		0% (0 to 26.5)	30%.0% (14.7 to 94.7)	87.5% (47.3 to 99.7)	100% (2.5 to 100)		100% (92.1 to 100)
Hangzhou Alltest - IgG/IgM	CGIA	1 (1/8)	2 (21/42)	2 (57/68)			2 (0/45)
		12.5% (0.3 to 52.7)	50.0% (34.2 to 65.8)	83.8% (72.9 to 91.6)			100% (92.1 to 100)
Innovita Biological - Ab test (IgM/IgG)	CGIA	1 (7/13)	1 (7/8)	1 (21/23)			
		53.8% (25.1 to 80.8)	87.5% (47.3 to 99.7)	91.3% (72.0 to 98.9)			
Shenzhen YHLO	CLIA	2 (2/8)	2 (28/29)	2 (25/26)	2 (64/64)	1 (7/7)	7 (4/322)
		25.0% (3.2 to 65.1)	96.6% (82.2 to 99.9)	96.2% (80.4 to 99.9)	100% (94.4 to 100)	100% (59.0 to 100)	98.8% (96.9 to 99.7)
Snibe Diagnostic - MAGLUMI	CLIA	2 (11/40)	2 (35/48)	25/25			
		27.5% (14.6 to 43.9)	72.9% (58.2 to 84.7)	100.0% (86.3 to 100)			
Vivachek - VivaDiag IgM/IgG	CGIA						2 (0/42)

Table 8. Sensitivity and specificity by test brand (IgG) *(Continued)*

						100% (91.6 to 100)
Zhuhai Livzon	CGIA	1 (5/36)	1 (20/34)	1 (35/38)		2 (0/35)
		13.9% (4.7 to 29.5)	58.8% (40.7 to 75.4)	92.1% (78.6 to 98.3)		100% (90.0 to 100)
Zhuhai Livzon	ELISA	4 (17/80)	3 (163/288)	3 (197/223)	2 (91/104)	5 (5/351)
		21.3% (12.9 to 31.8)	56.6% (50.7 to 62.4)	88.3% (83.4 to 92.2)	87.5% (79.6 to 93.2)	98.6% (96.7 to 99.5)

CGIA: colloidal gold immunoassay; **CI:** confidence interval; **CLIA:** chemiluminescence immunoassay; **ELISA:** enzyme-linked immunosorbent assay; **FIA:** fluorescence immunoassay; **IIFT:** indirect immunofluorescence assay; **LFA:** lateral flow assay

[a]See Appendix 12 for details of manufacturer product codes, where available.

Table 9. Sensitivity and specificity by test brand (IgM)

Test name[a]	**Test method**	**IgM sensitivity by time since onset of symptoms** **Studies (true positives/COVID-19 cases)** **Sensitiivity (95% CI)**					IgM s**pecificity** **Studies (false positives/COVID-19 cases)** **Specificity (95% CI)**
		1-7 days	**8-14 days**	**15-21 days**	**22-35 days**	**> 35 days**	
Artron Laboratories IgM/IgG	CGIA		1 (5/7)	1 (12/15)	1 (8/8)		
			71.4% (29.0 to 96.3)	80.0% (51.9 to 95.7)	100% (63.1 to 100)		
Autobio Diagnostics IgM/IgG	CGIA		1 (6/7)	1 (14/15)	1(8/8)		
			85.7% (42.1 to 99.6)	93.3% (68.1 to 99.8)	100% (63.1 to 100)		
Beijing Hotgen	ELISA	1 (10/22)	1 (72/92)	1 (72/92)	1 (41/45)		1 (0/100)

Table 9. Sensitivity and specificity by test brand (IgM) *(Continued)*

		45.5% (24.4 to 67.8)	78.3% (68.4 to 86.2)	78.3% (68.4 to 86.2)	91.1% (78.8 to 97.5)	100% (96.4 to 100)
Beijing Hotgen	CGIA					1 (22/72)
						69.4% (57.5 to 79.8)
Beijing Wantai	ELISA					1 (3/513)
						99.4% (98.3 to 99.9)
Beijing Wantai	CGIA					1 (4/209)
						98.1% (95.2 to 99.5)
Bioscience Co (Chongqing)	CLIA	1 (34/67)	1 (34/67)	1 (131/134)	1 (13/13)	
		50.7% (38.2 to 63.2)	50.7% (38.2 to 63.2)	97.8% (93.6 to 99.5)	100% (75.3 to 100)	
CTK Biotech OnSite IgG/IgM	CGIA		1 (5/7)	1 (14/15)	1 (8/8)	
			71.4% (29.0 to 96.3)	93.3% (68.1 to 99.8)	100% (63.1 to 100)	
Darui Biotech	ELISA					1 (14/64)
						78.1% (66.0 to 87.5)
Dynamiker Biotechnology IgG/IgM	CGIA		1 (5/7)	1 (14/15)	1 (8/8)	
			71.4% (29.0 to 96.3)	93.3% (68.1 to 99.8)	100% (63.1 to 100)	
EUROIMMUN	ELISA					1 (76/82)
						92.7% (84.8 to 97.3)

Table 9. Sensitivity and specificity by test brand (IgM) *(Continued)*

EUROIMMUN Anti-SARS-Cov	IIFT					1 (1/10)
						90.0% (55.5 to 99.7)
Hangzhou Alltest - IgG/IgM	CGIA	1 (1/8)	2 (23/42)	2 (58/68)		2 (0/45)
		12.5% (0.3 to 52.7)	54.8% (38.7 to 70.2)	85.3% (74.6 to 92.7)		100% (92.1 to 100)
Shenzhen YHLO	CLIA					7 (10/321)
						96.9% (94.3 to 98.5)
Vivachek - VivaDiag IgM/IgG	CGIA					2 (1/42)
						97.6% (87.4 to 99.9)
Xiamen InnodDx Biotech	CLIA					1 (2/300)
						99.3% (97.6 to 99.9)
Zhuhai Livzon	CGIA	1 (7/36)	1 (31/34)	1 (35/38)		2 (0/35)
		19.4% (8.2 to 36.0)	91.2% (76.3 to 98.1)	92.1% (78.6 to 98.3)		100% (90.0 to 100)
Zhuhai Livzon	ELISA	3 (14/66)	2 (150/202)	2 (159/166)	1 (43/45)	5 (3/351)
		21.2% (12.1 to 33.0)	74.3% (67.7 to 80.1)	95.8% (91.5 to 98.3)	95.6% (84.9 to 99.5)	99.1% (97.5 to 99.8)

CGIA: colloidal gold immunoassay; **CI:** confidence interval; **CLIA:** chemiluminescence immunoassay; **ELISA:** enzyme-linked immunosorbent assay; **FIA:** fluorescence immunoassay; **IIFT:** indirect immunofluorescence assay; **LFA:** lateral flow assay

[a]See Appendix 12 for details of manufacturer product codes, where available.

Table 10. Sensitivity and specificity by test brand (IgG/IgM)

Test name[a]	Test method	IgG/IgM sensitivity by time since onset of symptoms				IgG/IgM specificity

Table 10. Sensitivity and specificity by test brand (IgG/IgM) *(Continued)*

		Studies (true positives/COVID-19 cases) Sensitiivity (95% CI)					Studies (false positives/COVID-19 cases) Specificity (95% CI)
		1-7 days	**8-14 days**	**15-21 days**	**22-35 days**	**> 35 days**	
Acro Biotech - IgG/IgM	CGIA						1 (3/15)
							80.0% (51.9 to 95.7)
Artron Laboratories IgM/IgG	CGIA		1 (5/7)	1 (12/15)	1 (8/8)		1 (0/17)
			71.4% (29.0 to 96.3)	80.0% (51.9 to 95.7)	100% (63.1 to 100)		100% (80.5% to 100)
Autobio Diagnostics IgM/IgG	CGIA		1 (6/7)	1 (14/15)	1(8/8)		1 (0/32)
			85.7% (42.1 to 99.6)	93.3% (68.1 to 99.8)	100% (63.1 to 100)		100% (89.1 to 100)
Beijing Hotgen	ELISA	1 (10/22)	1 (72/92)	1 (72/92)	1 (41/45)		1 (0/100)
		45.5% (24.4 to 67.8)	78.3% (68.4 to 86.2)	78.3% (68.4 to 86.2)	91.1% (78.8 to 97.5)		100% (96.4 to 100)
Bioscience Co (Chongqing)	CLIA	1 (34/67)	1 (34/67)	1 (131/134)	1 (13/13)		2 (7/148)
		50.7% (38.2 to 63.2)	50.7% (38.2 to 63.2)	97.8% (93.6 to 99.5)	100% (75.3 to 100)		95.3% (90.5 to 98.1)
CTK Biotech OnSite IgG/IgM	CGIA		1 (5/7)	1 (14/15)	1 (8/8)		1 (0/32)
			71.4% (29.0 to 96.3)	93.3% (68.1 to 99.8)	100% (63.1 to 100)		100% (89.1 to 100)
Dynamiker Biotechnology IgG/IgM	CGIA		1 (5/7)	1 (14/15)	1 (8/8)		1 (0/32)

Table 10. Sensitivity and specificity by test brand (IgG/IgM) *(Continued)*

			71.4% (29.0 to 96.3)	93.3% (68.1 to 99.8)	100% (63.1 to 100)	100% (89.1 to 100)
Hangzhou Alltest - IgG/IgM	CGIA	1 (1/8)	2 (23/42)	2 (58/68)		3 (2/60)
		12.5% (0.3 to 52.7)	54.8% (38.7 to 70.2)	85.3% (74.6 to 92.7)		96.7% (88.5 to 99.6)
Shenzhen YHLO	CLIA					2 (7/96)
						92.7% (85.6 to 97.0)
Vivachek - VivaDiag IgM/IgG	CGIA					3 (14/162)
						91.4% (85.9 to 95.2)
Zhuhai Livzon	CGIA	1 (7/36)	1 (31/34)	1 (35/38)		2 (0/35)
		19.4% (8.2 to 36.0)	91.2% (76.3 to 98.1)	92.1% (78.6 to 98.3)		100% (90.0 to 100)
Zhuhai Livzon	ELISA	3 (14/66)	2 (150/202)	2 (159/166)	1 (43/45)	4 (4/291)
		21.2% (12.1 to 33.0)	74.3% (67.7 to 80.1)	95.8% (91.5 to 98.3)	95.6% (84.9 to 99.5)	98.6% (96.5 to 99.6)

CGIA: colloidal gold immunoassay; **CI:** confidence interval; **CLIA:** chemiluminescence immunoassay; **ELISA:** enzyme-linked immunosorbent assay; **FIA:** fluorescence immunoassay; **IIFT:** indirect immunofluorescence assay; **LFA:** lateral flow assay

[a]See Appendix 12 for details of manufacturer product codes, where available.

APPENDICES

Appendix 1. Summary of World Health Organization and Chinese National Health Commission Guidelines for the diagnosis of SARS-CoV-2

Table A: World Health Organization guidelines for the diagnosis of SARS-CoV-2[a]

Includes laboratory testing guidelines and global surveillance guidelines

Date range (2020)	Definition of confirmed case	Definition of confirmed non-case	Definition of suspect case	Definition of probable case	Role of serology in testing
10-30 January	10-30 January: no documentation to define at this time (before first date of global guidelines) 31 January onwards: a confirmed case is a person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms. No prescribed test in laboratory guidelines, suggested tests from 10 January include broad coronavirus RT-PCR (with sequencing of precise virus in test positives), whole genome sequencing, broad coronavirus serology on paired samples, microscopy, culture. (Lab 10 January) Four suggested tests from 17 January: broad coronavirus RT-PCR (with sequencing of precise virus in test positives), NAAT for SARS-CoV-2 when it becomes available, whole genome sequencing, and broad coronavirus serology on paired samples.	None stated	No definition of 'suspect case' at this time, but case definitions for surveillance are defined as a combination of symptoms and exposure, with more severe symptoms requiring less evidence for exposure	No definition at this time	Serological testing may be useful to confirm immunologic response to a pathogen from a specific viral group, e.g. coronavirus. Best results from serologic testing requires the collection of paired serum samples (in the acute and convalescent phase) from cases under investigation.
31 January-26 February	States that once specific NAAT assays are developed and validated, confirmation will be based on specific detection of unique sequences of viral nucleic acid by RT-PCR.	None stated	Suspect case defined as combination of symptoms and exposure, with more severe symptoms requiring less evidence for exposure	A suspect case with inconclusive laboratory results or is test-positive using a pan-coronavirus assay without laboratory evidence of other respiratory pathogens. (global 31 January)	
27 February-1 March		None stated	Suspect case defined as combination of symptoms and exposure, with more severe symp-	A suspected case with inconclusive laboratory results	
2 March-19 March	A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms. (global 31 January, 27 February, 20 March)	One or more negative			In cases where NAAT assays are negative and

(Continued)

19 March-present	Laboratory confirmation of cases by NAAT specific to SAR-CoV-2 such as real-time reverse-transcription polymerase chain reaction (rRT-PCR) with confirmation by nucleic acid sequencing when necessary. The viral genes targeted so far include the N, E, S and RdRP genes. In areas with no known COVID-19 virus circulation confirmation requires: • NAAT positive for at least two different targets on the COVID-19 virus genome, of which at least one target is preferably specific for COVID-19 virus (or SARS-like coronavirus) using a validated assay; OR • NAAT-positive result for betacoronavirus, and COVID-19 virus identified by sequencing partial/whole genome of virus (sequence target larger or different from the amplicon probed in the NAAT assay). Discordant results should be resampled. In areas where COVID-19 virus is widely spread a simpler algorithm might be adopted (e.g. RT-PCR of a single discriminatory target)	results do not rule out the possibility of COVID-19 virus infection.	toms requiring less evidence for exposure, OR defined by symptoms requiring hospitalisation and an absence of alternative explanation.	(global 27 February) Probable case A suspect case for whom testing for the COVID-19 virus is inconclusive. OR A suspect case for whom testing could not be performed for any reason.	there is a strong epidemiological link to COVID-19 infection, paired serum samples (in the acute and convalescent phase) could support diagnosis once validated serology tests are available. Serological assays will play an important role in research and surveillance but are not currently recommended for case detection.

NAAT: nucleic acids amplification test; **RT-PCR:** reverse transcription polymerase chain reaction; Source: WHO 2020.

[a]Source data from *Laboratory testing of 2019 novel coronavirus (2019-nCoV) in suspected human cases: interim guidance, World Health Organization*. (2020), 10 January, 17January, 2nd March, 19 March, 21st March, and *Global surveillance for COVID-19 caused by human infection with COVID-19 virus, interim guidance*, 31st January, 27 February, and 20 March.

Table B: Summary of Chinese National Health Commission guidelines for diagnosis and treatment for novel coronavirus pneumonia (trial versions 1-7)

Dates in effect	Definition of confirmed case	Definition of confirmed non-case	Definition of suspect case	Role of serology in testing
16-17 January 2020 (version 1)	Cases (not confirmed cases) defined as virus genome highly homologous to coronaviruses	Not defined	Observation cases: defined as combination of exposure in Wuhan and symptoms focused on pneumonia, leukopenia and lack of improvement.	No role
18 January-2 March (versions 2, 3, 4, 5, 5 revised, and 6)	Suspect cases with either • real-time fluorescent RT-PCR indicates positive for new coronavirus nucleic acid; OR • viral gene sequence is highly homologous to known new coronaviruses.	Suspect cases can be ruled out after 2 consecutive negative respiratory tract nucleic acid tests taken at least 24-hours apart.	Suspect cases: combination of exposure (such as residence in/travel to Wuhan or exposure to a confirmed case within 14 days of onset) AND clinical features (such as symptoms: fever, respiratory symptoms, and tests: chest imaging, white blood cell and lymphocyte count). Exact definition varies slightly with version	No role
3 March-present (version 7)	Suspect cases with either	Suspect cases can be ruled out after 2 negative NAATs,	Suspect cases: combination of exposure (such as residence in/travel to Wuhan or exposure to a confirmed	Part of definition of cases and

(Continued)

• real-time fluorescent RT-PCR indicates positive for new coronavirus nucleic acid; OR • viral gene sequence is highly homologous to known new coronaviruses. OR • NCP virus-specific IgM and IgG are detectable in serum; NCP virus-specific IgG is detectable or reaches a titration of at least 4-fold increase during convalescence compared with the acute phase.	taken at least 24-hours apart, and the NCP virus-specific IgM and IgG are negative after 7 days from onset.	case within 14 days of onset) AND clinical features (such as symptoms: fever, respiratory symptoms, and tests: chest imaging, white blood cell and lymphocyte count).	confirmed non-cases

NAAT: nucleic acids amplification test; **NCP:** novel coronavirus pneumonia; **RT-PCR:** reverse transcription polymerase chain reaction; Source: CDC China 2020.

Appendix 2. Antibody test 'use case' scenarios

Use Case[a]	Advantages	Limitations	Considerations
Diagnosis			
Aid diagnosis of suspect cases, especially when RT-PCR negative but X-Ray/CT suggestive	May improve overall sensitivity of diagnosis Diagnosis of patients presenting late or for post-infectious syndromes (low viral load) Diagnosis of patients when lower respiratory tract sampling not available	Unlikely to catch early-stage infection (< 7 days) May not detect asymptomatic cases Negative test cannot rule out infection IgM appears early, but is less specific	Total antibody may have best sensitivity Should be confirmed by PCR, where possible Rising titres and seroconversion can improve sensitivity and specificity
Aid diagnosis of suspect cases when PCR is not available **(would require careful development of interpretive guidelines)**	As above and could enable decentralised/community testing in settings where the availability of PCR testing is limited.		
Identification of individuals with protective immune status **(conditional upon identifying correlates of protection for SARS-CoV-2)**			
Identify convalescent plasma donors	Treatment for critically ill patients	Ideal timing of collection unknown to optimise efficaciousness	Preferentially patients recovered from moderate to severe disease (high titre). Theoretically may be derived from vaccinated donors

CT: computed tomography; **RT-PCR:** reverse transcription polymerase chain reaction;

[a]Table from Cheng 2020b

Appendix 3. Cochrane COVID-19 Study Register searches

Source	Strategy
CT.gov	COVID-19[a]
WHO ICTRP	Health topic: 2019-nCov / COVID-19
PubMed	(("2019 nCoV"[tiab] OR 2019nCoV[tiab] OR "2019 novel coronavirus"[tiab] OR "COVID 19"[tiab] OR COVID19[tiab] OR "new coronavirus"[tiab] OR "novel coronavirus"[tiab] OR "novel corona virus"[tiab] OR "SARS CoV-2"[tiab] OR (Wuhan[tiab] AND (coronavirus[tiab] OR "corona virus"[tiab])) OR "COVID-19"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])) NOT (editorial[pt] OR comment[pt] OR letter[pt] OR newspaper article[pt])

[a]Automatic term mapping links results for 2019-nCoV, 2019 novel coronavirus, SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Appendix 4. Living search from the University of Bern

The following information is taken from the university of Bern website (see: ispmbern.github.io/covid-19/living-review/collectingdata.html).

The register is updated daily and CSV file downloads are made available.

1 April 2020

From 1 April 2020, we will retrieve the curated BioRxiv/MedRxiv dataset (connect.medrxiv.org/relate/content/181).

26 to 31 March 2020

MEDLINE: (\"Wuhan coronavirus\" [Supplementary Concept] OR \"COVID-19\" OR \"2019 ncov\"[tiab] OR ((\"novel coronavirus\"[tiab] OR \"new coronavirus\"[tiab]) AND (wuhan[tiab] OR 2019[tiab])) OR 2019-nCoV[All Fields] OR (wuhan[tiab] AND coronavirus[tiab])))))

Embase: (nCoV or 2019-nCoV or ((new or novel or wuhan) adj3 coronavirus) or covid19 or covid-19 or SARS-CoV-2).mp.

BioRxiv/MedRxiv: ncov or corona or wuhan or COVID or SARS-CoV-2

With the kind support of the Public Health & Primary Care Library PHC (www.unibe.ch/university/services/university_library/faculty_libraries/medicine/public_health_amp_primary_care_library_phc/index_eng.html), and following guidance of the Medical Library Association (www.mlanet.org/p/cm/ld/fid=1713).

1 January 2020 to 25 March 2020

MEDLINE: ("Wuhan coronavirus" [Supplementary Concept] OR "COVID-19" OR "2019 ncov"[tiab] OR (("novel coronavirus"[tiab] OR "new coronavirus"[tiab]) AND (wuhan[tiab] OR 2019[tiab])) OR 2019-nCoV[All Fields] OR (wuhan[tiab] AND coronavirus[tiab])))))

Embase: ncov OR (wuhan AND corona) OR COVID

BioRxiv/MedRxiv: ncov or corona or wuhan or COVID

Appendix 5. CDC Library, COVID-19 Research Articles Downloadable Database

Embase records from the Stephen B. Thacker CDC Library, Covid-19 Research articles Downloadable database

Records were obtained by the CDC library by searching Embase through Ovid using the following search strategy.

Source	Strategy

(Continued)

Embase	coronavir* OR corona virus* OR betacoronavir* OR covid19 OR covid 19 OR nCoV OR novel CoV OR CoV 2 OR CoV2 OR sarscov2 OR 2019nCoV OR wuhan virus*).mp. OR ((wuhan OR hubei OR huanan) AND (severe acute respiratory OR pneumonia*) AND outbreak*).mp. OR Coronavirus infection/ OR coronavirinae/ OR exp betacoronavirus/ Limits: 2020- OR (novel coronavir* OR novel corona virus* OR covid19 OR covid 19 OR nCoV OR novel CoV OR CoV 2 OR CoV2 OR sarscov2 OR 2019nCoV OR wuhan virus*).mp. OR ((wuhan OR hubei OR huanan) AND (severe acute respiratory OR pneumonia*) AND outbreak*).mp. OR ((wuhan OR hubei OR huanan) AND (coronavir* OR betacoronavir*)).mp. Limits: 2019-

Appendix 6. Data extraction items

Patient sampling items	Patient characteristics and setting items	Index test items	Reference standard items	Flow and timing items	Notes items
A0 Test type (antibody/antigen etc)	COVID patients (or all patients if single group study)				
A1 Purpose	B1 Setting	D1.1 Test name	E1 Reference standard for cases including threshold	F1 What was the time interval between index and reference tests?	G1: Funding
A2 Design (and description of groups labelled [1] [2] …)	B2 Location (include name of institution if available)	D1.2 Manufacturer	E2 Samples used	F2 Did all patients receive the same reference standard?	G2: Publication status
A3 Recruitment	B3 Country	D1.3 Antibody targets	E3 Timing of reference standard (preferably since symptom onset only, if not from a different time points)	F3 Missing data	G3: Source (preprint or journal name)
A4 Were cases recruited prospectively or retrospectively?	B4 Dates	D1.4 Antigens used	E4 Was it blind to index test?	F4 Uninterpretable results	G4: Study author COI (including any manufactur-

(Continued)

					er affiliations)
A5 Sample size (virus/ COVID cases)	B5 Symptoms and severity	D1.5 Point-of-care or laboratory (is the test designed to be used at point-of-care or in laboratory, and was it used as point-of-care or in laboratory)?	E5 Did it incorporate index test?	F5 Indeterminate results	G5 Comment
A6 Inclusion and exclusion criteria	B6 Demographics	D1.6 Test method		F6 Samples or patients	
A7 Comment	B7 Exposure history	D1.7 When were samples taken (preferably since symptom onset only, if not from a different time points)?	E6 Reference standard for non-cases	F7 Comment	
	B8 Comment	D1.8 Samples used	E7 Samples used		
	Non-COVID patients (if additional groups)	D1.9 Who applied the test	E8 Timing of reference standard (preferably since symptom onset only, if not from a different time points)		
	C1.1 Group name	D1.10 How was positive defined?	E9 Was it blind to index test?		
	C1.2 Source and time	D1.11 Blinded to reference standard	E10 Did it incorporate index test?		
	C1.3 Characteristics	D1.12 Threshold predefined	E11 Comment		
	C2.1 Group name	D1.13 Comment			
	C2.2 Source and time				
	C2.3 Characteristics				
	C4 Comment				

Appendix 7. Criteria for assessment of study quality (QUADAS-2)

DOMAIN: PARTICIPANT SELECTION	
Was a consecutive or random sample of patients enrolled?	This will be similar for all index tests, target conditions, and populations. YES: if a study explicitly stated that all participants within a certain time frame were included; that this was done consecutively; or that a random selection was done. NO: if it was clear that a different selection procedure was employed; for example, selection based on clinician's preference, or based on institutions.

(Continued)

	UNCLEAR: if the selection procedure was not clear or not reported.
Was a case-control design avoided?	This will be similar for all index tests, target conditions, and populations. YES: if a study explicitly stated that all participants came from the same group of (suspected) patients. NO: if it was clear that a different selection procedure was employed for the participants depending on their COVID-19 status or SARS-CoV-2 infection status; or if only participants with SARS-CoV-2 infection were included UNCLEAR: if the selection procedure was not clear or not reported.
Did the study avoid inappropriate exclusions?	Studies may have excluded patients, or selected patients in such a way that they avoided including those who were difficult to diagnose or likely to be borderline. Although the inclusion and exclusion criteria will be different for the different index tests, inappropriate exclusions and inclusions will be similar for all index tests: for example, only elderly patients excluded, or children (as sampling may be more difficult). This needs to be addressed on a case-to-case basis. YES: if a high proportion of eligible patients was included without clear selection. NO: if a high proportion of eligible patients was excluded without providing a reason; if, in a retrospective study, participants without index test or reference standard results were excluded. UNCLEAR: if the exclusion criteria were not reported.
Did the study avoid inappropriate inclusions?	Some laboratory studies may have intentionally included groups of patients in whom the accuracy was likely to differ, such as those with particularly low or high viral loads, or who had other diseases, such that the sample over-represented these groups. This needs to be addressed on a case-to-case basis. Artificial spiked samples are a clear example. YES: if samples included were likely to be representative of the spectrum of disease. NO: if the study oversampled patients with particular characteristics likely to affect estimates of accuracy. UNCLEAR: if the exclusion criteria were not reported.
Could the selection of patients have introduced bias?	HIGH: if one or more signalling questions were answered with NO, as any deviation from the selection process may lead to bias. LOW: if all signalling questions were answered with YES. UNCLEAR: all other instances.
Is there concern that the included participants do not match the review question?	HIGH: for two-group studies that included healthy or other disease controls, whether pre-pandemic or contemporaneous; studies that only included people with COVID-19 (whether reverse transcription polymerase chain reaction (RT-PCR)-confirmed only, participants meeting official guideline criteria); LOW: for single-group studies recruiting participants with signs and symptoms of COVID-19; or for two-group studies where control groups suspected of COVID-19 were separately recruited. UNCLEAR: if a description about the participants was lacking.
DOMAIN: INDEX TESTS	
Were the index test results interpreted without knowledge of the results of the reference standard?	YES: if blinding was explicitly stated or index test was recorded before the results from the reference standard were available. NO: if it was explicitly stated that the index test results were interpreted with knowledge of the results of the reference standard.

(Continued)

	UNCLEAR: if blinding was unclearly reported.
If a threshold was used, was it prespecified?	YES: if the test was dichotomous by nature, or if the threshold was stated in the methods section, or if study authors stated that the threshold as recommended by the manufacturer was used. NO: if a receiver operating characteristic curve was drawn or multiple threshold reported in the results section; and the final result was based on one of these thresholds. UNCLEAR: if threshold selection was not clearly reported.
Could the conduct or interpretation of the index test have introduced bias?	HIGH: if one or more signalling questions were answered with NO, as even in a laboratory situation knowledge of the reference standard may lead to bias. LOW: if all signalling questions were answered with YES. UNCLEAR: all other instances.
Is there concern that the index test, its conduct, or interpretation differ from the review question?	For evaluations of laboratory-based tests, HIGH: if tests were built in-house, or if commercially available tests using SARS-Cov antigens instead of SARS-CoV-2-specific antigens. LOW: most other laboratory-evaluations UNCLEAR: name of the test was withheld For evaluations of lateral flow assays, HIGH: if tests were built in-house; if only serum or plasma instead of fingerprick or whole blood samples were used; if test evaluated in laboratory settings rather than at the point of care LOW: commercially available tests, using whole blood or fingerprick samples, and that were conducted in the intended setting for the test (i.e. point-of-care). UNCLEAR: name of the test was withheld; mixed sample types; or did not report the evaluation setting
DOMAIN: REFERENCE STANDARD	
Is the reference standard likely to correctly classify the target condition?	We will define acceptable reference standards using a consensus process once the list of reference standards that have been used has been obtained from the eligible studies. For COVID-19 cases YES: RT-PCR; confirmed or suspected case using official criteria (WHO, CDC) or a clearly set out combination of signs/symptoms/exposure. NO: RT-PCR not used, or if inadequate combination of clinical characteristics used in PCR negatives, e.g. computed tomography alone UNCLEAR: if definition of COVID-19 was not reported For absence of COVID-19 YES: if at least 2 negative RT-PCR results reported if suspected COVID-19 based on signs/symptoms; single negative RT-PCR test for asymptomatic contacts or contemporaneous controls with no clinical suspicion of COVID-19; only pre-pandemic sources of control samples used. NO: single RT-PCR or number of negative RT-PCRs not reported for COVID-19 suspects; no RT-PCR reported (untested) for asymptomatic contacts or contemporaneous controls UNCLEAR: if timing of control samples (pre-pandemic or contemporaneous) was not reported
Were the reference standard results interpreted without	YES: if it was explicitly stated that the reference standard results were interpreted without knowledge of the results of the index test, or if the result of the index test was obtained after the reference standard.

(Continued)

knowledge of the results of the index test?	NO: if it was explicitly stated that the reference standard results were interpreted with knowledge of the results of the index test or if the index test was used to make the final diagnosis. UNCLEAR: if blinding was unclearly reported.
Did the definition of the reference standard incorporate results from the index test(s)?	YES: if results from the index test were a component of the reference standard definition. NO: if the reference standard did not incorporate the index standard test. UNCLEAR: if it was unclear whether the results of the index test formed part of the reference standard.
Could the conduct or interpretation of the reference standard have introduced bias?	HIGH: if one or more signalling questions were answered with NO. LOW: if all signalling questions were answered with YES. UNCLEAR: all other instances.
Is there concern that the target condition as defined by the reference standard does not match the review question?	Applicability was judged primarily on the definition of disease-positive. HIGH: if RT-PCR alone used to define cases LOW: if clinical criteria, including RT-PCR, were used to define cases, regardless of whether official criteria were used, as long as the criteria were explicitly described. UNCLEAR: if definition of COVID-19 cases was not provided, including if some clinically diagnosed cases were included but the clinical criteria used were not described.
DOMAIN: FLOW AND TIMING	
Did all participants receive the same reference standard?	YES: if all participants received the same reference standard (clearly no differential verification). NO: if (part of) the index test-positives or index test-negatives received a different reference standard. UNCLEAR: if it was not reported.
Were all participants included in the analysis?	YES: if it is clear that all eligible participants were included in the analyses. NO: if after the inclusion/exclusion process, participants were removed from the analyses for different reasons: no reference standard done, no index test done, intermediate results of both index test or reference standard, indeterminate results of both index test or reference standard, samples unusable. UNCLEAR: if it is not possible to determine whether all participants were included (e.g. from a STARD style participant flow diagram)
Did all participants receive a reference standard?	YES: if all participants received a reference standard (clearly no partial verification). NO: if only (part of) the index test positives or index test negatives received the complete reference standard. UNCLEAR: if it was not reported.
Were results presented per participant?	YES: if either only one sample per participant (regardless of disaggregation of results over time), or if multiple samples per participant but results are disaggregated by time period (at least week by week) NO: if multiple samples per participant and results are not disaggregated by time period UNCLEAR: if it is not possible to tell whether results presented are per participant or per sample

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Could the participant**flow have introduced bias?**	HIGH: if one or more signalling questions were answered with NO. LOW: if all signalling questions were answered with YES. UNCLEAR: all other instances.

CDC: Centers for Disease Control; **ICU:** intensive care unit; **RT-PCR:** real-time polymerase chain reaction; **SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2; **WHO:** World Health Organization

Footnotes

Appendix 8. Summary details of study design and participants

This Appendix includes two tables. Please note that square brackets indicate different tests within one study.

1. Table A. Single-group studies estimating sensitivity (and specificity)
2. Table B. Two-group or more studies estimating sensitivity and specificity

Table A. Single-group studies estimating sensitivity (and specificity)

Study (source)	Inclusion criteria • **method used to rule out COVID-19**	Instititution (recruitment dates)	Age (median) n, % male	Exposure history Symptoms/severity	Reference details (cases)	Missing or uninterpretable data
Single-group studies estimating sensitivity and specificity						
Cassaniti 2020 (B) (published; letter) 50 participants (50 samples)	COVID-19-suspected cases presenting at A&E with fever and respiratory syndrome (n = 50, including 38 RT-PCR-positive); • 2 x RT-PCR-negative required to rule out disease (Additional groups reported in Cassaniti 2020 (A))	A&E; Pavia, Italy (not stated)	61.5 years 34, 68%	Not stated Not stated	RT-PCR detecting RNA polymerase and E genes; nasal swab (On presentation at A&E)	Weakly positive results counted as test positive
Liu 2020a (preprint) 179 participants (179 samples)	Inpatients and outpatients attending hospital during pandemic including COVID-19-suspected cases (all inpatient, n = 114) and outpatients (n = 64) with 'other disease'. (n = 179, including 90 PCR-confirmed and 5 clinically confirmed cases) • Negative PCR and insufficient evidence for clinical confirmation required to rule out disease	Inpatient and outpatient; Wuhan, China (1 January-12 March 2020)	[1] mean 76 years [2+3] mean 56 years [1] 60, 67% [2+3] 38, 43%	Not reported Of 90 RT-PCR+, 44, 49% severe/critical cases	Clinical criteria (not clearly described) ≤ RT-PCR; nasal and pharyngeal swabs (NR)	Per sample data by time period is based on

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Long 2020 (A) (preprint) 164 participants (164 samples)	Cohort of close contacts of 2 index cases (n = 164, 16 PCR-positive cases) • 1 x RT-PCR-negative required to rule out disease	Close contacts; Wanzhou, China (31 January-9 February)	Not stated Not stated	All exposed 151 (92%) asymptomatic	RT-PCR; NP (within 17 days of contact with confirmed cases)	None stated
Paradiso 2020a (preprint) 191 participants (191 samples)	Symptomatic patients accessing A&E (n = 191, including 70 PCR-positive) • 1 x RT-PCR-negative required to rule out disease	A&E; Bari, Italy (23-29 March)	58.5 years 116, 61%	Not stated 14, 9% asymptomatic	RT-PCR (Allplex 2019-nCoV Assay; Seegene, Seoul, Republic of Korea); NP, OP (Simultaneous)	1 D+ missing from results
Zhang 2020b (preprint) 228 participants (228 samples)	Suspected COVID-19 cases admitted to fever clinic (n = 228, including 3 PCR-positive) • 1 x RT-PCR negative required to rule out disease (review team excluded additional reported groups)	Inpatients, Shengjing, China (21 January-16 February)	Mean 51 years (cases only) Not stated	1, 33% Wuhan contact history (cases only) Not stated	RT-PCR (required presence of ORF1ab and N gene for positive result); NP, OP (Timing not stated)	Not stated
Zhang 2020d (preprint) 814 participants (814 samples)	Participants suspected of harbouring COVID-19 (n = 814, including 154 cases; 122 RT-PCR-positive and 32 clinically diagnosed by CT) • 1 x RT-PCR negative required to rule out disease; unclear if CT used in all D- (n = 663)	Samples from 5 hospitals (in/outpatient not stated); centres including Wuhan, Shenyang and Beijing, China (Not stated)	Not stated	Not stated	Real-time PCR kit (no details on threshold); CT used in at least some PCR-negative NP swabs. (Timing not stated)	None stated
Single group studies estimating sensitivity alone						
Du 2020 (published; letter) 60 participants (60 samples)	Single group of convalescent inpatients 6-7 weeks after symptom onset (n = 60) • Non-COVID-19 cases not included	Hospital inpatients; Wuhan, China (12 January-5 February 2020)	Not stated	Not stated	Not described; not stated (During hospital stay)	None described
Gao 2020a (published; letter) 38 participants (38 samples)	Inpatient cohort of COVID-19 patients confirmed by Chinese Government-issued guidelines (5th edition) • non-COVID-19 cases not included	Inpatient; Fuyang, China (22 January-28 February 2020)	40.5 years 21, 55.3%	Not stated 3, 8% severe or critical, 35 mild	Chinese guideline (5th edition)	Not reported
Gao 2020b [A] (accepted manuscript	Confirmed COVID-19 cases (n = 22) • non-COVID-19 cases not included	Hospital inpatient; Shijiazhuang, Hebei, China (21 Janu-	40 years 14, 64%	11 (50%) recent travel to epidemic areas,	RT-PCR assay (2019-nCoV RNA Test Kit, Daan Gene Company, China); Nasal and	None described

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(peer reviewed; pre-proof) 22 participants (37 samples)		ary-24 February 2020)		10 (45%) close contacts with confirmed COVID-19 cases 22 (100%) typical CT findings; 'most' received oxygen therapy	pharyngeal swab specimens	
Garcia 2020 (B) (preprint) 63 participants (63 samples)	Patients admitted with a clinical and radiological diagnosis of pneumonia of unknown aetiology but RT-PCR-negative (n = 63) • non-COVID-19 cases not included Addional reported cohort extracted as Garcia 2020 (A)	Inpatient hospital (9 February-2 April)	67 years 47, 74%	Not stated	Clinical diagnosis of COVID-19 (no further detail); all PCR-negative	None reported
Hu 2020a (preprint) 211 participants (993 samples)	Confirmed COVID-19 patients (221) • non-COVID-19 cases not included	Inpatient; Chongqing, China (23 January-3 March)	Mean 47.8 years 135, 64%	Not stated 137, 62% with fever; 40, 19% severe	Chinese Government guidelines (version 6); included RT-PCR	None described; text states 993 samples but only 409 reported for IgM and 507 for IgG
Jia 2020 (preprint) 57 participants (57 samples)	1. RT-PCR confirmed (24) 2. Clinical diagnosis for RT-PCR negative (2 x negative results) according to Chinese Government guideline (6th ed) (33) • non-COVID-19 cases not included	Inpatients; Shenzhen, China (Not stated)	Not stated	Not stated	1. RT-PCR 2. Chinese CDC guideline (6th ed). (1 to 34 days from exposure to first PCR test)	None described
Li 2020a (accepted for publication and undergone full peer review) 525 participants	COVID-19 according to Chinese CDC guideline (5th ed) (525; 397 PCR-positive)) • non-COVID-19 cases not included	Potentially inpatient and outpatient; 6 provinces, China (Not stated)	Not stated	Not stated	Chinese CDC guideline (6th ed), including PCR; pharyngeal, sputum (Not stated)	None stated

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(525 samples)						
Lippi 2020 [A] (published; letter) 48 participants (48 samples)	Participants with suspected COVID-19; subgroup of cases (48/131 patients) with available data on days post-symptom onset data can be included • non-COVID-19 cases not included	Inpatients; Verona, Italy (Not stated)	Totlal sample of 131: mean 56 years 60/131, 46%	Not stated	RT-PCR (Seegene Allplex 2019-nCoV Assay. OP, NP swabs (During hospitalisation)	Excluded 83 patients with no time pso data
Liu 2020c (preprint) 133 participants (133 samples)	Patients diagnosed with SARS-Cov-2 according to Chinese CDC guideline (5th ed) (133) • non-COVID-19 cases not included	Inpatients; Wuhan, China (17 February-1 March)	Moderate 67.5 years; severe 68 years; critical 70 years 70, 53%	Not stated moderate 44, 33%; severe 52, 39%; critical 37, 29%	Clinical diagnosis (seems to be Chinese CDC guideline, 5th ed) Includes RT-PCR (GeneoDx Biotech, Shanghai, China); 2 tests per participant; Table 2 refers to NP.	None described
Long 2020 (B) (preprint) 262 participants (363 samples)	RT-PCR-positive confirmed cases (n = 285). No further detail of inclusion or exclusion criteria. Additional cohort extracted as Long 2020 (A); some additional cohorts excluded (see Characteristics of included studies) • non-COVID-19 cases not included	Inpatients; Chongqing, China (38384)	47 years 158, 55.4%	103, 36% exposure to transmission sources 39, 14% severe or critical in ICU	RT-PCR; nasal and pharyngeal swabs (during hospital stay)	23 patients with no information on time pso were excluded leaving 363 samples from 262 patients
Padoan 2020 (peer reviewed; published) 37 participants (87 samples)	Hospitalised patients with confirmed COVID-19 (n = 37) • non-COVID-19 cases not included	Inpatients; Padova, Italy (18 March-26 March 2020)	Not stated	Not stated	RT-PCR; NP (Not stated)	None described

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Pan 2020a (peer reviewed; published) 105 participants (134 samples)	COVID-19 patients according to CDC guideline (5th ed); confirmed by PCR (67) or clinical diagnosis (37) • non-COVID-19 cases not included	Inpatients; Wuhan, China (Not stated (symptom onset 7 January-18 February))	58 years 48, 46%	Not stated	RT-PCR following WHO guidelines (BioGerm, Shanghai, China), Clinical diagnosis according to CDC guideline (5th ed); throat swabs (Not stated)	Data reported only for those with symptom onset information; 26 samples excluded
To 2020a [A] (peer reviewed; published) 23 participants (108 serum samples)	Confirmed COVID-19 patients from 2 hospitals (n = 23, can only extract data for 16 with > 14-day pso data) • non-COVID-19 cases not included	Hospital inpatient, Hong Kong (22 January-12 February)	Not stated 13/23 (57%) age: median 62 years (range 37–75)	Not stated 10/23 (43%) severe; 5/23(22%) admitted to ICU, 3/23(13%) required intubation, 2/23(9%) died Fever in 22/23 (96%) patients, cough in 5/23 (22%), chills in 4/23 (17%), dyspnoea in 4/23 (17%)	Laboratory-confirmed - not further described; NP or sputum (Unclear)	7/23 (30%) were not tested between days 14 and 30
Xiao 2020a (accepted manuscript; pre-proof) 34 participants (34 samples)	Confirmed cases of COVID-19 according to Chinese CDC (5th ed) (34) • non-COVID-19 cases not included	Inpatients; Wuhan, China (1-29 February)	49 years (review team estimated) 22, 65%	Not stated Not described	COVID-19 according to CDC diagnosis and treatment guideline (5th ed)	None reported

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Xie 2020a (accepted manuscript; pre-proof) 56 participants (56 samples)	Participants with suspected COVID-19 based on Chinese CDC (5th ed) criteria (n = 56, including 16 PCR confirmed) • non-COVID-19 cases not included	Inpatients; Wuhan, China (15-25 February 2020)	56.5 years 24, 43%	Not stated 34, 61% severe	[1] RT-PCR QIAamp RNA virus kit (Qiagen, Heiden, Germany); NP and throat [2] clinical diagnosis (guideline, 5th edition	None reported
Xu 2020a (preprint) 10 participants (10 samples)	Confirmed (PCR) COVID-19 cases (n = 10) • non-COVID-19 cases not included	Hospital inpatients; Shanghai, China (Not stated)	Not stated 6, 60%	Not stated 10, 100% required oxygen	RT-PCR (cycle threshold value (Ct) < 37 defined as positive and Ct ≥ 40 defined as negative; pharyngeal swab (Not stated)	None reported
Yongchen 2020 (peer reviewed; published) 21 participants (≥ 42 samples)	Participants with COVID-19 (n = 16) and asymptomatic carriers (n = 5) • non-COVID-19 cases not included	Mixed; Jiangsu, China (25 January-18 March 2020)	37 years 13, 62%	Not stated 5, 24% severe; 5, 24% asymptomatic cases Illness severity defined according to the Chinese management guideline for COVID-19 (version 6.0).	RT-PCR, confirmed after 2 sequential positive respiratory tract sample results; throat swabs	None described
Zhang 2020a (preprint) 222 participants (222 samples)	Confirmed COVID-19 patients (RT-PCR detection or antibody assay) (n = 222) • non-COVID-19 cases not included	Inpatients; Wuhan, China (admitted 13 January 13-1 March)	62 years Not stated	Not stated 87, 39% severe	RT-PCR or anti-SARS-CoV-2 assay ; nasal or pharyngeal swabs (Not stated)	None reported
Zhang 2020c (peer reviewed; published) 16 participants (16 samples)	RT-PCR-confirmed COVID-19 patients (n = 139); included those with around 10 days of medical treatment after admission (n = 16) • non-COVID-19 cases not included	Inpatients; Wuhan, China (Not stated)	Not stated	Not stated	RT-PCR	< 10 days' medical treatment (n = 123)

A&E: Accident and Emergency Department; **CDC:** Center for Disease Control; **CT:** computed tomography; **CGIA:** colloidal gold immunoassay; **D+:** disease positive: **D-:** disease negative; **ed:** edition; **ELISA:** enzyme-linked immunosorbent assay; **HCW:** healthcare worker; **ICU:** intensive care unit; **LFA:** lateral flow assay; **n:** number; **NP:** nasopharyngeal; **NR:** not reported; **OP:** oropharyngeal; **PCR:**

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polymerase chain reaction; **pso:** post-symptom onset; **RNA:** ribonucleic acid; **RT-PCR:** reverse transcriptase polymerase chain reaction; **SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2; **suppl:** supplementary; **TB:** tuberculosis

Table B. Two-group studies or more estimating sensitivity and specificity

Study (source)	COVID-19 cases (n)	Non-COVID cases (n) (including method of verification)	Institution (Recruitment dates)	Age (median) n, % male	Exposure history Symptoms/severity	Reference details (cases)	Missing or uninterpretable data
Adams 2020 [A] (preprint) 182 participants (40 samples)	RT-PCR confirmed COVID-19 cases (n = 40)	Pre-pandemic controls (n = 142); prior to December 2019	Acute hospital (n = 16), recovering HCWs (n = 6), convalescent (n = 18); UK (Not stated)	57y Not stated	Not stated Asymptomatic (n = 1); mild (n = 26); severe (n = 4); critical (n = 9)	RT-PCR; nose/throat swabs (Not stated)	[B]–[J] tests evaluated in different numbers
Bendavid 2020 (preprint) 3481 samples participants (3324 samples)	COVID-19 cases were obtained from 3 different sources (n = 157 specimens) Confirmed cases from manufacturer data (n = 85); local cases (PCR- and ELISA-confirmed) (n = 37) or PCR-confirmed (6-10 days pso) (n = 35)	Non-COVID-19 cases were obtained from 13 different sources (n = 3324 specimens), Pre-pandemic (10 sources; n = 2811); pandemic era PCR-negative (n = 202); not stated (n = 311)	Multiple sources; USA, China, unclear (Not described)	Not stated	Not stated	PCR-positive only (n = 35); PCR and IgG or IgM confirmed by ELISA (n = 37); not stated (n = 85)	None described
Burbelo 2020 [A] (preprint) 67 participants (140 samples)	SARS-CoV-2 cases confirmed by PCR (n = 35 in results, n = 39 in methods)	Pre-pandemic blood donors (n = 32); prior to 2018 [Review authors excluded 3rd group with no reference standard reported (n = 10)]	Hospital (unclear whether inpatient or outpatient); San Diego, Seattle, Washington, USA (Not stated)	44 years 0.87	Not stated 13, 37% on a ventilator	RT-PCR; nasal and/or throat swabs (No information)	none described
Cai 2020 (preprint) 443 participants (443 samples)	RT-PCR confirmed (276)	Healthy, other controls; pre-December 2019 (167)	Inpatient (cases only); Chongqing, China (Not stated)	48 years 151, 55%	99, 36% known exposure	RT-PCR; no further details	None described

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Cassaniti 2020 (A) (published; letter) 60 participants (60 samples)	COVID-19-positive patients in ICU (n = 30) [Additional cohort reported in Cassaniti 2020 (B)]	Healthy volunteers with negative RT-PCR results (n = 30)	Infectious Diseases Unit or ICU, Tertiary hospital; Pavia, Italy (Not stated)	73.5 years 25, 42%	Not stated	RT-PCR detecting RNA polymerase and E genes; Respiratory samples (During patient care)	Weakly positive results counted as test positive
Chen 2020a (Accepted manuscript; peer reviewed, preproof) 19 participants (19 samples)	RT–PCR positive samples (n = 7)	RT–PCR-negative samples, but clinically suspicious for COVID-19 (n = 12) [Additional group of 'normal' samples (n = 51) used to derive threshold]	Unclear, presumably inpatients; Guangzhou, China (Not described)	Not stated	Not stated	RT–PCR; not stated (Not stated; prior to LFA)	None reported
Dohla 2020 (peer reviewed; published) 49 participants (49 samples)	[1] Attendees at community screening centre for COVID-19 (n = 12 PCR-positive), [2] Stored samples from 10 patients with confirmed diagnosis of COVID-19	[1] Attendees at community screening centre for COVID-19 (n = 27 PCR-negative)	Community screening centre [1] and unclear setting [2]; author institutions Bonn, Germany (Not stated)	46 years 25, 51%	Probable date of exposure identified in 22, 45% 5/49 (10%) asymptomatic. 71% dry cough; 65% fatigue; 46% runny nose (only %s reported)	[1] RT–qPCR (Altona Diagnostics) [2] RT–qPCR (unknown if same kit); throat swabs group [1]; not stated for group [2]. ([1] same time as index test. [2] not stated)	Weak signals counted as positive; no missing data reported
Freeman 2020 (preprint) 618 participants (618 samples)	Confirmed COVID-19 cases (n = 99)	Pre-pandemic healthy (n = 377) + other infection (n = 142)	Convalescent; USA (reference to CDC National Center for Immunization and Respiratory Diseases) (Not stated)	Not stated	Not stated	PCR; no further detail	None mentioned

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Garcia 2020 (A) (preprint) 100 participants (100 samples)	Suspected COVID-19 patients admitted to A&E; all RT-PCR-positive (n = 55) [Third cohort reported as Garcia 2020 (B)]	Pre-pandemic healthy controls (n = 45); 1 October-30 November, 2019	Inpatient; Madrid, Spain (1 March-6 April 2020)	63 years 33, 60%	Not stated	RT-PCR	None described
Grzelak 2020 [A] (preprint) 542 participants (652 samples)	Hospitalized COVID-19 patients (51) Review team excluded 2 additional cohorts with no reference standard (See COIS)	Pre-pandemic sera from healthy individuals (491)	Inpatient; Paris, France (Not stated)	Not described 47, 74%	Not stated	Not stated	None reported
Guo 2020a (accepted manuscript; corrected proof now available online) 275 participants (343 samples)	Confirmed (82) or probable (58) COVID-19 cases (provided 208 samples)	Pre-pandemic acute lower respiratory tract infection (135) Healthy individuals (150) used to define threshold	Inpatients; Wuhan and Beijing, China (cases) (43,831)	Not stated	Not stated Confirmed cases - 28, 34% severe Pobable cases - 5, 9% severe	Confirmed: deep sequencing or qPCR assay Probable: cases - clinical manifestation, chest X-ray and epidemiology but no virus detected by deep sequencing or qPCR; throat (Not stated)	None reported
Infantino 2020 (accepted publication; peer reviewed; preproof) 125 participants (125 samples)	[1] confirmed COVID-19 cases (n = 61)	[2] pre-pandemic (2018-19) control group with rheumatic and infectious diseases (n = 44) [3] blood donors (winter 2019) (n = 20)	Inpatient; Florence, Italy (Not stated)	mean 59 years 26, 43%	Not stated 30, 49% mild to moderate symptoms 31, 51% severe pneumonia requiring admission to ICU	RT-PCR (2 positive results required for confirmation); OP and NP swabs (Not stated)	None reported
Jin 2020 (peer reviewed; published)	Laboratory confirmed COVID-19 patients (n = 43)	COVID-19 suspects, discharged with 2 x RT-PCR-negative results with an interval of 24 h and who quarantined at home (n = 33)	Hospital inpatients; Hangzhou, China (January to 4 Mar 2020)	47 years 17, 40%	Not stated [1] COVID-19 patients: 27 (63%) fever;	RT-PCR; oral swab or sputum specimens	No data reported for 16 patients while PCR positive.

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76 participants (98 samples from 43 cases samples)	[Review team excluded results for 34 participants after becoming PCR-negative]				26 (61%) cough [2] Non-COVID-19 patients: 24/43 (73%) fever; 15/33 (46%) cough	(During hospital stay)	
Lassauniere 2020 [A] (preprint) 112 participants (112 samples)	COVID-19 PCR-positive patients (n = 30) admitted to intensive care	Pre-pandemic (n = 82) including blood donors (n = 10) and other infections (n = 72)	Intensive care; Hillerod, Denmark (Not stated)	Not stated	Not stated	Viral nucleic acid detection (no further detail)	Borderline results for tests [B] and [C] were considered test negative; for POC tests weak signals for IgM and IgG were considered positive. Some samples not tested with all assays.
Lin 2020a [A] (preprint) 159 participants (159 samples)	[1] Suspected COVID-19 cases (epidemiological risk, clinical features and RT-PCR respiratory specimen positive) from inpatient setting (specialised COVID-19 hospital) (n = 79)	RT-PCR negative controls (reportedly at least 3 x negative), including: [2] healthy volunteers; timing not reported, presumed contemporaneous (n = 29) [3] TB patients; timing not reported, presumed contemporaneous (n = 51)	Inpatients (specialised COVID hospital); Shenzhen, China (Not stated)	Not stated	Not stated	Epidemiological risk, clinical features and RT-PCR respiratory specimen positive' 'GeneoDX kit (Taqman RT-PCR method)	Only 65/79 D + and 64/80 D- serum samples available for ELISA; reason not given.
Liu 2020b (preprint) 358 participants (358 samples)	Confirmed (153) or suspected (85) COVID-19	Ordinary patients (70) and randomly sampled healthy blood donors (50); timing not reported, presumed to be contemporaneous	Inpatients; Hubei, China (6 -14 February)	55 years 138, 58%	Not stated Fever (87%); dry cough (54%); fatigue (33%). 235/238 (99%) had CT ground glass opac-	RT-PCR (Daan Gene) targeting ORF1ab and N gene (≤ 40 Ct); Clinical diagnosis according to Chinese Government-issued guideline (5th ed); pharyngeal swabs	None reported

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					ity/patchy shadowing	RT-PCR sampling throughout inpatient stay	
Liu 2020d [A] (evaluation; accepted manuscript) 314 participants (314 samples)	RT-PCR-confirmed COVID-19 cases (n = 214)	Healthy blood donors, presumed to be contemporaneous (n = 100)	Inpatient, Hubei, China (18 January-26 February)	Not stated	Not stated	RT-PCR; pharyngeal swabs. Median 15 days pso (range 0–55 days)	None described
Lou 2020 [A] (preprint) 380 participants (380 samples)	Confirmed COVID-19 cases according to Chinese Government-issued guidelines (6th edition) (n = 80)	Healthy people enrolled from the community, presumed contemporaneous selection (n = 300)	inpatient; Hangzhou, China (19 January-9 February 2020)	Mean 55 years 0.61	26, 33% critical	CDC guideline (6th ed); criteria described including PCR; deep sputum samples' (On admission)	Not all control group participants were tested by all index tests (range 100-300/300)
Ma 2020a (preprint) 570 participants (216 samples from 87 cases samples)	Confirmed (PCR-positive) COVID-19 patients (n = 87)	[2] Pre-pandemic healthy donors (n = 330) [3] Contemporaneous 'other diseases' (no mention of PCR) (n = 138) [4] Suspected COVID pneumonia but negative PCR (n = 15)	Inpatient; Hefei, China (26 January-5 March 2020)	Not stated	Not stated 56, 67% clinically moderate 17 severe 5 critical "few mild" [page 7]	Chinese Government-issued guidelines (7th edition) including RT-qPCR; serum (During hospital admission as part of "routine clinical testing". Performed before index test)	For comparison of sensitivity and specificity of 2 antigens only 20/total of 479 control sera were used (20/138 from 'other disease' group)
Okba 2020c (accepted manuscript; early release) 54 participants (76 samples)	RT-PCR-confirmed SARS-CoV-2 cases (n = 9, 31 samples)	Contemporaneous healthy blood donors (n = 45)	Inpatient; Munich, Germany (occurred after 23 January, discovered (presume PCR-positive) on 27 January 27)	Not stated	All identified through exposure to known cases Not stated	RT-PCR; OP, NP (day 1-5 of symptoms)	Indeterminate or unclear index results on graphs considered negative by review team

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Qian 2020 (preprint) 2113 participants (2113 samples)	[1] Confirmed COVID-19 cases (RT-PCR-positive) (n = 503) and [2] suspected COVID-19 cases based on epidemiological history, clinical symptoms and chest X-ray but 3 x PCR-negative (n = 52)	Apparently contemporaneous controls, including: [3] hospitalised with non-COVID-19 conditions (PCR testing not described) (n = 972) [4] healthy controls (n = 586)	Hospital inpatients; Hubei and other provinces, China (Unclear)	Not stated	Not stated	RT-PCR; NP ("early onset of the symptoms of COVID-19")	None described
Wan 2020 [A] (preprint) 17 participants (36 samples)	SARS-Cov-2 positive cases confirmed by RT-PCR (n = 7, 26 samples)	Prepandemic sera (n = 5); plus controls SARS-Cov-2 negative on two occasions (n = 5)	Inpatients; Singapore (Not stated)	Not stated	Not stated	RT-PCR	not stated
Wang 2020a [A] (accepted manuscript) 86 participants (86 samples)	COVID-19 patients, meeting Chinese Government guideline criteria (14)	Contemporaneous patients with different pathogen infections and related chronic diseases with no clinical symptoms or imaging evidence of COVID-19 (no PCR testing reported) (72)	Inpatient; Nanchong, China (25 January-15 February)	Not stated	Not stated	Chinese CDC guideline (5th ed)	none described
Xiang 2020a [A] (preprint) 98 participants (ELISA samples) , 126 participants (LFA samples) , 81 participants (PCR samples)	COVID-19 patients according to WHO interim guidance (suppl data reports PCR results for a subgroup); (n = 63 for ELISA, n = 91 for GICA, some overlap of cases)	Contemporaneous healthy individuals (n = 35)	Inpatient; Wuhan, China (admitted 1-28 January; sampled 2-4 February)	ELISA 65 years; LFA 61 years ELISA 35, 56% male LFA 49, 54% male	Not stated ELISA 4, 6% severe LFA 4, 4%	WHO interim guidance (subgroup of 82 also have PCR results); (PCR using throat swabs) (Not stated (PCR at 6-37 days post-admission))	Not stated
Xiang 2020b (peer reviewed; published)	[1] RT-PCR confirmed cases (n = 85) [2] Suspected cases with COVID-19 pneumonia	[3] Contemporaneous control group of healthy blood donors (hospital staff) or patients with other diseases	Hospital patients (likely inpatients but not explicit);	51 years 31, 26%	Not stated 18/85 (21%) severe	[1] RT-PCR [2] Clinical manifestations and PCR ; NP and/or OP	Not stated

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150 participants (216 samples from 85 cases samples)	manifestations and ≥ 2 negative RT-PCR (n = 24) classed as D+ for review purposes	in the same hospital (all PCR-negative) (n = 60)	Wuhan, China (19 January-2 March 2020)			(Unclear)	
Zeng 2020a (accepted manuscript; pre-proof) 63 participants (63 samples)	COVID-19 cases (n = 27); no details of confirmation process	Healthy controls, presume contemporaneous but not stated (n = 36)	Hospital inpatient; Wuhan, China (Not stated)	62 years 14, 52%	Not stated 17, 63% severe	No information; 'confirmed'; No information (No information)	None reported
Zhao 2020a (accepted manuscript; pre-proof) 386 participants (386 samples)	Confirmed RT-PCR positive COVID-19 cases (173)	Pre-pandemic healthy individuals (213)	Inpatients; Shenzhen, China (11 January-9 February)	48 years 84, 49%	126, 73% clear exposure 32, 18% critical	RT-PCR; respiratory (Not stated)	inadequate plasma samples for 2 IgM tests and 1 IgG test
Zhao 2020b (preprint) 481 participants (481 samples)	Hospitalised and/or recovered COVID-19 patients (n = 69)	Pre-pandemic 'normal' samples ("strong negatives"); presumed healthy (n = 257) Contemporaneous 'normal' samples ("negatives"); presumed healthy (n = 155)	Hospital (no detail); multiple author institutions, China (Not stated)	Not stated	Not stated	Not described; "hospitalized and/or recovered patients confirmed SARS-CoV-2 virus infection."	None reported
Zhong 2020 [A] (published; letter) 347 participants (347 samples)	PCR-positive COVID-19 patients (n = 47)	Pre-pandemic healthy controls (n = 300)	Not stated; China (Not described (symptom onset 15 January-13 February))	48 years 16, 34%	Not stated 11, 24% severe (6) or critical (5)	PCR	None reported

A&E: Accident and Emergency Department; **CDC:** Center for Disease Control; **COIS**: Characteristics of included studies table; **CT:** computed tomography; **CGIA:** colloidal gold immunoassay; **D+:** disease positive: **D-:** disease negative; **ed:** edition; **ELISA:** enzyme-linked immunosorbent assay; **HCW:** healthcare worker; **ICU:** intensive care unit; **LFA:** lateral flow assay; **n:** number; **NP:** nasopharyngeal; **NR:** not reported; **OP:** oropharyngeal; **PCR:** polymerase chain reaction; **pso:** post-symptom onset; **RNA:** ribonucleic

(Continued)

acid; **RT-PCR:** reverse transcriptase polymerase chain reaction; **RT-qPCR:** reverse transcriptase quantitative polymerase chain reaction; **SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2; **suppl:** supplementary; **TB:** tuberculosis;

Appendix 9. Summary details of index tests per study

Study	Test type	Index test (manufacturer)	Antigen	Antibodies measured (threshold)	Sample used	Index sample timing (days pso)	Data by time pso
Adams 2020 [A]	[A][a] Laboratory [B] to [J] LFAs	[A] ELISA (In-house) [B] to [J] name withheld	[A] tri S-based [B] to [J] details withheld	[A] IgG (> 0.4) and IgM (IgM > 0.07) (set in study) [B] and [C] not known [D] to [J] IgG and IgM (presumed from reported results)	Plasma	Day 4-62 (median and range per group: acute 10 (4 to 27); recovering HCW 13 (8 to 19); convalescent 48 (31 to 62))	Yes; per week
Bendavid 2020	LFA	No details (Premier Biotech, Minneapolis, MN))	Not specified	IgG, IgM (threshold not specified)	Serum, plasma, fingerstick blood, venous whole blood	Not described	No
Burbelo 2020 [A]	Laboratory	LIPS (in-house)	[A] N-based [B] S-based	Appears to be total Ab (threshold set in healthy control sample)	plasma or serum	Day 2-50	Yes; ≤ 14 d, and > 14 d
Cai 2020	Laboratory	CLIA (in-house)	S-based	IgM, IgG (both ≥ 0.7 CL)	Serum (day 2-27 pso)	Day 2-27	No
Cassaniti 2020 (A)	LFA	CGIA: VivaDiag COVID-19 IgM/IgG (VivaChek)	Not stated	IgM, IgG (visible line)	Serum or whole blood	On presentation at A&E	No
Cassaniti 2020 (B)	LFA	CGIA: VivaDiag COVID-19 IgM/IgG (VivaChek)	Not stated	IgM, IgG (visible line)	Serum or blood	Median 7 days (IQR 4 to 11) after first test	No
Chen 2020a	LFA	FIA (in-house; using lanthanide-doped polystyrene nanoparticles)	N-based	IgG (threshold: At (florescence peak of test line)/Ac (florescence peak of control line) ratio (R) > 0.0666)	Serum	Not stated	No
Dohla 2020	LFA	CGIA (suspect this is a description of an anonymised test; no manufacturer stated)	SARS-CoV-2 antigen	IgG/IgM (weakly visible or clearly visible (strong positive) test line)	Fingerprick blood (n = 39 in cohort [1]);	Median time from exposure–to–test	No

(Continued)

					stored serum for cohort [2]	18.5 d (IQR 15 to 24)	
Du 2020	Laboratory	Not stated; coded as CLIA based on reported threshold in AU/mL (Manufacturer not reported)	Not stated	IgM, IgG (threshold > 10 AU/mL)	Not stated	day 22 to > 35	Yes; by week from day 22
Freeman 2020	Laboratory	ELISA (in-house)	S-based	IgG and IgM (based on optical density signal)	Serum	All day ≥ 10	No
Gao 2020a	LFA	CGIA (Innovita Biological Technology Co)	Not reported	IgG, IgM (coloured line)	Serum	day 0 to > 14	Yes; by week from day 22
Gao 2020b [A]	[A] Laboratory [B] CGIA [C] Laboratory	[A] CLIA [B] CGIA [C] ELISA (all Beier Bioengineering Company, Beijing)	[A], [B], and [C] all S- and N-based	IgG and IgM ([A] ≥ 8 arbitrary unit (AU)/mL; [B] visible line; [C] method to calculate threshold reported)	Serum	Day 1-24	Yes; by week
Garcia 2020 (A)	LFA	CGIA, AllTest COV-19 IgG/IgM kit (AllTest Biotech, Hangzhou, China)	Not reported	IgG, IgM (visible line for either)	Serum	Day 0 to ≥ 14	Yes; by week
Garcia 2020 (B)	LFA	CGIA, AllTest COV-19 IgG / IgM kit (AllTest Biotech, Hangzhou, China))	Not reported	IgG and IgM (visible line for either)	Serum	Day 8 to ≥ 14	Yes; by week
Grzelak 2020 [A]	[A] to [E] all Laboratory	5 tests evaluated: [A] and [B] LIPS (in-house) [C] and [E] ELISA [D] S-flow	[A] S1-based [B] and [C] N-based [D] S-based [E] tri-S-based	a. IgG b. total Ab c. IgM or IgG d. total Ab (Not clearly stated, plotted on Figure 1)	Serum	Not stated; day 2-18 for 5 patients	No
Guo 2020a	Laboratory	In-house ELISA	N-based	IgM, IgG, IgA (threshold set in healthy control sample)	Blood/plasma	Day 1-39	Yes; week 1 only
Hu 2020a	Laboratory	Magnetic MCLIA kit (Bioscience Co., Ltd (Chongqing, China))	N- and S-based	IgM, IgG (S/CO ≥ 1.0 considered positive (ratio of the chemiluminescence signal to the cut-off value)	Serum	Day 1 to > 37	Yes; by week
Infantino 2020	Laboratory	SARS CoV-2 IgM and IgG CLIA kits (Shenzhen YHLO Biotech Co)	N- and S-based	IgM, IgG (multiple thresholds reported, including manufac-	Blood (discussion mentions serum)	Day 8-19	No

(Continued)

				turer recommended threshold ≥ 10 AU/mL)			
Jia 2020	LFA	FIA method (Beijing Diagreat Biotechnologies)	Not described	IgM (≥ 0.88 Flu) IgG (≥ 1.02 Flu) (threshold set in healthy control sample)	Not stated	Not stated	No
Jin 2020	Laboratory	SARS CoV-2 IgM and IgG CLIA kits (Shenzhen YHLO Biotech Co)	N- and S-based	IgM, IgG (> 10 AU/mL)	Serum	Day 1-55	Yes; by week
Lassauniere 2020 [A]	[A] to [C] laboratory, [D] to [I] LFA	[A] ELISA (Beijing Wantai) [B] IgG ELISA (EUROIMMUN) [C] IgA ELISA ELISA (EUROIMMUN) [D] to [F] all presumed to be CGIA [D] Dynamiker Biotech 2019-nCOV IgG/IgM Rapid Test [E] CTK Biotech - OnSiteTM COV-ID-19 IgG/IgM Rapid Test [F] Autobio Diagnostics Anti-SARS-CoV-2 Rapid Test [G] Artron Labs Coronavirus Diseases 2019 (COVID-19) IgM/IgG Antibody Test [H] Acro Biotech 2019-nCoV IgG/IgM Rapid Test Cassette [I] Hangzhou All test 2019-nCoV IgG/IgM Rapid Test Cassette	[A] S-based [B] and [C] S1-based [D] to [I] not stated	[A] Total Ab (calculated negative control value to 0.160) [B] IgG and [C] IgM (ratio < 0.8 is considered negative, ≥ 0.8 and < 1.1 borderline, and ≥ 1.1 positive) [D] to [I] IgG/IgM (Visual line change)	Serum	Day 7 to ≥ 21	Yes
Li 2020a	LFA	CGIA (Jiangsu Medomics Medical Technologies)	S-based	IgM, IgG (coloured line)	Serum, plasma	Not stated; for 1 site (n = 58), sampling day 8-33	No
Lin 2020a [A]	[A] and [B] laboratory	[A] In-house CLIA [B] ELISA (Darui Biotech, China)	[A] and [B] N-based	[A] IgM (RLU 162296); IgG (RLU 336697) (threshold set using ROC analysis) [B] IgM, IgG	Serum	Day 0 to ≥ 14	Yes; by week
Lippi 2020 [A]	[A] and [B] laboratory	[A] MAGLUMI 2019-nCoV CLIAs (Snibe Diagnostics -Shenzhen New Industries Biomedical Engineering Co., Ltd,)	[A] N- and S-based [B] Not stated	[A] IgM or IgG (≥ 1.10 AU/mL) [B] IgA or IgG (≥ 1.1 (absorbance of patient sample/absorbance of calibrator))	[A] Serum or plasma [B] Not stated	Day < 5-21	Yes; 5 day intervals

(Continued)

		[B] ELISAs (Euroimmun AG, Lübeck, Germany)					
Liu 2020a	LFA	CGIA (Not stated: 'Chinese biotechnology company')	Not stated	IgG, IgM (visible line)	Serum	Day 0 to ≥ 14	Yes; by week
Liu 2020b	Laboratory	ELISA kit (Lizhu, Zhuhai, China)	N-based	IgM, IgG (threshold set in healthy control sample)	Serum	Day 0 to ≥ 16	Yes; 5-day intervals
Liu 2020c	Laboratory	iFLash-SARS-CoV-2 CLIA (Shenzhen YHLO Biotech) [based on company contact]	Not described	IgM, IgG (not stated)	Serum	Not stated	No
Liu 2020d [A]	Laboratory	[A] ELISA (Hotgen, Beijing, China) [B] ELISA (Lizhu, Zhuhai, China)	[A] S-based [B] N-based	IgM, IgG (threshold not stated but method of calculation reported)	Serum	Day 0-30	Yes; unequal intervals
Long 2020 (A)	Laboratory	Magnetic CLIA (Bioscience (Chongqing) Co., Ltd)	N- and S-based	IgM, IgG (threshold not stated)	Serum	Not stated; 21-31 days after PCR test	No
Long 2020 (B)	Laboratory	Magnetic CLIA (Bioscience (Chongqing) Co., Ltd)	N- and S-based	IgM, IgG (threshold not described)	Serum	Day 2 to ≥ 23	Yes; by week
Lou 2020 [A]	[A] and [C] laboratory [B] LFA	[A] ELISA (Beijing Wantai) [B] CGIA (Beijing Wantai) [C] CLIA (Xiamen InnoDx)	[A] N- and S-based [B] and [C] not stated	IgG, IgM, Ab (thresholds as per manufacturer; NR)	Serum	Day 0-29	Yes; by week
Ma 2020a	Laboratory	CLIA (in-house)	S-based (RBD)	IgM, IgG, IgA (ROC analysis to determine optimal cut-off in RLU, which is not stated	Serum	Day 4-41	Yes; 5-day intervals
Okba 2020a	Laboratory	ELISA, beta version (EUROIMMUN)	Not stated	IgA, IgG IgM, IgG (threshold not stated but method of calculation reported)	Serum	Day 3 to > 23	Yes; by week
Padoan 2020	Laboratory	CLIA - MAGLUMI 2000 Plus nCoV (Snibe Diagnostics)	Not stated	IgM (1.0 AU/mL); IgG (1.1 AU/mL)	Serum	Day 0 to ≥ 13	Yes; by week
Pan 2020a	LFA	CGIA (Zhuhai Livzon Diagnositic Inc)	Not described	IgM, IgG (appearance of T line)	Serum or plasma	Day 1 to ≥ 15	Yes; by week

(Continued)

Paradiso 2020a	LFA	VivaDiag (Jiangsu Medomics Medical Technologies) [VivaChek?]	S-based	IgM, IgG (both indicated by presence of red/purple line)	Venous blood	Day 0 to > 15	No
Qian 2020	Laboratory	CLIA (states analysed using fully automated immune analyser from Shenzhen YHLO Biotech Co)	N- and S-based	IgM and IgG (RLU ≥ 10 AU/mL)	Serum	Not stated	Patients
To 2020a [A]	Laboratory	EIAs (in-house, considered with ELISA tests for analysis purposes)	[A] N-based [B] S-based	IgG, IgM (set as the mean value of 93 anonymous archived serum specimens from 2018, plus 3 SDs)	Used serum remnant from blood samples taken for routine biochemical testing	Day ≥ 14 (for subgroup with 2x2 data)	Samples
Wan 2020 [A]	[A] and [B] laboratory	[A] IIFT (EUROIMMUN) [B] In-house ELISA	[A] and [B] both SARS-CoV	a. Total antibody (≥ 400) b. IgM, IgG (threshold not stated)	Serum	Day 3-24	Yes; per week
Wang 2020a [A]	[A] Laboratory [B] LFA	[A] ELISA (Beijing Hotgen Biotechnology Co) [B] CGIA (Beijing Hotgen Biotechnology Co)	Not stated	IgM ([A] not stated; [B] coloured line)	Serum	Day 3-7	Yes (week 1 only)
Xiang 2020a [A]	[A] Laboratory [B] LFA	[A] ELISA (Zhu Hai Livzon Diagnostics) [B] CGIA (Zhu Hai Livzon Diagnostics)	Not stated	IgM, IgG ([A] threshold not stated; [B] coloured line)	[A] Serum, [B] Plasma	Not stated (can be estimated as 5-35 days post-admission)	No
Xiang 2020b	Laboratory	ELISA (ELISA kits, Zuhai Livzon Inc)	N-based	IgG, IgM (method to calculate threshold reported	Serum	day 0 to > 21	Yes; per week
Xiao 2020a	Laboratory	CLIA (Shenzhen YHLO Biotechnology Co. Ltd)	Not described	IgM, IgG (≤ 10 AU/mL)	Blood	Day 1-49	Yes; per week
Xie 2020a	Laboratory	CLIA (Shenzhen YHLO Biological Technology)	N- and S-based	IgG, IgM (≥ 10 AU/mL)	Serum	Day 0-41	No
Xu 2020a	LFA	CGIA (in-house)	S-based	IgG, IgM (coloured line)	Not stated	Day 15-30 of observation	No

(Continued)

Yongchen 2020	LFA	CGIA (Innovita Co. Ltd, China)	N- and S-based	IgG, IgM (coloured line)	Serum	Day 8-42	Yes; by week
Zeng 2020a	Laboratory	ELISA (Zhuhai Livzon Diagnostics)	Not stated	IgG and IgM (OD = 0.105)	Serum	Day 3-39; can extract for day 6 only	Yes; week 1 only
Zhang 2020a	Laboratory	CLIA - iFlash-SARS-CoV-2 IgG and iFlash-SARS-CoV-2 (Shenzhen YHLO Biotech Co. Ltd.)	Not described	IgM, IgG (threshold not described)	Serum	Day 1-35	No
Zhang 2020b	Laboratory	CLIA - iFlash-SARS-CoV-2 (Shenzhen YHLO Biotechnology Co Ltd) [derived from company contact]	N- and S-based	IgM, IgG (> 10.0 AU/mL); AU - antibody concentration per mL	Serum (frozen until analysis)	Day 4-18	No
Zhang 2020c	Laboratory	ELISA (in-house; anti-SARSr-CoV)	N-based (SARS-CoV)	IgM, IgG (threshold not described)	Serum	Day 0 and day 5	Yes; week 1 only
Zhang 2020d	LFA	CGIA (in-house)	S-based	Total antibodies (IgM, IgG) (Visible test and control lines)	Serum	Not stated	No
Zhao 2020a	Laboratory	ELISA (Shenzhen YHLO Biotech Co)	N- and S-based	Ab, IgM, IgG (Not stated)	Plasma	Day 1-39	Yes; week 1, 2 and 3+
Zhao 2020b	Laboratory	ELISA (in-house)	S1-based	Total antibodies (IgG or IgM) (threshold calculation method reported)	Plasma	Not stated; n = 45 during week 1	No
Zhong 2020 [A]	Laboratory	[A] and [B] in-house ELISA [C] CLIA (author institution is Maccura Biotech)	[A] N-based [B] S-based [C] N- and S-based (unclear)	IgM, IgG (optimal cut-off based on ROC analysis)	Serum	Day 1-29	No

A&E: Accident and Emergency Department; **Ab:** antibody; **AU:** arbitrary units; **CGIA:** colloidal gold immunoassay; **CL:** chemilumonescence units; **CLIA:** chemiluminescence immunoassay; **d:** days; **ELISA:** enzyme-linked immunosorbent assay; **FIA:** fluorescence immunoassay; **Flu:** fluorescence units; **HCW:** healthcare workers; **IIFT:** indirect immunofluorescence assay; **IQR:** interquartile range; **LFA:** lateral flow assay; **LIPS:** luciferase Immunoprecipitation System; **mL:** millilitre; **N-based:** nucleocapsid protein; **NR:** not reported; **OD**: Optical density; **pso:** post-symptom onset; **RBD:** receptor binding domain; **RLU:** relative light units; **ROC:** receiver operating characteristics; **S-based:** spike protein; **SD:** standard deviation; **S-flow:** flow-cytometry based test; **SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2; **SD:** standard deviation

Footnotes

[a]Please note that square brackets indicate different tests within one study.

Appendix 10. Study level assessments of study quality

Figure 10

Figure 10. Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study

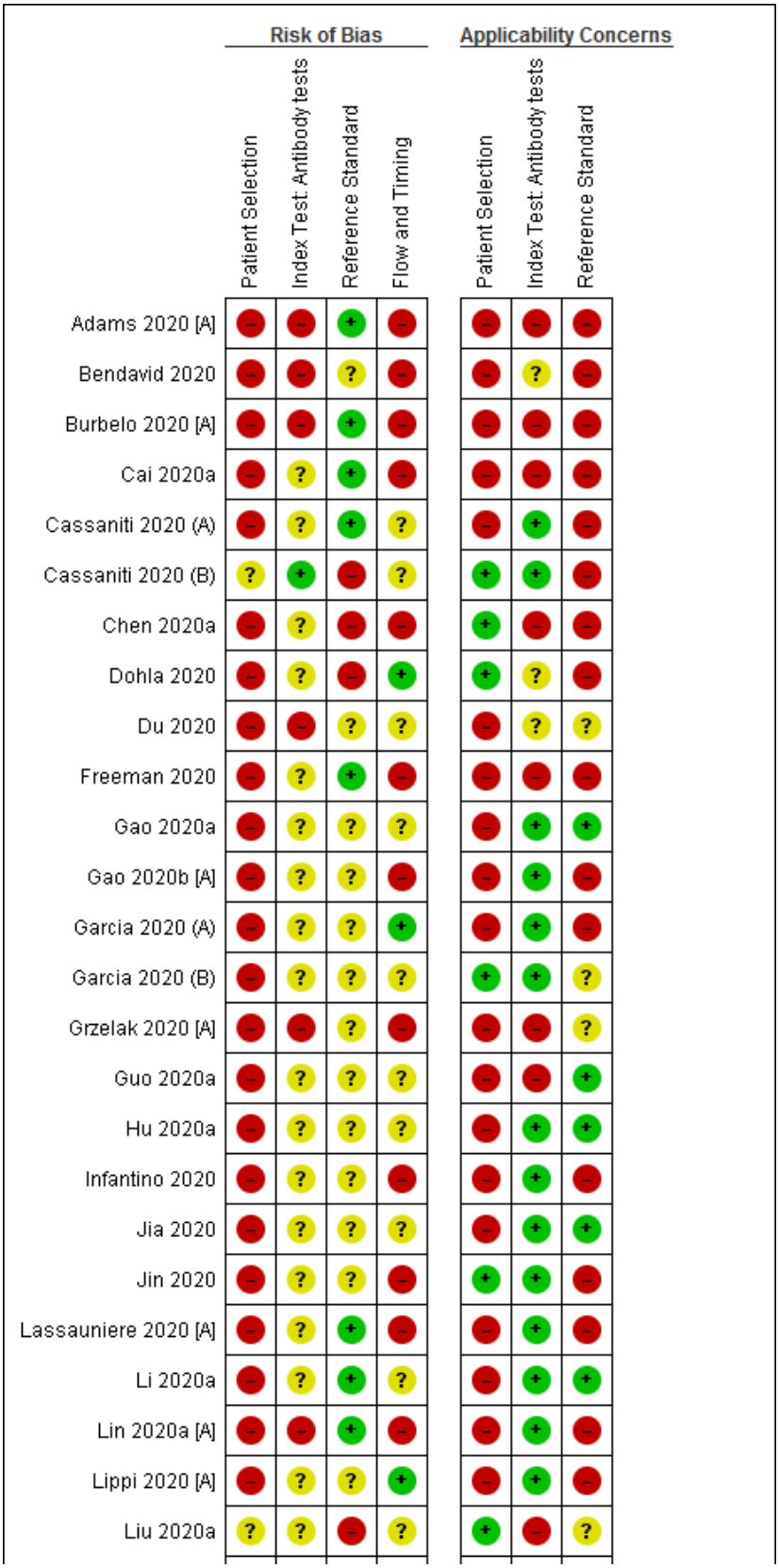
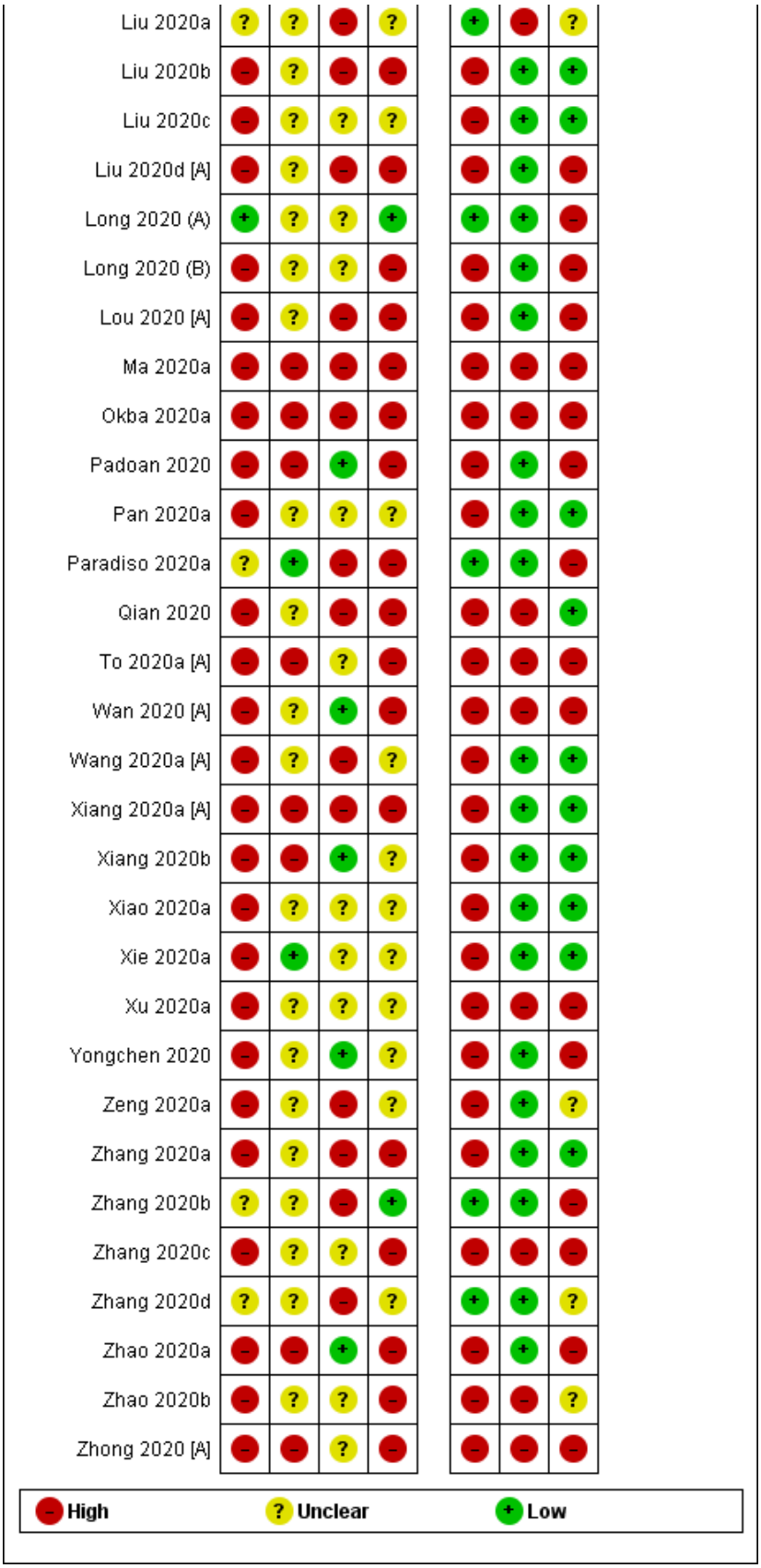


Figure 10. (Continued)



Appendix 11. Results of all studies across all time periods

Figure 11

Figure 11. Forest plot of studies evaluating tests for detection of IgG at all time post-symptom onset

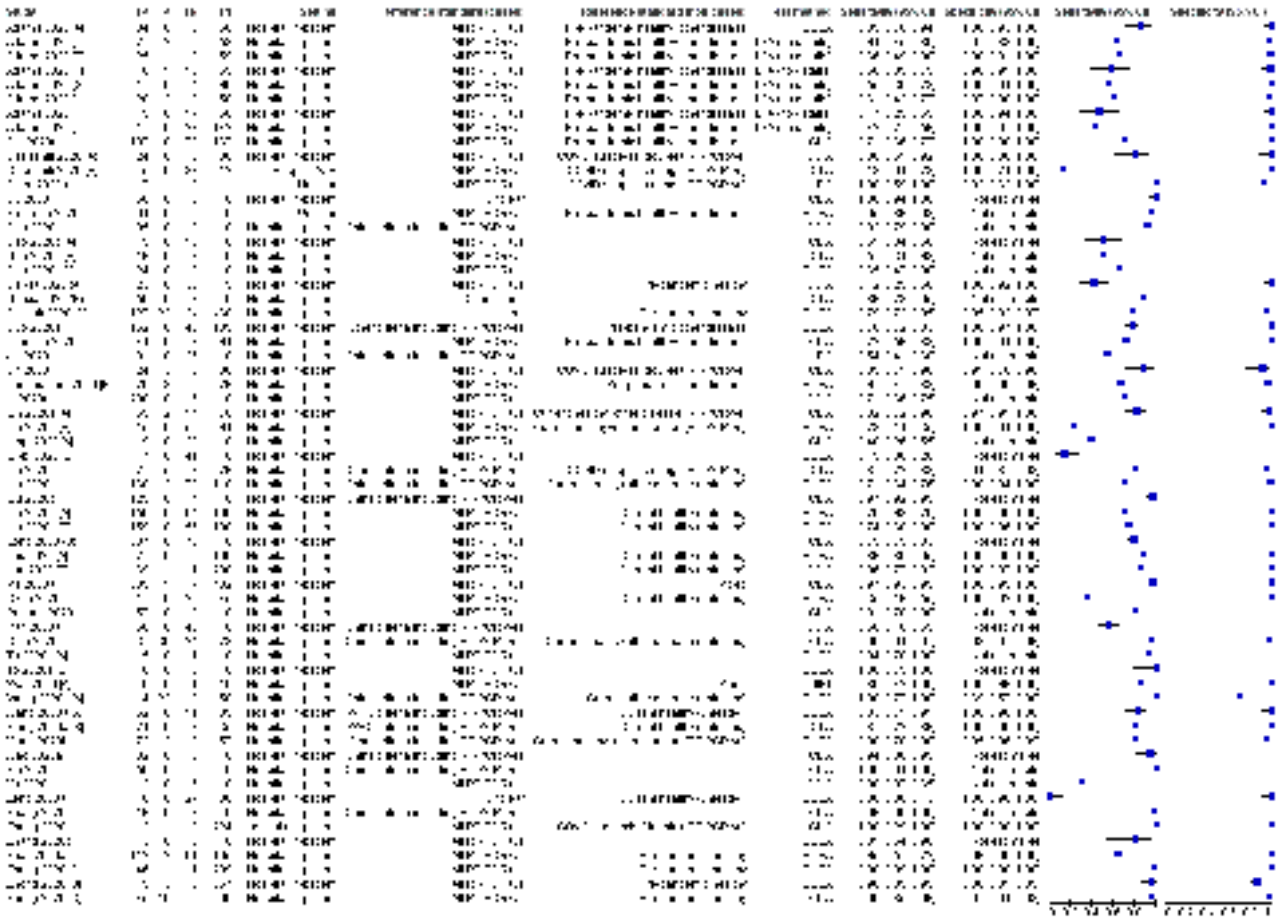


Figure 12;

Figure 12. Forest plot of studies evaluating tests for detection of IgM at all time post-symptom onset

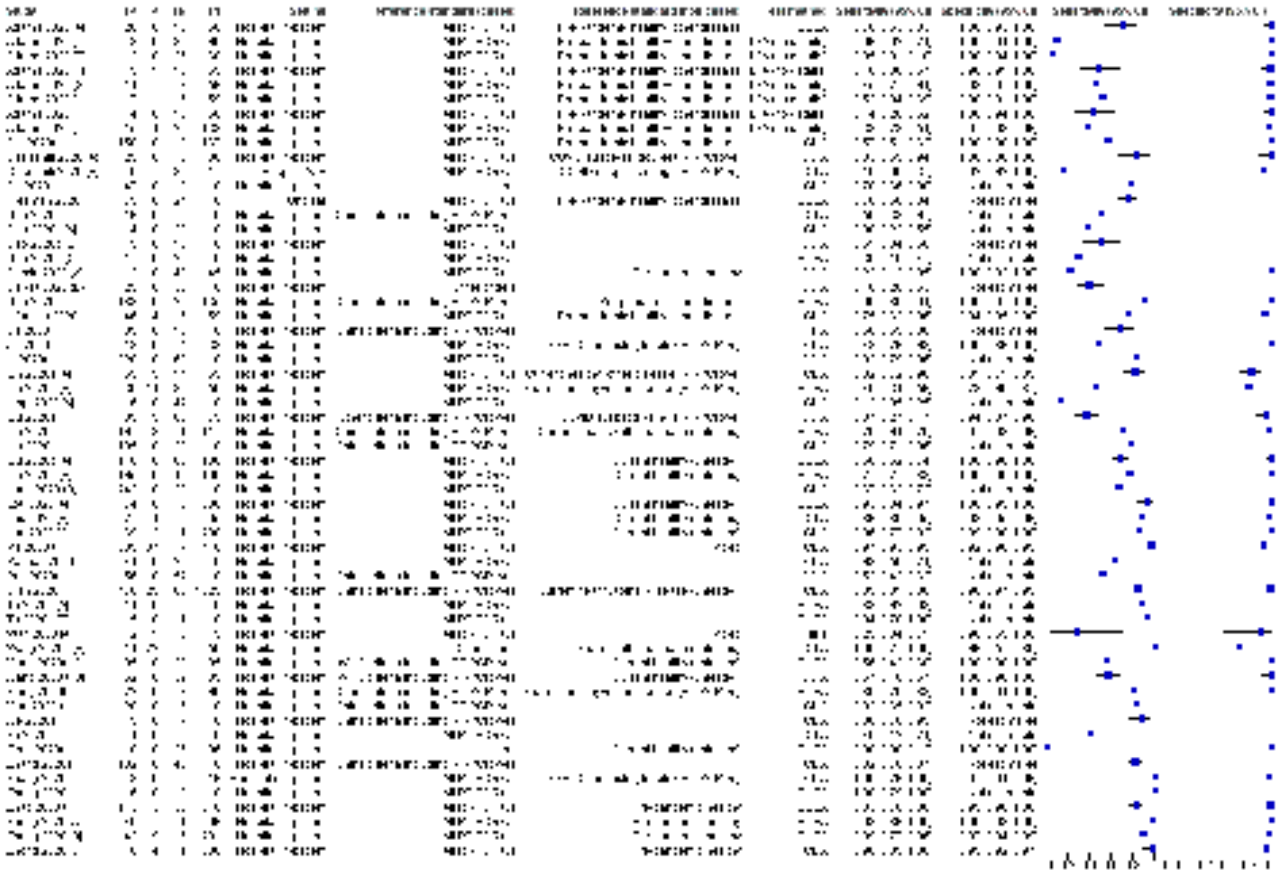


Figure 13

Figure 13. Forest plot of studies evaluating tests for detection of IgG/IgM at all time post-symptom onset.

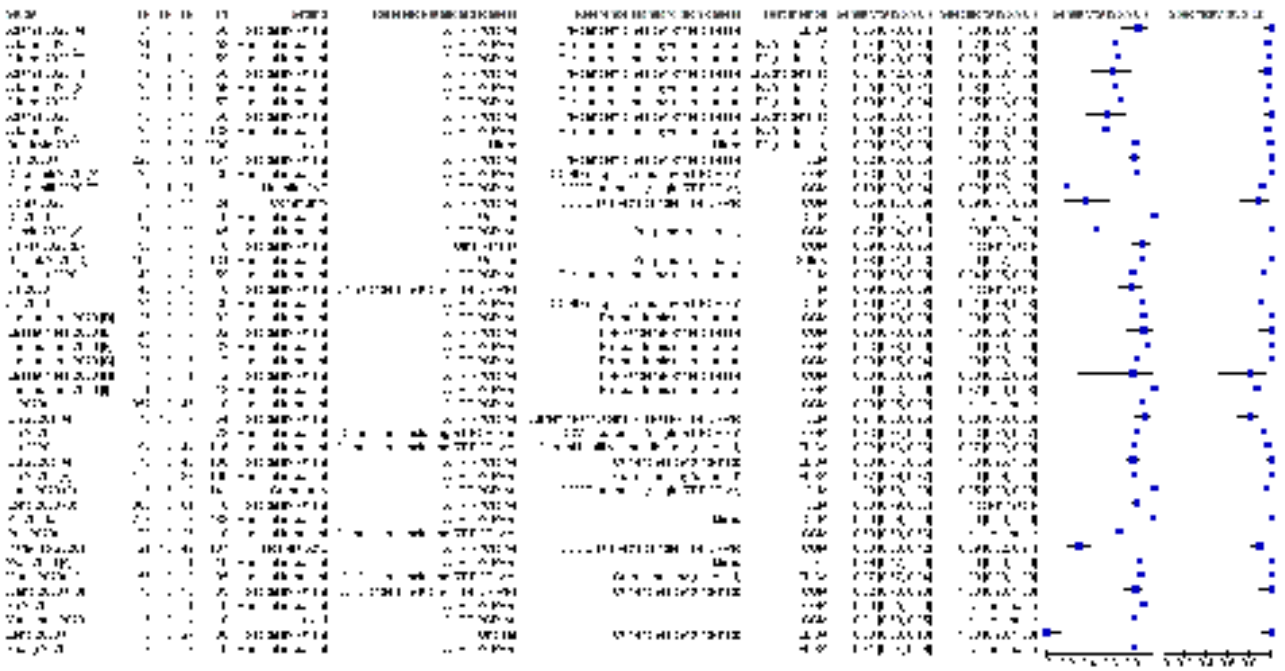
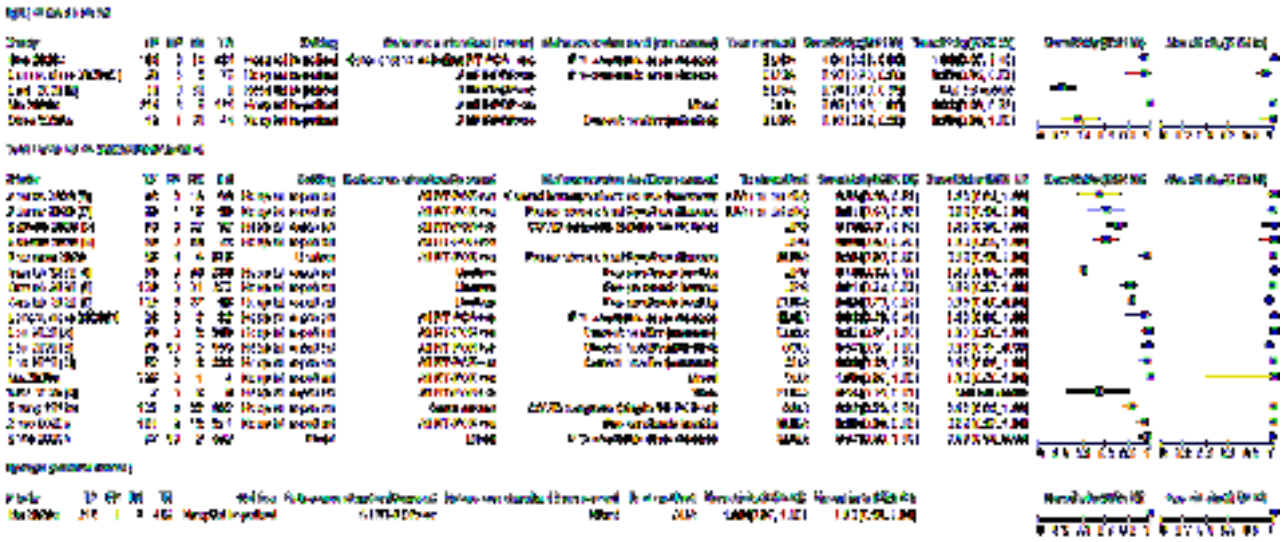


Figure 14

Figure 14. Forest plot of tests: 19 IgA (all time points), 25 Total antibodies (Ab) (all time points), 38 IgA/IgM (all time points).



Appendix 12. Manufacturer product code details identified

Test	Study	From paper	From company documentation/website
ELISA: Enzyme-linked immunosorbent assay			
Beijing Beier Bioengineering	Gao 2020b [C]	No product codes provided (Study author contacted 29 May 2020)	No IFU and not on company website, no product code identified
Beijing Hotgen	Wang 2020a [A]	ELISA (20200101 and 20200201)	No IFU, no product code identified www.hotgen.com.cn/ky/upt.html Unclear if test on website is ELISA although the company do produce ELISAs
	Liu 2020d [A]	No product code provided ; "The rS-based ELISA kit (Hotgen, Beijing, China)" Study author contacted 1 June 2020	
Beijing Wantai	Lassauniere 2020 [A]	SARS-CoV-2 Ab ELISA (CE-IVD) (WS-1096)	www.sanbio.nl/ws-1096
	Lou 2020 [A]	IgM, IgG; no product code reported in paper Study author responded: ELISA-Ab lot number NCOA20200201B ELISA-IgM lot number NCOM20200202B	

(Continued)

		ELISA-IgG lot number NCOnG20200201B	
	Zhao 2020a	No product code reported; "(ELISA) kits supplied by Beijing Wantai Biological Pharmacy Enterprise Co" Study author contacted 1 June 2020	
Darui Biotechnology	Lin 2020a [A]	No product code reported; "commercial enzyme-linked immunosorbent assay kit (Darui Biotech, CHINA)" Study author contacted 1 June 2020	No IFU, no product code on website (www.daruibiotech.com/eproduct/index_33.html)
EUROIMMUN	Lassauniere 2020 [B]; Lassauniere 2020 [C]	Anti-SARS-CoV-2 IgG (EI 2668-9601 G) Anti-SARS-CoV-2 IgA (EI 2606-9601 A)	IFU: Anti-SARS-CoV-2 ELISA (IgG) (EI 2606-9601 G) IFU: Anti-SARS-CoV-2 ELISA (IgA) (EI 2606-9601 A)
	Lippi 2020 [B]	No product code reported; "Anti-SARS-CoV-2 IgA and IgG … ELISAs; Euroimmun AG, Lübeck, Germany" Study author replied but could not supply product code	
	Okba 2020a	No product code reported; "β-versions of 2 commercial kits (EUROIMMUN)" (These are Beta versions)	Not available
Zhuhai Livzon	Xiang 2020a [A]	IgG/IgM antibody ELISA kits (lot number 2020010108)	No IFU identified; website only has the lateral flow assay en.livzon.com.cn/product/98.html No product code identified
	Xiang 2020b	ELISA kits (lot numbers IgM 20200308, IgG 20200308)	
	Zeng 2020a	No product code reported: ELISA "assay kits (Zhuhai Livzon Diagnostics INC.)" Study author contacted 1 June 2020	
Zhuhai Lizhu	Liu 2020b	No product code reported: ELISA kit "(Lizhu, Zhuhai, China)" Study author contacted 1 June 2020	Presumed to be same as above, following contact with FIND
	Liu 2020d [B]	No product code reported: ELISA kit (Lizhu, Zhuhai, China) Study author contacted 1 June 2020	
CLIA: chemiluminescence immunoassay			
Beijing Beier Bioengineering	Gao 2020b [A]	No product codes provided (Study author contacted 29 May 2020)	No IFU, not on website; no product code identified
Bioscience Co (Chongqing)	Hu 2020a	No product code reported; "(MCLIA) kit supplied by Bioscience Co., Ltd (Chongqing, China)" Study author contacted 1 June 2020	Review authors unable to find this company; no product code identified
	Long 2020 (A); Long 2020 (B)	No product code reported; "(MCLIA) kit supplied by Bioscience Co., Ltd China)" Study author supplied NMA approval numbers only:	

(Continued)

		MCLA IgG: China National Medical Products Administration approval number 20203400183; MCLA IgM: China National Medical Products Administration approval number20203400182	
Shenzhen YHLO	Infantino 2020	No product code reported; "IgM and IgG CLIA kits were from Shenzhen YHLO Biotech Co., Ltd (China)," Study author provided details: IgG anti-SARS Cov2 C86095G; IgM C86095M LOT NUMBER 207	Company flyer: iFlash-SARS-CoV-2 IgG (C86095G) iFlash-SARS-CoV-2 IgM (C86095G)
	Jin 2020	No product code reported; "(CLIA) kits used in this study were supplied by Shenzhen YHLO Biotech Co., Ltd (China)" Study author contacted 1 June 2020	
	Liu 2020c	No product code reported; "SARS-CoV-2 antibody detection kit (YHLO Biotech, Shenzhen, China" Study author contacted 1 June 2020	
	Xiao 2020a	No product code reported; "IgM and IgG were analyzed by … CLIA … (Shenzhen Yahuilong Biotechnology Co., Ltd). Study author contacted 1 June 2020	
	Xie 2020a	No product code reported; "IgG and IgM assays were purchased from YHLO Biological Technology Co., Ltd., Shenzhen, China" Study author contacted 1 June 2020	
	Zhang 2020a	No product code reported; "(CLIA) Assays panel (Shenzhen YHLO Biotech Co., Ltd., Shenzhen, China)" Study author contacted 1 June 2020	
	Zhang 2020b	No product code reported; "CLIA detection kit from Shenzhen Yahuilong Biotechnology Co Ltd" Study author contacted 1 June 2020	
Snibe Diagnostic - MAGLUMI	Lippi 2020 [A]	No product code reported; "MAGLUMI 2019-nCoV IgG and IgM". (IgM - 130219016M; IgG – 130219015M) Study author contacted 1 June 2020 Study author replied 1 June 2020 with IFU (no lot numbers provided; code from IFU added above)	From image on website: IgM - Ref 130219016M; Lot 2712000501 IgG - Ref 130219016M; Lot 2722000501 (www.snibe.com/zh_en/en_newsView.aspx?id=576)
	Padoan 2020	No product code reported; "MAGLUMI 2000 Plus (New Industries Biomedical Engineering Co., Ltd [Snibe], Shenzhen, China)" Study author supplied details: - for SARS-CoV-2 IgG lot number used for all the 87 measurements: 2722000102, kit number 8131;	

(Continued)

		- for SARS-CoV-2 IgM lot number used for all the 87 measurements: 2712000201, kit number 5122	
Xiamen InnoDx Biotech	Lou 2020 [C]	No product code reported; "CMIA reagents were supplied by Xiamen InnoDx Biotech Co., Ltd., China Study author supplied following details: CMIA-Ab product code CT0669 lot number 20200201 CMIA-IgM product code CT0667 lot number 20200201	Review authors unable to find website for this company
Other laboratory-based tests			
EUROIMMUN	Wan 2020 [A]	No product code reported; "Anti-SARS CoV Indirect 62 Immunofluorescence test (IIFT) (IgM & IgG) by Euroimmun (Germany)" (Test uses SARS-Cov not SARS-CoV-2)	
Lateral flow assays			
Acro Biotech	Lassauniere 2020 [H]	2019-nCoV IgG/IgM Rapid Test Cassette (INCP-402)	Code from IFU and Assay Genie website: INCP-402
Artron Laboratories	Lassauniere 2020 [G]	Coronavirus Diseases 2019 (COVID-19) IgM/IgG Antibody Test (A03-51-322),	Brochure only; but no product code www.artronlab.com/products/CoVBrochure-ver3.pdf
Autobio Diagnostics	Lassauniere 2020 [F]	Anti-SARS-CoV-2 Rapid Test (RTA0204)	Code from IFU: Anti-SARS-CoV-2 Rapid Test (RTA0203)
Beijing Beier Bioengineering	Gao 2020b [B]	No product codes provided (Study author contacted 29 May 2020)	No IFU and not on company website; Distributor: www.unifier.one/en/beier-new-2019-coronavirus-covid-19-rapid-test.html 2019- New Coronavirus IgM/IgG Rapid Test Casette (WB/S/P) No product code
Beijing Diagreat	Jia 2020	COVID IgM/IgG antibodies kit, which have sent to Beijing Institute of Medical Device Testing (BIMT) for product verification (lot: 20200214)	Manual from 2019-nCoV IgM Antibody Determination Kit (immunochromatographic Assay) Product No. P11802 2019-nCoV IgG Antibody Determination Kit (Immunochromatographic Assay) Product No. P11801

(Continued)

Beijing Hotgen	Wang 2020a [B]	Kit provided by Beijing Hotgen Biotechnology Co., Beijing, China: (lot number 20200208 and 105 20200229 for GICA)	No IFU, on website but no product code www.hotgen.com.cn/ky/up-t.html Coronavirus disease (COVID-19) Antibody Test (Colloidal Gold)
Beijing Wantai	Lou 2020 [B]	No product code reported Study author provided: LFIA-Ab lot number JNB20200202F LFIA-IgM lot number JNM20200203F LFIA-IgG lot number JNG20200201F	Code from IFU: WJ-2701, WJ-2710, WJ-2750 Website: Rapid test for coronavirus Ab (CE-IVD) (WJ-2750 www.sanbio.nl/wj-2750)
CTK Biotech - OnSite	Lassauniere 2020 [E]	OnSite COVID-19 IgG/IgM Rapid Test (R0180C)	IFU: OnSite COVID-19 IgG/IgM Rapid Test R0180C
Dynamiker Biotechnology	Lassauniere 2020 [D]	2019-nCOV IgG/IgM Rapid Test (DNK-1419-1)	IFU: 2019-nCOV IgG/IgM Rapid Test Catalogue No: DNK-1419-1
Hangzhou Alltest	Lassauniere 2020 [I]	2019-nCoV IgG/IgM Rapid Test Cassette (INCP-402)	IFU; 2019-nCoV IgG/IgM Rapid Test Cassette (Whole blood/serum/plasma) Package Insert INCP-402
	Garcia 2020 (A)	AllTest COV-19 IgG / IgM kit (no product code)	
	Garcia 2020 (B)	Study author provided IFU (product code NCP-402)	
Innovita Biological	Gao 2020a	No product code reported Study author contacted 1 June 2020	IFU: 2019-nCoV Ab Test (Colloidal gold); Catalogue No. YF 319C
	Yongchen 2020	No product code reported Study author provided lot number: 20200205	
Jiangsu Medomics	Li 2020a	No product code reported "SARS-CoV-2 rapid IgG-IgM combined antibody test kit" Study author contacted 1 June 2020	Review authors were unable to find this company; study was also provided to review authors by Lomina (www.test-covid19.com/); no product code identified
Vivachek - VivaDiag	Paradiso 2020a	No product code reported; "Viva-Diag™ kit *produced by Jiangsu Medomics* Medical Technologies kit (https://www.vivachek.com/vivachek/English/prods/prod-covid19.html)"; link no longer active. test considered to be Vivachek test Study author contacted 1 June 2020	Package insert VivaDiag SARS-CoV-2 IgM/IgG Rapid Test (VID35-08-011 / VID35-08-012 / VID35-08-013 / VID35-08-014 / VID35-08-015)

(Continued)

	Cassaniti 2020 (A) Cassaniti 2020 (B)	No product code reported; "VivaDiag COVID-19 IgM/IgG from VivaChek"; study also provided by Vivachek following company contact Study author provided lot number E2002002, REF VID35-08-011	
Zhuhai Livzon	Pan 2020a	No product code reported Study author contacted 1 June 2020	Product flyer; Diagnostic Kit for IgM/IgG Antibody to Coronavirus (SARS-CoV-2); Catalogue number: 01040048
	Xiang 2020a [B]	IgG/IgM antibody GICA kits (lot number 2001010220)	

FIND: Foundation for Innovative Diagnostics; **IFU:** instructions for use; **NMA:** China National Medical Products Administration

HISTORY

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CONTRIBUTIONS OF AUTHORS

JJD was the contact person with the editorial base.
JJD co-ordinated contributions from the co-authors and wrote the final draft of the review.
JJD, JDi, YT, CD, STP, IH, AA, LFR, MP, JDr, SB screened papers against eligibility criteria.
RS conducted the literature searches
JJD, JDi, YT, CD, STP, IH, AA, LFR, MP, JDr, SB appraised the quality of papers.
JJD, JDi, YT, CD, STP, IH, AA, LFR, MP, JDr, SB extracted data for the review and sought additional information about papers.
JJD and JDi entered data into Review Manager 2014.
JJD and JDi analysed and interpreted data.
JJD, JDi, YT, CD, STP, RS, ML, LH, AVB, DE, SD worked on the methods sections.
JJD and JDi responded to the comments of the referees.
JJD.is the guarantor of the update.

DECLARATIONS OF INTEREST

Jonathan J Deeks: none known

Jacqueline Dinnes: none known

Yemisi Takwoingi: none known

Clare Davenport: none known

René Spijker: the Dutch Cochrane Centre (DCC) has received grants for performing commissioned systematic reviews. In no situation, the commissioner had any influence on the results of the work.

Sian Taylor-Phillips: none known

Ada Adriano: none known

Sophie Beese: none known

Janine Dretzke: none known

Lavinia Ferrante di Ruffano: none known

Isobel Harris: none known

Malcolm Price: none known

Sabine Dittrich: is employed by FIND with funding from DFID and Australian Aid. FIND is a global non-for profit product development partnership and WHO Diagnostic Collaboration Centre. It is FIND's role to accelerate access to high quality diagnostic tools for low resource

settings and this is achieved by supporting both R&D and access activities for a wide range of diseases, including COVID-19. .FIND has several clinical research projects to evaluate multiple new diagnostic tests against published Target Product Profiles that have been defined through consensus processes. These studies are for diagnostic products developed by private sector companies who provide access to know-how, equipment/reagents, and contribute through unrestricted donations as per FIND policy and external SAC review.

Devy Emperador: is employed by FIND with funding from DFID and KFW. FIND is a global non-for profit product development partnership and WHO Diagnostic Collaboration Centre. It is FIND's role to accelerate access to high quality diagnostic tools for low resource settings and this is achieved by supporting both R&D and access activities for a wide range of diseases, including COVID-19. .FIND has several clinical research projects to evaluate multiple new diagnostic tests against published Target Product Profiles that have been defined through consensus processes. These studies are for diagnostic products developed by private sector companies who provide access to know-how, equipment/reagents, and contribute through unrestricted donations as per FIND policy and external SAC review.

Lotty Hooft: none known

Mariska MG Leeflang: none known

Ann Van den Bruel: none known

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Internal sources

- Liverpool School of Tropical Medicine, UK
- University of Birmingham, UK

External sources

- Department for International Development, UK

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- National Institute for Health Research (NIHR), UK
- NIHR Birmingham Biomedical Research Centre at the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham, UK

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

As we explained in the review, due to poor reporting, we were unable to identify studies that evaluated the test in patients who were symptomatic (active disease) separately from those who had recovered from their symptoms (convalescent). Our stratification of results according to days since onset of symptoms will in part be related to these categorisations.

We planned to check the following websites for eligible index tests, however these did not prove to be very accessible or easy to use and, after initial review, were not further considered:

- National Institute for Health Research (NIHR) Innovation Observatory (www.io.nihr.ac.uk/)
- www.rapidmicrobiology.com/test-method/testing-for-the-wuhan-coronavirus-a-k-a-covid-19-sars-cov-2-and-2019-ncov

We planned to check the following evidence repository for additional eligible studies however, the EPPI-Centre and Norwegian Institute of Public Health resources proved to be more accessible therefore we decided to prioritise our other sources of evidence.

- Meta-evidence (meta-evidence.co.uk/the-role-of-evidence-synthesis-in-covid19/)

QUADAS-2 (Whiting 2011), item "Was there an appropriate interval between index test(s) and reference standard?" was dropped from assessment because for antibody tests, the body's immune response to SARS-CoV-2 infection tends to increase over time such that the time between confirmation of the presence of SARS-CoV-2 an the index test is less relevant than the time from symptom onset to the application of the index test.

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ALLEGATO N. 3

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Short Communication

Test, test, test for COVID-19 antibodies: the importance of sensitivity, specificity and predictive powers

N. Kumleben [a], R. Bhopal [b], T. Czypionka [c, d], L. Gruer [b, e, *], R. Kock [f], J. Stebbing [g], F.L. Stigler [h]

[a] Greenmantle LLC, New York City, NY 10010, USA
[b] Usher Institute, University of Edinburgh, Edinburgh, EH8 9AG, UK
[c] Institute for Advanced Studies, 1080 Vienna, Austria
[d] London School of Economics and Political Science, London, UK
[e] Institute of Health and Wellbeing, University of Glasgow, G12 8RZ, UK
[f] Department of Pathobiology and Population Science, Royal Veterinary College, Hawkshead Lane, Hatfield, AL9 7TA, UK
[g] Imperial College, Hammersmith Hospital, London, W12 0HS, UK
[h] Österreichische Gesundheitskasse, 8010 Graz, Austria

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody tests of varying specificity and sensitivity are now available. For informing individuals whether they have had coronavirus disease 2019 (COVID-19), they need to be very accurate. For measuring population prevalence of past infection, the numbers of false positives and negatives need to be roughly equal.

With a series of worked examples for a notional population of 100,000 people, we show that even test systems with a high specificity can yield a large number of false positive results, especially where the population prevalence is low. For example, at a true population prevalence of 5%, using a test with 99% sensitivity and specificity, 16% of positive results will be false and thus 950 people will be incorrectly informed they have had the infection. Further confirmatory testing may be needed.

Giving false reassurance on which personal or societal decisions might be based could be harmful for individuals, undermine public confidence and foster further outbreaks.

To help reverse the current lockdowns while suppressing COVID-19 rates, we need to identify who currently has the infection and who has had it and recovered. As reverse transcriptase polymerase chain reaction (RT-PCR) testing to detect current infection has been recently discussed in detail,[1] we focus in this article on antibody tests. The presence or absence of antibodies can inform individuals if they have had the infection or not and guide personal and societal decisions about if and when they can return to normal activities. Antibody testing thus needs to be particularly accurate. It can also be used to provide an estimate of the population prevalence of previous infection. We demonstrate that for this purpose high accuracy is not required, but the numbers of false positives and false negatives need to be approximately equal.

Antibody tests are increasingly available but with variable accuracy. It is hoped they can be used to identify people who are at least partially immune. Immunity certificates, a more appropriate phrase than immunity passports that promises too much, for individuals thought to have recovered from COVID-19, are being discussed internationally.[2–4] Whether tests are carried out for clinical diagnosis, screening or immunity certificates, we need to have sufficient confidence they are accurate.

A sensitive test will detect the presence of antibodies to SARS-CoV-2 (the virus that causes COVID-19), and a specific test will not react to other antibodies e.g. to other coronaviruses. No diagnostic or screening test is perfect and incorrect results are inevitable, not least because the timing of the test is critical. Seroconversion takes time, with IgM, IgG and IgA antibodies usually developing in that order, and can be variable and dependent upon the severity of the illness and the individual's immune

* Corresponding author. Usher Institute, University of Edinburgh, Edinburgh, EH8 9AG, UK.
E-mail addresses: nicholas@gmantle.com (N. Kumleben), raj.bhopal@ed.ac.uk (R. Bhopal), czypionk@ihs.ac.at (T. Czypionka), gruer.health@gmail.com (L. Gruer), rkock@rvc.ac.uk (R. Kock), j.stebbing@imperial.ac.uk (J. Stebbing), florian.stigler@medunigraz.at (F.L. Stigler).

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system. Antibody levels subsequently decline with time. Antibody test systems may perform less well than the manufacturers' results suggest. For example, both Roche and Abbott reported their antibody test had 100% sensitivity for samples taken 14 days or more after the onset of symptoms, yet Public Health England found sensitivity at 14 or more days of only 87% and 93.4%, respectively.[5,6]

We show here how to measure the test's accuracy and how this changes along with the prevalence of disease (12 tables showing the results with varying sensitivity, specificity and population prevalence of 1%, 5%, 10% and 20% are available in the Supplementary File). The two key measures of its accuracy are sensitivity and specificity, set out in Table 1, with the cells identified as A (true positives), B (false positives), C (false negatives) and D (true negatives). Sensitivity (A/A + C) is the proportion of people with a disease who, when tested, receive a positive test result. It is also known as the true positive rate. Specificity (D/D + B) is the proportion of individuals without a disease who, when tested, receive a negative test result. It is also known as the true negative rate.

To establish sensitivity and specificity, we could test a sample of patients with proven disease (in this case laboratory detection of SARS-CoV-2), and a sample of people known to be free of disease (for example, using stored blood samples taken before COVID-19 existed in humans). In practice, a test's performance will usually be poorer than the values established due, for example, to problems in storing or transporting specimens or the variable time lag from the onset of infection until antibodies appear in the blood (seroconversion) and then decline. The proportion of test results that are false partly depends on the prevalence of the disease in the population. With a low prevalence, even a test with high sensitivity and specificity will produce a high proportion of false positives. In this article, we focus on the outcomes of tests of variable accuracy with 5% population prevalence in a hypothetical group of 100,000 people, of whom 5000 have had the infection and 95,000 have not. This is a plausible current prevalence of past COVID-19 in many countries[7–9] although it could be a lot higher in some areas.

Table 1 shows that if the sensitivity is 90%, 4500 people will correctly test positive, but 500 will incorrectly test negative and be wrongly told they have no antibody evidence of the disease. If the specificity is 90%, 85,500 people will correctly test negative, but 9500 will incorrectly test positive and be wrongly told they have antibody evidence of previous infection. Thus, of the 14,000 people who received positive test results, only 32% (4500/14,000; A/A + B) had the disease. This is referred to as the predictive value (or power) of a positive test. The other 68% would be given wrong information. Of the 86,000 people who received negative tests, 99% (85,500/86,000; D/C + D) would receive a correct result. This is called the predictive value (or power) of a negative test.

Sensitivity and specificity vary with different tests but, for any particular antibody test, these can be adjusted by altering the level of antibody required to determine a positive result. Requiring a higher level of antibody for a positive result would increase the specificity but lower the sensitivity. This would reduce the false positives (C) but increase the false negatives (B). Choosing a test that has 80% sensitivity and 99% specificity, as shown in Table 2, 81% of people who test positive have had the disease, an increase from 32%. Now, about one in five people who test positive will not have had the disease. This shows that when the prevalence of the disease is low, antibody testing, even with a specificity as high as 99%, still produces many false positives so the predictive power of a positive test is far from 100%.

If a test is extremely accurate, as is claimed for the Roche and Abbott systems, say 99% sensitivity and specificity, the results are shown in Table 3. Even now, the predictive power of a positive test has only risen from 81% with a sensitivity of 90%, to 83.8%. If the prevalence rises to 20% then the predictive power of a positive test is 96.1% and of a negative test 99.7% (Supplementary File Table A12).

If immunity certificates, or personal or societal decisions about returning to normality, are based on these results, a significant proportion will be incorrect. Where the disease has become highly prevalent, for example, among health care and care home workers,

Table 1
Predictive powers of a test with 90% sensitivity and specificity (5% prevalence).

Test result (90% sensitivity and 90% specificity)	People truly with disease	People truly without disease	Totals
Positive	4500 (A)	9500 (B)	14,000
Negative	500 (C)	85,500 (D)	86,000
Total	5000	95,000	100,000

Predictive value of a positive test: A/A + B = 32.1%.
Predictive value of a negative test: D/D + C = 99.4%.

Table 2
Predictive powers of a test with 80% sensitivity and 99% specificity (5% prevalence).

Test result (80% sensitivity and 99% specificity)	People truly with disease	People truly without disease	Totals
Positive	4000 (A)	950 (B)	4950
Negative	1000 (C)	94,050 (D)	95,050
Total	5000	95,000	100,000

Predictive value of a positive test: A/A + B = 80.8%.
Predictive value of a negative test: D/D + C = 98.9%.

Table 3
Predictive powers of a test with 99% sensitivity and 99% specificity (5% prevalence).

Test result (99% sensitivity and 99% specificity)	People truly with disease	People truly without disease	Totals
Positive	4950 (A)	950 (B)	5900
Negative	50 (C)	94,050 (D)	94,100
Total	5000	95,000	100,000

Predictive value of a positive test: A/A + B = 83.8%.
Predictive value of a negative test: D/D + C = 99.9%.

the power of a positive test would be higher, therefore more reliance could be placed on it. Even with a prevalence of 20% and 99% sensitivity and specificity, the test itself does not give a guarantee at the individual level, and personal and clinical judgements are required in applying the findings. A major hope of antibody testing is that those who test positive can resume work and social activities more fully and confidently than those who test negative. The presence of antibodies should signify the same illness will not recur, the person is not contagious and there is at least partial immunity to future COVID-19 infections. We need to establish whether this is true.[10]

If the purpose of antibody testing is to assess the prevalence of COVID-19 in a representative sample of the population, these clinical issues do not apply. The veracity of the prevalence derived by such measurements will depend upon achieving equal false positives and false negatives. For example, although the true prevalence is 5%, Tables 1–3 give a prevalence in the hypothetical population of 100,000 people of 14% (14,000 positives), 4.95% (4950 positives), and 5.9% (5900 positives), respectively. Perhaps surprisingly, the test with 80% sensitivity and 99% specificity (Table 2) gives the most accurate estimate at this level of population prevalence.

In conclusion, at currently reasonable estimates of the general population prevalence, even high sensitivity and specificity will produce an important number of false positives. People testing positive, especially those without indicative case histories, may need further testing to confirm the result. Given the current uncertainty about the level of immunity signalled by antibodies, all those testing positive for antibodies would be well advised to maintain protective measures. More information is also urgently needed to ascertain the strength and duration of immunity in people who have recovered from COVID-19, and whether some can still be infectious or become reinfected. Giving false security and reassurance could be harmful for individuals, undermine public confidence and foster further outbreaks.

Author statements

Ethical approval

Not required.

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Competing interests

None declared.

Author contributions

The article was conceived by J.S. during a discussion initiated by R.B. in the COVID-19 researchers Google Group. The manuscript was drafted by N.K. All authors commented on the drafts and agreed the final version. L.G. is the corresponding author and guarantor of the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2020.06.006.

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ALLEGATO N. 4

INDIZIONE DI GARA IN PROCEDURA SEMPLIFICATA E DI MASSIMA URGENZA
PER L'ACQUISIZIONE E DISTRIBUZION DI 2.000.000 KIT RAPIDI QUALITATIVI PER L'EFFETTUAZIONE DI TEST SIEROLOGICI SULL'INTERO TERRITORIO NAZIONALE PRIORITARIAMENTE DESTINATI AGLI OPERATORI SCOLASTICI

1. Informazioni concernenti l'Amministrazione aggiudicatrice e la procedura di aggiudicazione

La procedura competitiva semplificata è indetta dal Commissario straordinario per l'attuazione e il coordinamento delle misure occorrenti per il contenimento e il contrasto dell'emergenza epidemiologica COVID – 19 (di seguito: "Commissario straordinario per l'emergenza COVID – 19" oppure "ente aggiudicatore"), ai sensi dell'art. 122 del decreto-legge 17 marzo 2020, n. 18, con le modalità qui di seguito definite:

- Procedura competitiva, aperta alle aziende produttrici e relativi agenti o distributori per l'Italia dei materiali sanitari richiesti, mediante la presente "indizione di gara" ("call") postata sui siti istituzionali del Ministero della Salute, del Ministero dell'Istruzione e della Presidenza del Consiglio dei Ministri - Dipartimento della protezione civile, valida per la durata di sette giorni e comunque non oltre il 15 luglio 2020;
- Presentazione delle offerte, con modalità telematica, entro la stessa data;
- Valutazione delle offerte da parte della Commissione esaminatrice, con le modalità e la tempistica indicata al punto n. 8 e sulla base dei criteri di valutazione di cui al punto n. 7;
- Successiva sottoscrizione del contratto di fornitura, entro il 28 luglio 2020.

Per quanto concerne la presente procedura i riferimenti essenziali sono i seguenti:

- Referente e responsabile del procedimento: Roberto Rizzardo;
- Modalità di trasmissione delle offerte: piattaforma di e-procurement Invitalia;
- Recapiti per comunicazioni o richieste di chiarimenti: piattaforma e-procurement Invitalia.

2. Tipo e oggetto della procedura

La procedura è una procedura competitiva semplificata di massima urgenza, predisposta in deroga alle disposizioni del Codice dei contratti pubblici (D. Lgs. 18 aprile 2016, n. 50), e concerne la fornitura urgente di 2.000.000 di Kit sierologici rapidi per la rilevazione di specifiche per SARS CoV 2 , comprensivi di tutte le componenti necessarie a garantire utilizzo e risultato dell'analisi, aventi elevate caratteristiche di qualità, funzionalità e rapidità, adeguatamente validate da parte di laboratori qualificati o agenzie regolatorie a valenza nazionale o internazionale, con possibile successiva estensione della fornitura nelle circostanze e con le modalità di cui al punto 10.

3. Requisiti qualitativi dei beni oggetto della procedura

le caratteristiche essenziali dei prodotti oggetto della procedura sono:

a) La tipologia di Kit qualitativo rapido, per la rilevazione di IgG e IgM specifiche per SARS CoV-2, completo di relativi accessori perché sia immediatamente utilizzabile e che abbia tempi di ottenimento del risultato quanto più celeri possibile;
b) L'avvenuta validazione dei test da parte di laboratori qualificati o agenzie regolatorie operanti a livello nazionale o internazionale;

c) Una specificità dei test non inferiore al 95%;
d) Una sensibilità dei test non inferiore al 92 %;
e) La rapidità di trasporto e consegna della fornitura almeno nei capoluoghi di provincia di tutto il territorio nazionale secondo le indicazioni del committente e comunque entro e non oltre il 10 agosto 2020;
f) La capacità di assicurare la fornitura di un numero minimo di test pari a 500.000

L'assenza dei requisiti minimi descritti è condizione espressa di esclusione dalla gara.

4. Requisiti soggettivi degli operatori economici interessati

Sono richiesti i medesimi requisiti di onorabilità e affidabilità previsti dal Codice dei contratti pubblici (D. Lgs. 18 aprile 2016, n. 50), comprovabili, in considerazione dell'urgenza, anche mediante autocertificazioni.

Il mancato possesso dei requisiti previsti dall'art. 80 del predetto Codice è anch'esso motivo di esclusione dalla gara.

5. Modalità di inoltro delle offerte

Le offerte, corredate della documentazione occorrente, in formato PDF, andranno presentate tramite la piattaforma di e-procurement di Invitalia.

Il documento recante l'offerta qualitativa (descrizione dei prodotti e dei loro requisiti qualitativi come previsti al punto 3) e quello recante l'offerta economica dovranno essere sottoscritti digitalmente.

In particolare l'offerta economica dovrà indicare il prezzo unitario richiesto per ciascun Kit.

6. Commissione di gara

Le offerte saranno valutate da una Commissione di gara nominata dal Commissario straordinario per l'emergenza COVID – 19 e composta da:

a) due esperti designati del Comitato tecnico-scientifico istituito presso il Dipartimento della protezione civile per l'emergenza COVID-19
b) un rappresentante del Ministero della Salute (appartenente alla struttura ministeriale);
c) un rappresentante del Ministero dell'Istruzione (appartenente alla struttura ministeriale);
d) un esperto in materie giuridiche con funzioni di Presidente;
e) un componente della struttura alle dipendenze del Commissario Straordinario per l'emergenza da COVID – 19, con funzioni di segretario e senza diritto di voto.

Nell'espletamento delle procedure di gara, ove necessario, la Commissione potrà avvalersi del Comitato Tecnico Scientifico istituito presso il Dipartimento della protezione civile per l'emergenza COVID-19.

Tutti lavori della Commissione di gara possono svolgersi in videoconferenza o avvalendosi di altri collegamenti da remoto.

7. Criteri di valutazione delle offerte

L'appalto sarà aggiudicato secondo il criterio dell'offerta economicamente più vantaggiosa sulla base del miglior rapporto qualità/prezzo, secondo gli elementi di valutazione e le modalità di seguito indicati.

Il punteggio complessivo sarà dato dalla somma tra il punteggio conseguito per l'offerta tecnica ed il punteggio conseguito per l'offerta economica. Il punteggio massimo complessivo è pari a 100 punti, come di seguito distribuiti:

ID	ELEMENTI DI VALUTAZIONE	PUNTEGGIO MASSIMO
1	OFFERTA TECNICA	90
2	OFFERTA ECONOMICA	10
	TOTALE	**100**

La valutazione delle offerte pervenute sarà svolta in base ai criteri e sub-criteri di seguito indicati:

SUB CRITERI		Sub punteggi
A	a. Percentuale di specificità, oltre quelle minime richieste (95%)	38
B	b. Percentuale di sensibilità, oltre quelle minime richieste (92%)	37
C	c. Quantità di prodotti disponibili	10
D	d. Tempi di ottenimento del risultato del test	5
TOTALE OFFERTA TECNICA		90
E	Prezzo	10
TOTALE		100

L'individuazione dell'offerta economicamente più vantaggiosa sarà determinata in base alla seguente formula:

P= (a*38+b*37+c*10 + d*5+e*10)

I coefficienti **a** e **b** di natura quantitativa dei criteri **A** e **B**:

- saranno determinati mediante l'applicazione della seguente formula, attribuendo il coefficiente zero all'offerta meno conveniente per la Stazione Appaltante (ossia a quella che prevede la percentuale minima con riferimento a ciascun criterio – (95% per il

subcriterio A e 92% per il Subcriterio B) e il coefficiente uno all'offerta economica più conveniente (ossia a quella che offre la percentuale + alta):

$$\boldsymbol{P} = \frac{[\%\ \boldsymbol{offerta\ Concorente\ A} - \%\ \boldsymbol{minima}]}{[\%\ +\ \boldsymbol{alta\ ottenuta\ in\ gara}\ - \%\ \boldsymbol{minima}]} * \boldsymbol{punti\ criterio}$$

I coefficienti **c** di natura quantitativa del criterio **c**

sarà determinato con la seguente formula, adoperando il metodo dell'interpolazione lineare, attribuendo il coefficiente zero all'offerta minima possibile (ossia quantità pari a 500.000) e il coefficiente uno alla quantità più elevata offerta in sede di gara:

P *= Qa/Qmax *punti criterio*

I coefficienti **d** di natura quantitativa del criterio **D**

sarà applicata la formula del Minor Tempo:

P= punti criterio** $Tempo_{minimo}/Tempo_{i\text{-}esimo}$

Coefficienti di natura quantitativa del criterio D

sarà applicata la formula del Minor Prezzo:

P= punti criterio** $Prezzo_{minimo}/Prezzo_{i\text{-}esimo}$

Tutte le operazioni di moltiplicazione per il punteggio massimo attribuibile in relazione a ciascun criterio sarà effettuata troncando prima della terza cifra decimale, senza eseguire arrotondamenti.

8. Modalità di espletamento della gara

La valutazione delle offerte si svilupperà in tre fasi sequenziali, da concludersi, comunque entro il 25 luglio:

- Valutazione dei requisiti generali di ammissibilità sulla base della sola documentazione prodotta, entro il 16 luglio;
- Verifica della coerenza delle offerte rispetto all'oggetto della gara, da effettuarsi a cura del Comitato Tecnico Scientifico, con immediata esclusione delle offerte inammissibili perché non coerenti o comunque inferiori ai requisiti minimi richiesti, entro il 19 luglio;
- Valutazione delle offerte ammissibili, secondo i criteri di cui al punto 7, entro il 24 luglio;
- Aggiudicazione e definizione della graduatoria, entro il 25 luglio.

9 – Aggiudicazione a più operatori economici:

Nel caso di posizioni apicali di pari merito nella graduatoria finale, la fornitura sarà aggiudicata pro quota agli operatori economici interessati. Nel caso che l'offerta posizionatasi al primo posto nella graduatoria finale non sia sufficiente al completo soddisfacimento delle esigenze, quantificate in 2.000.000 di kit da acquisire entro il 10 agosto 2020, **o di ritardo o inadempimento parziale delle consegne,** i quantitativi restanti necessari a soddisfare il fabbisogno di 2.000.000 di Kit potranno essere forniti dall'operatore secondo classificato e, nel caso di ulteriore insufficienza**, ritardo** o inadempimento parziale delle consegne, da quelli successivi.

10 – Ripetibilità della prestazione

Nel caso che, nel corso dell'emergenza epidemiologica in atto, si verifichi l'urgente necessità di ulteriori somministrazioni del test sierologico al personale docente e non docente della scuola (compreso quello addetto alla scuola per l'infanzia e agli istituti per disabili), agli aggiudicatari della presente procedura possono essere richieste, per non più di due volte, ulteriori forniture del kit oggetto della gara, per quantitativi calcolati in proporzione a quelli aggiudicati, con un preavviso massimo di 15 giorni, salvo il sopraggiungere di cause di esclusione dalla gara o di risoluzione del contratto.

11 – Ulteriori fabbisogni

Nel caso che, nel corso dell'emergenza epidemiologica in atto, si verifichi l'urgente necessità di ulteriori somministrazioni del test sierologico si potrà provvedere con una procedura a negoziazione ristretta cui avranno diritto a partecipare gli operatori economici che siano stati inseriti nella graduatoria di cui al punto 8 del presento bando.

12 - Clausola di risoluzione immediata

La fornitura di prodotti che, per ogni 100 kit, dovessero risultare non rispondenti ai requisiti di qualità richiesti e/o dichiarati, comporta la immediata risoluzione del contratto, con oneri a carico del fornitore, fatto salvo l'eventuale risarcimento del danno.

ALLEGATO N. 5

Ministero delle Infrastrutture e dei Trasporti

IL CAPO DI GABINETTO

Al Comitato Tecnico-Scientifico
c/o Dipartimento della Protezione Civile
Sede
protezionecivile@pec.governo.it

Oggetto: Schema Protocollo sulle "Misure per la gestione dell'emergenza epidemiologica da COVID-19 a bordo delle navi da crociera".
Richiesta parere

Si trasmette lo schema di Protocollo concernente le "Misure per la gestione dell'emergenza epidemiologica da COVID-19 a bordo delle navi da crociera", redatto allo scopo di raccogliere ed organizzare le indicazioni fornite dall'IMO sulla tematica in oggetto attraverso diverse circolari "4204", richiamate nella griglia di cui all'allegato 1 del medesimo Protocollo per specifico argomento.

Il lavoro è stato condotto da un Gruppo che ha visto il coinvolgimento di rappresentanti del Comando Generale del Corpo delle Capitanerie di Porto, del Ministero della Salute, delle Associazioni di categoria e delle Organizzazioni Sindacali.

Lo stesso Protocollo si applicherà alle navi di qualsiasi nazionalità impiegate in servizi di crociera, con più di 36 passeggeri, che scalano i porti nazionali, allo scopo di indirizzare in modo adeguato la corretta implementazione di misure per affrontare i rischi da COVID 19 (o SARS-Cov-2) per tutte le persone coinvolte sia a bordo che nell'interfaccia nave/terra.

Si segnala, in particolare, che le Società di gestione interessate dovranno identificare una funzione a bordo con la responsabilità di supervisionare ed implementare tale Protocollo e di assicurarsi che, presso i porti di scalo, i passeggeri ed i membri dell'equipaggio possano ricevere, se necessario, cure mediche adeguate, nonché possano essere organizzati rimpatri e cambi di equipaggio.

Al riguardo, si chiede il parere di codesto Comitato circa l'adeguatezza delle misure di cui al citato Protocollo ai fini della gestione dell'emergenza in argomento a bordo delle navi suindicate.

Cons. Alberto Stancanelli

Misure per la gestione dell'emergenza epidemiologica da COVID-19 a bordo delle navi da crociera.

Preambolo

In considerazione dell'attuale scenario globale determinato dalla pandemia da Coronavirus, sono state adottate a livello internazionale, così come nell'ambito dei trasporti e della logistica, stringenti limitazioni: tra di esse, anche il cosiddetto distanziamento sociale.

Ai sensi del codice ISM, le Società di gestione sono tenute a identificare e valutare i rischi associati alle proprie navi ed al personale navigante allo scopo di progettare adeguate misure di mitigazione.

Di conseguenza, le Società di gestione delle navi da crociera di qualsiasi bandiera – meglio identificate nell'allegato Protocollo – che scalano i porti nazionali, dovranno sviluppare piani e procedure per fronteggiare i rischi associati all'emergenza in argomento, secondo le indicazioni fornite nel Protocollo annesso alla presente circolare condiviso, preliminarmente, con il Ministero della Salute, le Associazioni di categoria e le Organizzazioni sindacali.

Il numero di passeggeri e di equipaggio a bordo deve essere adeguatamente diminuito per assicurare il distanziamento sociale e garantire le misure di isolamento temporaneo/quarantena contenute nell'allegato Protocollo.

Le Società di gestione devono:

- identificare una funzione a bordo che avrà la responsabilità di supervisionare ed implementare il Protocollo allegato fornendo il necessario supporto e collaborazione allo stesso per l'epletamento delle sue attività; e
- assicurarsi che presso i porti di scalo i passeggeri e i membri dell'equipaggio possano ricevere, se necessario, cure mediche così come possano essere organizzati rimpatri e cambi di equipaggio.

Il presente lavoro è stato condotto allo scopo di raccogliere e mettere a fattor comune le molteplici indicazioni fornite dall'IMO, sulla tematica in discorso, attraverso la copiosa produzione di Circolari 4204 (vds. griglia in allegato 1), organizzandole secondo una struttura più armonica e ordinandole per specifico argomento.

In considerazione della continua evoluzione della normativa vigente in materia di contrasto al COVID-19, la presente Circolare sarà soggetta a periodico riesame e discendente, necessario, aggiornamento.

Protocollo sulle misure per la gestione dell'emergenza epidemiologica da COVID-19 a bordo delle navi da crociera.

MISURE PER LA GESTIONE DELL'EMERGENZA EPIDEMIOLOGICA DA COVID-19 A BORDO DELLE NAVI DA CROCIERA

A. Premessa e campo di applicazione

Il presente Protocollo si applica alle navi di qualsiasi nazionalità - interessate dalla sospensione del servizio di cui alla normativa in vigore - impiegate in servizi di crociera con più 36 (trentasei) passeggeri che scalano i porti nazionali ed ha lo scopo di indirizzare, in modo adeguato, la corretta implementazione di misure per affrontare i rischi da COVID-19 (o SARS-Cov-2) per tutte le persone coinvolte sia a bordo che, necessario ed inevitabile, nell'interfaccia nave/terra.

B. Informazioni sul coronavirus (COVID-19)

I coronavirus sono una vasta famiglia di virus noti per causare malattie che vanno dal comune raffreddore a malattie più gravi come la Sindrome respiratoria mediorientale (MERS, *Middle East Respiratory Syndrome*) e la Sindrome respiratoria acuta grave (SARS, *Severe Acute Respiratory Syndrome*).

1. Sintomi e periodo di incubazione

I sintomi più comuni di una persona affetta da COVID-19 sono rappresentati da febbre, stanchezza e tosse secca.

Alcuni pazienti possono presentare indolenzimento e dolori muscolari, congestione nasale, naso che cola, mal di gola o diarrea. Questi sintomi sono generalmente lievi e crescono gradualmente.

Recentemente sono state segnalati, come sintomi legati all'infezione da COVID-19, anche l'anosmia/iposmia (perdita /diminuzione dell'olfatto) e, in alcuni casi, l'ageusia (perdita del gusto).

Nei casi più gravi, l'infezione può causare polmonite, sindrome respiratoria acuta grave, insufficienza renale e persino la morte.

Alcune persone si infettano ma non sviluppano alcun sintomo mentre nei bambini e nei giovani i sintomi sono lievi e ad inizio lento. Circa 1 (una) persona su 5 (cinque) con COVID-19 si ammala gravemente e presenta difficoltà respiratorie, richiedendo il ricovero in ambiente ospedaliero. Le persone adulte a partire dai 65 (sessantacinque) anni di età nonché quelle con malattie preesistenti, come ipertensione, malattie cardiache o diabete e i pazienti immunodepressi (per patologia congenita o acquisita o in trattamento con farmaci immunosoppressori, trapiantati) hanno maggiori probabilità di sviluppare forme gravi di malattia.

Attualmente si stima che il periodo di incubazione vari fra 2 (due) e 11 (undici) giorni, fino ad un massimo di 14 (quattordici) giorni.

2. Trasmissione

La trasmissione da uomo a uomo di COVID-19 si verifica principalmente attraverso il Flügge di persona affetta da COVID-19 (come ad esempio tosse e starnuti o materiale che può cadere su oggetti e superfici).

Altre persone quindi potrebbero essere contagiate COVID-19 che, toccando questi oggetti o superfici, portano le mani agli occhi, al naso o alla bocca. Le persone possono

anche essere contagiate se respirano il Flügge di persona affetta da COVID-19 che tossisce, starnutisce o espira Flügge.
Le persone a bordo, siano essi marittimi (a bordo della nave o a terra in franchigia), passeggeri, tecnici ecc., qualora abbiano/hanno visitato zone dove il COVID-19 è stato segnalato negli ultimi 14 (quattordici) giorni o siano stati a stretto contatto di soggetti con sintomi respiratori, sono tenuti ad informare il personale medico di bordo e, se in porto in Italia l'Ufficio di Sanità Marittima Aerea e di Frontiera (USMAF) locale.
Se tale personale ha febbre, tosse o difficoltà respiratorie, è importante rivolgersi immediatamente al medico e/o ad una struttura sanitaria.

3. Protezione personale e prevenzione delle infezioni:

Le precauzioni standard di protezione e controllo delle infezioni sottolineano l'importanza fondamentale dell'igiene delle mani e delle vie respiratorie.
In particolare:

- lavaggio frequente delle mani (equipaggio e passeggeri) con acqua calda e sapone o a base di alcol (almeno 60%[1]) strofinando per almeno 20 secondi;
- evitare di toccare il viso - compresi bocca, naso e occhi - con le mani non lavate (in particolare se le mani abbiano potuto toccare superfici contaminate dal virus);
- i marittimi (e i passeggeri) devono essere incoraggiati a coprire il naso e la bocca con un tessuto usa e getta - quando starnutiscono, tossiscono, puliscono e soffiano il naso – da smaltire immediatamente dopo averlo usato;
- se un tessuto usa e getta non è disponibile, l'equipaggio deve coprire il naso e la bocca e tossire o starnutire all'interno del proprio gomito flesso;
- tutti i tessuti usati devono essere smaltiti prontamente, dopo l'uso, in un apposito contenitore o cestino dedicato;
- il marittimo deve mantenere una distanza di almeno un metro dalle altre persone, in particolare da quelle che tossiscono o starnutiscono o possono avere la febbre;
- non stringere la mano ma limitarsi ad un cenno;
- coerentemente con le buone pratiche di sicurezza alimentare, la carne, il latte o i prodotti di origine animale devono essere sempre maneggiati con cura, per evitare contaminazioni incrociate di alimenti crudi.

È importante che i marittimi abbiano il tempo e l'opportunità di lavarsi le mani dopo aver tossito, starnutito, usato tessuti usa e getta o dopo un possibile contatto con secrezioni respiratorie o oggetti o superfici che potrebbero essere contaminati.
I poster riportati in allegato 2, scaricabili dal sito web dell'International Chamber of Shipping (ICS) all'indirizzo www.ics-shipping.org/free-resources, possono essere utilizzati a bordo per fornire un promemoria delle migliori pratiche da adottare.

4. Test e trattamento

Per la conferma della diagnosi di infezione da nuovo coronavirus è necessario effettuare test di laboratorio (Real Time PCR) su campioni respiratori e/o siero. Con la circolare del 27 gennaio 2020, il Ministero della Salute ha fornito le

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[1] *CDC. How to Protect Yourself & Others - Coronavirus Disease 2019. 24th April 2020:* https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html
CDC: Guideline for Hand Hygiene in Health Care Settings - Recommendations of the Healthcare Infection Control Practices. 25th October 2002. - https://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf
https://www.fda.gov/drugs/information-drug-class/qa-consumers-hand-sanitizers-and-covid-19

raccomandazioni per i test di laboratorio e la raccolta e l'invio di campioni biologici. La diagnosi di laboratorio del virus va effettuata, dove possibile, su campioni biologici prelevati dalle basse vie respiratorie (espettorato, aspirato endotracheale o lavaggio bronco-alveolare). Se i pazienti non presentano segni di malattia delle basse vie respiratorie, o se la raccolta dei materiali dal tratto respiratorio inferiore non è possibile seppur clinicamente indicata, si raccomanda la raccolta di campioni prelevati dalle alte vie respiratorie (aspirato rinofaringeo, tamponi nasofaringei e orofaringei combinati).
In caso di risultato negativo di un test condotto su un campione biologico da paziente fortemente sospetto, si raccomanda di ripetere il prelievo di campioni biologici in tempi successivi e da diversi siti del tratto respiratorio (naso, espettorato, aspirato endotracheale).
Campioni biologici aggiuntivi quali sangue, urine e feci possono essere raccolti per monitorare la presenza di virus nelle diverse parti del corpo. I campioni devono essere immediatamente trasportati in laboratorio e impiegati nella diagnosi molecolare. La raccolta dei campioni biologici deve avvenire adottando precauzioni e dispositivi di protezione individuale utili a minimizzare la possibilità di esposizione a patogeni.
Per quanto attiene il trattamento, non ne esistono di specifici per le infezioni causate dai coronavirus e non sono disponibili, al momento, vaccini per proteggersi dal virus. Inoltre, non esistono, al momento, terapie specifiche; vengono curati i sintomi della malattia (cosiddetta terapia di supporto) in modo da favorire la guarigione, ad esempio fornendo supporto respiratorio.

5. Consapevolezza e formazione

Le Società di gestione devono fornire, alle persone imbarcate, una guida su come riconoscere i segni e i sintomi di COVID-19.
Si deve, altresì, richiamare l'equipaggio all'osservanza del piano e delle procedure da seguire se un passeggero o un membro dell'equipaggio a bordo mostra segni e sintomi di malattia respiratoria acuta. Il personale medico di bordo, se presente, deve, inoltre, essere informato e aggiornato sul COVID-19 e su qualsiasi nuova guida disponibile. A tal fine, si consiglia – tra l'altro – di consultare il sito web dell'Organizzazione Mondiale della Sanità (OMS) sul COVID-19.
Devono, comunque, essere tenuti in considerazione anche gli orientamenti specifici per singolo Paese visitato in merito alle misure di prevenzione.

C. Misure adottate a terra prima dell'imbarco

Prerequisito di imbarco per i passeggeri, visitatori ed ospiti

Per prerequisito di imbarco si intende la misurazione della temperatura, la compilazione di un questionario ed, eventualmente, test molecolari RT-PCR che saranno eseguiti, dal personale medico di bordo, in percentuale del 100% sui passeggeri la cui temperatura, o le evidenze anamnestiche e/o epidemiologiche o i contenuti del questionario portino a considerarli passeggeri casi sospetti. Inoltre, i test molecolari RT-PCR verranno effettuati all'imbarco a quei passeggeri di provenienza dalle aree ad alto rischio.
I passeggeri che sono guariti recentemente dal COVID-19 e dimessi secondo i criteri individuati da ECDC, possono evitare il test PCR.

Screening pre-imbarco

Prima di accedere all'imbarco, tutti i visitatori, ospiti ed equipaggio saranno sottoposti ad un attento screening pre-imbarco:

a) primario: misurazione della temperatura, compilazione, non oltre le 6 (sei) ore prima dell'imbarco, dello stampato in allegato 4 ovvero un questionario – predisposto dalla Società di gestione – contenente, almeno, i dati di cui al facsimile in allegato 4 e valutazione iniziale da parte di personale non medico che attraverso le risposte al questionario individuerà eventuali condizioni di rishio;
b) secondario: coloro che non supereranno il controllo della temperatura o per i quali il questionario evidenzierà criticità, che presentano segni o sintomi compatibili con il COVID-19 o che sono stati potenzialmente esposti alla SARS-CoV-2, saranno sottoposti ad un colloquio e screening condotto da un medico tramite anamnesi, esame medico e di laboratorio con una seconda misurazione della temperatura. L'accertamento sarà svolto in un'idonea area – precedentemente identificata dalla Autorità del porto di approdo in collaborazione con l'Autorità sanitaria locale – presidiata da personale di bordo adeguatamente formato ed eventualmente supportato dal personale sanitario della nave.

Non potrà, pertanto, accedere all'imbarco chi:

1. mostri sintomi ascrivibili a COVID-19 (es. persone alle quali verrà riscontrata temperatura corporea superiore a 37,5 °C, persone che riportino o evidenzino tosse o difficoltà respiratorie);
2. abbia avuto contatti negli ultimi 14 giorni (o nei 2 giorni precedenti l'esordio dei sintomi) con un caso confermato di COVID-19;
3. sia stato in "contatto stretto"[2] con casi confermati di COVID-19, per i quali sia stata fatta regolare denuncia alle competenti Autorità sanitarie;

Qualora si riscontrassero persone ricadenti nella tipologia di cui ai punti 1. e 2., il personale sanitario di bordo e/o quello individuato dalla Società di gestione, provvederà a separare i casi sospetti indirizzandoli verso un'area "sicura" precedentemente indicata dall'Autorità del porto di approdo. I referenti della Società di gestione daranno immediata comunicazione alle Autorità sanitarie locali dei casi sospetti a cui non è stato consentito l'imbarco.

Coloro i quali risulteranno ricadere nella tipologia di cui al punto 3., anche se asintomatici, non potranno prendere imbarco. La Società di gestione, in tal caso, consegnerà agli interessati una comunicazione contenente la motivazione del mancato imbarco.

D. Misure di bordo per affrontare i rischi associati a COVID-19

1. Misure per proteggere la salute e prevenire le infezioni:
   a) *Monitoraggio e screening*:
      1. *Equipaggio:*
         è necessario che il monitoraggio di tutto l'equipaggio a bordo sia effettuato giornalmente – attraverso la rilevazione della temperatura corporea di ogni singola persona – con successiva comunicazione allo staff medico di bordo; Inoltre, devono essere effettuati test "cd. rapidi", ad intervalli regolari di 15 (quindici) giorni, al 50% del personale navigante, al fine di coprire l'intero equipaggio ogni 30 (trenta) giorni. Eventuali casi positivi devono essere sottoposti al test PCR e trattati secondo le previsioni del punto E. In ogni caso ogni mese almeno il 20% dei membri dell'equipaggio deve essere comunque sottoposto al test molecore RT-PCR. La percentuale del 20%

[2] Vds. paragrafo E.3

sarà soggetta ad incremento nel caso di mutazione della situazione epidemiologica di bordo.

2. *Passeggeri*:
La misurazione della temperatura corporea dei passeggeri avverrà attraverso l'utilizzo di termocamere in entrata ed in uscita dalla nave; i passeggeri che soggiornino a bordo verranno incoraggiati ad utilizzare le stazioni dedicate di misurazione presenti sulla nave. Nel caso in cui non sia prevista l'installazione di termocamere a bordo, la rilevazione della temperatura avverrà attraverso termometri personali messi a disposizione dei passeggeri.

Qualora la temperatura corporea risultasse superiore a 37,5°C la persona dovrà indossare la mascherina e presentarsi, per la necessaria valutazione medica, presso l'ospedale di bordo oppure recarsi o rimanere nella propria cabina informando il personale medico di bordo. Nel caso in cui la nave si trovi in Italia dovrà essere informato l'USMAF locale e la persona dovrà essere, momentaneamente, isolata.

b) *Dispositivi di protezione (DP)*[3]:
L'uso di mascherine fa parte di un pacchetto completo di misure di prevenzione e controllo che possono limitare la diffusione di alcune malattie virali respiratorie, tra cui il COVID-19.
Le mascherine possono essere utilizzate sia da persone sane (indossate per proteggersi quando si viene a contatto con un individuo infetto) o da persone infette per impedire la successiva trasmissione.
Tuttavia, l'uso di una mascherina da sola non è sufficiente per fornire un livello adeguato di protezione e, quindi, altre misure a livello personale e di comunità dovrebbero essere adottate per evitare la trasmissione di virus respiratori.
Indipendentemente dal fatto che vengano utilizzate o meno le mascherine, il rispetto dell'igiene delle mani, il distanziamento fisico e altre misure di prevenzione dalle infezioni sono fondamentali per prevenire la trasmissione umana da COVID-19.
Per quanto attiene, invece, coloro che sono coinvolti nella distribuzione e gestione dei dispositivi di protezione (DP), nonché il personale di bordo che presta assistenza sanitaria si dovrà fare riferimento, tra l'altro, al documento dell'OMS[4] che fornisce informazioni sull'uso appropriato dei DP.
Infine, sull'uso e smaltimento delle mascherine nel contesto COVID-19 sia fatto riferimento all'allegato 3 ed al rapporto ISS COVID-19 n° 26/2020 del 18 maggio 2020 recante "*Indicazioni ad interim su gestione e smaltimento di mascherine e guanti monouso provenienti da utilizzo domestico e non domestico.*"

c) *Auto-distanziamento a bordo*:

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[3] *Advice on the use of masks in the context of COVID-19* dell'OMS datato 5 giugno 2020.
[4] *Rational use of personal protective equipment for coronavirus disease (COVID-19) and considerations during severe shortages* dell'OMS datato 6 aprile 2020.

L'auto-distanziamento a bordo può essere messa in atto attraverso, per esempio, le seguenti misure:

- mantenere la distanza sociale di almeno un metro;
- evitare qualsiasi contatto non essenziale o stretta vicinanza con altre persone; quando possibile, ma solo se le condizioni e le circostanze lo consentono ed è sicuro farlo, utilizzare scale esterne/vie di fuga per spostarsi a bordo della nave. È altresì consentito l'uso degli ascensori con limitazione del numero massimo di persone nel rispetto del distanziamento sociale e, comunque, con l'obbligo dell'uso della mascherina. Soluzioni a base di alcool devono essere poste ad entrambi i lati dei corridoi di accesso agli ascensori e l'equipaggio deve essere istruito a sollecitare tutti i passeggeri, sia in uscita che in entrata, ad usare tali apprestamenti sanitari.
  L'ascensore deve essere lavato regolarmente e con particolare attenzione per le aree/dotazioni soggette ad utilizzo frequente (es. maniglie e tasti).

Per quanto attiene al personale navigante:

- disinfezione delle aree di lavoro, delle attrezzature e degli strumenti dopo l'uso;
- porre la massima attenzione nell'utilizzo delle aree comuni a bordo, come la sala mensa, la zona lavanderia o aree ricreative quando utilizzate da altri.

Nel caso in cui non possa essere assicurato, per il personale navigante, il distanziamento sociale o i DP:

- ritornare nella propria cabina immediatamente dopo aver completato l'orario di lavoro;
- restare nella propria cabina durante le ore di riposo, tranne quando sono in atto disposizioni o misure che permettano loro di trascorrere ore di riposo sui ponti; e
- ricevere e consumare tutti i pasti nella propria cabina, purché sia sicuro farlo.

d) *Coorti (numerosità minima): distribuzione dei passeggeri ed equipaggio in coorti chiuse così da facilitare il 'Contact Tracing'.*

Nell'ottica di ridurre l'interazione tra passeggeri, tra l'equipaggio e tra passeggeri ed equipaggio si suggerisce, per quanto possibile, di dividere l'equipaggio e i passeggeri in coorti.

Ogni interazione tra coorti diverse dovrebbe, per quanto possibile, essere evitata; è importante attenersi a questa misura in quanto consentirebbe di gestire più efficacemente un potenziale caso di COVID-19 ed i relativi contatti ed a diminuire il numero delle persone esposte.

È particolarmente importante che queste misure vengano applicate dall'equipaggio quando sul luogo di lavoro il distanziamento non può essere garantito.

I membri dell'equipaggio che lavorano a contatto di casi COVID-19, probabili o confermati, dovrebbero avere la cabina posizionata in modo tale che il loro accesso alle aree comuni della nave sia ridotto al minimo.

Ogni specifico gruppo potrebbe avere orari comuni per l'accesso al servizio di ristorazione, per l'imbarco e lo sbarco e per la partecipazione a qualsiasi attività a bordo o a terra. Se non fosse possibile attuare una separazione per coorti a bordo, questa deve essere garantita almeno per ogni attività a terra.

In considerazione della tecnologia e dei sistemi presenti a bordo delle navi da crociera è considerato equivalente l'utilizzo dei metodi alternativi per il "contact tracing" (vedasi anche lettera E. punto 3)

e) *Pulizia e disinfezione:*

Per quanto attiene:

- le procedure giornaliere di pulizia e sanificazione appropriate (in aggiunta ai rigorosi regimi di pulizia e sanificazione già esistenti) per le cabine, le aree di preparazione del servizio di ristorazione e le aree comuni delle navi, con particolare attenzione alle sale da pranzo, ai luoghi di intrattenimento e ad altre grandi aree di ritrovo, nonché alle superfici frequentemente toccate, come, tra gli altri, i pulsanti degli ascensori e i telecomandi; e
- l'uso di disinfettanti per la pulizia delle superfici;

si dovrà fare riferimento alla vigente normativa nazionale, unionale ed internazionale.

f) *Misure igienico sanitarie:*

i. lavarsi spesso le mani. Si raccomanda di mettere a disposizione in tutti i locali comuni, come salette, saloni, palestre, negozi, farmacie e altri luoghi di aggregazione, soluzioni idroalcoliche per il lavaggio delle mani;
ii. evitare il contatto ravvicinato con persone che soffrono di infezioni respiratorie acute;
iii. evitare abbracci e strette di mano;
iv. mantenere, nei contatti sociali, una distanza interpersonale di almeno un metro;
v. praticare l'igiene respiratoria (starnutire e/o tossire in un fazzoletto, evitando il contatto delle mani con le secrezioni respiratorie ovvero all'interno del gomito flesso);
vi. evitare l'uso promiscuo di bottiglie e bicchieri, in particolare durante l'attività sportiva;
vii. non toccarsi occhi, naso e bocca con le mani;
viii. coprirsi bocca e naso se si starnutisce o tossisce;
ix. non prendere farmaci antivirali e antibiotici, a meno che siano prescritti dal medico;
x. pulire le superfici con disinfettanti a base di cloro o alcol;
xi. è fortemente raccomandato, in tutti i contatti sociali, di utilizzare protezioni delle vie respiratorie come misura aggiuntiva alle altre misure di protezione individuale igienico-sanitarie.

g) *Igiene degli alimenti*

Fare riferimento alla vigente normativa nazionale, unionale ed internazionale.

h) *Riscaldamento, ventilazione e area condizionata (HVAC)*

Organizzare il funzionamento dei sistemi HVAC allo scopo di massimizzare la circolazione dell'aria fresca nel sistema, in linea con le raccomandazioni del produttore del sistema, le capacità di bordo e le considerazioni operative.

Fare riferimento alla normativa vigente nazionale, unionale ed internazionale.

Inoltre, al fine di garantire un adeguato e completo isolamento, le Società di gestione di navi da crociera avranno cura di riservare – in via esclusiva un numero di cabine dotate di impianto di ventilazione dedicato (vds. anche lettera E. punto 4). Le stesse devono essere destinate a ricevere le persone da isolare, garantire alle stesse ogni necessaria assistenza nonchè tutelare, contestualmente, il restante personale presente a bordo.

i) *Utilizzo di ristoranti, bar, discoteche, SPA, teatri, negozi di bordo, cinema, sale giochi, casinò, palestre ecc.*
Fare riferimento alla normativa vigente nazionale, unionale ed internazionale.

j) *Gestione dei fluidi biologici e delle acque (potabili e ricreative)*
La gestione dei fluidi biologici assieme alla sorveglianza sanitaria delle acque (potabili e ricreative) deve avvenire rispettando standard e procedure basati su linee guida specifiche internazionalmente riconosciute (es. *VSP operational guideline - European Manual for Hygiene Standards and communicable disease surveillance on Passenger Ship*)

k) *Segnaletica e cartellonistica*
Le aree ed i posti a sedere disponibili per i passeggeri devono essere opportunamente contrassegnati. In assenza di norme che stabiliscano la simbologia da utilizzarsi, se ne rimette – al momento – la scelta alla singola Società di gestione che avrà l'obbligo di apporla e di esporre, in luoghi ben visibili, adeguata cartellonistica esplicativa.

2. Misure per la gestione dei rischi durante l'imbarco:
L'imbarco dell'equipaggio e dei passeggeri sulle navi deve essere gestito con cura al fine di ridurre il rischio che una persona infetta da COVID-19 che sale a bordo della nave possa trasmettere lo stesso ad altre persone.
Misure per ridurre il rischio che l'equipaggio, così come i passeggeri, diffondano a bordo l'infezione COVID-19 include la compilazione di questionari di screening così come la scansione o misurazione della temperatura. In caso di rilevate criticità, la persona sarà condotta in un'apposita area del terminal dove riceverà ulteriori test e valutazione medica. In base all'esito di questa valutazione, l'imbarco sarà autorizzato o negato (con relativa gestione della casistica).
Le Società di gestione devono, quindi, come indicato sopra, introdurre procedure per lo screening dell'equipaggio e dei passeggeri che salgono a bordo della nave richiedendo loro di compilare un questionario di screening (autocertificazione sanitaria) e sottoporre gli stessi a scansione o misurazione della temperatura corporea al momento dell'imbarco. Un esempio di modulo di autodichiarazione relativa alla salute dei passeggeri e dell'equipaggio è riportato in allegato 4.
L'imbarco non dove essere consentito per coloro che registrano una temperatura superiore a 37,5°C. Deve essere altresì considerato che la misurazione della temperatura corporea è una misura utile da mettere in atto, ma che la stessa, al contempo, non è totalmente efficace atteso che prove scientifiche hanno dimostrato che alcune persone infette potrebbero non presentare tale sintomo mentre altre potrebbero non sviluppare alcun sintomo fino ad un massimo di 10 (dieci) giorni.
L'esperienza maturata suggerisce, inoltre, che le persone asintomatiche possano trasmettere il virus ad altri, quindi il test di reazione a catena della polimerasi (PCR), da eseguirsi prima dell'imbarco, può aiutare a identificare tali persone che non sono state individuate con altre misure di screening.
Un test PCR comporta un tampone del naso o gola per l'identificazione della presenza del virus come meglio successivamente specificato.

Il test PCR dovrà essere eseguito, per i passeggeri, ogni qualvolta sia identificato un caso sospetto o si verifichino condizioni particolari come, ad esempio, passeggeri che sono stati a contatto con casi positivi o provenienti da aree a rischio.
Le Società di gestione dovranno anche considerare la possibilità di richiedere agli equipaggi di completare un periodo di auto-distanziamento per i primi 14 (quattordici) giorni a bordo della nave dopo l'imbarco al fine di monitorare la loro salute e gestire il rischio che possano essere infetti e senza che questo pregiudichi lo svolgimento delle funzioni e responsabilità assegnati. In alternativa, l'equipaggio sarà sottoposto ad un tampone entro 7 (sette) giorni prima dell'imbarco e ripetuto, immediatamente, appena arrivato a bordo. I due tamponi non dovranno essere eseguiti in un arco temporale inferiore a 48 (quarantotto) ore tra loro. Con risultato negativo dei 2 (due) tamponi consecutivi, il membro dell'equipaggio potrà essere impiegato per il servizio a bordo senza dover scontare alcun periodo di quarantena.
Ai membri dell'equipaggio risultati positivi non deve essere permesso di salire a bordo della nave. Gli stessi dovranno essere sottoposti a ulteriori valutazioni o test medici.
Poiché un test PCR negativo non garantisce che le persone siano immuni da COVID-19 e le stesse potrebbero, comunque, potenzialmente trasportare il virus a bordo della nave, chiunque sviluppi un sintomo di infezione del tratto respiratorio (tosse, febbre, mal di gola, ecc.) deve essere sottoposto a ulteriori valutazioni o test medici prima di essere imbarcato.

3. <u>Informazioni per i passeggeri e per l'equipaggio</u>:
Un poster intitolato "Informazioni sul COVID 19" – tradotto in una o più lingue comprese dall'equipaggio e dai passeggeri ospitati e, comunque, almeno in inglese, francese, tedesco e spagnolo – deve essere esposto nelle cabine quale informativa delle azioni aggiuntive intraprese a bordo.
Fermo restando le comunicazioni inerenti la sicurezza della navigazione, dovranno essere previsti messaggi, da diffondere attraverso gli schermi TV della nave, nonché video con le istruzioni per il lavaggio delle mani.
Gli stessi dovranno essere trasmessi almeno ogni ora sui canali video di *entertainment e revenue* e sugli schermi nelle aree pubbliche (es. schermi di servizio e mense equipaggio).
Durante tutti gli annunci giornalieri il Comandante provvederà affinché sia incoraggiato il lavaggio delle mani e contattato il centro medico di bordo per una consulenza medica gratuita in caso di insorgenza di ogni problema respiratorio.
Il Comandante provvederà affinché, almeno una volta al giorno, gli annunci periodici sia agli ospiti che all'equipaggio includano il seguente esempio di testo, tradotto in una o più lingue da essi comprese:
"Considerata l'attenzione mondiale per il Coronavirus, questa compagnia sta seguendo tutte le indicazioni dell'Organizzazione Mondiale della Sanità, delle Autorità sanitarie locali e dell'Amministrazione di bandiera. Desideriamo informarvi di avere aumentato la sanificazione delle aree pubbliche e delle superfici di maggior contatto in tutta la nave. Il migliore modo per rimanere in salute è lavarsi le mani spesso, almeno per 20 secondi, evitando di toccare il proprio viso, gli occhi, la bocca e il naso. Se avete febbre o sintomi di difficoltà respiratoria, siete invitati a contattare il Centro Medico di bordo al più presto. La vostra collaborazione è più che gradita. Contattate la reception in caso di ogni necessità."

4. <u>Misure per la gestione dei rischi durante lo sbarco</u>:

Lo sbarco del personale navigante e dei passeggeri dalle navi deve essere gestito con cura al fine di ridurre il rischio di infezione dal COVID-19 durante lo sbarco dalla nave (compresa l'interazione con qualsiasi persona o infrastrutture nel porto/terminal).
La salute degli stessi deve essere monitorata prima dello sbarco per garantire che, per quanto ragionevole e praticabile, siano sufficientemente sani da poter sbarcare e viaggiare ai fini del rimpatrio. Quanto sopra attraverso: scansione o misurazione della temperatura. Ulteriori indicazioni per le Società di gestione sullo sbarco dei marittimi sono fornite in P7 e P8 della lettera Circolare IMO n. 4204/Add.14 del 5 maggio 2020.
In allegato 6, invece, il poster che può essere utilizzato per consigliare all'equipaggio come tutelare la salute durante il viaggio da e verso la propria nave.

5. Misure per gestire i rischi associati all'interfaccia nave/terra:
La pandemia COVID-19 ha creato criticità anche nel l'interfaccia tra persone a bordo e personale di terra durante le soste in porto.
Le Società di gestione devono istruire le loro navi affinché – prima dell'arrivo in porto – siano comunicate – a tutte le *entities* con le quali esse si interfacceranno ed a tutto il personale di terra che potrebbe salire a bordo– anche attraverso la figura dell'Agente raccomandatario, le loro esigenze ed aspettative.
A tal proposito si faccia riferimento alla "*Guida per garantire un'interfaccia di bordo sicura tra nave e personale a terra*"[5] edita da ICS ed alla Circolare IMO 4204/Add. 16 del 6 maggio 2020 della quale si riporta, in allegato 7, una gerarchia di attività da compiersi come guida per stabilire misure efficaci di controllo e ridurre il rischio.
Inoltre, rispettivamente in allegato 8 e 9, sono presenti esempi di poster che possono essere utilizzati a bordo per consigliare all'equipaggio come salutare i visitatori in sicurezza e come proteggere tutti durante le visite a bordo.

E. Gestire un focolaio di COVID-19 a bordo della nave

1. *Azioni necessarie se una persona a bordo mostra sintomi di COVID-19*:
Quando una persona mostra i sintomi riconducibili ad infezione da COViD-19, la stessa deve essere segnalata immediatamente ed il piano di gestione dell'epidemia attivato. La persona deve essere considerata come un caso sospetto di COVID-19 ed isolata nella propria cabina, nell'ospedale della nave o nelle cabine appositamente riservate in attesa di ulteriori accertamenti. Questa valutazione deve, tra l'altro, accertare se esiste un'altra causa probabile, come ad esempio allergia, tonsillite.
Le navi devono essere dotate di apparecchiature per l'esecuzione di test molecolari (PCR) da utilizzare quando si sospetta che un passeggero o un membro dell'equipaggio sia infetto.
Deve essere istituito un protocollo rigoroso per i pasti, il contatto con altre persone che dovrà garantire l'accesso a una toilette separata. Il Comandante o il personale medico di bordo possono consultare, per la gestione del caso, il Centro Internazionale Radio Medico (CIRM) (in navigazione o in porto estero) e l'USMAF locale (in porto in Italia).

2. *Definizione di un caso sospetto di COVID-19*:
Un caso sospetto è:
   A. un soggetto:
      - con grave infezione respiratoria acuta (cioè febbre e tosse che richiedono ricovero in ospedale);

[5] *Guidance for Ensuring a Safe Shipboard Interface Between Ship and Shore-Based Personnel* dell'11 maggio 2020.

- febbre di origine non identificata (maggiore di 37,5°C)
- senza altra eziologia[6] che possa spiegare il quadro clinico;
- che ha effettuato un viaggio o ha avuto residenza/dimora in un Paese con trasmissione diffusa della malattia COVID-19 durante i 14 (quattordici) giorni prima dell'inizio dei sintomi; ovvero

B. un paziente con qualsiasi malattia respiratoria acuta e, almeno, una delle seguenti ipotesi avvenute durante i 14 (quattordici) giorni prima dell'insorgenza dei sintomi:
   a. contatto con un caso confermato o probabile di malattia COVID-19; o
   b. che lavora o ha visitato una struttura sanitaria dove sono ricoverati pazienti con la malattia COVID-19 confermata o probabile e che erano/sono in trattamento.

3. *Identificazione di contatti stretti e tracciamento dei contatti*:
Al fine di evitare ritardi nell'attuazione delle misure sanitarie, dopo che un caso sospetto è stato identificato a bordo dovrebbe iniziare immediatamente la ricerca dei contatti senza attendere i risultati di laboratorio. Ogni sforzo dovrebbe essere fatto per ridurre al minimo il rischio che altre persone – equipaggio o passeggeri – siano soggetti ad esposizioni ambientali in luoghi della nave nei quali era presente il caso sospetto. I soggetti che hanno avuto, con esso, contatti stretti devono essere separati dagli altri viaggiatori il più presto possibile.
Tutte le persone a bordo devono essere valutate in relazione al loro rischio di esposizione e classificate come a "*stretto contatto con un alto rischio di esposizione*" o con un "*basso rischio di esposizione*".
Una persona che abbia avuto un'esposizione ad alto rischio è quella che rientra in una delle seguenti condizioni/criteri:
- sia rimasta nella stessa cabina di un caso sospetto o confermato COVID-19;
- aveva uno stretto contatto o era chiusa in un ambiente con un caso sospetto o confermato COVID-19 (ovvero erano entro 1 metro di distanza e per almeno 15 minuti):
  - per i passeggeri, ciò può comprendere la partecipazione ad attività comuni sulla nave o a terra dove il distanziamento sociale non può essere sempre assicurato;
  - per i membri dell'equipaggio, questo include le attività sopra descritte, come applicabile, oltre alla interazione diretta con il caso COVID-19 sospetto o confermato (es. steward di cabina che ha pulito la camera o il personale del ristorante che ha consegnato cibo in cabina, così come istruttori di palestra che hanno fornito assistenza ravvicinata);
- operatore sanitario o un'altra persona che ha prestato assistenza ad un caso COVID-19 sospetto o confermato.

Qualora si verificasse una estesa trasmissione COVID-19 a bordo di una nave, i membri dell'equipaggio ed i passeggeri dovrebbero essere valutati al fine di determinare se sono stati esposti al caso sospetto o confermato. In caso di difficoltà nell'identificare i contatti stretti o se viene identificata una trasmissione diffusa, tutti i viaggiatori (ovvero passeggeri, equipaggio ed altro personale) a bordo della nave devono essere considerati alla stregua di "contatti stretti che hanno avuto un'esposizione ad alto rischio". A supporto dell'identificazione dei contatti, ci sarà

[6] Parte di una scienza che studia le cause di un fenomeno

l'utilizzo delle registrazioni video, i sistemi di prenotazione dei servizi di bordo, l'utilizzo della carta di bordo e le interviste individuali.
Fino a quando non saranno disponibili i risultati di laboratorio per il caso sospetto, a tutte le persone a bordo che rientrano nella definizione di "contatto stretto" – come appena sopra definito – dovrà essere richiesto di completare lo stampato in allegato 5 ovvero un questionario, predisposto dalla Società di gestione, contenente almeno i dati di cui al facsimile in allegato 5 – di rimanere nelle proprie cabine o in una struttura a terra appositamente designata secondo le istruzioni ricevute dalle Autorità sanitarie del porto in cui la nave si trova. Se il risultato di laboratorio è positivo, tutti i contatti stretti devono essere messi in quarantena. Le persone in quarantena che hanno avuto stretti contatti con un caso confermato dovrebbero, immediatamente, informare i servizi sanitari se sviluppano sintomi entro 14 (quattordici) giorni dal loro ultimo contatto con il caso confermato. Se entro 14 (quattordici) giorni dall'ultima esposizione non compaiono sintomi, il contatto non è più considerato a rischio di sviluppare la malattia COVID-19. L'implementazione di queste precauzioni specifiche può essere modificata in base alle valutazioni del rischio dei singoli casi e dei loro contatti condotti dalle Autorità sanitarie pubbliche.
Se il risultato di laboratorio è positivo, tutti gli altri viaggiatori che non soddisfano la definizione di contatto stretto sono considerati quali soggetti con esposizione a basso rischio; deve essere loro richiesto di completare lo stampato in allegato 5 ovvero uno stampato, predisposto dalla Società di gestione contenente, almeno, i dati di cui al facsimile in allegato 5 con i propri dati di contatto e i luoghi in cui alloggeranno per i successivi 14 (quattordici) giorni. L'implementazione di queste precauzioni può essere modificata a seconda della valutazione dei rischi condotta dalle Autorità sanitarie pubbliche che possono fornire ulteriori e specifiche istruzioni.

4. *Isolamento di casi sospetti e confermati da COVID-19*:
Il numero di cabine necessarie all'isolamento/quarantena viene calcolato come segue.
Se non è possibile far sbarcare i casi confermati entro 24 (ventiquattro) ore dall'individuazione del primo potenziale caso di COVID 19, in accordo con quanto scritto nel "contingency plan", il numero massimo di cabine riservate a passeggeri ed equipaggio che devono osservare la quarantena o l'isolamento è stabilito intorno al 5% del numero di passeggeri ed al 5% del numero dell'equipaggio. In caso di possibilità di sbarco le percentuali di cui sopra sono ridotte all'1%. Tale meccanismo di calcolo delle cabine di isolamento/quarantena si applica solo nelle fasi iniziali di riavvio delle operazioni (ovvero fino al 31 agosto 2020) e andranno riconsiderate ed eventualmente revisionate sulla base degli sviluppi della situazione epidemiologica.
Isolare il paziente in infermeria o in aree appositamente destinate per l'isolamento e assicurarsi di indossare una maschera chirurgica quando si è in contatto con altre persone. Il paziente deve avere accesso ad un servizio igienico privato.
Chiunque entri nella stessa cabina di un sospetto caso di COVID-19 deve indossare DP che includano una maschera facciale, un grembiule o un abito impermeabile (se disponibile), guanti e occhiali o una visiera. Il contatto con il caso sospetto deve essere limitato ad un massimo di altri 2 (due) membri dell'equipaggio. Lavarsi accuratamente le mani immediatamente prima e dopo aver lasciato la cabina del paziente.
In conformità al Regolamento Sanitario Internazionale (2005), l'ufficiale responsabile della nave contatterà immediatamente l'Autorità competente del porto di scalo successivo, per concordare le azioni più adeguate da adottare e ricevere le relative

istruzioni. È importante che tutti gli accordi siano condotti il più rapidamente possibile per ridurre al minimo la permanenza a bordo della nave di eventuali casi sintomatici gravi.
In relazione al numero, alla tipologia di casi positivi da COVID-19 a bordo ed alle misure di contenimento che sono attuate dalla Società di gestione, potrebbe rendersi necessario – sentito il personale medico di bordo e la Società di gestione per quanto attiene i luoghi da scalare – valutare l'opportunità di interrompere la crociera.

5. *Cura dei casi sospetti e confermati da COVID-19*:

Il trattamento di supporto può includere il sollievo dal dolore e dalla febbre, garantendo l'assunzione di liquidi sufficienti e ossigeno e altri trattamenti se necessario e come consigliato dal CIRM.
Il paracetamolo deve essere somministrato per alleviare il dolore e la febbre. L'ibuprofene dovrebbe essere usato solo dopo aver consultato il personale medico di bordo e, in porto in Italia, l'USMAF locale. La prescrizione a bordo di un qualsiasi farmaco aggiuntivo dovrebbe anche essere, preliminarmente, discussa con un medico a terra.
Le condizioni del paziente devono essere valutate regolarmente – due o tre volte al giorno – di persona o tramite telefono. In caso di peggioramento delle condizioni del paziente, contattare il CIRM. Il paziente deve essere messo in grado di contattare gli altri in caso di necessità.
Una registrazione della valutazione medica, delle cure e di quanto emerso dal colloquio con il paziente deve essere effettuata nel registro medico che deve riportare:

- chiunque a bordo sia stato nella struttura medica come caso sospetto ed isolato e le misure di igiene adottate;
- qualsiasi contatto ravvicinato o contatto occasionale con esposizione a basso rischio; e,
- i dati della persona che ha avuto contatti occasionali con individui a basso rischio che sbarcheranno e le posizioni in cui rimarranno nei successivi 14 (quattordici) giorni.

I contatti stretti dovrebbero essere invitati a:

- monitorare i sintomi da COVID-19, inclusa febbre, tosse o difficoltà respiratoria, per 14 (quattordici) giorni dalla loro ultima esposizione; e
- isolarsi immediatamente e contattare i servizi sanitari in caso di comparsa di sintomi nei 14 (quattordici) giorni. Se entro 14 (quattordici) giorni dall'ultima esposizione non compaiono sintomi, si ritiene che la persona che ha avuto il contatto non sviluppi il COVID-19.

Le Autorità sanitarie dello Stato di approdo devono essere informate di eventuali casi sospetti che possano anche condurre all'individuazione delle persone con cui hanno avuto contatti da gestire in linea con le norme nazionali del luogo di approdo.
Le misure di quarantena nel contesto di COVID-19, come da linee guida dell'OMS, dovranno includere anche:

- monitoraggio attivo da parte delle autorità sanitarie per 14 (quattordici) giorni dall'ultima esposizione;
- monitoraggio quotidiano (inclusa febbre di qualsiasi grado, tosse o difficoltà respiratoria);

- evitare i contatti sociali e i viaggi; e
- essere raggiungibile per l'esecuzione del monitoraggio attivo.

L'attuazione di precauzioni specifiche può essere modificata in seguito alla valutazione del rischio di singoli casi ed alla consulenza ricevuta dalle Autorità sanitarie.
L'allegato 10 fornisce un poster che contiene avvisi sulle cure a bordo di persone con caso sospetto o confermato di COVID-19.
Se un caso positivo grave viene rilevato a bordo, lo stesso dovrà essere sbarcato al primo porto di scalo in accordo con le Autorità sanitarie locali.

6. *Segnalazione al prossimo porto di scalo*

Informare sempre l'Autorità competente del prossimo scalo se vi è un caso sospetto a bordo. La gestione dei contatti avverrà secondo le politiche nazionali del porto di sbarco e secondo il "contingency plan" per la gestione delle emergenze della nave da crociera e del porto.
Per le navi impiegate in viaggi internazionali, il Regolamento sanitario internazionale (IHR) stabilisce che la dichiarazione dovrebbe essere completata e inviata all'Autorità competente in conformità con i requisiti locali sia per l'equipaggio che per membri dell'equipaggio deceduti.
Per le navi che approdano in porti italiani è richiesta l'informativa all'USMAF, competente a ricevere la dichiarazione di sanità per il rilascio della "libera pratica sanitaria", circa l'evoluzione della situazione sanitaria a bordo e di ogni suo cambiamento.
Il Comandante deve immediatamente informare l'Autorità sanitaria competente del successivo scalo anche di qualsiasi caso sospetto, al fine di verificare se è disponibile il trasporto, l'isolamento e la cura dell'individuo; tale Autorità sanitaria, anche sulla base di pianificazioni locali, provvede a fornire indicazioni sulla possibilità di effettuare lo scalo pianificato ovvero sulla necessità che la nave prosegua verso un porto più attrezzato per affrontare l'emergenza sanitaria a bordo.
Le Autorità sanitarie locali potranno consentire al resto dei passeggeri della nave – sulla base del numero, della tipologia di casi positivi da COVID-19 a bordo e delle misure di contenimento che sono attuate dalla Società di gestione – di continuare la crociera rilasciando alla nave la libera pratica sanitaria.

7. *Sbarco di casi sospetti e confermati da COVID-19*:

Quando si sbarca un caso sospetto o confermato da COVID-19, secondo quanto richiesto o suggerito dalle autorità sanitarie locali, devono essere prese le seguenti precauzioni:

- lo sbarco deve essere controllato per evitare qualsiasi contatto con altre persone a bordo;
- il paziente (caso sospetto o confermato da COVID-19) deve indossare una maschera chirurgica durante lo sbarco; e
- il personale di bordo che accompagna il paziente (caso sospetto o confermato da COVID-19) durante lo sbarco deve indossare DP adeguati, che possono includere una maschera facciale, un grembiule o impermeabile (se disponibile), guanti e protezione per gli occhi (occhiali o visiera).

La Società di gestione deve garantire ogni utile supporto a tutte le persone presenti a bordo (passeggeri ed equipaggio), in caso di sbarco, attraverso la predisposizione di:

- adeguati servizi di accoglienza nel porto o in località limitrofe ritenute idonee;
- adeguati servizi di assistenza e trasporto, ai fini del trasferimento nei rispettivi luoghi di provenienza, sulla base delle valutazioni ed indicazioni fornite dal Ministero della Salute;
- eventuali alloggi o sistemazioni, ritenute idonee dall'Unità di Crisi regionale, per le persone destinatarie dei provvedimenti di quarantena.

8. *Pulizia e disinfezione della nave*:
Le cabine e gli alloggi dei pazienti e dei contatti stretti devono essere puliti utilizzando protocolli di pulizia e disinfezione per cabine infette (come per *Norovirus* o altre malattie trasmissibili).
Le superfici devono essere pulite accuratamente con acqua calda, detergente e applicazione di comuni disinfettanti (ad es. ipoclorito di sodio). Una disinfettazione di routine deve essere eseguita sulle superfici che molte persone possono toccare, ad es. aree mensa, maniglie delle porte, ringhiere, pulsanti per ascensori/sciacquone, telefoni, pannelli di navigazione.
Una volta che un paziente ha lasciato la nave, la cabina o le zone di isolamento devono essere accuratamente puliti e disinfettati da parte del personale addestrato e dotato di DP.
Lavanderia, utensili per la ristorazione e rifiuti delle cabine di casi sospetti e contatti stretti devono essere trattati come infetti, in conformità con le procedure per la manipolazione dei materiali infetto a bordo. Devono essere usati i guanti quando si maneggiano questi oggetti che devono, altresì, rimanere coperti durante il trasporto verso la lavatrice/lavastoviglie/contenitore appropriato.
In allegato 11 un poster che indica come trattare la biancheria.
Per maggiori dettagli si dovrà fare riferimento alla vigente normativa nazionale, unionale ed internazionale.

F. Altri problemi medici a bordo per il personale navigante

Le circostanze associate all'attuale epidemia di COVID-19 possono rappresentare sfide uniche per il personale navigante e per le loro famiglie. I marittimi possono annoiarsi, sentirsi frustrati o sentirsi soli, così come le loro famiglie. Ognuno reagisce in modo diverso agli eventi e ai cambiamenti con possibili ripercussioni – che possono anche variare nel tempo – nei pensieri, nei sentimenti e nel comportamento. I marittimi devono nutrire la propria mente e il proprio corpo e cercare un supporto se richiesto. Diverse strategie per migliorare la salute mentale e il benessere del personale navigante sono riportate in allegato 12.

1. *Gestione dei sintomi fisici innescati da stress e ansia*:
I seguenti sintomi di breve durata possono insorgere nelle persone di cattivo umore o con ansia:
   - battito cardiaco più veloce, irregolare o più evidente;
   - sensazione di capogiro/stordimento e vertigini/nausea;
   - mal di testa; e
   - dolori al petto o perdita di appetito.

   Può essere difficile riconoscere quali sono le cause di questi sintomi; spesso si verificano a causa di stress, ansia o malumore e possono peggiorare quando le persone si concentrano sul loro stato di salute.

I marittimi che sono preoccupati per i loro sintomi fisici devono parlare con le persone responsabili dell'assistenza medica a bordo e, se necessario, chiedere consiglio al medico di bordo e laddove non presente al CIRM.
Nel caso in cui personale dell'equipaggio, a causa del COVID-19, non possa essere sostituito e resti a bordo – con suo consenso e previa stipula di nuovo contratto – oltre i limiti previsti dal contratto (MLC,2006 o CCNL), le Società di gestione devono mettere gratuitamente a disposizione del personale navigante:

- schede telefoniche o accesso a Internet per i collegamenti con la famiglia;
- videoconferenza o contatti telefonici con psicologi.

In allegato 13 il poster che rispettivamente riportano come affrontare lo stress durante l'emergenza COVID-19.

2. *Gestione di una crisi di salute mentale e di un'emergenza*:
Lo stress aggiuntivo dovuto al COVID-19 può avere un impatto sulla salute mentale e, pertanto, le Società di gestione devono occuparsene come se fosse un'emergenza fisica. Il personale navigante potrebbe non sentirsi più in grado di far fronte o controllare la propria situazione o lo stato emotivo e quindi:
   - provare grande stress emotivo o ansia;
   - essere incapace di far fronte alla vita quotidiana o al lavoro;
   - considerare l'autolesionismo o persino il suicidio; e
   - sentire voci (allucinazioni).

   In questo caso, bisogna consultare immediatamente un esperto di salute mentale per la valutazione del caso. Se la persona è già sotto la cura di un centro di salute mentale, si rende necessario contattare il consulente specifico.

3. *Prescrizioni sanitarie*:
In considerazione dell'attuale incertezza e del tempo necessario per effettuare i cambi di equipaggio, il personale navigante deve richiedere, senza indugio, l'accesso a farmaci personali a lungo termine su prescrizione medica che si stanno esaurendo in modo tale che possano essere acquistati e consegnati come articoli essenziali. A tal proposito la persona deve:
   a. informare il comandante della nave della necessità di ottenere una prescrizione, fornendo dettagli precisi sulle cure necessarie, compreso il dosaggio corretto al fine di ottenere il farmaco;
   b. ove possibile, ottenere una prescrizione elettronica dal proprio medico prima di arrivare in un porto o fornire una copia cartacea della prescrizione (se disponibile) per consentire la verifica e l'acquisto;
   c. se è richiesta la riservatezza e i marittimi non desiderano informare il comando nave, essi devono contattare il servizio *welfare* della gente di mare per ottenere informazioni sulla consegna e l'acquisto di medicinali tenendo in considerazione che –a motivo delle attuali restrizioni – l'attività dei servizi *welfare* è stato fortemente limitato;
   d. se possibile, richiedere l'invio di forniture dal loro Paese di residenza.

   Nell'allegato 14 una tabella che delinea i requisiti per la richiesta di prescrizioni ripetute per i marittimi i cui farmaci personali si stanno esaurendo. L'elenco non è esaustivo ed è importante contattare le Autorità locali o gli assistenti sociali locali prima dell'arrivo in porto per definire il modo migliore per conseguire, tempestivamente, tale obiettivo.

Circ. 4204 Add.	Operazioni Commerciali	Certificazione nave	Cambi equipaggi Rimpatri	Interferenza traffici	Gestione personale	CoCs CoPs	Ritardo Consegna navi	PSC	Off-Shore	DPI	Interfaccia Nave-porto	Single Window
1	X		X									
2				X								
3					X							
4					X						X	
4-1			X		X						X	
5						X						
5-1								X				
6	X		X								X	
7							X					
8								X				
9				X								
10				X								
11			X									
12				X								
12-1	X			X								
13									X			
14			X									
15										X		
16											X	
17												X
18			X									
19		X										
20	X											
21	X											
22			X									

COVID-19
Protect yourself and others from getting sick

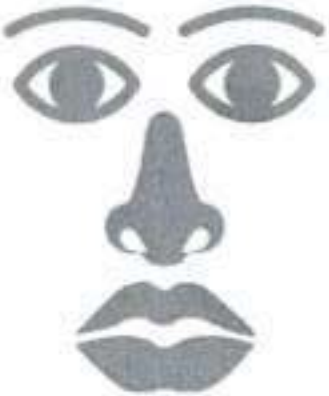
When coughing and sneezing, cover your nose and mouth with a tissue or a flexed elbow

Throw the tissue into a closed bin immediately after use

Clean your hands with an alcohol-based hand rub or with soap and hot water for at least 20 seconds:

- After coughing or sneezing
- When caring for the sick
- Before, during and after preparing food
- Before eating
- After toilet use
- When hands are visibly dirty

Avoid touching eyes, nose and mouth



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COVID-19
Practise Food Safety

Meat products can be safely consumed if they are cooked thoroughly and properly handled during food preparation

Do not eat sick or diseased animals

Use different chopping boards and knives for raw meat and cooked foods

Wash your hands with soap and hot water for at least 20 seconds between handling raw and cooked food

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COVID-19
Stay healthy while travelling

Avoid these modes of travel if you have a fever or a cough

Eat only well-cooked food

Avoid spitting in public

Avoid close contact and travel with sick animals, particularly in wet markets

When coughing and sneezing, cover your mouth and nose with a tissue or flexed elbow. Throw the tissue into a closed bin immediately after use and clean your hands

Frequently clean your hands with an alcohol-based hand rub or with soap and hot water for at least 20 seconds

Avoid touching eyes, nose and mouth

Avoid close contact with people suffering from a fever or a cough

If wearing a face mask, be sure it covers your mouth and nose and do not touch it once on. Immediately discard single-use masks after each use and clean your hands after removing masks

If you become sick while travelling, tell crew or ground staff

Seek medical care early if you become sick, and share your history with your health provider

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WHO has issued interim guidance advising on the use of masks in the context of COVID-19. It reviews the use of masks in communities, home care and health care settings in areas reporting COVID-19 cases. Whilst intended for individuals ashore, public health and infection prevention and control (IPC) professionals and health care workers, WHO has stated that the advice also applies to situations on board. Current information and evidence suggests that:

- The two main transmission routes for COVID-19 are respiratory droplets and contact. Respiratory droplets are generated when an infected person coughs or sneezes. Any person in close contact (within 1m) with someone with respiratory symptoms (coughing, sneezing) is at risk of exposure to potentially infective respiratory droplets. Droplets may also land on surfaces where COVID-19 could remain viable; thus, the immediate environment of an infected individual can be a source of contact transmission.
- Incubation for COVID-19 (time between exposure and symptom onset) is on average 5–6 days but can be up to 14 days. During this time, some infected persons can be contagious and transmit the virus to others. Data suggests that some people can test positive from 1–3 days before developing symptoms and may infect others.
- Pre-symptomatic transmission still requires the virus to spread via infectious droplets or through touching contaminated surfaces.
- WHO defines medical masks as flat or pleated surgical or procedure masks (some shaped like cups) affixed to the head with straps. They are tested using standardised test methods to balance high filtration, adequate breathability and, optionally, fluid penetration resistance.
- Wearing a medical mask is a prevention measure to try to limit the spread of certain respiratory viral diseases, including COVID-19. **However, use of a mask alone is insufficient to provide an adequate level of protection, and other measures should also be adopted.** Maximum compliance with hand hygiene and other IPC measures are critical to prevent transmission.
- Use of a medical mask can prevent the spread of infectious droplets from an infected person to someone else and potential environmental contamination from droplets. Limited evidence suggests wearing a medical mask by healthy individuals among contacts of a sick patient may be beneficial as a preventive measure but there is no evidence that mask wearing (medical or other type) by healthy persons prevents infection.
- Community use of medical masks may create a false sense of security and neglect of other essential measures, such as hand hygiene practices and physical distancing, and may lead to touching the face under the masks and under the eyes. This could result in unnecessary costs and a shortage of masks for health care workers.

Masks provided specifically for medical purposes should be reserved for those providing medical care on board.

There are mixed opinions on **the wide use of masks by healthy people on board** due to uncertainties and critical risks, including:

- Self-contamination can occur by touching and reusing a contaminated mask.
- Depending on type of mask used, potential breathing difficulties.
- False sense of security, risking less adherence to other preventive measures e.g. physical distancing and hand hygiene.
- Diversion of mask supplies and consequent shortage of masks for health care providers.

WHO advises that use of non-medical masks, e.g. masks made of cotton fabric, for communal use has not been well evaluated and argues there is currently no evidence to recommend for or against their use. Nevertheless, some national decision makers are suggesting use of non-medical masks can control potential spread from asymptomatic carriers. Some templates to produce such masks are provided at **Annex E.** The following features should be considered:

How many layers of fabric /tissue	Water repellence/hydrophobic qualities	Breathability of material
Shape of mask	Fit of mask	

Cloth masks should not be used by those providing on board medical care due to increased risk of infection compared to medical masks.

If production of cloth masks for use in on board medical care settings is proposed locally due to shortages, the local port medical authority should assess minimum standards and technical specification.

For any type of mask, appropriate use and disposal are essential to ensure that they are effective and to avoid any increase in transmission. WHO advises:

- Place the mask carefully covering the mouth and nose and tie securely to minimise any gaps between the face and mask.
- Avoid touching the mask while wearing it.
- Remove the mask using the appropriate technique: do not touch the front of the mask but untie it from behind.
- After removal or whenever a used mask is inadvertently touched, clean hands using an alcohol-based hand rub or soap and water if hands are visibly dirty.
- Replace masks as soon as they become damp with a new clean, dry mask.
- Do not re-use single-use masks.
- Discard single-use masks after each use and dispose of them immediately upon removal.

This form is consistent with the template found at the Appendix B in the IMO *Recommended framework of protocols for ensuring safe ship crew changes and travel during the coronavirus (COVID-19) pandemic* (IMO Circular Letter No.4204/Add.14).

Crew/Passenger Health Self-Declaration Form

This form should be completed by all persons prior to, or at the time of, embarkation on to the ship. It is intended to screen persons for COVID-19 infection and collect other relevant information. [Insert reference or link to relevant data protection/privacy policy.]

Date:

Full Name
(as found on passport or other ID)

Last (Family) Name:

First (Given) Name:

Name of Ship:

1. Have you received information and guidance on the coronavirus (COVID-19), including about standard health protection measures and precautions? Yes / No

2. Do you understand and comply with applicable standard health protection measures and precautions to prevent the spread of the coronavirus (COVID-19), such as proper hand washing, coughing etiquette, appropriate social distancing? Yes / No

During the last 14 days, have you:

3. Tested positive for being infected with the coronavirus (COVID-19)? Yes / No

   If "Yes", please provide date of test and name of test:

4. Tested positive for the antibodies for the coronavirus (COVID-19)? Yes / No

   If "Yes", please provide date of test and name of test:

5. Shown any symptoms associated with the coronavirus (COVID-19), specifically:

A fever:	Yes / No
A dry cough:	Yes / No
Tiredness:	Yes / No
Shortness of breath:	Yes / No
Aches and pains:	Yes / No
Sore throat:	Yes / No
Diarrhoea:	Yes / No
Nausea:	Yes / No
Loss or change in taste/smell:	Yes / No
Rash:	Yes / No

6. Completed a period of self-isolation related to the coronavirus (COVID-19)? Yes / No

If "Yes", please explain the circumstances and the length of self isolation:

7. Had close contact with anyone that has tested positive for coronavirus (COVID 19)? Yes / No
("Close contact" means being at a distance of less than one metre for more than 15 minutes.)

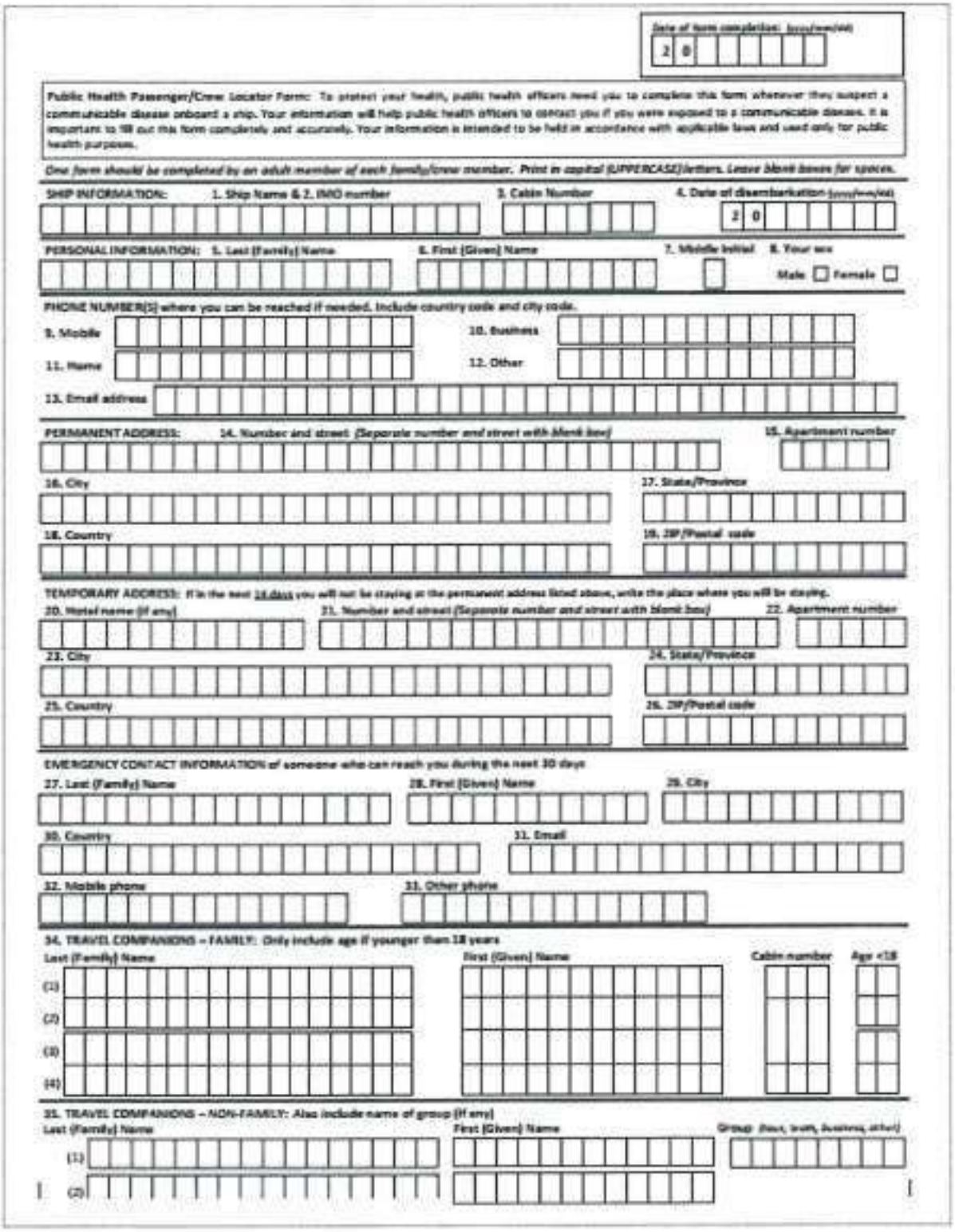
8. Had close contact with anyone with symptoms of the coronavirus (COVID-19)? Yes / No
("Close contact" means being at a distance of less than one metre for more than 15 minutes.)

9. Maintained good personal hygiene and complied with applicable health protection measures and precautions? Yes / No

I confirm that the information provided above is correct to the best of my knowledge.

Signature:

Date:



Date of form completion: (yyyy/mm/dd) 2 0

Public Health Passenger/Crew Locator Form: To protect your health, public health officers need you to complete this form whenever they suspect a communicable disease onboard a ship. Your information will help public health officers to contact you if you were exposed to a communicable disease. It is important to fill out this form completely and accurately. Your information is intended to be held in accordance with applicable laws and used only for public health purposes.

One form should be completed by an adult member of each family/crew member. Print in capital (UPPERCASE) letters. Leave blank boxes for spaces.

SHIP INFORMATION: 1. Ship Name & 2. IMO number | 3. Cabin Number | 4. Date of disembarkation (yyyy/mm/dd) 2 0

PERSONAL INFORMATION: 5. Last (Family) Name | 6. First (Given) Name | 7. Middle Initial | 8. Your sex: Male ☐ Female ☐

PHONE NUMBER(S) where you can be reached if needed. Include country code and city code.

9. Mobile | 10. Business

11. Home | 12. Other

13. Email address

PERMANENT ADDRESS: 14. Number and street *(Separate number and street with blank box)* | 15. Apartment number

16. City | 17. State/Province

18. Country | 19. ZIP/Postal code

TEMPORARY ADDRESS: If in the next 14 days you will not be staying at the permanent address listed above, write the place where you will be staying.

20. Hotel name (if any) | 21. Number and street *(Separate number and street with blank box)* | 22. Apartment number

23. City | 24. State/Province

25. Country | 26. ZIP/Postal code

EMERGENCY CONTACT INFORMATION of someone who can reach you during the next 30 days

27. Last (Family) Name | 28. First (Given) Name | 29. City

30. Country | 31. Email

32. Mobile phone | 33. Other phone

34. TRAVEL COMPANIONS – FAMILY: Only include age if younger than 18 years

	Last (Family) Name	First (Given) Name	Cabin number	Age <18
(1)				
(2)				
(3)				
(4)				

35. TRAVEL COMPANIONS – NON-FAMILY: Also include name of group (if any)

	Last (Family) Name	First (Given) Name	Group (tour, youth, business, other)
(1)			
(2)			

COVID-19 A3

Stay healthy while travelling

Avoid these modes of travel if you have a fever or a cough

Eat only well-cooked food

Avoid spitting in public

Avoid close contact and travel with sick animals, particularly in wet markets

When coughing and sneezing, cover your mouth and nose with a tissue or flexed elbow. Throw the tissue into a closed bin immediately after use and clean your hands

Frequently clean your hands with an alcohol-based hand rub or with soap and hot water for at least 20 seconds

Avoid touching eyes, nose and mouth

Avoid close contact with people suffering from a fever or a cough

If wearing a face mask, be sure it covers your mouth and nose and do not touch it once on. Immediately discard single-use masks after each use and clean your hands after removing masks

If you become sick while travelling, tell crew or ground staff

Seek medical care early if you become sick, and share your history with your health provider

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1 Eliminare	L'eliminazione del pericolo è la misura più efficace per ridurre i rischi. I lavori a bordo non devono essere condotti se esiste un metodo più sicuro per intraprendere l'attività per non andare su una nave. In un numero di casi ad es. condurre audit, survey, ispezioni e formazione esistono possibilità remote che possono eliminare la necessità di salire a bordo o ridurre il numero di personale che deve partecipare	• La frequenza a bordo è necessaria in questo momento? • Il lavoro può essere svolto in remoto? • il lavoro può essere rinviato? Se la frequenza a bordo non può essere eliminata, è possibile ridurre il rischio? Ad esempio, il numero dei presenti può essere ridotto e/o parte del lavoro normalmente svolto a bordo può essere ridotto ad es. la revisione documentale, le interviste, ecc. possono essere condotte in remoto?
2 Ridurre	La frequenza a bordo può essere ridotta? Laddove non sia possibile eliminare completamente i pericoli, il rischio potrebbe essere ridotto minimizzando il lavoro a bordo	• È possibile ridurre il numero di persone presenti a bordo e/o la durata del tempo trascorso a bordo ridotta? • È possibile svolgere parte del lavoro in remoto, ad es. ispezioni visive, esercitazioni, interviste? • È necessario partecipare a bordo di persona o è possibile organizzare riunioni in remoto per ridurre il numero di partecipanti e ridurre la durata? • È possibile fornire informazioni per la revisione remota per ridurre la presenza a bordo? Una volta che la presenza a bordo è stata ridotta il più possibile, è necessario considerare come controllare il rischio residuo
3 Comunicare	Se la presenza a bordo del personale di terra non può essere eliminata, comunicare e comprendere i requisiti dei partecipanti. Garantire che i requisiti di ciascuna parte, della nave e dell'organizzazione di terra siano stati comunicati in tempo utile tra loro e siano state valutate e comprese. In caso di differenze nelle esigenze, le misure di controllo devono essere concordate e comprese da tutte le parti prima dell'intervento a bordo della nave.	• I requisiti delle navi e delle organizzazioni di terra relativi alla gestione dei rischi e al controllo del COVID-19 sono stati comunicati in tempo utile a tutte le parti prima dell'arrivo? È previsto che l'agente della nave dovrà svolgere un ruolo importante in questo senso. • I requisiti di ciascuna parte sono compresi dall'altra parte? • I requisiti sono allineati, ad es. requisiti per l'uso dei DPI? Se la gestione del rischio e i requisiti di una parte non sono allineati o non sono stati compresi, ulteriori misure di controllo potrebbero essere necessarie.
4 Controllare	Se i requisiti di ciascuna parte, della nave e dell'organizzazione a terra sono stati tra loro comunicati e valutati e non sono stati compresi o ci sono differenze, allora devono essere prese	Se le misure di controllo della nave e dell'organizzazione a terra inizialmente non allineati o non completamente compresi devono essere identificate le azioni necessarie per correggere la situazione.

	misure di controllo in modo che tutti i requisiti siano compresi e che i requisiti possono essere reciprocamente concordati e compresi da tutte le parti prima dell'intervento a bordo della nave	Le considerazioni dovrebbero includere: • È necessario fornire una spiegazione aggiuntiva dei requisiti forniti? • Se i requisiti non sono compresi e o allineati, misure di controllo possono essere implementate chiarendo i requisiti e/o concordando requisiti reciprocamente accettabili? • Quali misure di protezione sono in atto a bordo e per il personale che sale? • Sono accettabili misure alternative, ad es. fornitura della nave di DPI al personale di terra? • È possibile mantenere il distanziamento sociale? • L'ingresso nelle zone alloggio dell'equipaggio può essere evitato/minimizzato? Una volta che i requisiti che differiscono dalla normale pratica per ciascuna delle parti sono concordati da parte di tutte le parti interessate, gli stessi dovrebbero essere comunicati in modo chiaro a tutte le parti coinvolte, vale a dire a tutto l'equipaggio e tutti i partecipanti di terra.
5 DPI	Comprendere quali DPI sono richiesti e che dovrebbero essere utilizzati dall'equipaggio e dal personale di terra durante le presenze a bordo ed in quali orari.	Oltre a comprendere le aspettative sui DPI reciprocamente concordate sia dall'equipaggio della nave che del personale di terra, dovrebbe essere valutato quanto segue: • I DPI concordati sono disponibili per entrambe le parti? In caso contrario, può essere fornito dall'altra parte, se necessario, prima o al momento dell'imbarco? • I DPI disponibili sono conformi alle specifiche raccomandate ed appropriate nonché compatibili con gli altri DPI e le attrezzature da indossare durante l'intervento. I DPI forniti consentono l'esecuzione efficace dei lavori previsti? • Il DPI è sterile, laddove applicabile? • L'utente è stato istruito su come ispezionare, indossare, utilizzare e smaltire i DPI?

COVID-19 **A5**

How to safely greet others

Avoid physical contact.

Safe greetings include
a wave, a nod
or a bow

For more information, go to
ics-shipping.org/covid19

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Allegato 9

COVID-19 A7

Protecting everyone during ship visits

COVID-19 is spread through small droplets from the nose or mouth of an infected person which may be inhaled or land on objects and surfaces other people touch, after which they then touch their eyes, nose or mouth.

Protect through social distancing and good hygiene

Keep a minimum of 1-2 metres distance.

No handshakes or physical contact.

Wash hands frequently and thoroughly, keeping contact surfaces clean, and touch your face less.

Prepare for visitors

Wipe down areas and objects visitors are likely to touch with an anti-bacterial solution.

Restrict access into the ship's accommodation – keeps doors locked and post 'no entry' signs.

Provide alcohol hand gel ready for use upon entry onto the ship and around the ship.

Have designated toilet and handwashing facilities for visitors, which are well-stocked with soap.

Try to prepare and complete documents digitally – avoid handling paper and laminated documents.

Have PPE, such as disposable gloves, ready to use in unavoidable close contact situations.

Keep your guard up

Maintain effective ship and gangway security and prevent unauthorised personnel boarding the ship.

If someone trying to board the ship exhibits symptoms – refuse access and report it.

Continue to sanitise contact areas throughout the ship's stay in port.

Take it outside

Where possible, hold conversations and meetings with visitors on the open deck or open bridge wings.

If visitors must be inside, limit the number of crew nearby to the absolute minimum.

Based on information kindly provided by the North of England P & I Club

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For more information, go to **ics-shipping.org/covid19**

COVID-19 A6

Shipboard care for people with suspected or confirmed COVID-19

For ill crew members

Clean hands frequently with soap and water or with alcohol-based hand rub.

Stay in your cabin and do not attend work. Rest, drink plenty of fluids and eat healthy food.

Stay in a separate cabin from other people. If this is not possible, wear a mask and keep a distance of at least 1m away. Keep the cabin well-ventilated and if possible use a dedicated bathroom.

When coughing or sneezing, cover your mouth and nose with flexed elbow or use disposable tissue and discard after use. If you experience difficulty breathing, contact radio medical.

For caregivers

Clean hands frequently with soap and water or with alcohol-based hand rub.

Wear a medical mask when in the same cabin with an ill person. Do not touch your face during use and discard it afterward.

Use dedicated dishes, cups, eating utensils, towels and bed linen for the ill person. Wash everything used by the ill person with soap and water.

Identify surfaces frequently touched by the ill person and clean and disinfect them daily.

Contact radio medical immediately if the ill person worsens or experiences difficulty breathing.

For all crew members

Clean hands frequently with soap and water or with alcohol-based hand rub.

Avoid unnecessary exposure to the ill crew member and avoid sharing items, such as eating utensils, dishes, drinks and towels.

When coughing or sneezing, cover your mouth and nose with flexed elbow or use disposable tissue and discard after use.

Monitor everyone's health for symptoms such as fever or a cough. If anyone has difficulty breathing, contact radio medical immediately.

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For more information, go to **ics-shipping.org/covid19**

COVID-19 A9

How to deal with laundry

How to wash and dry clothes, towels and bed linen if a crew member is a suspected COVID-19 patient

Wash the patient's clothes, towels and bed linen separately.

If possible, wear heavy-duty gloves before handling them.

Never carry soiled linen near your body; place soiled linen in a clearly labelled, leak-proof container (e.g. bag, bucket).

Scrape off solid excrement (e.g. faeces or vomit) with a flat, firm object and place it in the patient's toilet before putting linen in the designated container. Place the excrement in a covered bucket to dispose of in a toilet if this is not in the patient's cabin.

Wash and disinfect linen: machine wash at 60–90°C with laundry detergent. Alternatively, soak linen in hot water and soap in a large drum, using a stick to stir, avoid splashing. If hot water is not available, soak linen in 0.05% chlorine for approximately 30 minutes. Rinse with clean water and let linen dry in sunlight.

Do not forget to wash hands at the end of the process.

Do I need to use a washing machine and drier to wash and dry clothes, towels and bed linen if no one in the crew is a suspected COVID-19 patient?

No need to use a washing machine or drier, nor extremely hot water.

Do laundry as normal using detergent or soap.

Once dry, clean your hands before handling and storing clothes, towels and bed linen.

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For more information, go to **ics-shipping.org/covid19**

Measures to Enhance Mental Health and Wellbeing	General Wellbeing	Those with general mental health issues	Obsessive compulsive disorder (OCD)	Learning Disability	Autism	Older people
Consider how to connect with others and help and support them						
Contacting trusted friends, family and colleagues is key to mental wellbeing.	✓	✓	✓	✓	✓	✓
Make regular contact via telephone, video calls or social media instead of meeting up.	✓	✓	✓	✓	✓	✓
Identify how to provide help and support to others. Message a friend or family member nearby. Join community groups to support family while at sea.	✓	✓				
Try to accept other people's concerns, worries or behaviours.	✓	✓	✓	✓	✓	✓
Maintain daily physical wellbeing						
Physical health impacts on emotional and mental feelings. At difficult times, it can be easy to adopt unhealthy behaviours which can make things worse. Eat healthy, well-balanced meals, drink enough water, exercise where possible, and avoid smoking and alcohol.	✓	✓				✓
Life is changing for everyone. Staying on board or social distancing will cause disruption to the normal routine. Review how to adapt and create positive new routines, engage in useful activities (e.g. cleaning or exercise) or meaningful ones (e.g. reading or calling a friend). It may be helpful to write a daily plan.	✓	✓				✓
Manage panic and anxiety						
When having panic attacks or flashbacks plan a 'safe space' to go to.	✓	✓	✓	✓	✓	✓
If spending more time on board, seafarers may feel trapped or claustrophobic and should try if possible to go outside daily. Open windows if possible to let in fresh air, and sit with an external view. Change rooms visited (if possible) to give a sense of space.	✓	✓	✓	✓	✓	✓
Manage worry and stress and seek help when struggling						
The COVID-19 outbreak may be stressful and cause worry about changes that occur because of it, including having to stay on board.	✓	✓		✓	✓	
Do not forget about other health conditions and take any medication prescribed.	✓	✓		✓		
Share feelings and coping strategies with family and friends, or contact ISWAN Seafarer Help or a Seafarers' Mission to help.	✓	✓	✓	✓	✓	✓
If needing medical treatment, share medical information or diagnosis with medical staff.	✓	✓	✓	✓	✓	✓
Request help for example with shopping or running errands and let those around you know what they can do or contact Seafarers help or the local port welfare provider.	✓	✓				✓
Manage difficult feelings						
Seafarers should focus on things they can control by acquiring information and better preparation. Worries outside personal control and repetitive thoughts are unhelpful.	✓	✓				
OCD can make it hard to absorb advice due to problematic washing or hygiene behaviours.			✓			
Avoid re-reading advice about Covid-19 if this is unhelpful	✓	✓	✓	✓	✓	✓
Advise others when struggling, for example, ask them not to discuss the news	✓	✓	✓	✓	✓	✓
Set limits	✓	✓	✓	✓	✓	✓

Measures to Enhance Mental Health and Wellbeing	General Wellbeing	Those with general mental health issues	Obsessive compulsive disorder (OCD)	Learning Disability	Autism	Older people
Plan something to do to change focus	✓	✓	✓	✓	✓	✓
Contact the mental health team						
Contact the mental health team to discuss continuing care and to update medical plans.		✓	✓	✓	✓	✓
Improve sleep						
Anxiety or worries can make it harder to get a good night's sleep. Good quality sleep enhances mental and physical wellbeing. Maintain regular sleeping patterns and good practices, avoid screens before bed, reduce caffeine and create a restful environment.	✓	✓				✓
Manage personal media and information intake						
24-hour news and constant social media updates can increase worry. Limit time to a maximum of twice daily checks to watch, read, or listen to media coverage.	✓	✓	✓	✓	✓	✓
Gather information from this guidance document to accurately determine risks of contracting COVID-19 to take reasonable precautions. Inaccurate information can also negatively affect others so do not share information without fact-checking sources.	✓	✓	✓	✓	✓	✓
Set goals and plan to keep mentally well						
Setting goals and achievement gives a sense of control and purpose so identify things to do on board. Watch a film, read a book or learn something online.	✓	✓	✓	✓	✓	✓
Exercise on board and download 10 minute work outs or other exercise videos.	✓	✓				
Continue normal activities to keep well. If support is available from others, plan how to remain well and relaxed with them.	✓	✓			✓	
Keep a diary	✓	✓			✓	
View Brain in Hand https://www.autism.org.uk/services/education/brain-in-hand.aspx					✓	
Use strategies that have helped previously.	✓	✓				
Do enjoyable things and keep an active mind						
People may do enjoyable things less often, or not at all when anxious, lonely or low. Pursuing a favourite hobby, learning something new or taking time to relax indoors should provide relief from anxiety and can enhance mood.	✓	✓	✓	✓	✓	✓
If unable to do activities due to staying on board, adapt them, or try something new.	✓	✓	✓	✓	✓	✓
Read, write, play games, do crossword puzzles, sudokus, jigsaws or drawing and painting. Many free tutorials and courses are available online and people are producing innovative online solutions like online pub quizzes and streamed live music concerts.	✓	✓	✓	✓	✓	✓
Relax and focus on the present						
This can help with difficult emotions, worries about the future and improve wellbeing. Relaxation techniques can also help some people manage feelings of anxiety.	✓	✓	✓	✓	✓	✓
Spend time outside, or bring nature in						
Social distancing guidelines enable seafarers to exercise outside daily to enhance wellbeing. If unable to get outside there can be positive effects by opening windows (if possible) to provide fresh air, arrange space to sit for a nice view and get some natural sunlight.	✓	✓	✓	✓	✓	✓
If walking outside follow the recommended social distancing guidance.	✓	✓	✓	✓	✓	✓
With increased risk of severe illness and need to stringently follow social distancing measures when onboard, some older people, particularly those with pre-existing medical conditions, may be concerned or affected by changes required to daily life.	✓	✓				✓
Alcohol reduction						
It can be dangerous to stop quickly without support. If physical withdrawal symptoms occur (like shaking, sweating or anxiety until having the first daily drink), seek medical advice.	✓	✓	✓	✓	✓	✓

ALLEGATO N. 6

ECDC TECHNICAL REPORT

Guidelines for the use of non-pharmaceutical measures to delay and mitigate the impact of 2019-nCoV

February 2020

Scope of this document

This document provides guidance on the application of non-pharmaceutical countermeasures to minimise the spread of the 2019 novel coronavirus (2019-nCoV) in the population. Some of the measures proposed refer specifically to certain phases of the epidemic (containment or mitigation phases), and can be adapted depending on the assessed severity/impact of the infection. Other measures are valid for all phases of an epidemic.

The guidance is based on the current knowledge of the 2019-nCoV and evidence available on other viral respiratory pathogens, mainly the Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), the Middle East Respiratory Syndrome-related coronavirus (MERS-CoV) and seasonal or pandemic influenza viruses.

ECDC will update this guidance as and when new relevant information becomes available or as required by the epidemiological situation.

Target audience

Public health authorities in the EU/EEA Member States (MS) and the UK.

Background

Since it was first identified in Wuhan, Hubei province, thousands of cases of the 2019-novel coronavirus (2019-nCoV) infection have been reported in China. Several cases have also been reported in other countries across the continents of Asia, Europe, America, and Oceania, either as imported cases from China or as result of autochthonous transmission.

Coronaviruses are usually transmitted by direct contact through large respiratory droplets, but other modes of transmission have been identified. To date, human-to-human transmission through direct contact is the most common transmission mode for 2019-nCoV [1]. Although there is no evidence of airborne transmission, a precautionary approach is recommended due to uncertainties surrounding the potential for aerosol-mediated transmission of the virus. Other routes of transmission, such as contact with contaminated fomites and inhalation of aerosols during aerosol-generating procedures, may have occurred in some cases [2]. The RNA of the virus has been detected in the faeces of a confirmed patient with gastrointestinal symptoms, hence faecal–oral transmission cannot be ruled out [3]. The current estimated basic reproductive number (R0) is 2.2 (95% CI, 1.4 to 3.9) [4].

This document is based on an ECDC Expert Opinion on non-pharmaceutical countermeasures currently under development for use against pandemic influenza. Since there are uncertainties concerning the infectious period of the 2019-nCoV and its R0 and how these differ from influenza [4,5], this document should be interpreted with caution. However, it is plausible that measures effective against influenza would also work against 2019-nCoV.The primary objective of non-pharmaceutical countermeasures is to reduce the impact of an outbreak by reducing the number of contacts that result in disease transmission. Depending on the extent to which they are implemented, non-pharmaceutical countermeasures can delay the time to epidemic peak and reduce the overall number of cases,

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the number of cases at epidemic peak, and the total number of severe cases and deaths. Reducing the number of cases during the epidemic peak and the subsequent spread of cases over a longer time-period would play a crucial role in reducing the burden on the healthcare and other sectors, thus allowing more effective treatment of infected patients. This is an important goal of the current 2019-vCoV containment strategy in Europe (i.e. to delay the possible spread of 2019-nCoV until the end of the ongoing influenza season, hence reducing the strain on healthcare systems). Furthermore, delaying the introduction of 2019-nCoV into Europe would allow for more surge capacity in public health and healthcare services (including laboratories) while also minimising the need for differential diagnoses. Finally, this would also gain time for the development, production and distribution of effective and safe pharmaceuticals (i.e. vaccines and antiviral drugs).

Non-pharmaceutical countermeasures may be implemented at all stages of an epidemic but the choice of the most suitable measures may differ during the containment and mitigation phases. These measures range from standard precautions, such as hand, respiratory and environmental hygiene, in the form of personal protective action taken by individuals, to actions requiring the engagement of communities and the involvement of local, regional or national authorities (i.e. social distancing and travel-related measures).

Therefore, one of the key factors for the effective application of non-pharmaceutical measures is the correct identification and definition of triggers for their activation/deactivation during the various epidemic phases (e.g. school closures or travel restrictions). Non-pharmaceutical measures should ideally be combined with other approaches, as individual measures may not be so effective when implemented alone [6,7]. In the early epidemic phases, a combined approach may contain the pathogen or delay its spread, thus allowing for unaffected areas to activate their preventive measures in the meantime. During a widespread epidemic, a synergistic effect may increase the effectiveness of individual non-pharmaceutical measures and mitigate the disease impact, whilst reducing costs to society and the economy [7]. Despite the anticipated effectiveness of each measure, non-pharmaceutical countermeasures need to be evaluated in terms of their necessity, acceptability and feasibility. National planning and public health action should therefore be tailored to the severity and impact of the epidemic and to the local epidemiological situation. EU decision no 1082/2013/EU on serious cross-border threats to health regulates the risk assessment, communication and coordination of responses in situations such as the current spread of 2019-nCoV, and ensures that EU/EEA Member States take risk management measures in consultation with one another and the European Commission (EC).

Personal protective measures

Personal protective measures refer to hand and respiratory hygiene, cough etiquette and use of respirators or facemasks.

Hand hygiene

The risk of transmitting or acquiring 2019-nCoV infection can be reduced by the correct application of hand hygiene. Hand hygiene refers to the frequent washing of hands with soap and water or cleaning of hands with alcoholic solutions, gels or tissues. Hands should be washed regularly using soap and water for 20–40 seconds [8]. Alcohol-based hand sanitisers provide limited added benefit over soap and water in community settings, and if used should contain 60–85% alcohol [8,9]. If hands are soiled, soap and water should precede the use of alcohol-based hand sanitisers. Since the 2019-nCoV virus can be transmitted by direct contact through droplets or indirectly through hand-mediated transfer of respiratory or possibly other secretions, we recommend applying hand-hygiene measures in all community settings (home, schools, workplaces, etc.) during all phases of the epidemic. Proper hand hygiene would also prevent the transmission of other communicable diseases.

In healthcare settings, proper hand hygiene will need to be performed immediately before and after contact with a patient, before wearing or removing personal protective equipment (PPE) and after contact with potentially infectious material, such as respiratory or other secretions. The same applies to patients or people caring for patients at home.

Recommending hand hygiene is considered to be a rational precaution, involving limited costs and no significant associated risks. Its effectiveness is likely to increase in combination with other measures (e.g. facemasks used in healthcare settings). The effectiveness of hand hygiene depends on the ability to ensure that people comply, through appropriate and repeated training and an adequate and regular supply of soap, tissues and alcohol-based hand sanitisers.

Cough etiquette

Cough etiquette refers to covering the mouth and nose when coughing and sneezing (e.g. using a paper tissue or cloth handkerchief) with the aim of reducing person-to-person transmission through droplets which are a known mode of transmission for coronaviruses.

Cough etiquette is widely recommended in public health guidelines for all community settings (home, schools, workplaces, healthcare settings, etc.) at all times. Supply of materials (e.g. tissues, no-touch waste bins, etc.)

needs to be ensured. It is important that tissues are properly disposed of immediately after the use and hands are then washed with soap and water, as described in the hand hygiene section of this document.

Facemasks and respirators

This measure refers to the use of facemasks or respirators. For optimal use of these non-pharmaceutical countermeasures, it is important to have a sound estimate of the duration of the infectious period - which is not as yet available for 2019-nCoV infection.

Facemasks range from simple, even homemade masks, to cloth and surgical (medical) masks. They vary in thickness and permeability. They can protect against larger respiratory droplets but are not guaranteed to protect users from airborne infection. Cloth/gauze masks may induce moisture retention and poor filtration and it is unclear whether they confer clinical protection [10].

Respirators are specifically designed to protect users from small airborne particles, including aerosols [11,12]. They are usually available in three sizes (small, medium or large) to allow for differences in face contours. European standard (EN 149:2001+A1:2009) defines classes for respirators entirely or substantially constructed of filtering material [filtering face pieces (FFP) 1-3] [10]. Because the various respirators fit users differently, they need to be fitted individually in order to match each user with the appropriate respirator.

Surgical masks or respirators should be changed frequently in order to maintain their effectiveness. The frequency of change depends on several factors. As a general rule, a mask should be changed as soon as it becomes moist and, in healthcare settings, whenever moving from one patient to another.

Use of facemasks and respirators in healthcare settings

In healthcare settings, facemasks or respirators are used to reduce transmission and protect healthcare workers, patients and visitors against infection. Suspected 2019-nCoV cases should be offered a surgical mask which they should wear correctly while in public areas or while visiting areas where other people are present. Suspected cases arriving in healthcare settings should, where possible, immediately be offered a surgical mask in order to mitigate the risk of droplet spread when in triage or waiting areas or during transportation within the facility.

During the assessment of a suspected case or the management of a confirmed case, healthcare workers should use FFP respirators class 2 or 3 (FFP2 or FFP3) which protect both from droplet and aerosol transmission. In the absence of FFP respirators, a surgical mask should be worn that protects from droplet transmission. It is recommended that healthcare workers performing procedures that are likely generate aerosol should wear an FFP3 respirator. If FFP2 or FFP3 respirators are not available, the use of a surgical facemask is recommended. When using this type of PPE, the limitations and risks connected to its use should be assessed on a case-by-case basis.

Proper mask disposal and combined measures (e.g. proper hand hygiene) will probably increase the effectiveness of individual measures. For more information please consult the ECDC document on 'Infection prevention and control for the care of patients with 2019-nCoV in healthcare settings' [13]. ECDC has also published an adaptable template leaflet providing advice to healthcare workers on handling and caring for patients.

Use of facemasks in other high-exposure situations

It is still unclear whether the use of surgical facemasks by healthy people who might be exposed to 2019-nCoV will be beneficial. This uncertainty is mainly due to the low filtration efficiency of surgical masks, the risk of infection due to inappropriate use of the mask in high-risk community settings and the false sense of security offered by wearing a mask.

The following groups at risk of high-exposure could consider the use of surgical masks:

- care-providers for symptomatic suspected 2019-nCoV cases (before their hospitalisation);
- people in occupations who have extensive face-to-face contact with the public where there is ongoing transmission.

Furthermore, the wearing of a surgical mask can be considered for groups at risk of developing severe complications if infected (e.g. individuals in older age groups or having underlying conditions).

Relevant documents for the management of cases on ships and aircraft have been published by EU Healthy Gateways Joint Action: 'Interim advice for preparedness and response to cases of the 2019-nCoV acute respiratory disease at points of entry in the European Union (EU)/EEA Member States' [14]. Proper use and disposal of masks and proper hand hygiene need to be ensured by training users before distributing masks.

Use of facemasks in community settings

Surgical masks may be used as an infection control measure or as a mitigation measure in community settings when worn by individuals with respiratory symptoms before seeking medical advice and while being assessed. In the event that a symptomatic person cannot wear a facemask, close contacts should consider wearing one instead. During the containment phase, suspected cases can be offered a facemask as a precautionary measure.

There is no evidence on the usefulness of facemasks worn by persons who are not ill as a community mitigation measure. In the EU, it is not customary for health people to wear masks in the wider community. If masks are

used, best practices for should be followed donning, doffing, and disposing of them. The hand hygiene measures detailed above should always be followed after removing a mask.

Other personal protective equipment

Other personal protective equipment (PPE), such as eye protection (goggles, face shield or procedural masks), body protection (long-sleeved water-resistant gowns), and hand protection (gloves), should be used by healthcare workers or those caring for a patient or suspected 2019-nCoV case, especially when performing aerosol-generating procedures or when the risk of exposure to body secretions is high. Although the most common route of 2019-nCoV transmission is via respiratory droplets, it is not yet clear to what extent other secretions play a role. The use of PPE must be accompanied by appropriate training. Disposable PPE needs to be disinfected and disposed of immediately after use in accordance with routine safety procedures and used in combination with proper hand hygiene measures.

There are separate ECDC documents on 'Infection prevention and control for the care of patients with 2019-nCoV in health care settings' [13] and 'Personal protective equipment (PPE) needs in healthcare settings for the care of patients with suspected or confirmed novel coronavirus (2019-nCoV)' [15].

Environmental measures

Environmental measures refer to:

- routine cleaning of frequently used surfaces, clothes and objects;
- minimising the sharing of objects;
- ensuring appropriate ventilation.

These measures aim to enhance protection and reduce the risk of infection for 2019-nCoV and other communicable diseases in various settings (healthcare settings, long-term care facilities, educational settings, workplaces, public places and homes).

The survival time of 2019-nCoV in the environment is currently unknown. The survival of SARS-CoV is estimated to be several days and MERS-CoV >48 hours at an average room temperature (20°C) on different surfaces [16-18].

Although available evidence on the effectiveness of environmental measures in mitigating the impact of respiratory virus epidemics is limited, it is plausible that these measures may reduce viral transmission and, as such, it is recommended that they are used at all times and in all settings during the containment and mitigation phases of the epidemic [19]. Such measures include the routine cleaning of frequently used surfaces and objects (such as phones, tablets, doorknobs, toilets and keyboards) with water and detergent (such as bleach solution), washing laundry according to the detergent manufacturer's instructions at the warmest indicated temperature, and minimal sharing of objects (such as drinking glasses, eating utensils, towels and bed linen). Air ventilation in rooms is especially important in settings where people gather regularly. Lessons learnt from the SARS-CoV outbreaks show that it is possible for the virus to spread within a building through the mechanical ventilation system and therefore building maintenance measures should be taken into account [20].

In healthcare settings, it is especially important that thorough cleaning and disinfection is consistently performed. Cleaning with water, detergent and common hospital disinfectants should be sufficient, although there is lack of specific evidence for their effectiveness against 2019-nCoV virus. Routine safety procedures for disinfection and/or disposal of PPE, medical equipment, utensils, laundry and contaminated waste should be applied in case of 2019-nCoV suspected and confirmed cases. ECDC has published a document 'Interim guidance for environmental cleaning in non-healthcare facilities exposed to 2019-nCoV' [21].

Social distancing measures

Quarantine or self-isolation of 2019-nCoV cases and contacts during the containment phase

Quarantine and self-isolation imply that a person should remain in a designated setting or at home for a defined period after exposure to a situation where transmission of 2019-nCoV virus may have occurred. Evidence relating to influenza pandemics indicates that quarantining exposed people may delay the peak of local epidemics during the early stages of an epidemic, thus helping to reduce the burden of disease and delay further spread [19]. Therefore, this option can be considered during the early stages of 2019-nCoV virus introduction into Europe, as part of the Member States' containment efforts. When implementing quarantine measures, Member States should be aware of the disadvantages and possible compliance issues in order to weigh these against expected benefits.

The duration of the quarantine depends on the estimated incubation period of the virus. Early estimates indicated that the mean incubation period for 2019-nCoV is 5.2 days (95% confidence interval [CI], 4.1 to 7.0), with the 95th percentile of the distribution at 12.5 days [22]. A duration of 14 days is therefore considered sufficient for

monitoring persons having had contact with 2019-nCoV cases [4]. These guidelines will be updated if new data reveals different incubation and infectious periods. Rapid identification of cases enhances the effectiveness of quarantine measures.

There are considerable logistical, social and communication challenges in implementing quarantine measures. Education on infection control using personal protective and environmental measures in the home or other quarantine setting would be necessary.

The efficiency and resources needed to implement quarantine or self-isolation are dependent on the definition and, in particular, the scale of exposure in the target population. The more specifically the exposure is defined and confined, the more feasible such a measure will be. Implementing quarantine measures for subsets of healthy populations with unclearly defined exposure is unlikely to be an efficient use of resources. ECDC's contact management technical report [23] should be used to assess the potential risk and plan the actions associated with visitors from areas with presumed community transmission of 2019-nCoV. Quarantine is unlikely to be effective as soon as multiple introductions start to occur into EU/EEA countries and the UK from places other than China.

Suspected, probable or confirmed cases of 2019-nCov should be reported to the public health authorities and managed in accordance with national guidance and/or WHO's patient management guidelines. Contacts should be isolated and/or monitored in accordance with national guidance and/or ECDC's technical document 'Public health management of persons having had contact with novel coronavirus cases in the European Union' [23]. This document classifies contacts as 'close' or 'casual' and proposes actions, including self-isolation of close contacts and self-monitoring of casual contacts. If symptoms of illness occur, the quarantined persons should then self-isolate and seek medical advice.

Voluntary isolation of symptomatic 2019-nCoV cases not requiring hospitalisation during mitigation phase

Self-isolation of individuals with symptoms of a respiratory infection is one of the most important measures for reducing disease transmission and limiting the spread of the virus in the community during an epidemic [19]. During a community mitigation phase, this measure refers to persons presenting with an acute respiratory infection and probable or confirmed 2019-nCoV virus infection, who do not need hospital care. These individuals would usually be requested to voluntarily remain at home or in a designated setting, in a single, dedicated, adequately ventilated room and preferably use a dedicated toilet while displaying symptoms or for a defined period of time. This recommendation will be revised if new information becomes available on the infectious period for 2019-nCoV.

Early identification of cases to ensure rapid isolation is of paramount importance to prevent further spreading of the virus in the community. Based on current knowledge of 2019-nCoV clinical presentation, the most commonly observed symptoms are fever, cough, myalgia, fatigue and other non-specific respiratory symptoms, similar to those for other respiratory virus infections. This makes clinical suspicion particularly challenging during the influenza season [24]. Fever has been the most commonly reported symptom for 2019-nCoV but this may not be present in some patients, such as the very young, elderly or immunocompromised persons [24]. A small number of patients have reported gastrointestinal symptoms (such as vomiting and diarrhoea) [3,24]. The effectiveness of voluntary isolation would be reduced if there were transmission via asymptomatic or pre-symptomatic cases.

A combination of personal protective and environmental measures during isolation will increase intervention effectiveness [19]. There are complicated logistical issues associated with this measure (e.g. food provision, medical supplies, medical care) and training and supplies will therefore be essential to ensure support and infection control (e.g. PPE, proper waste disposal) for household members caring for the person who is ill.

In the absence of strong evidence on the infectious period, it is not possible to make evidence-based recommendations for isolation by case classification or stage of infection. These guidelines assume that infectiousness coincides with the symptomatic period, which is currently a reasonable assumption. Suggested non-pharmaceutical measures for cases and contacts during the containment and mitigation phases are summarised in Table 1.

Table 1. Non-pharmaceutical measures during containment and mitigation phases: quarantine, self-isolation and self-monitoring of confirmed, probable and suspected cases and close or casual contacts

A. Containment phase

Case	Suggested measure
Confirmed	Isolation (at home or in healthcare setting depending on clinical conditions) and monitoring by public health authorities in accordance with national guidance
Probable	Isolation (at home or in healthcare setting depending on clinical conditions) and monitoring by public health authorities in accordance with national guidance
Suspected	Immediate testing for 2019-nCoV and application of non-pharmaceutical measures throughout the process.
Contact of confirmed or probable case	
Close contacts	Isolation at home or in dedicated settings and active daily monitoring by public health authorities in accordance with national guidance[1]
Casual contacts	Self-monitoring - seek public health and medical assistance if symptoms develop.

B. Mitigation phase

Case	Suggested measure
Suspected	Contact local healthcare services for advice on clinical management and on the need for testing. Suspected cases with mild clinical symptoms may be advised to self-isolate at home or to limit social contacts for the duration of symptoms.
Confirmed (symptomatic)	Follow the recommendations from the healthcare service that made the diagnosis and adhere to national guidelines for dealing with confirmed cases during the mitigation phase.

Interventions in educational and child care settings

Schoolchildren and children attending day-care facilities are considered to be one of the main drivers of respiratory virus spread in the community. However, it is not yet known how much 2019-nCoV transmission will occur among children.

Proactive school and day care closures

Proactive closures refer to the early and planned closure of schools and day-care facilities to limit local virus transmission and spread at schools and into the community. School closures can be associated with significant costs to society and the economy.

During the containment phase, school closures are not justified. There are also no data to support informed decisions on proactive school closures in terms of their anticipated effectiveness in mitigating the 2019-nCoV epidemic, due to the unknown level of transmission of this virus among children.

Given that the influenza virus is circulating in the community during the ongoing influenza season across the EU/EEA, in order to reduce the burden on healthcare systems, proactive school closures may be considered if there is ongoing transmission of 2019-nCoV in an area. The decision concerning school closures and their optimal timing and duration would need to be carefully considered on a case-by-case basis. Bearing in mind the impact of school closure, the decision should weigh the expected impact of the epidemic against the adverse effects of such closures on the community.

Evidence originating from seasonal and pandemic influenza modelling studies have shown that proactive school closures before the peak of influenza virus activity have had a positive impact in reducing community transmission [19]. There will be a need to minimise contacts between children and the general population outside of schools to reduce opportunities for transmission. In the event of proactive school closures, plans for society in general and inter-sectorial collaboration should be considered to mitigate the significant secondary effects. Plans to help mitigate transmission within schools, while children continue to attend may include smaller school groups, physical distance of children in the class, promotion of other non-pharmaceutical countermeasures and outdoor classes. In the event of illness, voluntary isolation at home is advisable.

Reactive school and day-care closures

Reactive closures of schools may be necessary as a consequence of widespread virus transmission in the community and educational settings. Reactive school and day-care closures will probably not reduce the impact of the epidemic, but may be enforced, due to high absenteeism and operational issues, especially if the spread of 2019-nCoV coincides with the ongoing influenza season in an EU/EEA country. Communities therefore need to prepare for this eventuality and consider plans for society in general and the inter-sectorial collaboration needed to mitigate secondary effects. As with proactive school closures, the timing and duration of the closures will need to be carefully considered on a case-by-case basis.

[1] There is no evidence directly comparing the effectiveness and cost-effectiveness of self-isolation at home versus isolation in dedicated settings. In both instances, effectiveness is expected to depend on compliance with recommended behaviour and procedures.

Measures in the workplace

Based on studies on seasonal and pandemic influenza, measures at workplaces can be modestly effective in mitigating an epidemic and may be considered during the mitigation phase.

The 2019-nCoV can transmit from person-to-person at workplaces and in other public settings where people gather in contained spaces for long periods. Viral transmission may therefore be reduced by decreasing the frequency and length of social interactions and the physical contacts between individuals. However, there are still insufficient data available to assess the extent of 2019-nCoV transmission in these settings.

Workplace measures refer to a variety of actions to reduce the risk of transmission in the workplace and the community. These measures include: flexible working schedules/shifts for employees, the opportunity of distance working/teleworking, encouraging physical distancing measures within the workspace, increased use of email and teleconferences to reduce close contacts, reduced contact between employees and customers, reduced contact between employees, adoption of flexible leave policies and promoting the use of other personal protective countermeasures [7]. In the event of acute respiratory illness, self-isolation is advisable.

The selection of measures will depend on the company and the type of work and some may have significant economic consequences. Personal protective and environmental measures should be applied in combination at workplaces.

Workplace closures may be justified in exceptional circumstances, for example during pandemics of higher severity. Employees should be encouraged to self-isolate at home if experiencing respiratory symptoms.

Measures related to mass gatherings

Data originating from seasonal and pandemic influenza models indicate that during the mitigation phase, cancellations of mass gatherings before the peak of epidemics or pandemics may reduce virus transmission.

Mass gatherings increase the number of close contacts between people for long periods, sometimes in contained spaces. Therefore mass gatherings may lead to the introduction of the virus into the community hosting the event and/or facilitate virus transmission and spread.

Measures to reduce the risk posed by mass gatherings include interpersonal distancing measures to avoid crowding and organisational measures, such as cancellation, postponement or re-arrangement of an event. These measures include other non-pharmaceutical countermeasures, such as hand and respiratory hygiene.

During the containment phase, the cancellation of mass gatherings in the EU/EEA may be justified in exceptional cases (e.g. large conferences with a significant number of participants from a highly-affected area). The decision to cancel will need to be coordinated by the organiser and the public health and other national authorities on a case-by-case basis. ECDC's contact management technical report [23] can be used to assess the potential risk associated with visitors to the event and to plan further public health actions.

Due to the significant secondary effects of cancelling gatherings, the decision should be based on a risk assessment, taking into consideration the severity of the epidemic, the local epidemiological situation, the timing, duration, type of venue (indoor/outdoor), the size of the event and the area the attendees are coming from (affected or non-affected). Instead of cancellation, postponement or re-scheduling may be considered.

The extent of transmission during mass gatherings may justify the application of other measures (e.g. web-casting, education campaigns on good hygiene, enhanced environmental measures) and a risk assessment, depending on the type of event. Individuals in high-risk groups with a possibility of severe complications may choose to refrain from attending mass gatherings during an epidemic. Individuals that experience respiratory symptoms should self-isolate and seek medical advice.

Travel-related measures

International and domestic travel advice

Travel advice (or travel recommendations) refers to official government advice, which has legal and economic implications, that travellers should consider in order to minimise their risk of infection. Travel and trade restrictions are regulated under the International Health Regulations (IHR) part III. ECDC has published a template leaflet for travel advice relating to 2019-nCoV.

Travelling facilitates the spread of the 2019-nCoV from infected to uninfected areas. Although there is lack of evidence on the effectiveness of travel advice, close contact with people increases the risk of disease transmission and spread during travel [19]. Advising against travel during an epidemic aims to reduce the number of people who are infected during a trip to areas or countries where community transmission is ongoing; reduce the risk of importation from affected countries and reduce transmissions among travellers (e.g. in airport queues or on planes.)

In the context of travel recommendations, travellers should also be reminded to follow all the other appropriate preventive measures (environmental and personal protective measures) described in this document.
EU/EEA countries should review their procedures for informing travellers to and from affected areas, providing updates on the situation concerning 2019-nCoV at their points of entry, advising on personal protective measures and, for persons who develop 2019-nCoV-compatible symptoms after their return, providing information on how to seek medical advice and assistance. Member States may consider directing these cases to a particular call centre or healthcare facility, depending on their planning.

Screening at entry points

This measure refers to entry screening at national borders, airports, or other places where travellers from affected areas may enter another country. Screening is usually undertaken using devices such as non-contact infrared thermometers to assess whether individuals have symptoms of infection. However, measures may also include proactive sharing of information on the infection, advice on how to seek medical assistance should symptoms develop and on how to reduce the risk of infecting others. Overall these measures aim to reduce the number of infectious people entering a country, focusing on those coming from countries that are experiencing an epidemic [25,26].

Although some imported 2019-nCoV cases have been detected through entry screening procedures at destination airports, the available evidence from peer-reviewed publications and unpublished modelling work undertaken at ECDC suggests that border control measures are not effective in delaying or mitigating a pandemic. This is due to the low sensitivity of the systems used to detect mildly symptomatic infections and their inability to detect cases during the incubation period [19,27].

EU Healthy Gateways has published a document entitled 'Interim advice for preparedness and response to cases of the 2019-nCoV acute respiratory disease at points of entry in the European Union (EU)/EEA Member States' on the management of 2019-nCoV at points of entry [14].

Domestic travel restrictions

There is evidence that close contact of people increases transmission and spread of the virus during travel [1]. This measure refers to travel restrictions (e.g. airport and train station closures) implemented within a country or region to prevent or limit the geographical extent of virus transmission.

Broad domestic travel restrictions may have a small positive impact in delaying an epidemic only if they are implemented during its early stages [19]. Such restrictions may be effective in specific, isolated settings, but are unlikely to have a substantial impact on transmission in modern, mainly urban, societies within the EU. They are expected to have significant economical, legal and ethical implications. Therefore, such restrictions may be considered only during the containment phase of epidemics of high severity.

Border closures

This measure refers to the closure of international borders due to an epidemic which is regulated under the IHR. Border closures aim to reduce the risk of importation from countries with high transmission by implementing travel restrictions to or from an affected area.

Based on evidence from modelling studies, mainly relating to influenza pandemics, borders closures may delay the introduction of the virus into a country only if they are almost complete and when they are rapidly implemented during the early phases, which is feasible only in specific contexts (e.g. for small, isolated, island nations.) [19]. Available evidence therefore does not support recommending border closures which will cause significant secondary effects and societal and economic disruption in the EU.

The ECDC contact management technical report can be used to assess the potential risk and plan public health actions relating to travellers who have recently been in areas with presumed community transmission of 2019-nCoV, or elsewhere where they may have been exposed to a case of 2019-nCoV [23]. People with a travel history to areas with presumed community transmission of 2019-nCoV are classified as 'casual contacts', unless they meet any of the criteria for becoming a 'close contact' as a result of high-risk exposure either in the area with sustained community transmission or on board an aircraft. The management of these people would then differ depending on their classification.

Due to public health risks, border closures are regulated internationally under the IHR. Within the EU, freedom of movement may be limited for public health reasons within the limits of the EU Treaties and in accordance with Directive 2004/38/EC (art. 29).

Contributing ECDC experts (in alphabetical order)

Orlando Cenciarelli, Angeliki Melidou, Pasi Penttinen

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ALLEGATO N. 7

INTERIM GUIDANCE
FOR PREPAREDNESS AND RESPONSE TO CASES OF COVID-19 AT POINTS OF ENTRY IN THE EUROPEAN UNION (EU)/EEA MEMBER STATES (MS)

Interim advice for restarting cruise ship operations after lifting restrictive measures in response to the COVID-19 pandemic

Version 1

30 June 2020 ·

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1. Introduction

In January 2020 the EU HEALTHY GATEWAYS joint action switched from operating under the inter-epidemic mode to operating in an emergency mode, at the request of the European Commission's Directorate-General for Health and Food Safety (DG SANTE). As stated in the Grant Agreement, the objective of the emergency mode is to support coherent response of EU MS according to Decision No 1082/2013/EU and the implementation of temporary recommendations issued by the World Health Organization (WHO). Under this emergency mode, EU HEALTHY GATEWAYS is available to respond to any specific requests from DG SANTE or EU MS to provide technical support, advice or ad-hoc training at points of entry as needed.

An ad-hoc working group was established with members from the EU HEALTHY GATEWAYS joint action consortium. The names and affiliations of the working group members who prepared this document are listed at the end of the document. The working group produced the following guidance, considering the Communications issued by the Commission: a) "A European roadmap to lifting coronavirus containment measures"(1), b) "Towards a phased and coordinated approach for restoring freedom of movement and lifting internal border controls"(2), c) "COVID-19: EU Guidance for the progressive resumption of tourism services and for health protocols in hospitality establishments"(3), d) "COVID-19: Guidelines on the progressive restoration of transport services and connectivity"(4), e) "Tourism and transport in 2020 and beyond"(5). Moreover, current evidence, the temporary recommendations from the WHO (https://www.who.int/emergencies/diseases/novel-coronavirus-2019) (6-28) and the technical reports of the European Centre for Disease Prevention and Control (29-46) (ECDC) (https://www.ecdc.europa.eu/en/coronavirus/guidance-and-technical-reports) on COVID-19 (as of 30 June 2020) were taken into consideration. Lastly, this guidance has been prepared considering the evidence currently available about SARS-CoV-2 transmission (human-to-human transmission via respiratory droplets or contact), and also contains some proactive guidelines considering the lack of evidence to exclude other transmission modes (airborne or after touching contaminated environmental surfaces) (47). It should be noted that SARS-CoV-2 has been found in faecal samples without any further information on how this finding is implicated in the mode of transmission. The virus can be transmitted from both asymptomatic and symptomatic infected people, as well as from a person that is infected even two days before showing symptoms.

The guidance provided in this document is based on the current situation of the pandemic, and will be revised as needed after considering the epidemiological situation.

2. Purpose

Cruise ships are semi-closed environments providing shared facilities for many people on board the ship. Since the beginning of the COVID-19 epidemic, outbreaks have been reported on board cruise ships affecting both passengers and crew. Unprecedented challenges were faced by both the cruise ship industry, the public health authorities and all related sectors in dealing with cruise ship evacuations and management of outbreaks of COVID-19. As on-going transmission is currently reported in many countries worldwide and considering that several cases are asymptomatic, it is expected that both asymptomatic and symptomatic COVID-19 cases will most likely occur on board

cruise ships, as in similar touristic venues ashore. In addition to measures aimed at excluding infected persons from boarding a cruise ship, early detection and isolation of the first case, disembarkation, and quarantine of close contacts[2] in facilities ashore are all essential elements for effectively preventing future COVID-19 outbreaks on board cruise ships. Implementation of the International Health Regulations 2005 provisions by both the competent authorities at ports and the ship operators in regard to the availability of contingency plans at designated ports and on board ships and core capacities for health measures application, are imperative to prevent COVID-19 outbreaks, as well as passengers and crew members from being stuck at sea in the future.

The purpose of this document is to provide general guidance to EU/EEA MS and to cruise lines about options for measures on travel and tourism that could be applied after lifting the restrictive measures implemented in response to the COVID-19 pandemic.

Public health risks for COVID-19 transmission are a new reality globally. Similar to other holiday-makers, for cruise passengers, those exist not only while travelling on board cruise ships, but during the entire journey beginning from home to the cruise ship, including the sites of embarkation/ disembarkation, and at all destinations visited en route.

The current guidance provides a list of measures to reduce the risk for introduction of COVID-19 onto the ship, transmission during cruise ship voyage, embarkation and disembarkation, and further provides options for preparedness to respond to potential COVID-19 cases among travellers (passengers and crew).

A strategy for reducing the risks for COVID-19 among cruise ship passengers and crew should cover the entire process, beginning at the time of booking and extending until passengers and crew have returned to their homes. National policies for accepting incoming tourists to cross borders and to board cruise ships at the turnaround ports should also be considered in cruise line plans.

It is suggested that a gradual approach to restarting cruise ship operations should be considered. When resuming operations, cruise lines may initially consider using itineraries of a short duration (e.g. 3 to 7 days) and to perhaps limit the number of port visits in the itinerary. The willingness and capacity of countries included in the itinerary should be explored, and arrangements should be in place to accept possible or confirmed COVID-19 cases disembarking from cruise ships, as well as possible contacts and anyone else wishing to disembark.

[2] A contact of a COVID-19 case is any person who had contact with a COVID-19 case within a timeframe ranging from 48 hours before the onset of symptoms of the case to 14 days after the onset of symptoms. If the case had no symptoms, a contact person is defined as someone who had contact with the case within a timeframe ranging from 48 hours before the sample which led to confirmation was taken to 14 days after the sample was taken. Furthermore, a contact is defined as:
- a person who has stayed in the same cabin with a possible/confirmed COVID-19 case;
- a cabin steward who cleaned the cabin of a possible/confirmed COVID-19 case;
- a person who had face-to-face contact within two metres for more than 15 minutes, or physical contact, or unprotected direct contact with infectious secretions of a COVID-19 case or was in a closed environment with a possible/confirmed COVID-19 case for more than 15 minutes (for passengers this may include participating in common activities on board or ashore, participating in the same immediate travelling group, dining at the same table; for crew members this may include working together in close proximity in the same area of the ship or friends having face to face contact);
- a healthcare worker or other person providing care for a COVID-19 case, without recommended PPE or with a possible breach of PPE

3. Essential prerequisites

According to the International Health Regulations (IHR) 2005, designated ports must have the capacities to provide appropriate public health emergency response, by establishing and maintaining a public health emergency contingency plan. Interoperability of the port public health emergency contingency plan with the cruise ship contingency plan/outbreak management plan should be ensured.

For each cruise ship operating in the waters of an EU MS, a ship contingency plan/outbreak management plan for responding to a COVID-19 event should be prepared by the operating cruise line and submitted to the competent authority of at least one of the ports of call (preferably the home port or another port which can provide sufficient facilities in the cruise ship itinerary), in order to be reviewed and ensure interoperability with the port public health emergency contingency plan. In particular, before cruise lines resume operations, competent authorities in the EU MS and ship operators should ensure that the following conditions are met and have been fully addressed in this cruise ship contingency plan/outbreak management plan:

3.1. Monitoring of epidemiological situation, rules and restrictions worldwide

Before starting journeys and throughout cruise ship operations, it is essential that cruise lines monitor the epidemiological situation worldwide and at the cruise ship destinations, as well as at the places of origin of incoming passengers and crew (ECDC's COVID-19 Country Overview page: http://covid19-country-overviews.ecdc.europa.eu/#1_introduction). This will help assess the risk and adapt policies for screening and evaluating cruise ship passengers and crew members from countries with a high incidence of COVID-19, and furthermore to avoid destinations in countries with a high incidence of COVID-19. Cruise lines should have access to real-time information on the situation regarding borders, travel restrictions, travel advice, public health measures and safety measures at the destination ports (48). The European Commission has a dedicated website with an interactive map combining information from Member States and the tourism and travel industry, which is available at: https://ec.europa.eu/info/live-work-travel-eu/health/coronavirus-response/travel-and-transportation-during-coronavirus-pandemic_en (48).

3.2. Written contingency plan/outbreak management plan for COVID-19

Each cruise ship should have in place a written contingency plan/outbreak management plan for the prevention and control of possible cases of COVID-19 as described and in paragraph 5.1.2.

3.3. Arrangements for medical treatment and ambulance services

Before starting journeys, cruise ship operators should check and ensure with ports of call that, if needed, arrangements can be made for passengers and crew members to receive medical treatment (48) ashore (including possible air evacuation if needed). This should be clearly

described in both written contingency plans of cruise ships and at least of one of the ports of call (preferably the home port, with the possibility of also using other ports during the voyage).

3.4. Arrangements for repatriation

Before starting journeys, cruise ship operators should ensure with ports along the route that, if needed, repatriations and crew changes can be organised (48). It is suggested that cruise lines have in place repatriation plans for passengers and crew members, considering different scenarios for partial or complete ship evacuation in the event of a COVID-19 outbreak. Cruise ships' home ports (or at least one of the ports of call) should have airports operating international flights allowing repatriation of passengers and crew as necessary. Criteria for allowing repatriation and air travel based on exposure to COVID-19 cases and laboratory results of passengers and crew should also be considered in the planning process by the competent authorities at ports and the cruise ship operator. In addition, airline public health policies and public health policies of home countries should be considered in planning of repatriation processes.

3.5. Arrangements for quarantine of close contacts (exposed passengers or crew members with negative RT-PCR test results for SARS-CoV-2)

Before starting journeys, arrangements should be made between the cruise line and the local authorities of the home port (or at least one of the ports of call) for quarantine[3] facilities and procedures to be followed for close contacts. The facilities should be agreed upon and pre-specified (e.g. hotels), as well as the cost recovery for the health measures implementation. Residents of the country of disembarkation could be quarantined at home, according to local rules and procedures. Transport plans and hygiene protocols should be included in the contingency plan of the port, as well as the cruise ship contingency plan/outbreak management plan.

The procedures for management of close contacts can be found in the EU HEALTHY GATEWAYS Interim advice for ship operators for preparedness and response to the outbreak of COVID-19, available at: https://www.healthygateways.eu/Novel-coronavirus.

Close contacts that have been exposed to a confirmed case of COVID-19 should disembark as soon as possible, and be quarantined and monitored (self-monitored or otherwise according to the country procedures) for a period of 14 days in quarantine facilities ashore. Different scenarios with the expected numbers of persons to be quarantined should be considered and included in the planning and arrangements.

[3] Quarantine: the restriction of activities and/or separation from others of suspect persons who are not ill or of suspect baggage, containers, conveyances or goods in such a manner as to prevent the possible spread of infection or contamination.

3.6. Arrangements for isolation of asymptomatic/ pre-symptomatic travellers (passengers or crew members with positive RT-PCR test results for SARS-CoV-2)

Before starting journeys, arrangements should be made between the cruise line and the local authorities of the home port (or at least one of the ports of call) for isolation[4] procedures and facilities for asymptomatic/ pre-symptomatic infected travellers (persons with positive RT-PCR test results for SARS-CoV-2). The facilities should be pre-specified (e.g. hospitals, hotels), as should the cost recovery for the health measure implementation. Any person who has tested positive for SARS-CoV-2 should disembark as soon as possible, be isolated in a facility ashore and monitored until the ECDC criteria for discharge are met (49). Different scenarios with the expected number of persons to be isolated should be considered and included in the planning and arrangements made between the cruise line and the local authority.

3.7. Adequate testing capacity for SARS-CoV-2 infection on board or in cooperation with shore-based laboratories

Before starting journeys, arrangements should be made to ensure that cruise ships have adequate laboratory testing capacity for SARS-CoV-2 on board or through arrangements with shore side laboratories, to be used when a passenger or crew member is suspected of being infected (48). Arrangements should be made between the cruise line and laboratories ashore to ensure that RT-PCR tests can be organised and conducted ashore. Medical staff should be trained in sample collection and the field laboratory testing performance on board the cruise ship would need to be verified, with their routine use quality assured in accordance with national regulations and international professional standards for medical laboratory services. The ECDC guidelines for clinical specimens' collection and testing should be followed (50).

3.8. Training of crew about COVID-19

All persons intending to work on board (ship officers, crew members) as well as external contractors who interact with passengers or crew on board or ashore should complete training about COVID-19, as described in paragraph 5.1.1. For external contractors, this training may be conducted internally, or they may be supplied with written guidance describing the symptoms and requesting them to report symptoms, perform hand hygiene frequently, practise physical distancing and wear face masks.

Regular table-top exercises or drills should be conducted (e.g. before resuming operations and thereafter on a monthly basis) to test training of all staff on procedures related to prevention, surveillance and response to COVID-19, response time, department cooperation, procedures and equipment. A drill/table-top exercise normally includes participant instructions, scenario and evaluation tools.

[4] Isolation: separation of ill or contaminated persons or affected baggage, containers, conveyances, goods or postal parcels from others in such a manner as to prevent the spread of infection or contamination.

3.9. Commitment for immediate reporting to the next port of call of any possible case

An essential pre-requisite for resuming cruise ship operations is the immediate reporting of any possible case of infection, including possible[5] COVID-19 cases, to the next port of call by submitting the Maritime Declaration of Health (MDH). Early detection and immediate reporting are key factors for preventing outbreaks of COVID-19 on board ships. Before cruise ship operations begin, all involved parties (National Single Window, ship agents, port state control authorities, and health authorities at all levels) must ensure that written and clearly defined procedures are agreed upon and implemented for immediate reporting through the MDH of any possible case of infection, to the health authority at the next port of call.

Any previous practice/policies for reporting of Influenza-Like Illness (ILI) aggregated data at the end of voyages should be stopped. This approach should be replaced by actively looking for any person on board meeting the definition of a possible COVID-19 case, immediately reporting to the next port of call, and activating a ship contingency plan/outbreak management plan for management of the case and contacts.

It is suggested that EU MS competent authorities at the port level use the SHIPSAN Information System (SIS) to record health measures taken in response to possible or confirmed COVID-19 cases on board cruise ships. In parallel, the authorities at central level must always be informed by the authorities at a local level.

3.10. Estimation of the maximum number of passengers and crew on board cruise ships

Cruise ship operators should reduce the number of passengers and crew on board to ensure that measures related to physical distancing on board ships can be maintained, and that temporary isolation and quarantine of passengers and crew can take place individually in cabins.

When estimating the maximum number of passengers and crew on board except from ensuring physical distancing cruise ship operators are advised to ensure they are able to individually and temporarily isolate or quarantine (in a single cabin) possible COVID-19 cases/contacts:

- 5% of passengers and 5% of crew on board (until disembarkation and quarantine/isolation according to the contingency plan/outbreak management plan will take place), for ships where it will not be possible to disembark crew and passengers who need to be quarantined or isolated within 24 hours from detection of the first possible COVID-19 case, according to the ship contingency plan/outbreak management plan.

[5] Possible case: any person with at least one of the following symptoms: cough, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia. Additional less specific symptoms may include headache, chills, muscle pain, fatigue, vomiting and/or diarrhoea (source: Case definition for coronavirus disease 2019 (COVID-19), as of 29 May 2020. https://www.ecdc.europa.eu/en/covid-19/surveillance/case-definition).

- 1% of passengers and 1% of crew for ships where it will be possible to disembark crew and passengers who need to be quarantined or isolated within 24 hours from detection of the first possible COVID-19 case.

These proportions apply only to the initial phase of restarting operations, and will be re-considered and revised as appropriate depending on the epidemiological situation. Moreover, as far as possible, it is advised that the maximum number of crew members living in the same cabin should be two persons.

Consideration should be given to embarking a sufficient number of critical staff on board, in order to respect and maintain the Minimum Safe Manning requirements in case of a COVID-19 outbreak on board.

3.11. Focused inspection on COVID-19 prevention and control for resuming cruise ship voyages by EU HEALTHY GATEWAYS

EU HEALTHY GATEWAYS will support the competent health authorities in EU MS to perform focused inspections on board each cruise ship and ashore, and review procedures and written plans of each cruise ship and cruise line, to ensure that the below mentioned measures are met by both the cruise ship operator and the port authority. The EU HEALTHY GATEWAYS joint action will support the inspections by providing: a checklist based on the advice document; training of inspectors working at local authorities (through webinars); scheduling at an EU level to avoid duplication of inspections; and the EU database to record inspections. The inspections will be scheduled in cooperation with the companies and the competent authorities. It will not be necessary to conduct the inspection before starting the cruise ship operations. This could be arranged at any date and at any port, in agreement with the company and the inspectors.

4. Options for measures to prevent COVID-19 infectious passengers from starting holidays

4.1. Exclusion policy

Cruise lines should develop an exclusion policy with regard to COVID-19 and inform the travelling public about the policy through their travel agents, travel companies, cruise line operators and other businesses operating in the tourism sector. Harmonisation of this policy in the cruise industry, or consistent wording would facilitate acceptance and understanding by the public. Symptomatic and potentially exposed passengers should be discouraged from travelling, as is in place for air travel. In this respect, any person experiencing symptoms compatible with COVID-19, or if identified, anyone who has been in contact during the last 14 days with a confirmed case of COVID-19, or anyone who is tested positive for SARS-CoV-2 by RT-PCR would not be accepted on board cruise ships.

4.2. High risk groups

As long as the pandemic continues, special precautions may be applied to passengers and crew belonging to high risk groups. Passengers in high risk groups including people over 65 years of age or people of any age with underlying medical conditions (chronic diseases including cardiovascular disease, diabetes, respiratory diseases and immunocompromised individuals) should be advised to visit a doctor for pre-travel medical consultation to assess if they are fit to travel. Activities and services on board cruise ships could be organized according to age group, so that older individuals are separated from other age groups. Crew members in high risk groups could work in positions where there is little or no interaction with other individuals. Moreover, advanced respiratory protection may be used specifically by crew members belonging to vulnerable groups.

4.3. Exclusion policy information

Cruise line operators and tour operators should provide all relevant information about the exclusion policy, as well as any pre-requisites and country specific rules on their websites and electronic reservation systems. Ideally, it should be obligatory to read the information in order to complete the reservation. These materials should be available in the national language, English and, where needed, other languages based on the most common language profiles of the passengers travelling on the respective cruise ship. Moreover, relevant information could be shared directly with passengers via email, text message, mail, website or other means of communication.

5. Preparedness for responding to COVID-19 events on board cruise ships

5.1. General principles

5.1.1. Information, education and communication

Communication strategy and training plans

A communication strategy should be designed and implemented targeting the travelling public and the crew, defining the messages, the appropriate communication means and timing. The communication plan should cover processes related to ticketing, at pre-arrival, at the terminal, on board, as well as the procedures in case of a COVID-19 event.

Each cruise ship operator should design a training plan for their employees, with regular and on-going training. For example, a short webinar covering the topics listed in the following paragraph could be conducted.

Training content for crew

Cruise line operators should provide training and instructions to their crew regarding the recognition of the signs and symptoms compatible with COVID-19. Attention should be given to crew well-being.

Cruise line crew should be reminded of the procedures that should be followed when a passenger or a crew member displays signs and symptoms indicative of COVID-19. Each member of the crew should be trained in their role and responsibilities to implement measures as per the contingency plan/outbreak management plan. It is suggested that training takes place every 30 days.

Crew should also be instructed that if they develop symptoms compatible with COVID-19, they should not come to work. If symptoms develop while working, the crew should immediately self-isolate, wear appropriate personal protective equipment (PPE) and inform their designated supervisor/manager and medical crew immediately. Symptoms should be reported for both themselves and other crew members or passengers, if noted.

The cruise ship operator should also reassure crew that those who report symptoms and are unable to work will continue to be paid.

Cruise line operators should also provide training and instructions to crew regarding physical distancing measures, managing crowds, use of PPE, as well as protocols for cleaning and disinfection.

Crew who visit or stay in local areas at the various destinations should be informed in a timely manner about any national or local preventive measures or laws established by local or national public health authorities regarding COVID-19.

Medical crew on board should be trained in appropriate sample collection as well as storage and transport of the samples.

Information and communication to passengers

Cruise lines, travel companies and travel agencies should provide relevant pre-travel information about mitigating the risk of COVID-19 infection to their passengers and crew as a part of their travel information. In this context, information regarding the symptoms of COVID-19, the associated health risks especially for vulnerable groups, and the importance of preventive measures should be provided together with bookings. To support on board preventive measures, cruise lines may share details of recommended personal hygiene items to carry during their travel from home and during their time on board the ship (e.g. alcohol-based hand rub solution, PPE etc.).

Companies and travel agencies should inform travellers that they may be refused boarding if they have symptoms which are compatible with COVID-19, have had positive RT-PCR test results for SARS-CoV-2 or have been exposed to a COVID-19 confirmed case, as per the company's exclusion policy. The ticketing process should include information regarding the latest health and safety considerations, including those posed by COVID-19. During the ticketing process passengers should be informed about eligibility requirements.

Content of information and communication messages to crew and passengers

Before travelling, and, if applicable, regularly during the voyage, information should be provided to passengers and crew members (e.g. through electronic posters, recorded messages etc.). The information should include:

- boarding screening measures where applied;
- any requirements for COVID-19 testing prior to travel/embarkation;
- symptoms compatible with COVID-19, including sudden onset of at least one of the following: newly developed cough, fever, shortness of breath, sudden loss of taste/smell;
- likelihood of being denied boarding if they have developed symptoms or have been in contact during the last 14 days with a COVID-19 patient;
- advice on the risk of travelling for all individuals with chronic diseases (cardiovascular disease, diabetes, respiratory diseases) and immunocompromised individuals;
- recommendation for passengers over 65 years of age to consult with their medical care provider to obtain advice on their ability to travel;
- hygiene measures: hand washing with soap and water or hand hygiene with alcohol-based hand rub solution (containing at least 60% ethanol or 70% isopropanol), respiratory (coughing and sneezing) etiquette, disposal of used tissues, physical distancing (including the elimination of handshaking), use of face masks, avoiding touching the nose, eyes and mouth without previously washing hands (38) etc.;
- actions to take in case COVID-19 compatible symptoms develop;
- rules and health measures implemented on board cruise ships at the destination (e.g. physical distancing, use of face masks[6] (medical mask if available or non-medical "community" mask), disembarkation);
- the need to immediately report to cruise ship crew if they develop respiratory symptoms during travel, including means of reporting to crew (e.g. providing dedicated number or location to contact), crew will then inform the designated officer for the contingency plan/outbreak management plan implementation;
- the need to self-isolate and seek immediate medical care (including how to seek medical care) if developing fever, cough, difficulty breathing, sudden loss of taste/smell, and to share previous travel history with the health care provider.

[6] **Medical face mask (also known as surgical or procedure mask):** medical device covering the mouth, nose and chin ensuring a barrier that limits the transition of an infective agent between the hospital staff and the patient. They are used by healthcare workers to prevent large respiratory droplets and splashes from reaching the mouth and the nose of the wearer and help reduce and/or control at the source the spread of large respiratory droplets from the person wearing the face mask. Medical face mask comply with requirements defined in European Standard EN 14683:2014.
Non-medical face masks (or "community" masks): include various forms of self-made or commercial masks or face covers made of cloth, other textiles or other materials such as paper. They are not standardized and are not intended for use in healthcare settings or by healthcare professionals (European Centre for Disease Prevention and Control. Using face masks in the community. Stockholm: ECDC; 2020.) https://www.ecdc.europa.eu/sites/default/files/documents/COVID-19-use-face-masks-community.pdf

5.1.2. Contingency planning on board

Operators of cruise ships should have in place written contingency plan/outbreak management plans for the prevention and control of COVID-19 transmission on board the ship. For the implementation and execution of the written plan, one dedicated position/named individual/coordinator (e.g. a ship officer with alternate) or an outbreak management committee should be appointed, who will be designated in the written plan. It is good practice to have a dedicated Public Health Officer or medical person who will coordinate the execution of the company's infection prevention and control program. The contingency plan/outbreak management plan should include the following as applicable:

A. Preventive measures

- Physical distancing
- Personal hygiene rules
- PPE use
- Health monitoring of symptoms for cruise ship crew, and when applicable passengers through daily contactless temperature measurements and record keeping
- Procedures for responding to a -possible case (temporary isolation, arrangements for medical examination and laboratory testing)
- Standard Operating Procedures (SOP) for cleaning and disinfection covering all types of surfaces and materials, defining the disinfectants and the methods to be used
- SOP for laundry of linen and clothing
- SOP for cleaning and disinfection of body fluid spills in the environment
- Food safety management (e.g. dining and food service arrangements)
- Potable water safety management
- Recreational water safety management
- Ventilation of indoor areas
- Communication plan including reporting public health events to the competent authorities
- Data management of health and screening documents (e.g. Passenger/Crew Locator Forms, Maritime Declaration of Health)

B. Measures for response and management of a possible case COVID-19

- Isolation/quarantine plan of the possible case and their close contacts
- Collaboration with the national competent authorities for contact tracing, quarantine of contacts and isolation of cases
- Cleaning and disinfection procedures of contaminated spaces, objects and equipment (daily and final cleaning and disinfection)
- Communication strategy for informing the contacts of a confirmed COVID-19 case among the passengers/crew, retrospectively

5.1.3. Supplies and equipment

Adequate medical supplies and equipment should be available on board cruise ships to respond to a case or an outbreak. Adequate supplies of disinfectants and hand hygiene supplies should be carried on board cruise ships and also made available at the embarkation facilities. Supplies of PPE including gloves, long-sleeved impermeable gowns, goggles or face shields, medical face masks and filtering face-piece (FFP) respirators (prioritized for use during aerosol generating procedures) should also be carried on board.
An adequate supply of RT-PCR diagnostic panel test kits and equipment for collecting specimens to be tested at ashore facilities or on board should be available.
Adequate supplies of PPE for use by passengers and crew should also be available (please see Annex 1).

Further recommendations for the type of PPE required according to the job position and the setting can be found here: https://www.healthygateways.eu/Novel-coronavirus

Further details about supplies specific to COVID-19 can be found at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance (please see disease commodity package).

Additional medical crew should be considered to be available on board if required (e.g. based on passenger load/demographics etc.) in order to support surveillance, testing and case management.

6. Options for measures to prevent COVID-19 infectious travellers (passengers and crew) from boarding cruise ships

Pre-boarding screening aims at assessing the presence of symptoms and/or the exposure to COVID-19 cases of arriving travellers. Travellers identified as exposed to or potentially infected with COVID-19 will be quarantined or isolated and treated, respectively.

Pre-boarding screening can identify symptomatic travellers and those who truthfully declare their past exposure. Screening measures may not identify mild symptoms, asymptomatic, incubating travellers or those concealing symptoms (e.g. by using antipyretics) (52-54). Those travellers may not be detected and therefore may still board the ship.

Pre-boarding screening measures are generally conducted as a two-step process: primary screening and secondary screening (57, 58). Primary screening normally includes an initial assessment by personnel, who may not be public health or medically trained. This may include observing travellers for any signs of infectious disease and checking their body temperature. This can be supported by completion of a health screening questionnaire on the day of departure, asking about the presence of relevant symptoms and/or exposure to any COVID-19 cases. An example pre-boarding health declaration questionnaire is included in **Annex 2**. Where feasible, the use of electronic questionnaires is preferable to hard copy questionnaires, in order to help minimise crew contact. Requirements under the General

Data Protection Legislation (GDPR) must be followed for any personal data collected from individuals, in hard copy or electronically.

Travellers who have COVID-19 compatible signs or symptoms, or have been potentially exposed to SARS-CoV-2, should be referred to secondary screening. Secondary screening should be carried out by personnel with public health or medical training. It includes an in-depth interview, a focused medical (and if necessary laboratory) examination, and a second temperature measurement (56). Possible cases should not be allowed to embark, and a decision about allowing embarkation should be taken after considering the laboratory results, the symptoms and exposure. A standard policy should be implemented for denial of boarding to any exposed or symptomatic possible case among passengers and crew.

As an additional layer of measures applied, cruise lines could consider performing laboratory molecular testing for SARS-CoV-2 to all incoming passengers, ideally before boarding to start a cruise. When the laboratory results become available, and if positive results are found, then the contingency plan/outbreak management plan for management of cases available on board should be activated and implemented.

However, laboratory testing should not give a false sense of security, since it has several limitations: a) it cannot detect travellers with incubating infection, b) negative test results can be confounded by the stage of infection and the amount of viral RNA in clinical specimens collected, c) the diagnostic sensitivity is related with the characteristics of the RT-PCR or equivalent test, d) the sensitivity is related with quality/adequacy of specimen sampling and specimen transport and storage conditions before testing e) practicalities arising due to large number of specimens collected and the availability of laboratory tests.

Pooling of five samples from asymptomatic persons per pool before RNA extraction and RT-PCR amplification could be considered (according to guidance provided from international organizations) after proper validation in the laboratory. This can increase testing capacity with existing equipment. If there is a positive result from a pooled sample, then RT-PCR needs to be repeated for the individual samples within this pool, to identify the infected person(s), thus potentially substantially reducing the number of tests needed (51).

Testing passengers for antibodies as a condition for boarding ships is not supported by the current scientific knowledge. There are uncertainties about the immune response to SARS-CoV-2 (e.g. duration of human antibodies), as well as the performance of available specific antibody testing methods (laboratory based and point-of-care); therefore, antibody tests cannot be used at this point for inclusion or exclusion of passengers. However, passengers or crew members that have recently recovered from COVID-19 and the ECDC criteria for discharge have been met, may avoid measures such as RT-PCR test for SARS-CoV-2. ECDC guidance for discharge and ending isolation in the context of widespread community transmission of COVID-19 can be found here: https://www.ecdc.europa.eu/sites/default/files/documents/covid-19-guidance-discharge-and-ending-isolation-first%20update.pdf

7. Measures for preventing and limiting transmission of COVID-19 on board cruise ships

7.1. Health monitoring and laboratory testing

Routine on board health monitoring for all crew can help with early detection of symptomatic COVID-19 cases. Daily contactless temperature measurement and immediately reporting to supervisors of any mild or severe symptoms compatible with COVID-19 is of high importance. Any crew with a temperature at or above 38°C should immediately self-isolate, be provided with appropriate PPE and inform their designated supervisor/manager and medical crew. Salaries should continue to be paid in these cases. In the event of a possible COVID-19 case on board, the frequency of contactless temperature measurement of crew may be increased (e.g. to twice per day). However, body temperature measurement should be considered as an additional layer of measures applied, which has its own limitations: not all COVID-19 cases will have fever; incubating patients will not present with fever and fever can be masked with antipyretics.

Before resuming operations, cruise lines should perform laboratory molecular testing for SARS-CoV-2 to all crew members that are already on board the cruise ships, as well as to the incoming crew members (new employments or crew returning to the ship from home leave). If positive results are found, then the contingency plan/outbreak management plan for management of cases available on board should be activated and implemented, as described in the EU HEALTHY GATEWAYS advice "Advice for ship operators for preparedness and response to the outbreak of COVID-19" available here: https://www.healthygateways.eu/Novel-coronavirus.

In addition to this, periodic testing for SARS-CoV-2 can be conducted for all crew members at regular intervals (e.g. every two weeks) using the pool sample methods described in paragraph 6. This practice should be considered as an additional layer of measures applied, and should not create a false sense of security. Other control measures should be implemented in addition to laboratory testing (e.g. hand hygiene, physical distancing, PPE, cleaning and disinfection etc.).

Daily contactless temperature measures for all passengers may also be conducted to support early detection of symptomatic COVID-19 cases. Any passenger with a temperature at or above 38°C should immediately self-isolate, report symptoms to medical staff for further evaluation and be provided with appropriate PPE. In the event of a possible COVID-19 case on board, the frequency of contactless temperature measurement may be increased (e.g. to twice per day).

7.2. Protecting vulnerable groups

Efforts should be made to protect passengers and crew that belong to vulnerable groups (see paragraph 4.2). For example, crew belonging to vulnerable groups could be assigned responsibilities that have no direct interaction with passengers if this is feasible. If it is not feasible, advanced respiratory protection could be used for daily work activities.

Consideration should be given to passengers requiring assistance, and those with reduced mobility.

7.3. Limiting interaction

In order to limit interaction among passengers, among crew, and between crew and passengers, it may be possible to divide passengers and crew into cohorts with appropriate numbers of people. Each group could be given scheduled times for food service, embarking and disembarking and participating in some on board activities. If it is not possible to maintain separate cohorts/groups on board, cohorts/groups should be maintained for shore based activities. Interaction between each cohort should be avoided as much as possible. This will help in the management of any potential COVID-19 case and their contacts, and should help to limit the number of exposed persons, as well as tracing possible close contacts.

This is particularly important for crew members where physical distancing and interaction cannot be avoided in the work place.

In case cohorts cannot be guaranteed because of operational constraints, operators should implement ad hoc risk mitigation measures.

All crew designated to work with identified possible/confirmed COVID-19 cases should ideally have cabins in similar locations and dine together as a group, which minimises their traversal of the ship through common areas.

7.4. Physical distancing

Physical distancing of at least 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call) should be maintained at waiting areas and during boarding at transport stations, by adopting special markings and controlled entry measures. When physical distancing cannot be maintained, the use of face masks should be required.

Cruise ship crew could oversee the process and compliance with physical distancing measures. Operating procedures could be implemented to control the flow of passengers. Moreover, to decrease crowding and support physical distancing, outdoor spaces could be utilized for group events and procedures like muster drills could be staggered.

Special floor markings could be considered at all possible traveller congestion points, such as ticket offices, passenger services, bars, restaurants, shops, entertainment areas and shared toilets to ensure physical distance is maintained.

If appropriate physical distancing cannot be guaranteed, the use of protective transparent (e.g. glass or plastic) panels should be considered at places such as reception areas, at bars and restaurants.

Each port terminal should conduct an initial assessment and identify the areas where passengers and crew queue in order to implement measures ensuring physical distancing, including signage, audio announcements, floor markings, directional arrows for traveller flows and management by crew. This should include outdoor sunshades where travellers gather during the summer months to await boarding. During embarkation/disembarkation, several gangways should be used if possible to avoid crowding of passengers.

Where there are permanent non-moving seats either indoors or outdoors, there should be special markings on where a passenger is and is not allowed to sit, in order to maintain physical distance.

7.5. Personal hygiene measures

Good hand hygiene should be maintained, with frequent and thorough hand washing conducted by passengers and crew using soap and water. If hands are not visibly soiled, then alcohol-based hand rub solutions may be used (these should contain at least 60% ethanol or 70% isopropanol). The use of gloves should not replace good hand hygiene; gloves can provide a false sense of security.

Stations with alcohol-based hand rub solutions (containing at least 60% ethanol or 70% isopropanol) should be available at all entrances/gangways to the ship and in other areas such as crew/work areas, check-in areas, entertainment venues, casinos, bars and restaurants.

Cruise ship operators should provide information to passengers and cruise ship crew on hand hygiene related issues, and where necessary the appropriate facilities and equipment (59):

- Hand washing techniques (use of soap and water, rubbing hands for at least 20 seconds etc.)
- When hand washing is essential (frequent and meticulous hand washing must be performed and can be done for example before boarding and after disembarkation, after assisting an ill traveller or after contact with environmental surfaces they may have contaminated, prior to eating/drinking, after using restrooms etc.)
- When hand rubbing with an alcohol-based solution can be used, instead of hand washing and how this can be performed
- Respiratory etiquette during coughing and sneezing with disposable tissues or clothing
- Avoid touching with hands the eyes, nose or mouth
- Appropriate waste disposal
- Use of face masks (medical masks and non-medical ‘community’ masks)
- Avoiding close contact with people suffering from acute respiratory infections

7.6. Respiratory etiquette

Respiratory etiquette should be advised: the nose and mouth should be covered with disposable paper tissues when sneezing or coughing and then the tissue should be disposed

of immediately in a no touch bin, followed by meticulous hand hygiene using water and soap or an alcohol-based hand rub solution. It is important to have relevant supplies available in different areas around the cruise ship (e.g. tissues or paper towels and disposable gloves, no touch bins etc.). If disposable paper tissues are not available, coughing or sneezing into the elbow is recommended.

Information about respiratory etiquette should be provided to passengers via recorded communications, leaflets, infographics, electronic posters etc.

7.7. Preventing droplet transmission by the use of face masks

Face masks (medical masks, or if not available non-medical "community" masks) should be used at the terminal stations and on board cruise ships while indoors by cruise ship crew and passengers, as described in Annex 1**.** If the passenger does not arrive with their own face mask, face masks could be made available for passengers at the terminal. Additional PPE could be provided upon request on board the ship.

Information about the correct use of face masks should be provided to passengers via audio messages, leaflets, TV, infographics, websites or electronic posters etc. and at the terminal stations. Further advice for the use of face masks in the community is available in Annex 1 and from the following:

- ECDC: https://www.ecdc.europa.eu/en/publications-data/using-face-masks-community-reducing-covid-19-transmission
- WHO: https://www.who.int/publications/i/item/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak
- EU HEALTHY GATEWAYS joint action: https://www.healthygateways.eu/Novel-coronavirus

7.8. Adequate ventilation

The following recommendations are based on the ECDC guidance: "Heating, ventilation and air-conditioning systems in the context of COVID-19" (available here: https://www.ecdc.europa.eu/en/publications-data/heating-ventilation-air-conditioning-systems-covid-19) and on the REHVA guidance: "How to operate and use building services in order to prevent the spread of the coronavirus disease (COVID-19) virus (SARS-CoV-2) in workplaces".

The ventilation of all occupied spaces of the ship should operate continuously; the ventilation rate should be such as to provide as much outside air as possible. The use of timers or CO2 detectors that control the ventilation rate (demand-control ventilation) should be avoided. The minimum required air changes per hour for each space on the ship should be respected, and if possible, the air changes per hour should be further increased in order to reduce the risk of transmission. When possible, direct air flow should be diverted from

groups of passengers. Exhaust fans of bathrooms should be functional and operate continuously.

All of the air handling units (AHUs) should be switched from recirculation to 100% outside air by closing the recirculation dampers (via the Building Management System or manually) whenever possible. In case it is not possible to completely stop the recirculation of the air, the ship should explore improving air filtration as much as possible and using HEPA filters or Ultraviolet Germicidal Irradiation (UVGI).

In case any of the AHUs have heat recovery equipment (such as enthalpy wheels or plate heat exchangers), they should be inspected in order to ensure that leakages between the supply and the exhaust air is avoided.

All maintenance works related to the HVAC system, including changing the central outdoor air and extract air filters should be conducted according to the usual maintenance schedule. Duct cleaning should be avoided during the COVID-19 pandemic. Regular filter replacement and maintenance work shall be performed with common protective measures including adequate PPE. The medical facilities as well as the designated isolation spaces, should be connected to separate AHU's. If aerosol-generating procedures are performed in the medical facilities of the ship, then the area should be under negative pressure and achieve at least 10 air changes per hour. The return air from the medical facilities and the isolation spaces should be either be HEPA-filtered or exhausted to the outside.

7.9. Cleaning and disinfection

Enhanced cleaning and disinfection should be implemented in accordance with the EU HEALTHY GATEWAYS guidance on "Suggested procedures for cleaning and disinfection of ships during the COVID-19 pandemic (Version 2 – 20/04/2020)" and with an increased frequency in shared public areas/facilities (dining rooms, entertainment venues etc.) and for surfaces that are frequently touched by crew and passengers (e.g. handrails, elevator buttons). Other items that are frequently touched in common areas such as magazines/brochures, should be removed and information provided in alternative ways, including through announcements, additional signage or directly to mobile devices. Special protocols for cleaning and disinfection should be implemented after a possible or confirmed COVID-19 case has been identified on board. There should be adequate PPE for the cleaning crew available on board (e.g. gloves, face masks, gowns).

EU HEALTHY GATEWAYS guidance produced on suggested procedures for cleaning and disinfection of ships during the pandemic of COVID-19 (VERSION 2 - 20/04/2020) can be found here: https://www.healthygateways.eu/Portals/0/plcdocs/EU_HEALTHY_GATEWAYS_COVID-19_Cleaning_Disinfection_ships_21_4_2020_F.pdf?ver=2020-04-21-154731-953

This document includes advice about specifications for the training of cleaning crew and use of PPE, information about the cleaning equipment and materials to be used, and a summary

of antimicrobial agents effective against coronaviruses. It further outlines suggested procedures for cleaning and disinfection for different areas of the ships.

7.10. Special considerations for cabins

Between check out and check in, all cabins should be thoroughly cleaned and adequately ventilated (for at least one hour after cleaning and disinfection, and before the next passengers enter). It is advised that any item that cannot be cleaned and disinfected between cabin occupancies should be removed from the cabin (e.g. shared multiple use items such as menus, magazines and other objects that cannot be disinfected, coffee or tea packaging, mini bar products etc.).

Moreover, it is recommended to remove coffee machines, kettles, and all mini bar products from the cabin, unless these products are offered from a dispenser or can be disinfected between occupancies. It is preferable that the above devices or mini bar products be made available upon a passenger's request, so that their disinfection is ensured. The mini bar can be used as a refrigerator by passengers and should be disinfected after each check out.

A disposable cover should be placed on the TV and the air-conditioning remote controls to facilitate proper disinfection, unless these items can be easily and adequately cleaned and disinfected.

All types of surfaces and materials which may be touched, including textile surfaces (e.g. sofas, cushions, rugs, furniture, wallpaper) should be cleaned between occupancies.

During occupancy of a cabin by the same passenger/passengers, clothing and towels should be changed upon a passenger's request or routinely, but it is recommended that routine changes are made less frequent than normal (e.g. avoid changing of towels twice daily).

For natural ventilation of spaces, doors and windows (if applicable) should be opened daily.

It is recommended that individual alcohol-based hand rub solutions are placed in each cabin, which passengers can carry with them when moving outside of the cabin.

Specific advice for cleaning and disinfection of affected cabins is given in the EU HEALTHY GATEWAYS guidance on suggested procedures for cleaning and disinfection of ships during the pandemic of COVID-19 (VERSION 2 - 20/04/2020), available here: https://www.healthygateways.eu/Portals/0/plcdocs/EU_HEALTHY_GATEWAYS_COVID-19_Cleaning_Disinfection_ships_21_4_2020_F.pdf?ver=2020-04-21-154731-953.

7.11. Food safety rules

Food hygiene rules must be strictly followed as described in the "European Manual for Hygiene Standards and Communicable Disease Surveillance on passenger ships" available here: http://www.shipsan.eu/Home/EuropeanManual.aspx. The additional special provisions for preventing COVID-19 in food service areas and food operations should be

described in a written plan, and crew should be trained on the procedures based on their specific duties.

During food loading and storage, precautions such as physical distancing, use of PPE and hand hygiene should be applied. Crew should be reminded to avoid contact with potentially contaminated items/surfaces (e.g. packaging, invoices, products, equipment) and then touch their face, nose, mouth etc. Where necessary, external packaging may be disinfected or removed to avoid any potential contamination of environmental surfaces on board the ship food areas.

It is recommended that self-service food operations are avoided, and if this is not feasible, these facilities can operate only if additional specific hygiene management precautions are implemented as described in the following paragraphs. It is preferable that food is delivered by crew to passengers in closed packages or wrapped when it is delivered.

Disposable salt, pepper and other relevant containers should be used unless these containers can be disinfected between uses. Cutlery, plates, trays, napkins, soft drinks, straws etc. should be handed by crew to the passengers; the passengers should not collect these items themselves.

Physical distance should be maintained by travellers at all food service areas, including à la carte restaurants, specialty restaurants, service areas/breakfast areas, indoor and outdoor bars etc. It is recommended to limit food service provided in public areas of the ship. It is also recommended that only persons staying in the same cabin and/or persons from the same household or same travelling unit dine at the same table. A distance of 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call) between chairs of different tables should be maintained.

It is also recommended that crew and passengers are divided into cohorts (designated groups) and are served food at different times to limit interactions. In addition, limiting seating capacities in dining areas or using reservations to control passenger crowds could be implemented. The duration that restaurants are open could be extended to allow the rotating attendance of passengers in cohorts. The frequency of food service could also be increased to limit crowding and ensure physical distancing is maintained.

Special care should be taken to keep physical distances of 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call) among crew working in the galley or other food areas.

Any person entering/working in the galley should wash their hands and wear a face mask (see Annex 1). Only food handlers should be allowed to enter the galley. In case visitors (e.g. maintenance staff) must enter the galley, they should perform hand hygiene and be provided with the appropriate PPE (medical mask, hair covering, apron etc.), which will be available at the entrance of the galley.

Passengers should disinfect their hands (with an alcohol-based hand rub solution) upon entering and exiting the food service areas. Crew members could be present to monitor passenger compliance, especially during peak service times.

Towels, tablecloths and utensils should be washed even if they have not been used. Restaurant linen should always be changed between passengers.

If it is not possible to avoid buffet service (especially in the crew food service area), then the following precautions should be used:

- If hand washing stations are not available, at the entrance of the buffet area passengers and crew should be provided with an alcohol-based hand rub solution, and crew should ensure that passengers or crew disinfect their hands.
- The required physical distance should be maintained at all times in the service area.
- Suitable protection (e.g. sneeze guards/transparent dividers) should be installed between passengers/crew who will be served and the food, in order for the food to be completely protected from all sides (except the side where the crew member can serve food).
- Only the designated crew should be allowed to serve food. Crew serving food should wear appropriate PPE (face masks, disposable gloves) and should follow strict hygiene rules. Under no circumstances should crew or passengers who will be served food use any commonly shared utensils or other items. These should be removed from the service so that only a designated crew can distribute them.
- Self-service of dispensed items, plates, cutlery, utensils by passengers or crew should not be allowed. Food handlers should serve any dispensed items (for example water, coffee, juice etc.). Food handlers should wear appropriate PPE (face masks, disposable gloves) and follow strict hygiene rules.

Individual dining options, including room service, are recommended to provide food to passengers' cabins, in order to avoid overcrowding in restaurants and other food service areas. Room service crew should maintain appropriate physical distancing and use PPE. All normal food hygiene standards and precautions should be followed during the transport of food on board. Particular care should be taken with the safe collection and warewashing of room service items and utensils that have been used by passengers.

Crew providing individual dining options, including room service, should endeavour to maintain physical distance and use PPE. It is preferable that crew not enter the cabin, but rather deliver food to the door. Likewise, used plates and utensils should be collected by crew from outside the door.

7.12. Reducing face-to-face interactions

On-line bookings, orders and purchases should be encouraged, as well as the use of contactless cards for payments. Forms that need to be completed may be made available on-line for electronic completion.

Where face-to-face interaction without physical distancing between crew and passengers cannot be avoided, then protective screens or barriers may be used instead, where feasible.

7.13. Special considerations at reception

Reception staff should be able to provide passengers with details about the on board communicable disease controls and policies, as well as measures that have been taken to address possible cases of COVID-19 on board. Furthermore, reception staff should inform passengers how to get medical advice on board, and may also be able to provide PPE when requested.

It is recommended that written information, videos or electronic posters are made available to provide basic health instructions translated into English, and other languages based on the most common language(s) spoken by passengers and crew members on board. In addition where feasible, health advice may be provided through a mobile phone application.

Special equipment should be available (e.g. disposable gloves, face masks, and alcohol-based hand rub solutions) in the event that a possible case is identified, or if a passenger seeks help at reception.

Reception staff should be able to recognize the signs and symptoms of COVID-19 and report any issues directly to medical staff.

The use of a sneeze guard/transparent screen at the reception and other service and information points is recommended.

Alcohol-based hand rub solutions should be available for use by passengers at the reception desk. Crew should also monitor and encourage compliance with good hand hygiene in this area.

Regular cleaning and disinfection of reception desks/counters is recommended. Key cards should be disinfected (see paragraph 7.9).

In order to maintain appropriate physical distancing, the cruise ship should configure the reception desk, add deck markings at distances of at least 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call) where passengers will stand/proper distance marking in the waiting area, properly arrange furniture and manage the queue to reduce waiting times and avoid crowding. Overcrowding during check-in and check-out should be avoided and physical distances should be maintained.

It is recommended to use electronic alternatives for check-in and check-out (e.g. mobile concierge or use of electronic devices that can be disinfected after each use). The possibility of using an outdoor based check-in may also be considered. It is recommended that passenger expenses are paid electronically where possible (cash should be accepted only in exceptional cases) and that bills, invoices and receipts are sent electronically, as well.

7.14. Nursery and play areas for children

It is preferable to operate the outdoor children's play areas only or maximise their use. If this is not possible, the number of children using the indoor areas should be reduced to levels which help staff maintain physical distancing. The areas should be cleaned and disinfected according to the protocol on board and as required in the European Manual for Hygiene Standards and Communicable Disease Surveillance on Passenger Ships (available here: http://www.shipsan.eu/Home/EuropeanManual.aspx).

The number of children in the outdoor children's play areas/playgrounds may also be limited at one time. Consideration may be given to cohorting groups of children for the duration of the voyage. The child centre staff should monitor children for any signs or symptoms compatible with COVID-19, and the child exclusion policy should include possible COVID-19 cases. Child activities should be limited to those where physical distancing measures can be adhered to.

7.15. Entertainment venues

Overcrowding should be prevented in these areas (e.g. theatres) to maintain appropriate physical distancing, and the frequency of entertainment events may be increased to reduce numbers. The maximum allowable capacity of venues should be defined so that physical distancing of at least 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call) is maintained.

Alcohol-based hand rub solutions should be made available to passengers at the entrance of entertainment venues, with crew members monitoring compliance of hand hygiene. Additional alcohol-based hand rub solution equipment (e.g. dispensers) may also be provided in entertainment venues. It is recommended that facilities are cleaned and disinfected after each use.

7.16. Casinos

Physical distancing of least 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call) should be applied in all casino areas. Face masks should be worn as described in Annex 1.

Casino layouts should be reviewed so that physical distancing of least 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call) is respected and the maximum capacity of passengers allowed to enter the casino area should be determined to avoid overcrowding. At gaming tables, the number of players per table should also be estimated and defined to help ensure physical distancing measures are maintained.

Staff should supervise all casino areas to ensure that the capacity limits and all other measures are respected.

Floor markings should be placed in the entrance to the casino area to ensure physical distancing measures are respected in case lines or queues form, and if necessary seats may be removed or taken out of use from slot and electronic gaming machines, and from gaming tables where they are closer together than 1.5 metres.

Appropriate signage should be displayed at the entrance of the casino area informing passengers of the maximum capacity limits in the casino, advising them to apply regularly alcohol-based hand rub solutions, not to touch their face and to respect physical distancing measures.

Slot and electronic gaming machines and gaming tables should be positioned so as to maintain the physical distancing measures between passengers. Physical distancing at slot and electronic gaming machines and at gaming tables may be achieved by relocating the machines or tables, removing chairs, by disabling some slot and electronic gaming machines to create appropriate distances between them and by adding protective screens.

Staff should ensure that passengers do not congregate around slot and electronic gaming machines and around gaming tables.

It is recommended that food service is suspended in the casino area.

Alcohol-based hand rub solutions should be placed at the casino entrances and passengers should be advised to use them when entering and exiting the area as well as throughout the casino area.

Cleaning and disinfection should follow routine procedures, but with an increased frequency in the casino area.

Slot and electronic gaming machines should be cleaned and disinfected between use. This should be done by staff where possible. Additionally, passengers may be provided with disinfectant wipes or solutions to wipe frequently touched hand contact surfaces.

7.17. Hairdressers, beauty salons, gyms and shared facilities

This paragraph applies to the following services and facilities: massage services, beauty salons, hairdressers, gyms, saunas, Hammams and spas. Hygiene rules on those facilities must be strictly followed as described in the "European Manual for Hygiene Standards and Communicable Disease Surveillance on passenger ships" available here http://www.shipsan.eu/Home/EuropeanManual.aspx.

All public spaces (e.g. reception spa, hairdresser, near public toilets) should have hand rub alcohol-based solution for the passengers.

Where possible, the installation of sneeze guards/transparent screens or dividers at the spa's and the hairdressers' reception is recommended. Crew and passengers should wear appropriate PPE as described in Annex 1.

The operator should prevent overcrowding of the shared facilities.

Crew should advise passengers to immediately stop using shared facilities if they start to feel unwell and report this to staff working in these areas.

In the gym/fitness centre the following precautions are recommended:

- a record of any persons using the gym should be maintained,
- hand washing or disinfection using alcohol-based hand rubs should be required when entering and leaving the gym,
- machines should be positioned so as to ensure physical distancing of at least 2 metres,
- all touched surfaces of equipment should be disinfected after each use.

If classes are scheduled, it is advised to use same groups as far as possible and allow time for ventilation of the room (at least 30 minutes between classes).

7.18. Potable water

In case the potable water system of the cruise ship has not been operated as per the European Manual standards, or the cruise ship was in dry dock for more than a month, the steps described in "ESGLI Guidance for managing Legionella in building water systems during the COVID-19 pandemic" should be followed.

7.19. Sewage and grey water

The ship should have standard well-maintained plumbing, such as sealed bathroom drains, and backflow valves on sprayers and faucets to prevent aerosolized faecal matter from entering the plumbing or ventilation system.

Deck drains sanitary devices connected to the black water should always operate correctly and their water seals should not be left to dry out. In case the sanitary devices connected to them are not operated for long periods, water should be added to them in order for the water seal to work correctly. Water should be added regularly and dependent on the climate (e.g. every three weeks). The black water holding tanks should vent to the outside of the ships and ensure vented gases do not enter the ship through any air intakes. The vents of the black water holding tank should be located outside of the ship and away from air intake points of the ventilation system.

7.20. Recreational water facilities

The operation of indoor swimming pools is not recommended. However, the operation of indoor swimming pool venues that can be converted as outdoor after lifting/removing

walls/roofs facilities with natural ventilation could be allowed.

The showers for the outdoor recreational water facilities should be separated, in order to ensure bather's privacy and to facilitate the efficient showering of the bathers before they enter the pool. Bathers should be strongly advised to shower before entering the pools and there should be relevant signs informing them to do so. The cruise ship should provide all necessary items for showering (e.g. soap, shower gel, etc.). Additionally, the entrances of showers should be equipped with hand rub alcohol-based solutions.

Positioning of seats (sunbeds, chairs, poufs, lounge chairs, etc.) should be such that the distance between the edges of the seats of two passengers from different umbrellas or two passengers from different rooms is at least 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call) in any direction.

It is recommended that the seats, tables, small safes, call buttons for the waiters and menus, are made, or covered with, materials that are suitable for cleaning and disinfection.

After the change of passengers, the seats, tables, small safes, call buttons for the waiters and menus should be disinfected.

It is recommended that the facility provides towels or other washable coverings that can cover the entire surface of the seat and that the seats are disinfected after each use. It is recommended that the textile surfaces of the sunbeds are removed.

It is recommended that bathers are separated by a schedule or if possible, by different facilities for swimming and service for different groups.

The maximum allowable number of bathers at any time in the swimming pools should be one bather per 4 m^2 of water surface, regardless of the depth of the pool. Small hot tubs (with depth less than 1 m and tub volume less than 6 m^3) should be used only by bathers of the same household or by bathers staying in the same cabin at a time. For larger spa/hydrotherapy pools (with depth more than 1 m and tub volume more than 6 m^3), the maximum bather load is one person per 20 L per minute of recirculation flow (as per the European Manual); in any case, the total number of co-bathers should not exceed one bather per 4 m^2 of water surface.

7.21. Decorative fountains

The standards of the European Manual for Hygiene Standards and Communicable Diseases Surveillance on Passenger Ships (http://www.shipsan.eu/Home/EuropeanManual.aspx) for decorative fountains should be applied. In case the fountain remained out of operation for more than a month, the steps described in “ESGLI Guidance for managing Legionella in building water systems during the COVID-19 pandemic” should be followed.

7.22. Commercial stores inside the accommodation facility

Physical distancing, electronic payments, cleaning and disinfection should be followed in

commercial stores on board cruise ships. Clothes and other items should not be tried on (unless they can be laundered or disinfected afterwards) and shoppers should be encouraged not to handle items on display.

7.23. Other public spaces (indoor and outdoor)

Passengers should be advised to avoid the use of the elevators. It is recommended that the maximum capacity of elevators should be revised and reduced based on the physical distancing guidance. Moreover, it can be recommended that persons use face masks when using elevators as described in Annex 1. Hand rub alcohol-based solution should be placed at elevator entrances and crew should advise passengers to use upon entering and exiting the area. The elevators should be regularly cleaned and attention should be paid to frequently touched surfaces (buttons, knobs etc.).

To help ensure physical distancing, other precautions such as floor markings, placement of cones etc. may be implemented.

Other public spaces should be supplied with hand rub alcohol-based solution stations.

Furniture should be arranged in such a way to help avoid overcrowding in shared spaces (4 persons/10 m^2).

The use of business centres may be suspended or the operation changed to provide services to clients to avoid 'self-service'. Alternatively, access to Wi-Fi, printing services or other business centre services may be completed remotely using mobile phone apps etc.

Public toilet use should be managed to try to avoid any overcrowding. Passengers should be advised to flush the toilets with the lid closed to help prevent possible transmission through aerosolised faeces.

7.24. Interface between ship and shore-based personnel

To protect both crew and shore-based personnel who temporarily board the ship, precautions should be taken to minimize exposure risks to both. Where it is necessary for shore-based personnel to come on board, only the minimum number of personnel required should be allowed to embark. Furthermore, everyone who comes on board should observe hygiene protocols, screening measures and the use of appropriate PPE where necessary (see Annex 1).

7.25. Port visits, shore based activities and excursions

Alcohol-based hand rub solutions should be made available at gangway exits, and all persons who disembark and re-embark the cruise ship should be requested to use them. Upon re-boarding of the cruise ship health screening assessing the presence of COVID-19 symptoms or other relevant illnesses and contactless temperature measurements may be conducted.

Shore excursion/tour staff should be trained in the procedures to be followed if possible cases are identified. Symptomatic passengers should immediately wear a medical face mask and be transferred to an isolation or medical area for evaluation. All close contacts of potential cases should also be identified.

EU MS, cruise lines and terminal operators at destinations should ensure that appropriate measures are implemented to reduce overcrowding and maintain appropriate physical distancing when passengers disembark and re-board the ship.

Cruise lines should check that external excursion and tour providers offer similar precautions as on board, including physical distancing measures, use of PPE, and cleaning and disinfection protocols, while also following any local health regulations. Any external provider who interacts with passengers (such as tour guides) should follow cruise line protocols (e.g. for health screening). If tender boats or other means of transport are used to move passengers, physical distancing measures and protocols for frequent cleaning and disinfection should be implemented in line with on board procedures. Cleaning and disinfection of frequently touched surfaces of transport, including tender boats, should be conducted between each use.

While travelling in groups, it should be ensured that passenger groups maintain physical distance from other tour groups.

Cruise lines may consider making available appropriate PPE (e.g. face masks) to passengers on excursions and should refrain from organising visits to crowded areas during the pandemic.

8. Managing COVID-19 cases on board cruise ships and at terminal stations

8.1. Management of a possible case

Following a preliminary medical examination, if the ship's designated officer determines that there is a possible case of COVID-19 on board[7], the patient should be isolated in an isolation ward, cabin, room or quarters and infection control measures continued until they are disembarked and transferred to a hospital ashore. Cruise lines should designate single cabins to be used specifically for isolation of cases on board. The designated cabins should be located near the ship's medical facility for ease of accessibility by crew and if possible, have windows to promote appropriate air exchange. Contact with patients in isolation should be restricted to only those necessary, and crew in contact with the isolated patient (e.g. medical personnel) should wear appropriate PPE.

Further advice, including the definition of a possible case, management of possible cases and use of the Passenger/Crew Locator Forms (PLFs) can be found in the EU HEALTHY GATEWAYS Interim advice for ship operators for preparedness and response to the outbreak of COVID-19, available at: https://www.healthygateways.eu/Novel-coronavirus

Surveillance for influenza like illness (ILI) should integrate COVID-19 surveillance, as symptoms compatible with COVID-19 include those for ILI (as currently cruise ships will be implementing measures for early detection of COVID-19 possible cases)[8].

[7] ECDC, Case definition for coronavirus disease 2019 (COVID-19), as of 29 May 2020 https://www.ecdc.europa.eu/en/covid-19/surveillance/case-definition

[8] https://www.ecdc.europa.eu/en/publications-data/strategies-surveillance-covid-19

Depending on the assessment of the COVID-19 event on board, it may be necessary to shorten or terminate the cruise as described in the EU HEALTHY GATEWAYS "Advice for ship operators for preparedness and response to the outbreak of COVID-19" document, which can be downloaded here: https://www.healthygateways.eu/Portals/0/plcdocs/EU_HEALTHY_GATEWAYS_COVID-19_MARITIME_20_2_2020_FINAL.pdf?ver=2020-02-21-123842-480

When a possible case of COVID-19 is detected, laboratory testing should be performed according to the instructions provided by ECDC (https://www.ecdc.europa.eu/en/novel-coronavirus/laboratory-support).

Negative results do not rule out the possibility of a COVID-19 virus infection. A number of factors could lead to a negative result in an infected individual, including:

• Poor quality of the specimen, containing little patient material (as a control, consider determining whether there is adequate human DNA in the sample by including a human target in the PCR testing);
• When the specimen was collected late or very early in the infection;
• If the specimen was not handled or shipped appropriately;
• Technical reasons inherent in the test, e.g. virus mutation or PCR inhibition.

If a negative result is obtained from a patient with a high index of suspicion for COVID-19 virus infection, particularly when only upper respiratory tract specimens were collected, additional specimens, including from the lower respiratory tract if possible (hospitalized in ashore facilities), should be collected and tested.

Each Nucleic-acid Amplification Test (NAAT) run should include both external and internal controls, and laboratories are encouraged to participate in external quality assessment schemes when they become available. It is also recommended to laboratories that order their own primers and probes to perform entry testing/validation on functionality and potential contaminants.

When it has been confirmed that the specimen collection and the testing for COVID-19 has been performed correctly, and as soon as the repeated results are negative for COVID-19 according to the criteria by ECDC, then the case should be tested for influenza virus by means of viral detection through PCR techniques, not relying on rapid diagnostic tests. In the patient is positive for influenza, then the "Guidelines for the prevention and control of influenza-like illness on passenger ship" of the European Manual should be followed for the case management.

8.2. Management of contacts

Cruise lines should designate single cabins to be used specifically for quarantine of close contacts on board. Children should be quarantined in the cabin with one of their parents and similar consideration given to supporting those with special needs. The designated cabins should be located near the ship's medical facility for ease of accessibility by crew, and if possible have windows to promote appropriate air exchange.

Management of contacts should be in accordance with the national policies of the port of disembarkation and as detailed in the contingency plan/outbreak management plans of the cruise ship and the port. Advice for management of contacts and use of the Passenger/Crew Locator Forms (PLFs) in **Annex 3** can be found in the EU HEALTHY GATEWAYS Interim advice for ship operators for preparedness and response to the outbreak of COVID-19, available at: https://www.healthygateways.eu/Novel-coronavirus

8.3. Embarkation/disembarkation

As soon as a possible case is detected on board and for the duration of the journey until arrival at the final destination, a risk assessment of the event should be conducted (in cooperation of the port health authority and the ship officers) in order to decide if new passengers should not be allowed to board at intermediate destinations.

The competent authorities at the next port or destination will provide advice on the management of the possible case and their contacts.

8.4. Reporting

In accordance with the International Health Regulations (2005), the officer in charge of the ship must immediately inform the competent authority at the next port of call about any possible case of COVID-19[21].

For ships on international voyage, the MDH must be completed and sent to the competent authority in accordance with the local requirements at the port of call.

Ship operators must facilitate application of the health measures and provide all relevant public health information requested by the competent authority at the port. The officer in charge of the ship should immediately contact the competent authority at the next port of call regarding the possible case, to determine if the necessary capacity for transportation, isolation, laboratory diagnosis and care of the possible case/cluster of cases of COVID-19 is available at the port. The ship may be asked to proceed to another port in close proximity if this capacity is not available, or if warranted by the medical status of the possible case/cluster of cases of COVID-19. It is important that all arrangements are conducted as quickly as is feasible to minimise the stay of symptomatic possible case/cases on board the ship.

9. Responding to COVID-19 events retrospectively

Contact tracing is one of the most important public health activities in the response to the COVID-19 pandemic, and is extremely important in this adjustment phase.[9,10] It is

[9] ECDC, Contact tracing: Public health management of persons, including healthcare workers, having had contact with COVID-19 cases in the European Union - second update at: https://www.ecdc.europa.eu/en/covid-19-contact-tracing-public-health-management
[10] ECDC, Mobile applications in support of contact tracing for COVID-19 - A guidance for EU EEA Member States at: https://www.ecdc.europa.eu/en/publications-data/covid-19-mobile-applications-support-contact-tracing

recommended to use Passenger/Crew Locator Forms to ensure that contact information of passengers and crew is available, in order to facilitate contact tracing if a case of COVID-19 is detected. Contact tracing will be conducted as instructed by the competent public health authority.

Passenger/Crew Locator Forms could be disseminated before boarding or during boarding and collected by cruise ship crew prior to disembarkation. Electronic completion of Passenger/Crew Locator Forms before boarding could be used in the future. If the company collects and keeps all information exactly as it is described in **Annex 3** "Passenger/Crew Locator Forms (PLFs)", then it will not be necessary to complete the PLF, provided that this information can be extracted and sent to the competent health authority in accordance with local rules.

Annex 3 provides details of the Passenger/Crew Locator Forms for cruise ships, which are also available from the EU HEALTHY GATEWAYS joint action website here: https://www.healthygateways.eu/Translated-Passenger-Locator-Forms.

It is suggested that the Passenger/Crew Locator Forms for ships also be completed by all crew members who disembark and are on rotation.

Other means of contact tracing to identify and inform passengers of possible exposure may be employed by cruise lines, such as investigations by response teams, analysis of ship's CCTV, use of mobile contact tracing applications and analysis of passenger key card usage.

10. Considerations for cruise terminals

10.1. Physical distancing

Physical distancing of at least 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call) should be maintained in combination with the use of face masks in all internal and external areas of the terminal.

Competent authorities in EUMS and/or terminal operators may consider only allowing passengers, crew and other shore-based/terminal personnel, workers and contractors to enter indoor cruise facilities, in order to avoid overcrowding and maintain the physical distancing measures.

The use of floor markers to ensure spacing, arrows to indicate directional flow, signage and audio announcements for travellers and optimizing layouts so as to restrict number of indoor cruise terminal users should be considered.

Dedicated lanes or separation of different user flows and dividing of terminals into designated zones (e.g. arrival, screening, post-screening) through which travellers must pass through for arrival, any screening/testing and document processing (before being cleared for boarding and embarkation) may be considered.

Check-in, disembarkation, luggage handling, passenger queuing (inside and outside the terminal), and provision handling should be adjusted to reduce overcrowding and maintain

physical distancing. Work and break schedules of crew who work in the terminal should be reviewed and adjusted to avoid overlap of crew.

For the protection of cruise terminal staff and ship crew, the use of protective glass or plastic panels and provisions of appropriate PPE should be considered at locations where physical distancing cannot be maintained.

Cruise terminal operators should consider removing facilities at the terminal that encourage crowding e.g. tables, benches etc. Where there are permanent, non-moving seats either indoors or outdoors, there should be a special marking on where a passenger is and is not allowed to sit in order to maintain physical distance. When conditions allow, terminal users should be encouraged to use outdoor spaces. Health promotion information material should be prominently displayed and provided to incoming and outgoing passengers.

In public toilets, the minimum number of users should be managed to maintain physical distancing of 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call) between users (or otherwise in accordance with national policy).

Digital methods should be used for as many processes as possible at the terminal, such as on-line purchasing, issuing of boarding passes, automatic passport and ID scanners, in order to help reduce the time that passengers spend in the terminal and to avoid congestion.

Terminal operators may consider limiting the number of taxis, coaches, buses present on the terminal to control/limit overcrowding in waiting areas.

Where physical distancing is more challenging to maintain, additional safeguards and measures to ensure equivalent levels of protection should be used.

Designated terminal personnel should oversee the process and compliance with the physical distancing measures.

10.2. Preventing droplet transmission by the use of face masks

Competent authorities should consider advising passengers and other users of the cruise terminal, who are not ill or showing symptoms compatible with COVID-19 to wear a face mask, taking into consideration their national epidemiological aspects and the international spread of disease. In countries that have chosen to implement face mask or PPE policies, this should be communicated at the time of the ticket booking. Adequate PPE should be provided and distributed to all terminal staff, along with instructions for their proper use.

10.3. Respiratory etiquette

Good respiratory etiquette should be encouraged in terminals: the nose and mouth should be covered with disposable paper tissue when sneezing or coughing and then the tissue should be disposed of immediately in a no touch bin, and meticulous hand hygiene should be performed by using water and soap or an alcohol-based hand rub solution. It is important

to have relevant supplies available in different areas around the terminal (e.g. disposable tissues or paper towels and disposable gloves, no touch bins etc.). If disposable paper tissues are not available, coughing or sneezing into the elbow is recommended. Information about good respiratory etiquette should be provided to users of the terminal via announcements, TV, screens, leaflets, infographics, electronic posters etc.

10.4. Hand hygiene

Good hand hygiene should be encouraged by all terminal users. This may be achieved by hand washing using soap and water, or where hands are not visibly soiled, an alternative alcohol-based hand rub solution may be used. The use of gloves does not replace hand hygiene. Stations with alcohol-based hand-rub solutions (containing at least 60% ethanol or 70% isopropanol) should be available at all entrances of the terminal and other areas such as toilets, counters, terminal zones and at embarkation etc. Designated terminal personnel may oversee the process and help encourage compliance with hand hygiene requirements.

10.5. Cleaning and disinfection

Cleaning and disinfection should take place in accordance with routine procedures and with an increased frequency for surfaces that are frequently touched by terminal staff and users. Cleaning of and disinfection of the terminal should be conducted before and after each embarkation. Cleaning and disinfection should follow the same protocols to those used on board cruise ships as described in paragraph 7.9. Special protocols for cleaning and disinfection should be available and implemented after a possible or confirmed case has been identified, either at the terminal or on board a ship, if they used the terminal facilities.

10.6. Ventilation

Indoor areas at cruise terminals should be adequately ventilated. Natural ventilation is preferable where possible. In case of mechanical ventilation, the number of air exchanges per hour should be maximised together with the fresh air supply as much as possible. However, draughts should be avoided since these could create a risk of spreading any aerosolized droplets further.

10.7. Health monitoring of terminal staff

Terminal staff should practice frequent hand hygiene and wear appropriate PPE based on their specific work duties. It is recommended that terminal staff follow the same screening protocols as travellers for entry to the terminal. Laboratory testing for COVID-19 of terminal workers could be conducted on a regular basis.

10.8. Management of possible cases and their contacts at the cruise terminal

Once a possible case is detected a contingency plan/outbreak management plan should be activated.

The possible case should be asked to wear a medical face mask as soon as they are identified.

An appropriate isolation space/room should be designated for isolating possible cases of COVID-19. The isolation room should be equipped with appropriate supplies (medical face mask, tissues and appropriate waste disposal bins etc.). The door should be kept closed at all times and entrance should be restricted only to personnel trained for responding to possible cases of COVID-19.

As soon as a possible case is detected, the public health competent authorities should be informed immediately in order to conduct any preliminary interviews and to manage the possible case and close contacts in accordance with the national protocols.

10.9. Baggage handling

Baggage handlers should perform frequent hand hygiene. Gloves are not required unless used for protection against mechanical hazards. Disinfection of luggage and especially the hand contact parts may be considered before loading luggage on board.

Annexes

Annex 1: Overview of suggested personal protective equipment (PPE) on cruise ships

This annex provides an overview of recommended PPE to be used on board cruise ships in the context of lifting restrictive measures in response to the COVID-19 pandemic. The following tables list recommended PPE for crew members and passengers based on specific settings, situations and levels of interaction with others on board.

Cruise ships are workplace settings for crew members employed on board. Specific measures can be implemented in these settings in the context of COVID-19 as operations gradually restart, to prevent and minimize the risk of virus transmission and protect the health of both crew members and passengers. Personal protective measures and environmental measures should be implemented together in workplaces, in this case on board cruise ships (60).

Examples of measures that can be applied in all workplace settings include (61, 62):

- Encouragement of frequent and proper hand hygiene by all crew members and passengers
- Promotion of proper respiratory etiquette and ensuring medical face masks are available in case a crew member or passenger develops symptoms compatible with COVID-19
- For use of face masks to prevent droplet transmission, providing information on proper face mask use (e.g. how to wear, remove and dispose of)
- Encouragement of physical distancing of at least 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call). If physical distancing cannot be maintained, additional mitigation measures can be implemented to limit contact/interaction between crew members and between crew members and passengers (e.g. sneeze guards/transparent dividers or staggering of workspaces to provide separation)
- Ensuring cleaning and disinfection of surfaces and objects according to routine procedures and with increased frequency in the areas and on surfaces that are touched frequently by crew members and passengers
- Education, training and risk communication on personal protective measures and environmental measures
- Ensuring appropriate ventilation of closed environments

General considerations for use of face masks (including non-medical "community" masks)

- It is important that face masks fit against the face snugly but comfortably, entirely covering an individual's face from their nose to their chin.
- Non-medical cloth coverings should include several layers of fabric while allowing the wearer to breathe comfortably without restriction.
- Proper wearing (donning) and removing (doffing) procedures/best practices for face masks should be followed. Face masks (including cloth coverings) should be secured with ties or ear loops. Face masks should be removed from behind and the wearer should be careful to avoid touching the mask (front side) or their mouth/nose/eyes.
- Perform frequent hand hygiene with an alcohol-based rub or soap and water, including before wearing and after removing a face mask. Hand hygiene must be performed immediately after removing the mask and disposing of it.

- A face mask should be changed whenever it gets moist.
- Ensure safe disposal of disposable face masks (e.g. in a closed bin or in a closed bag) and perform hand hygiene immediately after disposal.
- Reusable face masks should be laundered after each use, as soon as possible, using common detergent at 60°C. It is important that laundering face masks does not change the fit or damage the face mask.
- Maintain a distance of at least 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call) from others at all times as far as practicable.
- Face masks should not be worn by children under the age of 2 years, individuals with breathing difficulties or those who are unconscious or unable to remove a mask on their own.

Advice for the use of face masks by passengers and crew

In situations where no interaction between crew members will occur, there is no need for the use of a face mask. Specific situations as outlined in **Table 1** include when crew members are working on their own or at times when they are alone in their cabin. In these situations, crew members should still observe proper and frequent hand hygiene (e.g. washing hands with soap and water or with an alcohol-based hand rub solution).

Table 1: Crew - no interaction

WHO	WHEN	WHAT
Crew members	• Working independently (no contact with other crew members) • Located in their own individual cabin on board	**No PPE recommended** **Perform frequent hand hygiene**

When there is interaction among crew members (settings or situations where crew members work together), there is no need for the use of a face mask as long as physical distancing of at least 1.5 metres (or otherwise as per national/local health authority requirements of the home port or the port of call) between crew members can be maintained at all times.

In the event that physical distancing measures between crew members cannot be maintained, crew are recommended to use a face mask (please see **Table 2** below).

Crew members should also observe proper and frequent hand hygiene (e.g. washing hands with soap and water or with an alcohol-based hand rub solution).

Table 2: Crew - interaction with other crew[11]

WHO	WHEN	WHAT
Crew members	• Working with other crew members **AND** • Physical distance of 1.5 meters[12] maintained **AND** • Working in areas in which appropriate ventilation can be maintained (See section 7.8)	**No PPE recommended** **Perform frequent hand hygiene**

[11] This table does not refer to crew working in the galley. Any person entering/working in the galley should wash hands and wear a face mask.

[12] or otherwise as per national/local health authority requirements of the home port or the port of call

	• Working with other crew members **BUT** • Physical distance of 1.5 metres **cannot** be maintained	**Medical face mask**[13] If not available, a non-medical "community" face mask[14]	 ©ECDC **OR** 
		Perform frequent hand hygiene	

Where passengers may interact with one another but appropriate physical distancing can be maintained (at least 1.5 metres), there is no need for the use of PPE. However, as seen in **Table 3** proper and frequent hand hygiene should be performed.

**For passengers who are travelling together such as a family unit or travelling unit (e.g. cohabitants, friends etc.), no PPE are required when they are interacting, and physical distancing between them is not required.

When passengers are interacting with others outside of their family unit or travelling unit and a physical distance of 1.5 metres cannot be maintained, it is suggested that passengers use a face mask.

At all times frequent and proper hand hygiene should be observed.

Table 3: Passengers – interaction with other passengers

WHO	WHEN	WHAT	
Passengers	• Interacting with other passengers **AND** • Physical distance of 1.5 metres maintained	**No PPE recommended**	
		Perform frequent hand hygiene	
	• Interacting with other passengers **BUT** • Physical distance of 1.5 metres **cannot** be maintained**	**Medical face mask** If not available, a non-medical "community" face mask	 ©ECDC **OR** 
		Perform frequent hand hygiene	

[13] **Medical face mask (also known as surgical or procedure mask):** medical device covering the mouth, nose and chin ensuring a barrier that limits the transition of an infective agent between the hospital staff and the patient. They are used by healthcare workers to prevent large respiratory droplets and splashes from reaching the mouth and the nose of the wearer and help reduce and/or control at the source the spread of large respiratory droplets from the person wearing the face mask. Medical face mask comply with requirements defined in European Standard EN 14683:2014.

[14] **Non-medical face masks (or "community" masks):** include various forms of self-made or commercial masks or face covers made of cloth, other textiles or other materials such as paper. They are not standardized and are not intended for use in healthcare settings or by healthcare professionals (European Centre for Disease Prevention and Control. Using face masks in the community. Stockholm: ECDC; 2020.) https://www.ecdc.europa.eu/sites/default/files/documents/COVID-19-use-face-masks-community.pdf

In settings where crew members are in contact with passengers on board, a face mask should be used by crew members. As listed in **Table 4** below, examples of contact between crew members and passengers include food handlers and crew members cleaning cabins on board.

Table 4: Crew members - interaction with passengers

WHO	WHEN	WHAT	

Crew members	• Crew members are in contact/interacting with passengers including when:
	  • Handling food
	  • Cleaning cabins
		Medical face mask
		If not available, a non-medical "community" face mask
			
			©ECDC
			OR
			 

		Perform frequent hand hygiene	

There are certain settings outlined in **Table 5** where the use of face masks is strongly recommended for both crew members and passengers.

Face masks should be used in any situation where contact or interaction with others will occur and maintaining a physical distance of 1.5 metres is challenging or not possible. On board cruise ships, such settings include walking through or passing others in narrow corridors, taking an elevator etc. Furthermore, a face mask should be used when visiting a medical facility on board for any purpose. In the event that a possible COVID-19 case is being cared for in the medical facility on board, entering the isolation area requires the use of a medical face mask and other appropriate PPE (e.g. gloves, goggles or face shield and long-sleeved impermeable gown) (63). Only crew providing care should be admitted to the isolation area.

Face masks should also be used in areas outside the cruise ship where a high density of people may congregate and physical distancing is challenging, including during embarkation at the terminal, during transfers on buses (46), on board lifeboats and when walking in the corridors in the various decks.

As in all cases passengers and crew members should observe frequent and proper hand hygiene in these settings.

Table 5: Settings where face mask use is strongly recommended

WHO	WHEN	WHAT	

Crew members and Passengers	• Any area where interaction with others occurs and maintaining physical distancing measures (1.5 metres) **cannot** be guaranteed
	
	AND
	
	• Specific settings including:
	  • During embarkation at the terminal
	  • On buses during transport
	  • Walking/passing in narrow corridors on board
	  • In elevators on board
	  • Visiting the medical facility on board
	  • On board lifeboats
		Medical face mask	
			©ECDC

		Perform frequent hand hygiene	

Annex 2: Pre-boarding health declaration questionnaire

(The questionnaire is to be completed by all adults before embarkation)

NAME OF VESSEL	CRUISE LINE	DATE AND TIME OF ITINERARY	PORT OF DISEMBARKATION
Contact telephone number for the next 14 days after disembarkation:			
First Name as shown in the Identification Card/Passport:	**Surname as shown in the Identification Card/Passport:**	**Father's name:**	**CABIN NUMBER:**
First Name of all children travelling with you who are under 18 years old:	**Surname of all children travelling with you who are under 18 years old:**	**Father's name:**	**CABIN NUMBER:**

Questions

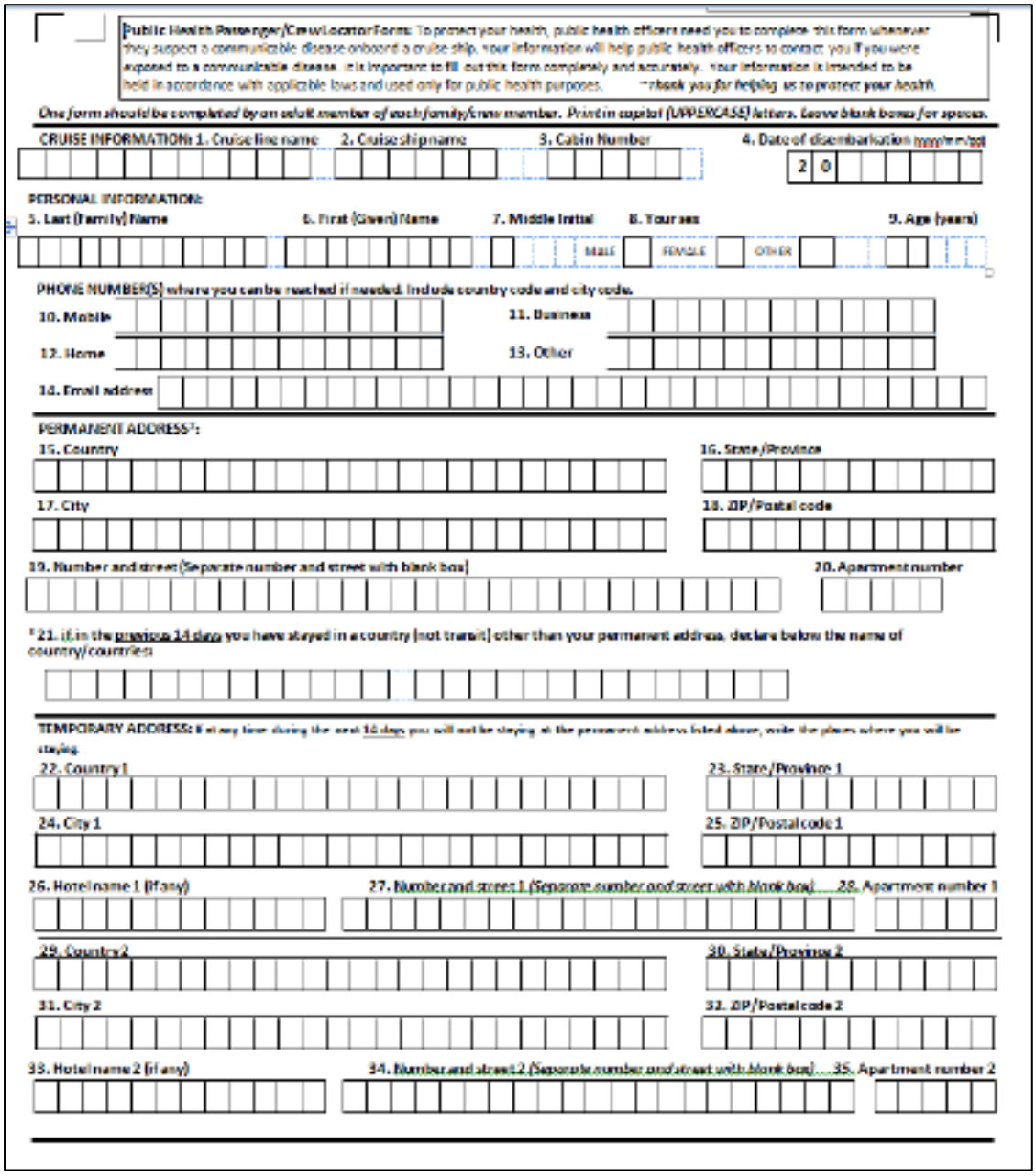
Within the past 14 days	**YES**	**NO**
1. Have you or has any person listed above, presented sudden onset of symptoms of fever or cough or difficulty in breathing?		
2. Have you, or has any person listed above, had close contact with anyone diagnosed as having coronavirus COVID-19?		
3. Have you, or has any person listed above, provided care for someone with COVID-19 or worked with a health care worker infected with COVID-19?		
4. Have you, or has any person listed above, visited or stayed in close proximity to anyone with COVID-19?		
5. Have you, or has any person listed above, worked in close proximity to or shared the same classroom environment with someone with COVID-19?		
6. Have you, or has any person listed above, travelled with a patient with COVID-19 in any kind of conveyance?		
7. Have you, or has any person listed above, lived in the same household as a patient with COVID-19?		

Annex 3: Passenger/Crew Locator Form (PLF) for cruise ships

The form is available in Word format from the following link:

https://www.healthygateways.eu/Translated-Passenger-Locator-Forms

Considerations on passenger locator data can be found here: https://www.ecdc.europa.eu/en/publications-data/passenger-locator-data-entry-exit-screening-health-declaration



Public Health Passenger/Crew Locator Form: To protect your health, public health officers need you to complete this form whenever they suspect a communicable disease onboard a cruise ship. Your information will help public health officers to contact you if you were exposed to a communicable disease. It is important to fill out this form completely and accurately. Your information is intended to be held in accordance with applicable laws and used only for public health purposes. Thank you for helping us to protect your health.

One form should be completed by an adult member of each family/crew member. Print in capital (UPPERCASE) letters. Leave blank boxes for spaces.

CRUISE INFORMATION: 1. Cruise line name 2. Cruise ship name 3. Cabin Number 4. Date of disembarkation (dd/mm/yy)

PERSONAL INFORMATION:

5. Last (Family) Name 6. First (Given) Name 7. Middle Initial 8. Your sex MALE FEMALE OTHER 9. Age (years)

PHONE NUMBER(S) where you can be reached if needed. Include country code and city code.

10. Mobile 11. Business

12. Home 13. Other

14. Email address

PERMANENT ADDRESS[1]:

15. Country 16. State/Province

17. City 18. ZIP/Postal code

19. Number and street (Separate number and street with blank box) 20. Apartment number

[1] 21. If in the previous 14 days you have stayed in a country (not transit) other than your permanent address, declare below the name of country/countries:

TEMPORARY ADDRESS: If at any time during the next 14 days you will not be staying at the permanent address listed above, write the places where you will be staying.

22. Country 1 23. State/Province 1

24. City 1 25. ZIP/Postal code 1

26. Hotel name 1 (if any) 27. Number and street 1 (Separate number and street with blank box) 28. Apartment number 1

29. Country 2 30. State/Province 2

31. City 2 32. ZIP/Postal code 2

33. Hotel name 2 (if any) 34. Number and street 2 (Separate number and street with blank box) 35. Apartment number 2

36. TRAVEL COMPANIONS – FAMILY: Only include age if younger than 18 years

	Last (Family) Name	First (Given) Name	Cabin number	Age <18
(1)				
(2)				
(3)				
(4)				

37. TRAVEL COMPANIONS – NON-FAMILY/NON-SAME HOUSEHOLD: Also include name of group (if any)

	Last (Family) Name	First (Given) Name	Group (tour, team, business, other)
(1)			
(2)			

To be completed by CREW only:

38. Working sector on board:

39. Co-habitants in cabin:

	Last (Family) Name	First (Given) Name
(1)		
(2)		
(3)		
(4)		

Working group members

Barbara Mouchtouri[1], Martin Dirksen-Fischer[2], Mauro Dionisio[3], Miguel Dávila-Cornejo[4], Brigita Kairiene[5], Peter Otorepec[6], Boris Kopilovic[6], Finán Ó Gallchobhair[7], Lemonia Anagnostopoulou[1], Elina Kostara[1], Leonidas Kourentis[1], Jan Heidrich[8], Agoritsa Baka[9], Eeva Broberg[9], Orlando Cenciarelli[9], Massimo Ciotti[9], Margot Einoder-Moreno[9], Pete Kinross[9], Katrin Leitmeyer[9], Angeliki Melidou[9], Daniel Palm[9], Diamantis Plachouras[9], Paul Riley[9], Marc Struelens[9], Carl Suetens[9], Svetla Tsolova[9], Klaus Weist[9], Emma Wiltshire[9] and Christos Hadjichristodoulou[1]

1. Laboratory of Hygiene and Epidemiology, Faculty of Medicine, University of Thessaly, Larissa, Greece
2. Institute for Hygiene and Environment of the Hamburg State Department for Health and Consumer Protection, Hamburg, Germany
3. Italian Ministry of Health, Rome, Italy
4. Ministry of Health, Social Services and Equality, Madrid, Spain
5. National Public Health Centre under The Ministry of Health, Klaipeda, Lithuania
6. National Institute of Public Health, Ljubljana, Slovenia
7. Environmental Health Service, Ireland
8. Institute for Occupational and Maritime Medicine, Hamburg, Germany
9. European Centre for Disease Prevention and Control

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Michael McCarthy, Royal Caribbean Cruises Ltd.
Nikos Mertzanidis, Cruise Lines International Association (CLIA) Europe
Members of Cruise Lines International Association (CLIA) Europe
Ukko Metsola, Royal Caribbean Cruises Ltd.
Adrijana Pesic, Royal Caribbean Cruises Ltd.
Julien Prodhomme, Carnival Corporation
Kathryn Ramsdale, Carnival Corporation

Ernie Rubi, Royal Caribbean Cruises Ltd.
Eddie Segev, Royal Caribbean Cruises Ltd.
Adrianna Siniscalchi, Royal Caribbean Cruises Ltd.
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Grant Tarling, Carnival Corporation
Frank Tuscano, Royal Caribbean Cruises Ltd.
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For any questions or support related to the points of entry including ports, airports, ground crossings, please email info@healthygateways.eu

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Ministero delle Infrastrutture e dei Trasporti

IL CAPO DI GABINETTO

ALLEGATO N. 8

Al Comitato Tecnico-Scientifico
c/o Dipartimento della Protezione Civile
SEDE
protezionecivile@pec.governo.it
coordinamento.emergenza@protezionecivile.it

Oggetto: Misure per il contenimento del rischio di contagio da COVID-19 – Linee guida per il trasporto pubblico – Richiesta parere.

Con l'allegata nota del 23 giugno 2020, a firma dei competenti assessori delle Regioni Liguria, Piemonte, Lombardia, Veneto e Friuli Venezia Giulia, è stato chiesto di valutare la possibilità di rivedere le linee guida dettate a livello nazionale per il contenimento del rischio di contagio da COVID-19 per il trasporto pubblico relativamente alla capacità di riempimento dei mezzi di trasporto, in funzione della necessità di far fronte al notevole incremento della domanda di trasporto.

Questa Amministrazione è consapevole delle attuali vigenti disposizioni adottate per contrastare la diffusione del contagio da COVID-19 di particolare rilevanza in materia di trasporto, quali, ad esempio, quelle contenute nella circolare prot. n. 14916 del 29 aprile 2020 del Ministero della Salute, che, nel fornire indicazioni per la rimodulazione delle misure contenitive di fase 2, in relazione al trasporto pubblico collettivo terrestre, nell'ottica della ripresa del pendolarismo, ha ribadito come il distanziamento tra gli utenti del trasporto costituisca un fattore essenziale, al fine di prevenire il rischio di contagio, in linea con quanto previsto nelle raccomandazioni dell'Organizzazione Mondiale della Sanità. A ciò si aggiunga che le linee guida del 5 giugno u.s., la stessa OMS, nel disciplinare l'uso delle mascherine e nel sottolineare l'importanza dell'utilizzo delle stesse, ha ribadito che l'uso della sola mascherina non sia sufficiente a garantire la sicurezza, evidenziando come il distanziamento interpersonale sia la misura principale per contrastare la diffusione del contagio.

Con l'allegato 15 del Decreto del Presidente del Consiglio dei Ministri 11 giugno 2020, emanato in attuazione di quanto disposto dal decreto-legge 16 maggio 2020, n.33, poi, ferma restando l'indicazione del distanziamento interpersonale di un metro quale regola

generale di prevenzione, è stata prevista, nell'ambito delle linee guida per l'informazione agli utenti e le modalità organizzative per il contenimento della diffusione del COVID-19 nel settore del trasporto pubblico, la possibilità per le Regioni e Province autonome di introdurre specifiche prescrizioni, in ragione delle diverse condizioni territoriali e logistiche e delle rispettive dotazioni di parco mezzi, in relazione all'andamento della situazione epidemiologica sul territorio.

Come è peraltro noto, alcune regioni hanno autonomamente nell'ambito della propria competenza sanitaria e specifica responsabilità adottato ordinanze del Presidente della Regione, in relazione al contesto territoriale di riferimento, con le quali hanno previsto misure che consentono di derogare nei mezzi di trasporto regionali alle regole del distanziamento interpersonale di un metro.

In relazione a quanto sopra, si chiede a codesto Comitato se, allo stato, della situazione epidemiologica nel Paese e di altri elementi conosciuti dalla comunità scientifica, in merito alle modalità di diffusione e contagio del virus covid-19, la richiesta avanzata dalle citate Regioni di superare la prescrizione del distanziamento interpersonale di un metro nei mezzi di trasporto, utilizzando in alternativa la mascherina chirurgica, l'aereazione e le porte dedicate per salita e la discesa, possa essere accolta, senza che ciò metta in pericolo la salute dei viaggiatori.

Cons. Alberto Stancanelli

REGIONE LIGURIA · REGIONE PIEMONTE · RegioneLombardia · REGIONE DEL VENETO · REGIONE AUTONOMA FRIULI VENEZIA GIULIA

Data, 23 giugno 2020.
Prot. PG/2020/196697
Inoltro a mezzo di posta certificata

Gentilissima
Ministro delle Infrastrutture e dei Trasporti
On.le Paola De Micheli

Gentilissima Ministro,

alla luce di questa nuova fase di ripresa delle attività economiche del Paese e, con esse, della normale mobilità delle persone, sia per esigenze di lavoro che di turismo, appare necessario rivedere le misure organizzative per il contenimento della diffusione del Covid-19 in materia di trasporto pubblico, disposte con il DPCM del 26 aprile 2020 e riprese dal DPCM dell'11 giugno 2020.

Infatti tali misure, che impongono il distanziamento sociale tra gli occupanti dei mezzi pubblici, confliggono con la necessità di garantire il diritto alla mobilità dei cittadini che, dopo aver pagato il biglietto, si vedono negata la possibilità di accedere al servizio a causa della limitazione alla capacità di carico dei mezzi.

Purtroppo nell'immediato non è possibile, a causa della carenza di risorse e di materiale rotabile, garantire un servizio sufficiente a soddisfare la domanda alle attuali condizioni.

Sicuramente prima di tutto occorre garantire la salute e le misure organizzative hanno tale scopo, tuttavia le disposizioni consentono una specifica deroga al distanziamento interpersonale a bordo degli aeromobili.

Senza voler entrare nel merito di tali disposizioni, si chiede di riconsiderare quanto previsto per il trasporto terrestre, e tenuto conto delle misure precauzionali adottate, tra cui l'obbligo all'utilizzo di mascherina chirurgica per la protezione del naso e della bocca, l'utilizzo delle porte dedicate per la salita e la discesa e l'aereazione dei mezzi, rivedere le linee guida al fine di consentire il riempimento fino alla capienza massima, considerato il notevole incremento della domanda registrato in questi ultimi giorni, in analogia a quanto già previsto per altri sistemi di mobilità.

Certi di un Suo cortese riscontro Le porgiamo i nostri più cordiali saluti

Assessore	Assessore	Assessore	Assessore	Assessore
Giovanni Berrino	Marco Gabusi	Claudia MariaTerzi	Elisa De Berti	Graziano Pizzimenti

ALLEGATO N. 9

Stimato Signor Prefetto,

il percorso nelle varie fasi di riapertura che il Governo sta autorizzando fa emergere sempre di più anche nella vita ecclesiale l'urgenza di ritornare all'esercizio della prassi pastorale, a partire dall'esperienza liturgica, perché sempre più consona con l'incontro con il Signore e con la Comunità.

Facendosi interprete delle segnalazioni che giungono dai Pastori di numerose Diocesi, codesta Segreteria Generale sottopone la richiesta di superare il limite del numero di 200 partecipanti alle celebrazioni che si svolgono nelle chiese. La richiesta, se diventa impellente in occasione di ordinazioni sacerdotali ed episcopali, è veicolata pure da Vescovi e parroci che nella quotidianità hanno responsabilità ministeriali di edifici religiosi di ampie dimensioni, dove il rispetto per il distanziamento personale – oltre che per tutte le altre misure di carattere sanitario – è comunque assicurato senza difficoltà.

A tal proposito, una soluzione potrebbe forse essere quella di garantire a sua volta una congrua distanza tra insiemi – gruppi di 200 persone – cercando contestualmente di evitare assembramenti sia al momento dell'ingresso in chiesa che in quello del congedo.

Un altro quesito concerne la possibilità per i familiari che già vivono quotidianamente tra le stesse pareti di casa: per queste persone si chiede che possano partecipare alle celebrazioni evitando tra loro il criterio del distanziamento.

Infine, ma non meno rilevante per la qualità delle celebrazioni, si sottopone anche l'urgenza di tornare ad ammettere la figura dei cantori: a quali condizioni è proponibile?

Grati per l'attenzione,

✠ Stefano Russo
Segretario Generale

Roma, 29 giugno 2020

CIRCONVALLAZIONE AURELIA, 50 – 00165 ROMA – Tel. 06 66.398.1 – fax 06 66.23.037 – e-mail: segrgen@chiesacattolica.it

ALLEGATO N. 10

AGENZIA ITALIANA DEL FARMACO

Ufficio Segreteria Organismi Collegiali

COMMISSIONE CONSULTIVA TECNICO SCIENTIFICA

SCHEDA VALUTAZIONE STUDIO COVID-19

Data e numero di protocollo interno: 81BISa/2020 – **EMENDAMENTO**
Data di avvio procedura di valutazione Commissione Tecnico Scientifica AIFA: 30.06.2020
Data parere FINALE Commissione Tecnico Scientifica AIFA: 06.07.2020

IDENTIFICAZIONE DELLA SPERIMENTAZIONE CLINICA
TITOLO STUDIO: Studio randomizzato di Fase II sull'efficacia e la sicurezza di Acalabrutinib in aggiunta alle migliori terapie di supporto verso le migliori terapie di supporto in soggetti ricoverati con COVID-19.
PROMOTORE (specificare anche se profit o no-profit) Acerta Pharma BV
SPONSOR: Acerta Pharma BV
SPERIMENTATORE RESPONSABILE DELLO STUDIO (richiedente) Nome e Cognome: Wyndham Wilson, MD PhD, Center for Cancer Research, National Cancer Institute, Building 10, Room 12C-442, Bethesda, MD 20892
CENTRO COORDINATORE *(solo per studi multicentrici):* CON IL NUOVO PROTOCOLLO VIENE PROPOSTO Comitato etico dell'INMI Spallanzani
CENTRI COINVOLTI NELLA SPERIMENTAZIONE: CON IL NUOVO PROTOCOLLO VENGONO PROPOSTI - INMI Spallanzani - Roma (prof. Antinori) - Ospedale San Raffaele - Milano (prof. Ghia) - Azienda Ospedaliero-Universitaria Careggi - Firenze (prof. Bartoloni) - Policlinico di Tor Vergata - Roma (prof. Andreoni) - Policlinico Gemelli - Roma (prof. Cauda) - Policlinico S. Orsola Malpighi - Bologna (prof. Viale) - Ospedale Sacco - Milano (prof. Galli)

FARMACO/I O INTERVENTO TERAPEUTICO

breve descrizione del razionale, delle caratteristiche del/i farmaco/i e del meccanismo d'azione/funzionamento

Acalabrutinib è una "piccola molecola", potente inibitore della tirosin chinasi di Bruton (BTK). Acalabrutinib e il suo metabolita attivo ACP-5862, formano un legame covalente con un residuo di cisteina nel sito attivo di BTK, portando ad una inibizione dell'attività enzimatica di BTK. La BTK, membro della famiglia delle chinasi Tec, è un'importante molecola delle vie del segnale del recettore per l'antigene dei linfociti B (BCR) e del recettore per le citochine. Il ruolo centrale della BTK nella trasmissione del segnale dai recettori di superficie delle cellule B provoca l'attivazione delle vie necessarie per il trafficking, la chemiotassi e l'adesione delle cellule B.

Btk è anche coinvolta nei seguenti processi biologici: trasduzione del segnale FcγR nelle cellule mieloidi, degranulazione dei mastociti,differenziazione degli osteoclasti,e trasduzione del segnale attraverso i recettoriToll-like (TLRs) nei macrofagi e nei neutrofili. L' inibizione di Btk è associata ad una riduzione delle citochine proinfiammatorie in pazienti con neoplasie ematologiche.

I pazienti con neoplasie ematologiche trattati con acalabrutinib hanno mostrato riduzioni statisticamente significative delle seguenti citochine: TNFα ($p<0.001$), IL-10 ($p<0.001$), eMCP-1 ($p<0.01$) (Byrd et al, 2016) e IL-6 ($p<0.05$) (dati non disponibili, dichiarati dall'azienda on file). La riduzione di queste citochine immunomodulanti potrebbe mitigare la risposta fisiopatologica che porta alle morbidità più gravi e mortalità associate all'infezione virale.

Acalabrutinib non è attualmente approvato in Europa, ma è approvato negli Stati Uniti per il trattamento dei pazienti con linfoma a cellule mantellari e leucemia linfocitica cronica/linfoma linfocitico a piccole cellule.

<u>CON IL NUOVO PROTOCOLLO VIENE TRASMESSO</u>

Il manoscritto di un lavoro in valutazione per la pubblicazione che riporta un piccolo studio preliminare con acalabrutinib effettuato presso 5 ospedali statunitensi che ha coinvolto 19 pazienti che necessitavano di ossigeno e di cui il 42% (8) era in ventilazione meccanica. Lo studio è stato finanziato dall'NIH e il farmaco fornito dal Walter Reed National Military Medical Center. Ad eccezione di un paziente tutti presentavano elevati livelli di proteina C reattiva e, ad eccezione di tre, una linfocitopenia. In 15 pazienti (79%) è stato osservato un miglioramento dell'ossigenazione che ha comportato la riduzione dei flussi di ossigeno, fino alla sua cessazione in 4, e in 1/4 dei pazienti intubati l'estubazione. Nessuno dei pazienti arruolati ha avuto un esito fatale. Due degli 11 pazienti (18%) che hanno iniziato acalabrutinib senza ossigenoterapia invasiva sono stati successivamente intubati tra il 3° e il 4° giorno di trattamento, uno di questi è stato estubato dopo 3 giorni. Non sono state osservate tossicità riferibili ad acalabrutinib.

L'ipotesi degli autori è che l'azione di acalabrutinib interferisca con la "sindrome da attivazione macrofagica" e quindi con l'intera tempesta citochinica che caratterizza i casi gravi di CoViD-19.

TIPO DI STUDIO

Indicare se lo studio è osservazionale (prospettico o retrospettivo) o sperimentale. Nel caso si tratti di uno studio sperimentale indicarne brevemente le caratteristiche (se randomizzato, se in cieco ecc.), la fase (1-2-3-4), si dovrà poi indicare se si tratta di uno studio di superiorità, di equivalenza o di non inferiorità.

Il promotore propone uno studio multricentrico, globale, di fase 2, in aperto, di 2 parti che arruoleranno contemporaneamente.

<u>La Parte 1</u> dello studio è randomizzata (2:1) e valuta l'aggiunta di acalabrutinib all'attuale BSC per COVID-19 in soggetti ospedalizzati verso BSC..

Assumendo una perdita del 5%, la dimensione del campione di 408 pazienti per la Parte 1 produce una dimensione effettiva del campione di 387 che permette con il 90% di potenza ed un errore di tipo 1 a 2 code di 0.05, di rilevare una differenza del 15% (cioè, una riduzione del 50% del rischio relativo) nel fallimento della terapia tra acalabrutinib + BSC e BSC, assumendo il 30% di fallimenti nel braccio BSC vs 15% nel braccio acalabrutinib + BSC.

La Parte 2 di questo protocollo include una coorte di soggetti nell'unità di terapia intensiva (ICU). La parte 2 non è randomizzata. I soggetti nella coorte di terapia intensiva sono soggetti ammessi nella terapia intensiva per il trattamento dei sintomi della COVID-19 (non si possono includere soggetti della Parte 1).

POPOLAZIONE IN STUDIO

breve descrizione delle caratteristiche della popolazione proposta per lo studio che comprenda solo i più rilevanti criteri di inclusione/esclusione

Principali criteri di inclusione per la Parte 1 (bracci 1 e 2)

1. Possibilità di dare un valido consenso informato scritto
2. Pazienti maggiorenni
3. Infezione COVID-19 confermata con "sospetta" polmonite che richiede ospedalizzazione, SpO2<94% in aria ambiente o che richiede 2-5 L/min di ossigeno, con almeno 1 dei seguenti parametri di laboratorio:
    a. ferritina > 300 ng/mL per gli uomini e > 150 ng/mL per le donne
    b. PCR ≥ 10 mg/L
    c. D-dimero > 1 mg/L
    d. conta assoluta dei linfociti < 1000 cellule/µL
4. Capacità di deglutire capsule o ricevere il contenuto delle capsule mediante sondino naso gastrico o tubo di nutrizione enterale

Principali criteri di inclusione per la Parte 2

1. Possibilità di dare un valido consenso informato scritto
2. Pazienti maggiorenni
3. Infezione COVID-19 confermata che richiede ricovero in terapia intensiva e che richiede ≥ 6 L/min di ossigeno o PaO2/FiO2 ≤300 mm Hg
4. In grado di ingoiare capsule o ricevere il contenuto delle capsule mediante sondino naso gastrico o tubo di nutrizione enterale

Principali criteri di esclusione per la Parte 1 e per la Parte 2 (tutti i soggetti)

1. Gravidanza o allattamento
2. Sospetta infezione attiva non controllata batterica, fungina o virale (ad eccezione del COVID-19)
3. Sopravvivenza stimata inferiore a 28 giorni a causa di altre patologie
4. ALT o AST >5 volte la norma misurate entro 24 ore dallo screening
5. Conta assoluta dei neutrofili<500/µL allo screening
6. Conta piastrinica < 50,000/µL allo screening
7. Cardiopatia non controllata e sintomatica
8. HBV o HCV attiva che richiede terapia
9. Partecipazione in altri trial clinici (la partecipazione ai trial degli antivirali per il COVID-19 può essere permessa se approvata dal Medical Monitor)
10. I pazienti hanno ricevuto agenti antirigetto o immunomodulanti (incluso tocilizumab) negli ultimi 30 giorni
11. Utilizzo concomitante di corticosteroidi sistemici o inalatori
12. Utilizzo di anticoagulanti (warfarin o altri antagonisti della vitamina K) entro 7 giorni dalla prima dose di acalabrutinib
13. Utilizzo concomitante di altri inibitori JAK, PI3K, o Btk (oltre acalabrutinib)

INTERVENTO

Specificare trattamento e n. pazienti

Il numero totale di soggetti in questo studio è 428.

Nella Parte 1

Acalabrutinib 100 mg 2 volte al giorno (bid) x 10 giorni + BSC (n=272)

I soggetti saranno randomizzati sulla base dei seguenti fattori di stratificazione, che sono considerati fattori prognostici per scarso risultato:

- Età (≥65 verso< 65 anni)
- Comorbidità (presenti o assenti).

Le comorbidità considerate sono: Malattie cardiovascolari definite sia come insufficienza cardiaca di classe NYHA ≥2 o ipertensione che richiede trattamento; Diabete mellito che richiede trattamento; BPCO o asma che richiede trattamento; Presenza di tumore solido attivo o neoplasie ematologiche.

Nella Parte 2

20 soggetti saranno arruolati nella Coorte ICU (Intensive Care Unit). e riceveranno acalabrutinib 100 mg 2 volte al giorno per 10 giorni più BSC. Le informazioni sulla sicurezza e sull'efficacia della coorte ICU saranno confrontate con i dati dei controlli storici per determinare se uno studio formale randomizzato debba essere condotto in questa popolazione di pazienti.

CONTROLLO

Specificare trattamento e n. pazienti

Il controllo è previsto esclusivamente nella Parte 1 dello studio e consiste in Best Supportive Care, che sarà a discrezione dello sperimentatore e secondo le linee guida dell'ospedale (n=136).

I soggetti del braccio di controllo sottoposti a ventilazione assistita (ad esempio, considerati fallimenti del trattamento) possono ricevere acalabrutinib 100 mg 2 volte al giorno per un massimo di 10 giorni a discrezione dello sperimentatore.

TERAPIE CONCOMITANTI
consentite e non consentite

ESITI

Obiettivo primario**:**

L'obiettivo generale dello studio è valutare l'efficacia dell'aggiunta di acalabrutinib a BSC per il trattamento di COVID-19

*Endpoint primario***:**

L'endpoint primario è il tasso di fallimento del trattamento, in cui il fallimento del trattamento è definito come l'uso della ventilazione assistita o la morte.

*Endpoint secondari***:**

- Numero di giorni in vita liberi da ventilazione assistita a 30 giorni dopo la randomizzazione /arruolamento
- Numero di giorni con utilizzo del ventilatore a 30 giorni dopo la randomizzazione/arruolamento
- Numero di giorni ospedalizzati a 30 giorni dopo la randomizzazione /arruolamento
- Numero di giorni in terapia intensiva a 30 giorni dopo la randomizzazione /arruolamento
- Numero di giorni in vita al di fuori dell'ospedale a 30 giorni dopo la randomizzazione / arruolamento
- Numero di giorni in vita al di fuori dell'ospedale a 90 giorni dopo la randomizzazione / arruolamento

Endpoint secondari di sicurezza

Tipo, frequenza, gravità e correlazione con il trattamento in studio di eventuali eventi avversi emergenti dal trattamento (TEAE) o anomalie degli esami di laboratorio, eventi avversi seri (SAE) o eventi avversi (AEs) che portano alla sospensione del trattamento in studio

Endpoint esplorativi

- Modifica di INF-ɣ, TNF-α, IL-1β, IL-6, IL-8, IL-10, IL-18, MCP-1; marker infiammatori associati proteina C-reattiva (CRP), D-dimero, procalcitonina (se disponibile), fibrinogeno e ferritina; e conta linfocitaria assoluta dal basale
- Modifica dei livelli e della sierologia del virus SARS-CoV-2 rispetto al basale
- Occupazione BTK e alterazioni delle cellule linfoidi e mieloidi rispetto al basale
- Analisi correlativa con effetti del trattamento per determinare se eventuali biomarcatori possono prevedere la risposta, nonché qualsiasi correlazione ai livelli di esposizione al farmaco

Durata dello studio:

Periodo di arruolamento (ove applicabile): La data stimata del primo paziente arruolato è il Q2 2020. La data stimata dell'ultimo paziente completato è il Q3 2020.

Periodo di Follow-up (ove applicabile):

COMMENTI/RIFLESSIONI SULLO STUDIO

(deve contenere oltre ai commenti specifici sullo studio in esame, osservazioni sulla rilevanza dello studio, sull'adeguatezza del disegno relativamente agli obiettivi prefissati e sulla pubblicazione dei risultati)

COMMENTI SULLA PRIMA PRESENTAZIONE DEL PROTOCOLLO

Generale

Non sono indicati il centro coordinatore né i centri italiani coinvolti nella sperimentazione.

Razionale biologico

L'inibizione di BTK è anche associata ad una riduzione delle citochine proinfiammatorie in pazienti con neoplasie ematologiche. La riduzione di queste citochine immunomodulanti potrebbe mitigare la risposta fisiopatologica che porta alle morbidità più gravi e mortalità associate all'infezione virale.

L'ipotesi di studio presenta una certa plausibilità biologica, ma non esiste alcuna evidenza clinica dell'effetto della somministrazione di acalabrutinib in pazienti senza neoplasie ematologiche e del ruolo che potrebbe avere sui linfociti B non neoplastici, con rischio di riduzione dell'attivazione dei linfociti B nei confronti delle infezioni virali.

Posologia e durata trattamento

Acalabrutinib non è attualmente approvato in Europa, ma è approvato negli Stati Uniti per il trattamento dei pazienti con linfoma a cellule mantellari o leucemia linfocitica cronica/linfoma linfocitico a piccole cellule.

Il dosaggio proposto è 100 mg 2 volte al giorno per 10 giorni.

Si sottolinea che non esiste alcun dato clinico riguardante l'attività antiinfiammatoria di acalabrutinib quando somministrato per 10 giorni (i pazienti ematologici assumono il trattamento anche per diversi anni).

Disegno dello studio.

Nella Parte 1 408 soggetti saranno randomizzati 2:1 nel Braccio 1 (acalabrutinib + BSC) o 2 (BSC). Nella Parte 2 20 soggetti saranno arruolati nella Coorte ICU (Intensive Care Unit). Le Parti 1 e 2 arruoleranno contemporaneamente.

Al contrario della parte 1, che presenta una randomizzazione e un'ipotesi statistica, la Parte 2 di questo protocollo include esclusivamente una coorte di soggetti nell'unità di terapia intensiva (ICU). La parte 2 non è randomizzata e senza alcuna ipotesi formale statistica. Pertanto i risultati ottenibili da questa coorte sono puramente descrittivi.

Criteri di inclusione

I criteri di inclusione dello studio comportano una grande eterogeneità clinica nella Parte 1. È richiesto esclusivamente che i pazienti siano "ospedalizzati", con "sospetta" polmonite da COVID-19. I pazienti ricoverati possono avere caratteristiche estremamente eterogenee e sarebbe più appropriato includere esclusivamente pazienti con polmonite "documentata". I pazienti verranno stratificati in base ad età Età (≥65 verso< 65 anni) e comorbidità (presenti o assenti). Per quanto riguarda le comorbidità sarebbe utile stratificare non solo per la presenza, ma anche per il numero di comorbidità, che porta a un rischio prognostico notevolmente diverso.

Terapie concomitanti

Non viene specificata la tipologia di trattamento concomitante, anzi viene riportato che essa sarà a discrezione dello sperimentatore e delle linee guida dell'ospedale. È controindicato l'utilizzo di tocilizumab e JAK inibitori, mentre è permesso l'arruolamento in trial che testano terapie antivirali per il COVID-19. Essendo questo uno studio multicentrico internazionale, inevitabilmente le terapie concomitanti potrebbero essere diverse tra i pazienti arruolati, con rischio di confondimento per quanto riguarda i risultati finali.

End-point dello studio

L'endpoint primario è il tasso di fallimento del trattamento, in cui il fallimento del trattamento è definito come l'uso della ventilazione assistita o la morte. Tale end-point quindi va a valutare esclusivamente l'assenza di peggioramento, non il miglioramento, che è l'obiettivo principale dei pazienti meno gravi affetti da COVID-19, che tra l'altro rappresenta la storia naturale di malattia in un'alta percentuale di pazienti. Non vengono inoltre specificati i timepoints di valutazione.

Per quanto riguarda gli endpoints secondari, vengono valutati molteplici parametri clinici a 28 giorni,

sarebbe utile avere anche una valutazione intermedia a 14 giorni, che permetterebbe di capire l'evoluzione clinica dei pazienti.

Sicurezza/interazioni farmacologiche

L'impego di acalabrutinib è caratterizzato da molteplici eventi avversi (emorragie, infezioni, riattivazione epatite B, nausea, vomito, diarrea) che andranno accuratamente monitorati nel corso dello studio.

Per quanto riguarda le interazioni farmacologiche, acalabrutinib è in gran parte metabolizzato dal CYP3A, pertanto andrebbe considerat l'opportunità di terapie concomitanti diverse rispetto ad inibitori forti del CYP3A (es. lopinavir e ritonavir, cobicistat, telaprevir, indinavir e ritonavir, etc). Inoltre andrebbe evitato l'uso concomitante di inibitori di pompa protonica.

Per quanto sopra, la CTS ha espresso PARERE NON FAVOREVOLE sulla base delle considerazioni sopra riportate. In particolare per una valutazione del rapporto beneficio/rischio dovrebbe essere soppesato il rischio che comporta l'uso di una terapia che interferisce con meccanismi di risposta immunitaria adattativa ed innata in un elevato numero di pazienti in condizioni non gravi. Mancano infatti evidenze anche preliminari di utilizzo del farmaco in patologie di origine virale e sull'effetto che può avere nella produzione di risposte immunitarie protettive contro le infezioni.

COMMENTI SULLA SECONDA PRESENTAZIONE DEL PROTOCOLLO

I dati presentati sotto forma di manoscritto, pur non superando i limiti di una serie aneddotica di casi, suggeriscono che acalabrutinib possa esercitare un'azione favorevole in pazienti con decorso ingravescente dell'insufficienza respiratoria. La limitatezza del campione non consente di trarre conclusioni anche se l'assenza di decessi in una popolazione di gravità elevata, almeno nella maggior parte se non quasi totalità dei casi, supporta una più ampia valutazione dell'efficacia dell'intervento. È da rilevare che lo studio di Xu e coll. (PNAS pre-print 29 aprile 2020), sul quale si sono basate le proposte di studio con tocilizumab, era assimilabile come numerosità della casistica che era però di gravità inferiore (solo 10% in ventilazione invasiva verso il 42% in questo) e la riduzione della richiesta di ossigeno è stata osservata nel 73% dei casi contro il 79% dello studio con acalabrutinib anche se c'era stata la dimissione dall'ospedale in tutti i 21 casi.

Rimane non superato il dubbio che un intervento su di una via di segnale importante per i linfociti B, oltre che per alcuni effettori dell'immunità innata (aspetto su cui per la loro precedente esperienza scientifica particolarmente insistono gli autori), possa interferire con l'eliminazione del virus anche se la dimissione di 3 pazienti e l'avvio alla riabilitazione respiratoria per altri 2 potrebbe far pensare che si sia comunque ottenuta la negativizzazione virale.

Il protocollo è stato emendato rispondendo in parte ad alcuni commenti della CTS, secondari rispetto alla preoccupazione che il farmaco potesse interferire con la risposta antivirale, in particolare è stata eliminata la parte 2 dello studio non controllata e senza ipotesi statistica che arruolava pazienti in UTI e precisato che la polmonite deve essere radiologicamente accertata per l'inclusione del paziente.

I criteri di inclusione ed esclusione dello studio caratterizzano una popolazione arruolabile di gravità inferiore rispetto a quella dello studio statunitense a supporto del razionale. In particolare non è richiesta la supplementazione con ossigeno, sono esclusi pazienti con insufficienza respiratoria definita dalla presenza di una delle seguenti condizioni:

a) intubazione e ventilazione meccanica;
b) somministrazione di ossigeno con cannula nasale ad alto flusso (>20 L/min con O_2 ≥0.5);
c) Non-invasive positive pressure ventilation o continuous positive airway pressure;
d) Extracorporeal membrane oxygenation.

Non viene inoltre previsto un criterio di inclusione relativo allo stato infiammatorio del paziente.

Sono stati modificati gli endpoint e le sezioni sulle interazioni farmacologiche.

Sulla base di quanto sopra, la CTS ha espresso PARERE SOSPENSIVO per chiedere al proponente di produrre dati sulla sieroconversione o sulla negativizzazione dei pazienti inseriti nello studio presentato a supporto

Infatti, benché la nuova documentazione fornita dall'azienda supporti l'opportunità di valutare in una

sperimentazione clinica l'efficacia di acalabrutinib nell'infezione da SARS-CoV-2, permane la criticità relativa alla possibile interferenza del trattamento con la risposta protettiva dell'ospite che potrebbe tradursi in una maggior persistenza del virus.

VALUTAZIONE INTEGRAZIONI/OSSERVAZIONI FORNITE DAL PROPONENTE

L'azienda ha chiarito che non dispone dei dati sulla negativizzazione o sieroconversione dei pazienti inclusi nello studio statunitense che descriveva un potenziale effetto dell'acalabrutinib nella polmonite in corso di CoViD-19 perché non era prevista nel consenso fornito dai pazienti la raccolta di campioni per esami diagnostici.
A supporto della ridotta probabilità che il trattamento con un inibitore di BTK vengono citati precedenti studi con ibrutinib nei quali è stata osservata una risposta alle vaccinazioni in pazienti cronicamente trattati con il farmaco. Inoltre l'azienda argomenta che la breve durata del trattamento e il ruolo dominante della risposta T-mediata nella risoluzione delle malattie virali contribuiscono ulteriormente a far considerare improbabile il rischio che il breve corso di trattamento con acalabrutinib abbia un effetto negativo sulla clearance virale. Durante lo studio saranno monitorate la risposta umorale e il carico virale nonché l'eventuale insorgenza di infezioni opportunistiche.

PARERE CTS

PARERE FAVOREVOLE

In considerazione dell'attuale fase calante dell'epidemia, e del conseguente rischio che l'attivazione di ulteriori studi possa entrare in competizione con quelli già in atto, vanificando la possibilità di portare a termine le sperimentazioni, lo sponsor dovrebbe inoltre indicare quanti pazienti italiani prevede di includere nello studio e verificarne l'effettiva possibilità di arruolamento.

VERIFICA DELLA DOCUMENTAZIONE INVIATA DAL PROPONENTE PER ACCETTAZIONE CONDIZIONI

L'Azienda ha comunicato di aver verificato la possibilità di includere 15 pazienti italiani nello studio multicentrico internazionale.

PARERE CTS

La CTS prende atto della comunicazione e conferma il PARERE FAVOREVOLE

VALUTAZIONE DELL'EMENDAMENTO PROPOSTO (30.06.2020)

L'emendamento, oltre a numerose modifiche di carattere non sostanziale, propone:

- l'aggiunta dei seguenti due endpoint secondari di efficacia
    - tempo intercorso al miglioramento clinico di almeno 2 punti (dalla randomizzazione) su 9 punti categoria su scala ordinale fino al Giorno 28 (vedi Sezione 8.8.1)
    - tempo a SpO2 >94% in aria ambiente
- l'estensione del tempo massimo ammissibile tra lo screening e l'inizio del trattamento da 24 ore a 3 giorni
- la modifica della periodicità durante il periodo di ospedalizzazione dei controlli ematici di D-dimero, PT, INR, aPTT e procalcitonina da giornaliero a ogni due giorni

Commento
Le modifiche proposte non modificano il giudizio precedentemente espresso.

PARERE CTS SULL'EMENDAMENTO

PARERE FAVOREVOLE