EUnetHTA Joint Action 3 WP4

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RAPID COLLABORATIVE REVIEW ON THE CURRENT ROLE OF ANTIBODY TESTS FOR NOVEL CORONAVIRUS SARS-COV-2 IN THE MANAGEMENT OF THE PANDEMIC

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Conflict of interest

All authors, co-authors and dedicated reviewers involved in the production of this assessment have declared they have no conflicts of interest in relation to the technology and comparator(s) assessed according to the EUnetHTA declaration of interest (DOI) form, which was evaluated following the EUnetHTA Procedure Guidance for handling DOI form (https://eunethta.eu/doi).

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LIST OF ABBREVIATIONS

CE	Conformité Européenne
CLIA	Chemiluminescenceimmunoassay
COVID-19	Coronavirus disease 2019
ECDC	European Centre for Disease Prevention and Control
ELISA	Enzyme-Linked Immunosorbent Assay
EUnetHTA	European Network for Health Technology Assessment
FIA	Fluorescent Immunoassay
HAS	Haute Autorité de Santé (France)
HCW	Healthcare Worker
HIQA	Health Information and Quality Authority (Ireland)
HTA	Health Technology Assessment
HTW	Health Technology Wales
ICTRP	International Clinical Trials Registry Platform
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, Insitute for Quality and Efficiency in Healthcare
IgA	Immunglobulin A
IgG	Immunglobulin G
IgM	Immunglobulin M
IVD	In-Vitro Diagnostic
JA	Joint Action
JRC	Joint Research Centre
LFA	Lateral Flow Assay
MERS	Middle East respiratory syndrome
N/A	Not Applicable
NAAT	Nucleic Acid Amplification Test
NIPH	Norwegian Institute of Public Health
NR	Not Reported

OECD	Organisation for Economic Co-operation and Development
PCR	Polymerase chain reaction
PoC	Point of Care
PROSPERO	International Prospective Register of Systematic Reviews
qPCR	quantitative Polymerase Chain Reaction
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies-2
RDT	Rapid Diagnostic Test
REA	Relative Effectiveness Assessment
RER	Regione Emilia-Romagna
ROC	Receiver Operating Characteristics Curve
RODT	Rapid Diagnostic Orientation Test
RT-PCR	Reverse Transcription Polymerase Chain Reaction
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SHTG	Scottish Health Technologies Group
SR	Systematic Review
THL	Institute for Health and Welfare (Finland)
UK	United Kingdom
WHO	World Health Organization
WP	Work Package

EXECUTIVE SUMMARY OF THE ASSESSMENT OF ANTIBODY TESTS FOR NOVEL COROANVIRUS SARS-COV-2

Introduction

At the EUnetHTA Plenary Assembly held on the 1st and 2nd of April 2020 partners agreed that the collaborative network would take actions to be responsive to the COVID-19 pandemic and meet decision makers' urgent needs for trustworthy scientific information on the safety and effectiveness of disease management health technologies. Following this input, a EUnetHTA Assessment Team convened for this Rapid Collaborative Review on the current role of antibody tests for novel coronavirus SARS-CoV-2 in the management of the pandemic with the general objective of addressing the most pressing health policy questions related to screening, diagnosis and monitoring of the disease's course.

The pandemic of coronavirus disease 2019 has suddenly and quickly affected most of the world.
COVID-19, the disease caused by SARS-CoV-2, usually starts as upper respiratory tract infection, with non-specific symptoms including fever and cough, followed by sore throat, fatigue, rhinorrhoea, headache, chest and back pain. However, many cases show different presentations, among which are gastrointestinal symptoms (i.e. diarrhoea, nausea, vomiting, poor appetite, and anorexia), neurological signs and symptoms (i.e. ageusia, anosmia), fainting, redness of eye, and rash. These symptoms are related to the establishment of a viral pneumonia, which in severe cases can be complicated by additional viral and bacterial infections, heart problems, and acute respiratory distress syndrome (ARDS), requiring intensive care and resulting in death in a high proportion of patients. In a minority of patients, pneumonia is followed by a systemic hyperinflammation status, leading to life-threatening complications including vasculitis, multi-organ failure, blood clots, and shock.
As SARS-CoV-2 has been detected for the first time in humans in 2019, nobody has prior immunity, making the entire human population potentially susceptible to infection and disease. The very high transmissibility of SARS-CoV-2 and the susceptibility of the world population, led to over 7 million confirmed cases of infection and over 400,000 related deaths worldwide, from 31st December 2019 up to mid June 2020. The European Union (EU) and European Economic Area (EEA) countries were the first affected by high local transmission outside China, and reached over one and half million confirmed cases and over 170,000 deaths in the same time span.
Precise definitions of the incubation and infectious periods are still debated, and current available evidence shows potential transmission from 2 days before symptom onset up to 7-12 days in moderate cases, or up to an average of two weeks in severe cases. However, uncertainties remain about transmission by asymptomatic persons.

Objectives and scope

The aim of this EUnetHTA Rapid Collaborative Review is to provide a reliable synthesis of the available evidence on a number of intended clinical uses of antibody tests. It comprises an assessment of the clinical benefit and safety of antibody tests in the management of the current SARS-CoV-2 pandemic.

This Rapid Collaborative Review will address the following questions:

Whether and with which testing strategies, antibodiy tests can be reliably used for:

1. surveillance for early detection of new asymptomatic cases of SARS-CoV-2 acute infection in the general population and/or specific subpopulations;

2. diagnosis of SARS-CoV-2 acute infection in patients presenting symptoms suggestive of SARS-CoV-2 infection:

How antibody tests can be used for:

3 measuring seroprevalence in communities;

4 ruling out risk of transmission in patients who recovered from SARS-CoV-2 infection;

5 assessing protective immunity in subjects with past and resolved SARS-CoV-2 infection.

This review does not assess the analytical performance of antibody tests and does not review performance assessment studies of test methods and devices for COVID-19. To retrieve such information the reader is invited to refer to the working document published on 16 of April 2020 by the expert group from the Joint Research Centre (JRC) set up by the European Commission (1), as well as the JRC COVID-19 In Vitro Diagnostic Devices and Test Methods Database which provides a continuously updated list of diagnostic devices that are commercialised or in development (https://covid-19-diagnostics.jrc.ec.europa.eu).

Five different PICO questions and Scope have been developed for the five questions stated in the objective.

Table 0 - 1: Scope of the assessment

Description	**Project scope – Question 1 (Surveillance)**
Population	• Asymptomatic people from general population ○ Subpopulations: asymptomatic healthcare workers
Index test/ testing strategy	• Antibody tests (IgM and IgG): ○ As standalone tests ○ in triage ○ as add-on
Reference Standard	• RT-PCR tests • RT-PCR test combined with clinical assessment and/or CT imaging
Outcomes	Primary outcomes • Sensitivity, Specificity, Positive/Negative Predictive Value, Aarea Under the ROC Curve.
Study design	• Cohort and cross sectional diagnostic accuracy studies

Description	Project scope – Question 2 (Diagnosis of active infection)
Population	• Patients with symptoms for SARS-CoV-2 acute infection
Index test/ testing strategy	• Antibody tests (IgM and IgG) o standalone o in triage o add-on
Reference Standard	• RT-PCR tests • RT-PCR test combined with clinical assessment and/or CT imaging]
Outcomes	Primary outcomes • Sensitivity, Specificity, Positive/Negative Predictive Value, Area Under the ROC Curve.
Study design	• Cohort and cross sectional diagnostic accuracy studies *Case control studies will also be considered if no or very limited data available from cohort and cross sectional studies*

Description	Project scope – Question 3 (Seroprevalence)
Population	• General Population o Sub-populations: e.g. healthcare workers, blood donors
Testing strategy	• Any antibody test
Comparison	• Prevalence of SARS-CoV2 infection (acute and resolved infection) before seroprevalence study
Outcomes	• Seroprevalence • Difference in SARS-CoV-2 infection estimated prevalence in the same sample or population at different time points
Study design	• Cross sectional prevalence studies • Cohort studies

Description	Project scope – Question 4 (risk of transmission)
Population	• Patients recovered from SARS-CoV-2 infection (RT-PCR negative)
Testing strategy	• Antibody tests (IgM and IgG) in conjunction with RT-PCR
Outcomes	• Virus transmission due to RT-PCR re-positivity for acute SARS-CoV-2 infection
Study design	• Cohort studies

Description	Project scope – Question 5 (immunity)
Population	• Asymptomatic subjects with past and resolved SARS-CoV-2 infection
Intervention	• Antibody tests (IgM and IgG)
Outcomes	• Recurrence of SARS-CoV-2 acute infection
Study design	• Longitudinal cohort studies

Methods

A systematic information retrieval for relevant studies or documents was carried out to obtain comprehensive information using the following sources: MEDLINE, U.S. National Institutes of Health. ClinicalTrials.gov, World Health Organization. International Clinical Trials Registry Platform Search Portal. The PRESS (Peer Review of Electronic Search Strategies) checklist was used for the quality check of search strategies in bibliographic databases.
The last search was performed on 7 May 2020.
Selection of relevant studies was performed by two persons independently of each other using Covidence and discrepancies were resolved by discussion. Inclusion criteria for each research questions are reported In Table 0-2.

Table 0 - 2: Inclusion criteria for research questions

Characteristics	Research question 1: Surveillance	Research question 2: Diagnosis	Research question 3: Seroprevalence	Research question 4: Transmission	Research question 5 Immunity
Population	Asymptomatic people (in general population and/or subgroups such as healthcare workers)	Subjects with symptoms for SARS-CoV-2 acute infection	General population and subpopulations (i.e. healthcare workers, blood donors)	Patients recovered from SARS-CoV-2 acute infection (NAAT / PCR negative)	Asymptomatic subjects with past and resolved SARS-CoV-2 infection
Index test / Testing strategy	Any antibody test including laboratory based and point-of-care, quantitative and qualitative tests.				
Reference standard	Any testing strategy including NAAT or NAAT in combination with clinical findings or clinical Follow-up		Not applicable		
Outcome	2x2 table reporting sensitivity and specificity	2x2 table reporting sensitivity and specificity	Seroprevalence estimates	Virus transmission after repositivity for acute infection	Recurrence of SARS-CoV-2 acute infection
Study design	Cross-sectional studies, cohort studies	Cross-sectional and cohort diagnostic accuracy studies (case-control studies)	Cross-sectional studies, cohort studies	Cohort studies	Longitudinal cohort studies
Sample size	At least 10 human beings (or their blood samples) are included.				
Unit of analysis	Individual patient/subject				
Language	Full text references in English, Italian or German.				
NAAT: Nucleic acid amplification test, PCR: Polymerase chain reaction					

During the COVID-19 pandemic, sharing scientific information worldwide as quickly as possible became paramount, and most of the scientific literature has been made available in great haste and without being peer-reviewed. In order not to lose any potentially useful data, less appropriate study designs have been included in this first edition of the review, such as case control and retrospective cohort studies. Appropriate references and comments to quality of the information and uncertainty of the results have been made. The subsequent updates will apply more stringent inclusion criteria, as evidence of better quality is expected to become available.

The QUADAS-2 tool was used for the quality assessment of diagnostic accuracy studies. The assessment of risk of bias follows the criteria described in the two EUnetHTA guidelines on the internal validity of RCTs and non-randomised studies on interventions. Risk of bias was assessed at the study level.

Details on statistical analysis are reported in the main text.

Results

Overall,40 primary studies were included in this assessment and allocated to the appropriate research questions.
Results are summarized for each research question

Question 1: surveillance for early detection of new cases of SARS-CoV-2 infection in the general population and/or specific subpopulations

Most countries have initiated surveillance for SARS-CoV-2 infection either in sub-groups of the general population or in health,care workers. However, the evidence on the diagnostic accuracy of antibody test is still scarce and the data from the only two included studies did not allow calculations of pooled estimates.
In a screening program using two consecutive tests, it is of paramount importance that the triage test has a very high sensitivity, in order to identify asymptomatic people with acute SARS-CoV-2 infection. While waiting for results from adequate surveillance studies, the estimated accuracy of antibody tests over the course of the disease reported for symptomatic patients can provide some insights (see Table 4.3-2 in Question 2). The meta-analysis shows that sensitivity increases with time since infection/symptom onset. This finding is consistent with what is known about the immune response to infection. Unfortunately, point estimates of sensitivity and specificity in symptomatic population cannot be extrapolated to an asymptomatic population due to different pre-test probabilities. Nevertheless the observed trend in increasing sensitivity with time elapsed from infection to testing is expected to be valid also in asymptomatic people. Even if evidence is lacking, it can be assumed that sensitivity will be higher, for asymptomatic subjects tested in a late phase of infection. This dependence of test sensitivity with time implies that the test may more accurately identify asymptomatic subjects for whom isolation measures would be much belated with respect to their time of infectivity. In contrast, the test may less accurately identify subjects close to infection and with longer time to infect others, hindering early detection and prompt isolation of new cases at the onset of infection. Moreover, screening programs carried out weeks or months after start of epidemic will detect a growing number of subjects with past and resolved infection, affecting the specificity of the tests.

Question 2: diagnosis of SARS-CoV-2 infection in symptomatic patients

Nineteen studies were included and analysed to investigate the role of antibody tests in the diagnosis of SARS-CoV-2 infection in symptomatic patients. Most of the included studies did not have an adequate study design and the overall quality of the retrieved evidence is judged very low (Ta-

ble A3 – Appendix3) . Nevertheless, there was a sufficient number of studies to calculate pooled estimates, although high heterogeneity was found.

At week 1 from symptom onset the pooled estimates of sensitivity and specificity for tests combining IgG and IgM were:
Sen 33.8 (CI: 27 - 41.4) and Sp 92 (CI: 84.7 - 96) for rapid tests;
Sen 83.3 (CI: 50.9 - 97.1) and Sp 80 (69.3 - 87.8) for CLIA-based tests;
Sen 37.8 (CI: 27 - 49.9) and Sp 95.4 (CI: 8.6 - 100) for ELISA-based tests.

At week 2 from symptom onset, the pooled estimates of sensitivity and specificity for tests combining IgG and IgM were:
Sen 71.5 (CI: 65.7 - 76.6) and Sp 90.2 (CI: 75.9 - 96.4) for rapid tests;
Sen 87.9 (CI: 70.9 - 96) and Sp 80 (CI: 69.3 - 87.8) for CLIA based-tests;
Sen 84.8 (CI: 70.3 - 92.9) and Sp 95.4 (CI: 8.6-100) for ELISA based-tests.

Consistent with the expected course of development and detection of antibodies, both IgM and IgG resulted adequately detected from the second week of symptom onset. The combined detection of IgM and IgG seems to improve the diagnostic performance of serological tests.
No studies reported clinical effectiveness outcomes, thereforecalculations were performed to highlight benefits (i.e. symptomatic patients correctly diagnosed with COVID-19 or correctly classified as not infected with SARS-CoV-2) and risks (i.e. symptomatic patients incorrectly classified as COVID-19 patients or COVID-19 patients incorrectly classified as affected by another condition). Calculations were performed with data related to the first and second week from symptom onset, as these are the time windows during which patients typically seek healthcare and a diagnosis is made. The calculations showed a higher risk of misdiagnosis with antibody tests at week 1 than at week 2, with the molecular test RT-PCR performing better than any type of serological test in both time windows.

Question 3: measuring seroprevalence in communities

Seroprevalence studies have been recommended to understand how much the virus has spread during the pandemic, to provide baseline estimates for epidemiological surveillance using surveys at repeated intervals and for future information, should some form of immunity from re-infection be established. There are several surveys on-going on different target populations (general population, healthcare workers, blood donors etc.) and we report preliminary data from 17 studies published so far. Only three studies were judged at low risk of bias, and most of the studies presented issues of generalizability of results to the target population due to sample selection. The preliminary data are presented only in a descriptive way, as heterogeneity of studies did not allow any inference.

Question 4: ruling out of infection and risk of transmission in patients who have recovered from SARS-CoV-2

We did not identify studies that could be included for this research question and provide data on whether antibody tests are useful in ruling out risk of virus transmission in recovered COVID-19 patients. The Korea Centers for Disease Control and Prevention, after conducting an epidemiological and contact investigation on re-positive detected cases and their contacts, concluded that no evidence was found indicating infectivity for re-detected positive cases. Unfortunately, the role of antibody tests was not investigated in this study.

Question 5: assessing protective immunity of subjects with past SARS-CoV-2 infection

To date no studies have been retrieved investigating correlations between antibody presence or concentrations and protective immunity. No evidence was found suggesting that the presence of antibodies can confer immunity or any other form of protection against re-infection from SARS-CoV-2. While in three out of the four common coronaviruses causing milder respiratory diseases, reinfections are known to occur, uncertainties persist on the immune response to COVID-19 regarding the required level and durability of neutralising antibodies, as well as the correlation between IgG response and immunity. People who have recovered from COVID-19 will be advised and requested to continue observing public health advice and measures to control virus spread transmission.

Discussion

Given the sparseness of data on immunity and transmissibility, the present report focused on test accuracy of serological testing and on seroprevalence results. Data were heterogeneous and the validity of primary studies was far from good. Furthermore, test accuracy is insufficient to inform decisions on how to best implement or reduce isolation measures. Only very few data is currently available on SARS-CoV-2 transmission by recovering patients (question 4 of this report) and no valid information is there to estimate whether prior infections confers immunity (question 5). Antibody testing may support the diagnosis of SARS-CoV-2 (question 2), but the delayed development of IgM and IgG antibodies after infection strongly limits the practical use of these tests. For similar reasons, serological testing for screen and early disease detection (Question 1) is likely to prove unsuitable. The current role of antibody testing, therefore, would be mainly limited to estimating seroprevalence (question 3).

As expected, sensitivity and specificity of antibody tests increase over the first weeks after infection or symptom onset. For a full assessment of seroconversion over time, studies performing repetitive testing in infected patients are most valuable. The duration of antibody responses to SARS-CoV-2 is another open question, which is most relevant for immunity considerations. However, the aim of the present report was to assess potential application of antibody tests rather than the time course of seroconversion. Besides timing, other factors obviously affected test accuracy, as results were heterogeneous. It was not possible to identify specific attributes of studies, tests or enrolled subjects that might lead to lower test accuracy. Given the quickly evolving nature of this field, optimization and standardization of individual tests will probably lead to more homogeneous and reliable test results.

It is likely that the current data on test accuracy are overoptimistic, because the majority of contributing studies had a case-control rather than a cohort design. As cases were selected from symptomatic (or even severe) patients and control samples came from healthy volunteers, such studies mostly failed to include asymptomatic SARS-CoV-2 infections and patients with other viral diseases or symptoms typical for COViD-19. This selection process leads to spectrum bias, which causes overestimated test accuracy results. Specifically, the non-inclusion of other viral diseases precludes detecting cross-reactivity in these studies. Cohort studies could avoid this problem, but would in turn lead to an imperfect reference standard, because no valid test is available to rule out prior infection in a person who tested negative on antibody testing. Theoretically, virus neutralization tests could serve as an independent reference test, but such tests require highest levels of biosafety in the laboratory, and although preliminary results seem promising it is therefore likely that test accuracy will remain somewhat uncertain over the next weeks and months.

Due to the urgency of the situation, both, the present assessment and the included primary studies were performed very swiftly. This haste increases the risk of inaccuracies. In order to compensate for this problem, the assessment will be updated, as this not only allows to correct any shortcomings but also to include new evidence that has become available in the meantime.

Concluding summary

There is wide consensus that antibody tests can be used for estimating seroprevalence and for confirming prior SARS CoV-2 infection. Quite uncertain, however, is the potential role of serological testing in diagnosis of acute and asymptomatic cases, in ascertaining immunity (both on a individual and on a population level), in estimating transmissibility, in selecting plasma donors from Covid-19 convalescents, or in evaluating future vaccines against SARS CoV-2. Nevertheless, the many potential uses of antibody tests indicate that these tests deserve close attention in the forthcoming months.

Due to the low quality and the limited number of eligible studies, the present assessment confirms the persistence of uncertainty on the role of antibody tests in SARS-CoV-2 diagnosis and management. Since many studies are still ongoing and their results expected to become available in the near future, this assessment will be updated when evidence suitable to reduce this uncertainty will be published.

1. BACKGROUND

At the EUnetHTA Plenary Assembly held on the 1st and 2nd of April 2020 partners agreed that the collaborative network would take actions to be responsive to the COVID-19 pandemic and meet decision makers' urgent needs for trustworthy scientific information on the safety and effectiveness of disease management health technologies. Following this call, a small group of partners set up a EUnetHTA COVID-19 group to lay down a course of action involving a consultation with all partners aimed at setting up collaborative projects.

In April, the EUnetHTA Secretariat invited partners to share questions and requests for information posed by national decision makers as well as any on-going or published work carried out by the HTA bodies. A list of questions was obtained, ranging from patient screening and diagnosis to treatment and recovery, and a formal commitment was undertaken by the EUnetHTA Executive Board to sustain and facilitate collaborative work on assessment of COVID-19 related health technologies. A EUnetHTA Task Force on SARS-COV-2 diagnostics was subsequently set up which selected the following health policy questions:

- how to best screen asymptomatic subjects and monitor close contacts in order to promptly detect infections among the general population and healthcare workers;
- how to best test patients with clinical manifestations of SARS-CoV-2 in order to confirm a diagnosis of COVID-19;
- which tests should be used to monitor the course of disease and inform decisions on treatment, hospitalisation etc. and to determine viral clearance of recovered patients in order to allow re-entry into the community.

Diagnostic tests play a central role in the understanding of the disease and of its natural course. As diagnostic tools for SARS-CoV-2 infection evolve, a systematic and regularly updated review of the scientific evidence represents the basis for the understanding and correct interpretation of test results (2). A EUnetHTA Assessment Team convened for this Rapid Collaborative Review on the current role of antibody tests for novel coronavirus SARS-CoV-2 in the management of the pandemic and the Project Plan was published on the EUnetHTA website on 13th of May 2020 (https://eunethta.eu/sars-cov-2-antibody-tests/)

This report is the first output of the above-described collaborative effort. In order to provide timely information, this review was undertaken with very restricted timelines and as such, it differs from a standard EUnetHTA Relative Effectiveness Assessment, which requires longer timelines and the involvement of external experts and stakeholders. As a substantial body of evidence on the role of antibody tests is expected to develop and be published in the near future, this review will be updated as more evidence becomes available.

1.1. Overview of the disease, health condition and target population

The health condition in the scope of the present assessment is Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection and the associated disease named Coronavirus Disease 2019 (COVID-19).

The pandemic of coronavirus disease 2019 has suddenly and quickly affected most of the world. On 31 December 2019 the World Health Organization (WHO) received a first report of a pneumonia of unknown cause detected in Wuhan, China. One month later COVID-19 was declared a public health emergency (3).

Within three months of the first report, COVID-19 was characterised as a pandemic (4).

SARS-CoV-2 is a new strain of coronavirus identified in humans for the first time in 2019 in China, provisionally named “2019 novel coronavirus” (2019-nCoV) and “human coronavirus 2019” (HCoV-19 or hCoV-19) prior to the official definition by WHO (5, 6)

Coronaviruses are viruses circulating among animals of different species, such as bats who are natural hosts and act as reservoirs. Other beta-coronaviruses have spilled over infecting and spreading in humans, with respiratory droplets and fomites as primary routes of transmission. They cause illnesses ranging from a common cold to severe respiratory syndromes with high case fatality rates, such as those caused by SARS-CoV and MERS-CoV, mainly in Southeastern Asia in 2002 and Arabian Peninsula countries in 2012, respectively (6-8).

SARS-CoV-2 infection is closely related genetically to the SARS-CoV infection sharing disease severity and clinical features, while characterised by a higher basic reproduction number (R_0) (expected number of cases directly generated by one case in a fully susceptible population), estimated as between 2 to 4, leading to a faster and wider spread worldwide (7).

As SARS-CoV-2 was detected for the first time in humans in 2019, nobody has prior immunity, making the entire human population potentially susceptible to infection and disease (8). According to the available evidence, children and young adults showed lower risk of severe disease when infected, but this lower risk of SARS-CoV-2 infection is still debated, since absence of symptom affects chance of detection. Women also seem to experience less severe disease compared to men, with similar risk of infection at lower risk of hospitalisation and death (9).

The WHO has provided a definition of confirmed cases (a person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms) and of probable cases (a suspect case for whom testing for COVID-19 is inconclusive (10, 11).

The WHO assigned an emergency ICD-10 code of ‘U07.1 COVID-19, virus identified’ for disease diagnosis of COVID-19 confirmed by laboratory testing, and an emergency ICD-10 code of ‘U07.2 COVID-19, virus not identified’ for a clinical or epidemiological diagnosis of COVID-19 where laboratory confirmation is inconclusive or not available (12). Both codes should be used in mortality coding of cause of death (13).

In ICD-11, the code for the confirmed diagnosis of COVID-19 is RA01.0, while the code for the clinical diagnosis (suspected or probable) of COVID-19 is RA01.1 (14).

The transmissibility characteristics of SARS-CoV-2 infection and the susceptibility of the world population, led to over 7 million confirmed cases of infection and over 400,000 related deaths worldwide, from 31 December 2019 up to mid-June 2020. The European Union (EU) and European Economic Area (EEA) countries reached over one and a half million confirmed cases and over 170,000 deaths in the same time span (15).

The current underestimation of the virus spread is due to both the clinical spectrum of COVID-19, ranging from completely asymptomatic patients to severe Acute Respiratory Distress Syndrome (ARDS), and the differences in country-level testing strategies, initially aimed at prioritising those with higher symptom burden or at higher risk (16). Extended testing strategies including serologic surveys could provide more reliable data on infection spread.

While a decreasing trend in notification rates observed in 30 out of 31 EU/EEA countries and the UK by 4 of June 2020 has prompted lifting lockdown measures, social-distancing and preventive hygiene measures are still recommended to the General Population to avoid new epidemic waves (9). Moreover, contact-and-tracing activities are being implemented in order to control local outbreaks, while optimal testing strategies remain yet to be defined.

SARS-CoV-2 virions are 50–200 nanometres in diameter, composed by four structural proteins: the N (nucleocapsid) protein, holding the RNA genome, and the S (spike), E (envelope), M (membrane) proteins creating the envelope (17). The spike protein is responsible for virus attachment and fusion with host cells, and it has been found to have enough affinity to the angiotensin converting enzyme 2 (ACE2) receptor on human cells to use them as a mechanism of entry (18).

The affinity to ACE2 receptors allows SARS-CoV-2 to affect different human organs that express ACE2 protein, such as lung alveolar epithelial cells and enterocytes of the small intestine, causing a systemic disease (19).

Symptoms of COVID-19 vary greatly among infected people, ranging from no symptoms at all (asymptomatic people) to mild non-specific symptoms (pre-symptomatic people), up to severe respiratory distress syndromes and life threatening systemic complications, requiring admission to Intensive Care Units.

The proportion of asymptomatic people is yet to be defined since symptom-based screening strategies miss most of them, but estimates range from 5% to 80% of laboratory-confirmed COVID-19. Available evidence suggest that over 50% SARS-CoV-2 of individuals have no symptoms at the time of diagnosis (pre-symptomatic), and develop them over the following week (16).

For those who develop symptoms, the average incubation period (i.e. time from infection to symptom onset) lasts 5 to 6 days, ranging from 2 to 14 days (20). The clinical course of COVID-19 varies across individuals and could follow different stages, and each of these stages could progress towards more severe ones up to disease recovery or death (21).

COVID-19 usually starts as upper respiratory tract infection, with non-specific symptoms including the more common fever (45-80% of symptomatic cases) and cough (46-66%), followed by sore throat, fatigue, rhinorrhoea, headache, chest and back pain. However, many cases show different presentations, among which were gastrointestinal symptoms (i.e. diarrhoea, nausea, vomiting, poor appetite, and anorexia) neurological signs and symptoms (i.e. ageusia, anosmia) fainting, redness of eye, and rash (22). In mild or moderate cases, these symptoms can last for many days, up to weeks before complete recovery, while in severe cases, they usually worsen in the second week after symptoms onset including development of chest pain and dyspnoea, leading patients to seek for medical support (23). These symptoms are related to the establishment of a viral pneumonia, that in severe cases can be complicated by additional viral and bacterial infections, heart problems, and acute respiratory distress syndrome (ARDS), requiring intensive care and resulting in death in a high proportion of patients. In a minority of patients, pneumonia is followed by a systemic hyperinflammation status, leading to life-threatening complications including vasculitis, multi-organ failure, blood clots, and shock (23, 24).

Since the viral infection directly causes the first two phases of disease (i.e. early infection and lungs involvement) but plays a limited direct role in the systemic hyperinflammatory status - mainly driven by an uncontrolled host immunity response -, therapeutic strategies differ substantially and are still being tested in many ongoing clinical trials (23, 25).

The duration of the infectious period is still debated, and current available evidence shows potential transmission from two days before symptoms onset up to 7-12 days in moderate cases, or up to an average of two weeks in severe cases. However, uncertainties remain about transmission by asymptomatic persons, as well as from pet animals (8).

According to the European Centre for Disease Prevention and Control (ECDC) report, 35% of COVID-19 cases reported in the EU/EEA countries and the UK had been hospitalised at mid-June 2020. Among hospitalised patients, 11% required ICU and/or respiratory support, and the average mortality rate was 22%, although there was wide heterogeneity between countries (9). The im-

pact of COVID-19 on overall mortality in 24 European countries collaborating with the EuroMOMO network (European mortality monitoring activity) was 172,400 excess deaths from week 10 to week 22 during 2020, mainly driven by deaths in people over 65 years of age, but with mortality excess also in the age group 45-64 years and 15-44 years (26).

Several risk factors for severe COVID-19 progression have been recognised, but genetic and individual genetic susceptibility to SARS-CoV-2 infection and to life-threatening complications remain under investigation (27).

Sex might play a role, with women showing slightly higher or equal incidence of infection but lower risk of severe symptoms and death, compared to men. Age 70 or above is associated with higher risk of death, while infected children seem to be generally asymptomatic or with mild disease, even if the association between SARS-CoV-2 infection and a life-threatening systemic inflammatory disease in younger ages is still under investigation (8, 28). Finally, people with underlying health conditions (e.g. hypertension, diabetes, cardiovascular disease, chronic respiratory disease and cancer) are at higher risk of developing severe symptoms, hospitalization and death (8, 9).

1.2. Current diagnostic clinical practice

Diagnostic testing for SARS-CoV-2 infection is critical for tracking the viral spread, understanding epidemiology, informing case management, and reducing transmission (29).

In a document published on 16 of April 2020, the Organisation for Economic Co-operation and Development (OECD) identifies three main goals that testing strategies could achieve (30):

1) suppressing the resurgence of local outbreaks;

2) identifying people who have developed some form of immunity and can safely return to work;

3) gaining knowledge on the evolution of the pandemic, including on when a threshold for herd immunity has been reached.

Data on confirmed cases of SARS-CoV-2 infection are systematically collected and communicated in daily updated reports. The data on confirmed cases are based on all subjects diagnosed with real-time reverse-transcription polymerase chain reaction (RT-PCR) swab testing. Testing policies have varied during the outbreak of the pandemic. Following the recommendations by the WHO (31), the initial approach was to test those presenting with signs and symptoms for the disease and history of travelling or personal contact to persons with known or suspected SARS-CoV-2 infection, followed by more extensive testing also on asymptomatic or pauci-symptomatic subjects.

Diagnostic tests for SARS-CoV-2 infection are currently divided into two main categories: those that detect the presence of SARS-CoV-2 pathogen and are primarily used to diagnose an active COVID-19 infection, and those that detect the presence of an immune response to the pathogen through the presence of antibodies against SARS-CoV-2.

Pathogen detection tests include: molecular methods to detect viral RNA including RT-PCR, isothermal RNA amplification methods and genetic sequencing; antigen detection tests and viral culture (32).

Antigen detection tests are still in development, while genetic sequencing and viral culture are not recommended for routine diagnostic procedures (29). Compared with RT-PCR, reported advantages of loop-mediated Isothermal RNA amplification methods include a faster turnaround time and requiring fewer laboratory resources. At the time of writing this review these technologies were still in development and no CE marked devices were yet available (1).

As currently recommended by the WHO, routine confirmation of cases of COVID-19 in suspected subjects is based on detection of unique sequences of virus RNA by nucleic acid amplification tests (NAAT), such as RT-PCR, with confirmation by nucleic acid sequencing when necessary or feasible (29). RT-PCR, performed using nasopharyngeal swabs or other upper respiratory specimens, have to date been regarded as the most reliable means to diagnose SARS-CoV-2 infection. This technique has been proven reliable and feasible when public health emergencies need to be addressed. Nevertheless, some limitations have been highlighted, such as its suboptimal sensitivity (the ability to detect the virus in infected subjects), the long turnaround times and the need for specialised equipment and reagents and technically skilled staff (32). According to the available data, viral load seems to peak early in illness and then declines, although viral shedding has also been found to persist over several weeks (33). It is uncertain whether the virus still shed after resolution of symptoms is still infectious (34).

A large proportion of the general population is currently not undergoing any kind of testing, potentially meaning a serious underestimation of cases and thus compromising the potential effects of lockdown policies. The fast spread of SARS-CoV-2 infection in areas with high rates of hospitalisation has also raised the issue of how health workers are contributing to the spread of the disease within hospitals and in the community. Testing policies for the early detection of infected health workers have been implemented in order to activate prompt isolation and counteract transmission.

A testing strategy capable of reliably identifying subjects who have been (knowingly or unknowingly) infected and successfully recovered from the infection would permit to obtain a more accurate estimate of the prevalence of the disease and increase knowledge on how widely the virus has spread and circulated among the population.

1.3. Features of the intervention

1.3.1. Index test

Antibodies are produced as part of the body's immune response to infection, and tests that can detect these antibodies can provide information on a person's immune status. After infection, the first antibodies to appear in the blood are of the immunoglobulin A (IgA) and IgM type. IgA antibodies, which appear around the same time as the IgM, are mainly present in the mucosa and at lower concentrations in the blood. IgG antibodies appear later.

Following infection from SARS-CoV-2, IgM and IgG antibodies are produced and become detectable in most infected individuals within a time frame that can range from days to weeks from onset of symptoms (34).Data on timing of seroconversion vary among studies with window periods that can range from 15 to 20 days frome exposure and 9 to 15 days from symptoms onset (35). Generally, the presence of antibodies precedes viral load decline: viral load tends to peak early in illness before declining, whereas antibody titers increase in the subsequent two to three weeks post symptom onset (34).

Typically, IgM antibodies disappear in several weeks to months after infection, but IgG can remain present in the blood for many years, or even for the rest of the individual's life, potentially playing a role in protective immunity (1).

Antibody testing is based on the application of immunological reactions to capture the presence of IgA, IgM and IgG antibodies specific to SARS-CoV-2. These tests, called immunoassays, determine the immune response of the body against the SARS-CoV-2 virus, thus informing on past or on-going infection with the virus (1).

There are several types of immunoassays available, using different viral antigens for antibody detection, such as the spike (S), membrane (M), envelope (E), nucleocapsid (N) proteins. The most common antigens used for indirect assays are the recombinant spike protein, which contains the domain for attachment to the host cells, and the nucleocapsid protein, involved in the processes of the virus including viral replication, transcription and assembly (36).

The methods for detection include enzyme-linked immunosorbent assays (ELISAs), immunofluorescence assays (IFAs), lateral flow assays (LFA), chemiluminescence enzyme based immunoassay (CLIA), multiplex-bead array assays (MBAA) or luciferase immuno precipitation system (LIPS) (37).

The majority of antibody test methods do not require complex laboratory equipment and multiple sets of reagents. A drop of sample is usually used (either whole blood or serum/plasma) and time of execution and turnaround for a qualitative result (test positive or test negative) are claimed to be fast. Some tests analyse a unique antibody isotype (IgM or IgG) while others analyse both isotypes simultaneously (IgM and IgG). Tests that detect both IgG and IgM at the same time providing separate results, are considered superior to the ones testing for only one antibody isotype (1). Tests can be manual or automated and many of the available assays are immunochromatographic with results being visualised as coloured bands.

In Europe, tests for SARS-CoV-2 infection can be placed on market provided they are CE marked in accordance with the In Vitro Diagnostic Medical Devices Directive (IVDD; 98/79/EC). Under this Directive, manufacturers are required to specify device performance characteristics and self-declare conformity with the safety and performance characteristics outlined in the Directive. Self-tests for SARS-CoV-2 infection require independent assessment by a Notified Body to ensure the requirements of the IVD Directive are met (32).

After being placed on the market, the performance of the device can be further tested in order to confirm manufacturer's specifications, but this validation is not legally required, although highly recommended for public health decision making (1).

Two categories of commercial CE-marked tests can be distinguished: tests automated for use on analyser machines, and rapid tests, defined as qualitative or semi-quantitative devices, used singly or in a small series, which involve non-automated procedures and have been designed to give a fast result (38).

A large and growing number of antibody tests are commercially available, and a full list is available from the continuously updated EU database (1). At the time of writing this report, there are approximately 200 CE marked immunoassay antibody testing devices and four CE marked immunochromatography antibody testing devices listed in the JRC COVID-19 In Vitro Diagnostic Devices and Test Methods Database.

Antibody testing should not be considered as a competing alternative for RT-PCR testing, and both approaches are clinically relevant at different time points during the clinical course of infection (32). Measuring subjects' immune response to SARS-CoV-2 infection can represent an additional means to detect COVID-19, as the detection of IgM antibodies might imply recent or potentially active infection, while detection of IgG could identify past exposure. Development of neutralising IgG could in principle provide long-lasting immunity against re-infection with the same virus. However, several uncertainties surround antibody detection for SARS-CoV-2. There have been reports of patients not developing a humoral immune response and of others developing it very late in the illness. The relationship between development of antibodies and clinical outcome is still uncertain. Although greater severity of disease might correlate with higher antibody titers, these

do not seem to correlate with better outcomes (34, 39). In mild cases, seroconversion can take place after resolution of symptoms (40) .

Due to the lack of available knowledge on the validation and accuracy of antibody testing, these tests have not been recommended for clinical use. However, the ECDC has recommended collection and storage of serum samples from patients during the different phases of the disease to carry out studies on the validation of antibody tests and on seroconversion (41).

1.3.2. Reference standard

The chosen reference standard for acute infection is the test currently recommended by the WHO for routine confirmation of cases of COVID-19, i.e. detection of virus RNA by nucleic acid amplification tests (NAAT), such as RT-PCR (29) .

RT-PCR is routinely used to detect causative viruses from respiratory secretions. RT-PCR, performed on upper respiratory specimens or - most commonly - on nasopharyngeal swabs, was identified as the Reference Standard for acute infection in this assessment as it is considered the most reliable test to detect and measure viral RNA at this time. Viral RNA is detected through the measurement of the number of replication cycles required to produce a fluorescent signal, with lower values representing higher viral RNA (2).

There are consistent data indicating that - in general - the viral RNA becomes detectable as early as one day from onset of symptoms and starts to decline by the third week, subsequently becoming undetectable (2). Persistence of detectable viral load seems to vary with severity of illness, with mild cases achieving clearance earlier than severely ill or hospitalised patients (33), but cases of long persistence of viral shedding in asymptomatic and recovered patients have also been reported (42).

Although RT-PCR is considered a feasible and reliable technology to deploy in public health laboratories during international health emergencies (43), detection of viral RNA through RT-PCR performed on upper respiratory specimens cannot be considered as a gold standard for diagnosis of COVID-19, and its use as a reference standard must take into considerations some of its limitations.

Two systematic reviews on diagnostic accuracy of RT-PCR in COVID-19 suspected subjects reported a pooled sensitivity of 89% (44, 45). In its laboratory testing technical guidance, the WHO states that negative results by NAAT do not rule out the presence of COVID-19 infection (31), as false negative results could be due to several factors, ranging from timing of sample collection in relation to illness onset to poor quality of the specimen. Despite an estimated specificity of 98% (43), concerns have been expressed over the possibility of false positive results in recovered patients, as it has been suggested that positivity reflects the detection of viral RNA but does not necessarily indicate presence of transmissible virus (7).

Due to the above considerations, confirmation with RT-PCR plus clinical manifestations of COVID-19 (such as severe respiratory symptoms or CT scans suggestive of interstitial pneumonia) has also been considered as the Reference Standard.

Confirmation via nucleic acid sequencing and viral culture could have been considered as the Reference Standard, but they are not recommended and used as routine diagnostic practice (29).

2. OBJECTIVES AND SCOPE

The aim of this EUnetHTA Rapid Collaborative Review is to provide a reliable synthesis of the available evidence on a number of intended clinical uses of antibody tests. It comprises an assessment of the clinical benefit and safety of antibody tests in the management of the current SARS-CoV-2 pandemic.

This Rapid collaborative review will address the following questions:

Whether and with which testing strategies, antibody tests can be reliably used for:

1 surveillance for early detection of new asymptomatic cases of SARS-CoV-2 acute infection in the general population and/or specific subpopulations;

2 diagnosis of SARS-CoV-2 acute infection in patients presenting symptoms suggestive of SARS-CoV-2 infection:

How antibody tests can be used for:

3 measuring seroprevalence in communities;

4 ruling out risk of transmission in patients who recovered from SARS-CoV-2 infection;

5 assessing protective immunity in subjects with past and resolved SARS-CoV-2 infection.

This review does not assess the analytical performance of antibody tests and does not review performance assessment studies of test methods and devices for COVID-19. To retrieve such information the reader is invited to refer to the working document published on 16 of April 2020 by the expert group of the Joint Research Centre (JRC) set up by the European Commission (1), as well as the JRC COVID-19 In Vitro Diagnostic Devices and Test Methods Database which provides a continuously updated list of diagnostic devices that have been commercialised or are in development (https://covid-19-diagnostics.jrc.ec.europa.eu).

Five different PICO questions and scopes have been developed for the five questions stated in the objective.

Table 1 - 1: Scope of the assessment

Description	Project scope – Question 1 (surveillance)
Population	• Asymptomatic people from general population ○ Subpopulations: asymptomatic healthcare workers
Index test/ testing strategy	• Antibody tests (IgM and IgG) : ○ as standalone tests ○ in triage ○ as add-on
Reference Standard	• RT-PCR tests • RT-PCR test combined with clinical assessment and/or CT imaging
Outcomes	Primary outcomes • Sensitivity, Specificity, Positive/Negative Predictive Value, Area Under the ROC Curve.
Study design	• Cohort and cross sectional diagnostic accuracy studies

Description	Project scope – Question 2 (diagnosis of active infection)
Population	• Patients with symptoms for SARS-CoV-2 acute infection
Index test/ testing strategy	• Antibody tests (IgM and IgG) ○ standalone ○ in triage ○ add-on
Reference Standard	• RT-PCR tests • RT-PCR test combined with clinical assessment and/or CT imaging]
Outcomes	Primary outcomes • Sensitivity, Specificity, Positive/Negative Predictive Value, Area Under the ROC Curve.
Study design	• Cohort and cross sectional diagnostic accuracy studies *Case control studies will also be considered if no or very limited data available from cohort and cross sectional studies*

Description	Project scope – Question 3 (seroprevalence)
Population	• General Population ○ Subpopulations: e.g. healthcare workers, blood donors
Testing strategy	• Any antibody test
Comparison	• Prevalence of SARS-CoV2 infection (acute and resolved infection) before seroprevalence study
Outcomes	• Seroprevalence • Difference in SARS-CoV-2 infection estimated prevalence in the same sample or population at different time points
Study design	• Cross sectional prevalence studies • Cohort studies

Description	Project scope – Question 4 (risk of transmission)
Population	• Patients recovered from SARS-CoV-2 infection (RT-PCR negative)
Testing strategy	• Antibody tests (IgM and IgG) in conjunction with RT-PCR
Outcomes	• Virus transmission due to RT-PCR re-positivity for acute SARS-CoV-2 infection
Study design	• Cohort studies

Description	Project scope – Question 5 (immunity)
Population	• Asymptomatic subjects with past and resolved SARS-CoV-2 infection
Intervention	• Antibody tests (IgM and IgG)
Outcomes	• Recurrence of SARS-CoV-2 acute infection
Study design	• Longitudinal cohort studies

3. METHODS

3.1. Clinical effectiveness and safety

3.1.1. Information retrieval

A systematic information retrieval for relevant studies or documents was carried out to obtain comprehensive information. The following sources of information as well as search techniques were used.

Main information sources

- Bibliographic databases
  - MEDLINE

A preliminary search indicated that there is limited additional literature available on COVID-19 in Embase and Central. Therefore, a search in these standard sources was omitted:

- Study registries
  - U.S. National Institutes of Health. ClinicalTrials.gov
  - World Health Organization. International Clinical Trials Registry Platform Search Portal

The PRESS (Peer Review of Electronic Search Strategies) checklist was used for the quality check of search strategies in bibliographic databases.

The search strategies are displayed in Appendix 1. The last search was performed on 07 May 2020.

Further information sources and search techniques

To identify further relevant studies or documents, depending on the research question, further information sources are used and further search techniques are applied.

- Application of further search techniques
  - Screening of reference lists of included Systematic Reviews/Health Technology Aseessment reports
  - Searching preprint servers: Europe PMC
  - Hand search
- Queries to authors

3.1.2. Selection of relevant studies and documents

All selection steps were performed by two persons independently of each other. Discrepancies were resolved by discussion.

EndNote was used for citation management. Study selection was performed in Covidence.

Inclusion criteria differ by research question and are presented in Table **3.1**.

Table 3 - 1: Criteria for study inclusion and exclusion

Characteristics	Research question 1: Surveillance	Research question 2: Diagnosis e	Research question 3: Seroprevalence	Research question 4: Transmission	Research question 5: Immunity
Population	Asymptomatic people (in general population and/or subgroups such as healthcare workers)	Subjects with symptoms for SARS-CoV-2 acute infection	General population and subpopulations (i.e. healthcare workers, blood donors)	Patients recovered from SARS-CoV-2 acute infection (NAAT / PCR negative)	Asymptomatic subjects with past and resolved SARS-CoV-2 infection
Index test / Testing strategy	Any antibody test including laboratory based and point-of-care, quantitative and qualitative tests				
Reference standard	Any testing strategy including NAAT or NAAT in combination with clinical findings or clinical follow-up		Not applicable		
Outcome	2x2 table reporting sensitivity and specificity	2x2 table reporting sensitivity and specificity	Seroprevalence estimates	Virus transmission after re-positivity for acute infection	Recurrence of SARS-CoV-2 acute infection
Study design	Cross-sectional studies, cohort studies	Cross-sectional and cohort diagnostic accuracy studies (case-control studies)	Cross-sectional studies, cohort studies	Cohort studies	Longitudinal cohort studies
Sample size	At least 10 individuals (or their blood samples) are included.				
Unit of analysis	Individual patient/subject				
Language	Full text references in English, Italian or German.				
NAAT: Nucleic acid amplification test, PCR: Polymerase chain reaction					

During the COVID-19 pandemic, sharing scientific information worldwide as quickly as possible became paramount, and most of the scientific literature was made available in great haste and without being peer-reviewed. In order not to lose any potentially useful data, less appropriate study designs have been included in this first edition of the review, such as case control and retrospective cohort studies. This has been deemed necessary in order to promptly provide decision makers with the available, albeit incomplete, information to balance benefits and harms of antibody test's deployment (46). Appropriate references and comments related to quality of the information and uncertainty of the results have been made. The updates that will follow, however, will apply more stringent inclusion criteria, as evidence of better quality is expected to become available.

3.1.3. Data extraction

The following study characteristics were extracted by authors and co-authors for all included studies.

- Study characteristics: year, country, study design, stated objective and conclusion of the authors, flow and timing, related research question.

- Participants: Inclusion criteria, exclusion criteria, population, number of participants, age, sex, underlying health conditions, COVID-19-related symptoms, time since onset of symptoms, target condition.

- Index test: Antibody test class, (commercial) name of index test, manufacturer, target, sample type, setting of index test, reported cut-off values, reported analytical sensitivity, reported analytical specificity, regulatory status.

- Reference test: Reference standard, sample type, setting of reference test.

- Outcome: Diagnostic accuracy outcome measures (sensitivity, specificity, true and false positives, true and false negatives)

All necessary information for the assessment was extracted from the documents on the included studies into standardised tables. If discrepancies arose in the comparison of the information from different documents on a study (but also from multiple data on an aspect within a document itself) which could have a considerable influence on the interpretation of the results, this is shown in the corresponding places in the results section of the report.

3.1.4. Quality rating / Risk of bias assessment

The QUADAS-2 tool (47) was used for the quality assessment of diagnostic accuracy studies. Risk of bias was assessed at study level.

3.1.5. Data analyses and synthesis

The information in the included documents on study design, study methods, populations, endpoints (patient relevance, validity, and operationalisation) and study results were evaluated. The results of this evaluation are presented and are used for identification of relevant analyses and considered for the conclusions of the assessment report.

3.1.5.1. Effect measures (Diagnostic accuracy studies)

The measures are based on 2 x 2 tables for true positives (TP), false negatives (FN), false positives (FP) and true negatives (TN). The calculations are as follows:

Sensitivity = TP / (TP + FN)

Specificity = TN / (TN + FP)

Positive predictive value = TP / (TP + FP)

Negative predictive value = TN / (TN + FN)

95% confidence intervals for these measures were calculated based on the score method (48, 49). The predictive values are highly dependent on the prevalence. Thus, predictive values have to be interpreted with caution when representative prevalence cannot be estimated.

3.1.5.2. Meta-analyses

Overall, the extracted 2 x 2 tables compose a complex data set. Multiple antibody targets were analysed for several testing methods within a study, subjects were measured multiple times with the same test, and the 'negative' subjects for the specificity were sampled in different ways (e.g. samples from blood donors from the pre-COVID-19 era, PCR-negative subjects with and without symptoms). Thus, the basic assumption for bivariate meta-analysis cannot be presumed, i.e. that the pairs of sensitivity and specificity are on one Receiver Operating Characteristics Curve (ROS). Therefore, univariate meta-analyses were performed for sensitivity and specificity. Furthermore, separate meta-analyses were performed for combinations of the following three factors:

1. The type of test:
    - rapid diagnostic test (RDT)
    - enzyme-linked immunosorbent assay (ELISA)
    - chemiluminescent immunoassay (CLIA)
2. Antibody target:
    - IgM
    - IgG
    - IgM and/or IgG
3. Period from the time of the onset of symptoms:
    - overall
    - week 1
    - week 2
    - week 3
    - week 4

Assignment of data to specific periods of the time of the onset of symptoms was carried out.

3.1.5.3. Subgroup characteristics and other effect modifiers

The results were examined with regard to potential effect modifiers, i.e. factors influencing the effects. The aim was to uncover possible differences in effects between time periods and assays.

In order to evaluate the variation of the diagnostic measures in time from the onset of symptoms, the data were divided into time periods of one week. If data were provided in shorter time periods or different periods, attempts were made to assign the data to one of the designated periods to reduce redundancies. Data from later time points were aggregated in one period in order to guarantee that sufficient data are available. Furthermore, for the overall analysis as well as the analysis by period, each subject was considered only once for each specific combination.

If more than one 2 x 2 was identified for a specific combination, a univariate meta-analysis for sensitivity and specificity was performed with a generalized linear mixed model (50, 51). The measure of between-study heterogeneity, τ, corresponds to the width of the underlying distribution of random effects in terms of the standard deviation.The meta-analyses of sensitivity and specificity might be hampered if the between-study heterogeneity cannot be reliably estimated (52). This might be the case in the presented results, especially if only few sparse 2 x 2 tables, containing cells with small counts and/or zeros, were available.

As considerable heterogeneity was identified for the meta-analyses of sensitivity and specificity, no meta-analyses were performed for the predictive values.

Software

The data analysis for this report was generated using SAS/STAT® software (version 15.1).

3.2. Division of work within the project

Regione Emilia-Romagna (RER), as first author, conceived the idea of this assessment, developed the Project Plan, took part in the screening of studies, in the data extraction of the included studies, regularly updated the EndNote database and managed the citations, wrote the drafts and final report.

Institute for Quality and Efficiency in Health Care (iqwig), as co-author, carried out all the statistical analyses, the literature search, set up the Covidence database, took part in the screening of studies, in the data extraction of the included studies, set up and regularly updated the EndNote database, contributed to, read and approved drafts, final Project Plan, and final report.

Health Technology Wales, as co-author, contributed to the literature search and the data extraction of the included studies, reviewed, and approved the draft and final report.

Health Information and Quality Authority (HIQA) and NHS Healthcare Improvement Scotland, as dedicated reviewers, reviewed the first and second drafts of this assessment, provided valuable comments and timely feedback and contributed to the editing the whole document.

3.3. Deviations from project plan

Health Technology Assessment Wales joined the Assessment Team after the Project Plan was published and it is now reported among the Co-authors.

To clearly distinguish a diagnostic role of antibody tests from other intended use, the order of the five objectives of the Project Plan has been re-arranged.
The Project Plan reported inclusion criteria only for diagnostic accuracy studies, relevant for research question 1 and 2, and failed to report detailed inclusion criteria for the remaining questions 3a, 3b and 3c. This information has been integrated in the full report. There was no time to report results from the search for ongoing studies, but these will be monitored in view of the next update of this report.

4. RESULTS: CLINICAL EFFECTIVENESS AND SAFETY

4.1. Information retrieval

Figure 1: Flow chart of information retrieval for the diagnostic accuracy of antibody tests and/ or on their potential use in different scenarios.

shows the results of the information retrieval in the main and further information sources based on the predefined inclusion criteria. References of the documents that have been checked in full-texts but were excluded are presented in Appendix 2 with the reason for their exclusion.

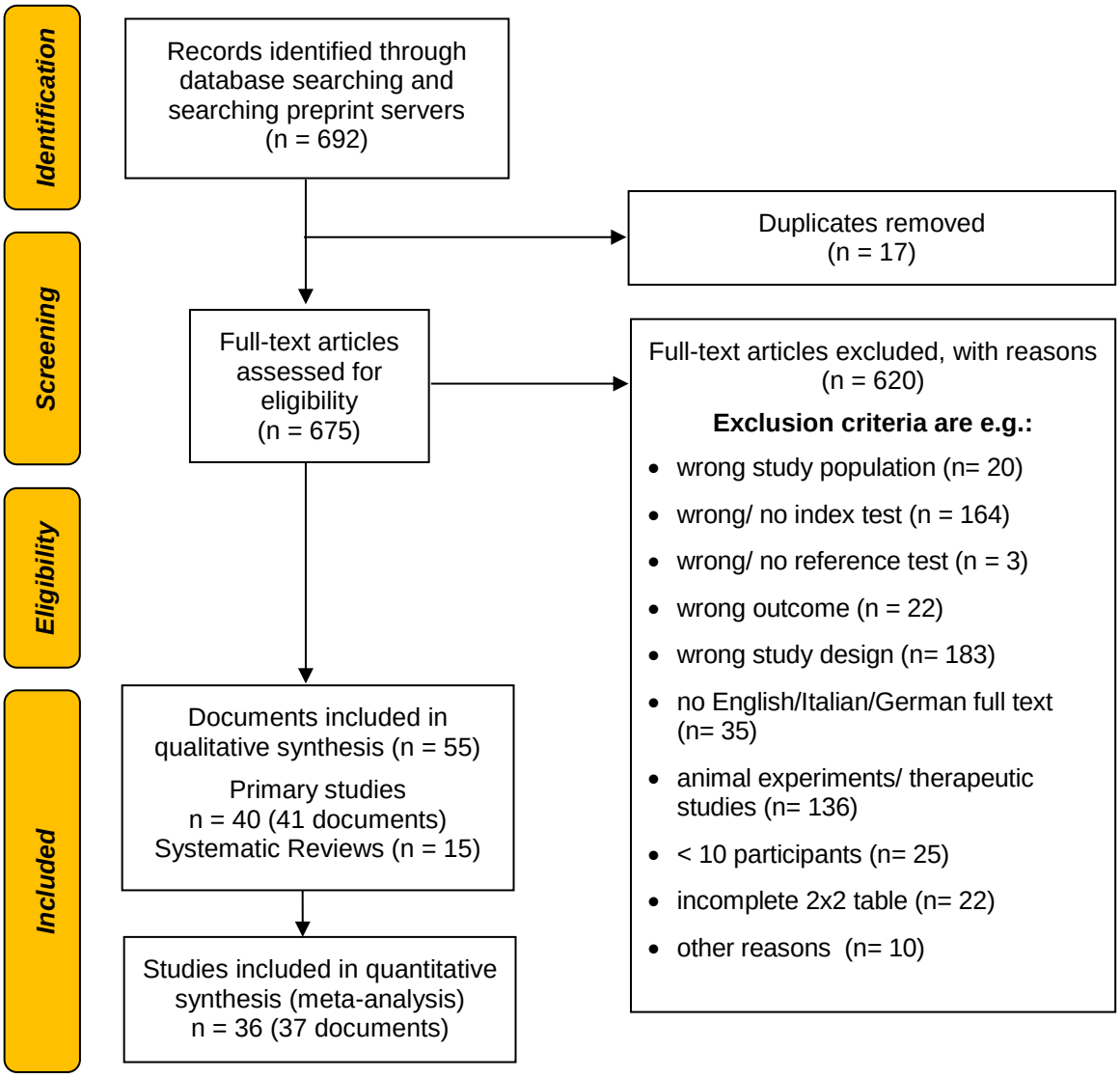

Figure 1: Flow chart of information retrieval for the diagnostic accuracy of antibody tests and/ or on their potential use in different scenarios.

Information retrieval identified 40 studies (41 documents) as relevant for the research questions. The last search took place on 7th of May 2020.

4.2. Studies included in the assessment

The full list of the relevant studies used for this assessment is reported in Appendix 2 (Table A1), An overview of the included studies is reported for each research question.

4.3. Description of the evidence used

The table of the characteristics of the included studies (Table A2) and the table reporting the risk of bias of the included diagnostic accuracy studies (Table A3) are presented in Appendix 3. A narrative description of the evidence used is reported for each research question.

Results presented in the following sections for each research question.

4.4. Question 1

What role can antibody tests have in general and/or specific population surveillance programmes for the early detection of new cases of SARS-CoV-2 infection in asymptomatic people?

Rationale

A robust surveillance strategy is paramount to flattening the COVID-19 epidemic curve. Effective testing strategies are the core means to meet some of the surveillance objectives identified by the ECDC, such as monitoring the intensity, geographic spread and severity of COVID-19 in the population, monitoring changes in risk groups and monitoring the impact of any mitigation measures (53). At the national level the following additional objectives have been identified: detection and containment of nosocomial outbreaks to protect healthcare workers and patients, as well as detection and containment of outbreaks in long-term facilities and other closed communities. The WHO strongly recommends active case finding and testing as well as contact tracing in all transmission scenarios (11, 54). In the EU document on testing strategy, effective – i.e. timely and accurate – testing is recommended to support decisions on infection control strategies and to detect asymptomatic cases that need to be isolated in order to avoid further spread of the virus (55).

In the absence of a vaccine and with limited effective targeted treatments available, isolation remains the most effective way of containing spread of SARS-CoV-2 infection, especially when accompanied by efficient contact tracing (56, 57). The ECDC document on contact tracing for COVID-19 reports extensive evidence on the effectiveness of this public health measure in reducing transmission and in increasing safety of de-escalation measures (58).

The ECDC and WHO recommend molecular tests for detection of the SARS-CoV-2 virus RNA, which require specific laboratory equipment and highly skilled professionals. Due to the substantial amount of resources required, the use of molecular test in comprehensive surveillance programmes could put a strain on national health systems' capacity. While less resource intensive molecular tests with faster turnaround are still in development (59), the availability of reliable serological tests may contribute to expand testing capacity and to relieve pressure on resources.

A systematic review of the literature was undertaken in order to address the following questions:

- What is the diagnostic accuracy of antibody tests in general population surveillance programs for the early detection of new cases of SARS-CoV-2 infection?

- What is the diagnostic accuracy of antibody tests in healthcare workers' and other high-risk groups' surveillance programs for the early detection of new cases of SARS-CoV-2 infection?

The purpose of this intended use of antibody tests is to promptly isolate asymptomatic and pre-symptomatic subjects testing positive for acute SARS-CoV-2 infection and activate contact tracing in order to avoid transmission, and to provide early healthcare expected to improve clinical out-

comes. Subjects testing negative will safely remain within their own living and working community and continue to exercise all necessary and prescribed protective behaviour.

Important patient outcomes to be taken in consideration for assessing relative effectiveness of the use of antibody tests in the general population for surveillance purposes are listed in Table 4 – 1.

Table 4 - 1: Patient important outcomes for question 1

Patient important outcomes	
BENEFITS	**RISKS**
Individuals are diagnosed with acute SARS-CoV-2 infection at an early stage, are promptly isolated and receive necessary healthcare. Contact tracing is promptly activated (True Positive)	Individuals are incorrectly diagnosed with acute SARS-CoV-2 infection, unnecessarily withdrawn from the community and might receive inappropriate health interventions. Their contacts are unnecessarily traced (False Positive)
Individuals have their healthy status confirmed and remain safely in the community (True Negative)	Individuals and their contacts are misclassified as being healthy/not at risk, remain in the community representing a risk of transmission to others (False Negative)

Results

Our research strategy yielded two studies meeting our inclusion criteria (60, 61)

The first study (60) investigated the diagnostic accuracy of antibody tests (MCLIA) in 164 asymptomatic close contacts of confirmed COVID-19 patients. All the 16 individuals thattested positive by RT-PCR at the beginning of February 2020 resulted positive for IgM and/or IgG on 1March 2020. Additionally, positive antibody results were found in 7 individuals previously tested negative by RT-PCR. In the second study (61),142 healthcare workers being dispatched to Hubei as well as 284 healthcare workers remaining in Hefei were tested using both antibody test (CLIA) and RT-PCR. In the group dispatched to Hubei, tests were applied on the same day upon return, while in the other group timing of the tests was not reported. None of the tests showed positive results.

Due to the limited number of studies, we could not perform calculations of sensitivity and specificity estimates applicable to asysmptomatc general population or to the subgroup ofasymptomatic healthcare workers subgroup.

Summary and discussion

Most countries have initiated surveillance for SARS-CoV-2 infection either in sub-groups of the general population or in healthcare workers. However, the evidence on the diagnostic accuracy of antibody test is still scarce and the data from the only two included studies did not allow pooled estimates calculations.

In a screening program using two consecutive tests, it is of paramount importance that the triage test has a very high sensitivity in order to identify asymptomatic people with acute SARS-CoV-2 infection. While waiting for results from adequate surveillance studies, the estimated accuracy of antibody tests over the course of the disease reported for symptomatic patients can provide some

insights (see Table 4-2 in Question 2). The meta-analysis shows that sensitivity increases with time since infection/symptom onset.This finding is consistent with what is known about the immune response to infection. Unfortunately, point estimates of sensitivity and specificity in symptomatic population cannot be extrapolated to an asymptomatic population due to different pre-test probabilities. Nevertheless, the observed trend in increasing sensitivity with time elapsed from infection to testing is expected to be valid also in asymptomatic people. Even if evidence is lacking, it can be assumed that sensitivity will be higher for asymptomatic subjects tested in a late phase of infection. This dependence of test sensitivity with time implies that the test may more accurately identify asymptomatic subjects for whom isolation measures would be much belated with respect to their time of infectivity. In contrast, the test may less accurately identify subjects close to infection and with longer time to infect others, hindering early detection and prompt isolation of new cases at the onset of infection. Moreover, screening programs carried out weeks or months after start of epidemic will detect a growing number of subjects with past and resolved infection, affecting the specificity of the tests.

4.5. Question 2

What role can antibody tests have in diagnosing SARS-CoV-2 infection in patients presenting symptoms suggestive of SARS-CoV-2 infection?

Rationale

As currently recommended by the WHO, routine confirmation of COVID-19 in suspected subjects is based on detection of unique sequences of virus RNA by nucleic acid amplification tests (NAAT), such as RT-PCR, with confirmation by nucleic acid sequencing when necessary or feasible (29). Researchers and study authors reporting on characteristics of patients and on COVID-19 outbreak patterns and trends have used the WHO definitions of confirmed and probale cases of SARS-CoV-2 infections (62, 63). A substantial body of research reveals a high incidence of “probable cases”, i.e. COVID-19 patients in whom RT-PCR test does not confirm presence of virus RNA (64, 65).

The current sub-optimal sensitivity of RT-PCR (42, 43) is a serious cause for concern, while the broad spectrum of symptoms – common to other influenza-like conditions – calls for a testing strategy that allows effective and timely differential diagnosis. Some studies have suggested a potential added value in the inclusion of serological tests within the diagnostic work up for COVID-19 in patients with SARS-CoV-2 symptoms and in patients presenting late in illness when viral load might have started to decrease (2, 66, 67).

A systematic review of the literature was undertaken in order to address the following questions:

- What is the diagnostic accuracy of antibody tests in diagnosing acute SARS-CoV-2 infection in patients presenting symptoms suggestive of SARS-CoV-2 infection?

The purpose of this intended use of the antibody tests is to place a prompt diagnosis of COVID-19 for subjects testing positive in order to initiate treatment, place the patient in isolation and activate contact tracing. Differential diagnosis and appropriate care for other conditions is provided for subjects testing negative.

Results

Inclusion criteria for studies addressing this question were cross-sectional and cohort studies, enrolling symptomatic patients, performing any serological antibody test including laboratory based and point-of-care, quantitative and qualitative tests, reporting data that allowed the construction of a contingency table reporting sensitivity and specificity. Case-control studies were also included at this first stage of the review.

Nineteen studies were included in this analysis, of which 10 studies assessed rapid tests (35, 68-76), 7 studies assessed CLIA-based tests (72, 77-81), and 7 studies assessed ELISA-based tests, and 7 studies assessed ELISA-based tests (35, 72, 73, 77, 82-84) . Of the included studies only 4 met our study design inclusion criteria and presented a cross-sectional or cohort design, the remaining 15 were case-control studies or retrospective cohort studies. Of the four studies meeting our inclusion critery for study design, one was judged at high risk of bias and presented concerns for applicability to our research question (70) while the remaining three were judged at moderate risk of bias and low concerns for applicability (69, 71, 74), The case control and retrospective cohort studies were all judged at high risk of bias and presented concerns for applicability to our research question.

Despite the substantial number of retrieved studies, the overall quality of the evidence is considered very low, meaning that we expect results from future well-conducted and good quality studies to change the estimates reported in the results.

Diagnostic accuracy

We first report pooled estimates for tests combining IgM and IgG, as these are the most used ones in clinical practice. Separate pooled estimates are reported for the three types of tests (rapid, CLIA-based and ELISA-based) calculated overall, i.e. irrespective of test timing since symptom onset, and at week 1, 2, 3, and 4 since symptom onset (Table 4-2). In Tables 4-3 and 4-4 results are reported for IgM and IgG. All data extracted from each study and detailed pooled estimates are reported in the Appendix (Tables A4 and A5).

Separate results for IgM and IgG are reported in Tables 4-3 and 4-4. The pooled estimates confirm the progress overtime of the development of antibodies, with IgM and IgG detection picking up more or less at the same time and from the second week from symptom onset.

As most patients typically seek healthcare and receive diagnostic testing within the first two weeks from symptom onset, we considered the estimates of diagnostic accuracy of antibody tests carried out at week 1 (0-7 days from symptoms) and at week 2 (8-14 days from symptoms) to be most relevant.

At week 1 from symptom onset, the pooled estimates of sensitivity and specificity for tests combining IgG and IgM were:
Sen 33.8 (CI: 27 - 41.4) and Sp 92 (CI: 84.7 - 96) for rapid tests;
Sen 83.3 (CI: 50.9 - 97.1) and Sp 80 (69.3 - 87.8) for CLIA-based tests;
Sen 37.8 (CI: 27 - 49.9) and Sp 95.4 (CI: 8.6 - 100) for ELISA-based tests.

At week 2 from symptom onset, the pooled estimates of sensitivity and specificity for tests combining IgG and IgM were:
Sen 71.5 (CI: 65.7 - 76.6) and Sp 90.2 (CI: 75.9 - 96.4) for rapid tests;
Sen 87.9 (CI: 70.9 - 96) and Sp 80 (CI: 69.3 - 87.8) for CLIA based-tests;
Sen 84.8 (CI: 70.3 - 92.9) and Sp 95.4 (CI: 8.6-100) for ELISA based-tests.

Tables 4-2, 4-3 and 4-4 report heterogeneity for the above estimates, which is also shown by the wide confidence intervals of the pooled estimates.

We could only retrieve data on head-to-head comparisons between antibody tests and RT-PCR and cannot provide pooled estimates of sensitivity and specificity of antibody tests used in triage or as add-on to RT-PCR.

Pre-test probability

A pre-test probability of 57% was calculated from the cohort studies included, which is applicable to patients suspected to have COVID-19 during a peaking epidemic (not applicable to the general population and/or periods where infection transmission has decreased).

Table 4 - 2: Sensitivity and Specificity estimates for IgM+IgG tests

RAPID DIAGNOSTIC TESTS					
Time since symptoms onset **Pooled estimate**	**Overall** **(9 studies)**	**Week 1** **(12 studies)**	**Week 2** **(13 studies)**	**Week 3** **(13 studies)**	**Week 4** **(10 studies)**
Sensitivity **overall**	68.8 (46.3 - 85)	33.8 (27 - 41.4)	71.5 (65.7 - 76.6)	81.6 (71.9-88.5)	87.8 (78.4-93.4)
Heterogeneity τ^2	1.39	0.08	0.10	0.51	0.0
Specificity	93.2 (71.8 – 98).7	92 (84.7 – 96)	90.2 (75.9 - 96.4)	89.7 (72.8 - 96.6)	92.1 (83.2 - 96.5)
Heterogeneity τ^2	4.14	0.87	2.54	3.23	0.95
CLIA (chemiluminescent immunoassay) 4 studies					
Time since symptoms onset **Pooled estimate**	**Overall** **(2 studies)**	**Week 1** **(1study)**	**Week 2** **(1study)**	**Week 3** **(1 study)**	**Week 4** **No studies**
Sensitivity **overall**	91.8 (9.4-99.9)	83.3 (50.9-97.1)	87.9 (70.9-96)	97.1 (82.9-99.8)	-
Heterogeneity τ^2	0.0				-
Specificity	76.5 (14.3-98.4)	80 (69.3-87.8)	80 (69.3 - 87.8)	80 (69.3-87.8)	-
Heterogeneity τ^2	0.0				-
ELISA (enzyme-linked immunosorbent assay)- 2 studies					
Time since symptoms onset **Pooled estimate**	**Overall** **(2 studies)**	**Week 1** **(3 studies)**	**Week 2** **(3 studies)**	**Week 3** **(3 studies)**	**Week 4** **(3 studies)**
Sensitivity **overall**	84.5 (21.8 - 99.1)	37.8 (27 - 49.9)	84.8 (70.3 - 92.9)	88.1 (56.4 - 97.7)	90.7 56. 5-98.7
Heterogeneity τ^2	0.06	0.0	0.0	0.16	0.0
Specificity	98.5 (0 - 100)	95.4 (8.6 - 100)	95.4 (8.6 – 100)	95.4 (8.6 - 100)	95.4 (8.6 - 100)
Heterogeneity τ^2	19.0	3.48	3.48	3.48	3.48

Table 4 - 3: Sensitivity and Specificity estimates for IgM tests.

RAPID DIAGNOSTIC TESTS					
Time since symptoms onset Pooled estimate	**Overall (4 studies)**	**Week 1 (10 studies)**	**Week 2 (11 studies)**	**Week 3 (11 studies)**	**Week 4 (9 studies)**
Sensitivity	61.5 (14.7 - 93.7)	28 (20.8 - 36.5)	63.6 (47.9 - 76.8)	63.2 (50.3 - 74.5)	86 (66.4 - 95.1)
Heterogeneity τ^2	1.88	0.09	0.77	0.40	1.14
Specificity	91.8 (57.8 - 98.9)	92.1 (85 - 96)	90.4 (81 - 95.4)	89.9 (80 - 95.2)	92.3 (84.5 - 96.3)
Heterogeneity τ^2	1.59	0.57	0.94	1.04	0.63
CLIA (chemiluminescent immunoassay)					
Time since symptoms onset Pooled estimate	**Overall (6 studies)**	**Week 1 (2 studies)**	**Week 2 (2 studies)**	**Week 3 (2 studies)**	**Week 4 (1 study)**
Sensitivity	90.4 (82.1 - 95)	78.5 (1.2 - 99.9)	96 (0 - 100)	98 (0 – 100)	100 (93.6 - 100)
Heterogeneity τ^2	0.30	>0.0	5.67	2.11	-
Specificity	95.5 (88 - 98.4)	88.6 (7.3 - 99.9)	88.6 (7.3 - 99.9)	88.6 (7.3 - 99.9)	92.3 (89.5 - 94.5)
Heterogeneity τ^2	0.91	0.20	0.20	0.20	-
ELISA (enzyme-linked immunosorbent assay)					
Time since symptoms onset Pooled estimate	**Overall (4 studies)**	**Week 1 (3 studies)**	**Week 2 (3 studies)**	**Week 3 (4 studies)**	**Week 4 (2 studies)**
Sensitivity	83.9 (31.1 - 98.4)	33.6 (12.6 - 64)	75.6 (45.3 – 92,1)	83.9 (56,1 -95,5)	82.9 (6.2 - 99.7)
Heterogeneity τ^2	2.11	0.12	0.20	0.58	0.0
Specificity	99.8 (22.1 - 100)	99.9 (0.6 – 100)	99.9 (0,6 -100)	99,9 (7,7 -100)	99 (0 - 100)
Heterogeneity τ^2	12.27	6.78	6,78	7,33	1.19

Table 4 - 4: Sensitivity and Specificity estimates for IgG tests

RAPID DIAGNOSTIC TESTS					
Time since symptoms onset Pooled estimate	**Overall (3 studies)**	**Week 1 (10 studies)**	**Week 2 (11 studies)**	**Week 3 (11 studies)**	**Week 4 (9 studies)**
Sensitivity	67.4 (22.9 - 93.5)	26.9 (21.5 - 33.1)	62.1 (54.7 - 69.1)	73.9 (60.8 - 83.9)	82.8 (71.8 - 90.1)
Heterogeneity τ^2	0.56	0.0	0.12	0.56	0.0
Specificity	85.6 (0.3 - 100)	94.5 (89.5 - 97.2)	92.8 (78.2 - 97.9)	92.4 (75.2 - 98)	95 (90 - 97.6)
Heterogeneity τ^2	8.76	0.42	2.90	3.63	0.40
CLIA (chemiluminescent immunoassay)					
Time since symptoms onset Pooled estimate	**Overall (5 studies)**	**Week 1 (2 studies)**	**Week 2 (2 studies)**	**Week 3 (2 studies)**	**Week 4 (1 study)**
Sensitivity overall	91.1 (82 - 95.9)	62.2 (1.5 - 99.5)	88.3 (0 – 100)	98.9 (0 – 100)	100 (93.6 - 100)
Heterogeneity τ^2	0.27	0.0	1.01	0.0	-
Specificity	98 (96.7 - 98.8)	99.4 (0.1 - 100)	99.4 (0.1 – 100)	99.4 (0.1 – 100)	99.8 (98.7 - 100)
Heterogeneity τ^2	0.02	0.90	0.90	0.90	-
ELISA (enzyme-linked immunosorbent assay)					
Time since symptoms onset Pooled estimate	**Overall (3 studies)**	**Week 1 (2 studies)**	**Week 2 (2 studies)**	**Week 3 (3 studies)**	**Week 4 (2 studies)**
Sensitivity overall	74.9 (1.6 - 99.8)	37.8 (3.5 - 91)	78.4 (17.4 - 98.4)	87.5 (75.7 - 92.1)	87.6 (1.9 -100)
Heterogeneity τ^2	4.1	0.0	0.01	0.0	0.0
Specificity	99.8 (86.2 - 100)	98.7 (0 - 100)	98.7 (0 - 100)	96.9 (19.9 - 100)	98.7 (0 – 100)
Heterogeneity τ^2	0.0	10.05	8.25	2.61	8.25

Relative effectiveness / Risks and benefits assessment

The main objective of the test in this intended use would be the diagnosis and care for COVID-19 as well as prompt isolation of subjects from other patients or households. Important patient outcomes to be taken in consideration for assessing relative effectiveness of the use of antibody tests in diagnosing symptomatic patients are listed in Table 4 – 5.

Table 4 - 5: Patient important outcomes for question 2

Patient important outcomes	
BENEFITS	**RISKS**
Symptomatic subjects are diagnosed with COVID-19 at an early stage of disease, are promptly isolated and receive necessary healthcare. Contact tracing is activated (True Positive)	Symptomatic subjects are incorrectly diagnosed with SARS-CoV-2 infection, might receive inappropriate health interventions and are unnecessarily put in isolation. Their contacts are unnecessarily traced (False Positive)
Symptomatic subjects are correctly classified as not infected with SARS-CoV-2 and might be diagnosed and receive healthcare for other condition; no contact tracing for SARS-CoV-2 infection is activated (True Negative)	Symptomatic subjects are incorrectly diagnosed for a condition other than SARS-CoV-2 infection, might not receive appropriate care, are not placed in isolation and their contacts are not traced, representing a risk of transmission to others (False Negative)

As the included studies neither provide any data on clinical outcomes, nor compare different testing strategies, natural frequencies (85) for a risk-benefit relative assessment have been calculated, applying the diagnostic accuracy estimates of the differente tests on a hypothetical population of 1,000 symptomatic patients being tested for SARS-CoV-2 acute infection. The calculations were developed for the following scenarios:

- Symptomatic patients presenting at 0-7 days from symptom onset (week 1)
- Symptomatic patients presenting at 8-14 days from symptoms onset (week 2)

Symptomatic patients presenting within 7 days of symptom onset (week 1) and undergoing a rapid serological test, CLIA-based test, ELISA-based test or RT-PCR

With an estimated prevalence of disease of **57%** we would expect **570 s**ubjects with acute infection from SARS-CoV-2 out of a 1,000 tested. The estimated sensitivities and specificities at week 1 are 33.8% and 92%, respectively, for rapid serological tests, 83.3 % and 80% for CLIA-based test, 37.8% and 95.4% for ELISA-based test and 89% and 98% for RT-PCR (44, 45). Natural frequencies calculations for different tests, based on the pre-test probability of 57% are reported in Table 4 - 6. False negatives and false positives are highlighted.

Table 4 - 6: Natural frequencies - Week 1 from symptom onset

WEEK 1		N of patients out 1,000* submitted to test			
		Rapid IgM + IgG	CLIA IgM + IgG	ELISA IgM + IgG	RT-PCR
Subjects **with** SARS-CoV-2 infection (N. 570)	Testing positive	193	475	215	507
	Testing negative	377	95	355	63
Subjects **without** SARS-CoV-2 infection (N. 430)	Testing negative	396	344	410	421
	Testing positive	34	86	20	9
	Total	1,000	1,000	1,000	1,000

*Pre-test probability 57%

At one week from symptoms' onset, according to the above estimates and calculations, out of the 570 expected subjects with SARS-CoV-2 infection, IgM and IgG rapid tests would correctly diagnose 93 patients with COVID-19, while the remaining 377 COVID-19 patients would remain undetected. CLIA-based tests would correctly classify 475 COVID-19 patients and miss COVID-19 diagnosis in 95 patients. ELISA-based tests would correctly diagnose 215 COVID-19 patients and not detect 355, while under RT-PCR test 507 COVID-19 would be diagnosed and 63 undiagnosed for COVID-9. False positive results in subjects without SARS-CoV-2 infection would amount to 34 with rapid antibody test, 86 with CLIA, 20 with ELISA and 9 with RT-PCR.

Symptomatic patients presenting within 8-14 days of symptom onset (week 2) and undergoing a rapid serological test, CLIA-based test, ELISA-based test or RT-PCR.

The estimated sensitivities and specificities at week 2 are 71.5% and 90.2% respectively for rapid serological tests, 87.9% and 80% for CLIA-based tests, 84.8% and 95.4% for ELISA-based tests and 84.8% and 98% for RT-PCR (44, 45). Natural frequencies calculations for different tests, based on the pre-test probability of 57%, are reported in Table 4 - 7. False negatives and false positives are highlighted.

Table 4 - 7: Natural frequencies - Week 2 from symptom onset

WEEK 2		N of patients out 1,000* submitted to test			
		Rapid IgM + IgG	CLIA IgM + IgG	ELISA IgM + IgG	RT-PCR
Subjects **with** SARS-CoV-2 infection (N. 570)	Testing positive	408	501	483	507
	Testing negative	162	69	87	63
Subjects **without** SARS-CoV-2 infection (N. 430)	Testing negative	388	344	410	421
	Testing positive	42	86	20	9
	Total	1,000	1,000	1,000	1,000

*Pre-test probability 57%

At two weeks from symptoms' onset, according to the above estimates and calculations, out of the 570 expected subjects with SARS-CoV-2 infection, IgM and IgG rapid test would correctly diagnose 408 patients with COVID-19, while the remaining 162 COVID-19 patients would remain undetected. CLIA-based tests would correctly classify 501 COVID-19 patients and miss COVID-19 diagnosis in 69 patients ELISA-based test would correctly diagnose 4837 COVID-19 patients and not detect 87, while under RT-PCR test 507 COVID-19 would be diagnosed and 63 undiagnosed for COVID-19. False positive results in subjects without SARS-CoV-2 infection would amount to 42 with rapid antibody test, 86 with CLIA, 20 with ELISA and 9 with RT-PCR.

Additional analysis

Evolution of infection's spread affects the pre-test probability of an individual to have caught the infection. At the beginning of the epidemic, this pre-test probability would have been low, while during peak times of disease spread the pre-test probability would have increased, to start decreasing after implementation of lockdown measures. The local applicability of the above calculated estimates, therefore, depends both on the pre-test probability of SARS-CoV-2 infection of the population of interest as well as the number of the included subjects. To facilitate transferability of analysis to different contexts and levels of infection's spread, we provide calculations for several pre-test probability estimates and numbers of tested subjects (Table 4 - 8) with projections of number of COVID-19 patients at risk of being misdiagnosed (false negatives) and number of individuals without the infection at risk of being wrongly diagnosed with COVID-19 (false positives) according to the different scenarios.

Table 4 - 8: Number of subjects who will be falsely identified as positive (FP) or negative (FN), depending on pre-test probability and population size.

Population size	Pre-test probability	Number of false-positive results			Number of false-negative results		
		RDT	CLIA	ELISA	RDT	CLIA	ELISA
100	1%	5	20	8	1	1	1
	10%	4	18	7	6	2	7
	25%	3	15	6	16	4	17
	50%	2	10	4	31	8	33
50.000	1%	2,277	9,900	3,960	311	83	331
	10%	2,070	9,000	3,600	3,110	835	3,310
	25%	1,725	7,500	3,000	7,775	2087	8,275
	50%	1,150	5,000	2,000	15,550	4,175	16,550
8.000.000	1%	364,320	1,58,4000	633,600	49,760	13,360	5,2960
	10%	331,200	1,440,000	576,000	497,600	133,600	529,600
	25%	276,000	1,200,000	480,000	1,244,000	334,000	1,324,000
	50%	184,000	800,000	320,000	2,488,000	668,000	2648,000

***** Test performance: RDT: sensitivity: 33.8 %, specificity: 92%, CLIA: sensitivity: 83.3 %, specificity: 80%, ELISA: sensitivity: 37.8 %, specificity: 95.4%

Positive and negative predictive values are also a useful means to interpret test results and they are an alternative way of representing risks and benefits. The positive predictive value (PPV) indicates the probability that a person testing positive is infected by SARS-CoV-2, while the negative predictive value (NPV) indicates the probability that a person testing negative is not affected by SARS-CoV-2 infection. Figure 2 represents how, given the performance of each type of test, PPV and NVP vary depending on the pre-test probability.

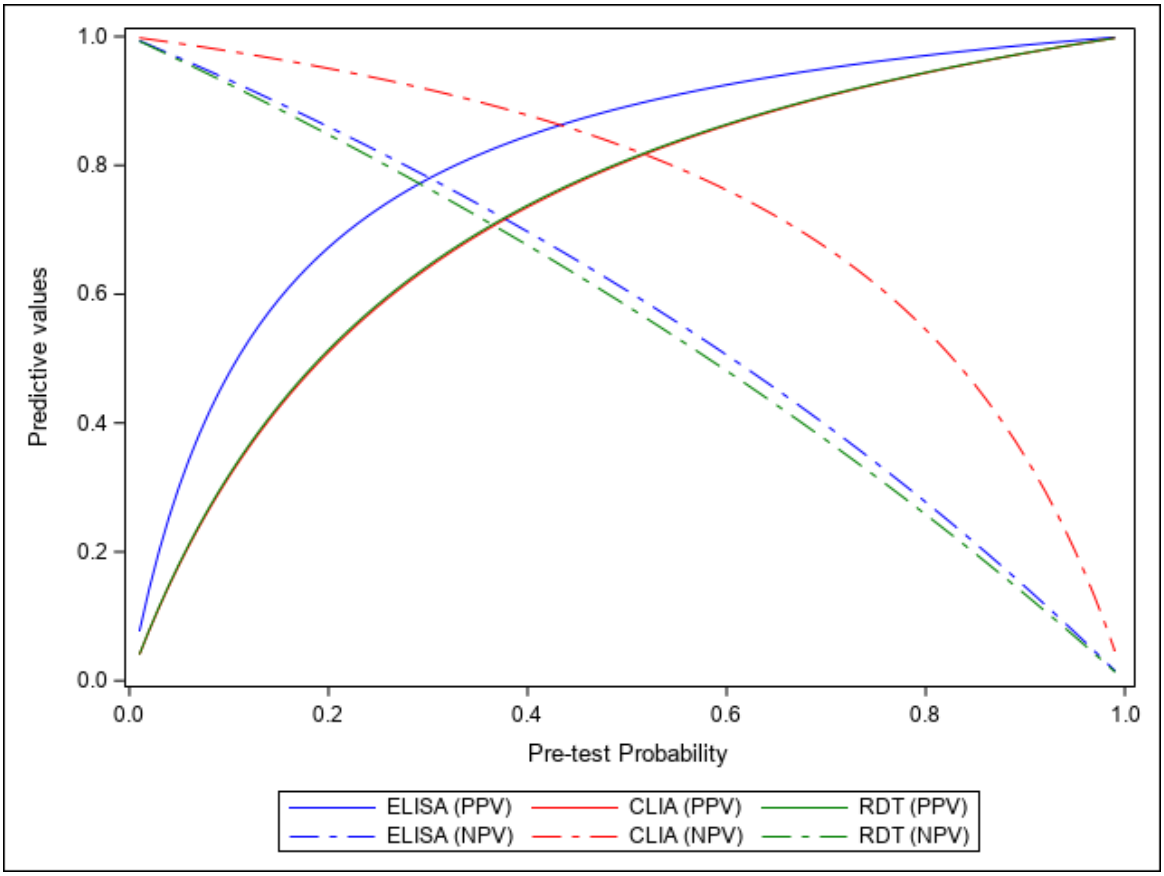

Figure 2: Positive predictive vales (PPV) and negative predictive values (NPV) for a range of pre-test probabilities (0.01 – 0.99). Test performance: RDT: sensitivity: 33.8 %, specificity: 92%, CLIA: sensitivity: 83.3 %, specificity: 80%, ELISA: sensitivity: 37.8 %, specificity: 95.4%

Summary and discussion

Nineteen studies were included and analysed to investigate the role of antibody tests in the diagnosis of SARS-CoV-2 infection in symptomatic patients. Most of the included studies did not have an adequate study design and the overall quality of the retrieved evidence is judged very low. Nevertheless, there was a sufficient number of studies to calculate pooled estimates, although high heterogeneity was found.

Consistent with the expected course of development and detection of antibodies, both IgM and IgG resulted adequately detected from the second week of symptom onset. The combined detection of IgM and IgG seems to improve the diagnostic performance of serological tests.

No studies reported clinical effectiveness outcomes and calculations were performed to highlight benefits (i.e. symptomatic patients correctly diagnosed with COVID-19 or correctly classified as not infected with SARS-CoV-2) and risks (i.e. symptomatic patients incorrectly classified as COVID-19 patients or COVID-19 patients incorrectly classified as affected by another condition).

Calculations were performed with data related to the first and second week from symptom onset, as these are the time windows during which patients typically seek healthcare and a diagnosis is made. The calculations showed a higher risk of misdiagnosis with antibody tests at week 1 than at week 2, with the molecular test RT-PCR performing better than any type of serological test in both time windows.

4.6. Question 3

What role can antibody tests have in measuring seroprevalence in communities?

Rationale

At the beginning of the novel SARS-CoV-2 infection outbreak, seroprevalence in the general population was assumed to be very low, due to the initial limited circulation of the virus, and expected to increase with the steep increase in infection transmission. Initial surveillance and testing for virus RNA has focused on patients presenting with symptoms suggestive of acute SARS-CoV-2 infection. It is now known that the spectrum of the disease manifestation is quite broad, ranging from very severe patients to asymptomatic infected subjects. The proportion of asymptomatic subjects is not known yet and their role in the transmission of the infection is not wholly understood. Underestimation of the disease prevalence affects the reliability of other epidemiological parameters, such as case fatality ratio (CFR). Seroprevalence studies could provide information on how much the virus has circulated in a given population/community, by identifying how many have had the disease, knowingly or unknowingly and irrespective of whether they had received a confirmation of diagnosis. Such an estimate would be important and necessary to calculate Infection Fatality Ratio (IFR). Moreover, understanding the virus' spread in a community can help to estimate the proportion of individuals still susceptible to acquire and transmit the virus.

As indicated by the ECDC, once validated, SARS-CoV-2 antibody tests could prove to be essential for performing large-scale seroepidemiological population surveys and for assessing the immune status of first-line responders (86). Several seroprevalence studies are ongoing in countries throughout Europe (7, 87).

In its protocol for population-based seroepidemiological investigation the WHO identified two main objectives for the investigation: to determine the extent of infection in the general population and age-specific infection cumulative incidence, as determined by seropositivity; and to determine the fraction of asymptomatic or subclinical infections (88). The WHO protocol recommends that both IgM and IgG tests be carried out in seroepidemiological survey. Besides the validity of the deployed tests, the confidence in the seroprevalence estimates and their generalizability to the target population is also determined by the way subjects and samples are identified and selected. Appropriate actions need to be taken to ensure recruitment of a representative sample of the target population.

A systematic review of the literature was undertaken to address the following question:

- What seroprevalence rates of SARS-CoV-2 infection do IgM and/or IgG antibody tests provide when used in general population seroepidemiological surveys and how do they impact on prevalence estimates?
- What are the documented seroprevalence rates in different subgroups of the general population?

The purpose of this intended use of the antibody tests is to measure seroprevalence for SARS-CoV-2 within a community, complementing data on confirmed cases, in order to characterize the community in terms of virus' spread.

Results

According to the WHO protocol, the following study designs were considered for inclusion:

- Cross sectional investigation
- Repeated cross-sectional investigation in the same geographic area (but not necessarily the same individual each time)
- Longitudinal cohort study with serial sampling of the same individuals each time (89).

Quality of the studies was judged in terms of selection bias.

Following the recommendations of the WHO and the ECDC, several European countries began seroprevalence surveys, many of which are still on-going, on general population or at risk populations, such as healthcare workers (90). We only included data reported in published studies satisfying our language inclusion criteria and 17 such studies are included in this report (Appendix 4 Table A6).

Most of the surveys have been conducted in Europe. Three studies were conducted in Italy, two in the U.S.A, and the remaining 12 studies come from Spain, Scotland, the Netherlands, France, Denmark, Germany, Luxembourg, Switzerland, Belgium, China and Iran.

Except for two studies reporting consecutive weekly seroprevalence (91, 92), the remaining 14 were all cross sectional studies. Among the studies carried out in healthcare setting, five studies recruited healthcare workers (93-97), one study recruited hospitalised patients (98) and one study outpatients (99). Population surveys were carried out on samples from the general population by four studies (92, 100-102), on a whole German town population by one study (103), on subjects from selected households by one study (104), on blood donors by four studies (91, 105-107), and on school pupils and their close contacts by one study (106).

Among the studies that specified time of survey, one study covered a period between February and early April 2020 (95), three studies were carried out during the last week of March 2020 (91, 94, 106). The majority, eight studies, were carried out within the first two weeks of April 2020 (98, 100, 101, 103-107) and one study during the last week of April (97). Two studies covered the whole month of April 2020 (92, 102).

Regarding testing methods, only one study (95) used a quantitative test; rapid tests were used in three studies (94, 104, 107), while CLIA or ELISA-based methods were used in the remaining studies.

Of the six general population surveys, two studies were judged to be at high risk of bias (100, 101), one at moderate risk of bias (104) and the remaining three at low risk of bias for sample selection (92, 102, 103). All studies on blood donors (91, 105-107) recruited a selected opportunistic population sample, not representative of the general population, and are considered at high risk of bias for generalizability of results (Table A3 – Appendix3).

Seroprevalence estimates

Heterogeneity of studies, in terms of time of survey, context and country does not allow calculating pooled estimates. As only preliminary data are available, we report descriptive results for the three main groups of samples (general population, blood donors and healthcare workers):

- Seroprevalence estimates in general population: range from 1.5% (95%CI 1.1-2.0) to 25.9% (95%CI 22.6-29.4). Sample sizes ranged from 528 to 3,330.
- Seroprevalence estimates in blood donors: range from 1.0 (95%CI 0.4-2.5) to 3.1 (95%CI 2.7-3.6). Sample sizes ranged from 200 and 9496.
- Seroprevalence estimates in healthcare workers: range from 4.5% (95%CI 1.8-10.5) to 17.2% (95%CI 14.6-20.2). Sample sizes ranged from 133 to 727.

Very few studies reported information on how the seroprevalence survey contributed to reconsidering the disease prevalence provided by confirmed cases. Among the survey conducted on health workers the Spanish study (95) reported an increase of 38.9% in confirmed cases with respect to the disease prevalence from confirmed cases. Of two studies conducted on blood donors, one reported a seroprevalence of 3.1% against the Netherlands' general population confirmed cases prevalence of 0.22% (105), while the Danish study (107) reported a seroprevalence of 1.8% against a general population confirmed cases prevalence of 0.08%.

The two studies reporting consecutive measures showed a change in prevalence from 0% to 1% in one week for blood donors (91) and a change over five weeks from 4.8% to 10.8% in the general population (92).

Relative effectiveness / Risks and benefits assessment

The main objective of the test in this intended use would be to measure the population's seroprevalence for SARS-CoV-2. Seroprevalence estimates should be used with caution, if intended to be extrapolated to the whole target population, as the technical validity and diagnostic accuracy of most of the commercialized tests remain to be confirmed. The implication of such limitations needs to be adequately communicated to subjects enrolled in seroprevalence studies, in order not to compromise their adoption of the appropriate protective measures and behaviour.

Summary and discussion

Seroprevalence studies have been recommended to understand how much the virus has spread during the pandemic, to provide baseline estimates for epidemiological surveillance using surveys at repeated intervals and for future information, should some form of immunity from re-infection be established. There are several surveys on-going on different target populations (general population, healthcare workers, blood donors etc.) and we have reported preliminary data from 17 studies published so far. Only three studies were judged at low risk of bias, and most of the studies presented issues of generalizability of results to the target population due to sample selection. The preliminary data have been presented only in a descriptive way, as heterogeneity of studies do not allow any inference.

4.7. Question 4

What role can antibody tests have in ruling out risk of transmission in patients who recovered from SARS-CoV-2 infection?

Rationale

Current internationally agreed criteria for determining clearance from acute SARS-Cov-2 infection and/or discharge of COVID-19 patients are relief from symptoms and two consecutive negative viral nucleic acid results from respiratory samples at 24 hours interval (108). Towards the end of February and beginning of March 2020, initial data began to emerge on patients recovered from COVID-19 and retesting positive at RT-PCR days or weeks after discharge, suggesting that RT-PCR testing could yield false negative results (109) and that a proportion of recovered patients may still be virus carriers (110, 111). As prolonged detection of IgM has been associated with the acute phase of infection (112) and poor patient recovery (113), it has been suggested that convalescent patients that are IgM positive but RT-PCR negative should be considered as still having active infection (114).

Although viral shedding has been noted to decline during the course of the disease, it could persist for quite a long time after relief of symptoms (115). Besides concerns for false negative RT-PCR results at discharge, it has been suggested that a positive PCR result might not indicate the presence of transmissible virus (2). Reports of prolonged detection of RNA without direct correlation to viral culture have led the Centre for Disease Control to revise their criteria for return to work of healthcare workers with suspected or confirmed COVID-19 (116) . The updated criteria now include a symptom-based strategy for patients having presented symptoms (at least 3 days since recovery defined as resolution of fever without the use of fever-reducing medications and improvement in respiratory symptoms and at least 10 days since symptoms first appeared) and a time strategy for patients that never developed symptoms (10 days since the date of the first positive COVID-19 diagnostic test).

Nevertheless, as the possibility of re-infection still remains to be studied (7), there is ongoing concern that a proportion of recovered patients re-entering their community might still be infected and be a vector for transmission of the virus. Given that seroconversion, expected to occur in all patients during the course of the disease (60), seems to coincide with a slow but steady decline of viral load (34), antibody testing could contribute to better understand and monitor the recovery process from viral infection.

A systematic review of the literature was undertaken in order to address the following question:

- Can antibody tests contribute to rule out risk of virus transmission in patients that have recovered from acute SARS-CoV-2 infection?

The purpose of this intended use of the antibody tests is to correctly rule out persistent infection and risk of transmission of SARS-CoV-2 allowing a diagnosis of viral clearance and safe return in the community. Only patients assessed as being still at risk of transmission would remain in isolation.

Results

Inclusion criteria for studies addressing this question were cohort studies of recovered and/or discharged COVID-19 patients, with a follow-up of at least 14 days since recovery, and assessing virus transmission (infectivity) in those re-testing positive.

We could not identify studies matching our question and inclusion criteria. Nevertheless, we report findings from two small studies investigating re-positivity rates of recovered patients after two consecutive negative RT-PCR tests.

The first study (117) enrolled 262 COVID-19 recovered patients discharged from hospital and followed up for at least 14 days. Thirty-eight patients (14.5%) were found to re-test positive with RT-PCR. Plasma antibody levels at discharge were similar for patients re-testing positive and for those re-testing negative.

The second study (118) reports data on a cohort of 74 recovered COVID-19 patients testing negative for RT-PCR at discharge from hospital, and followed up for the following 14 days. IgM and IgG antibody tests were undertaken after 7 and 1 days from discharge. Thirty-nine patients (52.7%) retested positive witht RT-PCR during the 14 days follow-up. Compared to patients re-testing negative, patients re-testing positive had a significantly lower IgG concentrations within 7 days from discharge, but the difference in IgM concentration was not significant.

We also report data on infectivity of COVID-19 recovered patients re-testing positive with RT-PCR after discharge retrieved from an official national report of the Korea Centers for Disease Control and Prevention (119). The Korea Centers for Disease Control and Prevention (119) has reported the outcome of an epidemiological and contact investigation on 285 out of 447 re-positive detected cases and on their 790 contacts. Forty-four per cent of the investigated cases were symptomatic on re-presentation and the average number of days from discharge to re-testing positive was found to be 14.3. After investigating the 790 contacts of the 285 subjects, the authors of the investigation concluded that no evidence was found indicating infectivity for re-detected positive cases.

Summary and Discussion

We did not identify studies that could be included for this research question and provide data on whether antibody tests are useful in ruling out risk of virus transmission in recovered COVID-19 patients. The Korea Centers for Disease Control and Prevention, after conducting an epidemiological and contact investigation on re-positive detected cases and their contacts, concluded that no evidence was found indicating infectivity for re-detected positive cases. Unfortunately, the role of antibody tests was not investigated in this study.

4.8. Question 5

What role can antibody tests have in assessing protective immunity in subjects with past SARS-CoV-2 infection?

Rationale

The body immune response to a viral infection has an early non-specific innate response, followed by a specific adaptive response (34). During the adaptive immune response, Cytotoxic T-cells recognise and eliminate infected cells, and antibodies activate the humoral (b cell) response binding to an element that affects the viral infectivity. The adaptive response process, measured also by the presence of antibodies in the blood, contributes to clear the virus and may prevent re-infection by the same virus (120).

It has been hypothesized that detection of antibodies to SARS-CoV-2 could provide information on the recovered patients' status of immunity to future re-infection from SARS-CoV-2. Besides

one study conducted on animals (121), evidence of persistence of antibody responses to coronavirus is provided by very few data collected from patients recovered from SARS-CoV (SARS) (122). This longitudinal study on 176 convalescent SARS patients reported that levels of IgG, detected in all patients at end of illness, remained detectable after 2 years in over 90% of patients, while during the third year this proportion dropped below 50%. No data on re-exposure to infection and protective role of antibodies were reported.

Antibody tests available at the moment are mainly qualitative, indicating purely the presence or absence of SARS-CoV-2, and the quantitative methods have not yet shown to distinguish neutralising antibodies (Nab), although high titers of IgG antibodies detected by quantitative techniques are thought to positively correlate with presence of neutralizing antibodies (40).
Knowing whether post infection immunity can occur and how long it persists is important for the development of serologic therapies and vaccines, as well as to scale population-based interventions (40, 123).
Even if some governments have proposed the use of antibody tests for the issue of immunity certificates in order to manage safe return to the workforce and re-starting of the economy, the WHO warns against the use of “immunity passports” or “risk free certificates”(124) as currently there is not enough evidence on the effectiveness of antibody-mediated immunity. However, assuming that all recovered patients develop an immunity, the percentage of “immune” people, calculated with current figures provided by world daily bulletins would approximate 0.33% of the total population in Italy and 0.21% in Germany. Even if applied to subgroups such as healthcare workers, national healthcare systems would not be able to run on such a small proportion of previously exposed (and presumed immune) healthcare workers (see seroprevalence data in Question 3). Therefore, protective immunity is currently explored to inform individuals on their risk of re-infection.

A systematic review of the literature was undertaken in order to address the following question:

- Can antibody tests contribute to determine protective immunity in subjects with past SARS-CoV-2 infection?

As a next step, the purpose of this intended use of the antibody tests would be to correctly classify recovered patients with adequate neutralising antibodies titers as protected against a subsequent re-infection.

Results

The study inclusion criteria for this research question were longitudinal cohort studies recruiting patients recovered from COVID-19 and closely monitored for signs and symptoms of recurrent illness, possibly documenting re-exposure events.

No studies matching our research question and meeting our inclusion criteria were identified.

Summary and Discussion

To date no studies were retrieved investigating correlations between antibody presence or concentrations and protective immunity. No evidence was found suggesting that the presence of antibodies can confer immunity or any other form of protection against re-infection from SARS-CoV-2. While in three out of the four common coronaviruses causing milder respiratory diseases, reinfections are known to occur, uncertainties persist on the immune response to COVID-19 regarding the required level and durability of neutralising antibodies, as well as the correlation between IgG response and immunity. People who have recovered from COVID-19 will be advised and requested to continue observing public health advice and measures to control virus spread transmission.

5. OVERALL DISCUSSION

Given the sparseness of data on immunity and transmissibility, the present report focused on test accuracy of serological testing and on seroprevalence results. Data were heterogeneous and the validity of primary studies was far from good. Furthermore, test accuracy is insufficient to inform decisions on how to best implement or reduce isolation measures. Only very few data is currently available on SARS-CoV-2 transmission by recovering patients (question 4 of this report) and no valid information is there to estimate whether prior infection confers immunity (question 5). Antibody testing may support the diagnosis of SARS-CoV-2 (question 2), but the delayed development of IgM and IgG antibodies after infection strongly limits the practical use of these tests. For similar reasons, serological testing for screen and early disease detection (Question 1) is likely to prove unsuitable. The current role of antibody testing, therefore, would be mainly limited to estimating seroprevalence (question 3).

As expected, sensitivity and specificity of antibody tests increase over the first weeks after infection or symptom onset. For a full assessment of seroconversion over time, studies performing repetitive testing in infected patients are most valuable. The duration of antibody responses to SARS-CoV-2 is another open question, which is most relevant for immunity considerations. However, the aim of the present report was to assess potential application of antibody tests rather than the time course of seroconversion. Besides timing, other factors obviously affected test accuracy, as results were heterogeneous. It was not possible to identify specific attributes of studies, tests or enrolled subjects that might lead to lower test accuracy. Given the quickly evolving nature of this field, optimization and standardization of individual tests will probably lead to more homogeneous and reliable test results.

Previous meta-analyses have reported mixed and less precise estimates of test accuracy, mainly because fewer studies were available up to April 2020. Based on 9 heterogeneous studies published up to April 25th, Caini et al. calculated a pooled sensitivity of 85% and a specificity of 99% for quantitative tests, such as ELISA or CLIA (125). Since cohort studies of infected patients were also included, Kontou et al. was able to pool data from 38 studies (available up to April 17) and found ELISA tests to provide highest test accuracy, with sensitivities in the range of 94% and specificities over 96% (126). Compared to these two meta-analyses, the present results on ELISA-based tests (sensitivity 85%, specificity 95%) show a similar, albeit slightly lower, accuracy. The meta-analysis by Riccò et al., which focused only on point-of-care tests, noted a lower sensitivity of 65% for this type of test (127). This figure corresponds well to the present findings. Due to the higher test accuracy of ELISA-based, combined IgG/IgM tests, this type of antibody test can be expected to evolve as a future standard.

It is likely that the current data on test accuracy are overoptimistic, because the majority of contributing studies had a case-control rather than a cohort design. As cases were selected from symptomatic (or even severe) patients and control samples came from healthy volunteers, such studies mostly failed to include asymptomatic SARS-CoV-2 infections and patients with other viral diseases or symptoms typical for COViD-19. This selection process leads to spectrum bias, which causes overestimated test accuracy results. Specifically, the non-inclusion of other viral diseases precludes detecting cross-reactivity in these studies. Cohort studies could avoid this problem, but would in turn lead to an imperfect reference standard, because no valid test is available to rule out prior infection in a person who tested negative on antibody testing. Theoretically, virus neutralization tests could serve as an independent reference test, but such tests require highest levels of biosafety in the laboratory. Although first studies gave promising results (128, 129) it is likely that these tests' accuracy results will remain somewhat uncertain over the next weeks and months.

Due to the urgency of the situation, both, the present assessment and the included primary studies were performed very swiftly. This haste increases the risk of inaccuracies. In order to compensate for this problem, the assessment will be updated, as this not only allows to correct any shortcomings, but also to include new evidence that has become available in the meantime.

The present results are in line with the current international recommendations on antibody testing. In a statement issued in April 2020, the WHO did “not recommend the use of antibody-detecting rapid diagnostic tests for patient care” (130). Already very early in the course of the pandemic, the ECDC warned that “SARS-CoV-2 antibody detection tests have limited usefulness for early COVID-19 diagnosis” (131). Furthermore, the US Centers for Disease Control (CDC) stated that “serologic testing should not be used to determine immune status”, but “can be offered as a method to support diagnosis of acute COVID-19 illness for persons who present late” (132). In May 2020, the American Medical Association (AMA) warned “that public health decisions, such as discontinuation of physical distancing, should not be made on the basis of results” of serological tests (133).

High quality studies addressing health policy-oriented research questions are urgently needed.

6. CONCLUDING SUMMARY

There is wide consensus that antibody tests can be used for estimating seroprevalence and for confirming prior SARS CoV-2 infection. Quite uncertain, however, is the potential role of serological testing in diagnosis of acute and asymptomatic cases, in ascertaining immunity (both on a individual and on a population level), in estimating transmissibility, in selecting plasma donors from Covid-19 convalescents, or in evaluating future vaccines against SARS CoV-2. Nevertheless, the many potential uses of antibody tests indicate that these tests deserve close attention in the forthcoming months.

Due to the low quality and the limited number of eligible studies, the present assessment confirms the persistence of uncertainty on the role of antibody tests in SARS-CoV-2 diagnosis and management. Since many studies are still ongoing and their results expected to become available in the near future, this assessment will be updated when evidence suitable to reduce this uncertainty will be published.

REFERENCES

1. European Commision. Current performance of COVID-19 test methods and devices and proposed performance criteria: working document of Commission services 2020 [updated 17.04.2020. Available from: https://ec.europa.eu/docsroom/documents/40805.
2. Sethuraman N, Jeremiah SS, Ryo A. Interpreting Diagnostic Tests for SARS-CoV-2. JAMA. 2020.
3. World Health Organization. COVID-19 Public Health Emergency of International Concern (PHEIC) Global research and innovation forum. 2020.
4. Kyhlstedt M, Andersson SW. Diagnostic and digital solutions to address the COVID-19 pandemic: The need for international collaboration to close the gap. Health Policy Technol2020.
5. World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it. 2020.
6. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol. 2020;5(4):536-44.
7. ECDC - European Centre for Disease Prevention and Control. Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK- ninth update. 2020.
8. ECDC - European Centre for Disease Prevention and Control. Q & A on COVID-19. 2020.
9. ECDC - European Centre for Disease Prevention and Control. COVID - 19 Surveillance report. 2020.
10. World Health Organization. Global surveillance for COVID-19 caused by human infection with COVID-19 virus: interim guidance, 20 March 2020. 2020.
11. World Health Organization. Global surveillance for COVID-19 caused by human infection with COVID-19 virus. 2020.
12. World Health Organization. COVID-19 coding in ICD-10. 2020.
13. World Health Organization. INTERNATIONAL GUIDELINES FOR CERTIFICATION AND CLASSIFICATION (CODING) OF COVID-19 AS CAUSE OF DEATH. 2020.
14. World Health Organization. Emergency use ICD codes for COVID-19 disease outbreak. 2020.
15. ECDC - European Centre for Disease Prevention and Control. Situation Update. 2020.
16. CEBM - The Centre for Evidence-Based Medicine develops padbefh. COVID-19: What proportion are asymptomatic? 2020.
17. Wu C, Liu Y, Yang Y, Zhang P, Zhong W, Wang Y, et al. Analysis of therapeutic targets for SARS-CoV-2 and discovery of potential drugs by computational methods. Acta Pharm Sin B. 2020;10(5):766-88.
18. Xu X, Chen P, Wang J, Feng J, Zhou H, Li X, et al. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. Sci China Life Sci. 2020;63(3):457-60.

19. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol. 2004;203(2):631-7.
20. World Health Organization. Coronavirus disease 2019 (COVID-19) Situation Report – 73. 2020.
21. Matricardi PM, Dal Negro RW, Nisini R. The first, holistic immunological model of COVID-19: implications for prevention, diagnosis, and public health measures. Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology. 2020.
22. CEBM - The Centre for Evidence-Based Medicine develops padbefh. In patients of COVID-19, what are the symptoms and clinical features of mild and moderate cases? 2020.
23. Siddiqi HK, Mehra MR. COVID-19 illness in native and immunosuppressed states: A clinical-therapeutic staging proposal. J Heart Lung Transplant. 2020;39(5):405-7.
24. Mayo Clinic. Coronavirus disease 2019 (COVID-19). 2020.
25. World Health Organization. COVID-19 Studies from the World Health Organization Database. 2020.
26. EuroMOMO. EuroMOMO Bulletin, Week 22, 2020. 2020.
27. GEN-COVID. Impact of Host Genome on COVID-19 clinical variability 2020.
28. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al. Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2. JAMA. 2020.
29. World Health Organization. Laboratory testing strategy recommendations for COVID-19 2020 [updated 21.03.2020. Available from: https://apps.who.int/iris/bitstream/handle/10665/331509/WHO-COVID-19-lab_testing-2020.1-eng.pdf.
30. Organisation for Economic Co-operation and Development. Testing for COVID-19: a way to lift confinement restrictions 2020 [updated 04.05.2020. Available from: https://read.oecd-ilibrary.org/view/?ref=129_129658-l62d7lr66u&title=Testing-for-COVID-19-A-way-to-lift-confinement-restrictions.
31. World Health Organization. Coronavirus disease (COVID-19) technical guidance: surveillance and case definitions 2020 [updated 2020. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/surveillance-and-case-definitions.
32. Health Information and Quality Authority. Rapid health technology assessment of alternative diagnostic testing approaches for the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): HIQA; 2020 [updated 05.05.2020. Available from: https://www.hiqa.ie/reports-and-publications/health-technology-assessment/rapid-hta-alternative-diagnostic-testing.
33. Zheng S, Fan J, Yu F, Feng B, Lou B, Zou Q, et al. Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study. BMJ. 2020;369:m1443.
34. Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. Nature. 2020;581(7809):465-9.

35. Lou B, Li T, Zheng S, Su Y, Li Z, Liu W, et al. Serology characteristics of SARS-CoV-2 infection since the exposure and post symptoms onset. medRxiv; 2020.
36. Gonzalez J, Shelton J, Diaz-Vallejo M, Rodriguez-Castellanos V, Zuluaga JD, Chamorro D, et al. Immunological assays for SARS-CoV-2: an analysis of available commercial tests to measure antigen and antibodies. medRxiv; 2020.
37. Li M, Jin R, Peng Y, Wang C, Ren W, Lv F, et al. Generation of antibodies against COVID-19 virus for development of diagnostic tools. medRxiv; 2020.
38. European Commission. COMMUNICATION FROM THE COMMISSION Guidelines on COVID-19 in vitro diagnostic tests and their performance 2020 [Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52020XC0415(04).
39. To KK, Tsang OT, Leung WS, Tam AR, Wu TC, Lung DC, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. The Lancet Infectious diseases. 2020;20(5):565-74.
40. Kirkcaldy RD, King BA, Brooks JT. COVID-19 and Postinfection Immunity: Limited Evidence, Many Remaining Questions. JAMA. 2020.
41. ECDC - European Centre for Disease Prevention and Control. Laboratory support for COVID-19 in the EU/EEA 2020 [updated 15.04.2020. Available from: https://www.ecdc.europa.eu/en/novel-coronavirus/laboratory-support.
42. P M, F V, M V, C P, E L, E B, et al. Temporal profile and determinants of viral shedding and confirmation of viral clearance on nasopharyngeal swabs from SARS-CoV-2 positive subjects: a population-based study in Reggio Emilia. 2020.
43. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin. 2020;25(3).
44. Health Technology Wales. The clinical effectiveness of tests to detect the presence of SARS-CoV-2 virus, and antibodies to SARS-CoV-2, to inform COVID-19 diagnosis 2020 [updated 04.2020. Available from: https://www.healthtechnology.wales/wp-content/uploads/2020/04/EAR025-COVID19-diagnostics-report.pdf.
45. Arevalo-Rodriguez I, Buitrago-Garcia D, Simancas-Racines D, Zambrano-Achig P, del Campo R, Ciapponi A, et al. FALSE-NEGATIVE RESULTS OF INITIAL RT-PCR ASSAYS FOR COVID-19: A SYSTEMATIC REVIEW. medRxiv. 2020:2020.04.16.20066787.
46. Weinstein MC, Freedberg KA, Hyle EP, Paltiel AD. Waiting for Certainty on Covid-19 Antibody Tests - At What Cost? N Engl J Med. 2020.
47. University of Bristol. QUADAS-2: University of Bristol; 2020 [Available from: https://www.bristol.ac.uk/population-health-sciences/projects/quadas/quadas-2/.
48. Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. Stat Med. 1998;17(8):857-72.
49. Vollset SE. Confidence-Intervals for a Binomial Proportion. Stat Med. 1993;12(9):809-24.
50. Schwarzer G, Chemaitelly H, Abu-Raddad LJ, Rucker G. Seriously misleading results using inverse of Freeman-Tukey double arcsine transformation in meta-analysis of single proportions. Res Synth Methods. 2019;10(3):476-83.

51. Stijnen T, Hamza TH, Özdemir P. Random effects meta-analysis of event outcome in the framework of the generalized linear mixed model with applications in sparse data. Stat Med. 2010;29(29):3046-67.
52. Higgins JP, Thompson SG, Spiegelhalter DJ. A re-evaluation of random-effects meta-analysis. J R Stat Soc Ser A Stat Soc. 2009;172(1):137-59.
53. ECDC - European Centre for Disease Prevention and Control. Strategies for the surveillance of COVID-19. 2020.
54. World Health Organization. Critical preparedness, readiness and response actions for COVID-19. 2020.
55. European Commission. COVID-19 EU recommendations for testing strategies1. 2020.
56. Bruinen de Bruin Y, Lequarre AS, McCourt J, Clevestig P, Pigazzani F, Zare Jeddi M, et al. Initial impacts of global risk mitigation measures taken during the combatting of the COVID-19 pandemic. Saf Sci. 2020;128:104773.
57. Anderson RM, Heesterbeek H, Klinkenberg D, Hollingsworth TD. How will country-based mitigation measures influence the course of the COVID-19 epidemic? Lancet. 2020;395(10228):931-4.
58. ECDC - European Centre for Disease Prevention and Control. Contact tracing for COVID-19: current evidence, options for scale-up and an assessment of resources needed. 2020.
59. Flodgren GM. Immunity after SARS-CoV-2 infection: a rapid review. Oslo: Norwegian Institute of Public Health; 2020.
60. Long QX, Liu BZ, Deng HJ, Wu GC, Deng K, Chen YK, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med. 2020.
61. Wang W, Min Y-Z, Yang C-M, Hong H-O, Xue T, Gao Y, et al. Association of Personal Protective Equipment Use with Successful Protection Against COVID-19 Infection Among Health Care Workers. medRxiv; 2020.
62. Wang Y, Kang H, Liu X, Tong Z. Combination of RT-qPCR testing and clinical features for diagnosis of COVID-19 facilitates management of SARS-CoV-2 outbreak. J Med Virol. 2020.
63. [The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(2):145-51.
64. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology. 2020:200642.
65. Liu L, Liu W, Zheng Y, Jiang X, Kou G, Ding J, et al. A preliminary study on serological assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 238 admitted hospital patients. Microbes Infect. 2020;22(4):206-11.
66. Guo L, Ren L, Yang S, Xiao M, Chang D, Yang F, et al. Profiling Early Humoral Response to Diagnose Novel Coronavirus Disease (COVID-19). Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.
67. Jia X, Zhang P, Tian Y, Wang J, Zeng H, Wang J, et al. Clinical significance of IgM and IgG test for diagnosis of highly suspected COVID-19 infection. medRxiv; 2020.

68. Spicuzza L, Montineri A, Manuele R, Crimi C, Pistorio MP, Campisi R, et al. Reliability and usefulness of a rapid IgM-IgG antibody test for the diagnosis of SARS-CoV-2 infection: A preliminary report. The Journal of infection. 2020.
69. Cassaniti I, Novazzi F, Giardina F, Salinaro F, Sachs M, Perlini S, et al. Performance of VivaDiag COVID-19 IgM/IgG Rapid Test is inadequate for diagnosis of COVID-19 in acute patients referring to emergency room department. J Med Virol. 2020.
70. Li Z, Yi Y, Luo X, Xiong N, Liu Y, Li S, et al. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. J Med Virol. 2020.
71. Shen B, Zheng Y, Zhang X, Zhang W, Wang D, Jin J, et al. Clinical evaluation of a rapid colloidal gold immunochromatography assay for SARS-Cov-2 IgM/IgG. American journal of translational research. 2020;12(4):1348-54.
72. Zhong L, Chuan J, Gong B, Shuai P, Zhou Y, Zhang Y, et al. Detection of serum IgM and IgG for COVID-19 diagnosis. Science China Life sciences. 2020;63(5):777-80.
73. Whitman J, Hiatt J, Mowery C, Shy B, Yu R, Yamamoto T, et al. Test performance evaluation of SARS-CoV-2 serological assays. medRxiv; 2020.
74. Paradiso AV, De Summa S, Loconsole D, Procacci V, Sallustio A, Centrone F, et al. Clinical meanings of rapid serological assay in patients tested for SARS-Co2 RT-PCR. medRxiv; 2020.
75. Liu Y, Liu Y, Diao B, Ren F, Wang Y, Ding J, et al. Diagnostic Indexes of a Rapid IgG/IgM Combined Antibody Test for SARS-CoV-2. medRxiv; 2020.
76. Garcia FP, Perez Tanoira R, Romanyk Cabrera JP, Arroyo Serrano T, Gomez Herruz P, Cuadros Gonzalez J. Rapid diagnosis of SARS-CoV-2 infection by detecting IgG and IgM antibodies with an immunochromatographic device: a prospective single-center study. medRxiv; 2020.
77. Lin D, Liu L, Zhang M, Hu Y, Yang Q, Guo J, et al. Evaluations of serological test in the diagnosis of 2019 novel coronavirus (SARS-CoV-2) infections during the COVID-19 outbreak. medRxiv; 2020.
78. Hu X, Deng H, Shang Y, Fan M, Yue F. Simple Strategy for Rapid and Sensitive Detection of 2019 novel coronavirus Based on Antibody. Research Square; 2020.
79. Ma H, Zeng W, He H, Zhao D, Yang Y, Jiang D, et al. COVID-19 diagnosis and study of serum SARS-CoV-2 specific IgA, IgM and IgG by chemiluminescence immunoanalysis. medRxiv; 2020.
80. Qian C, Zhou M, Cheng F, Lin X, Gong Y, Xie X, et al. Development and Multicenter Performance Evaluation of The First Fully Automated SARS-CoV-2 IgM and IgG Immunoassays. medRxiv; 2020.
81. Wan Y, Li Z, Wang K, Li T, Liao P. Performance verification of detecting COVID-19 specific antibody by using four chemiluminescence immunoassay systems. medRxiv; 2020.
82. Liu W, Liu L, Kou G, Zheng Y, Ding Y, Ni W, et al. Evaluation of Nucleocapsid and Spike Protein-based ELISAs for detecting antibodies against SARS-CoV-2. J Clin Microbiol. 2020.
83. Xiang F, Wang X, He X, Peng Z, Yang B, Zhang J, et al. Antibody Detection and Dynamic Characteristics in Patients with COVID-19. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.

84. Liu L, Liu W, Wang S, Zheng S. A preliminary study on serological assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 238 admitted hospital patients. medRxiv; 2020.
85. Gigerenzer G, Gaissmaier W, Kurz-Milcke E, Schwartz LM, Woloshin S. Helping Doctors and Patients Make Sense of Health Statistics. Psychol Sci Public Interest. 2007;8(2):53-96.
86. ECDC - European Centre for Disease Prevention and Control. Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK - eighth update. 2020.
87. Bobrovitz N, Arora RK, Yan T, Rahim H, Duarte N, Boucher E, et al. Lessons from a rapid systematic review of early SARS-CoV-2 serosurveys. medRxiv. 2020:2020.05.10.20097451.
88. World Health Organization. Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection. 2020.
89. WHOc. Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection. 2020.
90. ECDC - European Centre for Disease Prevention and Control. Rapid Risk Assessment: Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK - tenth update. 2020.
91. Thompson C, Grayson N, Paton R, Lourenço J, Penman B, Lee LN, et al. Neutralising antibodies to SARS coronavirus 2 in Scottish blood donors - a pilot study of the value of serology to determine population exposure. medRxiv; 2020.
92. Stringhini S, Wisniak A, Piumatti G, Azman AS, Lauer SA, Baysson H, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study. Lancet. 2020.
93. Comar M, Brumat M, Concas MP, Argentini G, Bianco A, Bicego L, et al. COVID-19 experience: first Italian survey on healthcare staff members from a Mother-Child Research hospital using combined molecular and rapid immunoassays test. medRxiv; 2020.
94. Paradiso AV, De Summa s, Silvestris N, Tommasi S, Tufaro A, De Palma G, et al. RAPID SEROLOGICAL TESTS HAVE A ROLE IN ASYMPTOMATIC HEALTH WORKERS COVID-19 SCREENING. medRxiv; 2020.
95. Garcia-Basteiro A, Moncunill G, Tortajada M, Vidal M, Guinovart C, Jimenez A, et al. Seroprevalence of antibodies against SARS-CoV-2 among health care workers in a large Spanish reference hospital. medRxiv; 2020.
96. Tosato F, Pelloso M, Gallo N, Giraudo C, Llanaj G, Cosma C, et al. Severe Acute Respiratory Syndrome Coronavirus 2 Serology in Asymptomatic Healthcare Professionals: Preliminary Experience of a Tertiary Italian Academic Center. medRxiv; 2020.
97. Steensels D, Oris E, Coninx L, Nuyens D, Delforge ML, Vermeersch P, et al. Hospital-Wide SARS-CoV-2 Antibody Screening in 3056 Staff in a Tertiary Center in Belgium. JAMA. 2020.
98. Wu X, Fu B, Chen L, Feng Y. Serological tests facilitate identification of asymptomatic SARS-CoV-2 infection in Wuhan, China. J Med Virol. 2020.
99. Doi A, Iwata K, Kuroda H, Hasuike T, Nasu S, Kanda A, et al. Estimation of seroprevalence of novel coronavirus disease (COVID-19) using preserved serum at an outpatient setting in Kobe, Japan: A cross-sectional study. 2020.

100. Bendavid E, Mulaney B, Sood N, Shah S, Ling E, Bromley-Dulfano R, et al. COVID-19 Antibody Seroprevalence in Santa Clara County, California. medRxiv; 2020.
101. Bryan A, Pepper G, Wener M, Fink S, Morishima C, Chaudhary A, et al. Performance Characteristics of the Abbott Architect SARS-CoV-2 IgG Assay and Seroprevalence Testing in Idaho. medRxiv; 2020.
102. Snoeck C, Vaillant M, Abdelrahman T, Satagopam V, Turner J, Beaumont K, et al. Prevalence of SARS-CoV-2 infection in the Luxembourgish population: the CON-VINCE study. medRxiv; 2020.
103. Streeck H, Schulte B, Kuemmerer B, Richter E, Hoeller T, Fuhrmann C, et al. Infection fatality rate of SARS-CoV-2 infection in a German community with a super-spreading event. medRxiv; 2020.
104. Shakiba M, Hashemi Nazari SS, Mehrabian F, Rezvani SM, Ghasempour Z, Heidarzadeh A. Seroprevalence of COVID-19 virus infection in Guilan province, Iran. medRxiv; 2020.
105. Slot E, Hogema B, Reusken CBEM, Reimerink J, Molier M, Karregat JHM, et al. Herd immunity is not a realistic exit strategy during a COVID-19 outbreak. Research Square; 2020.
106. Fontanet A, Tondeur L, Madec Y, Grant R, Besombes C, Jolly N, et al. Cluster of COVID-19 in northern France: A retrospective closed cohort study. medRxiv; 2020.
107. Erikstrup C, Hother CE, Pedersen OBV, Mølbak K, Skov RL, Holm DK, et al. Estimation of SARS-CoV-2 infection fatality rate by real-time antibody screening of blood donors. medRxiv; 2020.
108. Huang J, Mao T, Li S, Wu L, Xu X, Li H, et al. Long period dynamics of viral load and antibodies for SARS-CoV-2 infection: an observational cohort study. medRxiv; 2020.
109. Xiao AT, Tong YX, Zhang S. False-negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: Rather than recurrence. J Med Virol. 2020.
110. Chen D, Xu W, Lei Z, Huang Z, Liu J, Gao Z, et al. Recurrence of positive SARS-CoV-2 RNA in COVID-19: A case report. Int J Infect Dis. 2020;93:297-9.
111. Lan L, Xu D, Ye G, Xia C, Wang S, Li Y, et al. Positive RT-PCR Test Results in Patients Recovered From COVID-19. JAMA. 2020;323(15):1502-3.
112. Xiao AT, Gao C, Zhang S. Profile of specific antibodies to SARS-CoV-2: The first report. The Journal of infection. 2020.
113. Fu H, Xu H, Zhang N, Xu H, Li Z, Chen H, et al. Association between Clinical, Laboratory and CT Characteristics and RT-PCR Results in the Follow-up of COVID-19 patients. medRxiv; 2020.
114. Du Z, Zhu F, Guo F, Yang B, Wang T. Detection of antibodies against SARS-CoV-2 in patients with COVID-19. J Med Virol. 2020.
115. Li N, Wang X, Lv T. Prolonged SARS-CoV-2 RNA shedding: Not a rare phenomenon. J Med Virol. 2020.
116. CDC - Centers for Disease Control and Prevention. Criteria for Return to Work for Healthcare Personnel with Suspected or Confirmed COVID-19 (Interim Guidance). 2020.
117. An J, Liao X, Xiao T, Qian S, Yuan J, Ye H, et al. Clinical characteristics of the recovered COVID-19 patients with re-detectable positive RNA test. medRxiv; 2020.
118. Hu Q, Cui X, Liu X, Peng B, Jiang J, Wang X, et al. The production of antibodies for SARS-CoV-2 and its clinical implication. medRxiv; 2020.

119. KCDC - Korea Centers for Diseases and Control & Prevention. Findings from investigation and analysis of re-positive cases. 2020.
120. Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, et al. Coronavirus infections and immune responses. J Med Virol. 2020;92(4):424-32.
121. Bao L, Deng W, Gao H, Xiao C, Liu J, Xue J, et al. Lack of Reinfection in Rhesus Macaques Infected with SARS-CoV-2. bioRxiv; 2020.
122. Wu LP, Wang NC, Chang YH, Tian XY, Na DY, Zhang LY, et al. Duration of antibody responses after severe acute respiratory syndrome. Emerg Infect Dis. 2007;13(10):1562-4.
123. Suthar MS, Zimmerman M, Kauffman R, Mantus G, Linderman S, Vanderheiden A, et al. Rapid generation of neutralizing antibody responses in COVID-19 patients. medRxiv. 2020:2020.05.03.20084442.
124. World Health Organization. "Immunity passports" in the context of COVID-19. 2020.
125. Caini S, Bellerba F, Corso F, Díaz-Basabe A, Natoli G, Paget J, et al. Meta-analysis of diagnostic performance of serological tests for SARS-CoV-2 antibodies up to 25 April 2020 and public health implications. Euro Surveill. 2020;25(23).
126. Kontou P, Braliou G, Dimou N, Nikolopoulos G, Bagos P. Antibody tests in detecting SARS-CoV-2 infection: a meta-analysis. medRxiv; 2020.
127. Riccò M, Ferraro P, Gualerzi G, Ranzieri S, Henry BM, Said YB, et al. Point-of-Care Diagnostic Tests for Detecting SARS-CoV-2 Antibodies: A Systematic Review and Meta-Analysis of Real-World Data. J Clin Med. 2020;9(5).
128. Premkumar L, Segovia-Chumbez B, Jadi R, Martinez DR, Raut R, Markmann A, et al. The receptor binding domain of the viral spike protein is an immunodominant and highly specific target of antibodies in SARS-CoV-2 patients. Sci Immunol. 2020;5(48).
129. Okba NMA, Muller M, Li W, Wang C, GeurtsvanKessel C, Corman V, et al. SARS-CoV-2 specific antibody responses in COVID-19 patients. medRxiv; 2020.
130. world Health Organization. Advice on the use of point-of-care immunodiagnostic tests for COVID-19: scientific brief. 2020.
131. ECDC - European Centre for Disease Prevention and Control. An overview of the rapid test situation for COVID-19 diagnosis in the EU/EEA. 2020.
132. CDC - Centers for Disease Control and Prevention. Interim Guidelines for COVID-19 Antibody Testing. 2020.
133. AMA - American Medical Association. Serological testing for SARS-CoV-2 antibodies. 2020.
134. Long Q-x, Deng H-j, Chen J, Hu J, Liu B-z, Liao P, et al. Antibody responses to SARS-CoV-2 in COVID-19 patients: the perspective application of serological tests in clinical practice. medRxiv; 2020.
135. Snoeck CJ, Vaillant M, Abdelrahman T, Satagopam VP, Turner JD, Beaumont K, et al. Prevalence of SARS-CoV-2 infection in the Luxembourgish population: the CON-VINCE study 2020 [updated 18.05.2020. Available from: https://www.medrxiv.org/content/10.1101/2020.05.11.20092916v1.
136. Streeck H, Schulte B, Kümmerer BM, Richter E, Höller T, Fuhrmann C, et al. Infection fatality rate of SARS-CoV-2 infection in a German community with a super-

spreading event 2020 [updated 02.06.2020. Available from: https://www.medrxiv.org/content/10.1101/2020.05.04.20090076v2.
137. Stringhini S, Wisniak A, Piumatti G, Azman AS, Lauer SA, Baysson H, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study. Lancet. 11.06.2020 [Epub ahead of print].
138. Zhang P, Gao Q, Wang T, Ke Y, Mo F, Jia R, et al. Evaluation of recombinant nucleocapsid and spike proteins for serological diagnosis of novel coronavirus disease 2019 (COVID-19). medRxiv; 2020.

7. APPENDIX 1

Documentation of the Search Strategies

Search in bibliographic databases

1. PubMed

Interface: NLM

#	Searches
1	covid-19 OR sars-cov-2 OR 2019-ncov OR 2019-novel coronavirus
2	((antibod* OR antigen* OR igg OR igm OR nucleic acid* OR serological*) AND (diagnos* OR test OR testing OR tests OR immunoassay* OR assay* OR response* OR detect*)) OR elisa

2. Europe PMC Preprints

Searches
("covid-19" OR "sars-cov-2" OR "2019-ncov" OR "2019-novel coronavirus") AND (((antibod* OR antigen* OR igg OR igm OR (nucleic* AND acid*) OR serological*) AND (diagnos* OR test* OR immunoassay* OR assay* OR response* OR detect*)) OR elisa*) AND (SRC:PPR)

Search in study registries

1. ClinicalTrials.gov

Provider: U.S. National Institutes of Health

- URL: http://www.clinicaltrials.gov
- Input surface: Advanced Search

Suchstrategie
(Covid-19 OR SARS-Cov-2 OR 2019-nCov) AND (antibody OR antigen OR igg OR igm OR nucleic acid OR serological) AND (diagnostic OR test OR ELISA OR assay OR response OR detect)

2. International Clinical Trials Registry Platform Search Portal

Provider: World Health Organization

- URL: http://apps.who.int/trialsearch
- Input surface: Advanced Search

Suchstrategie
Covid-19 AND antibody test OR Covid-19 AND diagnostic test OR Covid-19 AND ELISA OR Covid-19 AND serological assay OR SARS-Cov-2 AND antibody test OR SARS-Cov-2 AND diagnostic test OR SARS-Cov-2 AND ELISA OR SARS-Cov-2 AND serological assay OR 2019-nCov AND antibody test OR 2019-nCov AND diagnostic test OR 2019-nCov AND ELISA OR 2019-nCov AND serological assay

8. APPENDIX 2 - LIST OF EXCLUDED STUDIES

E1 wrong study population

1. Ackerman CM, Myhrvold C, Thakku SG, Freije CA, Metsky HC, Yang DK, et al. Massively multiplexed nucleic acid detection using Cas13. Nature. 2020.
2. Adams E, Anand R, Andersson M, Auckland K, Baillie K, Barnes E, et al. Evaluation of antibody testing for SARS-Cov-2 using ELISA and lateral flow immunoassays. medRxiv; 2020.
3. Döhla M, Boesecke C, Schulte B, Diegmann C, Sib E, Richter E, et al. Rapid point-of-care testing for SARS-CoV-2 in a community screening setting shows low sensitivity. Public Health. 2020;182:170-2.
4. Freeman B, Lester S, Mills L, Rasheed MAU, Moye S, Abiona O, et al. Validation of a SARS-CoV-2 spike protein ELISA for use in contact investigations and sero-surveillance. bioRxiv; 2020.
5. Gordon CJ, Tchesnokov EP, Feng JY, Porter DP, Götte M. The antiviral compound remdesivir potently inhibits RNA-dependent RNA polymerase from Middle East respiratory syndrome coronavirus. The Journal of biological chemistry. 2020;295(15):4773-9.
6. Guo X, Guo Z, Duan C, chen Z, Wang G, Lu Y, et al. Long-Term Persistence of IgG Antibodies in SARS-CoV Infected Healthcare Workers. medRxiv; 2020.
7. Hoffman T, Nissen K, Krambrich J, Rönnberg B, Akaberi D, Esmaeilzadeh M, et al. Evaluation of a COVID-19 IgM and IgG rapid test; an efficient tool for assessment of past exposure to SARS-CoV-2. Infection ecology & epidemiology. 2020;10(1):1754538.
8. Imai K, Tabata S, Ikeda M, Noguchi S, Kitagawa Y, Matuoka M, et al. Clinical evaluation of an immunochromatographic IgM/IgG antibody assay and chest computed tomography for the diagnosis of COVID-19. medRxiv; 2020.
9. Jia X, Zhang P, Tian Y, Wang J, Zeng H, Wang J, et al. Clinical significance of IgM and IgG test for diagnosis of highly suspected COVID-19 infection. medRxiv; 2020.
10. Lassaunière R, Frische A, Harboe Z, Nielsen ACY, Fomsgaard A, Krogfelt K, et al. Evaluation of nine commercial SARS-CoV-2 immunoassays. medRxiv; 2020.
11. Lee YL, Liao CH, Liu PY, Cheng CY, Chung MY, Liu CE, et al. Dynamics of anti-SARS-Cov-2 IgM and IgG antibodies among COVID-19 patients. The Journal of infection. 2020.
12. Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, et al. Coronavirus infections and immune responses. J Med Virol. 2020;92(4):424-32.
13. Qian S, Jia X, Gao Z, Zhang W, Xu Q, Li Z. Isolation and Identification of Porcine Deltacoronavirus and Alteration of Immunoglobulin Transport Receptors in the Intestinal Mucosa of PDCoV-Infected Piglets. Viruses. 2020;12(1).
14. Qu J, Wu C, Li X, Zhang G, Jiang Z, Zhu Q, et al. Profile of IgG and IgM antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.
15. Solodky ML, Galvez C, Russias B, Detourbet P, N'Guyen-Bonin V, Herr AL, et al. Lower detection rates of SARS-COV2 antibodies in cancer patients vs healthcare workers after symptomatic COVID-19. Annals of oncology : official journal of the European Society for Medical Oncology. 2020.
16. Stryhn A, Kongsgaard M, Rasmussen M, Harndahl MN, Østerbye T, Bassi MR, et al. A systematic, unbiased mapping of CD8+ and CD4+ T cell epitopes in Yellow Fever vaccinees. bioRxiv; 2020.
17. Wang Q, Du Q, Guo B, Mu D, Lu X, Ma Q, et al. A method to prevent SARS-CoV-2 IgM false positives in gold immunochromatography and enzyme-linked immunosorbent assays. J Clin Microbiol. 2020.
18. Yangchun F. Optimize Clinical Laboratory Diagnosis of COVID-19 from Suspect Cases by Likelihood Ratio of SARS-CoV-2 IgM and IgG antibody. medRxiv; 2020.
19. Zhang Z, Xiao T, Wang Y, Yuan J, Ye H, Wei L, et al. Early viral clearance and antibody kinetics of COVID-19 among asymptomatic carriers. medRxiv; 2020.
20. Zhao R, Li M, Song H, Chen J, Ren W, Feng Y, et al. Serological diagnostic kit of SARS-CoV-2 antibodies using CHO-expressed full-length SARS-CoV-2 S1 proteins. medRxiv; 2020.

E2 wrong/ no index test

1. Ai J, Gong J, Xing L, He R, Tian F, Wang J, et al. Analysis of factors associated early diagnosis in coronavirus disease 2019 (COVID-19). medRxiv; 2020.
2. Ai J-W, Zhang H-C, Xu T, Wu J, Zhu M, Yu Y-Q, et al. Optimizing diagnostic strategy for novel coronavirus pneumonia, a multi-center study in Eastern China. medRxiv; 2020.

3. Akçay Ş, Özlü T, Yılmaz A. Radiological approaches to COVID-19 pneumonia. Turkish journal of medical sciences. 2020;50(Si-1):604-10.
4. alam I, Kamau A, Kulmanov M, Arold S, Pain A, Gojobori T, et al. Functional pangenome analysis suggests inhibition of the protein E as a readily available therapy for COVID-2019. bioRxiv; 2020.
5. Annamalai P, Kanta M, Ramu P, Ravi B, Veerapandian K, Srinivasan R. A SIMPLE COLORIMETRIC MOLECULAR DETECTION OF NOVEL CORONAVIRUS (COVID-19), AN ESSENTIAL DIAGNOSTIC TOOL FOR PANDEMIC SCREENING. medRxiv; 2020.
6. Azhar M, Phutela R, Ansari AH, Sinha D, Sharma N, Kumar M, et al. Rapid, field-deployable nucleobase detection and identification using FnCas9. bioRxiv; 2020.
7. Aziz M, Fatima R, Assaly R. Elevated Interleukin-6 and Severe COVID-19: A Meta-Analysis. J Med Virol. 2020.
8. Baruah V, Bose S. Immunoinformatics-aided identification of T cell and B cell epitopes in the surface glycoprotein of 2019-nCoV. J Med Virol. 2020;92(5):495-500.
9. Benchoufi M, Bokobza J, Anthony Chauvin A, Dion E, Baranne M-L, Levan F, et al. Lung injury in patients with or suspected COVID-19 : a comparison between lung ultrasound and chest CT-scanner severity assessments, an observational study. medRxiv; 2020.
10. Benelli G, Buscarini E, Canetta C, La Piana G, Merli G, Scartabellati A, et al. SARS-COV-2 comorbidity network and outcome in hospitalized patients in Crema, Italy. medRxiv; 2020.
11. Benussi A, Pilotto A, Premi E, Libri I, Giunta M, Agosti C, et al. Clinical features and outcomes of inpatients with neurological disease and COVID-19. medRxiv; 2020.
12. Bhadra S, Riedel T, Lakhotia S, Tran N, Ellington A. High-surety isothermal amplification and detection of SARS-CoV-2, including with crude enzymes. bioRxiv; 2020.
13. Boorla VS, Chowdhury R, Maranas C. De novo design of high-affinity antibody variable regions (scFv) against the SARS-CoV-2 spike protein. bioRxiv; 2020.
14. Brat G, Weber G, Gehlenborg N, Avillach P, Palmer N, Chiovato L, et al. International Electronic Health Record-Derived COVID-19 Clinical Course Profiles: The 4CE Consortium. medRxiv; 2020.
15. Brown J, Atkinson L, Shah D, Harris K. Validation of an extraction-free RT-PCR protocol for detection of SARS-CoV2 RNA. medRxiv; 2020.
16. Buscarini E, Manfredi G, Brambilla G, Menozzi F, Londoni C, Alicante S, et al. Gastrointestinal symptoms as Covid-19 onset in hospitalized Italian patients. medRxiv; 2020.
17. Chen X, Zhao B, Qu Y, Chen Y, Xiong J, Feng Y, et al. Detectable serum SARS-CoV-2 viral load (RNAaemia) is closely correlated with drastically elevated interleukin 6 (IL-6) level in critically ill COVID-19 patients. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.
18. Chen X, Zhao B, Qu Y, Chen Y, Xiong J, Feng Y, et al. Detectable serum SARS-CoV-2 viral load (RNAaemia) is closely associated with drastically elevated interleukin 6 (IL-6) level in critically ill COVID-19 patients. medRxiv; 2020.
19. Chen Y, Bai W, Liu B, Huang J, Laurent I, Deng W, et al. Re-evaluation of Nucleic Acid Retested Positive Cases in the Recovered COVID-19 Patients: Report from a Designated Transfer Hospital in Chongqing, China. Research Square; 2020.
20. Chu J, Yang N, Wei Y, Yue H, Zhang F, Zhao J, et al. Clinical characteristics of 54 medical staff with COVID-19: A retrospective study in a single center in Wuhan, China. J Med Virol. 2020.
21. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin. 2020;25(3).
22. Deng W, Guang T-w, Yang M, Li J-r, Jiang D-p, Li C-y, et al. Positive results for patients with COVID-19 discharged from hospital in Chongqing, China. 2020.
23. Detoc M, Bruel S, Frappe P, Botelho-Nevers E, Gagneux-Brunon A. Intention to participate in a COVID-19 vaccine clinical trial and to get vaccinated against COVID-19 in France during the pandemic. medRxiv; 2020.
24. Diao B, Wen K, Chen J, Liu Y, Yuan Z, Han C, et al. Diagnosis of Acute Respiratory Syndrome Coronavirus 2 Infection by Detection of Nucleocapsid Protein. medRxiv; 2020.
25. Ding X, Yin K, Li Z, Lalla R, Ballesteros E, Sfeir M, et al. All-in-One Dual CRISPR-Cas12a (AIOD-CRISPR) Assay: A Case for Rapid, Ultrasensitive and Visual Detection of Novel Coronavirus SARS-CoV-2 and HIV virus at the Point of Care. Research Square; 2020.
26. Dong J, Wu L, Jin Q, Chen J, He J. Chest CT Scan of Hospitalized Patients with COVID-19: A Case-Control Study. medRxiv; 2020.
27. Eis-Hübinger AM, Hönemann M, Wenzel JJ, Berger A, Widera M, Schmidt B, et al. Ad hoc laboratory-based surveillance of SARS-CoV-2 by real-time RT-PCR using minipools of RNA prepared from routine respi-

ratory samples. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology. 2020;127:104381.
28. El-Tholotha M, Bau H, Song J. A Single and Two-Stage, Closed-Tube, Molecular Test for the 2019 Novel Coronavirus (COVID-19) at Home, Clinic, and Points of Entry. ChemRxiv; 2020.
29. Farfan M, Torres J, Oryan M, Olivares M, Gallardo P, Salas C. Optimizing RT-PCR detection of SARS-CoV-2 for developing countries using pool testing. medRxiv; 2020.
30. Fu H, Xu H, Zhang N, Xu H, Li Z, Chen H, et al. Association between Clinical, Laboratory and CT Characteristics and RT-PCR Results in the Follow-up of COVID-19 patients. medRxiv; 2020.
31. Gil-Agudo A, Rodriguez-Cola M, Jimenez-Velasco I, Gutierrez-Henares F, Lopez-Dolado E, Gambarrutta-Malfatti C, et al. Clinical features of coronavirus disease 2019 (COVID-19) in a cohort of patients with disability due to spinal cord injury. medRxiv; 2020.
32. Gong J, Ou J, Qiu X, Jie Y, Chen Y, Yuan L, et al. A Tool to Early Predict Severe 2019-Novel Coronavirus Pneumonia (COVID-19) : A Multicenter Study using the Risk Nomogram in Wuhan and Guangdong, China. medRxiv; 2020.
33. Gonzalez-Gonzalez E, Lara-Mayorga IM, Garcia-Rubio A, Garciamendez-Mijares CE, Guerra-Alvarez GE, Garcia-Martinez G, et al. Scaling diagnostics in times of COVID-19: Rapid prototyping of 3D-printed water circulators for Loop-mediated Isothermal Amplification (LAMP) and detection of SARS-CoV-2 virus. medRxiv; 2020.
34. Gonzalez-Gonzalez E, Trujillo-de Santiago G, Lara-Mayorga IM, Martinez-Chapa SO, Alvarez MM. Portable and accurate diagnostics for COVID-19: Combined use of the miniPCR thermocycler and a well-plate reader for SARS-CoV-2 virus detection. medRxiv; 2020.
35. Gudbjartsson D, Helgason A, Jonsson H, Magnusson O, Melsted P, Norddahl G, et al. Early Spread of SARS-Cov-2 in the Icelandic Population. medRxiv; 2020.
36. Guo L, Sun X, Wang X, Liang C, Jiang H, Gao Q, et al. SARS-CoV-2 detection with CRISPR diagnostics. bioRxiv; 2020.
37. Gupta N, Bhatnagar T, Rade K, Murhekar M, Gangakhedkar RR, Nagar A. Strategic planning to augment the testing capacity for COVID-19 in India. The Indian journal of medical research. 2020;151(2 & 3):210-5.
38. Han R, Huang L, Jiang H, Dong J, Peng H, Zhang D. Early Clinical and CT Manifestations of Coronavirus Disease 2019 (COVID-19) Pneumonia. AJR American journal of roentgenology. 2020:1-6.
39. He R, Lu Z, Zhang L, Fan T, Xiong R, Shen X, et al. The clinical course and its correlated immune status in COVID-19 pneumonia. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology. 2020;127:104361.
40. Hogan CA, Sahoo MK, Huang C, Garamani N, Stevens B, Zehnder J, et al. Comparison of the Panther Fusion and a laboratory-developed test targeting the envelope gene for detection of SARS-CoV-2. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology. 2020;127:104383.
41. Hu X, Xing Y, Jia J, Ni W, Liang J, Zhao D, et al. Factors associated with negative conversion of viral RNA in patients hospitalized with COVID-19. The Science of the total environment. 2020;728:138812.
42. Hu Y, Shen L, Xu Z, Zhou J, Zhou H. SARS-CoV-2 May Persist in Digestive Tract Longer than Respiratory Tract. Preprints.org; 2020.
43. Hu Z, Song C, Xu C, Jin G, Chen Y, Xu X, et al. Clinical Characteristics of 24 Asymptomatic Infections with COVID-19 Screened among Close Contacts in Nanjing, China. 2020.
44. Hu Z, Song C, Xu C, Jin G, Chen Y, Xu X, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Science China Life sciences. 2020;63(5):706-11.
45. Hua J, Chen R, Zhao L, Wu X, Guo Q, He C, et al. Epidemiological features and medical care-seeking process of patients with COVID-19 in Wuhan, China. ERJ open research. 2020;6(2).
46. Huang D, Huang K, Dai Y, Hu R, Li J, Jiang D, et al. Children are less affected by COVID-19: a family case study. Research Square; 2020.
47. Huang G, Zeng W, Wang W, Song Y, Mo X, Li J, et al. Triaging patients in the outbreak of the 2019 novel coronavirus. medRxiv; 2020.
48. Lavezzo E, Franchin E, Ciavarella C, Cuomo-Dannenburg G, Barzon L, Del Vecchio C, et al. Suppression of COVID-19 outbreak in the municipality of Vo, Italy. medRxiv; 2020.
49. L'Huillier A, Torriani G, Pigny F, Kaiser L, Eckerle I. Shedding of infectious SARS-CoV-2 in symptomatic neonates, children and adolescents. medRxiv; 2020.
50. Li B, Li X, Wang Y, Han Y, Wang C, Zhang G, et al. Diagnostic value and key features of computed tomography in Coronavirus Disease 2019. Emerging microbes & infections. 2020;9(1):787-93.
51. Li D, Wang D, Dong J, Wang N, Huang H, Xu H, et al. False-Negative Results of Real-Time Reverse-Transcriptase Polymerase Chain Reaction for Severe Acute Respiratory Syndrome Coronavirus 2: Role of Deep-Learning-Based CT Diagnosis and Insights from Two Cases. Korean J Radiol. 2020;21(4):505-8.

52. Li H-W, Zhuo L-H, Yan G-W, Wang J-S, Huang G-P, Li J-B, et al. High resolution computed tomography for the diagnosis of 2019 novel coronavirus (2019-nCoV) pneumonia: a study from multiple medical centers in western China. Research Square; 2020.
53. Li J, Zhang Y, Wang F, Liu B, Li H, Tang G, et al. Sex differences in clinical findings among patients with coronavirus disease 2019 (COVID-19) and severe condition. medRxiv; 2020.
54. Li K, Wang W, Zhao C-W, Wu L, Zhu Y-N, Ran R-Y, et al. Corona virus disease 2019: hysteresis effect of chest CT and the correlation of its severity with lymphocyte count in peripheral blood. Research Square; 2020.
55. Li Q, Ding X, Xia G, Chen HG, Chen F, Geng Z, et al. Eosinopenia and elevated C-reactive protein facilitate triage of COVID-19 patients in fever clinic: a retrospective case-control study. EClinicalMedicine. 2020:100375.
56. Li X-j, Shuai B-X, Zhang Z-W, Kang Y. COVID-19 versus non-COVID-19 pneumonia: A retrospective cohort study. medRxiv; 2020.
57. Li Y, Hu Y, Yu Y, Zhang X, Li B, Wu J, et al. Positive result of Sars-Cov-2 in faeces and sputum from discharged patient with COVID-19 in Yiwu, China. J Med Virol. 2020.
58. Li Y, Xia L. Coronavirus Disease 2019 (COVID-19): Role of Chest CT in Diagnosis and Management. AJR American journal of roentgenology. 2020:1-7.
59. Li YK, Peng S, Li LQ, Wang Q, Ping W, Zhang N, et al. Clinical and Transmission Characteristics of Covid-19 - A Retrospective Study of 25 Cases from a Single Thoracic Surgery Department. Current medical science. 2020;40(2):295-300.
60. Liao J, He X, Gong Q, Yang L, Zhou C, Li J. Analysis of vaginal delivery outcomes among pregnant women in Wuhan, China during the COVID-19 pandemic. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2020.
61. Liao Y, Feng Y, Wang B, Wang H, Huang J, Wu Y, et al. Clinical Characteristics and Risk factors for developed COVID-19 patients transferring to designated hospital from Jianghan Fangcang shelter Hospital: a retrospective, observational study. medRxiv; 2020.
62. Lim ZY, Khoo HW, Hui TCH, Kok SSX, Kwan KEL, Young BE, et al. Variable computed tomography appearances of COVID-19. Singapore Med J. 2020.
63. Lin C, Xiang J, Yan M, Li H, Huang S, Shen C. Comparison of throat swabs and sputum specimens for viral nucleic acid detection in 52 cases of novel coronavirus (SARS-Cov-2)-infected pneumonia (COVID-19). Clin Chem Lab Med. 2020.
64. Ling Y, Xu SB, Lin YX, Tian D, Zhu ZQ, Dai FH, et al. Persistence and clearance of viral RNA in 2019 novel coronavirus disease rehabilitation patients. Chin Med J (Engl). 2020;133(9):1039-43.
65. Lista MJ, Page R, Sertkaya H, Matos P, Ortiz-Zapater E, Maguire TJA, et al. Resilient SARS-CoV-2 diagnostics workflows including viral heat inactivation. medRxiv; 2020.
66. Liu R, Han H, Liu F, Lv Z, Wu K, Liu Y, et al. Positive rate of RT-PCR detection of SARS-CoV-2 infection in 4880 cases from one hospital in Wuhan, China, from Jan to Feb 2020. Clinica chimica acta; international journal of clinical chemistry. 2020;505:172-5.
67. Liu R, Ma Q, Han H, Su H, Liu F, Wu K, et al. The value of urine biochemical parameters in the prediction of the severity of coronavirus disease 2019. Clin Chem Lab Med. 2020.
68. Liu R, Ming X, Xu O, Zhou J, Peng H, Xiang N, et al. Association of Cardiovascular Manifestations with In-hospital Outcomes in Patients with COVID-19: A Hospital Staff Data. medRxiv; 2020.
69. Liu W, Tao ZW, Wang L, Yuan ML, Liu K, Zhou L, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Chin Med J (Engl). 2020;133(9):1032-8.
70. Liu Y, Liao W, Wan L, Xiang T, Zhang W. Correlation Between Relative Nasopharyngeal Virus RNA Load and Lymphocyte Count Disease Severity in Patients with COVID-19. Viral Immunol. 2020.
71. Loeffelholz MJ, Alland D, Butler-Wu SM, Pandey U, Perno CF, Nava A, et al. Multicenter Evaluation of the Cepheid Xpert Xpress SARS-CoV-2 Test. J Clin Microbiol. 2020.
72. Lopez-Rincon A, Tonda A, Mendoza-Maldonado L, Claassen E, Garssen J, Kraneveld A. Accurate Identification of SARS-CoV-2 from Viral Genome Sequences using Deep Learning. bioRxiv; 2020.
73. Lu R, Wang J, Li M, Wang Y, Dong J, Cai W. SARS-CoV-2 detection using digital PCR for COVID-19 diagnosis, treatment monitoring and criteria for discharge. medRxiv; 2020.
74. Lu R, Wu X, Wan Z, Li Y, Jin X, Zhang C. A Novel Reverse Transcription Loop-Mediated Isothermal Amplification Method for Rapid Detection of SARS-CoV-2. Int J Mol Sci. 2020;21(8).
75. Lyu Z, Ren M, Wu L-M, Yang Y, Lu Y-B, Li L, et al. The multicenter study of Chest HRCT imaging characteristics of 2019 Novel Coronavirus (COVID-19) Pneumonia. Research Square; 2020.
76. Mahari S, Roberts A, Shahdeo D, Gandhi S. eCovSens-Ultrasensitive Novel In-House Built Printed Circuit Board Based Electrochemical Device for Rapid Detection of nCovid-19 antigen, a spike protein domain 1 of SARS-CoV-2. bioRxiv; 2020.

77. Mai M, Juan Wang, Xia D, Xinming Guo, Fei Li, Chen Y, et al. Survey of Anxiety and Depression in Patients with Suspected and Confirmed Cases of COVID-19 During Hospitalization and Isolation. Research Square; 2020.
78. Marzinotto S, Mio C, Cifu A, Verardo R, Pipan C, Schneider C, et al. A streamlined approach to rapidly detect SARS-CoV-2 infection, avoiding RNA extraction. medRxiv; 2020.
79. Meng H, Xiong R, He R, Lin W, Hao B, Zhang L, et al. CT imaging and clinical course of asymptomatic cases with COVID-19 pneumonia at admission in Wuhan, China. The Journal of infection. 2020.
80. Meng Y, Guo E, Liu J, Huang X, Sun C, Wu P, et al. Value and Challenges: Nucleic Acid Amplification Tests for SARS-CoV-2 in Hospitalized COVID-19 Patients. The Journal of infection. 2020.
81. Metsky H, Freije C, Kosoko-Thoroddsen T-S, Sabeti P, Myhrvold C. CRISPR-based surveillance for COVID-19 using genomically-comprehensive machine learning design. bioRxiv; 2020.
82. Mutnal M, Arroliga A, Walker K, Mohammad A, Brigmon M, Beaver R, et al. Early trends for SARS-CoV-2 infection in central and north Texas and impact on other circulating respiratory viruses. medRxiv; 2020.
83. Nelson A, Auch B, Schomaker M, Gohl D, Grady P, Johnson D, et al. Analytical Validation of a COVID-19 qRT-PCR Detection Assay Using a 384-well Format and Three Extraction Methods. bioRxiv; 2020.
84. Nerli S, Sgourakis N. Structure-based modeling of SARS-CoV-2 peptide/HLA-A02 antigens. bioRxiv; 2020.
85. Nordor A, Siwo G. Predicting Broad-Spectrum Antiviral Drugs against RNA Viruses Using Transcriptional Responses to Exogenous RNA. Preprints.org; 2020.
86. Nunez-Bajo E, Kasimatis M, Cotur Y, Asfour T, Collins A, Tanriverdi U, et al. Ultra-Low-Cost Integrated Silicon-based Transducer for On-Site, Genetic Detection of Pathogens. bioRxiv; 2020.
87. Pan Y, Long L, Zhang D, Yan T, Cui S, Yang P, et al. Potential false-negative nucleic acid testing results for Severe Acute Respiratory Syndrome Coronavirus 2 from thermal inactivation of samples with low viral loads. Clin Chem. 2020.
88. Pan Y, Yu X, Du X, Li Q, Li X, Qin T, et al. Epidemiological and clinical characteristics of 26 asymptomatic SARS-CoV-2 carriers. The Journal of infectious diseases. 2020.
89. Parazzini F, Bortolus R, Mauri PA, Favilli A, Gerli S, Ferrazzi E. Delivery in pregnant women infected with SARS-CoV-2: A fast review. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2020.
90. Patterson B, Seethamraju H, Dhody K, Corley M, Kazempour K, Lalezari J, et al. Disruption of the CCL5/RANTES-CCR5 Pathway Restores Immune Homeostasis and Reduces Plasma Viral Load in Critical COVID-19. medRxiv; 2020.
91. Peng S, Pan L, Zhang S, Liu Y, Zhang H, Tan L, et al. Clinical and Imaging features in COVID-19 Patients: Analysis of Data from Patients in Non-pandemic areas. 2020.
92. Qiu G, Gai Z, Tao Y, Schmitt J, Kullak-Ublick GA, Wang J. Dual-Functional Plasmonic Photothermal Biosensors for Highly Accurate Severe Acute Respiratory Syndrome Coronavirus 2 Detection. ACS nano. 2020.
93. Qiu R, Liu M-w, Zhao C, Li W-m. Analysis on Diagnosis of Family Clustering Infection of SARS-CoV-2. Research Square; 2020.
94. Rahman H, Carter I, Basile K, Donovan L, Kumar S, Tran T, et al. Interpret with caution: An evaluation of the commercial AusDiagnostics versus in-house developed assays for the detection of SARS-CoV-2 virus. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology. 2020;127:104374.
95. Rasheed MA, Raza S, Zohaib A, Yaqub T, Rabbani M, Riaz MI, et al. In Silico Identification of Novel B Cell and T Cell Epitopes of Wuhan Coronavirus (2019-nCoV) for Effective Multi Epitope-Based Peptide Vaccine Production. Preprints.org; 2020.
96. Renieri A, Benetti E, Tita R, Spiga O, Ciolfi A, Birolo G, et al. ACE2 variants underlie interindividual variability and susceptibility to COVID-19 in Italian population. medRxiv; 2020.
97. Robertson M, Kulkarni S, Berry A, Mirzayi C, Maroko A, Zimba R, et al. A national prospective cohort study of SARS/COV2 pandemic outcomes in the U.S.: The CHASING COVID Cohort. medRxiv; 2020.
98. Rossi JJ, Rossi D. Oligonucleotides and the COVID-19 Pandemic: A Perspective. Nucleic Acid Ther. 2020.
99. Seo G, Lee G, Kim MJ, Baek SH, Choi M, Ku KB, et al. Rapid Detection of COVID-19 Causative Virus (SARS-CoV-2) in Human Nasopharyngeal Swab Specimens Using Field-Effect Transistor-Based Biosensor. ACS nano. 2020;14(4):5135-42.
100. Shen N, Zhu Y, Wang X, Peng J, Liu W, Wang F, et al. Characteristics and diagnosis rate of 5,630 subjects receiving SARS-CoV-2 nucleic acid tests from Wuhan, China. JCI insight. 2020.
101. Soares F, Villavicencio A, Fogliatto FS, Rigatto MHP, Anzanello MJ, Idiart M, et al. A novel specific artificial intelligence-based method to identify COVID-19 cases using simple blood exams. medRxiv; 2020.

102. Song W, Li J, Zou N, Guan W, Pan J, Xu W. Clinical features of pediatric patients with coronavirus disease (COVID-19). Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology. 2020;127:104377.
103. Srivatsan S, Han P, van Raay K, Wolf C, McCulloch D, Kim A, et al. Preliminary support for a "dry swab, extraction free" protocol for SARS-CoV-2 testing via RT-qPCR. bioRxiv; 2020.
104. Sun Y, Koh V, Marimuthu K, Ng OT, Young B, Vasoo S, et al. Epidemiological and Clinical Predictors of COVID-19. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.
105. Tammaro A, Adebanjo GAR, Parisella FR, Pezzuto A, Rello J. Cutaneous manifestations in COVID-19: the experiences of Barcelona and Rome. Journal of the European Academy of Dermatology and Venereology : JEADV. 2020.
106. Tan YP, Tan BY, Pan J, Wu J, Zeng SZ, Wei HY. Epidemiologic and clinical characteristics of 10 children with coronavirus disease 2019 in Changsha, China. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology. 2020;127:104353.
107. Vandenberg O. Development and potential usefulness of the COVID-19 Ag Respi-Strip diagnostic assay in a pandemic context. medRxiv; 2020.
108. Vermeiren C, Marchand-Senécal X, Sheldrake E, Bulir D, Smieja M, Chong S, et al. Comparison of Copan Eswab and FLOQswab for COVID-19 PCR diagnosis: working around a supply shortage. J Clin Microbiol. 2020.
109. Wan WY, Lim SH, Seng EH. Cross-reaction of sera from COVID-19 patients with SARS-CoV assays. medRxiv; 2020.
110. Wang K, Kang S, Tian R, Zhang X, Wang Y. Imaging manifestations and diagnostic value of chest CT of coronavirus disease 2019 (COVID-19) in the Xiaogan area. Clin Radiol. 2020;75(5):341-7.
111. Wang M, Fu A, Hu B, Tong Y, Liu R, Gu J, et al. Nanopore target sequencing for accurate and comprehensive detection of SARS-CoV-2 and other respiratory viruses. medRxiv; 2020.
112. Wang M, Wu Q, Xu W, Qiao B, Wang J, Zheng H, et al. Clinical diagnosis of 8274 samples with 2019-novel coronavirus in Wuhan. medRxiv; 2020.
113. Wang Q, Wang X, Lin H. The role of triage in the prevention and control of COVID-19. Infect Control Hosp Epidemiol. 2020:1-15.
114. Wang QX, Zeng XH, Zheng SL. The nucleic acid test of induced sputum should be used for estimation of patients cure with 2019-nCov. Eur Rev Med Pharmacol Sci. 2020;24(7):3437.
115. Wang S, Kang B, Ma J, Zeng X, Xiao M, Guo J, et al. A deep learning algorithm using CT images to screen for Corona Virus Disease (COVID-19). medRxiv; 2020.
116. Wang Y, Liu Y, Liu L, Wang X, Luo N, Ling L. Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China. The Journal of infectious diseases. 2020.
117. Wang Z, Weng J, Li Z, Hou R, Zhou L, Ye H, et al. Development and Validation of a Diagnostic Nomogram to Predict COVID-19 Pneumonia. medRxiv; 2020.
118. Wee SK, Sivalingam SP, Yap EPH. Rapid direct nucleic acid amplification test without RNA extraction for SARS-CoV-2 using a portable PCR thermocycler. bioRxiv; 2020.
119. Weiwei G, Xia Z, Zhiliang H, Yun C, shan ZY, mei HC, et al. Quantifying the clinical characteristics of coronavirus disease 2019 (COVID-19) of different age segments based on 60 patients. Research Square; 2020.
120. Wong HYF, Lam HYS, Fong AH, Leung ST, Chin TW, Lo CSY, et al. Frequency and Distribution of Chest Radiographic Findings in COVID-19 Positive Patients. Radiology. 2019:201160.
121. Woo CH, Jang S, Shin G, Jung GY, Lee JW. Sensitive one-step isothermal detection of pathogen-derived RNAs. medRxiv; 2020.
122. Woodruff M, Ramonell R, Cashman K, Nguyen D, Ley A, Kyu S, et al. Critically ill SARS-CoV-2 patients display lupus-like hallmarks of extrafollicular B cell activation. medRxiv; 2020.
123. Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science. 2020;367(6483):1260-3.
124. Wu G, He S, Chen Q, Ling L, Yan S, Wu X, et al. Study on the Age of SARS-CoV-2 in Respiratory and Digestive Tract Samples: A Retrospective Study guixian-wu1,dongqin-lv*,susu-He,qian-chen,lin-ling,shaungquan-yan,xiaomai-wu,yongpo-jiang. Research Square; 2020.
125. Wu J, Liu J, Li S, Peng Z, Xiao Z, Wang X, et al. Detection and analysis of nucleic acid in various biological samples of COVID-19 patients. Travel Med Infect Dis. 2020:101673.
126. Wu J, Liu J, Zhao X, Liu C, Wang W, Wang D, et al. Clinical Characteristics of Imported Cases of COVID-19 in Jiangsu Province: A Multicenter Descriptive Study. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.

127. Wu Q, Xing Y, Shi L, Li W, Gao Y, Pan S, et al. Epidemiological and Clinical Characteristics of Children with Coronavirus Disease 2019. medRxiv; 2020.
128. Wu Y, Guo W, Liu H, Qi B, Liang K, Xu B, et al. Clinical outcomes of 402 patients with COVID-2019 from a single center in Wuhan, China. medRxiv; 2020.
129. Wu Y, Liu C, Dong L, Zhang C, Chen Y, Liu J, et al. Coronavirus disease 2019 among pregnant Chinese women: Case series data on the safety of vaginal birth and breastfeeding. BJOG : an international journal of obstetrics and gynaecology. 2020.
130. Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. Pediatr Pulmonol. 2020;55(5):1169-74.
131. Xia XY, Wu J, Liu HL, Xia H, Jia B, Huang WX. Epidemiological and initial clinical characteristics of patients with family aggregation of COVID-19. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology. 2020;127:104360.
132. Xiao AT, Tong YX, Zhang S. False-negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: Rather than recurrence. J Med Virol. 2020.
133. Xie C, Jiang L, Huang G, Pu H, Gong B, Lin H, et al. Comparison of different samples for 2019 novel coronavirus detection by nucleic acid amplification tests. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2020;93:264-7.
134. Xie Y, Yang L, Dong H, Peng H, Yu Y, Tu G, et al. CT scores predict mortality in 2019-nCoV pneumonia. Research Square; 2020.
135. Xing Q, Li G, Xing Y, Chen T, Li W, Ni W, et al. Precautions are Needed for COVID-19 Patients with Coinfection of Common Respiratory Pathogens. medRxiv; 2020.
136. Xiong Y, Li Z-Z, Zhuang Q-Z, Chao Y, Li F, Ge Y-Y, et al. Comparative performance of four nucleic acid amplification tests for SARS-CoV-2 virus. bioRxiv; 2020.
137. Xu H, Liu E, Xie J, Smyth R, Zhou Q, Zhao R, et al. A follow-up study of children infected with SARS-CoV-2 from Western China. 2020.
138. Xu H, Yan L, Qiu C, Jiao B, Chen Y, Tan X, et al. Analysis and Prediction of False Negative Results for SARS-CoV-2 Detection with Pharyngeal Swab Specimen in COVID-19 Patients: A Retrospective Study. medRxiv; 2020.
139. Xu Z-Q, Wang J-Z, Wang H-R, He J-F, Wang B, Yang Y-C, et al. Research on COVID-19 prevention and control strategies, and the effect of home quarantine in Shenzhen, China, 2020. Research Square; 2020.
140. Xue X, Ma J, Zhao Y, Zhao A, Liu X, Guo W, et al. Correlation between hypophosphatemia and the severity of Corona Virus Disease 2019 patients. medRxiv; 2020.
141. Yang L, Tang Y-P, Chen G-X, Wang L, Lan X, Ji C, et al. Research on pneumonia exacerbation in patients infected with SARS-CoV-2 in Wuhan, China. 2020.
142. Yang N, Che S, Zhang J, Wang X, Tang Y, Wang J, et al. Breastfeeding of Infants Born to Mothers with COVID-19: A Rapid Review. medRxiv; 2020.
143. Yang P, Wang X, Liu P, Wei C, He B, Zheng J, et al. Clinical characteristics and risk assessment of newborns born to mothers with COVID-19. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology. 2020;127:104356.
144. Yang Q, Liu Q, Xu H, Lu H, Liu S, Li H. Imaging of coronavirus disease 2019: A Chinese expert consensus statement. Eur J Radiol. 2020;127:109008.
145. Yang W, Dang X, Wang Q, Xu M, Zhao Q, Zhou Y, et al. Rapid Detection of SARS-CoV-2 Using Reverse transcription RT-LAMP method. medRxiv; 2020.
146. Yu J, Xiang T, Xu X, Zuo W, Zhou C, Liu Y, et al. Changes in the clinical characteristics of severe Corona Virus Disease 2019 in Jiangxi Province. Research Square; 2020.
147. Yuan B, An Y-W, Chen Y-X, Yang J, Wang J-C, Li W-X, et al. Epidemiological Characteristics of 417 patients infected with COVID-19 and 368 discharged cases among them in Shenzhen City, China. Research Square; 2020.
148. Yun H, Sun Z, Wu J, Tang A, Hu M, Xiang Z. Laboratory data analysis of novel coronavirus (COVID-19) screening in 2510 patients. Clinica chimica acta; international journal of clinical chemistry. 2020;507:94-7.
149. Zhai P, Ding Y, Wu X, Long J, Zhong Y, Li Y. The epidemiology, diagnosis and treatment of COVID-19. Int J Antimicrob Agents. 2020:105955.
150. zhang c, Hong D, Chen W, Ren Q, Guan Q. Clinical analysis of 17 deaths associated with the 2019 novel coronavirus. Research Square; 2020.
151. Zhang H, Lu L, Hu W, Zhang J, Zhu W, He Q, et al. Analysis of clinical characteristics of SARS-CoV-2 infected cases: a retrospective study of medical records. Research Square; 2020.
152. Zhang H, Shang W, Liu Q, Zhang X, Zheng M, Yue M. Clinical characteristics of 194 cases of COVID-19 in Huanggang and Taian, China. Research Square; 2020.

153. Zhang J, Wang S, Xue Y. Fecal specimen diagnosis 2019 novel coronavirus-infected pneumonia. J Med Virol. 2020.
154. zhang s. Simultaneous Detection of 2019 Novel Coronavirus and Influenza Virus by Double Fluorescent RT-PCR. Research Square; 2020.
155. Zhang Y. Gastrointestinal tract symptoms in coronavirus disease 2019: Analysis of clinical symptoms in adult patients. medRxiv; 2020.
156. Zhang Y, Chen R, Wang J, Gong Y, Zhou Q, Cheng H-h, et al. Anaesthetic managment and clinical outcomes of parturients with COVID-19: a multicentre, retrospective, propensity score matched cohort study. medRxiv; 2020.
157. Zhen-Dong YP, Gao-Jun ZP, Run-Ming J, Zhi-Sheng L, Zong-Qi DP, Xiong X, et al. Clinical and Transmission Dynamics Characteristics of 406 Children with Coronavirus Disease 2019 in China: A Review. The Journal of infection. 2020.
158. Zheng G, Xie C, Liu D, Ye G, Chen X, Wang P, et al. Clinical analysis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children. Research Square; 2020.
159. Zheng S, Fan J, Yu F, Feng B, Lou B, Zou Q, et al. Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study. BMJ. 2020;369:m1443.
160. Zheng Y, Xiong C, Liu Y, Qian X, Tang Y, Liu L, et al. Epidemiological and Clinical Characteristics Analysis of COVID-19 in the Surrounding Areas of Wuhan, Hubei Province in 2020. Pharmacol Res. 2020:104821.
161. Zhifeng J, Feng A, Li T. Consistency analysis of COVID-19 nucleic acid tests and the changes of lung CT. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology. 2020;127:104359.
162. zhou y, Pei F, Wang L, Zhao H, Li H, Ji M, et al. Sensitivity evaluation of 2019 novel coronavirus (SARS-CoV-2) RT-PCR detection kits and strategy to reduce false negative. medRxiv; 2020.
163. Zhou Y, Yang L, Han M, Huang M, Sun X, Zhen W, et al. Clinical Reports on Early Diagnosis of Novel Coronavirus (2019-nCoV) Pneumonia in Stealth Infected Patients. Preprints.org; 2020.
164. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. Translational pediatrics. 2020;9(1):51-60.

E3 wrong/ no reference test

1. Du Y, Zhang T-h, Meng X, Shi Y, Hu M, Yuan S, et al. Development of high affinity monobodies recognizing SARS-CoV-2 antigen. Research Square; 2020.
2. Peng L, Liu KY, Xue F, Miao YF, Tu PA, Zhou C. Improved Early Recognition of Coronavirus Disease-2019 (COVID-19): Single-Center Data from a Shanghai Screening Hospital. Arch Iran Med. 2020;23(4):272-6.
3. Zhang X, Wu X, Wang D, Lu M, Hou X, Wang H, et al. Proteome-wide analysis of differentially-expressed SARS-CoV-2 antibodies in early COVID-19 infection. medRxiv; 2020.

E4 wrong outcome

1. Adams E, Augustin Y, Byrne R, Clark D, Cocozza M, Cubas-Atienzar A, et al. Rapid development of COVID-19 rapid diagnostics for low resource settings: accelerating delivery through transparency, responsiveness, and open collaboration. medRxiv; 2020.
2. Cai X, Chen J, Hu J, Long Q, Deng H, Fan K, et al. A Peptide-based Magnetic Chemiluminescence Enzyme Immunoassay for Serological Diagnosis of Corona Virus Disease 2019 (COVID-19). medRxiv; 2020.
3. de Lusignan S, Lopez Bernal J, Zambon M, Akinyemi O, Amirthalingam G, Andrews N, et al. Emergence of a Novel Coronavirus (COVID-19): Protocol for Extending Surveillance Used by the Royal College of General Practitioners Research and Surveillance Centre and Public Health England. JMIR public health and surveillance. 2020;6(2):e18606.
4. Diao B, Wang C, Wang R, Feng Z, Tan Y, Wang H, et al. Human Kidney is a Target for Novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection. medRxiv; 2020.
5. Dong C, Ni L, Ye F, Chen M-L, Feng Y, Deng Y-Q, et al. Characterization of anti-viral immunity in recovered individuals infected by SARS-CoV-2. medRxiv; 2020.
6. Du Z, Zhu F, Guo F, Yang B, Wang T. Detection of antibodies against SARS-CoV-2 in patients with COVID-19. J Med Virol. 2020.

7. Garcia FP, Perez Tanoira R, Romanyk Cabrera JP, Arroyo Serrano T, Gomez Herruz P, Cuadros Gonzalez J. Rapid diagnosis of SARS-CoV-2 infection by detecting IgG and IgM antibodies with an immunochromatographic device: a prospective single-center study. medRxiv; 2020.
8. GeurtsvanKessel C, Okba NMA, Igloi Z, Embregts CWE, Laksono B, Leijten L, et al. Towards the next phase: evaluation of serological assays for diagnostics and exposure assessment. medRxiv; 2020.
9. Grzelak L, Temmam S, Planchais C, Demeret C, Huon C, Guivel F, et al. SARS-CoV-2 serological analysis of COVID-19 hospitalized patients, pauci-symptomatic individuals and blood donors. medRxiv; 2020.
10. Guo L, Ren L, Yang S, Xiao M, Chang D, Yang F, et al. Profiling Early Humoral Response to Diagnose Novel Coronavirus Disease (COVID-19). Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.
11. Infantino M, Grossi V, Lari B, Bambi R, Perri A, Manneschi M, et al. Diagnostic accuracy of an automated chemiluminescent immunoassay for anti-SARS-CoV-2 IgM and IgG antibodies: an Italian experience. J Med Virol. 2020.
12. Jin Y, Wang M, Zuo Z, Fan C, Ye F, Cai Z, et al. Diagnostic value and dynamic variance of serum antibody in coronavirus disease 2019. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2020;94:49-52.
13. Khan S, Nakajima R, Jain A, de Assis RR, Jasinskas A, Obiero J, et al. Analysis of Serologic Cross-Reactivity Between Common Human Coronaviruses and SARS-CoV-2 Using Coronavirus Antigen Microarray. bioRxiv; 2020.
14. Li N, Wang X, Lv T. Prolonged SARS-CoV-2 RNA shedding: Not a rare phenomenon. J Med Virol. 2020.
15. Lippi G, Salvagno GL, Pegoraro M, Militello V, Caloi C, Peretti A, et al. Assessment of immune response to SARS-CoV-2 with fully automated MAGLUMI 2019-nCoV IgG and IgM chemiluminescence immunoassays. Clin Chem Lab Med. 2020.
16. Norman M, Gilboa T, Ogata A, Maley A, Cohen L, Cai Y, et al. Ultra-Sensitive High-Resolution Profiling of Anti-SARS-CoV-2 Antibodies for Detecting Early Seroconversion in COVID-19 Patients. medRxiv; 2020.
17. Padoan A, Cosma C, Sciacovelli L, Faggian D, Plebani M. Analytical performances of a chemiluminescence immunoassay for SARS-CoV-2 IgM/IgG and antibody kinetics. Clin Chem Lab Med. 2020.
18. Perera RA, Mok CK, Tsang OT, Lv H, Ko RL, Wu NC, et al. Serological assays for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), March 2020. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin. 2020;25(16).
19. Suo T, Liu X, Guo M, Feng J, Hu W, Yang Y, et al. ddPCR: a more sensitive and accurate tool for SARS-CoV-2 detection in low viral load specimens. medRxiv; 2020.
20. Tan CW, Chia WN, Chen MIC, Hu Z, Young B, Tan Y-J, et al. A SARS-CoV-2 surrogate virus neutralization test (sVNT) based on antibody-mediated blockage of ACE2-spike (RBD) protein-protein interaction. Research Square; 2020.
21. Wang Z, Li H, Li J, Yang C, Guo X, Hu Z, et al. Elevated serum IgM levels indicate poor outcome in patients with coronavirus disease 2019 pneumonia: A retrospective case-control study. medRxiv; 2020.
22. Xiang J, Yan M, Li H, Liu T, Lin C, Huang S, et al. Evaluation of Enzyme-Linked Immunoassay and Colloidal Gold- Immunochromatographic Assay Kit for Detection of Novel Coronavirus (SARS-Cov-2) Causing an Outbreak of Pneumonia (COVID-19). medRxiv; 2020.

E5 wrong study design

1. The race against COVID-19. Nature nanotechnology. 2020;15(4):239-40.
2. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). Intensive Care Med. 2020:1-34.
3. Ali M, Zaid M, Saqib MAN, Ahmed H, Afzal MS. SARS-CoV-2 and the Hidden Carriers - Sewage, Feline, and Blood Transfusion. J Med Virol. 2020.
4. Amanat F, Stadlbauer D, Strohmeier S, Nguyen T, Chromikova V, McMahon M, et al. A serological assay to detect SARS-CoV-2 seroconversion in humans. medRxiv; 2020.
5. An P, Song P, Lian K, Wang Y. CT Manifestations of Novel Coronavirus Pneumonia: A Case Report. Balkan medical journal. 2020;37(3):163-5.
6. Armengaud J, Delaunay-Moisan A, Thuret JY, van Anken E, Acosta-Alvear D, Aragón T, et al. The Importance Of Naturally Attenuated Sars-Cov-2 In The Fight Against Covid-19. Environ Microbiol. 2020.
7. Assis Rd, Jain A, Nakajima R, Jasinskas A, Felgner J, Obiero J, et al. Analysis of SARS-CoV-2 Antibodies in COVID-19 Convalescent Plasma using a Coronavirus Antigen Microarray. bioRxiv; 2020.

8. Baig AM. The Devil in its Details: Unravelling the Epitopes in COVID-19 Surface Glycoprotein with the potential for Vaccination and Antibody Synthesis. 2020.
9. Bastian I, Waring L. The Royal College of Pathologists of Australasia (RCPA) position statement on COVID-19. Australian journal of general practice. 2020;49.
10. Bedford T, Greninger A, Roychoudhury P, Starita L, Famulare M, Huang M-L, et al. Cryptic transmission of SARS-CoV-2 in Washington State. medRxiv; 2020.
11. Beeching NJ, Fletcher TE, Beadsworth MBJ. Covid-19: testing times. BMJ. 2020;369:m1403.
12. Bennett S, Steyvers M. Estimating COVID-19 Antibody Seroprevalence in Santa Clara County, California. A re-analysis of Bendavid et al. 2020.
13. Bouman J, Bonhoeffer S, Regoes R. Estimating seroprevalence with imperfect serological tests: a cutoff-free approach. bioRxiv; 2020.
14. Brufsky A. Hyperglycemia, hydroxychloroquine, and the COVID-19 pandemic. J Med Virol. 2020.
15. Burbelo P, Riedo F, Morishima C, Rawlings S, Smith D, Das S, et al. Detection of Nucleocapsid Antibody to SARS-CoV-2 is More Sensitive than Antibody to Spike Protein in COVID-19 Patients. medRxiv; 2020.
16. Chen H, Ai L, Lu H, Li H. Clinical and imaging features of COVID-19. Radiology of infectious diseases (Beijing, China). 2020.
17. Chen L-D, Li H, Ye Y-M, Wu Z, Huang Y-P, Zhang W-L, et al. A COVID-19 patient with multiple negative results for PCR assays outside Wuhan, China: a case report. Research Square; 2020.
18. Chen Z, Zhang Z, Zhai X, Li Y, Lin L, Zhao H, et al. Rapid and Sensitive Detection of anti-SARS-CoV-2 IgG, Using Lanthanide-Doped Nanoparticles-Based Lateral Flow Immunoassay. Anal Chem. 2020.
19. Chi X, Liu X, Wang C, Zhang X, Ren L, Jin Q, et al. Humanized Single Domain Antibodies Neutralize SARS-CoV-2 by Targeting Spike Receptor Binding Domain. bioRxiv; 2020.
20. Davoodi L, Taghavi M, Razavi A. COVID-19 presented with Deep Vein Thrombosis: An unusual case report. Research Square; 2020.
21. Deforche K. An age-structured epidemiological model of the Belgian COVID-19 epidemic. 2020.
22. Delius G, Powell B, Bees M, Constable G, MacKay N, Pitchford J. More prevalent, less deadly? Bayesian inference of the COVID19 Infection Fatality Ratio from mortality data. 2020.
23. Desautels T, Zemla A, Lau E, Franco M, Faissol D. Rapid in silico design of antibodies targeting SARS-CoV-2 using machine learning and supercomputing. 2020.
24. Di Giambenedetto S, Ciccullo A, Posteraro B, Lombardi F, Borghetti A, Sanguinetti M. Still much to learn about the diagnostic role of SARS-CoV-2 antibody detection. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.
25. di Mauro G, Cristina S, Concetta R, Francesco R, Annalisa C. SARS-Cov-2 infection: Response of human immune system and possible implications for the rapid test and treatment. Int Immunopharmacol. 2020;84:106519.
26. Djaileb A, Charron B, Jodaylami MH, Thibault V, Coutu J, Stevenson K, et al. A Rapid and Quantitative Serum Test for SARS-CoV-2 Antibodies with Portable Surface Plasmon Resonance Sensing. ChemRxiv; 2020.
27. Esbin MN, Whitney ON, Chong S, Maurer A, Darzacq X, Tjian R. Overcoming the bottleneck to widespread testing: A rapid review of nucleic acid testing approaches for COVID-19 detection. RNA (New York, NY). 2020.
28. Feng H, Bu L. 18F-FDG PET/CT uptake in COVID-19: case report of a patient with lung metastases after treatment of nasal cavity malignancy. Research Square; 2020.
29. Fuhrmann J, Barbarossa MV. The Signicance of the Detection Ratio for Predictions on the Outcome of an Epidemic - A Message from Mathematical Modelers. Preprints.org; 2020.
30. German R, Djanatliev A, Maile L, Bazan P, Hackstein H. Modeling Exit Strategies from COVID-19 Lockdown with a Focus on Antibody Tests. 2020.
31. Golinelli D, Fantini MP, Maietti E. COVID-19 in Italy: Is the Virus Running Through an Ancient Roman road? : Preprints.org; 2020.
32. Gonzalez J, Shelton J, Diaz-Vallejo M, Rodriguez-Castellanos V, Zuluaga JD, Chamorro D, et al. Immunological assays for SARS-CoV-2: an analysis of available commercial tests to measure antigen and antibodies. medRxiv; 2020.
33. Gray N, Calleja D, Wimbush A, Miralles-Dolz E, Gray A, De-Angelis M, et al. "No test is better than a bad test": Impact of diagnostic uncertainty in mass testing on the spread of Covid-19. medRxiv; 2020.
34. Hachim A, Kavian N, Cohen C, Chin AWH, Chu DKW, Mok CKP, et al. Beyond the Spike: identification of viral targets of the antibody response to SARS-CoV-2 in COVID-19 patients. medRxiv; 2020.
35. Hao Q, Wu H, Wang Q. Difficulties in False Negative Diagnosis of Coronavirus Disease 2019: A Case Report. Research Square; 2020.
36. Hong Y, Huang J, Chen D, Ye Y, Su F, Dai J, et al. Clinical characteristics of Coronavirus Disease 2019 outside Wuhan and development of early risk stratification tool. 2020.

37. Hoque N, Chaudhury A, Akanda MAM, Hossain A, Islam MT. Genomic Diversity and Evolution, Diagnosis, Prevention, and Therapeutics of the Pandemic COVID-19 Disease. Preprints.org; 2020.
38. Hosier H, Farhadian S, Morotti R, Deshmukh U, Lu-Culligans A, Campbell K, et al. First case of placental infection with SARS-CoV-2. medRxiv; 2020.
39. Hsin F, Chao T-L, Chan Y-R, Kao H-C, Liu W-D, Wang J-T, et al. Distinct Inductions of and Responses to Type I and Type III Interferons Promote Infections in Two SARS-CoV-2 Isolates. bioRxiv; 2020.
40. Hu K, Zhao Y, Wang M, Zeng Q, Wang X, Wang M, et al. Identification of a super-spreading chain of transmission associated with COVID-19. 2020.
41. Hu X, An T, Situ B, Hu Y, Ou Z, Li Q, et al. Heat inactivation of serum interferes with the immunoanalysis of antibodies to SARS-CoV-2. medRxiv; 2020.
42. Huang H, Fan C, Li M, Nie HL, Wang FB, Wang H, et al. COVID-19: A Call for Physical Scientists and Engineers. ACS nano. 2020;14(4):3747-54.
43. Huang L, Shi Y, Gong B, Jiang L, Liu X, Yang J, et al. Blood single cell immune profiling reveals the interferon-MAPK pathway mediated adaptive immune response for COVID-19. medRxiv; 2020.
44. Iacobucci G. Covid-19: Antibody tests will not be rolled out in UK until at least May, MPs hear. BMJ. 2020;369:m1449.
45. Iwasaki A, Yang Y. The potential danger of suboptimal antibody responses in COVID-19. Nat Rev Immunol. 2020.
46. Jahan Y, Rahman S, Rahman A. COVID-19: A case report from Bangladesh perspective. Respiratory medicine case reports. 2020:101068.
47. Jain N, Shankar U, Majee P, Kumar A. Scrutinizing the SARS-CoV-2 protein information for the designing an effective vaccine encompassing both the T-cell and B-cell epitopes. bioRxiv; 2020.
48. Jiang H-w, Li Y, Zhang H-n, Wang W, Men D, Yang X, et al. Global profiling of SARS-CoV-2 specific IgG/IgM responses of convalescents using a proteome microarray. medRxiv; 2020.
49. Joly E. Confronting Covid-19 by exploring the possibility of vaccinating with live SARS-CoV-2 virus itself, via a route that would reduce the incidence of pulmonary complications. F1000Res; 2020.
50. Joosten R, Abhishta A. A simulation-based procedure to estimate base rates from Covid-19 antibody test results I: Deterministic test reliabilities. 2020.
51. Ju B, Zhang Q, Ge X, Wang R, Yu J, Shan S, et al. Potent human neutralizing antibodies elicited by SARS-CoV-2 infection. bioRxiv; 2020.
52. Larremore D, Fosdick B, Bubar K, Zhang S, Kissler S, Metcalf J, et al. Estimating SARS-CoV-2 seroprevalence and epidemiological parameters with uncertainty from serological surveys. 2020.
53. Lee NY, Li CW, Tsai HP, Chen PL, Syue LS, Li MC, et al. A case of COVID-19 and pneumonia returning from Macau in Taiwan: Clinical course and anti-SARS-CoV-2 IgG dynamic. Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi. 2020.
54. Lehrer S. Inhaled biguanides and mTOR inhibition for influenza and coronavirus (Review). World Academy of Sciences journal. 2020;2(3).
55. Lesniewski A. Estimating population immunity without serological testing. 2020.
56. Levesque J, Maybury D. A note on COVID-19 seroprevalence studies: a meta-analysis using hierarchical modelling. 2020.
57. Lin F, Huang Y, Zhang H, He X, Yin Y, Liu J. Evaluating the different control policies for COVID-19 between mainland China and European countries by a mathematical model in the confirmed cases. 2020.
58. Lin L, Lu L, Cao W, Li T. Hypothesis for potential pathogenesis of SARS-CoV-2 infection-a review of immune changes in patients with viral pneumonia. Emerging microbes & infections. 2020;9(1):727-32.
59. Lipsitch M, Kahn R, Mina MJ. Antibody testing will enhance the power and accuracy of COVID-19-prevention trials. Nat Med. 2020.
60. Liu PP, Blet A, Smyth D, Li H. The Science Underlying COVID-19: Implications for the Cardiovascular System. Circulation. 2020.
61. Liu WD, Chang SY, Wang JT, Tsai MJ, Hung CC, Hsu CL, et al. Prolonged virus shedding even after seroconversion in a patient with COVID-19. The Journal of infection. 2020.
62. Liu X, Wu J, Liu M, Dai Y, Zhou D, Li W, et al. Presymptomatic transmission of COVID-19 in a cluster of cases occurred in confined space: a case report. Research Square; 2020.
63. Loeffelholz MJ, Tang YW. Laboratory diagnosis of emerging human coronavirus infections - the state of the art. Emerging microbes & infections. 2020;9(1):747-56.
64. Loghin C, Chauhan S, Lawless SM. Pseudo acute myocardial infarction in a young COVID-19 patient. JACC Case reports. 2020.

65. Lourenco J, Paton R, Ghafari M, Kraemer M, Thompson C, Simmonds P, et al. Fundamental principles of epidemic spread highlight the immediate need for large-scale serological surveys to assess the stage of the SARS-CoV-2 epidemic. medRxiv; 2020.
66. Lu D, Sang L, Du S, Li T, Chang Y, Yang XA. Asymptomatic COVID-19 infection in late pregnancy indicated no vertical transmission. J Med Virol. 2020.
67. Ma XP, Wang H, Bai DM, Zou Y, Zhou SM, Wen FQ, et al. Prevention program for the COVID-19 in a children's digestive endoscopy center. World journal of clinical cases. 2020;8(8):1343-9.
68. Mahase E. Covid-19: Confidentiality agreements allow antibody test manufacturers to withhold evaluation results. BMJ. 2020;369:m1816.
69. Mallapaty S. Will antibody tests for the coronavirus really change everything? Nature. 2020;580(7805):571-2.
70. Mamedov T, Soylu I, Mammadova G, Hasanova G. Sequence Analysis and Amino Acid Variations of Structural Proteins Deduced From Novel Coronavirus SARS-CoV-2 Strains, Isolated in Different Countries. Preprints.org; 2020.
71. Manikyam H, Joshi S. Computational methods to develop potential neutralizing antibody Fab region against SARS-CoV-2 as therapeutic and diagnostic tool. bioRxiv; 2020.
72. Matricardi PM, Dal Negro RW, Nisini R. The first, holistic immunological model of COVID-19: implications for prevention, diagnosis, and public health measures. Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology. 2020.
73. Maxmen A. The researchers taking a gamble with antibody tests for coronavirus. Nature. 2020.
74. McCarthy MW. Harnessing the potential of CRISPR-based platforms to advance the field of hospital medicine. Expert Rev Anti Infect Ther. 2020:1-7.
75. McDade T, McNally E, D'Aquila RT, Mustanski B, Miller A, Vaught L, et al. Enzyme immunoassay for SARS-CoV-2 antibodies in dried blood spot samples: A minimally-invasive approach to facilitate community- and population-based screening. medRxiv; 2020.
76. Melgaço JG, Azamor T, Ano Bom APD. Protective immunity after COVID-19 has been questioned: What can we do without SARS-CoV-2-IgG detection? Cell Immunol. 2020;353:104114.
77. Mercurio I, Tragni V, Busco F, De Grassi A, Pierri CL. Protein structure analysis of the interactions between SARS-CoV-2 spike protein and the human ACE2 receptor: from conformational changes to novel neutralizing antibodies. bioRxiv; 2020.
78. Meyerowitz EA, Vannier AGL, Friesen MGN, Schoenfeld S, Gelfand JA, Callahan MV, et al. Rethinking the role of hydroxychloroquine in the treatment of COVID-19. FASEB journal : official publication of the Federation of American Societies for Experimental Biology. 2020;34(5):6027-37.
79. Moriguchi T, Harii N, Goto J, Harada D, Sugawara H, Takamino J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2020;94:55-8.
80. Morrison AR, Johnson JM, Ramesh M, Bradley P, Jennings J, Smith ZR. Letter to the Editor: Acute hypertriglyceridemia in patients with COVID-19 receiving tocilizumab. J Med Virol. 2020.
81. Mukherjee A, Ahmad M, Frenia D. A Coronavirus Disease 2019 (COVID-19) Patient with Multifocal Pneumonia Treated with Hydroxychloroquine. Cureus. 2020;12(3):e7473.
82. Nguyen A, David JK, Maden SK, Wood MA, Weeder BR, Nellore A, et al. Human leukocyte antigen susceptibility map for SARS-CoV-2. J Virol. 2020.
83. Nguyen L, Smith B, Jain P. Enhancement of trans-cleavage activity of Cas12a with engineered crRNA enables amplified nucleic acid detection. bioRxiv; 2020.
84. Nicastri E, D'Abramo A, Faggioni G, De Santis R, Mariano A, Lepore L, et al. Coronavirus disease (COVID-19) in a paucisymptomatic patient: epidemiological and clinical challenge in settings with limited community transmission, Italy, February 2020. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin. 2020;25(11).
85. Novi G, Mikulska M, Briano F, Toscanini F, Tazza F, Uccelli A, et al. COVID-19 in a MS patient treated with ocrelizumab: does immunosuppression have a protective role? Multiple sclerosis and related disorders. 2020;42:102120.
86. Ong E, Wong M, Huffman A, He Y. COVID-19 coronavirus vaccine design using reverse vaccinology and machine learning. 2020.
87. Orsburn B, Jenkins C, Miller S, Neely B, Bumpus N. In silico approach toward the identification of unique peptides from viral protein infection: Application to COVID-19. bioRxiv; 2020.
88. Ou J, Zhou Z, Dai R, Zhang J, Lan W, Zhao S, et al. Emergence of RBD mutations in circulating SARS-CoV-2 strains enhancing the structural stability and human ACE2 receptor affinity of the spike protein. bioRxiv; 2020.

89. Ou X, Liu Y, Lei X, Li P, Mi D, Ren L, et al. Characterization of spike glycoprotein of SARS-CoV-2 on virus entry and its immune cross-reactivity with SARS-CoV. Nature communications. 2020;11(1):1620.
90. Ozma MA, Maroufi P, Khodadadi E, Köse Ş, Esposito I, Ganbarov K, et al. Clinical manifestation, diagnosis, prevention and control of SARS-CoV-2 (COVID-19) during the outbreak period. Infez Med. 2020;28(2):153-65.
91. Pachetti M, Marini B, Benedetti F, Giudici F, Mauro E, Storici P, et al. Emerging SARS-CoV-2 mutation hot spots include a novel RNA-dependent-RNA polymerase variant. J Transl Med. 2020;18(1):179.
92. Pan X, Zhou P, Fan T, Wu Y, Zhang J, Shi X, et al. Immunoglobulin fragment F(ab')2 against RBD potently neutralizes SARS-CoV-2 in vitro. 2020.
93. Park T, Lee S-Y, Kim S, Kim MJ, Kim HG, Jun S, et al. Spike protein binding prediction with neutralizing antibodies of SARS-CoV-2. bioRxiv; 2020.
94. Patel R, Babady E, Theel ES, Storch GA, Pinsky BA, St George K, et al. Report from the American Society for Microbiology COVID-19 International Summit, 23 March 2020: Value of Diagnostic Testing for SARS-CoV-2/COVID-19. mBio. 2020;11(2).
95. Pei S, Yuan X, Zhimin Zhang Z, Run Yao R, Xie Y, Minxue Shen M, et al. Convalescent Plasma to Treat COVID-19: Chinese Strategy and Experiences. medRxiv; 2020.
96. Peng Z, Wang J, Mo Y, Duan W, Xiang G, Yi M, et al. Unlikely SARS-CoV-2 vertical transmission from mother to child: A case report. Journal of infection and public health. 2020;13(5):818-20.
97. Petherick A. Developing antibody tests for SARS-CoV-2. Lancet (London, England). 2020;395(10230):1101-2.
98. Peto J, Alwan NA, Godfrey KM, Burgess RA, Hunter DJ, Riboli E, et al. Universal weekly testing as the UK COVID-19 lockdown exit strategy. Lancet (London, England). 2020;395(10234):1420-1.
99. Pfaender S, Mar K, Michailidis E, Kratzel A, Hirt D, V'kovski P, et al. LY6E impairs coronavirus fusion and confers immune control of viral disease. bioRxiv; 2020.
100. Pinto D, Park Y-J, Beltramello M, Walls A, Tortorici A, Bianchi S, et al. Structural and functional analysis of a potent sarbecovirus neutralizing antibody. bioRxiv; 2020.
101. Pizzorno A, Padey B, Julien T, Trouillet-Assant S, Traversier A, Errazuriz-Cerda E, et al. Characterization and treatment of SARS-CoV-2 in nasal and bronchial human airway epithelia. bioRxiv; 2020.
102. Poh CM, Carissimo G, Wang B, Amrun SN, Lee CY-P, Chee RS-L, et al. Potent neutralizing antibodies in the sera of convalescent COVID-19 patients are directed against conserved linear epitopes on the SARS-CoV-2 spike protein. bioRxiv; 2020.
103. Preskorn SH. Mental Health Care Providers Dealing With Coronavirus Disease 2019 (COVID-19): What Is the Definition of a Case, How Is That Changing, and What Kinds of Tests Are Available? J Psychiatr Pract. 2020.
104. Qamar MTu, Shahid F, Ashfaq UA, Aslam S, Fatima I, Fareed MM, et al. Structural modeling and conserved epitopes prediction against SARS-COV-2 structural proteins for vaccine development. Research Square; 2020.
105. Qiu R, Zhao C, Liang T, Hao X, Huang Y, Zhang X, et al. Core Outcome Set for Clinical Trials of COVID-19 based on Traditional Chinese and Western Medicine. 2020.
106. Rabaan A, Al-Ahmed S, Sah R, Tiwari R, Yatoo MI, Patel SK, et al. SARS-CoV-2/COVID-19 and Advances in Developing Potential Therapeutics and Vaccines to Counter this Emerging Pandemic Virus – A Review. Preprints.org; 2020.
107. Radon K, Saathoff E, Pritsch M, Guggenbuehl Noller JM, Kroidl I, Olbrich L, et al. Protocol of a population-based prospective COVID-19 cohort study Munich, Germany (KoCo19). 2020.
108. Rattanapisit K, Shanmugaraj B, Manopwisedjaroen S, Purwono PB, Siriwattananon K, Khorattanakulchai N, et al. Rapid and Scalable Production of Functional Anti-Coronavirus Monoclonal Antibody CR3022 in Plants. Research Square; 2020.
109. Ricke D, Malone R. Medical Countermeasures Analysis of 2019-nCoV and Vaccine Risks for Antibody-Dependent Enhancement (ADE). Preprints.org; 2020.
110. Rodrigues C, Baia I, Domingues R, Barros H. Pregnancy and breastfeeding during COVID-19 pandemic: A systematic review of published pregnancy cases. medRxiv; 2020.
111. Rokni M, Ghasemi V, Tavakoli Z. Immune responses and pathogenesis of SARS-CoV-2 during an outbreak in Iran: Comparison with SARS and MERS. Rev Med Virol. 2020.
112. Ruan ZR, Gong P, Han W, Huang MQ, Han M. A case of 2019 novel coronavirus infected pneumonia with twice negative 2019-nCoV nucleic acid testing within 8 days. Chin Med J (Engl). 2020.
113. Rubino S, Kelvin N, Bermejo-Martin JF, Kelvin D. As COVID-19 cases, deaths and fatality rates surge in Italy, underlying causes require investigation. Journal of infection in developing countries. 2020;14(3):265-7.
114. Santiago I. Trends and innovations in biosensors for COVID-19 mass testing. Chembiochem : a European journal of chemical biology. 2020.

115. Sarfraz I, Rasul A, Hussain G, Adem Se, Ali M. Natural Immune Boosters as First-Line Armours to Combat Viral Infection-COVID19: Myth or Science? : Preprints.org; 2020.
116. Schlickeiser R, Kröger M. Clues from the First Covid-19 Wave and Recommendations for Social Measures in the Future. 2020.
117. Sedaghat Z, Karimi N. Guillain Barre syndrome associated with COVID-19 infection: A case report. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. 2020.
118. Setti L, Passarini F, De Gennaro G, Barbieri P, Pallavicini A, Ruscio M, et al. Searching for SARS-COV-2 on Particulate Matter: A Possible Early Indicator of COVID-19 Epidemic Recurrence. Int J Environ Res Public Health. 2020;17(9).
119. Shen M, Zhou Y, Ye J, Abdullah Al-Maskri AA, Kang Y, Zeng S, et al. Recent advances and perspectives of nucleic acid detection for coronavirus. Journal of pharmaceutical analysis. 2020;10(2):97-101.
120. Shi Y, Wang Y, Shao C, Huang J, Gan J, Huang X, et al. COVID-19 infection: the perspectives on immune responses. Cell Death Differ. 2020;27(5):1451-4.
121. Simon P. Robust Estimation of Infection Fatality Rates during the Early Phase of a Pandemic. medRxiv; 2020.
122. Singh Labana K, K Mittal A, Gujral A. The epidemiology, evolution, transmission, and therapeutics of COVID-19 Outbreak: an update on the status. Preprints.org; 2020.
123. Slathia P, Sharma P. Prediction of T and B Cell Epitopes in the Proteome of SARS-CoV-2 for Potential Use in Diagnostics and Vaccine Design. ChemRxiv; 2020.
124. Song F, Zhang X, Zha Y, Liu W. COVID-19: Recommended sampling sites at different stage of the disease. J Med Virol. 2020.
125. Song L, Xiao G, Zhang X, Gao Z, Sun S, Zhang L, et al. A case of SARS-CoV-2 carrier for 32 days with several times false negative nucleic acid tests. medRxiv; 2020.
126. Stadlbauer D, Amanat F, Chromikova V, Jiang K, Strohmeier S, Arunkumar GA, et al. SARS-CoV-2 Seroconversion in Humans: A Detailed Protocol for a Serological Assay, Antigen Production, and Test Setup. Curr Protoc Microbiol. 2020;57(1):e100.
127. Suhail Y, Afzal J, Kshitiz. Incorporating and Addressing Testing Bias Within Estimates of Epidemic Dynamics for SARS-CoV-2. 2020.
128. Sullivan PS, Sailey C, Guest JL, Guarner J, Kelley C, Siegler AJ, et al. 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. JMIR public health and surveillance. 2020;6(2):e19054.
129. Taipale J, Romer P, Linnarsson S. Population-scale testing can suppress the spread of COVID-19. 2020.
130. Tetro JA. Is COVID-19 receiving ADE from other coronaviruses? Microbes Infect. 2020;22(2):72-3.
131. Thevarajan I, Nguyen THO, Koutsakos M, Druce J, Caly L, van de Sandt C, et al. Breadth of concomitant immune responses underpinning viral clearance and patient recovery in a non-severe case of COVID-19. medRxiv; 2020.
132. Thevarajan I, Nguyen THO, Koutsakos M, Druce J, Caly L, van de Sandt CE, et al. Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19. Nat Med. 2020;26(4):453-5.
133. Tomasik P, Krótki F, Jońca M, Anyszek T. COVID-19 rapid antibody cassette point of care tests: practical considerations. Polish archives of internal medicine. 2020.
134. Udugama B, Kadhiresan P, Kozlowski HN, Malekjahani A, Osborne M, Li VYC, et al. Diagnosing COVID-19: The Disease and Tools for Detection. ACS nano. 2020;14(4):3822-35.
135. Vashist SK. In Vitro Diagnostic Assays for COVID-19: Recent Advances and Emerging Trends. Diagnostics (Basel, Switzerland). 2020;10(4).
136. Vicini E, Galimberti V, Naninato P, Anna Rita AR, Ribeiro Fontana SK, Veronesi P. COVID-19: The European institute of oncology as a "hub" centre for breast cancer surgery during the pandemic in Milan (Lombardy region, northern Italy) - A screenshot of the first month. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 2020.
137. von der Thüsen J, van der Eerden M. Histopathology and genetic susceptibility in COVID-19 pneumonia. Eur J Clin Invest. 2020.
138. Wang C, Liu Z, Chen Z, Huang X, Xu M, He T, et al. The establishment of reference sequence for SARS-CoV-2 and variation analysis. J Med Virol. 2020.
139. Wang H, Li Y, Wang F, Du H, Lu X. Rehospitalization of a Recovered Coronavirus Disease 19 (COVID-19) Child With Positive Nucleic Acid Detection. The Pediatric infectious disease journal. 2020.
140. Wang X, Wen P, Sun Z-G, Xing C-Y, Li Y. Chest CT Could Be Used to Diagnose 2019 Novel Coronavirus Pneumonia Clinically in Hubei Province. Research Square; 2020.

141. Wang Y, Liu C, Meng Q, Gui S, Wu Y, Cheng P, et al. A case report of moderate COVID-19 with an extremely long-term viral shedding period in China. Research Square; 2020.
142. Wang Y, Wang Y, Xia C. Activating organ's immunizing power against COVID–19–learning from SARS. 2020.
143. Waters A. Vets can help government tackle Covid-19. The Veterinary record. 2020;186(14):429.
144. Weitz J, Beckett S, Coenen A, Demory D, Dominguez-Mirazo M, Dushoff J, et al. Intervention Serology and Interaction Substitution: Modeling the Role of 'Shield Immunity' in Reducing COVID-19 Epidemic Spread. 2020.
145. Wu F, Wang A, Liu M, Wang Q, Chen J, Xia S, et al. Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications. medRxiv; 2020.
146. Wu z, Xia h, zhu r, Cao J. A case report of an undiagnosed COVID-19 infection. Research Square; 2020.
147. Xia N-S, Wang G-Q, Gong W-F. Serological Test is an Efficient Supplement for Detecting RNA to Confirm SARS-CoV-2 Infection. Preprints.org; 2020.
148. Xie Q, Wang J, You J, Zhu S, Zhou R, Tian Z, et al. Effect of large-scale testing platform in prevention and control of the COVID-19 pandemic: an empirical study with a novel numerical model. medRxiv; 2020.
149. Xing YH, Ni W, Wu Q, Li WJ, Li GJ, Wang WD, et al. Prolonged viral shedding in feces of pediatric patients with coronavirus disease 2019. Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi. 2020.
150. Xiong H-L, Wu Y-T, Cao J-L, Yang R, Ma J, Qiao X-Y, et al. Robust neutralization assay based on SARS-CoV-2 S-bearing vesicular stomatitis virus (VSV) pseudovirus and ACE2-overexpressed BHK21 cells. bioRxiv; 2020.
151. Xu H, Hou K, Zhang N, Yang M, Guo Y. Chest CT imaging of pediatric COVID-19 infection: a case report. Research Square; 2020.
152. Xu R, Cui B, Duan X, Zhang P, Zhou X, Yuan Q. Saliva: potential diagnostic value and transmission of 2019-nCoV. International journal of oral science. 2020;12(1):11.
153. Yadav PD, Potdar VA, Choudhary ML, Nyayanit DA, Agrawal M, Jadhav SM, et al. Full-genome sequences of the first two SARS-CoV-2 viruses from India. The Indian journal of medical research. 2020;151(2 & 3):200-9.
154. Yan K, Zhang J, Zhang Y, Zhang S, Cai T, Zheng J. Computed tomography (CT) scan challenges the result of SARS-CoV-2 nucleic acid test in a suspected COVID-19 case. Infect Control Hosp Epidemiol. 2020:1-2.
155. Yan Y, Chang L, Wang L. Laboratory testing of SARS-CoV, MERS-CoV, and SARS-CoV-2 (2019-nCoV): Current status, challenges, and countermeasures. Rev Med Virol. 2020:e2106.
156. Yang JR, Deng DT, Wu N, Yang B, Li HJ, Pan XB. Persistent viral RNA positivity during recovery period of a patient with SARS-CoV-2 infection. J Med Virol. 2020.
157. Yang R, Gui X, Gao S, Mo P, Ke H, Zhang Y, et al. The reflection on an AIDS patient with asymptomatic COVID-19 Research Square; 2020.
158. Yang W, Sirajuddin A, Zhang X, Liu G, Teng Z, Zhao S, et al. The role of imaging in 2019 novel coronavirus pneumonia (COVID-19). Eur Radiol. 2020:1-9.
159. Yang Y, Peng F, Wang R, Guan K, Jiang T, Xu G, et al. The deadly coronaviruses: The 2003 SARS pandemic and the 2020 novel coronavirus epidemic in China. J Autoimmun. 2020;109:102434.
160. Yaqinuddin A, Kashir J. Innate immunity in COVID-19 patients mediated by NKG2A receptors, and potential treatment using Monalizumab, Cholroquine, and antiviral agents. Med Hypotheses. 2020;140:109777.
161. Yi Y, Lagniton PNP, Ye S, Li E, Xu RH. COVID-19: what has been learned and to be learned about the novel coronavirus disease. Int J Biol Sci. 2020;16(10):1753-66.
162. Yin R, Feng W, Wang T, Chen G, Wu T, Chen D, et al. Concomitant neurological symptoms observed in a patient diagnosed with coronavirus disease 2019. J Med Virol. 2020.
163. Yin X, Dong L, Zhang Y, Bian W, Li H. A mild type of childhood Covid-19 - A case report. Radiology of infectious diseases (Beijing, China). 2020.
164. Yu F, Du L, Ojcius DM, Pan C, Jiang S. Measures for diagnosing and treating infections by a novel coronavirus responsible for a pneumonia outbreak originating in Wuhan, China. Microbes Infect. 2020;22(2):74-9.
165. Yu Y, Xu J, Li Y, Hu Y, Li B. Breast Milk-fed Infant of COVID-19 Pneumonia Mother: a Case Report. Research Square; 2020.
166. Yuan H, Guo E, Gao Z, Hu F, Lu L. Coronavirus Disease 2019 in a Hemodialysis Patient. Blood Purif. 2020:1-4.

167. Yuan yuan C. Statistical methods for batch screening of input populations by stage and group in COVID-19 nucleic acid testing. 2020.
168. Zeng C, Hou X, Yan J, Zhang C, Li W, Zhao W, et al. Leveraging mRNAs sequences to express SARS-CoV-2 antigens in vivo. 2020.
169. Zhai P, Ding Y, Li Y. The impact of COVID-19 on ischemic stroke: A case report. Research Square; 2020.
170. Zhang J, Gharizadeh B, Lu D, Yue J, Yu M, Liu Y, et al. Navigating the Pandemic Response Life Cycle: Molecular Diagnostics and Immunoassays in the Context of COVID-19 Management. IEEE reviews in biomedical engineering. 2020.
171. Zhang J, Wu S, Xu L. Asymptomatic carriers of COVID-19 as a concern for disease prevention and control: more testing, more follow-up. Biosci Trends. 2020.
172. Zhang N, Wang L, Deng X, Liang R, Su M, He C, et al. Recent advances in the detection of respiratory virus infection in humans. J Med Virol. 2020;92(4):408-17.
173. Zhang P, Cai Z, Wu W, Peng L, Li Y, Chen C, et al. The novel coronavirus (COVID-19) pneumonia with negative detection of viral ribonucleic acid from nasopharyngeal swabs: a case report. BMC Infect Dis. 2020;20(1):317.
174. Zhang T, Cui X, Zhao X, Wang J, Zheng J, Zheng G, et al. Detectable SARS-CoV-2 viral RNA in feces of three children during recovery period of COVID-19 pneumonia. J Med Virol. 2020.
175. Zhang Y, Wang D, Lin M, Sun T, Chen J, Xu J, et al. Serum Amyloid A Protein as a Potential Biomarker Useful in Monitoring the Course of COVID-19 : A Retrospectively Studied. 2020.
176. Zhang Y, Xiao M, Zhang S, Xia P, Cao W, Jiang W, et al. Coagulopathy and Antiphospholipid Antibodies in Patients with Covid-19. N Engl J Med. 2020;382(17):e38.
177. Zhao J, Liao X, Wang H, Wei L, Xing M, Liu L, et al. Early virus clearance and delayed antibody response in a case of COVID-19 with a history of co-infection with HIV-1 and HCV. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.
178. Zhao K, Huang J, Dai D, Feng Y, Liu L, Nie S. Acute myelitis after SARS-CoV-2 infection: a case report. medRxiv; 2020.
179. Zhao R, Li M, Song H, Chen J, Ren W, Feng Y, et al. Early detection of SARS-CoV-2 antibodies in COVID-19 patients as a serologic marker of infection. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.
180. Zheng Z, Monteil V, Maurer-Stroh S, Yew CW, Leong C, Mohd-Ismail NK, et al. Monoclonal antibodies for the S2 subunit of spike of SARS-CoV cross-react with the newly-emerged SARS-CoV-2. bioRxiv; 2020.
181. Zhou G, Zhao Q. Perspectives on therapeutic neutralizing antibodies against the Novel Coronavirus SARS-CoV-2. Int J Biol Sci. 2020;16(10):1718-23.
182. Zimmermann P, Curtis N. Coronavirus Infections in Children Including COVID-19: An Overview of the Epidemiology, Clinical Features, Diagnosis, Treatment and Prevention Options in Children. The Pediatric infectious disease journal. 2020;39(5):355-68.
183. Zingone F, Buda A, Savarino EV. Screening for active COVID-19 infection and immunization status prior to biologic therapy in IBD patients at the time of the pandemic outbreak. Digestive and liver disease : official journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver. 2020.

E6 no English/Italian/German full text

1. Bai SL, Wang JY, Zhou YQ, Yu DS, Gao XM, Li LL, et al. [Analysis of the first cluster of cases in a family of novel coronavirus pneumonia in Gansu Province]. Zhonghua yu fang yi xue za zhi [Chinese journal of preventive medicine]. 2020;54(0):E005.
2. Cao L, Wang TY, Chen HZ, Qian Y, Chen BW, Fang P, et al. [A preliminary investigation on the serological and epidemiological characteristics of severe acute respiratory syndrome in children]. Zhonghua er ke za zhi = Chinese journal of pediatrics. 2004;42(11):840-4.
3. Chen S, Huang B, Luo DJ, Li X, Yang F, Zhao Y, et al. [Pregnant women with new coronavirus infection: a clinical characteristics and placental pathological analysis of three cases]. Zhonghua bing li xue za zhi = Chinese journal of pathology. 2020;49(0):E005.
4. Chen Y, Qiu F. [Spike protein in the detection and treatment of novel coronavirus]. Sheng wu yi xue gong cheng xue za zhi = Journal of biomedical engineering = Shengwu yixue gongchengxue zazhi. 2020;37(2):246-50.
5. Feng K, Yun YX, Wang XF, Yang GD, Zheng YJ, Lin CM, et al. [Analysis of CT features of 15 children with 2019 novel coronavirus infection]. Zhonghua er ke za zhi = Chinese journal of pediatrics. 2020;58(4):275-8.

6. Jiang NN, Wang DY, Chen L, Xie WG. [Treatment experience of burn patients combined with inhalation injury during epidemic period of Corona Virus Disease 2019]. Zhonghua shao shang za zhi = Zhonghua shaoshang zazhi = Chinese journal of burns. 2020;36(0):E007.
7. Li Y, Hu Y, Zhang X, Yu Y, Li B, Wu J, et al. [Follow-up testing of viral nucleic acid in discharged patients with moderate type of 2019 coronavirus disease (COVID-19)]. Zhejiang da xue xue bao Yi xue ban = Journal of Zhejiang University Medical sciences. 2020;49(1):0.
8. Ma SY, Luo YM, Hu TY, You ZC, Sun JG, Yu SY, et al. [Clinical application effect of modified nasopharyngeal swab sampling for 2019 novel coronavirus nucleic acid detection]. Zhonghua shao shang za zhi = Zhonghua shaoshang zazhi = Chinese journal of burns. 2020;36(0):E009.
9. Qiu YY, Wang SQ, Wang XL, Lu WX, Qiao D, Li JB, et al. [Epidemiological analysis on a family cluster of COVID-19]. Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi. 2020;41(4):506-9.
10. Ren YH, Wang SY, Liu M, Guo YM, Dai HP. [When COVID-19 encounters interstitial lung disease: challenges and management]. Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases. 2020;43(0):E039.
11. Shi Y, Wang N, Zou QM. [Progress and challenge of vaccine development against 2019 novel coronavirus (2019-nCoV)]. Zhonghua yu fang yi xue za zhi [Chinese journal of preventive medicine]. 2020;54(0):E029.
12. Tan FR, Qiu YL, Xu Z. [Bronchoalveolar lavage fluid was used to diagnose two cases of 2019-nCoV infection]. Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases. 2020;43(4):337-9.
13. Tan X, Huang J, Zhao F, Zhou Y, Li JQ, Wang XY. [Clinical features of children with SARS-CoV-2 infection: an analysis of 13 cases from Changsha, China]. Zhongguo dang dai er ke za zhi = Chinese journal of contemporary pediatrics. 2020;22(4):294-8.
14. van der Heide V. Neutralizing antibody response in mild COVID-19. Nat Rev Immunol. 2020.
15. Vásárhelyi B, Kristóf K, Ostorházi E, Szabó D, Prohászka Z, Merkely B. [A specifikus IgM- és IgG-antitesteket detektáló gyorstesztek értéke a SARS CoV-2 vírusfertőzés kimutatásában (A COVID-19-pandémia orvosszakmai kérdései)]. Orv Hetil. 2020;161(20):807-12.
16. Wang D, Ju XL, Xie F, Lu Y, Li FY, Huang HH, et al. [Clinical analysis of 31 cases of 2019 novel coronavirus infection in children from six provinces (autonomous region) of northern China]. Zhonghua er ke za zhi = Chinese journal of pediatrics. 2020;58(4):E011.
17. Wang H, Jin XY, Pang B, Liu CX, Zheng WK, Yang FW, et al. [Analysis on clinical study protocols of traditional Chinese medicine for coronavirus disease 2019]. Zhongguo Zhong yao za zhi = Zhongguo zhongyao zazhi = China journal of Chinese materia medica. 2020;45(6):1232-41.
18. Xiong Z, Fu L, Zhou H, Liu JK, Wang AM, Huang Y, et al. [Construction and evaluation of a novel diagnosis process for 2019-Corona Virus Disease]. Zhonghua yi xue za zhi. 2020;100(0):E019.
19. Xu K, Cai H, Shen Y, Ni Q, Chen Y, Hu S, et al. [Management of corona virus disease-19 (COVID-19): the Zhejiang experience]. Zhejiang da xue xue bao Yi xue ban = Journal of Zhejiang University Medical sciences. 2020;49(1):0.
20. Xu X, Chang XN, Pan HX, Su H, Huang B, Yang M, et al. [Pathological changes of the spleen in ten patients with new coronavirus infection by minimally invasive autopsies]. Zhonghua bing li xue za zhi = Chinese journal of pathology. 2020;49(0):E014.
21. Yang P, Shao FL, Wang GJ. [Clinical observation on increasing the positive rate of novel coronavirus nucleic acid tests by sputum excretion induced by nebulizer therapy]. Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases. 2020;43(4):335-6.
22. Yao XH, Li TY, He ZC, Ping YF, Liu HW, Yu SC, et al. [A pathological report of three COVID-19 cases by minimally invasive autopsies]. Zhonghua bing li xue za zhi = Chinese journal of pathology. 2020;49(0):E009.
23. Ye B, Fan C, Pan Y, Ding R, Hu HX, Xiang ML. [Which sampling method for the upper respiratory tract specimen should be taken to diagnose patient with COVID-19?]. Zhonghua er bi yan hou tou jing wai ke za zhi = Chinese journal of otorhinolaryngology head and neck surgery. 2020;55(0):E003.
24. Ye Z, Hong Y, Wu X, Hong D, Zhang Y, Dong X, et al. [Management of a colon cancer patient infected with corona virus disease 2019]. Zhejiang da xue xue bao Yi xue ban = Journal of Zhejiang University Medical sciences. 2020;49(1):0.
25. Zhang JZ, Zhou P, Han DB, Wang WC, Cui C, Zhou R, et al. [Investigation on a cluster epidemic of COVID-19 in a supermarket in Liaocheng, Shandong province]. Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi. 2020;41(0):E055.
26. Zhang L, Jiang Y, Wei M, Cheng BH, Zhou XC, Li J, et al. [Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province]. Zhonghua Fu Chan Ke Za Zhi. 2020;55(0):E009.
27. Zhang R, Li JM. [The way to reduce the false negative results of 2019 novel coronavirus nucleic acid detection]. Zhonghua yi xue za zhi. 2020;100(11):801-4.

28. Zhen L, Lin T, Zhao ML, Chen H, Chen T, Guo WH, et al. [Management strategy for the resumption of regular diagnosis and treatment in gastrointestinal surgery department during the outbreak of coronavirus disease 2019 (COVID-19)]. Zhonghua wei chang wai ke za zhi = Chinese journal of gastrointestinal surgery. 2020;23(4):321-6.
29. Zhong Q, Li Z, Shen X, Xu K, Shen Y, Fang Q, et al. [CT imaging features of patients with different clinical types of coronavirus disease 2019 (COVID-19)]. Zhejiang da xue xue bao Yi xue ban = Journal of Zhejiang University Medical sciences. 2020;49(1):0.
30. Zhou L, Liu K, Liu HG. [Cause analysis and treatment strategies of "recurrence" with novel coronavirus pneumonia (covid-19) patients after discharge from hospital]. Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases. 2020;43(0):E028.
31. Zhou Y, Yang GD, Feng K, Huang H, Yun YX, Mou XY, et al. [Clinical features and chest CT findings of coronavirus disease 2019 in infants and young children]. Zhongguo dang dai er ke za zhi = Chinese journal of contemporary pediatrics. 2020;22(3):215-20.
32. Zhu L, Cai MY, Shi Q, Wang P, Li QL, Zhong YS, et al. [Analysis of selective endoscopy results during the epidemic of coronavirus disease 2019 (COVID-19)]. Zhonghua wei chang wai ke za zhi = Chinese journal of gastrointestinal surgery. 2020;23(4):327-31.
33. Zhu ZB, Zhong CK, Zhang KX, Dong C, Peng H, Xu T, et al. [Epidemic trend of corona virus disease 2019 (COVID-19) in mainland China]. Zhonghua yu fang yi xue za zhi [Chinese journal of preventive medicine]. 2020;54(0):E022.
34. Zhuang GH, Shen MW, Zeng LX, Mi BB, Chen FY, Liu WJ, et al. [WITHDRAWN: Potential false-positive rate among the 'asymptomatic infected individuals' in close contacts of COVID-19 patients]. Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi. 2020;41(4):485-8.
35. Zou X, Wu YS, Liu XJ, Huang SL, He JF, Zhao J, et al. [Evaluation of the emergency response strategies and measures on the epidemic of COVID-19 in Shenzhen, China]. Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi. 2020;41(0):E056.

E7 animal experiments/ therapeutic studies

1. Anft M, Paniskaki K, Blazquez-Navarro A, Doevelaar AAN, Seibert F, Hoelzer B, et al. A possible role of immunopathogenesis in COVID-19 progression. medRxiv; 2020.
2. Ascierto PA, Fox B, Urba W, Anderson AC, Atkins MB, Borden EC, et al. Insights from immuno-oncology: the Society for Immunotherapy of Cancer Statement on access to IL-6-targeting therapies for COVID-19. Journal for immunotherapy of cancer. 2020;8(1).
3. Bao L, Deng W, Gao H, Xiao C, Liu J, Xue J, et al. Lack of Reinfection in Rhesus Macaques Infected with SARS-CoV-2. bioRxiv; 2020.
4. Behbahani M. In silico Design of novel Multi-epitope recombinant Vaccine based on Coronavirus surface glycoprotein. bioRxiv; 2020.
5. Benatia D, Godefroy R, Lewis J. Estimating COVID-19 Prevalence in the United States: A Sample Selection Model Approach. medRxiv; 2020.
6. Bian H, Zheng Z-H, Wei D, Zhang Z, Kang W-Z, Hao C-Q, et al. Meplazumab treats COVID-19 pneumonia: an open-labelled, concurrent controlled add-on clinical trial. medRxiv; 2020.
7. Bizzarri M, Laganà AS, Aragona D, Unfer V. Inositol and pulmonary function. Could myo-inositol treatment downregulate inflammation and cytokine release syndrome in SARS-CoV-2? Eur Rev Med Pharmacol Sci. 2020;24(6):3426-32.
8. Bojkova D, Klann K, Koch B, Widera M, Krause D, Ciesek S, et al. SARS-CoV-2 infected host cell proteomics reveal potential therapy targets. Research Square; 2020.
9. Bonilla-Aldana K, Cardona-Trujillo M, García-Barco A, Holguin-Rivera Y, Cortes-Bonilla I, Bedoya-Arias H, et al. MERS-CoV and SARS-CoV Infections in Animals: A Systematic Review and Meta-Analysis of Prevalence Studies. Preprints.org; 2020.
10. Boudewijns R, Thibaut HJ, Kaptein S, Li R, Vergote V, Seldeslachts L, et al. STAT2 signaling as double-edged sword restricting viral dissemination but driving severe pneumonia in SARS-CoV-2 infected hamsters. bioRxiv; 2020.
11. Cai H, Cai K, Li J. Identification of Novel Missense Mutations in a Large Number of Recent SARS-CoV-2 Genome Sequences. Preprints.org; 2020.
12. Cai SJ, Wu LL, Chen DF, Li YX, Liu YJ, Fan YQ, et al. [Analysis of bronchoscope-guided tracheal intubation in 12 cases with COVID-19 under the personal protective equipment with positive pressure protective hood]. Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases. 2020;43(0):E033.

13. Carneiro J, Pereira F. CoV2ID: Detection and Therapeutics Oligo Database for SARS-CoV-2. bioRxiv; 2020.
14. Ceribelli A, Motta F, De Santis M, Ansari AA, Ridgway WM, Gershwin ME, et al. Recommendations for coronavirus infection in rheumatic diseases treated with biologic therapy. J Autoimmun. 2020;109:102442.
15. Cesewski E, Johnson BN. Electrochemical biosensors for pathogen detection. Biosensors & bioelectronics. 2020;159:112214.
16. Chaari L, Golubnitschaja O. Covid-19 pandemic by the "real-time" monitoring: the Tunisian case and lessons for global epidemics in the context of 3PM strategies. The EPMA journal. 2020:1-6.
17. Chan JF, Zhang AJ, Yuan S, Poon VK, Chan CC, Lee AC, et al. Simulation of the clinical and pathological manifestations of Coronavirus Disease 2019 (COVID-19) in golden Syrian hamster model: implications for disease pathogenesis and transmissibility. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.
18. Chary MA, Barbuto AF, Izadmehr S, Hayes BD, Burns MM. COVID-19: Therapeutics and Their Toxicities. Journal of medical toxicology : official journal of the American College of Medical Toxicology. 2020.
19. Chen J, Zhang ZZ, Chen YK, Long QX, Tian WG, Deng HJ, et al. The clinical and immunological features of pediatric COVID-19 patients in China. Genes & diseases. 2020.
20. Chen JY, Qiao K, Liu F, Wu B, Xu X, Jiao GQ, et al. Lung transplantation as therapeutic option in acute respiratory distress syndrome for COVID-19-related pulmonary fibrosis. Chin Med J (Engl). 2020.
21. Chen R, Zhang Y, Huang L, Cheng BH, Xia ZY, Meng QT. Safety and efficacy of different anesthetic regimens for parturients with COVID-19 undergoing Cesarean delivery: a case series of 17 patients. Canadian journal of anaesthesia = Journal canadien d'anesthesie. 2020:1-9.
22. Chen T, Song J, Liu H, Zheng H, Chen C. Positive Epstein-Barr virus detection in corona virus disease 2019 (COVID-19) patients. Research Square; 2020.
23. Chen WH, Strych U, Hotez PJ, Bottazzi ME. The SARS-CoV-2 Vaccine Pipeline: an Overview. Current tropical medicine reports. 2020:1-4.
24. Chen X, Zheng F, Qing Y, Ding S, Yang D, Lei C, et al. Epidemiological and clinical features of 291 cases with coronavirus disease 2019 in areas adjacent to Hubei, China: a double-center observational study. medRxiv; 2020.
25. Cherian SS, Agrawal M, Basu A, Abraham P, Gangakhedkar RR, Bhargava B. Perspectives for repurposing drugs for the coronavirus disease 2019. The Indian journal of medical research. 2020;151(2 & 3):160-71.
26. Chow C, Chang J, Gerkin R, Vattikuti S. Global prediction of unreported SARS-CoV2 infection from observed COVID-19 cases. medRxiv; 2020.
27. Conti P, Younes A. Coronavirus COV-19/SARS-CoV-2 affects women less than men: clinical response to viral infection. J Biol Regul Homeost Agents. 2020;34(2).
28. Corrêa Giron C, Laaksonen A, Barroso da Silva F. On the interactions of the receptor-binding domain of SARS-CoV-1 and SARS-CoV-2 spike proteins with monoclonal antibodies and the receptor ACE2. bioRxiv; 2020.
29. Crawford KHD, Eguia R, Dingens A, Loes A, Malone K, Wolf C, et al. Protocol and reagents for pseudotyping lentiviral particles with SARS-CoV-2 Spike protein for neutralization assays. bioRxiv; 2020.
30. D'Annessa I, Marchetti F, Colombo G. Differential Antibody Recognition by Novel SARS-CoV-2 and SARS-CoV Spike Protein Receptor Binding Domains: Mechanistic Insights and Implications for the Design of Diagnostics and Therapeutics. bioRxiv; 2020.
31. Davoodi L, Jafarpour H, Kazeminejad A, Soleymani E, Akbari Z, Razavi A. Hydroxychloroquine-Induced Stevens-Johnson Syndrome in COVID-19: A rare Case Report. Research Square; 2020.
32. Della Gatta AN, Rizzo R, Pilu G, Simonazzi G. COVID19 during pregnancy: a systematic review of reported cases. Am J Obstet Gynecol. 2020.
33. Deng J, Jin Y, Liu Y, Sun J, Hao L, Bai J, et al. Serological survey of SARS-CoV-2 for experimental, domestic, companion and wild animals excludes intermediate hosts of 35 different species of animals. Transbound Emerg Dis. 2020.
34. Derraik J, Anderson W, Connelly E, Anderson Y. Rapid evidence summary on SARS-CoV-2 survivorship and disinfection, and a reusable PPE protocol using a double-hit process. medRxiv; 2020.
35. Díez J-M, Romero C, Gajardo R. Currently available intravenous immunoglobulin (Gamunex®-C and Flebogamma® DIF) contains antibodies reacting against SARS-CoV-2 antigens. bioRxiv; 2020.
36. Diurno F, Numis FG, Porta G, Cirillo F, Maddaluno S, Ragozzino A, et al. Eculizumab treatment in patients with COVID-19: preliminary results from real life ASL Napoli 2 Nord experience. Eur Rev Med Pharmacol Sci. 2020;24(7):4040-7.
37. Du YX, Chen XP. Favipiravir: Pharmacokinetics and Concerns About Clinical Trials for 2019-nCoV Infection. Clin Pharmacol Ther. 2020.

38. Duan K, Liu B, Li C, Zhang H, Yu T, Qu J, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad Sci U S A. 2020;117(17):9490-6.
39. Duan K, Liu B, Li C, Zhang H, Yu T, Qu J, et al. The feasibility of convalescent plasma therapy in severe COVID-19 patients: a pilot study. 2020.
40. Enayatkhani M, Hasaniazad M, Faezi S, Guklani H, Davoodian P, Ahmadi N, et al. Reverse vaccinology approach to design a novel multi-epitope vaccine candidate against COVID-19: an in silico study. Journal of biomolecular structure & dynamics. 2020:1-16.
41. Fast E, Altman R, Chen B. Potential T-cell and B-cell Epitopes of 2019-nCoV. bioRxiv; 2020.
42. Feng Y, Qiu M, Zou S, Li Y, Luo K, Chen R, et al. Multi-epitope vaccine design using an immunoinformatics approach for 2019 novel coronavirus in China (SARS-CoV-2). bioRxiv; 2020.
43. Fernandes J, Hinrichs A, Clawson H, Navarro Gonzales J, Lee B, Nassar L, et al. The UCSC SARS-CoV-2 Genome Browser. bioRxiv; 2020.
44. Ferrucci S, Romagnuolo M, Angileri L, Berti E, Tavecchio S. Safety of dupilumab in severe atopic dermatitis and infection of Covid-19: two case reports. Journal of the European Academy of Dermatology and Venereology : JEADV. 2020.
45. Franklin R, Young A, Neumann B, Fernandez R, Joannides A, Reyahi A, et al. Homologous protein domains in SARS-CoV-2 and measles, mumps and rubella viruses: preliminary evidence that MMR vaccine might provide protection against COVID-19. 2020.
46. Fu B, Xu X, Wei H. Why tocilizumab could be an effective treatment for severe COVID-19? J Transl Med. 2020;18(1):164.
47. Fu Y, Cheng Y, Wu Y. Understanding SARS-CoV-2-Mediated Inflammatory Responses: From Mechanisms to Potential Therapeutic Tools. Virol Sin. 2020.
48. Gagiannis D, Steinestel J, Hackenbroch C, Hannemann M, Umathum V, Gebauer N, et al. COVID-19-induced acute respiratory failure: an exacerbation of organ-specific autoimmunity? : medRxiv; 2020.
49. Gallotti R, Valle F, Castaldo N, Sacco P, De Domenico M. Assessing the risks of "infodemics" in response to COVID-19 epidemics. medRxiv; 2020.
50. Gao J, Yang M, Liu L, Guo S, Li Y, Cheng C. The Aggressive Surgical Treatment and Outcome of a Colon Cancer Patient Infected with SARS-CoV-2 in Wuhan, China and Our Experience Sharing. Research Square; 2020.
51. Gao Q, Bao L, Mao H, Wang L, Xu K, Yang M, et al. Rapid development of an inactivated vaccine for SARS-CoV-2. bioRxiv; 2020.
52. Gao T, Hu M, Zhang X, Li H, Zhu L, Liu H, et al. Highly pathogenic coronavirus N protein aggravates lung injury by MASP-2-mediated complement over-activation. medRxiv; 2020.
53. Geurdes H, Koutsaroff I. Histamine Antagonists to Temper the Cytokine Overproduction in Gastrointestinal Cells Infected by SARS-CoV-2. Preprints.org; 2020.
54. Giamarellos-Bourboulis EJ, Netea MG, Rovina N, Akinosoglou K, Antoniadou A, Antonakos N, et al. Complex Immune Dysregulation in COVID-19 Patients with Severe Respiratory Failure. Cell host & microbe. 2020.
55. Goyal A, Cardozo-Ojeda F, Schiffer J. Potency and timing of antiviral therapy as determinants of duration of SARS CoV-2 shedding and intensity of inflammatory response. medRxiv; 2020.
56. Grant O, Montgomery D, Ito K, Woods R. Analysis of the SARS-CoV-2 spike protein glycan shield: implications for immune recognition. bioRxiv; 2020.
57. Gu H, Chen Q, Yang G, He L, Fan H, Deng Y-q, et al. Rapid adaptation of SARS-CoV-2 in BALB/c mice: Novel mouse model for vaccine efficacy. bioRxiv; 2020.
58. Guo Y, Zeng J, Li Q, Li P, Luo FM, Zhang WZ, et al. [Preliminary clinical study of direct renin inhibitor aliskiren in the treatment of severe COVID-19 patients with hypertension]. Zhonghua Nei Ke Za Zhi. 2020;59(0):E011.
59. Gupta E, Mishra RK, Niraj RRK. Identification of potential vaccine candidates against SARS-CoV-2, A step forward to fight novel coronavirus 2019-nCoV: A Reverse Vaccinology Approach. bioRxiv; 2020.
60. Han Y, Jiang M, Xia D, He L, Lv X, Liao X, et al. COVID-19 in a patient with long-term use of glucocorticoids: A study of a familial cluster. Clinical immunology (Orlando, Fla). 2020;214:108413.
61. Harzallah I, Debliquis A, Drénou B. Lupus anticoagulant is frequent in patients with Covid-19. Journal of thrombosis and haemostasis : JTH. 2020.
62. Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med. 2020.
63. Heyd CP, Desiato VM, Nguyen SA, O'Rourke AK, Clemmens CS, Awad MI, et al. Tracheostomy protocols during COVID-19 pandemic. Head & neck. 2020.

64. Issa E, Merhi G, Panossian B, Salloum T, Tokajian S. SARS-CoV-2 and ORF3a: Non-Synonymous Mutations and Polyproline Regions. bioRxiv; 2020.
65. Jacobs JP, Stammers AH, St Louis J, Hayanga JWA, Firstenberg MS, Mongero LB, et al. Extracorporeal Membrane Oxygenation in the Treatment of Severe Pulmonary and Cardiac Compromise in COVID-19: Experience with 32 patients. ASAIO journal (American Society for Artificial Internal Organs : 1992). 2020.
66. Jawhara S. Could Intravenous Immunoglobulin Collected from Recovered Coronavirus Patients Protect against COVID-19 and Strengthen the Immune System of New Patients? Int J Mol Sci. 2020;21(7).
67. Ji H, Yan Y, Ding B, Guo W, Brunswick M, Niethammer A, et al. Novel decoy cellular vaccine strategy utilizing transgenic antigen-expressing cells as immune presenter and adjuvant in vaccine prototype against SARS-CoV-2 virus. Medicine in drug discovery. 2020;5:100026.
68. Joyce G, Sankhala R, Chen W-H, Choe M, Bai H, Hajduczki A, et al. A Cryptic Site of Vulnerability on the Receptor Binding Domain of the SARS-CoV-2 Spike Glycoprotein. bioRxiv; 2020.
69. Kalita P, Padhi A, Zhang KYJ, Tripathi T. Design of a Peptide-Based Subunit Vaccine against Novel Coronavirus SARS-CoV-2. Preprints.org; 2020.
70. Kashir J, Yaqinuddin A. Loop mediated isothermal amplification (LAMP) assays as a rapid diagnostic for COVID-19. Med Hypotheses. 2020;141:109786.
71. Khan A, Alam A, Imam N, Siddiqui MF, Ishrat R. Design of an Epitope-Based Peptide Vaccine against the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2): A Vaccine Informatics Approach. bioRxiv; 2020.
72. Kibria K, Islam MSb, Ullah H, Miah M. The multi-epitope vaccine prediction to combat Pandemic SARS-CoV-2, an immunoinformatic approach. Research Square; 2020.
73. Kim E, Erdos G, Huang S, Kenniston TW, Balmert SC, Carey CD, et al. Microneedle array delivered recombinant coronavirus vaccines: Immunogenicity and rapid translational development. EBioMedicine. 2020:102743.
74. Kim YI, Kim SG, Kim SM, Kim EH, Park SJ, Yu KM, et al. Infection and Rapid Transmission of SARS-CoV-2 in Ferrets. Cell host & microbe. 2020.
75. Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. Nature microbiology. 2020;5(4):562-9.
76. Li K, Li Z, Wohlford-Lenane C, Meyerholz DK, Channappanavar R, An D, et al. Single-Dose, Intranasal Immunization with Recombinant Parainfluenza Virus 5 Expressing Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Spike Protein Protects Mice from Fatal MERS-CoV Infection. mBio. 2020;11(2).
77. Li M, Jin R, Peng Y, Wang C, Ren W, Lv F, et al. Generation of antibodies against COVID-19 virus for development of diagnostic tools. medRxiv; 2020.
78. Li W. Structurally Observed Electrostatic Features of the COVID-19 Coronavirus-Related Experimental Structures inside Protein Data Bank: A Brief Update. Preprints.org; 2020.
79. Li Y, Zhang J, Wang N, Li H, Shi Y, Guo G, et al. Therapeutic Drugs Targeting 2019-nCoV Main Protease by High-Throughput Screening. bioRxiv; 2020.
80. Liu J, Babka A, Kearney B, Radoshitzky S, Kuhn J, Zeng X. Molecular Detection of SARS-CoV-2 in Formalin Fixed Paraffin Embedded Specimens. bioRxiv; 2020.
81. Liu X, Chen H, Shang Y, Zhu H, Chen G, Chen Y, et al. Efficacy of Chloroquine and Lopinavir/Ritonavir in mild/general COVID-2019: a prospective, open-label, multicenter randomized controlled clinical study. Research Square; 2020.
82. Liu X, Gao F, Gou L, Chen Y, Gu Y, Ao L, et al. Neutralizing Antibodies Isolated by a site-directed Screening have Potent Protection on SARS-CoV-2 Infection. bioRxiv; 2020.
83. Liu X, Zhang X, Xiao Y, Gao T, Wang G, Wang Z, et al. Heparin-induced thrombocytopenia is associated with a high risk of mortality in critical COVID-19 patients receiving heparin-involved treatment. 2020.
84. Liu Y, Chan W, Wang Z, Hur J, Xie J, Yu H, et al. Ontological and Bioinformatic Analysis of Anti-Coronavirus Drugs and Their Implication for Drug Repurposing against COVID-19. Preprints.org; 2020.
85. Lombardy Section Italian Society I, Tropical D. Vademecum for the treatment of people with COVID-19. Edition 2.0, 13 March 2020. Infez Med. 2020;28(2):143-52.
86. Luo P, Liu Y, Qiu L, Liu X, Liu D, Li J. Tocilizumab treatment in COVID-19: A single center experience. J Med Virol. 2020.
87. Lv H, Wu N, Tsang OT-Y, Yuan M, Perera R, Leung WS, et al. Cross-reactive antibody response between SARS-CoV-2 and SARS-CoV infections. bioRxiv; 2020.
88. Magar R, Yadav P, Farimani AB. Potential Neutralizing Antibodies Discovered for Novel Corona Virus Using Machine Learning. bioRxiv; 2020.

89. Magrone T, Magrone M, Jirillo E. Focus on Receptors for Coronaviruses with Special Reference to Angiotensin-converting Enzyme 2 as a Potential Drug Target - A Perspective. Endocr Metab Immune Disord Drug Targets. 2020.
90. Mahase E. Covid-19: Antibody test that claims to be 99% accurate is certified by EU. BMJ. 2020;369:m1742.
91. Malik YS, Sircar S, Bhat S, Sharun K, Dhama K, Dadar M, et al. Emerging novel coronavirus (2019-nCoV)-current scenario, evolutionary perspective based on genome analysis and recent developments. The veterinary quarterly. 2020;40(1):68-76.
92. Malone B, Simovski B, Moliné C, Cheng J, Gheorghe M, Fontenelle H, et al. Artificial intelligence predicts the immunogenic landscape of SARS-CoV-2: toward universal blueprints for vaccine designs. bioRxiv; 2020.
93. Martinez MA. Compounds with Therapeutic Potential against Novel Respiratory 2019 Coronavirus. Antimicrob Agents Chemother. 2020;64(5).
94. Mi B, Chen L, Panayi A, Xiong Y, Liu G. Serum Mycoplasma Pneumoniae IgG in COVID-19: A Protective Factor. medRxiv; 2020.
95. Musarrat F, Chouljenko V, Nabi R, Dahal A, Jois S, Kousoulas K. The anti-HIV Drug Nelfinavir Mesylate (Viracept) is a Potent Inhibitor of Cell Fusion Caused by the SARS-CoV-2 Spike (S) Glycoprotein Warranting further Evaluation as an Antiviral against COVID-19 infections. bioRxiv; 2020.
96. Mycroft-West C, Su D, Pagani I, Rudd T, Elli S, Guimond S, et al. Heparin inhibits cellular invasion by SARS-CoV-2: structural dependence of the interaction of the surface protein (spike) S1 receptor binding domain with heparin. bioRxiv; 2020.
97. Nie J, Li Q, Wu J, Zhao C, Hao H, Liu H, et al. Establishment and validation of a pseudovirus neutralization assay for SARS-CoV-2. Emerging microbes & infections. 2020;9(1):680-6.
98. Qian S, Gao Z, Cao R, Yang K, Cui Y, Li S, et al. Transmissible Gastroenteritis Virus Infection Up-Regulates FcRn Expression via Nucleocapsid Protein and Secretion of TGF-β in Porcine Intestinal Epithelial Cells. Front Microbiol. 2019;10:3085.
99. Quinlan B, Mou H, Zhang L, Guo Y, He W, Ojha A, et al. The SARS-CoV-2 receptor-binding domain elicits a potent neutralizing response without antibody-dependent enhancement. bioRxiv; 2020.
100. Rahman S, Hoque N, Islam R, Akter S, Rubayet-Ul-Alam ASM, Siddique MA, et al. Epitope-based chimeric peptide vaccine design against S, M and E proteins of SARS-CoV-2 etiologic agent of global pandemic COVID-19: an in silico approach. bioRxiv; 2020.
101. Ren W, Sun H, Gao G, Chen J, Sun S, Zhao R, et al. Recombinant SARS-CoV-2 spike S1-Fc fusion protein induced high levels of neutralizing responses in nonhuman primates. bioRxiv; 2020.
102. Rosales-Mendoza S. Will plant-made biopharmaceuticals play a role in the fight against COVID-19? Expert Opin Biol Ther. 2020;20(6):545-8.
103. Saha R, Prasad B. In silico approach for designing of a multi-epitope based vaccine against novel Coronavirus (SARS-COV-2). bioRxiv; 2020.
104. Shen C, Wang Z, Zhao F, Yang Y, Li J, Yuan J, et al. Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma. JAMA. 2020;323(16):1582-9.
105. Sia SF, Yan L-M, Chin AWH, Fung K, Poon LLM, Nicholls J, et al. Pathogenesis and transmission of SARS-CoV-2 virus in golden Syrian hamsters. Research Square; 2020.
106. Singh A, Thakur M, Sharma LK, Chandra K. Designing a multi-epitope peptide-based vaccine against SARS-CoV-2. bioRxiv; 2020.
107. Smith TRF, Patel A, Ramos S, Elwood D, Zhu X, Yan J, et al. Rapid development of a synthetic DNA vaccine for COVID-19. Research Square; 2020.
108. Srivastava S, Verma S, Kamthania M, Kaur R, Badyal RK, Saxena AK, et al. Structural basis to design multi-epitope vaccines against Novel Coronavirus 19 (COVID19) infection, the ongoing pandemic emergency: an in silico approach. bioRxiv; 2020.
109. Sun C, Chen L, Yang J, Luo C, Zhang Y, Li J, et al. SARS-CoV-2 and SARS-CoV Spike-RBD Structure and Receptor Binding Comparison and Potential Implications on Neutralizing Antibody and Vaccine Development. bioRxiv; 2020.
110. Sun F, Ganguli A, Nguyen J, Brisbin R, Shanmugam K, Hirschberg DL, et al. Smartphone-based multiplex 30-minute nucleic acid test of live virus from nasal swab extract. Lab Chip. 2020;20(9):1621-7.
111. Teixeira da Silva JA. Convalescent plasma: A possible treatment of COVID-19 in India. Medical journal, Armed Forces India. 2020.
112. Temmam S, Barbarino A, Maso D, Behillil S, Enouf V, Huon C, et al. Absence of SARS-CoV-2 infection in cats and dogs in close contact with a cluster of COVID-19 patients in a veterinary campus. bioRxiv; 2020.

113. ul Qamar MT, Rehman A, Ashfaq UA, Awan MQ, Fatima I, Shahid F, et al. Designing of a next generation multiepitope based vaccine (MEV) against SARS-COV-2: Immunoinformatics and in silico approaches. bioRxiv; 2020.
114. V'kovski P, Gultom M, Steiner S, Kelly J, Russeil J, Mangeat B, et al. Disparate temperature-dependent virus – host dynamics for SARS-CoV-2 and SARS-CoV in the human respiratory epithelium. bioRxiv; 2020.
115. Vashi Y, Jagrit V, Kumar S. Understanding the B and T cells epitopes of spike protein of severe respiratory syndrome coronavirus-2: A computational way to predict the immunogens. bioRxiv; 2020.
116. Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. Cell. 2020;181(2):281-92.e6.
117. Wan Y, Shang J, Sun S, Tai W, Chen J, Geng Q, et al. Molecular Mechanism for Antibody-Dependent Enhancement of Coronavirus Entry. J Virol. 2020;94(5).
118. Wang H, Hou X, Wu X, Liang T, Zhang X, Wang D, et al. SARS-CoV-2 proteome microarray for mapping COVID-19 antibody interactions at amino acid resolution. bioRxiv; 2020.
119. Wang K, Chen W, Zhou Y-S, Lian J-Q, Zhang Z, Du P, et al. SARS-CoV-2 invades host cells via a novel route: CD147-spike protein. bioRxiv; 2020.
120. Wang YX, Ma JR, Wang SQ, Zeng YQ, Zhou CY, Ru YH, et al. Utilizing integrating network pharmacological approaches to investigate the potential mechanism of Ma Xing Shi Gan Decoction in treating COVID-19. Eur Rev Med Pharmacol Sci. 2020;24(6):3360-84.
121. Wrapp D, De Vlieger D, Corbett K, Torres G, Van Breedam W, Roose K, et al. Structural Basis for Potent Neutralization of Betacoronaviruses by Single-domain Camelid Antibodies. bioRxiv; 2020.
122. Xia S, Chen X. Ultrasensitive and Whole-Course Encapsulated Field Detection of 2019-nCoV Gene Applying Exponential Amplification from RNA Combined with Chemical Probes. ChemRxiv; 2020.
123. Xu X, Han M, Li T, Sun W, Wang D, Fu B, et al. Effective treatment of severe COVID-19 patients with tocilizumab. Proc Natl Acad Sci U S A. 2020.
124. Yazdani Z, Rafiei A, Yazdani M, Valadan R. Design an efficient multi-epitope peptide vaccine candidate against SARS-CoV-2: An in silico analysis. bioRxiv; 2020.
125. Ye M, Fu D, Ren Y, Wang F, Wang D, Zhang F, et al. Treatment with convalescent plasma for COVID-19 patients in Wuhan, China. J Med Virol. 2020.
126. Yu K, Wu Y, He J, Liu X, Wei B, Wen W, et al. Thymosin alpha-1 Protected T Cells from Excessive Activation in Severe COVID-19. Research Square; 2020.
127. Yu P, Qi F, Xu Y, Li F, Liu P, Liu J, et al. Age-related rhesus macaque models of COVID-19. Animal models and experimental medicine. 2020;3(1):93-7.
128. Yuan S, Jiang S-C, Li Z-L. Early Oxygen Inhalation to Prevent SARS-CoV-2-Induced Acute Respiratory Distress Syndrome. 2020.
129. Zhang B-z, Hu Y-f, Chen L-l, Tong Y-g, Hu J-c, Cai J-p, et al. Mapping the Immunodominance Landscape of SARS-CoV-2 Spike Protein for the Design of Vaccines against COVID-19. bioRxiv; 2020.
130. Zhang Q, Wang Y, Qi C, Shen L, Li J. Clinical trial analysis of 2019-nCoV therapy registered in China. J Med Virol. 2020.
131. Zhang Q, Zhang H, Huang K, Yang Y, Hui X, Gao J, et al. SARS-CoV-2 neutralizing serum antibodies in cats: a serological investigation. bioRxiv; 2020.
132. Zhang Q, Zhao Q. Inactivating porcine coronavirus before nuclei acid isolation with the temperature higher than 56 °C damages its genome integrity seriously. bioRxiv; 2020.
133. Zhang X, Song K, Tong F, Fei M, Guo H, Lu Z, et al. First case of COVID-19 in a patient with multiple myeloma successfully treated with tocilizumab. Blood advances. 2020;4(7):1307-10.
134. Zhou Y, Fu B, Zheng X, Wang D, Zhao C, qi Y, et al. Aberrant pathogenic GM-CSF+ T cells and inflammatory CD14+CD16+ monocytes in severe pulmonary syndrome patients of a new coronavirus. bioRxiv; 2020.
135. Zhu Y, Yu D, Han Y, Yan H, Chong H, Ren L, et al. Cross-reactive neutralization of SARS-CoV-2 by serum antibodies from recovered SARS patients and immunized animals. bioRxiv; 2020.
136. Zolfaghari Emameh R, Nosrati H, Taheri RA. Combination of Biodata Mining and Computational Modelling in Identification and Characterization of ORF1ab Polyprotein of SARS-CoV-2 Isolated from Oronasopharynx of an Iranian Patient. Biol Proced Online. 2020;22:8.

E8 < 10 participants

1. Alzamora MC, Paredes T, Caceres D, Webb CM, Valdez LM, La Rosa M. Severe COVID-19 during Pregnancy and Possible Vertical Transmission. Am J Perinatol. 2020.

2. Baettig SJ, Parini A, Cardona I, Morand GB. Case series of coronavirus (SARS-CoV-2) in a military recruit school: clinical, sanitary and logistical implications. BMJ military health. 2020.
3. Cao G, Tang S, Yang D, Shi W, Wang X, Wang H, et al. One nosocomial cluster following with a familial cluster of COVID-19 cases: the potential transmission risk in patients with negative swab tests. Research Square; 2020.
4. Cao S, Wu A, Li J, Li Y, Xia M, Wu J. Recurrent recurrence of positive SARS-CoV-2 RNA in a COVID-19 patient. Research Square; 2020.
5. Chen HJ, Qiu J, Wu B, Wang ZP, Chen Y, Chen F. Clinical Characteristics of SARS-CoV-2 Infection in Haikou: a study of a family cluster. 2020.
6. Dahlke C, Heidepriem J, Kobbe R, Santer R, Koch T, Fathi A, et al. Distinct early IgA profile may determine severity of COVID-19 symptoms: an immunological case series. medRxiv; 2020.
7. Dong X, Cao YY, Lu XX, Zhang JJ, Du H, Yan YQ, et al. Eleven faces of coronavirus disease 2019. Allergy. 2020.
8. Fu W, Chen Q, Wang T. Letter to the Editor: Three cases of re-detectable positive SARS-CoV-2 RNA in recovered COVID-19 patients with antibodies. J Med Virol. 2020.
9. Gao J, Liu JQ, Wen HJ, Liu H, Hu WD, Han X, et al. The unsynchronized changes of CT image and nucleic acid detection in COVID-19: reports the two cases from Gansu, China. Respir Res. 2020;21(1):96.
10. Gao Z, Gao L, Chen X, Xu Y. A 49-year-old Woman Co-infected with SARS-COV-2 and Mycoplasma – A Case Report. Research Square; 2020.
11. Gutiérrez-Ortiz C, Méndez A, Rodrigo-Rey S, San Pedro-Murillo E, Bermejo-Guerrero L, Gordo-Mañas R, et al. Miller Fisher Syndrome and polyneuritis cranialis in COVID-19. Neurology. 2020.
12. Han M, Zou J, Tian W, Wei X, Zhou Y, Qiao J, et al. Cases Report of Cured Novel Coronavirus-infected Pneumonia Patients with Viral Nucleic Acid Test Positive in Fecal Specimens. Research Square; 2020.
13. Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, Seferovic MD, Aski SK, Arian SE, et al. Maternal Death Due to COVID-19 Disease. Am J Obstet Gynecol. 2020.
14. Haveri A, Smura T, Kuivanen S, Österlund P, Hepojoki J, Ikonen N, et al. Serological and molecular findings during SARS-CoV-2 infection: the first case study in Finland, January to February 2020. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin. 2020;25(11).
15. Hyun-Jung Lee C, Koohy H. In silico identification of vaccine targets for 2019-nCoV. F1000Research. 2020;9:145.
16. Lovly C, Boyd K, Gonzalez-Ericsson P, Lowe C, Brown H, Hoffman R, et al. Rapidly fatal pneumonitis from immunotherapy and concurrent SARS-CoV-2 infection in a patient with newly diagnosed lung cancer. medRxiv; 2020.
17. Okba NMA, Müller MA, Li W, Wang C, GeurtsvanKessel CH, Corman VM, et al. Severe Acute Respiratory Syndrome Coronavirus 2-Specific Antibody Responses in Coronavirus Disease 2019 Patients. Emerg Infect Dis. 2020;26(7).
18. Wan Y, Cao S, Fang Q, Wang M, Huang Y. Coronavirus disease 2019 complicated with Bell's palsy: a case report. 2020.
19. Wang C, Huang L, Lu W, Chen G, Cai Y, Li X, et al. Clinical characteristics of pneumonia patients of long courses infected with SARS-CoV-2. Research Square; 2020.
20. Weiskopf D, Schmitz K, Raadsen M, Grifoni A, Okba NMA, Endeman H, et al. Phenotype of SARS-CoV-2-specific T-cells in COVID-19 patients with acute respiratory distress syndrome. medRxiv; 2020.
21. Weiss S, Klingler J, Hioe C, Amanat F, Baine I, Kojic EM, et al. A High Through-put Assay for Circulating Antibodies Directed against the S Protein of Severe Acute Respiratory Syndrome Corona virus 2. medRxiv; 2020.
22. Yong SEF, Anderson DE, Wei WE, Pang J, Chia WN, Tan CW, et al. Connecting clusters of COVID-19: an epidemiological and serological investigation. The Lancet Infectious diseases. 2020.
23. Zhang H, Chen Y, Yuan Q, Xia QX, Zeng XP, Peng JT, et al. Identification of Kidney Transplant Recipients with Coronavirus Disease 2019. Eur Urol. 2020.
24. Zhang J, Liu J, Li N, Liu Y, Ye R, Qin X, et al. Serological detection of 2019-nCoV respond to the epidemic: A useful complement to nucleic acid testing. medRxiv; 2020.
25. Zhang L, Pang R, Xue X, Bao J, Ye S, Dai Y, et al. Anti-SARS-CoV-2 virus antibody levels in convalescent plasma of six donors who have recovered from COVID-19. Aging (Milano). 2020;12(8):6536-42.

E9 incomplete 2x2 table (cases only)

1. Abbasi J. The Promise and Peril of Antibody Testing for COVID-19. JAMA. 2020.

2. Fu S, Fu X, Song Y, Li M, Pan P-h, Tang T, et al. Virologic and clinical characteristics for prognosis of severe COVID-19: a retrospective observational study in Wuhan, China. medRxiv; 2020.
3. Gao HX, Li YN, Xu ZG, Wang YL, Wang HB, Cao JF, et al. Detection of serum immunoglobulin M and immunoglobulin G antibodies in 2019-novel coronavirus infected cases from different stages. Chin Med J (Engl). 2020.
4. Gao Y, Yuan Y, Li TT, Wang WX, Li YX, Li A, et al. Evaluation the auxiliary diagnosis value of antibodies assays for detection of novel coronavirus (SARS-Cov-2) causing an outbreak of pneumonia (COVID-19). medRxiv; 2020.
5. Huang J, Mao T, Li S, Wu L, Xu X, Li H, et al. Long period dynamics of viral load and antibodies for SARS-CoV-2 infection: an observational cohort study. medRxiv; 2020.
6. Liu C, Zeng F, Wang P, Wu H, Deng S, Liu J, et al. New perspectives into the clinical characteristics of COVID-19 disease. Research Square; 2020.
7. Liu R, Liu X, Han H, Shereen MA, Niu Z, Li D, et al. The comparative superiority of IgM-IgG antibody test to real-time reverse transcriptase PCR detection for SARS-CoV-2 infection diagnosis. medRxiv; 2020.
8. Padoan A, Sciacovelli L, Basso D, Negrini D, Zuin S, Cosma C, et al. IgA-Ab response to spike glycoprotein of SARS-CoV-2 in patients with COVID-19: A longitudinal study. Clinica chimica acta; international journal of clinical chemistry. 2020;507:164-6.
9. Pan Y, Li X, Yang G, Fan J, Tang Y, Zhao J, et al. Serological immunochromatographic approach in diagnosis with SARS-CoV-2 infected COVID-19 patients. The Journal of infection. 2020.
10. Sun B, Feng Y, Mo X, Zheng P, Wang Q, Li P, et al. Kinetics of SARS-CoV-2 specific IgM and IgG responses in COVID-19 patients. Emerging microbes & infections. 2020:1-36.
11. Tan W, Lu Y, Zhang J, Wang J, Dan Y, Tan Z, et al. Viral Kinetics and Antibody Responses in Patients with COVID-19. medRxiv; 2020.
12. To KK, Tsang OT, Leung WS, Tam AR, Wu TC, Lung DC, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. The Lancet Infectious diseases. 2020;20(5):565-74.
13. Wang X, Guo X, Xin Q, Pan Y, Li J, Chu Y, et al. Neutralizing Antibodies Responses to SARS-CoV-2 in COVID-19 Inpatients and Convalescent Patients. medRxiv; 2020.
14. Xiao AT, Gao C, Zhang S. Profile of specific antibodies to SARS-CoV-2: The first report. The Journal of infection. 2020.
15. Xie J, Ding C, Li J, Wang Y, Guo H, Lu Z, et al. Characteristics of Patients with Coronavirus Disease (COVID-19) Confirmed using an IgM-IgG Antibody Test. J Med Virol. 2020.
16. Yong G, Yi Y, Tuantuan L, Xiaowu W, Xiuyong L, Ang L, et al. Evaluation of the auxiliary diagnostic value of antibody assays for the detection of novel coronavirus (SARS-CoV-2). J Med Virol. 2020.
17. Yongchen Z, Shen H, Wang X, Shi X, Li Y, Yan J, et al. Different longitudinal patterns of nucleic acid and serology testing results based on disease severity of COVID-19 patients. Emerging microbes & infections. 2020;9(1):833-6.
18. Zeng F, Dai C, Cai P, Wang J, Xu L, Li J, et al. A comparison study of SARS-CoV-2 IgG antibody between male and female COVID-19 patients: a possible reason underlying different outcome between gender. medRxiv; 2020.
19. Zhang B, Zhou X, Zhu C, Feng F, Qiu Y, Feng J, et al. Immune phenotyping based on neutrophil-to-lymphocyte ratio and IgG predicts disease severity and outcome for patients with COVID-19. medRxiv; 2020.
20. Zhang G, Nie S, Zhang Z. Longitudinal Change of SARS-Cov2 Antibodies in Patients with COVID-19. The Journal of infectious diseases. 2020.
21. Zhang W, Du RH, Li B, Zheng XS, Yang XL, Hu B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerging microbes & infections. 2020;9(1):386-9.
22. Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020.

E10 other reasons

1. Cohen J, Kupferschmidt K. Labs scramble to produce new coronavirus diagnostics. Science. 2020;367(6479):727.
2. Ding X, Yin K, Li Z, Liu C. All-in-One Dual CRISPR-Cas12a (AIOD-CRISPR) Assay: A Case for Rapid, Ultrasensitive and Visual Detection of Novel Coronavirus SARS-CoV-2 and HIV virus. bioRxiv; 2020.

3. Ismail AAA. ANNALS EXPRESS: Serological tests for Covid-19 antibodies: limitations must be recognised. Ann Clin Biochem. 2020:4563220927053.
4. Klasse PJ, Moore J. Antibodies to SARS-CoV-2 and Their Potential for Therapeutic Passive Immunization. Preprints.org; 2020.
5. Lu H, Stratton CW, Tang YW. An Evolving Approach to the Laboratory Assessment of COVID-19. J Med Virol. 2020.
6. Okba NMA, Muller M, Li W, Wang C, GeurtsvanKessel C, Corman V, et al. SARS-CoV-2 specific antibody responses in COVID-19 patients. medRxiv; 2020.
7. Tan X, Lin C, Zhang J, Khaing Oo MK, Fan X. Rapid and quantitative detection of COVID-19 markers in micro-liter sized samples. bioRxiv; 2020.
8. Tu YF, Chien CS, Yarmishyn AA, Lin YY, Luo YH, Lin YT, et al. A Review of SARS-CoV-2 and the Ongoing Clinical Trials. Int J Mol Sci. 2020;21(7).
9. Wang B, Wang L, Kong X, Geng J, Xiao D, Ma C, et al. Long-term Coexistence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) with Antibody Response in Coronavirus Disease 2019 (COVID-19) Patients. medRxiv; 2020.
10. Wang B, Wang L, Kong X, Geng J, Xiao D, Ma C, et al. Long-term coexistence of SARS-CoV-2 with antibody response in COVID-19 patients. J Med Virol. 2020.

9. APPENDIX 3 – INCLUDED STUDIES

Table A 1: Study pool– list of relevant studies used for the assessment

Study reference / ID	Available documents[a]	Research question
An 2020	(117)	4*
Bendavid 2020	(100)	2
Bryan 2020	(101)	2 & 3
Cassaniti 2020	(69)	3
Comar 2020	(93)	2
Doi 2020	(99)	2*
Erikstrup 2020	(107)	2
Fontanet 2020	(106)	2
Garcia 2020	(76)	3
Garcia-Basteiro 2020	(95)	2
Hu 2020 (Production)	(118)	4*
Hu 2020 (Simple)	(78)	3
Li 2020 (Development)	(70)	3
Lin 2020 (evaluations)	(77)	3
Liu 2020 (Evaluation)	(82)	3
Liu 2020 (Diagnostic)	(75)	3
Liu 2020 (Preliminary)	(84)	3
Long 2020	(60, 134)	1
Lou 2020	(35)	3
Ma 2020	(79)	3
Paradiso 2020 (Rapid)	(94)	2
Paradiso 2020 (Clinical)	(74)	3
Qian 2020	(80)	3
Shakiba 2020	(104)	2
Shen 2020	(71)	3
Slot 2020	(105)	2
Snoeck 2020	(135)	2
Spicuzza 2020	(68)	3
Steensels 2020	(97)	2
Streeck 2020	(136)	2
Stringhini 2020	(137)	2
Thompson 2020	(91)	2
Tosato 2020	(96)	2
Wan 2020	(81)	3
Wang 2020 (Association)	(61)	1
Whitman 2020	(73)	3
Wu 2020	(98)	2
Xiang 2020 (Antibody)	(83)	3
Zhang 2020 (Evaluation)	(138)	3
Zhong 2020	(72)	3
*included but excluded from quantitative synthesis		

Table A 2: Characteristics of the studies included

Study reference	Study type	Total number of participants	Target population	Countries	Age	Reference standard	Antibody test class	Sample type	Diagnostic accuracy measures	RQ
Bendavid 2020	Cross-sectional	3330	Adults and children residents of Santa Clara	USA	0-4 yrs: 2.1% 5-18 yrs: 16.5% 19-64 yrs: 76.3% 65+ yrs: 5.1%	NR	LFIA	Blood	Detection rate	2
Bryan 2020	Cross-sectional	4856	NR	USA	0-19 yrs: 4.9% 20-29 yrs: 6.2% 30-39 yrs: 17.1% 40-49 yrs: 22.7% 50-59 yrs: 23.5% 60-69 yrs: 18.3% 70-79 yrs: 6.7% 80+ yrs: 0.5%	PCR	CMIA	Serum	Sensitivity, specificity, true positive, detection rate	2
Cassaniti 2020	Case-control / Cohort study	110	Cohort: adults, hospitalized positive controls: adults, hospitalized healthy volunteers: adults	Italy	cohort: Median: 61.50 Range: 33-97 positive controls: Median: 73.5 Range: 38-86 healthy volunteers: Median: 38.5 Range: 25-69	RT-PCR	LFIA	Serum or whole blood	Specificity, sensitivity, positive predictive value, and negative predictive value	3
Comar 2020	Cross-sectional	727	Health care workers and other workers in the hospital	Italy	Range: 22-77	RT-PCR	ELISA	Serum	True positive, true negative, false negative, false positive	2
Doi 2020	Cross-sectional	1000	Randomly selected preserved serum from patients who visited outpatient clinics of the hospital and received blood testing for any reason	Japan	<10 yrs: 0.8% 10-19 yrs: 2.7% 20-29 yrs: 3.6% 30-39 yrs: 9.0% 40-49 yrs: 15.5% 50-59 yrs: 16.4% 60-69 yrs: 17.1% 70-79 yrs: 16.6% 80-89 yrs: 16.4% 90+ yrs: 1.9%	NR	Immunochromatographic test	Serum	Serum samples tested from patients who visited the clinic from March 31 to April 7, 2020,	2

Study reference	Study type	Total number of participants	Target population	Countries	Age	Reference standard	Antibody test class	Sample type	Diagnostic accuracy measures	RQ
Erikstrup 2020	Cross-sectional	9496	General population/ convenience sample healthy blood donations, for test validation: plasma samples from blood donors giving blood before November 2019, plasma from 155 patients with previous SARS-CoV-2	Denmark	Range: 17-69	Number of infected and deceased due to COVID-19 by epidemiological surveillance report, pre-epidemic controls	Lateral flow test	Plasma or whole blood	Estimated number of infected individuals, seroprevalence, infection fatality rate, ratio between estimated antibody-positive individuals and number of confirmed cases	2
Fontanet 2020	Cohort study	661	Adults and Children, attending the same high school and blood donors living near the school	France	Median:37	NR	S-Flow assay; ELISA N assay; LIPS	Serum	NA	2
Garcia 2020	Case-control / cohort study	Group 1: 45 Group 2: 55 Group 3: 63	Group1: Pre-epidemic serum samples Group 2: hospitalised patients with RT PCR-positive for SARS-CoV-2 Group 3: hospitalised patients with RT-PCR negative for SARS-CoV-2 but clinical and radiological signs of pneumonia of unknown origin	Spain	Mean (IQR) Group 1: 55 (34-66) Group 2: 63 (50-79) Group 3: 67 (57-74)	Group 1: Pre-covid serum samples Group 2: clinical and radiological characteristics with positive PCR Group 3: clinical and radiological characteristics with negative PCR	Qualitative membrane-based immunoassay (immunochromatography)	Serum	Sensitivity, specificity	3
Garcia-Basteiro 2020	Cross-sectional	578	Health care workers from the human resources database of hospital clínic in Barcelona: physicians, nurses, assistants, technicians, stretcher-bearers or other support staff (administrative officers, cleaning, kitchen, laundry, maintenance, etc.)	Spain	Mean (SD): 42.1 (11.6)	RT-PCR	xMAP	Plasma	Seropositivity, prevalence of past or current infection	2

Study reference	Study type	Total number of participants	Target population	Countries	Age	Reference standard	Antibody test class	Sample type	Diagnostic accuracy measures	RQ
Hu 2020 (Simple)	Cohort study	41	Hospitalized	China	NR	RT-PCR	Colloidal gold-based immunochromatographic	Serum/ plasma or whole blood	Sensitivity	3
Li 2020 (Development)	Case-control	525	Samples were collected from various hospitals and CDC testing laboratories (total eight) at six different provinces of China	China	NR	RT-PCR	PoC LFIA	Vein blood	Sensitivity, specificity	3
Lin 2020 (evaluations)	Case-control	159	COVID-19 patients (N=79); healthy controls (N=29) & controls with tuberculosis (N=51)	China	Cases: NR control: range 16-72 control tuberculosis: NR	RT-PCR + clinical features	CLIA IgM + IgG (ELISA/ IgM + IgG for comparison)	Serum	True positive rate, false positive rate, detection rate, ROC	3
Liu 2020 (Evaluation)	Case-control	214	Patients diagnosed with COVID-19 who were hospitalized. All patients were laboratory confirmed (RT-PCR positive); 100 healthy blood donors were selected as controls	China	NR	RT-PCR	ELISA	Confirmed patients: NR; healthy donors: blood samples	None	3
Liu 2020 (Diagnostic)	Retrospective cohort study	179	Inpatient or outpatient	China	PCR Positive: mean (SD): 76 (15) PCR Negative: mean (SD): 56 (21)	RT-PCR	GICA	Serum samples from fasting blood	Sensitivity, specificity, PPV, NPV, accuracy, Kappa efficiency	3
Liu 2020 (Preliminary)	Case-control	Total: 358 total cases: 238 total control: 120	Adults	China	Median (IQR): 55 (38 - 65)	RT-PCR	ELISA	Serum samples	Sensitivity, specificity, detection rate	3
Long 2020	Cross-sectional	501	Patients with confirmed (RT-PCR positive) COVID-19 (n=285); patients admitted to hospital with suspected COVID-19 (n=52), who had respiratory symptoms or abnormal pulmonary imaging; a couple who were confirmed to be SARS-CoV-2 positive and a cluster of close contacts identified by a local centre for disease control (n=164)	China	Confirmed cases: Median (IQR): 47 (34-56)	PCR	MCLIA	Serum	NR	1

Study reference	Study type	Total number of participants	Target population	Countries	Age	Reference standard	Antibody test class	Sample type	Diagnostic accuracy measures	RQ
Lou 2020	Cohort study	380	Adults	China	Cases: Median (IQR): 55 (45-64)	RT-PCR	3 ELISA, 3 LFA, 2 CMIA	Plasma	Sensitivity, specificity	3
Ma 2020	Case-control	570	87 COVID-19 patients and 330 negative sera from healthy donors before Oct 2019, 138 interfering sera from no-COVID-19 patients with different underlying diseases, 15 sera from once suspected cases (PCR-negative but typical manifestation of pneumonia).	China	Cases with severe symptoms: Median: 62.5 moderate symptoms: Median: 46 mild symptoms: Median: 30	cases: RT-PCR; controls: NR	CLIA	Serum	Sensitivity, specificity, overall agreement, pair-wise test between each group.	3
Paradiso 2020 (Rapid)	Cross-sectional	525	Health care workers, enrolled in direct clinical activities (56%), laboratory practice (6%), administrative activities (8%), maintenance/cleaning (30%),	Italy	Median: 48 Range: 20-73	RT-PCR	Colloidal gold	Venous blood	Sensitivity, seropositivity	2
Paradiso 2020 (Clinical)	Cross-sectional	191	Patients presenting at the emergency room for SARS-CoV-2 testing purposes.	Italy	Median: 58.5	RT-PCR	Colloidal gold	Venous blood	Sensitivity, specificity, accuracy, precision, recall, kappa	3
Qian 2020	Case-control	2113	NR	China	NR	RT-PCR	CLIA	NR	Sensitivity specificity	3

Study reference	Study type	Total number of participants	Target population	Countries	Age	Reference standard	Antibody test class	Sample type	Diagnostic accuracy measures	RQ
Shakiba 2020	Cross-sectional + positive control sample	525	General population selected randomly from 20 geographic clusters; individuals and household members	Iran	< 5 yrs: 5% 5-18 yrs: 18% 18-60 yrs: 62% 60+ yrs: 13%	COVID-19 patients: RT-PCR suspected cases: no reference test hospitalized patients with other diseases: no reference test normal population: no reference test	NR	Serum or whole blood	Unadjusted, population weight adjusted and test-perfomance adjusted prevalence, infection fatality rate	2
Shen 2020	Cohort study	176	Suspected COVID-19 patients (n=150), defined as a pneumonia that had related epidemiological history and fulfilled two of these three criteria: fever and/or respiratory symptoms; imaging manifestations of pneumonia; low or normal white-cell count or low lymphocyte count. Clinical characteristics for this cohort were reported as PCR positive (n=97) and PCR negative (n=53) subgroups. 26 healthy blood donors from a blood centre	China	PCR positive: Median (IQR): 38 (46-56). PCR negative: Median (IQR): 32 (20-42.5)	PCR	GICA	Blood samples (peripheral venous blood)	True positive, true negative, false positive, false negative, sensitivity, specificity, PPV, NPV	3
Slot 2020	Cross-sectional + positive control sample	7361	Plasma and serum samples of 7,361 adult blood plasma donors and 153 convalescent plasma donors from throughout the Netherlands	Netherlands	Range: 18-72	RT-PCR	ELISA	Serum	Seroconversion rate, positive predictive value, specificity, seroprevalence	2

Study reference	Study type	Total number of participants	Target population	Countries	Age	Reference standard	Antibody test class	Sample type	Diagnostic accuracy measures	RQ
Snoeck 2020	Cohort study	1862	Adult general population	Luxembourg	Mean (SD): 47 (15) Range: 18–84	PCR only, PCR plus intensive care admission, pre-COVID samples	ELISA	Blood	Detection rate	2
Spicuzza 2020	Case-control	37	Patients with confirmed COVID-19 who had, according to the WHO definition, consistent radiological/clinical findings and positive molecular tests (n = 23); patients with suspected COVID-19 with suggestive radiological/clinical findings but negative molecular tests (n = 7); asymptomatic controls with negative molecular tests (n = 7)	Italy	Confirmed patients: Mean: 57 Suspected patients: Mean: 67	RT-PCR	PoC	Blood	Positive and negative rates for antibody and PCR tests; applying PCR as reference standard	3
Steensels 2020	Cross-sectional	3056	Adult, hospital staff	Belgium	IgG positive mean (SD): 39.5 (13.1) IgG negative mean (SD): 41.3 (12.4)	NR	single-lane rapid IgG/IgM lateral flow assay	NR	Detection rate	2
Streeck 2020	Cross-sectional	919	Adults and children. A random sample of 600 adults with different surnames and all household members contained in the Heinsberg region	Germany	Median: 53 Range: 1 - 90	RT-PCR	ELISA	Blood	Detection rate	2
Stringhini 2020	Cross-sectional	2766	Former participants of the Bus Santé study (yearly representative stratified sample of 500 men and 500 women from the general population) and their household members, aged > 5 years.	Switzerland	5-9 yrs: 4.4% 10-19 yrs: 12.0% 20-49 yrs: 39.6% 50-64 yrs: 30.6% 65+ yrs: 13.3%	RT-PCR	ELISA	Peripheral venous blood	NR	2
Thompson 2020	Cross-sectional + positive control sample	1100	Blood donors; samples collected across Scotland and pre-pandemic controls from 2019. Negative blood donor samples from anonymous archive collected between 09/2018 and 12/2019. 7 PCR-confirmed positive controls with asymptomatic infections collected at the discharge plus 28 day time-point.	Scotland, UK	Range: 18-75	None (only for inhouse-validation study)	PMN assay, ELISA for confirmation in a sample	Plasma	Standardised neutralisation percentage, raw serpoprevalence	2

Study reference	Study type	Total number of participants	Target population	Countries	Age	Reference standard	Antibody test class	Sample type	Diagnostic accuracy measures	RQ
Tosato 2020	Cross-sectional	133	Adult, healthcare providers	Italy	Mean (SD): 47 (10) Range: 39-55	100 pre-epidemic control samples; PCR for asymptomatic positive controls	CLIA	Serum	Seroprevalence	2
Wan 2020	Cross-sectional	180	Cases: patients with SARS -CoV-2 diagnosed in January 2020 Controls: 130 serum samples from patients with other conditions including 20 late pregnancy women, 20 patients with solid tumors, 20 patients with AIDS, 21 patients over 90 years old and 49 normal controls	China	NR	PCR	CLIA	Serum	Sensitivity, specificity AUC and Youden's index	3
Wang 2020 (Association)	Cross-sectional	426	Adults	China	Wuhan: 20-29 yrs: 28.17% 30-39 yrs: 50.71% 40-49 yrs: 19.01% 50-59 yrs: 2.11% Hefei: 20-29 yrs: 31.69% 30-39 yrs: 50.70% 40-49 yrs: 14.79% 50-59: 2.82%	PCR	Chemiluminescent kit	Blood	Detection rate, prevalence	1
Whitman 2020	Case-control	130 samples form 80 positive RT-PCR- individuals; 108 pre COVID negative controls; 52 samples from individuals with respiratory infections other than COVID-19	Adults	USA	Mean: 52.7 Range: 22-90	RT-PCR	LFA, ELISA	Plasma or serum	NR	3

Study reference	Study type	Total number of participants	Target population	Countries	Age	Reference standard	Antibody test class	Sample type	Diagnostic accuracy measures	RQ
Wu 2020	Cross-sectional/ cohort	1021	People applying for a permission to resume work (n = 1021); hospitalized patients (n = 381)	China	NR	PCR	GICA	Unclear	NR	2
Xiang 2020 (Antibody)	Case-control	169	People with suspected (n = 24) or confirmed (n = 85) COVID-19; control group (n = 60). Confirmation was through RT-PCR. Suspected diagnosis was based on negative RT-PCR, but satisfying one epidemiological factor and two clinical manifestations.	China	Confirmed group: Median (IQR): 51.0 (32.0-65); suspected group: Median (IQR): 44.0 (35.5-60.5); control group: Median (IQR): 34.0 (29.0-51.0)	RT-PCR	ELISA	Serum	True-positive, true-negative, false-positive, false-negative, sensitivity, specificity, PPV, NPV	3
Zhang 2020 (Evaluation)	Unclear	814	NR	China	NR	RT-PCR	GICA	NR	Sensitivity specificity positives negatives	3
Zhong 2020	Case-control	347	Adults	China	Mean: 48	RT-PCR plus CT	ELISA / CLIA	Serum	Sensitivity, specificity	3

Abbreviations: AUC: Area under the curve; CDC: Centers for Disease Control and Prevention; CLIA: Chemiluminescence immunoassay; CMIA: Chemiluminescence microparticle immunoassay; CT: Computed tomography; ELISA: Enzyme-linked immunosorbent assay; GICA: Gold immunochromatography assay; IQR: Interquartile range; IgG: Immunoglobulin G; IgM: Immunoglobulin M; LFIA: Lateral flow immunoassay; LFA: Lateral flow assay; LIPS: Luciferase immunoprecipitation system; MCLIA: Magnetic chemiluminescence immunoassay; NR: Not reported; NPV: Negative predictive value; PCR: Polymerase chain reaction; PMN: Polymorphonuclear leukocytes; PoC: Point of care; PPV: Positive predictive value; RT-PCR: Reverse transcription polymerase chain reaction; xMAP: Bead-based multiplexed immunoassay; yrs: Years

Table A 3: Risk of bias in diagnostic accuracy studies

Trial	Risk of Bias				Applicability concerns		
	Patient selection (Domain 1)	Index test (Domain 2)	Reference standard (Domain 3)	Flow and timing (Domain 4)	Patient selection (Domain 1)	Index test (Domain 2)	Reference standard (Domain 3)
Cassaniti 2020	low	low	high	low	low	low	low
Garcia 2020	high	high	low	low	high	low	low
Hu 2020 (Simple)	low	low	high	low	low	low	low
Li 2020 (De-velopment)	high	high	high	unclear	unclear	unclear	unclear
Lin 2020 (evaluations)	high	high	low	high	unclear	low	low
Liu 2020 (Evaluation)	high	high	low	low	high	low	low
Liu 2020 (Diagnostic)	unclear	low	high	low	low	low	low
Liu 2020 (Preliminary)	high	unclear	low	unclear	high	low	low
Long 2020	unclear	unclear	low	unclear	low	low	low
Lou 2020	high	high	high	high	high	low	low
Ma 2020	high	high	low	low	high	low	low
Paradiso 2020 (Clinical)	low	low	high	low	low	low	low
Qian 2020	high	high	high	high	high	low	low
Shen 2020	low	low	high	low	low	low	low
Spicuzza 2020	high	unclear	low	high	unclear	low	low
Wan 2020	high	high	low	low	high	low	low
Wang 2020 (Association)	low	low	low	low	low	low	low
Whitman 2020	high	low	low	low	high	low	low
Xiang 2020 (Antibody)	high	unclear	low	high	high	low	low
Zhang 2020 (Evaluation)	unclear	high	high	unclear	high	low	low
Zhong 2020	high	high	low	high	unclear	low	low
Abbreviations: NA: Not available							

10. APPENDIX 4 – DATA EXTRACTION TABLES

Table A 4: Estimates for sensitivity, specificity, positive and negative predictive value and prevalence with 95% confidence intervals.

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Cassaniti 2020	LFI	RDT		IgM and/or IgG	0	25	0	30	5	83.3 (64.5 - 93.7)	100 (88.4 - 100)	100 (86.3 - 100)	85.7 (69 - 94.6)	50 (37 - 63)
Cassaniti 2020	LFI	RDT		IgM and/or IgG	0	7	1	11	31	18.4 (8.3 - 34.9)	91.7 (59.8 - 99.6)	87.5 (46.7 - 99.3)	26.2 (14.4 - 42.3)	76 (61.5 - 86.5)
Garcia 2020	IC	RDT		IgG	0	23	56	7	32	41.8 (28.9 - 55.9)	11.1 (5 - 22.2)	29.1 (19.7 - 40.6)	17.9 (8.1 - 34.1)	46.6 (37.5 - 56)
Garcia 2020	IC	RDT		IgG	2	6	15	3	18	25 (10.6 - 47.1)	16.7 (4.4 - 42.3)	28.6 (12.2 - 52.3)	14.3 (3.8 - 37.4)	57.1 (41.1 - 71.9)
Garcia 2020	IC	RDT		IgG	3	16	41	4	7	69.6 (47 - 85.9)	8.9 (2.9 - 22.1)	28.1 (17.4 - 41.7)	36.4 (12.4 - 68.4)	33.8 (23.1 - 46.4)
Garcia 2020	IC	RDT		IgM	0	12	25	38	43	21.8 (12.2 - 35.4)	60.3 (47.2 - 72.2)	32.4 (18.6 - 49.9)	46.9 (35.9 - 58.3)	46.6 (37.5 - 56)
Garcia 2020	IC	RDT		IgM	2	3	7	11	21	12.5 (3.3 - 33.5)	61.1 (36.1 - 81.7)	30 (8.1 - 64.6)	34.4 (19.2 - 53.2)	57.1 (41.1 - 71.9)
Garcia 2020	IC	RDT		IgM	3	9	18	27	14	39.1 (20.5 - 61.2)	60 (44.4 - 73.9)	33.3 (17.2 - 54)	65.9 (49.3 - 79.4)	33.8 (23.1 - 46.4)
Garcia 2020	IC	RDT		IgM and/or IgG	0	26	56	7	29	47.3 (33.9 - 61.1)	11.1 (5 - 22.2)	31.7 (22.1 - 43)	19.4 (8.8 - 36.6)	46.6 (37.5 - 56)
Garcia 2020	IC	RDT		IgM and/or IgG	2	8	15	3	16	33.3 (16.4 - 55.3)	16.7 (4.4 - 42.3)	34.8 (17.2 - 57.2)	15.8 (4.2 - 40.5)	57.1 (41.1 - 71.9)
Garcia 2020	IC	RDT		IgM and/or IgG	3	17	41	4	6	73.9 (51.3 - 88.9)	8.9 (2.9 - 22.1)	29.3 (18.5 - 42.9)	40 (13.7 - 72.6)	33.8 (23.1 - 46.4)
Li 2020 (Development)	LFI	RDT		IgG	0	280	1	127	117	70.5 (65.7 - 74.9)	99.2 (95.1 - 100)	99.6 (97.7 - 100)	52 (45.6 - 58.4)	75.6 (71.7 - 79.2)
Li 2020 (Development)	LFI	RDT		IgM	0	328	10	118	69	82.6 (78.4 - 86.1)	92.2 (85.7 - 96)	97 (94.5 - 98.5)	63.1 (55.7 - 69.9)	75.6 (71.7 - 79.2)
Li 2020 (Development)	LFI	RDT		IgM and IgG	0	256	1	127	141	64.5 (59.5 - 69.2)	99.2 (95.1 - 100)	99.6 (97.5 - 100)	47.4 (41.3 - 53.5)	75.6 (71.7 - 79.2)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Li 2020 (Development)	LFI	RDT		IgM and/or IgG	0	352	12	116	45	88.7 (85 - 91.5)	90.6 (83.9 - 94.8)	96.7 (94.2 - 98.2)	72 (64.3 - 78.7)	75.6 (71.7 - 79.2)
Lin 2020 (evaluations)	CLIA	CLIA		IgG	0	65	2	78	14	82.3 (71.7 - 89.6)	97.5 (90.4 - 99.6)	97 (88.7 - 99.5)	84.8 (75.4 - 91.1)	49.7 (41.7 - 57.7)
Lin 2020 (evaluations)	CLIA	CLIA		IgG	1	8	2	78	4	66.7 (35.4 - 88.7)	97.5 (90.4 - 99.6)	80 (44.2 - 96.5)	95.1 (87.3 - 98.4)	13 (7.2 - 22.1)
Lin 2020 (evaluations)	CLIA	CLIA		IgG	2	24	2	78	9	72.7 (54.2 - 86.1)	97.5 (90.4 - 99.6)	92.3 (73.4 - 98.7)	89.7 (80.8 - 94.9)	29.2 (21.2 - 38.6)
Lin 2020 (evaluations)	CLIA	CLIA		IgG	3	33	2	78	1	97.1 (82.9 - 99.8)	97.5 (90.4 - 99.6)	94.3 (79.5 - 99)	98.7 (92.2 - 99.9)	29.8 (21.8 - 39.2)
Lin 2020 (evaluations)	CLIA	CLIA		IgM	0	65	15	65	14	82.3 (71.7 - 89.6)	81.3 (70.6 - 88.8)	81.3 (70.6 - 88.8)	82.3 (71.7 - 89.6)	49.7 (41.7 - 57.7)
Lin 2020 (evaluations)	CLIA	CLIA		IgM	1	10	15	65	2	83.3 (50.9 - 97.1)	81.3 (70.6 - 88.8)	40 (21.8 - 61.1)	97 (88.7 - 99.5)	13 (7.2 - 22.1)
Lin 2020 (evaluations)	CLIA	CLIA		IgM	2	24	15	65	9	72.7 (54.2 - 86.1)	81.3 (70.6 - 88.8)	61.5 (44.7 - 76.2)	87.8 (77.7 - 93.9)	29.2 (21.2 - 38.6)
Lin 2020 (evaluations)	CLIA	CLIA		IgM	3	31	15	65	3	91.2 (75.2 - 97.7)	81.3 (70.6 - 88.8)	67.4 (51.9 - 80)	95.6 (86.8 - 98.9)	29.8 (21.8 - 39.2)
Lin 2020 (evaluations)	CLIA	CLIA		IgM and IgG	0	58	1	79	21	73.4 (62.1 - 82.4)	98.8 (92.3 - 99.9)	98.3 (89.7 - 99.9)	79 (69.5 - 86.2)	49.7 (41.7 - 57.7)
Lin 2020 (evaluations)	CLIA	CLIA		IgM and IgG	1	8	1	79	4	66.7 (35.4 - 88.7)	98.8 (92.3 - 99.9)	88.9 (50.7 - 99.4)	95.2 (87.5 - 98.4)	13 (7.2 - 22.1)
Lin 2020 (evaluations)	CLIA	CLIA		IgM and IgG	2	19	1	79	14	57.6 (39.4 - 74)	98.8 (92.3 - 99.9)	95 (73.1 - 99.7)	84.9 (75.7 - 91.2)	29.2 (21.2 - 38.6)
Lin 2020 (evaluations)	CLIA	CLIA		IgM and IgG	3	31	1	79	3	91.2 (75.2 - 97.7)	98.8 (92.3 - 99.9)	96.9 (82 - 99.8)	96.3 (88.9 - 99.1)	29.8 (21.8 - 39.2)
Lin 2020 (evaluations)	CLIA	CLIA		IgM and/or IgG	0	72	16	64	7	91.1 (82 - 96.1)	80 (69.3 - 87.8)	81.8 (71.9 - 88.9)	90.1 (80.2 - 95.6)	49.7 (41.7 - 57.7)
Lin 2020 (evaluations)	CLIA	CLIA		IgM and/or IgG	1	10	16	64	2	83.3 (50.9 - 97.1)	80 (69.3 - 87.8)	38.5 (20.9 - 59.3)	97 (88.5 - 99.5)	13 (7.2 - 22.1)
Lin 2020 (evaluations)	CLIA	CLIA		IgM and/or IgG	2	29	16	64	4	87.9 (70.9 - 96)	80 (69.3 - 87.8)	64.4 (48.7 - 77.7)	94.1 (84.9 - 98.1)	29.2 (21.2 - 38.6)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Lin 2020 (evaluations)	CLIA	CLIA		IgM and/or IgG	3	33	16	64	1	97.1 (82.9 - 99.8)	80 (69.3 - 87.8)	67.3 (52.3 - 79.6)	98.5 (90.6 - 99.9)	29.8 (21.8 - 39.2)
Lin 2020 (evaluations)	ELISA	ELISA		IgG	0	15	0	64	50	23.1 (13.9 - 35.5)	100 (94.4 - 100)	100 (78.2 - 100)	56.1 (46.5 - 65.3)	50.4 (41.5 - 59.3)
Lin 2020 (evaluations)	ELISA	ELISA		IgM	0	30	14	40	35	46.2 (33.9 - 58.9)	74.1 (60.1 - 84.6)	68.2 (52.3 - 80.9)	53.3 (41.5 - 64.8)	54.6 (45.3 - 63.7)
Liu 2020 (Evaluation)	ELISA	ELISA		IgG	0	150	0	100	64	70.1 (63.4 - 76)	100 (96.4 - 100)	100 (97.6 - 100)	61 (53 - 68.4)	68.2 (62.6 - 73.2)
Liu 2020 (Diagnostic)	CLIA	CLIA		IgM and/or IgG	0	18	8	14	1	94.7 (71.9 - 99.7)	63.6 (40.8 - 82)	69.2 (48.1 - 84.9)	93.3 (66 - 99.7)	46.3 (31 - 62.4)
Liu 2020 (Diagnostic)	ELISA	ELISA		IgM and/or IgG	0	127	67	85	16	88.8 (82.2 - 93.3)	55.9 (47.7 - 63.9)	65.5 (58.3 - 72)	84.2 (75.2 - 90.4)	48.5 (42.7 - 54.3)
Liu 2020 (Diagnostic)	GICA	RDT		IgG	0	75	7	82	15	83.3 (73.7 - 90.1)	92.1 (83.9 - 96.5)	91.5 (82.7 - 96.2)	84.5 (75.5 - 90.8)	50.3 (42.8 - 57.8)
Liu 2020 (Diagnostic)	GICA	RDT		IgG	1	2	2	7	14	12.5 (2.2 - 39.6)	77.8 (40.2 - 96.1)	50 (9.2 - 90.8)	33.3 (15.5 - 56.9)	64 (42.6 - 81.3)
Liu 2020 (Diagnostic)	GICA	RDT		IgG	2	5	1	1	1	83.3 (36.5 - 99.1)	50 (2.7 - 97.3)	83.3 (36.5 - 99.1)	50 (2.7 - 97.3)	75 (35.6 - 95.5)
Liu 2020 (Diagnostic)	GICA	RDT		IgG	3	68	4	10	0	100 (94.7 - 100)	71.4 (42 - 90.4)	94.4 (85.7 - 98.2)	100 (69.2 - 100)	82.9 (72.7 - 90)
Liu 2020 (Diagnostic)	GICA	RDT		IgM	0	34	5	84	56	37.8 (28 - 48.7)	94.4 (86.8 - 97.9)	87.2 (71.8 - 95.2)	60 (51.4 - 68.1)	50.3 (42.8 - 57.8)
Liu 2020 (Diagnostic)	GICA	RDT		IgM	1	3	1	8	13	18.8 (5 - 46.3)	88.9 (50.7 - 99.4)	75 (21.9 - 98.7)	38.1 (19 - 61.3)	64 (42.6 - 81.3)
Liu 2020 (Diagnostic)	GICA	RDT		IgM	2	6	1	1	0	100 (54.1 - 100)	50 (2.7 - 97.3)	85.7 (42 - 99.2)	100 (2.5 - 100)	75 (35.6 - 95.5)
Liu 2020 (Diagnostic)	GICA	RDT		IgM	3	25	4	10	43	36.8 (25.6 - 49.4)	71.4 (42 - 90.4)	86.2 (67.4 - 95.5)	18.9 (9.9 - 32.4)	82.9 (72.7 - 90)
Liu 2020 (Diagnostic)	GICA	RDT		IgM and/or IgG	0	77	8	81	13	85.6 (76.2 - 91.8)	91 (82.6 - 95.8)	90.6 (81.8 - 95.6)	86.2 (77.2 - 92.1)	50.3 (42.8 - 57.8)
Liu 2020 (Diagnostic)	GICA	RDT		IgM and/or IgG	1	3	2	7	13	18.8 (5 - 46.3)	77.8 (40.2 - 96.1)	60 (17 - 92.7)	35 (16.3 - 59.1)	64 (42.6 - 81.3)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Liu 2020 (Diagnostic)	GICA	RDT		IgM and/or IgG	2	6	1	1	0	100 (54.1 - 100)	50 (2.7 - 97.3)	85.7 (42 - 99.2)	100 (2.5 - 100)	75 (35.6 - 95.5)
Liu 2020 (Diagnostic)	GICA	RDT		IgM and/or IgG	3	68	5	9	0	100 (94.7 - 100)	64.3 (35.6 - 86)	93.2 (84.1 - 97.5)	100 (66.4 - 100)	82.9 (72.7 - 90)
Liu 2020 (Evaluation)	ELISA	ELISA		IgG	1	22	0	100	38	36.7 (24.9 - 50.2)	100 (96.4 - 100)	100 (84.6 - 100)	72.5 (64.1 - 79.6)	37.5 (30.1 - 45.5)
Liu 2020 (Evaluation)	ELISA	ELISA		IgG	2	39	0	100	15	72.2 (58.1 - 83.1)	100 (96.4 - 100)	100 (91 - 100)	87 (79.1 - 92.3)	35.1 (27.7 - 43.2)
Liu 2020 (Evaluation)	ELISA	ELISA		IgG	3	48	0	100	7	87.3 (74.9 - 94.3)	100 (96.4 - 100)	100 (92.6 - 100)	93.5 (86.5 - 97.1)	35.5 (28.1 - 43.6)
Liu 2020 (Evaluation)	ELISA	ELISA		IgG	4	28	0	100	4	87.5 (70.1 - 95.9)	100 (96.4 - 100)	100 (87.7 - 100)	96.2 (89.9 - 98.8)	24.2 (17.4 - 32.6)
Liu 2020 (Evaluation)	ELISA	ELISA		IgG	5	6	0	100	0	100 (54.1 - 100)	100 (96.4 - 100)	100 (54.1 - 100)	100 (96.4 - 100)	5.7 (2.3 - 12.4)
Liu 2020 (Evaluation)	ELISA	ELISA		IgG	6	7	0	100	0	100 (59 - 100)	100 (96.4 - 100)	100 (59 - 100)	100 (96.4 - 100)	6.5 (2.9 - 13.5)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM	0	146	0	100	68	68.2 (61.5 - 74.3)	100 (96.4 - 100)	100 (97.5 - 100)	59.5 (51.7 - 66.9)	68.2 (62.6 - 73.2)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM	1	27	0	100	33	45 (32.3 - 58.3)	100 (96.4 - 100)	100 (87.2 - 100)	75.2 (66.8 - 82.1)	37.5 (30.1 - 45.5)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM	2	39	0	100	15	72.2 (58.1 - 83.1)	100 (96.4 - 100)	100 (91 - 100)	87 (79.1 - 92.3)	35.1 (27.7 - 43.2)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM	3	45	0	100	10	81.8 (68.6 - 90.5)	100 (96.4 - 100)	100 (92.1 - 100)	90.9 (83.5 - 95.3)	35.5 (28.1 - 43.6)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM	4	26	0	100	6	81.3 (63 - 92.1)	100 (96.4 - 100)	100 (86.8 - 100)	94.3 (87.6 - 97.7)	24.2 (17.4 - 32.6)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM	5	5	0	100	1	83.3 (36.5 - 99.1)	100 (96.4 - 100)	100 (47.8 - 100)	99 (93.8 - 99.9)	5.7 (2.3 - 12.4)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM	6	4	0	100	3	57.1 (20.2 - 88.2)	100 (96.4 - 100)	100 (39.8 - 100)	97.1 (91.1 - 99.2)	6.5 (2.9 - 13.5)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM and/or IgG	0	172	0	100	42	80.4 (74.3 - 85.3)	100 (96.4 - 100)	100 (97.9 - 100)	70.4 (62.1 - 77.6)	68.2 (62.6 - 73.2)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Liu 2020 (Evaluation)	ELISA	ELISA		IgM and/or IgG	1	29	0	100	41	41.4 (30 - 53.8)	100 (96.4 - 100)	100 (88.1 - 100)	70.9 (62.6 - 78.1)	41.2 (33.8 - 49)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM and/or IgG	2	48	0	100	6	88.9 (76.7 - 95.4)	100 (96.4 - 100)	100 (92.6 - 100)	94.3 (87.6 - 97.7)	35.1 (27.7 - 43.2)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM and/or IgG	3	52	0	100	3	94.5 (83.9 - 98.6)	100 (96.4 - 100)	100 (93.2 - 100)	97.1 (91.1 - 99.2)	35.5 (28.1 - 43.6)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM and/or IgG	4	30	0	100	2	93.8 (77.8 - 98.9)	100 (96.4 - 100)	100 (88.4 - 100)	98 (92.4 - 99.7)	24.2 (17.4 - 32.6)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM and/or IgG	5	6	0	100	0	100 (54.1 - 100)	100 (96.4 - 100)	100 (54.1 - 100)	100 (96.4 - 100)	5.7 (2.3 - 12.4)
Liu 2020 (Evaluation)	ELISA	ELISA		IgM and/or IgG	6	7	0	100	0	100 (59 - 100)	100 (96.4 - 100)	100 (59 - 100)	100 (96.4 - 100)	6.5 (2.9 - 13.5)
Lou 2020	CMIA	CLIA		Ab	0	77	2	298	3	96.3 (88.7 - 99)	99.3 (97.3 - 99.9)	97.5 (90.3 - 99.6)	99 (96.9 - 99.7)	21.1 (17.1 - 25.6)
Lou 2020	CMIA	CLIA		IgM	0	69	2	298	11	86.3 (76.3 - 92.6)	99.3 (97.3 - 99.9)	97.2 (89.3 - 99.5)	96.4 (93.5 - 98.1)	21.1 (17.1 - 25.6)
Lou 2020	ELISA	ELISA		Ab	0	78	0	300	2	97.5 (90.4 - 99.6)	100 (98.8 - 100)	100 (95.4 - 100)	99.3 (97.4 - 99.9)	21.1 (17.1 - 25.6)
Lou 2020	ELISA	ELISA		Ab	1	25	0	300	14	64.1 (47.2 - 78.3)	100 (98.8 - 100)	100 (86.3 - 100)	95.5 (92.5 - 97.4)	11.5 (8.4 - 15.5)
Lou 2020	ELISA	ELISA		Ab	2	74	0	300	1	98.7 (91.8 - 99.9)	100 (98.8 - 100)	100 (95.1 - 100)	99.7 (97.9 - 100)	20 (16.1 - 24.5)
Lou 2020	ELISA	ELISA		Ab	3	60	0	300	0	100 (94 - 100)	100 (98.8 - 100)	100 (94 - 100)	100 (98.8 - 100)	16.7 (13 - 21)
Lou 2020	ELISA	ELISA		IgM	0	74	0	300	6	92.5 (83.8 - 96.9)	100 (98.8 - 100)	100 (95.1 - 100)	98 (95.6 - 99.2)	21.1 (17.1 - 25.6)
Lou 2020	ELISA	ELISA		IgM	1	13	0	300	26	33.3 (19.6 - 50.3)	100 (98.8 - 100)	100 (75.3 - 100)	92 (88.4 - 94.6)	11.5 (8.4 - 15.5)
Lou 2020	ELISA	ELISA		IgM	2	65	0	300	10	86.7 (76.4 - 93.1)	100 (98.8 - 100)	100 (94.5 - 100)	96.8 (94 - 98.4)	20 (16.1 - 24.5)
Lou 2020	ELISA	ELISA		IgM	3	58	0	300	2	96.7 (87.5 - 99.4)	100 (98.8 - 100)	100 (93.8 - 100)	99.3 (97.4 - 99.9)	16.7 (13 - 21)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Lou 2020	LFI	RDT		Ab	0	78	10	199	2	97.5 (90.4 - 99.6)	95.2 (91.1 - 97.6)	88.6 (79.7 - 94.1)	99 (96.1 - 99.8)	27.7 (22.7 - 33.3)
Lou 2020	LFI	RDT		IgM	0	71	4	205	9	88.8 (79.2 - 94.4)	98.1 (94.9 - 99.4)	94.7 (86.2 - 98.3)	95.8 (91.9 - 97.9)	27.7 (22.7 - 33.3)
Ma 2020	CLIA	CLIA		IgA	1	15	9	474	2	88.2 (62.3 - 97.9)	98.1 (96.4 - 99.1)	62.5 (40.8 - 80.4)	99.6 (98.3 - 99.9)	3.4 (2.1 - 5.5)
Ma 2020	CLIA	CLIA		IgA	2	30	9	474	0	100 (88.4 - 100)	98.1 (96.4 - 99.1)	76.9 (60.3 - 88.3)	100 (99.2 - 100)	5.8 (4 - 8.3)
Ma 2020	CLIA	CLIA		IgA	3	55	9	474	0	100 (93.5 - 100)	98.1 (96.4 - 99.1)	85.9 (74.5 - 93)	100 (99.2 - 100)	10.2 (7.9 - 13.2)
Ma 2020	CLIA	CLIA		IgA	4	55	9	474	1	98.2 (89.2 - 99.9)	98.1 (96.4 - 99.1)	85.9 (74.5 - 93)	99.8 (98.6 - 100)	10.4 (8 - 13.4)
Ma 2020	CLIA	CLIA		IgA	5	58	9	474	0	100 (93.8 - 100)	98.1 (96.4 - 99.1)	86.6 (75.5 - 93.3)	100 (99.2 - 100)	10.7 (8.3 - 13.7)
Ma 2020	CLIA	CLIA		IgG	1	11	1	482	6	64.7 (38.6 - 84.7)	99.8 (98.7 - 100)	91.7 (59.8 - 99.6)	98.8 (97.2 - 99.5)	3.4 (2.1 - 5.5)
Ma 2020	CLIA	CLIA		IgG	2	29	1	482	1	96.7 (80.9 - 99.8)	99.8 (98.7 - 100)	96.7 (80.9 - 99.8)	99.8 (98.7 - 100)	5.8 (4 - 8.3)
Ma 2020	CLIA	CLIA		IgG	3	55	1	482	0	100 (93.5 - 100)	99.8 (98.7 - 100)	98.2 (89.2 - 99.9)	100 (99.2 - 100)	10.2 (7.9 - 13.2)
Ma 2020	CLIA	CLIA		IgG	4	56	1	482	0	100 (93.6 - 100)	99.8 (98.7 - 100)	98.2 (89.4 - 99.9)	100 (99.2 - 100)	10.4 (8 - 13.4)
Ma 2020	CLIA	CLIA		IgG	5	58	1	482	0	100 (93.8 - 100)	99.8 (98.7 - 100)	98.3 (89.7 - 99.9)	100 (99.2 - 100)	10.7 (8.3 - 13.7)
Ma 2020	CLIA	CLIA		IgM	1	13	37	446	4	76.5 (49.8 - 92.2)	92.3 (89.5 - 94.5)	26 (15.1 - 40.6)	99.1 (97.6 - 99.7)	3.4 (2.1 - 5.5)
Ma 2020	CLIA	CLIA		IgM	2	30	37	446	0	100 (88.4 - 100)	92.3 (89.5 - 94.5)	44.8 (32.8 - 57.4)	100 (99.2 - 100)	5.8 (4 - 8.3)
Ma 2020	CLIA	CLIA		IgM	3	55	37	446	0	100 (93.5 - 100)	92.3 (89.5 - 94.5)	59.8 (49 - 69.7)	100 (99.2 - 100)	10.2 (7.9 - 13.2)
Ma 2020	CLIA	CLIA		IgM	4	56	37	446	0	100 (93.6 - 100)	92.3 (89.5 - 94.5)	60.2 (49.5 - 70.1)	100 (99.2 - 100)	10.4 (8 - 13.4)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Ma 2020	CLIA	CLIA		IgM	5	55	37	446	3	94.8 (84.7 - 98.7)	92.3 (89.5 - 94.5)	59.8 (49 - 69.7)	99.3 (97.9 - 99.8)	10.7 (8.3 - 13.7)
Paradiso 2020 (Clinical)	LFI	RDT	Viva-Diag	IgM and/or IgG	0	21	13	107	49	30 (19.9 - 42.3)	89.2 (81.9 - 93.9)	61.8 (43.6 - 77.3)	68.6 (60.6 - 75.6)	36.8 (30.1 - 44.2)
Qian 2020	CLIA	CLIA		IgG	0	486	17	947	25	95.1 (92.8 - 96.7)	98.2 (97.1 - 98.9)	96.6 (94.5 - 98)	97.4 (96.2 - 98.3)	34.6 (32.2 - 37.1)
Qian 2020	CLIA	CLIA		IgG	0	45	7	581	5	90 (77.4 - 96.3)	98.8 (97.5 - 99.5)	86.5 (73.6 - 94)	99.1 (97.9 - 99.7)	7.8 (5.9 - 10.3)
Qian 2020	CLIA	CLIA		IgM	0	432	71	946	26	94.3 (91.7 - 96.2)	93 (91.2 - 94.5)	85.9 (82.5 - 88.7)	97.3 (96 - 98.2)	31.1 (28.7 - 33.5)
Qian 2020	CLIA	CLIA		IgM	0	38	14	583	3	92.7 (79 - 98.1)	97.7 (96 - 98.7)	73.1 (58.7 - 84)	99.5 (98.4 - 99.9)	6.4 (4.7 - 8.7)
Shen 2020	GICA	RDT		IgM and/or IgG	0	69	2	51	28	71.1 (60.9 - 79.7)	96.2 (85.9 - 99.3)	97.2 (89.3 - 99.5)	64.6 (52.9 - 74.8)	64.7 (56.4 - 72.2)
Shen 2020	GICA	RDT		IgM and/or IgG	1	22	2	51	18	55 (38.7 - 70.4)	96.2 (85.9 - 99.3)	91.7 (71.5 - 98.5)	73.9 (61.7 - 83.4)	43 (32.9 - 53.7)
Shen 2020	GICA	RDT		IgM and/or IgG	2	24	2	51	9	72.7 (54.2 - 86.1)	96.2 (85.9 - 99.3)	92.3 (73.4 - 98.7)	85 (72.9 - 92.5)	38.4 (28.3 - 49.5)
Shen 2020	GICA	RDT		IgM and/or IgG	3	23	2	51	1	95.8 (76.9 - 99.8)	96.2 (85.9 - 99.3)	92 (72.5 - 98.6)	98.1 (88.4 - 99.9)	31.2 (21.4 - 42.9)
Spicuzza 2020	PoC	RDT		IgM and/or IgG	0	19	1	13	4	82.6 (60.5 - 94.3)	92.9 (64.2 - 99.6)	95 (73.1 - 99.7)	76.5 (49.8 - 92.2)	62.2 (44.8 - 77.1)
Wan 2020	CLIA	CLIA	A	IgG	0	43	4	126	7	86 (72.6 - 93.7)	96.9 (91.8 - 99)	91.5 (78.7 - 97.2)	94.7 (89.1 - 97.7)	27.8 (21.5 - 35)
Wan 2020	CLIA	CLIA	A	IgM	0	41	8	122	9	82 (68.1 - 91)	93.8 (87.8 - 97.1)	83.7 (69.8 - 92.2)	93.1 (87 - 96.6)	27.8 (21.5 - 35)
Whitman 2020	ELISA	ELISA	Epitope	IgG	1	11	8	44	16	40.7 (23 - 61)	84.6 (71.4 - 92.7)	57.9 (34 - 78.9)	73.3 (60.1 - 83.5)	34.2 (24.1 - 45.8)
Whitman 2020	ELISA	ELISA	Epitope	IgG	2	59	8	44	12	83.1 (71.9 - 90.6)	84.6 (71.4 - 92.7)	88.1 (77.3 - 94.3)	78.6 (65.2 - 88)	57.7 (48.5 - 66.5)
Whitman 2020	ELISA	ELISA	Epitope	IgG	3	16	8	44	5	76.2 (52.5 - 90.9)	84.6 (71.4 - 92.7)	66.7 (44.7 - 83.6)	89.8 (77 - 96.2)	28.8 (19.1 - 40.7)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Whitman 2020	ELISA	ELISA	Epitope	IgG	4	10	8	44	1	90.9 (57.1 - 99.5)	84.6 (71.4 - 92.7)	55.6 (31.3 - 77.6)	97.8 (86.8 - 99.9)	17.5 (9.4 - 29.5)
Whitman 2020	ELISA	ELISA	Epitope	IgM	1	5	2	50	22	18.5 (7 - 38.7)	96.2 (85.7 - 99.3)	71.4 (30.3 - 94.9)	69.4 (57.3 - 79.5)	34.2 (24.1 - 45.8)
Whitman 2020	ELISA	ELISA	Epitope	IgM	2	46	2	50	25	64.8 (52.5 - 75.5)	96.2 (85.7 - 99.3)	95.8 (84.6 - 99.3)	66.7 (54.7 - 76.9)	57.7 (48.5 - 66.5)
Whitman 2020	ELISA	ELISA	Epitope	IgM	3	14	2	50	7	66.7 (43.1 - 84.5)	96.2 (85.7 - 99.3)	87.5 (60.4 - 97.8)	87.7 (75.7 - 94.5)	28.8 (19.1 - 40.7)
Whitman 2020	ELISA	ELISA	Epitope	IgM	4	9	2	50	2	81.8 (47.8 - 96.8)	96.2 (85.7 - 99.3)	81.8 (47.8 - 96.8)	96.2 (85.7 - 99.3)	17.5 (9.4 - 29.5)
Whitman 2020	ELISA	ELISA	Epitope	IgM and/or IgG	1	11	9	43	16	40.7 (23 - 61)	82.7 (69.2 - 91.3)	55 (32 - 76.2)	72.9 (59.5 - 83.3)	34.2 (24.1 - 45.8)
Whitman 2020	ELISA	ELISA	In house	IgM and/or IgG	1	10	7	45	17	37 (20.1 - 57.5)	86.5 (73.6 - 94)	58.8 (33.5 - 80.6)	72.6 (59.6 - 82.8)	34.2 (24.1 - 45.8)
Whitman 2020	ELISA	ELISA	Epitope	IgM and/or IgG	2	60	9	43	11	84.5 (73.5 - 91.6)	82.7 (69.2 - 91.3)	87 (76.2 - 93.5)	79.6 (66.1 - 88.9)	57.7 (48.5 - 66.5)
Whitman 2020	ELISA	ELISA	In house	IgM and/or IgG	2	58	7	45	13	81.7 (70.4 - 89.5)	86.5 (73.6 - 94)	89.2 (78.5 - 95.2)	77.6 (64.4 - 87.1)	57.7 (48.5 - 66.5)
Whitman 2020	ELISA	ELISA	Epitope	IgM and/or IgG	3	17	9	43	4	81 (57.4 - 93.7)	82.7 (69.2 - 91.3)	65.4 (44.4 - 82.1)	91.5 (78.7 - 97.2)	28.8 (19.1 - 40.7)
Whitman 2020	ELISA	ELISA	In house	IgM and/or IgG	3	17	7	45	4	81 (57.4 - 93.7)	86.5 (73.6 - 94)	70.8 (48.8 - 86.6)	91.8 (79.5 - 97.4)	28.8 (19.1 - 40.7)
Whitman 2020	ELISA	ELISA	Epitope	IgM and/or IgG	4	10	9	43	1	90.9 (57.1 - 99.5)	82.7 (69.2 - 91.3)	52.6 (29.5 - 74.8)	97.7 (86.5 - 99.9)	17.5 (9.4 - 29.5)
Whitman 2020	ELISA	ELISA	In house	IgM and/or IgG	4	9	7	45	2	81.8 (47.8 - 96.8)	86.5 (73.6 - 94)	56.3 (30.6 - 79.2)	95.7 (84.3 - 99.3)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	BioMedomics	IgG	1	6	4	48	20	23.1 (9.8 - 44.1)	92.3 (80.6 - 97.5)	60 (27.4 - 86.3)	70.6 (58.1 - 80.7)	33.3 (23.3 - 45)
Whitman 2020	LFI	RDT	Bioperfectus	IgG	1	7	6	39	20	25.9 (11.9 - 46.6)	86.7 (72.5 - 94.5)	53.8 (26.1 - 79.6)	66.1 (52.5 - 77.6)	37.5 (26.6 - 49.7)
Whitman 2020	LFI	RDT	DecomBio	IgG	1	7	2	50	18	28 (12.9 - 49.6)	96.2 (85.7 - 99.3)	77.8 (40.2 - 96.1)	73.5 (61.2 - 83.2)	32.5 (22.5 - 44.2)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Whitman 2020	LFI	RDT	DeepBlue	IgG	1	6	7	45	21	22.2 (9.4 - 42.7)	86.5 (73.6 - 94)	46.2 (20.4 - 73.9)	68.2 (55.4 - 78.8)	34.2 (24.1 - 45.8)
Whitman 2020	LFI	RDT	Innovita	IgG	1	7	2	26	20	25.9 (11.9 - 46.6)	92.9 (75 - 98.8)	77.8 (40.2 - 96.1)	56.5 (41.2 - 70.8)	49.1 (35.5 - 62.8)
Whitman 2020	LFI	RDT	Premier	IgG	1	6	1	51	21	22.2 (9.4 - 42.7)	98.1 (88.4 - 99.9)	85.7 (42 - 99.2)	70.8 (58.8 - 80.7)	34.2 (24.1 - 45.8)
Whitman 2020	LFI	RDT	Sure	IgG	1	5	0	52	22	18.5 (7 - 38.7)	100 (93.2 - 100)	100 (47.8 - 100)	70.3 (58.4 - 80.1)	34.2 (24.1 - 45.8)
Whitman 2020	LFI	RDT	UCP	IgG	1	7	2	50	20	25.9 (11.9 - 46.6)	96.2 (85.7 - 99.3)	77.8 (40.2 - 96.1)	71.4 (59.2 - 81.3)	34.2 (24.1 - 45.8)
Whitman 2020	LFI	RDT	VivaChek	IgG	1	7	1	48	17	29.2 (13.4 - 51.2)	98 (87.8 - 99.9)	87.5 (46.7 - 99.3)	73.8 (61.2 - 83.6)	32.9 (22.6 - 45)
Whitman 2020	LFI	RDT	BioMedomics	IgG	2	42	4	48	28	60 (47.6 - 71.3)	92.3 (80.6 - 97.5)	91.3 (78.3 - 97.2)	63.2 (51.3 - 73.7)	57.4 (48.1 - 66.2)
Whitman 2020	LFI	RDT	Bioperfectus	IgG	2	50	6	39	20	71.4 (59.2 - 81.3)	86.7 (72.5 - 94.5)	89.3 (77.4 - 95.6)	66.1 (52.5 - 77.6)	60.9 (51.3 - 69.7)
Whitman 2020	LFI	RDT	DecomBio	IgG	2	53	2	50	17	75.7 (63.7 - 84.8)	96.2 (85.7 - 99.3)	96.4 (86.4 - 99.4)	74.6 (62.3 - 84.1)	57.4 (48.1 - 66.2)
Whitman 2020	LFI	RDT	DeepBlue	IgG	2	39	7	45	32	54.9 (42.7 - 66.6)	86.5 (73.6 - 94)	84.8 (70.5 - 93.2)	58.4 (46.6 - 69.4)	57.7 (48.5 - 66.5)
Whitman 2020	LFI	RDT	Innovita	IgG	2	42	2	26	27	60.9 (48.4 - 72.2)	92.9 (75 - 98.8)	95.5 (83.3 - 99.2)	49.1 (35.3 - 63)	71.1 (60.9 - 79.7)
Whitman 2020	LFI	RDT	Premier	IgG	2	40	1	51	30	57.1 (44.8 - 68.7)	98.1 (88.4 - 99.9)	97.6 (85.6 - 99.9)	63 (51.5 - 73.2)	57.4 (48.1 - 66.2)
Whitman 2020	LFI	RDT	Sure	IgG	2	44	0	52	26	62.9 (50.4 - 73.9)	100 (93.2 - 100)	100 (92 - 100)	66.7 (55 - 76.7)	57.4 (48.1 - 66.2)
Whitman 2020	LFI	RDT	UCP	IgG	2	43	2	50	28	60.6 (48.2 - 71.7)	96.2 (85.7 - 99.3)	95.6 (83.6 - 99.2)	64.1 (52.4 - 74.4)	57.7 (48.5 - 66.5)
Whitman 2020	LFI	RDT	VivaChek	IgG	2	47	1	48	19	71.2 (58.6 - 81.4)	98 (87.8 - 99.9)	97.9 (87.5 - 99.9)	71.6 (59.1 - 81.7)	57.4 (47.8 - 66.5)
Whitman 2020	LFI	RDT	BioMedomics	IgG	3	14	4	48	7	66.7 (43.1 - 84.5)	92.3 (80.6 - 97.5)	77.8 (51.9 - 92.6)	87.3 (74.9 - 94.3)	28.8 (19.1 - 40.7)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Whitman 2020	LFI	RDT	Bioperfectus	IgG	3	14	6	39	7	66.7 (43.1 - 84.5)	86.7 (72.5 - 94.5)	70 (45.7 - 87.2)	84.8 (70.5 - 93.2)	31.8 (21.2 - 44.6)
Whitman 2020	LFI	RDT	DecomBio	IgG	3	14	2	50	6	70 (45.7 - 87.2)	96.2 (85.7 - 99.3)	87.5 (60.4 - 97.8)	89.3 (77.4 - 95.6)	27.8 (18.2 - 39.8)
Whitman 2020	LFI	RDT	DeepBlue	IgG	3	15	7	45	6	71.4 (47.7 - 87.8)	86.5 (73.6 - 94)	68.2 (45.1 - 85.3)	88.2 (75.4 - 95.1)	28.8 (19.1 - 40.7)
Whitman 2020	LFI	RDT	Innovita	IgG	3	9	2	26	5	64.3 (35.6 - 86)	92.9 (75 - 98.8)	81.8 (47.8 - 96.8)	83.9 (65.5 - 93.9)	33.3 (20 - 49.6)
Whitman 2020	LFI	RDT	Premier	IgG	3	14	1	51	7	66.7 (43.1 - 84.5)	98.1 (88.4 - 99.9)	93.3 (66 - 99.7)	87.9 (76.1 - 94.6)	28.8 (19.1 - 40.7)
Whitman 2020	LFI	RDT	Sure	IgG	3	14	0	52	7	66.7 (43.1 - 84.5)	100 (93.2 - 100)	100 (76.8 - 100)	88.1 (76.5 - 94.7)	28.8 (19.1 - 40.7)
Whitman 2020	LFI	RDT	UCP	IgG	3	14	2	50	7	66.7 (43.1 - 84.5)	96.2 (85.7 - 99.3)	87.5 (60.4 - 97.8)	87.7 (75.7 - 94.5)	28.8 (19.1 - 40.7)
Whitman 2020	LFI	RDT	VivaChek	IgG	3	14	1	48	7	66.7 (43.1 - 84.5)	98 (87.8 - 99.9)	93.3 (66 - 99.7)	87.3 (74.9 - 94.3)	30 (19.9 - 42.3)
Whitman 2020	LFI	RDT	BioMedomics	IgG	4	9	4	48	2	81.8 (47.8 - 96.8)	92.3 (80.6 - 97.5)	69.2 (38.9 - 89.6)	96 (85.1 - 99.3)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	Bioperfectus	IgG	4	9	6	39	1	90 (54.1 - 99.5)	86.7 (72.5 - 94.5)	60 (32.9 - 82.5)	97.5 (85.3 - 99.9)	18.2 (9.5 - 31.4)
Whitman 2020	LFI	RDT	DecomBio	IgG	4	10	2	50	1	90.9 (57.1 - 99.5)	96.2 (85.7 - 99.3)	83.3 (50.9 - 97.1)	98 (88.2 - 99.9)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	DeepBlue	IgG	4	9	7	45	2	81.8 (47.8 - 96.8)	86.5 (73.6 - 94)	56.3 (30.6 - 79.2)	95.7 (84.3 - 99.3)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	Innovita	IgG	4	4	2	26	2	66.7 (24.1 - 94)	92.9 (75 - 98.8)	66.7 (24.1 - 94)	92.9 (75 - 98.8)	17.6 (7.4 - 35.2)
Whitman 2020	LFI	RDT	Premier	IgG	4	9	1	51	2	81.8 (47.8 - 96.8)	98.1 (88.4 - 99.9)	90 (54.1 - 99.5)	96.2 (85.9 - 99.3)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	Sure	IgG	4	10	0	52	1	90.9 (57.1 - 99.5)	100 (93.2 - 100)	100 (69.2 - 100)	98.1 (88.6 - 99.9)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	UCP	IgG	4	9	2	50	2	81.8 (47.8 - 96.8)	96.2 (85.7 - 99.3)	81.8 (47.8 - 96.8)	96.2 (85.7 - 99.3)	17.5 (9.4 - 29.5)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Whitman 2020	LFI	RDT	VivaChek	IgG	4	9	1	48	1	90 (54.1 - 99.5)	98 (87.8 - 99.9)	90 (54.1 - 99.5)	98 (87.8 - 99.9)	16.9 (8.9 - 29.4)
Whitman 2020	LFI	RDT	BioMedomics	IgM	1	7	8	44	19	26.9 (12.4 - 48.1)	84.6 (71.4 - 92.7)	46.7 (22.3 - 72.6)	69.8 (56.8 - 80.4)	33.3 (23.3 - 45)
Whitman 2020	LFI	RDT	Bioperfectus	IgM	1	11	5	40	16	40.7 (23 - 61)	88.9 (75.2 - 95.8)	68.8 (41.5 - 87.9)	71.4 (57.6 - 82.3)	37.5 (26.6 - 49.7)
Whitman 2020	LFI	RDT	DecomBio	IgM	1	8	5	47	17	32 (15.7 - 53.6)	90.4 (78.2 - 96.4)	61.5 (32.3 - 84.9)	73.4 (60.7 - 83.3)	32.5 (22.5 - 44.2)
Whitman 2020	LFI	RDT	DeepBlue	IgM	1	12	14	38	15	44.4 (26 - 64.4)	73.1 (58.7 - 84)	46.2 (27.1 - 66.3)	71.7 (57.4 - 82.8)	34.2 (24.1 - 45.8)
Whitman 2020	LFI	RDT	Innovita	IgM	1	4	2	26	23	14.8 (4.9 - 34.6)	92.9 (75 - 98.8)	66.7 (24.1 - 94)	53.1 (38.4 - 67.2)	49.1 (35.5 - 62.8)
Whitman 2020	LFI	RDT	Premier	IgM	1	10	1	51	17	37 (20.1 - 57.5)	98.1 (88.4 - 99.9)	90.9 (57.1 - 99.5)	75 (62.8 - 84.4)	34.2 (24.1 - 45.8)
Whitman 2020	LFI	RDT	Sure	IgM	1	3	0	52	24	11.1 (2.9 - 30.3)	100 (93.2 - 100)	100 (29.2 - 100)	68.4 (56.6 - 78.3)	34.2 (24.1 - 45.8)
Whitman 2020	LFI	RDT	UCP	IgM	1	7	3	49	20	25.9 (11.9 - 46.6)	94.2 (83.1 - 98.5)	70 (35.4 - 91.9)	71 (58.7 - 81)	34.2 (24.1 - 45.8)
Whitman 2020	LFI	RDT	VivaChek	IgM	1	7	4	45	17	29.2 (13.4 - 51.2)	91.8 (79.5 - 97.4)	63.6 (31.6 - 87.6)	72.6 (59.6 - 82.8)	32.9 (22.6 - 45)
Whitman 2020	LFI	RDT	BioMedomics	IgM	2	47	8	44	23	67.1 (54.8 - 77.6)	84.6 (71.4 - 92.7)	85.5 (72.8 - 93.1)	65.7 (53 - 76.6)	57.4 (48.1 - 66.2)
Whitman 2020	LFI	RDT	Bioperfectus	IgM	2	54	5	40	16	77.1 (65.3 - 86)	88.9 (75.2 - 95.8)	91.5 (80.6 - 96.8)	71.4 (57.6 - 82.3)	60.9 (51.3 - 69.7)
Whitman 2020	LFI	RDT	DecomBio	IgM	2	53	5	47	27	66.3 (54.7 - 76.2)	90.4 (78.2 - 96.4)	91.4 (80.3 - 96.8)	63.5 (51.5 - 74.2)	60.6 (51.7 - 68.9)
Whitman 2020	LFI	RDT	DeepBlue	IgM	2	56	14	38	15	78.9 (67.3 - 87.3)	73.1 (58.7 - 84)	80 (68.4 - 88.3)	71.7 (57.4 - 82.8)	57.7 (48.5 - 66.5)
Whitman 2020	LFI	RDT	Innovita	IgM	2	24	2	26	44	35.3 (24.4 - 47.9)	92.9 (75 - 98.8)	92.3 (73.4 - 98.7)	37.1 (26.1 - 49.6)	70.8 (60.5 - 79.4)
Whitman 2020	LFI	RDT	Premier	IgM	2	53	1	51	17	75.7 (63.7 - 84.8)	98.1 (88.4 - 99.9)	98.1 (88.8 - 99.9)	75 (62.8 - 84.4)	57.4 (48.1 - 66.2)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Whitman 2020	LFI	RDT	Sure	IgM	2	37	0	52	43	46.3 (35.2 - 57.7)	100 (93.2 - 100)	100 (90.5 - 100)	54.7 (44.2 - 64.9)	60.6 (51.7 - 68.9)
Whitman 2020	LFI	RDT	UCP	IgM	2	47	3	49	24	66.2 (53.9 - 76.7)	94.2 (83.1 - 98.5)	94 (82.5 - 98.4)	67.1 (55 - 77.4)	57.7 (48.5 - 66.5)
Whitman 2020	LFI	RDT	VivaChek	IgM	2	48	4	45	18	72.7 (60.2 - 82.6)	91.8 (79.5 - 97.4)	92.3 (80.6 - 97.5)	71.4 (58.5 - 81.8)	57.4 (47.8 - 66.5)
Whitman 2020	LFI	RDT	BioMedomics	IgM	3	16	8	44	5	76.2 (52.5 - 90.9)	84.6 (71.4 - 92.7)	66.7 (44.7 - 83.6)	89.8 (77 - 96.2)	28.8 (19.1 - 40.7)
Whitman 2020	LFI	RDT	Bioperfectus	IgM	3	16	5	40	5	76.2 (52.5 - 90.9)	88.9 (75.2 - 95.8)	76.2 (52.5 - 90.9)	88.9 (75.2 - 95.8)	31.8 (21.2 - 44.6)
Whitman 2020	LFI	RDT	DecomBio	IgM	3	14	5	47	6	70 (45.7 - 87.2)	90.4 (78.2 - 96.4)	73.7 (48.6 - 89.9)	88.7 (76.3 - 95.3)	27.8 (18.2 - 39.8)
Whitman 2020	LFI	RDT	DeepBlue	IgM	3	16	14	38	5	76.2 (52.5 - 90.9)	73.1 (58.7 - 84)	53.3 (34.6 - 71.2)	88.4 (74.1 - 95.6)	28.8 (19.1 - 40.7)
Whitman 2020	LFI	RDT	Innovita	IgM	3	4	2	26	10	28.6 (9.6 - 58)	92.9 (75 - 98.8)	66.7 (24.1 - 94)	72.2 (54.6 - 85.2)	33.3 (20 - 49.6)
Whitman 2020	LFI	RDT	Premier	IgM	3	16	1	51	5	76.2 (52.5 - 90.9)	98.1 (88.4 - 99.9)	94.1 (69.2 - 99.7)	91.1 (79.6 - 96.7)	28.8 (19.1 - 40.7)
Whitman 2020	LFI	RDT	Sure	IgM	3	14	0	52	7	66.7 (43.1 - 84.5)	100 (93.2 - 100)	100 (76.8 - 100)	88.1 (76.5 - 94.7)	28.8 (19.1 - 40.7)
Whitman 2020	LFI	RDT	UCP	IgM	3	15	3	49	6	71.4 (47.7 - 87.8)	94.2 (83.1 - 98.5)	83.3 (57.7 - 95.6)	89.1 (77.1 - 95.5)	28.8 (19.1 - 40.7)
Whitman 2020	LFI	RDT	VivaChek	IgM	3	15	4	45	6	71.4 (47.7 - 87.8)	91.8 (79.5 - 97.4)	78.9 (53.9 - 93)	88.2 (75.4 - 95.1)	30 (19.9 - 42.3)
Whitman 2020	LFI	RDT	BioMedomics	IgM	4	9	8	44	2	81.8 (47.8 - 96.8)	84.6 (71.4 - 92.7)	52.9 (28.5 - 76.1)	95.7 (84 - 99.2)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	Bioperfectus	IgM	4	10	5	40	0	100 (69.2 - 100)	88.9 (75.2 - 95.8)	66.7 (38.7 - 87)	100 (91.2 - 100)	18.2 (9.5 - 31.4)
Whitman 2020	LFI	RDT	DecomBio	IgM	4	10	5	47	1	90.9 (57.1 - 99.5)	90.4 (78.2 - 96.4)	66.7 (38.7 - 87)	97.9 (87.5 - 99.9)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	DeepBlue	IgM	4	10	14	38	1	90.9 (57.1 - 99.5)	73.1 (58.7 - 84)	41.7 (22.8 - 63.1)	97.4 (84.9 - 99.9)	17.5 (9.4 - 29.5)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Whitman 2020	LFI	RDT	Innovita	IgM	4	1	2	26	5	16.7 (0.9 - 63.5)	92.9 (75 - 98.8)	33.3 (1.8 - 87.5)	83.9 (65.5 - 93.9)	17.6 (7.4 - 35.2)
Whitman 2020	LFI	RDT	Premier	IgM	4	10	1	51	1	90.9 (57.1 - 99.5)	98.1 (88.4 - 99.9)	90.9 (57.1 - 99.5)	98.1 (88.4 - 99.9)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	Sure	IgM	4	8	0	52	3	72.7 (39.3 - 92.7)	100 (93.2 - 100)	100 (63.1 - 100)	94.5 (83.9 - 98.6)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	UCP	IgM	4	10	3	49	1	90.9 (57.1 - 99.5)	94.2 (83.1 - 98.5)	76.9 (46 - 93.8)	98 (88 - 99.9)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	VivaChek	IgM	4	9	4	45	1	90 (54.1 - 99.5)	91.8 (79.5 - 97.4)	69.2 (38.9 - 89.6)	97.8 (87 - 99.9)	16.9 (8.9 - 29.4)
Whitman 2020	LFI	RDT	BioMedomics	IgM and/or IgG	1	8	11	41	18	30.8 (15.1 - 51.9)	78.8 (64.9 - 88.5)	42.1 (21.1 - 66)	69.5 (56 - 80.5)	33.3 (23.3 - 45)
Whitman 2020	LFI	RDT	Bioperfectus	IgM and/or IgG	1	11	8	37	16	40.7 (23 - 61)	82.2 (67.4 - 91.5)	57.9 (34 - 78.9)	69.8 (55.5 - 81.3)	37.5 (26.6 - 49.7)
Whitman 2020	LFI	RDT	DecomBio	IgM and/or IgG	1	8	6	46	17	32 (15.7 - 53.6)	88.5 (75.9 - 95.2)	57.1 (29.6 - 81.2)	73 (60.1 - 83.1)	32.5 (22.5 - 44.2)
Whitman 2020	LFI	RDT	DeepBlue	IgM and/or IgG	1	12	14	38	15	44.4 (26 - 64.4)	73.1 (58.7 - 84)	46.2 (27.1 - 66.3)	71.7 (57.4 - 82.8)	34.2 (24.1 - 45.8)
Whitman 2020	LFI	RDT	Innovita	IgM and/or IgG	1	7	3	25	20	25.9 (11.9 - 46.6)	89.3 (70.6 - 97.2)	70 (35.4 - 91.9)	55.6 (40.1 - 70)	49.1 (35.5 - 62.8)
Whitman 2020	LFI	RDT	Premier	IgM and/or IgG	1	10	2	50	17	37 (20.1 - 57.5)	96.2 (85.7 - 99.3)	83.3 (50.9 - 97.1)	74.6 (62.3 - 84.1)	34.2 (24.1 - 45.8)
Whitman 2020	LFI	RDT	Sure	IgM and/or IgG	1	5	0	52	22	18.5 (7 - 38.7)	100 (93.2 - 100)	100 (47.8 - 100)	70.3 (58.4 - 80.1)	34.2 (24.1 - 45.8)
Whitman 2020	LFI	RDT	UCP	IgM and/or IgG	1	7	3	49	20	25.9 (11.9 - 46.6)	94.2 (83.1 - 98.5)	70 (35.4 - 91.9)	71 (58.7 - 81)	34.2 (24.1 - 45.8)
Whitman 2020	LFI	RDT	VivaChek	IgM and/or IgG	1	7	4	45	17	29.2 (13.4 - 51.2)	91.8 (79.5 - 97.4)	63.6 (31.6 - 87.6)	72.6 (59.6 - 82.8)	32.9 (22.6 - 45)
Whitman 2020	LFI	RDT	Wondfo	IgM and/or IgG	1	10	0	41	15	40 (21.8 - 61.1)	100 (91.4 - 100)	100 (69.2 - 100)	73.2 (59.5 - 83.8)	37.9 (26.5 - 50.7)
Whitman 2020	LFI	RDT	BioMedomics	IgM and/or IgG	2	49	11	41	21	70 (57.7 - 80.1)	78.8 (64.9 - 88.5)	81.7 (69.1 - 90.1)	66.1 (52.9 - 77.4)	57.4 (48.1 - 66.2)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Whitman 2020	LFI	RDT	Bioperfectus	IgM and/or IgG	2	57	8	37	13	81.4 (70 - 89.4)	82.2 (67.4 - 91.5)	87.7 (76.6 - 94.2)	74 (59.4 - 84.9)	60.9 (51.3 - 69.7)
Whitman 2020	LFI	RDT	DecomBio	IgM and/or IgG	2	53	6	46	17	75.7 (63.7 - 84.8)	88.5 (75.9 - 95.2)	89.8 (78.5 - 95.8)	73 (60.1 - 83.1)	57.4 (48.1 - 66.2)
Whitman 2020	LFI	RDT	DeepBlue	IgM and/or IgG	2	56	14	38	15	78.9 (67.3 - 87.3)	73.1 (58.7 - 84)	80 (68.4 - 88.3)	71.7 (57.4 - 82.8)	57.7 (48.5 - 66.5)
Whitman 2020	LFI	RDT	Innovita	IgM and/or IgG	2	45	3	25	24	65.2 (52.7 - 76)	89.3 (70.6 - 97.2)	93.8 (81.8 - 98.4)	51 (36.5 - 65.4)	71.1 (60.9 - 79.7)
Whitman 2020	LFI	RDT	Premier	IgM and/or IgG	2	54	2	50	16	77.1 (65.3 - 86)	96.2 (85.7 - 99.3)	96.4 (86.6 - 99.4)	75.8 (63.4 - 85.1)	57.4 (48.1 - 66.2)
Whitman 2020	LFI	RDT	Sure	IgM and/or IgG	2	44	0	52	26	62.9 (50.4 - 73.9)	100 (93.2 - 100)	100 (92 - 100)	66.7 (55 - 76.7)	57.4 (48.1 - 66.2)
Whitman 2020	LFI	RDT	UCP	IgM and/or IgG	2	48	3	49	23	67.6 (55.3 - 78)	94.2 (83.1 - 98.5)	94.1 (82.8 - 98.5)	68.1 (55.9 - 78.3)	57.7 (48.5 - 66.5)
Whitman 2020	LFI	RDT	VivaChek	IgM and/or IgG	2	48	4	45	18	72.7 (60.2 - 82.6)	91.8 (79.5 - 97.4)	92.3 (80.6 - 97.5)	71.4 (58.5 - 81.8)	57.4 (47.8 - 66.5)
Whitman 2020	LFI	RDT	Wondfo	IgM and/or IgG	2	51	0	41	18	73.9 (61.7 - 83.4)	100 (91.4 - 100)	100 (93 - 100)	69.5 (56 - 80.5)	62.7 (52.9 - 71.6)
Whitman 2020	LFI	RDT	BioMedomics	IgM and/or IgG	3	17	11	41	4	81 (57.4 - 93.7)	78.8 (64.9 - 88.5)	60.7 (40.7 - 77.9)	91.1 (77.9 - 97.1)	28.8 (19.1 - 40.7)
Whitman 2020	LFI	RDT	Bioperfectus	IgM and/or IgG	3	17	8	37	4	81 (57.4 - 93.7)	82.2 (67.4 - 91.5)	68 (46.4 - 84.3)	90.2 (75.9 - 96.8)	31.8 (21.2 - 44.6)
Whitman 2020	LFI	RDT	DecomBio	IgM and/or IgG	3	14	6	46	6	70 (45.7 - 87.2)	88.5 (75.9 - 95.2)	70 (45.7 - 87.2)	88.5 (75.9 - 95.2)	27.8 (18.2 - 39.8)
Whitman 2020	LFI	RDT	DeepBlue	IgM and/or IgG	3	17	14	38	5	77.3 (54.2 - 91.3)	73.1 (58.7 - 84)	54.8 (36.3 - 72.2)	88.4 (74.1 - 95.6)	29.7 (19.9 - 41.6)
Whitman 2020	LFI	RDT	Innovita	IgM and/or IgG	3	9	3	25	5	64.3 (35.6 - 86)	89.3 (70.6 - 97.2)	75 (42.8 - 93.3)	83.3 (64.5 - 93.7)	33.3 (20 - 49.6)
Whitman 2020	LFI	RDT	Premier	IgM and/or IgG	3	17	2	50	4	81 (57.4 - 93.7)	96.2 (85.7 - 99.3)	89.5 (65.5 - 98.2)	92.6 (81.3 - 97.6)	28.8 (19.1 - 40.7)
Whitman 2020	LFI	RDT	Sure	IgM and/or IgG	3	15	0	52	6	71.4 (47.7 - 87.8)	100 (93.2 - 100)	100 (78.2 - 100)	89.7 (78.2 - 95.7)	28.8 (19.1 - 40.7)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Whitman 2020	LFI	RDT	UCP	IgM and/or IgG	3	15	3	49	6	71.4 (47.7 - 87.8)	94.2 (83.1 - 98.5)	83.3 (57.7 - 95.6)	89.1 (77.1 - 95.5)	28.8 (19.1 - 40.7)
Whitman 2020	LFI	RDT	VivaChek	IgM and/or IgG	3	15	4	45	6	71.4 (47.7 - 87.8)	91.8 (79.5 - 97.4)	78.9 (53.9 - 93)	88.2 (75.4 - 95.1)	30 (19.9 - 42.3)
Whitman 2020	LFI	RDT	Wondfo	IgM and/or IgG	3	17	0	41	4	81 (57.4 - 93.7)	100 (91.4 - 100)	100 (80.5 - 100)	91.1 (77.9 - 97.1)	33.9 (22.6 - 47.1)
Whitman 2020	LFI	RDT	BioMedomics	IgM and/or IgG	4	9	11	41	2	81.8 (47.8 - 96.8)	78.8 (64.9 - 88.5)	45 (23.8 - 68)	95.3 (82.9 - 99.2)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	Bioperfectus	IgM and/or IgG	4	10	8	37	0	100 (69.2 - 100)	82.2 (67.4 - 91.5)	55.6 (31.3 - 77.6)	100 (90.5 - 100)	18.2 (9.5 - 31.4)
Whitman 2020	LFI	RDT	DecomBio	IgM and/or IgG	4	10	6	46	1	90.9 (57.1 - 99.5)	88.5 (75.9 - 95.2)	62.5 (35.9 - 83.7)	97.9 (87.3 - 99.9)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	DeepBlue	IgM and/or IgG	4	10	14	38	1	90.9 (57.1 - 99.5)	73.1 (58.7 - 84)	41.7 (22.8 - 63.1)	97.4 (84.9 - 99.9)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	Innovita	IgM and/or IgG	4	5	3	25	1	83.3 (36.5 - 99.1)	89.3 (70.6 - 97.2)	62.5 (25.9 - 89.8)	96.2 (78.4 - 99.8)	17.6 (7.4 - 35.2)
Whitman 2020	LFI	RDT	Premier	IgM and/or IgG	4	10	2	50	1	90.9 (57.1 - 99.5)	96.2 (85.7 - 99.3)	83.3 (50.9 - 97.1)	98 (88.2 - 99.9)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	Sure	IgM and/or IgG	4	10	0	52	1	90.9 (57.1 - 99.5)	100 (93.2 - 100)	100 (69.2 - 100)	98.1 (88.6 - 99.9)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	UCP	IgM and/or IgG	4	10	3	49	1	90.9 (57.1 - 99.5)	94.2 (83.1 - 98.5)	76.9 (46 - 93.8)	98 (88 - 99.9)	17.5 (9.4 - 29.5)
Whitman 2020	LFI	RDT	VivaChek	IgM and/or IgG	4	9	4	45	1	90 (54.1 - 99.5)	91.8 (79.5 - 97.4)	69.2 (38.9 - 89.6)	97.8 (87 - 99.9)	16.9 (8.9 - 29.4)
Whitman 2020	LFI	RDT	Wondfo	IgM and/or IgG	4	9	0	41	2	81.8 (47.8 - 96.8)	100 (91.4 - 100)	100 (66.4 - 100)	95.3 (82.9 - 99.2)	21.2 (11.5 - 35.1)
Xiang 2020 (Antibody)	ELISA	ELISA		IgG	3	55	3	57	11	83.3 (71.7 - 91)	95 (85.2 - 98.7)	94.8 (84.7 - 98.7)	83.8 (72.5 - 91.3)	52.4 (43.3 - 61.3)
Xiang 2020 (Antibody)	ELISA	ELISA		IgM	3	51	0	60	15	77.3 (65 - 86.3)	100 (94 - 100)	100 (93 - 100)	80 (68.9 - 88)	52.4 (43.3 - 61.3)
Zhang 2020 (Evaluation)	GICA	RDT		IgM and/or IgG	0	127	4	656	27	82.5 (75.3 - 87.9)	99.4 (98.3 - 99.8)	96.9 (91.9 - 99)	96 (94.2 - 97.3)	18.9 (16.3 - 21.8)

Study reference	Test	Type of test	Test specifics	Target	Period	TP	FP	TN	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence
Zhong 2020	CLIA	CLIA		IgG	0	45	10	290	2	95.7 (84.3 - 99.3)	96.7 (93.8 - 98.3)	81.8 (68.6 - 90.5)	99.3 (97.3 - 99.9)	13.5 (10.2 - 17.7)
Zhong 2020	CLIA	CLIA		IgM	0	46	14	286	1	97.9 (87.3 - 99.9)	95.3 (92.1 - 97.3)	76.7 (63.7 - 86.2)	99.7 (97.8 - 100)	13.5 (10.2 - 17.7)
Zhong 2020	ELISA	ELISA		IgG	0	46	1	299	1	97.9 (87.3 - 99.9)	99.7 (97.9 - 100)	97.9 (87.3 - 99.9)	99.7 (97.9 - 100)	13.5 (10.2 - 17.7)
Zhong 2020	ELISA	ELISA		IgM	0	46	1	299	1	97.9 (87.3 - 99.9)	99.7 (97.9 - 100)	97.9 (87.3 - 99.9)	99.7 (97.9 - 100)	13.5 (10.2 - 17.7)

Abbreviations: **CLIA: Chemiluminescence immunoassay; CMIA: Chemiluminescence microparticle immunoassay**; ELISA: Enzyme-linked immunosorbent assay; FN: false negatives; FP: false positives; **; GICA: Gold immunochromatography assay; IC: immunochromatography; IgG: Immunoglobulin G; IgM: Immunoglobulin M; LFIA: Lateral flow immunoassay; LFA: Lateral flow assay; PoC: Point of care**; TN: true negatives; TP: true positives

Table A 5: Diagnostic accuracy

Type of test: Rapid Diagnostic Test (RDT)

Target: IgM

Period: overall

Study_ID	Author	Testclass	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#307	Li	LFI	328	10	118	69	82.6	78.4	86.1	92.2	85.7	96
#470	Lou	LFI	71	4	205	9	88.8	79.2	94.4	98.1	94.9	99.4
#473	Liu	GICA	34	5	84	56	37.8	28	48.7	94.4	86.8	97.9
#545	Garcia	IC	12	25	38	43	21.8	12.2	35.4	60.3	47.2	72.2
					Pooled estimate		61.5	14.7	93.7	91.8	57.8	98.9
					Heterogeneity τ^2		1.89			1.59		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgM

Period: Week 1

Study_ID	Author	Testclass	Test	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#386	Whitman	LFI	BioMedomics	7	8	44	19	26.9	12.4	48.1	84.6	71.4	92.7
#386	Whitman	LFI	Bioperfectus	11	5	40	16	40.7	23	61	88.9	75.2	95.8
#386	Whitman	LFI	DecomBio	8	5	47	17	32	15.7	53.6	90.4	78.2	96.4
#386	Whitman	LFI	DeepBlue	12	14	38	15	44.4	26	64.4	73.1	58.7	84
#386	Whitman	LFI	Innovita	4	2	26	23	14.8	4.9	34.6	92.9	75	98.8
#386	Whitman	LFI	Premier	10	1	51	17	37	20.1	57.5	98.1	88.4	99.9
#386	Whitman	LFI	Sure	3	0	52	24	11.1	2.9	30.3	100	93.2	100
#386	Whitman	LFI	UCP	7	3	49	20	25.9	11.9	46.6	94.2	83.1	98.5
#386	Whitman	LFI	VivaChek	7	4	45	17	29.2	13.4	51.2	91.8	79.5	97.4
#473	Liu	GICA		3	1	8	13	18.8	5	46.3	88.9	50.7	99.4
						Pooled estimate		28	20.8	36.5	92.1	85	96
						Heterogeneity τ^2		0.09			0.57		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgM

Period: Week 2

Study_ID	Author	Test-class	Test	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#386	Whitman	LFI	BioMedomics	47	8	44	23	67.1	54.8	77.6	84.6	71.4	92.7
#386	Whitman	LFI	Bioperfectus	54	5	40	16	77.1	65.3	86	88.9	75.2	95.8
#386	Whitman	LFI	DecomBio	53	5	47	27	66.3	54.7	76.2	90.4	78.2	96.4
#386	Whitman	LFI	DeepBlue	56	14	38	15	78.9	67.3	87.3	73.1	58.7	84
#386	Whitman	LFI	Innovita	24	2	26	44	35.3	24.4	47.9	92.9	75	98.8
#386	Whitman	LFI	Premier	53	1	51	17	75.7	63.7	84.8	98.1	88.4	99.9
#386	Whitman	LFI	Sure	37	0	52	43	46.3	35.2	57.7	100	93.2	100
#386	Whitman	LFI	UCP	47	3	49	24	66.2	53.9	76.7	94.2	83.1	98.5
#386	Whitman	LFI	VivaChek	48	4	45	18	72.7	60.2	82.6	91.8	79.5	97.4
#473	Liu	GICA		6	1	1	0	100	54.1	100	50	2.7	97.3
#545	Garcia	IC		3	7	11	21	12.5	3.3	33.5	61.1	36.1	81.7
						Pooled estimate		63.6	47.9	76.8	90.4	81	95.4
						Heterogeneity τ^2		0.77			0.94		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgM

Period: Week 3

Study_ID	Author	Test-class	Test	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#386	Whitman	LFI	BioMedomics	16	8	44	5	76.2	52.5	90.9	84.6	71.4	92.7
#386	Whitman	LFI	Bioperfectus	16	5	40	5	76.2	52.5	90.9	88.9	75.2	95.8
#386	Whitman	LFI	DecomBio	14	5	47	6	70	45.7	87.2	90.4	78.2	96.4
#386	Whitman	LFI	DeepBlue	16	14	38	5	76.2	52.5	90.9	73.1	58.7	84
#386	Whitman	LFI	Innovita	4	2	26	10	28.6	9.6	58	92.9	75	98.8
#386	Whitman	LFI	Premier	16	1	51	5	76.2	52.5	90.9	98.1	88.4	99.9
#386	Whitman	LFI	Sure	14	0	52	7	66.7	43.1	84.5	100	93.2	100
#386	Whitman	LFI	UCP	15	3	49	6	71.4	47.7	87.8	94.2	83.1	98.5
#386	Whitman	LFI	VivaChek	15	4	45	6	71.4	47.7	87.8	91.8	79.5	97.4
#473	Liu	GICA		25	4	10	43	36.8	25.6	49.4	71.4	42	90.4
#545	Garcia	IC		9	18	27	14	39.1	20.5	61.2	60	44.4	73.9
						Pooled estimate		63.2	50.3	74.5	89.9	80	95.2
						Heterogeneity τ^2		0.40			1.04		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgM

Period: Week 4

Study_ID	Author	Test-class	Test	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#386	Whitman	LFI	BioMedomics	9	8	44	2	81.8	47.8	96.8	84.6	71.4	92.7
#386	Whitman	LFI	Bioperfectus	10	5	40	0	100	69.2	100	88.9	75.2	95.8
#386	Whitman	LFI	DecomBio	10	5	47	1	90.9	57.1	99.5	90.4	78.2	96.4
#386	Whitman	LFI	DeepBlue	10	14	38	1	90.9	57.1	99.5	73.1	58.7	84
#386	Whitman	LFI	Innovita	1	2	26	5	16.7	0.9	63.5	92.9	75	98.8
#386	Whitman	LFI	Premier	10	1	51	1	90.9	57.1	99.5	98.1	88.4	99.9
#386	Whitman	LFI	Sure	8	0	52	3	72.7	39.3	92.7	100	93.2	100
#386	Whitman	LFI	UCP	10	3	49	1	90.9	57.1	99.5	94.2	83.1	98.5
#386	Whitman	LFI	VivaChek	9	4	45	1	90	54.1	99.5	91.8	79.5	97.4
						Pooled estimate		86	66.4	95.1	92.3	84.5	96.3
						Heterogeneity τ^2		1.14			0.63		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgG

Period: overall

Study_ID	Author	Testclass	TP	FP	TN	FN	se	se_ll	se_ul	sp	sp_ll	sp_ul
#307	Li	LFI	280	1	127	117	70.5	65.7	74.9	99.2	95.1	100
#473	Liu	GICA	75	7	82	15	83.3	73.7	90.1	92.1	83.9	96.5
#545	Garcia	IC	23	56	7	32	41.8	28.9	55.9	11.1	5	22.2
					Pooled estimate		67.4	22.9	93.5	85.6	0.3	100
					Heterogeneity τ^2		0.56			8.76		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgG

Period: Week 1

Study_ID	Author	Testclass	Test	TP	FP	TN	FN	se	se_ll	se_ul	sp	sp_ll	sp_ul
#386	Whitman	LFI	BioMedomics	6	4	48	20	23.1	9.8	44.1	92.3	80.6	97.5
#386	Whitman	LFI	Bioperfectus	7	6	39	20	25.9	11.9	46.6	86.7	72.5	94.5
#386	Whitman	LFI	DecomBio	7	2	50	18	28	12.9	49.6	96.2	85.7	99.3
#386	Whitman	LFI	DeepBlue	6	7	45	21	22.2	9.4	42.7	86.5	73.6	94
#386	Whitman	LFI	Innovita	7	2	26	20	25.9	11.9	46.6	92.9	75	98.8
#386	Whitman	LFI	Premier	6	1	51	21	22.2	9.4	42.7	98.1	88.4	99.9
#386	Whitman	LFI	Sure	5	0	52	22	18.5	7	38.7	100	93.2	100
#386	Whitman	LFI	UCP	7	2	50	20	25.9	11.9	46.6	96.2	85.7	99.3
#386	Whitman	LFI	VivaChek	7	1	48	17	29.2	13.4	51.2	98	87.8	99.9
#473	Liu	GICA		2	2	7	14	12.5	2.2	39.6	77.8	40.2	96.1
						Pooled estimate		26.9	21.5	33.1	94.5	89.5	97.2
						Heterogeneity τ^2		0			0.42		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgG

Period: Week 2

Study_ID	Author	Test-class	Test	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#386	Whitman	LFI	BioMedomics	42	4	48	28	60	47.6	71.3	92.3	80.6	97.5
#386	Whitman	LFI	Bioperfectus	50	6	39	20	71.4	59.2	81.3	86.7	72.5	94.5
#386	Whitman	LFI	DecomBio	53	2	50	17	75.7	63.7	84.8	96.2	85.7	99.3
#386	Whitman	LFI	DeepBlue	39	7	45	32	54.9	42.7	66.6	86.5	73.6	94
#386	Whitman	LFI	Innovita	42	2	26	27	60.9	48.4	72.2	92.9	75	98.8
#386	Whitman	LFI	Premier	40	1	51	30	57.1	44.8	68.7	98.1	88.4	99.9
#386	Whitman	LFI	Sure	44	0	52	26	62.9	50.4	73.9	100	93.2	100
#386	Whitman	LFI	UCP	43	2	50	28	60.6	48.2	71.7	96.2	85.7	99.3
#386	Whitman	LFI	VivaChek	47	1	48	19	71.2	58.6	81.4	98	87.8	99.9
#473	Liu	GICA		5	1	1	1	83.3	36.5	99.1	50	2.7	97.3
#545	Garcia	IC		6	15	3	18	25	10.6	47.1	16.7	4.4	42.3
						Pooled estimate		62.1	54.7	69.1	92.8	78.2	97.9
						Heterogeneity τ^2		0.12			2.90		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgG

Period: Week 3

Study_ID	Author	Test-class	Test	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#386	Whitman	LFI	BioMedomics	14	4	48	7	66.7	43.1	84.5	92.3	80.6	97.5
#386	Whitman	LFI	Bioperfectus	14	6	39	7	66.7	43.1	84.5	86.7	72.5	94.5
#386	Whitman	LFI	DecomBio	14	2	50	6	70	45.7	87.2	96.2	85.7	99.3
#386	Whitman	LFI	DeepBlue	15	7	45	6	71.4	47.7	87.8	86.5	73.6	94
#386	Whitman	LFI	Innovita	9	2	26	5	64.3	35.6	86	92.9	75	98.8
#386	Whitman	LFI	Premier	14	1	51	7	66.7	43.1	84.5	98.1	88.4	99.9
#386	Whitman	LFI	Sure	14	0	52	7	66.7	43.1	84.5	100	93.2	100
#386	Whitman	LFI	UCP	14	2	50	7	66.7	43.1	84.5	96.2	85.7	99.3
#386	Whitman	LFI	VivaChek	14	1	48	7	66.7	43.1	84.5	98	87.8	99.9
#473	Liu	GICA		68	4	10	0	100	94.7	100	71.4	42	90.4
#545	Garcia	IC		16	41	4	7	69.6	47	85.9	8.9	2.9	22.1
						Pooled estimate		73.9	60.8	83.9	92.4	75.2	98
						Heterogeneity τ^2		0.56			3.63		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgG

Period: Week 4

Study_ID	Author	Test-class	Test	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#386	Whitman	LFI	BioMedomics	9	4	48	2	81.8	47.8	96.8	92.3	80.6	97.5
#386	Whitman	LFI	Bioperfectus	9	6	39	1	90	54.1	99.5	86.7	72.5	94.5
#386	Whitman	LFI	DecomBio	10	2	50	1	90.9	57.1	99.5	96.2	85.7	99.3
#386	Whitman	LFI	DeepBlue	9	7	45	2	81.8	47.8	96.8	86.5	73.6	94
#386	Whitman	LFI	Innovita	4	2	26	2	66.7	24.1	94	92.9	75	98.8
#386	Whitman	LFI	Premier	9	1	51	2	81.8	47.8	96.8	98.1	88.4	99.9
#386	Whitman	LFI	Sure	10	0	52	1	90.9	57.1	99.5	100	93.2	100
#386	Whitman	LFI	UCP	9	2	50	2	81.8	47.8	96.8	96.2	85.7	99.3
#386	Whitman	LFI	VivaChek	9	1	48	1	90	54.1	99.5	98	87.8	99.9
						Pooled estimate		82.8	71.8	90.1	95	90	97.6
						Heterogeneity τ^2		0.0			0.40		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgM and/or IgG

Period: overall

Study_ID	Author	Testclass	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#221	Spicuzza	PoC	19	1	13	4	82.6	60.5	94.3	92.9	64.2	99.6
#301	Cassaniti	LFI	25	0	30	5	83.3	64.5	93.7	100	88.4	100
#301	Cassaniti	LFI	7	1	11	38	15.6	7	30.1	91.7	59.8	99.6
#307	Li	LFI	352	12	116	45	88.7	85	91.5	90.6	83.9	94.8
#326	Shen	GICA	69	2	51	28	71.1	60.9	79.7	96.2	85.9	99.3
#347	Zhang	GICA	127	4	656	27	82.5	75.3	87.9	99.4	98.3	99.8
#440	Paradiso	LFI	21	13	107	49	30	19.9	42.3	89.2	81.9	93.9
#473	Liu	GICA	77	8	81	13	85.6	76.2	91.8	91	82.6	95.8
#545	Garcia	IC	26	56	7	29	47.3	33.9	61.1	11.1	5	22.2
					Pooled estimate		68.8	46.3	85	93.2	71.8	98.7
					Heterogeneity τ^2		1.39			4.14		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgM and/or IgG

Period: Week 1

Study_ID	Author	Testclass	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#326	Shen	GICA	22	2	51	18	55	38.7	70.4	96.2	85.9	99.3
#386	Whitman	LFI	8	11	41	18	30.8	15.1	51.9	78.8	64.9	88.5
#386	Whitman	LFI	11	8	37	16	40.7	23	61	82.2	67.4	91.5
#386	Whitman	LFI	8	6	46	17	32	15.7	53.6	88.5	75.9	95.2
#386	Whitman	LFI	12	14	38	15	44.4	26	64.4	73.1	58.7	84
#386	Whitman	LFI	7	3	25	20	25.9	11.9	46.6	89.3	70.6	97.2
#386	Whitman	LFI	10	2	50	17	37	20.1	57.5	96.2	85.7	99.3
#386	Whitman	LFI	5	0	52	22	18.5	7	38.7	100	93.2	100
#386	Whitman	LFI	7	3	49	20	25.9	11.9	46.6	94.2	83.1	98.5
#386	Whitman	LFI	7	4	45	17	29.2	13.4	51.2	91.8	79.5	97.4
#386	Whitman	LFI	10	0	41	15	40	21.8	61.1	100	91.4	100
#473	Liu	GICA	3	2	7	13	18.8	5	46.3	77.8	40.2	96.1
					Pooled estimate		33.8	27	41.4	92	84.7	96
					Heterogeneity τ^2		0.08			0.87		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgM and/or IgG

Period: Week 2

Study_ID	Author	Testclass	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#326	Shen	GICA	24	2	51	9	72.7	54.2	86.1	96.2	85.9	99.3
#386	Whitman	LFI	49	11	41	21	70	57.7	80.1	78.8	64.9	88.5
#386	Whitman	LFI	57	8	37	13	81.4	70	89.4	82.2	67.4	91.5
#386	Whitman	LFI	53	6	46	17	75.7	63.7	84.8	88.5	75.9	95.2
#386	Whitman	LFI	56	14	38	15	78.9	67.3	87.3	73.1	58.7	84
#386	Whitman	LFI	45	3	25	24	65.2	52.7	76	89.3	70.6	97.2
#386	Whitman	LFI	54	2	50	16	77.1	65.3	86	96.2	85.7	99.3
#386	Whitman	LFI	44	0	52	26	62.9	50.4	73.9	100	93.2	100
#386	Whitman	LFI	48	3	49	23	67.6	55.3	78	94.2	83.1	98.5
#386	Whitman	LFI	48	4	45	18	72.7	60.2	82.6	91.8	79.5	97.4
#386	Whitman	LFI	51	0	41	18	73.9	61.7	83.4	100	91.4	100
#473	Liu	GICA	6	1	1	0	100	54.1	100	50	2.7	97.3
#545	Garcia	IC	8	15	3	16	33.3	16.4	55.3	16.7	4.4	42.3
					Pooled estimate		71.5	65.7	76.6	90.2	75.9	96.4
					Heterogeneity τ^2		0.10			2.54		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgM and/or IgG

Period: Week 3

Study_ID	Author	Testclass	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#326	Shen	GICA	23	2	51	1	95.8	76.9	99.8	96.2	85.9	99.3
#386	Whitman	LFI	17	11	41	4	81	57.4	93.7	78.8	64.9	88.5
#386	Whitman	LFI	17	8	37	4	81	57.4	93.7	82.2	67.4	91.5
#386	Whitman	LFI	14	6	46	6	70	45.7	87.2	88.5	75.9	95.2
#386	Whitman	LFI	17	14	38	5	77.3	54.2	91.3	73.1	58.7	84
#386	Whitman	LFI	9	3	25	5	64.3	35.6	86	89.3	70.6	97.2
#386	Whitman	LFI	17	2	50	4	81	57.4	93.7	96.2	85.7	99.3
#386	Whitman	LFI	15	0	52	6	71.4	47.7	87.8	100	93.2	100
#386	Whitman	LFI	15	3	49	6	71.4	47.7	87.8	94.2	83.1	98.5
#386	Whitman	LFI	15	4	45	6	71.4	47.7	87.8	91.8	79.5	97.4
#386	Whitman	LFI	17	0	41	4	81	57.4	93.7	100	91.4	100
#473	Liu	GICA	68	5	9	0	100	94.7	100	64.3	35.6	86
#545	Garcia	IC	17	41	4	6	73.9	51.3	88.9	8.9	2.9	22.1
					Pooled estimate		81.6	71.9	88.5	89.7	72.8	96.6
					Heterogeneity τ^2		0.51			3.23		

Type of test: Rapid Diagnostic Test (RDT)

Target: IgM and/or IgG

Period: Week 4

Study_ID	Author	Testclass	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#386	Whitman	LFI	9	11	41	2	81.8	47.8	96.8	78.8	64.9	88.5
#386	Whitman	LFI	10	8	37	0	100	69.2	100	82.2	67.4	91.5
#386	Whitman	LFI	10	6	46	1	90.9	57.1	99.5	88.5	75.9	95.2
#386	Whitman	LFI	10	14	38	1	90.9	57.1	99.5	73.1	58.7	84
#386	Whitman	LFI	5	3	25	1	83.3	36.5	99.1	89.3	70.6	97.2
#386	Whitman	LFI	10	2	50	1	90.9	57.1	99.5	96.2	85.7	99.3
#386	Whitman	LFI	10	0	52	1	90.9	57.1	99.5	100	93.2	100
#386	Whitman	LFI	10	3	49	1	90.9	57.1	99.5	94.2	83.1	98.5
#386	Whitman	LFI	9	4	45	1	90	54.1	99.5	91.8	79.5	97.4
#386	Whitman	LFI	9	0	41	2	81.8	47.8	96.8	100	91.4	100
					Pooled estimate		87.8	78.4	93.4	92.1	83.2	96.5
					Heterogeneity τ^2		0.0			0.95		

Type of test: chemiluminescent immunoassay (CLIA)

Target: IgM

Period: overall

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#272	Zhong	46	14	286	1	97.9	87.3	99.9	95.3	92.1	97.3
#282	Lin	65	15	65	14	82.3	71.7	89.6	81.3	70.6	88.8
#430	Qian	432	71	946	26	94.3	91.7	96.2	93	91.2	94.5
#430	Qian	38	14	583	3	92.7	79	98.1	97.7	96	98.7
#470	Lou	69	2	298	11	86.3	76.3	92.6	99.3	97.3	99.9
#597	Wan	41	8	122	9	82	68.1	91	93.8	87.8	97.1
				Pooled estimate		90.4	82.1	95	95.5	88	98.4
				Heterogeneity τ^2		0.30			0.91		

Type of test: chemiluminescent immunoassay (CLIA)

Target: IgM

Period: Week 1

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#282	Lin	10	15	65	2	83.3	50.9	97.1	81.3	70.6	88.8
#464	Ma	13	37	446	4	76.5	49.8	92.2	92.3	89.5	94.5
				Pooled estimate		78.5	1.2	99.9	88.6	7.3	99.9
				Heterogeneity τ^2		0.0			0.20		

Type of test: chemiluminescent immunoassay (CLIA)

Target: IgM

Period: Week 2

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#282	Lin	24	15	65	9	72.7	54.2	86.1	81.3	70.6	88.8
#464	Ma	30	37	446	0	100	88.4	100	92.3	89.5	94.5
				Pooled estimate		96	0	100	88.6	7.3	99.9
				Heterogeneity τ^2		5.67			0.20		

Type of test: chemiluminescent immunoassay (CLIA)

Target: IgM

Period: Week 3

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#282	Lin	31	15	65	3	91.2	75.2	97.7	81.3	70.6	88.8
#464	Ma	55	37	446	0	100	93.5	100	92.3	89.5	94.5
				Pooled estimate		98	0	100	88.6	7.3	99.9
				Heterogeneity τ^2		2.11			0.20		

Type of test: chemiluminescent immunoassay (CLIA)

Target: IgG

Period: overall

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#272	Zhong	45	10	290	2	95.7	84.3	99.3	96.7	93.8	98.3
#282	Lin	65	2	78	14	82.3	71.7	89.6	97.5	90.4	99.6
#430	Qian	486	17	947	25	95.1	92.8	96.7	98.2	97.1	98.9
#430	Qian	45	7	581	5	90	77.4	96.3	98.8	97.5	99.5
#470	Lou	69	1	208	11	86.3	76.3	92.6	99.5	97	100
#597	Wan	43	4	126	7	86	72.6	93.7	96.9	91.8	99
				Pooled estimate		91.1	82	95.9	98	96.7	98.8
				Heterogeneity τ^2		0.27			0.02		

Type of test: chemiluminescent immunoassay (CLIA)

Target: IgG

Period: Week 1

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#282	Lin	8	2	78	4	66.7	35.4	88.7	97.5	90.4	99.6
#464	Ma	11	1	482	6	64.7	38.6	84.7	99.8	98.7	100
				Pooled estimate		62.2	1.5	99.5	99.4	0.1	100
				Heterogeneity τ^2		0.0			0.90		

Type of test: chemiluminescent immunoassay (CLIA)

Target: IgG

Period: Week 2

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#282	Lin	24	2	78	9	72.7	54.2	86.1	97.5	90.4	99.6
#464	Ma	29	1	482	1	96.7	80.9	99.8	99.8	98.7	100
				Pooled estimate		88.3	0	100	99.4	0.1	100
				Heterogeneity τ^2		1.01			0.90		

Type of test: chemiluminescent immunoassay (CLIA)

Target: IgG

Period: Week 3

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#282	Lin	33	2	78	1	97.1	82.9	99.8	97.5	90.4	99.6
#464	Ma	55	1	482	0	100	93.5	100	99.8	98.7	100
				Pooled estimate		98.9	0	100	99.4	0.1	100
				Heterogeneity τ^2		0.0			0.90		

Type of test: chemiluminescent immunoassay (CLIA)

Target: IgM and/or IgG

Period: overall

Study_ID	Author	Testclass	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#282	Lin	CLIA	72	16	64	7	91.1	82	96.1	80	69.3	87.8
#518	Hu	CLIA	18	8	14	1	94.7	71.9	99.7	63.6	40.8	82
					Pooled estimate		91.8	9.4	99.9	76.5	14.3	98.4
					Heterogeneity τ^2		0			0		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgM

Period: overall

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	146	0	100	68	68.2	61.5	74.3	100	96.4	100
#272	Zhong	46	1	299	1	97.9	87.3	99.9	99.7	97.9	100
#282	Lin	30	14	40	35	46.2	33.9	58.9	74.1	60.1	84.6
#470	Lou	74	0	300	6	92.5	83.8	96.9	100	98.8	100
				Pooled estimate		83.9	31.1	98.4	99.8	22.1	100
				Heterogeneity τ^2		2.11			12.27		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgM

Period: Week 1

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	27	0	100	33	45	32.3	58.3	100	96.4	100
#386	Whitman	5	2	50	22	18.5	7	38.7	96.2	85.7	99.3
#470	Lou	13	0	300	26	33.3	19.6	50.3	100	98.8	100
				Pooled estimate		33.6	12.6	64	99.9	0.6	100
				Heterogeneity τ^2		0.12			6.78		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgM

Period: Week 2

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	39	0	100	15	72.2	58.1	83.1	100	96.4	100
#386	Whitman	46	2	50	25	64.8	52.5	75.5	96.2	85.7	99.3
#470	Lou	65	0	300	10	86.7	76.4	93.1	100	98.8	100
				Pooled estimate		75.6	45.3	92.1	99.9	0.6	100
				Heterogeneity τ^2		0.20			6.78		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgM

Period: Week 3

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	45	0	100	10	81.8	68.6	90.5	100	96.4	100
#146	Xiang	51	0	60	15	77.3	65	86.3	100	94	100
#386	Whitman	14	2	50	7	66.7	43.1	84.5	96.2	85.7	99.3
#470	Lou	58	0	300	2	96.7	87.5	99.4	100	98.8	100
				Pooled estimate		83.9	56.1	95.5	99.9	7.7	100
				Heterogeneity τ^2		0.58			7.33		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgM

Period: Week 4

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	26	0	100	6	81.3	63	92.1	100	96.4	100
#386	Whitman	9	2	50	2	81.8	47.8	96.8	96.2	85.7	99.3
				Pooled estimate		81.4	2.9	99.8	99	0	100
				Heterogeneity τ^2		0.0			1.19		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgG

Period: overall

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	150	0	100	64	70.1	63.4	76	100	96.4	100
#272	Zhong	46	1	299	1	97.9	87.3	99.9	99.7	97.9	100
#282	Lin	15	0	64	50	23.1	13.9	35.5	100	94.4	100
				Pooled estimate		74.9	1.6	99.8	99.8	86.2	100
				Heterogeneity τ^2		4.10			0		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgG

Period: Week 1

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	22	0	100	38	36.7	24.9	50.2	100	96.4	100
#386	Whitman	11	8	44	16	40.7	23	61	84.6	71.4	92.7
				Pooled estimate		37.8	3.5	91	98.7	0	100
				Heterogeneity τ^2		0			8.25		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgG

Period: Week 2

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	39	0	100	15	72.2	58.1	83.1	100	96.4	100
#386	Whitman	59	8	44	12	83.1	71.9	90.6	84.6	71.4	92.7
				Pooled estimate		78.4	17.4	98.4	98.7	0	100
				Heterogeneity τ^2		0.01			8.25		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgG

Period: Week 3

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	48	0	100	7	87.3	74.9	94.3	100	96.4	100
#146	Xiang	55	3	57	11	83.3	71.7	91	95	85.2	98.7
#386	Whitman	16	8	44	5	76.2	52.5	90.9	84.6	71.4	92.7
				Pooled estimate		87,5	75.7	92.1	96.9	19.9	100
				Heterogeneity τ^2		0.0			2.61		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgG

Period: Week 4

Study_ID	Author	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	28	0	100	4	87.5	70.1	95.9	100	96.4	100
#386	Whitman	10	8	44	1	90.9	57.1	99.5	84.6	71.4	92.7
				Pooled estimate		88.4	1.8	100	98.7	0	100
				Heterogeneity τ^2		0.0			8.25		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgM and/or IgG

Period: overall

Study_ID	Author	Testclass	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	ELISA	172	0	100	42	80.4	74.3	85.3	100	96.4	100
#480	Liu	ELISA	127	67	85	16	88.8	82.2	93.3	55.9	47.7	63.9
					Pooled estimate		84.5	21.8	99.1	98.5	0	100
					Heterogeneity τ^2		0.06			19.0		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgM and/or IgG

Period: Week 1

Study_ID	Author	Testclass	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	ELISA	29	0	100	41	41.4	30	53.8	100	96.4	100
#386	Whitman	ELISA	11	9	43	16	40.7	23	61	82.7	69.2	91.3
#386	Whitman	ELISA	10	7	45	17	37	20.1	57.5	86.5	73.6	94
					Pooled estimate		37.8	27	49.9	95.4	8.6	100
					Heterogeneity τ^2		0.00			3.48		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgM and/or IgG

Period: Week 2

Study_ID	Author	Testclass	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	ELISA	48	0	100	6	88.9	76.7	95.4	100	96.4	100
#386	Whitman	ELISA	60	9	43	11	84.5	73.5	91.6	82.7	69.2	91.3
#386	Whitman	ELISA	58	7	45	13	81.7	70.4	89.5	86.5	73.6	94
					Pooled estimate		84.8	70.3	92.9	95.4	8.6	100
					Heterogeneity τ^2		0.0			3.48		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgM and/or IgG

Period: Week 3

Study_ID	Author	Testclass	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	ELISA	52	0	100	3	94.5	83.9	98.6	100	96.4	100
#386	Whitman	ELISA	17	9	43	4	81	57.4	93.7	82.7	69.2	91.3
#386	Whitman	ELISA	17	7	45	4	81	57.4	93.7	86.5	73.6	94
					Pooled estimate		88.1	56.4	97.7	95.4	8.6	100
					Heterogeneity τ^2		0.16			3.48		

Type of test: enzyme-linked immunosorbent assay (ELISA)

Target: IgM and/or IgG

Period: Week 4

Study_ID	Author	Testclass	TP	FP	TN	FN	Sensitivity	Lower	Upper	Specificity	Lower	Upper
#112	Liu	ELISA	30	0	100	2	93.8	77.8	98.9	100	96.4	100
#386	Whitman	ELISA	10	9	43	1	90.9	57.1	99.5	82.7	69.2	91.3
#386	Whitman	ELISA	9	7	45	2	81.8	47.8	96.8	86.5	73.6	94
					Pooled estimate		90.7	56.6	98.7	95.4	8.6	100
					Heterogeneity τ^2		0.0			3.48		

Table A 6: Seroprevalence studies

Study reference	Study type	Period	Type of test	Population Subpopulation	Sample size	Number of subjects with positive antibody test	Prevalence (%) [95%-CI][a]	Increase in pre-study prevalence
Comar 2020	Cross-sectional	NR within 1 week	CLIA	Health care workers	727	125	17.2 [14.6, 20.2]	NR
				High risk[a]	335	65	19.4 [15.4, 24.1]	NR
				Medium risk[a]	277	49	17.7 [13.5, 22.8]	NR
				Low risk[a]	115	11	9.6 [5.1, 16.8]	NR
Paradiso 2020	Cross-sectional	March, 26 – April, 2	RDT	Health care workers	525	6	1.1 [0.5, 2.6]	NR
Garcia-Basteiro 2020	Cross-sectional	February, 9 – April, 2	Multiplex immunoassay	Health care workers	578	54[c]	9.3 [7.2, 12.1]	21 (38.9)
			Multiplex immunoassay + PCR test		578	65[c]	11.2 [8.8, 14.2]	26 (40)
Tosato 2020		NR	CLIA	Health professionals	133	6	4.5 [1.8, 10.0]	NR
			CLIA + PCR test		133	7	5.3 [2.3, 10.9]	NR
Wu 2020	Cross-sectional	April, 3 – 15	CLIA	Applying for permission of resume	1021	98[d]	9.6 [7.9, 11.6]	NR
			CLIA + PCR		1021	98[d]	9.6 [7.9, 11.6]	NR
		April, 3 – 15	CLIA	Hospitalized	381	40[d]	10.5 [7.7, 14.1]	NR
			CLIA + PCR		381	40[d]	10.5 [7.7, 14.1]	NR

Thompson 2020	Cross-sectional		Neutralization test	Blood donors				
		March, 17		Study sample 1	500	0	0.0 [0.0, 0.7]	NR
		March, 21 - 23		Study sample 2	500	5[e]	1.0 [0.4, 2.5]	NR
Slot 2020	Cross-sectional	April, 1 – 15	ELISA	Blood donors	7361	230	3.1 [2.7, 3.6]	General population 0.218% confirmed cases (37190/17.4 mio)
						200[f]	2.7 [2.4, 3.1]	
Shakiba 2020	Cross-sectional	April	RDT	Households	528[g] (196 households)	117[c]	21.2 [17.9, 24.9]	"*higher than confirmed cases*"
							33 [28, 39][c,h]	
Fontanet 2020	Cross-sectional	March, 30 – April, 4	ELISA	Pupils and their contacts	661	171	25.9 [22.6, 29.4]	NR
		March, 23 – 27	ELISA	Blood donors	200	6	3.0 [1.2, 6.7]	
Erikstrup 2020	Cross-sectional	April, 6 – 17	RDT	Blood donors	9496	173	1.8 [1.6, 2.1]	0.082% (82/100.000)
							1.7 [0.9, 2.3][h]	NR
Bryan 2020	Cross-sectional	April, within 1 week	CLIA	Cohort	4856	87	1.8 [1.4, 2.2]	NR
Bendavid 2020	Cross-sectional	April, 3 – 4	RDT	Cohort	3330[i]	50	1.5 [1.1, 2.0]	*"Confirmed cases prevalence 55-fold lower"*
							2.8 [1.3, 4.7][j]	

Streeck 2020	Cross-sectional	March, 31 – April, 6	ELISA[k]	Households	919[l] (405 households)	125	13.6 [11.5, 16.9]	NR
							14.11 [11.15, 17.27][h]	NR
			ELISA[k] + PCR		919[l] (405 households)	138	15.0 [12.8, 17.5]	NR
							15.53 [12.31, 18.96][h]	NR
Snoek 2020	Cross-sectional	April, 5 – May, 5	ELISA + PCR	Cohort	1835	35	2.1 [1.3, 2.8][m]	NR
Stringhini 2020	Cross-sectional	April, 6 – May, 9	ELISA	General population	2766	219	7.9 [7.0, 9.0]	
Doi 2020	Cross-sectional	March, 31 – April, 7	NR	Outpatients with blood testing for any reason	1000	33	3.3 [2.3, 4.7]	
							2.7 [1.8, 3.9][m]	
Steensels 2020	Cross-sectional	April 22, -April 30	RDT	Hospital workers	3056	197	6.4 [5.6, 7.4]	NR

a. own calculations, 95% CI based on the score method
b. conflicting information in the article
c. IgA and/or IgM and/or IgG positive
d. Numbers of positives based on target IgG; all tests for IgM except 1 in the hospitalized group were negative
e. 1 further subject was identified in a non-random subsample by ELISA
f. 30 subjects were also antibody positive in blood sample from the pre-COVID 19 era
g. 23 subjects without valid test results are not included
h. adjusted for estimated sensitivity and specificity of the test
i. 109 subjects were not included
j. adjusted for estimated sensitivity and specificity as well as for population characteristics
k. Number of positives based on target IgG
l. 88 subjects were not included
m. adjusted for population characteristics

NR: Data not reported