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MORNING BRIEF

Scientific Review

17 July 2020

The purpose of the Morning Brief is to summarize and present key information, research articles and other relevant publications pertaining to critical care and COVID-19.

Stellenbosch University Research Response Team

Content of the brief

SARS-CoV-2 antibody and seroprevalence studies

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Currently there are approximately 280 antibody tests for SARS-CoV-2 commercially available, but less than 10% of these approved.

For a list of approved tests:
https://www.centerforhealthsecurity.org/resources/COVID-19/serology/Serology-based-tests-for-COVID-19.html

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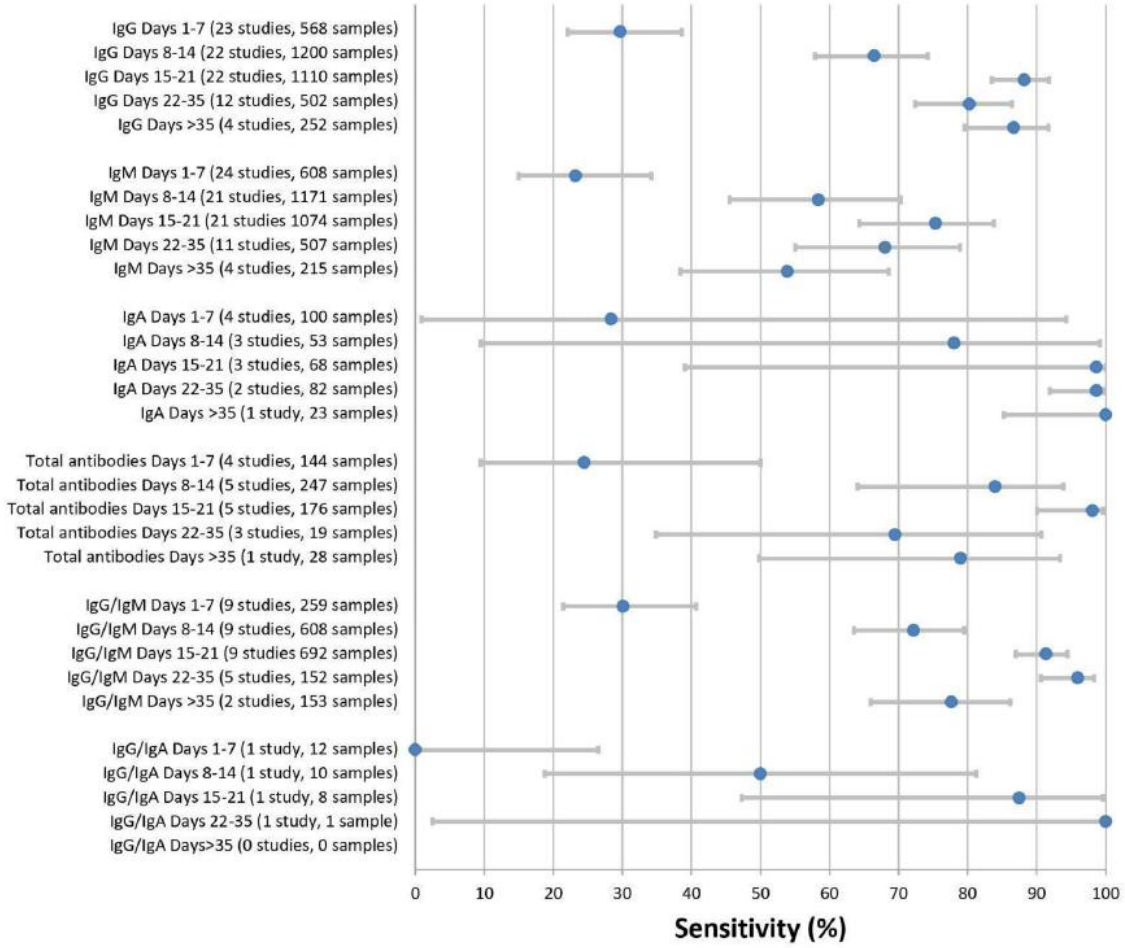
Cochrane Library

Cochrane Database of Systematic Reviews

Meta-analytical estimates of sensitivity (with 95% CI) by antibody class and time since symptom onset



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

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

Antibody testing depends on TIMING:

[pooled results of 54 studies with 15 976 samples]
The combination of IgG/IgM had a sensitivity of:
30.1% (95% CI 21.4 to 40.7) for 1 to 7 days
72.2% (95% CI 63.5 to 79.5) for 8 to 14 days
91.4% (95% CI 87.0 to 94.4) for 15 to 21 days
96.0% (95% CI 90.6 to 98.3) for 21 50 35 days

And it depends on which Ab's are being tested (IgA>IgG/IgA>Total Ig>IgG/IgM>IgG>IgM)

And it depends on the validity of the assay used

Seroprevalence studies

Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study

Marina Pollán, Beatriz Pérez-Gómez, Roberto Pastor-Barriuso, Jesús Oteo, Miguel A Hernán, Mayte Pérez-Olmeda, Jose L Sanmartín, Aurora Fernández-García, Israel Cruz, Nerea Fernández de Larrea, Marta Molina, Francisco Rodríguez-Cabrera, Mariano Martín, Paloma Merino-Amador, Jose León Paniagua, Juan F Muñoz-Montalvo, Faustino Blanco, Raquel Yotti, on behalf of the ENE-COVID Study Group*

Over 35000 households (>100 000 individuals) invited to participate, randomly selected through census data, proportionate to the size of the population within each municipality
NB: they EXCLUDED institutionalised people

Three 'waves' of sampling on all participants are planned, 2 – 4 weeks apart – THIS data is the first wave 27 April to 11 May
2 tests available to each participant:

1. Orient Gene Biotech COVID-19 IgG/IgM Rapid Test Cassette; Zhejiang Orient Gene Biotech, Zhejiang, China; a POC lateral-flow immunochromatographic assay sensitivity of 97·2% for IgG and 87·9% for IgM; specificity of 100% for both.(they only reported IgG)
2. SARS-CoV-2 IgG for use with ARCHITECT; Abbott Laboratories, Abbott Park, IL, USA; a chemiluminescent microparticle immunoassay for qualitative detection of IgG; Sensitivity 90-100%; specificity 100%

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POC performed on 61075
Serology performed on 51 958

Country-wide seroprevalence of 5.0% for POC and 4.7% with serology.
Range 3.7% (both tests positive) to 6.2% (either test positive)
HIGHEST prevalence was 14.4% in a central province

Infants <1 year, 1% prevalence
Children 3 – 9 years, 3%
Rising prevalence up to age 45 years, then plateau at around 6% (serology showed decline after age 85 again)

Health Care Workers: 8.3 – 11.1%
Asymptomatic positive test: 32.7% POC and 28.5% serology

Prevalence among people with NO reported contact with a known case of COVID was 2.7% - 3.2%
Prevalence among people who had a HOUSEHOLD MEMBER with known COVID was 15%

nature medicine

BRIEF COMMUNICATION

https://doi.org/10.1038/s41591-020-0949-6

Check for updates

Seroprevalence of immunoglobulin M and G antibodies against SARS-CoV-2 in China

Xin Xu[1,2,16], Jian Sun[1,2,16], Sheng Nie[1,2,16], Huiyuan Li[3,16], Yaozhong Kong[4,16], Min Liang[1,2], Jinlin Hou[1,2], Xianzhong Huang[3], Dongfeng Li[5], Tean Ma[6], Jiaqing Peng[7], Shikui Gao[8], Yong Shao[9], Hong Zhu[2], Johnson Yiu-Nam Lau[10], Guangyu Wang[11], Chunbao Xie[12], Li Jiang[12], Ailong Huang[13] ✉, Zhenglin Yang[12] ✉, Kang Zhang[14,15] ✉ and Fan Fan Hou[1,2,15] ✉

9 March 2020 and 10 April 2020
17,368 non-randomly selected individuals from four different geographic locations and different populations in China

During validation of their IgG/IgM assay against PCR positive cases, they noted that IgG rose high relatively early (7 Days after symptoms onset), and both IgM and IgG persisted at detectable levels past 28 days. They note that unlike other viral infections, the distinction between early IgM and late IgG response may not be as clear.
In the main data set, IgG performed better overall, but some individuals in their survey were only IgM positive.

Seropositvity was significantly higher in individuals older than 65 years (2.0% in those ≥65 years versus 1.3% in those <65 years, $P < 0.01$).

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In WUHAN (outbreak epicenter):

3.8% (2.6–5.4%, 95% CI) in the cohort of 714 healthcare workers,

3.8% (2.2–6.3%, 95% CI) in the cohort of 346 hotel staff members

3.2% (1.6–6.4%, 95% CI) in the cohort of 219 family members of the healthcare workers

Outside Wuhan:

Cities of Jinzhou and Honghu of Hubei Province, 1.3% (1.0–1.8%, 95% CI) in 3,091 healthcare workers and 3.6% (2.0–4.9%, 95% CI) in 979 asymptomatic patients who visited the hospital for routine maintenance hemodialysis.

City of Chongqing, 3.1% (1.7–5.7%, 95% CI) in 319 health care workers, and 3.8% (2.8–5.2%, 95% CI) in 993 hospital outpatients

City of Chengdu in Sichuan Province, 0.58% (0.45–0.76%, 95% CI) in 9,442 community residents

Guangzhou and Foshan, 2.8% (1.8–4.6%, 95% CI) in 563 haemodialysis patients, 1.2% (0.4–3.3%, 95% CI) in 260 health care workers, and 1.4% (0.6–2.9%, 95% CI) in 442 factory workers.

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LETTERS

https://doi.org/10.1038/s41591-020-0992-3

Check for updates

Population-based surveys of antibodies against SARS-CoV-2 in Southern Brazil

Mariângela F. Silveira[1], Aluísio J. D. Barros[1], Bernardo L. Horta[1], Lúcia C. Pellanda[2], Gabriel D. Victora[3], Odir A. Dellagostin[1], Claudio J. Struchiner[4], Marcelo N. Burattini[5], Andréia R. M. Valim[6], Evelise M. Berlezi[7], Jeovany M. Mesa[8], Maria Letícia R. Ikeda[9], Marilia A. Mesenburg[2], Marina Mantesso[10], Marinel M. Dall'Agnol[11], Raqueli A. Bittencourt[12], Fernando P. Hartwig[1], Ana M. B. Menezes[1], Fernando C. Barros[1], Pedro C. Hallal[1,13] ✉ and Cesar G. Victora[1,13]

Three rounds of sampling: 11-13 April; 25 -27 April; 9-11 May
'Population-based' samples of 500 people derived from households in census tracts from all 9 major cities in the state of Rio Grande do Sul. Excluded small towns and rural areas.

POC lateral flow assay (Wondfo) for IgG and IgM (sens 86.4%, Spec 99.6%)
Internal validation only picked up 64/83 (77%) who were +PCR
In demographics, slight overrepresentation of women and people aged >60 years and under representation of children

Tested 4151 in round 1, of whom 2 were +; 4460 in round 2 of whom 6 were +; 4500 in round 3 of whom 10 were + = very low prevalences <1%
Early in their outbreak, they will continue to do sampling every 2 weeks.

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Contents lists available at ScienceDirect

Annals of Epidemiology

ELSEVIER

Original article

Cumulative incidence and diagnosis of SARS-CoV-2 infection in New York

Eli S. Rosenberg, PhD [a,*], James M. Tesoriero, PhD [b], Elizabeth M. Rosenthal, MPH [a], Rakkoo Chung, PhD [b], Meredith A. Barranco, MPH [a], Linda M. Styer, PhD [c], Monica M. Parker, PhD [c], Shu-Yin John Leung, MA [b], Johanne E. Morne, MS [b], Danielle Greene, DrPH [b], David R. Holtgrave, PhD [a], Dina Hoefer, PhD [b], Jessica Kumar, DO [b], Tomoko Udo, PhD [a], Brad Hutton, MPH [b], Howard A. Zucker, MD [b]

April 19 - 28, 2020
Convenience sample of over 15,000 people attending 99 grocery stores across 26 counties in New York State

SARS-CoV IgG testing was conducted using a microsphere immunoassay developed and validated for DBS by the NYSDOH Wadsworth Center. Sens 87.9%, Spec 99.7%

1887 (12.5%) were reactive and 340 (2.3%) indeterminate. After weighting, 12.5% were estimated reactive and after further adjustment for test characteristics, estimated cumulative incidence as 14.0% (95% CI: 13.3%e14.7%).

Infer that only 8.9% of all infections in NY State are diagnosed by current testing strategy
And estimated infection fatality ratio 0.6%

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Seroprevalence of SARS-CoV-2–Specific Antibodies Among Adults in Los Angeles County, California, on April 10-11, 2020

JAMA June 16, 2020 Volume 323, Number 23

April 10 – 14, 2020
Participants invited from a random sample of a proprietary commercial database of residents of LA County
IgG and IgM antibodies using a lateral flow immunoassay test (Premier Biotech). Sensitivity 82.7% and specificity 99.5%
865 participants tested, 863 included. 13% of all reported at least 1 symptoms.
Slight overrepresentation of female, white, ages 35-54 years of age
Seroprevalence 4.0%

Infer that 2.3% of all infections in the region are diagnosed by current testing strategy.

Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study

Silvia Stringhini, Ania Wisniak, Giovanni Piumatti*, Andrew S Azman*, Stephen A Lauer, Hélène Baysson, David De Ridder, Dusan Petrovic, Stephanie Schrempft, Kailing Marcus, Sabine Yerly, Isabelle Arm Vernez, Olivia Keiser, Samia Hurst, Klara M Posfay-Barbe, Didier Trono, Didier Pittet, Laurent Gétaz, François Chappuis, Isabella Eckerle, Nicolas Vuilleumier, Benjamin Meyer, Antoine Flahault, Laurent Kaiser, Idris Guessous*

April 6 and May 9, 2020, enrolled 2766 participants from 1339 households
Randomised population-representative survey, planned for 12 weekly rounds, this report is the first 5 weeks
SARS-CoV-2 IgG antibodies using ELISA (Euroimmun; Lubeck, Germany), sensitivity of 93% and a specificity of 100%.

Week 1 seroprevalence 4.8%
Week 2 seroprevalence 8.5%
Week 3 seroprevalence 10.9%
Week 4 seroprevalence 6.6%
Week 5 seroprevalence 10.8%

Individuals aged 5–9 years (relative risk [RR] 0·32 [95% CI 0·11–0·63]) and those older than 65 years (RR 0·50 [0·28–0·78]) had a significantly lower risk of being seropositive than those aged 20–49 years

Estimate that for every reported confirmed case, there were 11·6 infections in the community

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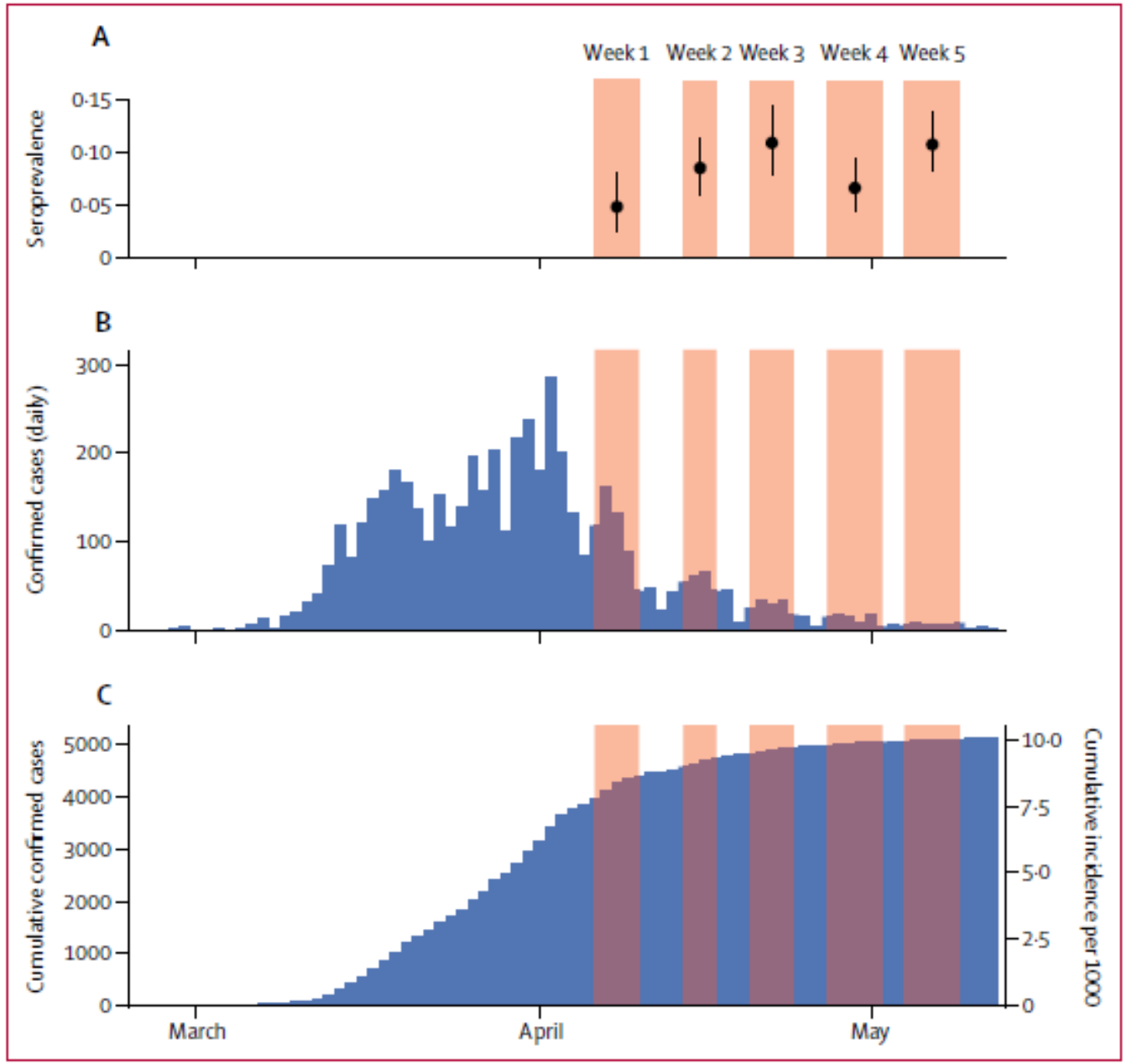

Figure: Seroprevalence estimates and 95% CIs for each week of the survey (A), daily confirmed COVID-19 cases reported in Geneva (B), and cumulative case counts per day and cumulative incidence rate of confirmed COVID-19 (C)

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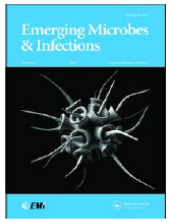

Emerging Microbes & Infections

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/temi20

High neutralizing antibody titer in intensive care unit patients with COVID-19

Li Liu , Kelvin Kai-Wang To , Kwok-Hung Chan , Yik-Chun Wong , Runhong Zhou , Ka-Yi Kwan , Carol Ho-Yan Fong , Lin-Lei Chen , Charlotte Yee-Ki Choi , Lu Lu , Owen Tak-Yin Tsang , Wai-Shing Leung , Wing-Kin To , Ivan Fan-Ngai Hung , Kwok-Yung Yuen & Zhiwei Chen

50 confirmed COVID patients (8 ICU, 42 hospitalised), serum assessed for neutralising ab activity
ICU patients had significantly higher peak NAb titer than non-ICU patients (ICU patients, 7280; non-ICU patients, 671) and peaked earlier (17 days after symptoms vs 20 days after symptoms).

Intensive Care Med
https://doi.org/10.1007/s00134-020-06171-7

LETTER

Serum antibody response in critically ill patients with COVID-19

Alban Longchamp[1,2,3], Justine Longchamp[1,3], Antony Croxatto[4], Gilbert Greub[4], Bienvenido Sanchez[1*], Julie Delaloye[1*] on behalf of the Study Group

28 Critically Ill COVID patients (96% ventilated, 20% died)
58% had SARS-CoV2-specific IgG+ on admission
IgG showed 2 peaks – on admission to ICU ; 20 days later
In the 1 month follow up 96% became seropositive
Levels of Ab correlated with time from symptom onset; no correlation with age or any other clinical or lab parameter
Levels were higher in patients who survived

117 patients who were laboratory confirmed as SARS-CoV-2 infection; 61 regular, 46 severe, 10 critically ill. Specific IgG antibodies to the SARS-CoV-2 in severe and critically ill patients were significantly lower than that in regular patients ($p < 0.05$).

International Journal of Hematology
https://doi.org/10.1007/s12185-020-02930-w

ORIGINAL ARTICLE

Changes of hematological and immunological parameters in COVID-19 patients

Xiaohong Yuan[1] · Wanling Huang[1] · Bing Ye[2] · Cunrong Chen[2] · Rongfeng Huang[3] · Feng Wu[4] · Qin Wei[5] · Wei Zhang[5] · Jianda Hu[1]