# **COVID-19 Science Update**



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### Vaccines

#### PEER-REVIEWED

Safety and efficacy data are needed to select SARS-CoV-2 vaccine candidates for phase 3 trials and ultimately to determine likely benefits and risks of large-scale administration. Few trials to date have studied SARS-CoV-2 vaccine effects specifically in older adults, who are at increased risk for severe COVID-19. Here we present early findings from studies of two different types of SARS-CoV-2 vaccine candidates, including data on safety and immunogenicity in older adults.

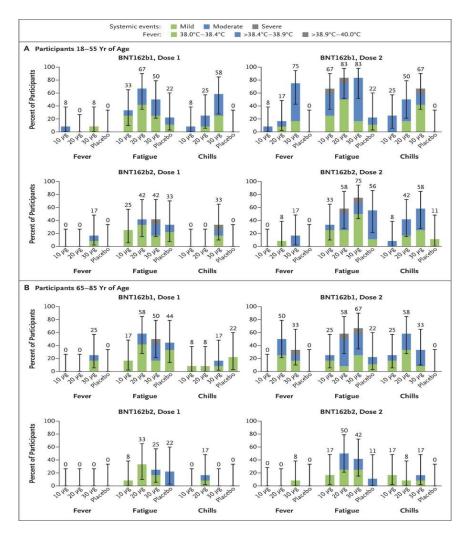
<u>Safety and immunogenicity of two RNA-based COVID-19 vaccine candidates.</u> Walsh *et al.* NEJM (October 14, 2020).

#### Key findings:

- BNT162b2 was associated with less frequent and less severe systemic reactions than BNT162b1, particularly in older adults (Figure 1).
  - Few younger recipients of BNT162b2, and no older recipients had severe systemic events.
  - After the first dose, systemic events were similar among older participants who received either BNT162b2 or placebo.
- Both vaccine candidates elicited dose-dependent SARS-CoV-2-neutralizing antibody titers in younger and older adults (Figure 2).
  - Titers were similar to or higher than those of a panel of SARS-CoV-2 convalescent serum samples.
  - IgG and virus-neutralizing responses were lower in older than in younger participants.

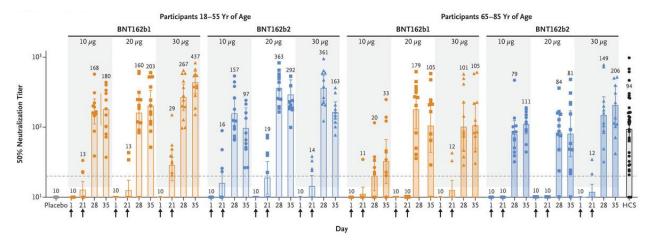
**Methods**: Randomized, placebo-controlled, blinded, dose-escalation, phase 1 trial including 195 participants aged 18–55 or 65–85 years who received placebo or one of two nucleoside-modified RNA vaccine candidates: BNT162b1 (encodes a secreted trimerized SARS-CoV-2 receptor-binding domain protein) or BNT162b2 (encodes a membraneanchored SARS-CoV-2 full-length spike protein). Participants in 13 groups received an injection of 10 µg, 20 µg, 30 µg or 100 µg of one of the vaccine candidates (12 participants/group) or placebo (3 participants/group) on days 1 and 21. Participants were evaluated for local and systemic reactions, adverse events and immune response. *Limitations*: Small, phase 1 study; most participants were white; persons with various comorbidities or previous COVID-19 diagnosis were excluded.

#### Figure 1



*Note*: Adapted from Walsh *et al.* Systemic events reported within 7 days after the administration of vaccine or placebo, according to age group. A: Participants aged 8–55 years. B: Participants aged 65–85 years. Fevers were scaled as **38.0°C-38.4°C**, >**38.4°C-38.9°C**, or **38.9°C-40.0°C**. Systemic events of fatigue and chills were graded as being **mild**, **moderate**, or **severe**. I bars represent 95% confidence intervals. The numbers above the I bars show the overall percentage of participants in each group who reported the specified systemic event. From NEJM, Walsh *et al.* Safety and immunogenicity of two RNA-based Covid-19 vaccine candidates. DOI: 10.1056/NEJMoa2027906, October 14, 2020. Copyright © 2020 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

#### Figure 2



*Note*: Adapted from Walsh *et al.* Serum neutralization titers with **BNT162b1** and **BNT162b2**. Arrows indicate days of vaccination. Immune responses in participants. All **placebo recipients** are combined (far left). Serum samples were obtained before injection (Day 1) and Days 21, 28, and 35 after the first dose. Human convalescent serum (**HCS**) were samples from 38 donors with RT-PCR-confirmed COVID-19 diagnosis (far right). Each data point represents the 50% SARS-CoV-2-neutralizing geometric mean titer (GMT) of a serum sample, the whisker bars represent the 95% CI of the GMT, and the dashed line is the lower limit of quantification. Data points for HCS samples, or the 10-µg dose of vaccine are shown as circles, for the 20-µg dose as squares, and for the 30-µg dose as triangles. The numbers above the bars show the GMT in the group. From NEJM, Walsh *et al.* Safety and immunogenicity of two RNA-based Covid-19 vaccine candidates. DOI: 10.1056/NEJMoa2027906, October 14, 2020. Copyright © 2020 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

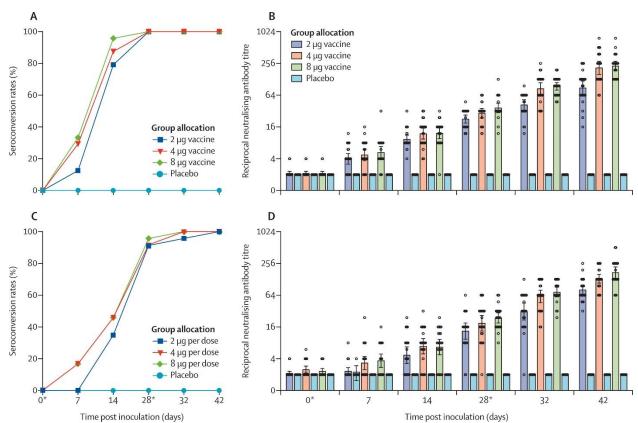
#### Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: A randomized, doubleblind, placebo-controlled, phase 1/2 trial. Xia *et al.* Lancet Infectious Diseases (October 15, 2020).

**Key findings:** 

- BBIBP-CorV was well tolerated in younger and older adults who received two 2 µg, 4 µg, or 8 µg injections.
  - All adverse reactions were mild or moderate severity.
  - Fever was the most common systematic adverse reaction (4% of phase 1 and 2% of phase 2 recipients).
- Neutralizing antibody (nAb) geometric mean titers (GMTs) were higher in vaccine than in placebo recipients for both younger and older participants (Figure 1).
  - All younger and 94% of older vaccine recipients seroconverted by day 28.
- By 28 days after last dose, nAb GMT differed by vaccine dose and schedule (Figure 2):
  - Single 8 μg injection GMT 14.7 (95% CI 11.6–18.8).
  - o Two 4 μg injections 14 days apart GMT 169.5 (95% CI 132.2-217.1).
  - o Two 4 μg injections 21 days apart GMT 282.7 (95% CI 221.2-361.4).
  - o Two 4 μg injections 28 days apart GMT 218.0 (95% CI 181.8-261.3.)

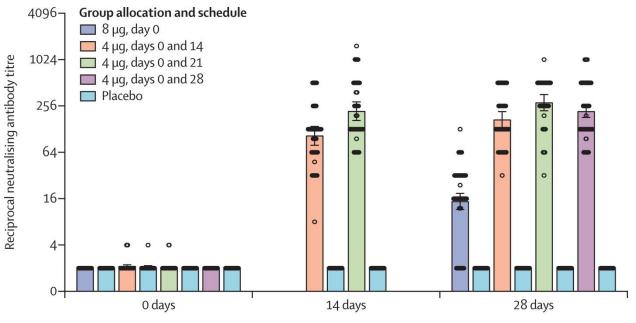
**Methods**: Randomized, double-blind, placebo-controlled, phase 1/2 dose escalation trial of BBIBP-CorV, an inactivated SARS-CoV-2 vaccine. In phase 1, healthy adults aged 18–59 years (n = 96) and  $\geq$ 60 years (n = 96) were randomly assigned to receive placebo or vaccine at a dose of 2 µg, 4 µg, or 8 µg, on Days 1 and 28. In phase 2, 448 healthy adults aged 18–59 years were randomly assigned to receive placebo or vaccine as a single 8 µg dose or in 2 doses of 4 µg, 14, 21, or 28 days apart. Primary outcomes were safety and tolerability and the secondary outcome was immunogenicity which was expressed as reciprocal neutralizing antibody titer in serum, with average for each group expressed as GMT. <u>Limitations</u>: Small study; short follow-up period; most participants were white; no evaluation in children or adolescents.





Note: Adapted from Xia *et al.* Seroconversion ratios and nAb titers for participants receiving 2 injections of vaccine at 2µg, 4µg, or placebo. Seroconversion rates (A and C) and reciprocal neutralizing antibody titer (B and D) for participants ages 18–59 years (A and B) and for participants aged ≥60 years (C and D) are shown. Each data point (B and D) represents a serum sample, and the top of each vertical bar represents the geometric mean with the 95% CI (I bar). Seroconversion was defined as a ≥4fold increase in post-vaccination titer from baseline. Reciprocal neutralizing antibody titer of ≤2 represents no nAb detected. \* indicates days of vaccination. This article was published in Lancet Infectious Diseases, Xia *et al.* Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomized, double-blind, placebo-controlled, phase 1/2 trial. DOI: https://doi.org/10.1016/S1473-3099(20)30831-8. Copyright Elsevier 2020. This article is currently available at the Elsevier COVID-19 resource centre: https://www.elsevier.com/connect/coronavirus-information-center.

#### Figure 2



Immunisation schedule

*Note*: Adapted from Xia *et al*. Neutralizing antibody titers for different immunization schedules. Reciprocal nAb titer of  $\leq 2$  represents no nAb detected. 14 days and 28 days refer to Days 14 and 28 *after the second inoculation*, except for the 8 µg group where the sample was obtained 28 days after single inoculation. The measurement of nAb at day 14 was not designed for the 4 µg days 0 and 14 or days 0 and 28 groups. Each data point represents a serum sample, and the I bar represents the 95% CI of the reciprocal nAb titer. This article was published in Lancet Infectious Diseases, Xia *et al*. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomized, double-blind, placebo-controlled, phase 1/2 trial. DOI: https://doi.org/10.1016/S1473-3099(20)30831-8. Copyright Elsevier 2020. This article is currently available at the Elsevier COVID-19 resource centre: https://www.elsevier.com/connect/coronavirus-information-center.

**Implications for both studies** (Walsh *et al.* & Xia *et al.*): Early studies of 2 different types of SARS-CoV-2 vaccines demonstrate tolerability and immunogenicity including in older adults; results from these studies have been used to select candidates and doses for larger safety and efficacy trials, for which the investigators are now recruiting participants. An editorial accompanying Xia *et al.* (Isakova-Sivak & Rudenko, <u>A promising inactivated whole-virion SARS-CoV-2 vaccine</u>) notes that this is the second study to report immunogenicity and low levels of adverse effects for an inactivated SARS-CoV-2 vaccine candidate, indicating reproducibility of results from vaccines across different manufacturers. According to the <u>Milken Institute's COVID-19 Treatment and Vaccine Tracker</u> BNT162b1/2 and BBIBP-CorV are both in phase 3 trials, with the former product selected for FDA fast track status and Operation Warp Speed in July 2020, and the latter receiving early approval for emergency use in China (August 2020) and the United Arab Emirates (September 2020).

## Epidemiology

#### PEER-REVIEWED

<u>Risk factors for SARS-CoV-2 infection in homeless shelters in Chicago, Illinois — March–May, 2020.</u> Ghinai *et al.* Open Forum Infectious Diseases (October 12, 2020).

#### Key findings:

• 27% of homeless shelter residents and staff tested RT-PCR positive for SARS-CoV-2.

- $\circ$  Prevalence was higher for residents (30%, n = 431) than for staff (15%, n = 41).
- 72% of residents reported no symptoms at testing or within two weeks of testing.
- $\circ$   $\,$  13% of residents were hospitalized and 4% admitted to the ICU.
- Prevalence among residents was associated with:
  - Sharing a room with >20 people compared to having a single room (adjusted prevalence ratio [aPR] = 2.25, 95% CI 1.87-3.58).
  - A 1% increase in proportion of residents leaving shelter and returning each day (aPR = 1.08, 95% Cl 1.01-1.16).
  - Private bathrooms in the shelter were associated with reduced prevalence (aPR for 1 additional private bathroom per 100 people = 0.92, 95% CI 0.87-0.98).

**Methods**: SARS-CoV-2 point prevalence surveys were conducted at all Chicago homeless shelters with a reported case of COVID-19 in either a resident or staff member, from March 1 to May 1, 2020. Cases were confirmed by RT-PCR. Adjusted prevalence ratios for individual and facility-level risk factors were estimated. *Limitations:* Most data describing tested persons were self-reported; only ongoing infections were detected by PCR assays.

**Implications**: Modifying housing arrangements and limiting daily movement of residents in and out of shelters may reduce shelter associated SARS-CoV-2 infections.

#### **<u>COVID-19 and parent-child psychological well-being.</u> Gassman-Pines** *et al.* **Pediatrics (October 1, 2020).**

#### Key findings:

- Constant parental negative mood increased 29% (p < 0.05) and work disruption increased 122% (p < 0.001).
- 86% of families experienced hardships including loss of household income (69%), job loss (60%), increased caregiving burden (45%), and household illness (12%).
- Families experiencing hardship had worse psychological well-being.
  - Each individual hardship was associated with worse parental mood, p <0.05.
  - Increased caregiving burden and household illness were associated with children's uncooperative behavior and worry, both p-values <0.05.</li>
  - Families with 2–4 hardships had worse parental mood and sleep quality, and more uncooperative child behavior than those with no hardships, all p-values <0.05.
    - Families with all 4 hardships also had significantly more child worry, p <0.05.

**Methods**: Hourly service workers with a child 2–7 years of age were surveyed daily by SMS text message, between February and April 2020 (n = 8,222 person-days from 645 people), in one large US city. Between March and April 2020, a subsample (n = 561) completed a one-time survey on hardships (job loss, income loss, caregiving burden, household illness) and psychological wellbeing (parental mood, parental sleep quality, child uncooperative behavior, children's worry) experienced as a result of COVID-19. *Limitations*: Participation limited to hourly workers in retail, food service, and hotel industry with mobile phone access; conducted in one city limiting generalizability.

**Implications**: The COVID-19 crisis has substantially affected the well-being of hourly service workers and their children illustrating that these families may require additional social support for mental health.

#### **PREPRINT (NOT PEER-REVIEWED)**

SARS-CoV-2 sequencing reveals rapid transmission from college student clusters resulting in morbidity and deaths in vulnerable populations. Richmond *et al.* MedRxiv (October 14, 2020).

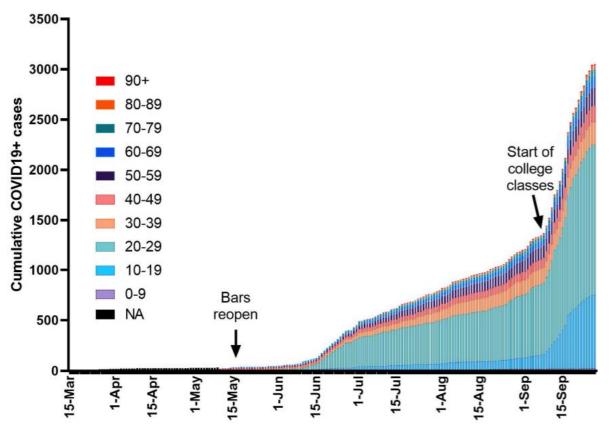
#### Key findings:

- A rapid increase in SARS-CoV-2 cases coincided with the return of college students to in-person instruction at three colleges in La Crosse, Wisconsin (Figure).
  - Growth in cases was concentrated in the immediate vicinity of the three colleges.
- Genomic sequencing revealed:
  - Majority of the increase was explained by two clusters, College A and College B.
  - 56.7% of isolates from College A and College B were from persons aged 17–29 years and 17.1% from persons ≥60 years.
  - Spread was rapid among persons aged 20–29 years.
  - College B cluster led to infections in two skilled nursing facilities infecting five patients and two staff and resulted in two patient deaths.

**Methods**: Surveillance between March 18 and September 23, 2020 of COVID-19 cases diagnosed by an integrated healthcare system providing care to area around La Crosse, WI with investigation of a rapid rise of cases in September 2020. Genomic sequencing was performed on viral isolates from 514 cases. <u>Limitations</u>: Unclear what incidence was prior to students' return to campus; case counts only from one health system and one college conducted diagnostic testing separately—neither captured all cases within the area; samples were not available for genomic sequencing and were not performed on all cases; investigation still ongoing.

**Implications**: Interim findings support an association between the start of college classes and increased SARS-CoV-2 cases among young adults, and also an increased risk of infection in older people in surrounding communities. Public health and university officials should consider the risks and develop plans to prevent SARS-CoV-2 outbreaks and community spread when reopening college campuses.

#### Figure:



*Note*: From Richmond *et al*. Cumulative SARS-CoV-2 case incidence in La Crosse County, WI, stratified by age group. Licensed under CC-BY-NC-ND 4.0.

## **Clinical Treatment & Management**

#### **PEER-REVIEWED**

<u>Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: A living systematic</u> <u>review</u>. Chai *et al*. Cochrane Database Systematic Reviews (October 12, 2020).

#### Key findings:

- There was low or very-low certainty evidence that convalescent plasma (CP) resulted in:
  - Decreased all-cause mortality at hospital discharge (risk ratio [RR] 0.55, 95% CI 0.22-1.34).
  - Decreased time-to-event mortality (hazard ratio 0.64, 95% CI 0.33-1.25).
  - Improved clinical symptoms (i.e., need for respiratory support):
    - Within 7 days after administration (RR 0.98, 95% CI 0.30-3.19).
    - Within 15 days (RR 1.34, 95% CI 0.85-2.11).
    - With 30 days (RR 1.13, 95% CI 0.88-1.43).
  - $\circ$   $\quad$  Increased risk of moderate to severe adverse events.

**Methods**: Major medical databases were searched for clinical studies on treatment with CP or hyperimmune immunoglobulin for persons with COVID-19. Nineteen studies with 38,160 participants (36,081 received CP) published prior to August 19, 2020 were identified. Meta-analyses were conducted to assess CP efficacy (2 randomized controlled trials [RCT]) and safety (2 RCTs, 8 controlled non-randomized studies (NSRI), and 9 non-

controlled NSRIs). <u>Limitations</u>: Few RCTs included; the assessment of potency of CP and hyperimmune immunoglobulin has not been well standardized; safety assessment limited due to limited numbers of controls; reporting of adverse events in reviewed studies varied.

**Implications**: Currently, there is little evidence that CP improves outcomes for persons with COVID-19. However, many trials are currently ongoing, including multiple RCTs, which will provide additional information. This Cochrane review is the second update of an ongoing review of CP efficacy and safety studies; subsequent updates may provide additional insight.

## Pulmonary function of patients with 2019 novel coronavirus induced-pneumonia: A retrospective cohort study. Lv *et al.* Annals of Palliative Medicine (September 11, 2020).

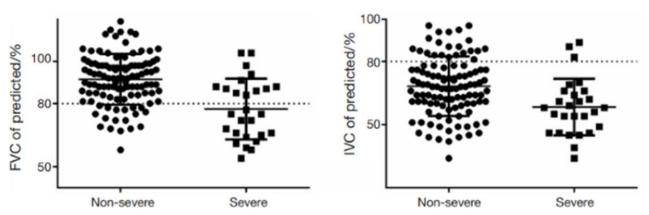
#### Key findings:

- 81% and 24% of patients had a post-discharge forced inspiratory volume (IVC, maximum volume of air that can be inspired after maximal expiration) or forced vital capacity (FVC, maximum volume of air that can be forcefully expired after maximal inspiration) below the predicted value, respectively (Figure).
  - IVC and FVC were significantly reduced in severe cases compared to non-severe cases, both p-values <0.05.
- Pulmonary function test results indicated decreased lung volume and small airway injury.

**Methods**: Retrospective, observational, single-center study conducted between January 31 and March 11, 2020. Pulmonary function tests were performed on 137 patients with history of SARS-CoV-2 pneumonia, two weeks after hospital discharge. Pulmonary function was compared in persons with history of non-severe (n = 110) and severe (n = 27, experienced respiratory distress, decreased oxygen saturation, or >50% progression of chest imaging lesion within 24–48 hours), COVID-19 when hospitalized. *Limitations:* Small sample size and short follow-up period.

**Implications**: The extent of potential long-term pulmonary effects after COVID-19 remains unknown. Similar to persons with influenza, some of whom have some level of pulmonary dysfunction post-recovery, these findings suggest that persons hospitalized for COVID-19 may need out-patient follow-up for pulmonary dysfunction.

Figure:



*Note*: Adapted from Lv *et al*. Pulmonary function parameters according to patient severity. Dotted line is the predicted normal value. Solid line is the mean value with 95% CI. Licensed under CC-BY-NC-ND 4.0.

#### **PREPRINT (NOT PEER-REVIEWED)**

Persistent symptoms after COVID-19: Qualitative study of 114 "long COVID" patients and draft quality criteria for services. Ladds et al. MedRxiv (October 14, 2020).

#### Key findings:

- Participants described their experience with COVID-19 as follows:
  - A frightening, confusing and debilitating illness often with relapsing-remitting symptoms.
  - Accessing care is complex, difficult and exhausting.
  - Interactions with healthcare providers who listened, believed, and effectively treated patients was less common than with providers who perceived symptoms as less serious or who failed to offer support.
  - Poor experience is exacerbated by absence of medical knowledge and guidance.
  - Emotional touch points included feelings of anger, frustration, fear, and hopelessness.

**Methods**: Qualitative data were gathered from 55 individual interviews, 8 focus groups (n = 59) and 11 symptom diaries between May and September 2020. Participants included persons from the UK with history of COVID-19 and symptoms lasting >3 weeks. Data were coded and analyzed according to sociological theories of illness experience, self-care, peer support, the clinical relationship, access to care, and service redesign. <u>Limitations:</u> Sample mainly female and white.

**Implications**: Healthcare providers should understand that patients' COVID-19 experience is physically and emotionally burdensome and care should involve compassionate communication and continuity of care.

### Laboratory Science

#### **PEER-REVIEWED**

<u>Cellular immunity in COVID-19 convalescents with PCR-confirmed infection but with undetectable</u> <u>SARS-CoV-2–specific IgG</u>. Schwarzkopf *et al.* Emerging Infectious Diseases (October 15, 2020).

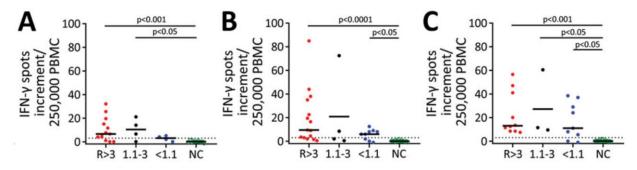
#### Key findings:

- 17% of potential convalescent plasma donors had borderline or negative IgG antibody titers to the SARS-CoV-2 S1 protein.
  - Of these, 78% showed T-cell responses against SARS-CoV-2.
    - The proportion with T-cell responses did not differ significantly from that of potential donors with high antibody titers (80%) but were substantially higher than those of negative controls (Figure).

**Methods**: Samples from 78 potential convalescent plasma donors, with history of PCR-confirmed SARS-CoV-2 infection were tested for IgG to SARS-CoV-2 S1 protein, up to 112 days post-symptom onset. Potential donors with strong antibody response (ratio of response in patient sample/negative control sample>3) were positive controls and participants with no symptoms of infection and no infected household contacts were negative controls. Interferon-γ ELISpot assay T-cell responses was used to determine T-cell responses. *Limitations:* Small sample in experimental test groups and participants biased toward healthy males with AB blood type.

Implications: In persons with minimal antibody response to SARS-CoV-2, immunity may be mediated by T-cells.

Figure:



*Note.* From Schwarzkopf *et al.* Cellular immunity against SARS-CoV-2 in potential convalescent plasma donors and negative controls (NC). Peripheral blood mononuclear cells of volunteers were stimulated by an S1 protein antigen of SARS-CoV-2 (**A**), peptide pools of S1/S2 (**B**) and membrane protein antigen of SARS-CoV-2 (**M**) (**C**). Each data point represents a serum sample: antibody ratio (**R**)>3 (n = 15), antibody ratio of 1.1–3 (n = 4), antibody ratio of <1.1 (n = 9), NC (n = 22). Dotted lines represent cutoff for a positive test. Horizontal solid black lines indicate median values. Open access journal; all content freely available.

## Orthogonal SARS-CoV-2 serological assays enable surveillance of low prevalence communities and reveal durable humoral immunity. Ripperger *et al.* Immunity (October 14, 2020).

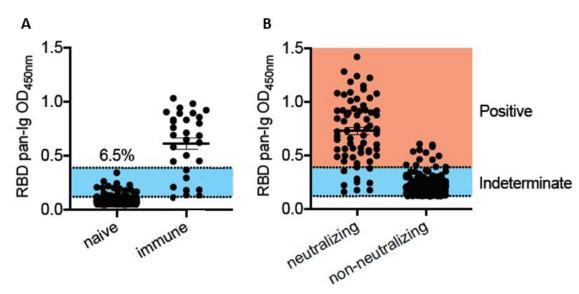
**Key findings:** 

- 6.5% of the negative control group were reactive for SARS-CoV-2 antibodies to the receptor binding domain (RBD) of the spike protein (Figure 1A).
- 13 of 73 samples (17.8%) with anti-RBD reactivity failed to neutralize SARS-CoV-2 (Figure 1B).
- If neutralization is considered the true measure of prior SARS-CoV-2 infection, the positive predictive value of anti-RBD reactivity alone was 82%.
- IgG antibody titers to SARS-CoV-2 S2 protein correlated well with neutralizing titers (Figure 2).
- Orthogonal testing with anti-RBD *and* anti-S2 achieved an empirically defined false positive rate of 0.02%.

**Methods:** To validate assay performance, testing for antibodies to RBD, N and S and neutralizing activity was performed using samples from 5,882 community volunteers from a low seroprevalence area, 129 persons with COVID-19 and 320 samples obtained prior to 2020. <u>Limitations:</u> May have missed individuals who seroreverted by time community cohort was tested; follow up limited to a maximum of 226 days.

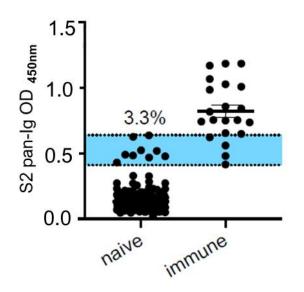
**Implications:** Because the positive predictive value of a test may be poor in low prevalence communities and serologic testing may not predict neutralization capacity, use of multiple independent assays may predict neutralization capacity and minimize false positive results.





*Note:* Adapted from Ripperger *et al.* **A:** Pan anti-RBD levels (IgA, IgG and IgM) expressed as an optical density (OD) measurement in samples from 352 pre-2020 negative controls (naïve) and 30 SARS-CoV-2 exposed individuals (immune). The **blue region** indicates overlap of OD values between negative and positive control samples and % indicates frequency of negative control values in this range. **B:** PRNT90 (plaque reduction neutralization test at which 90% viral neutralization occurred) analysis from community samples that displayed indeterminate or positive anti-RBD seroreactivity. Samples that neutralized 90% of virions were considered positive. Error bars depict mean values of data sets +/- standard error of the mean. Permission request in process.

Figure 2



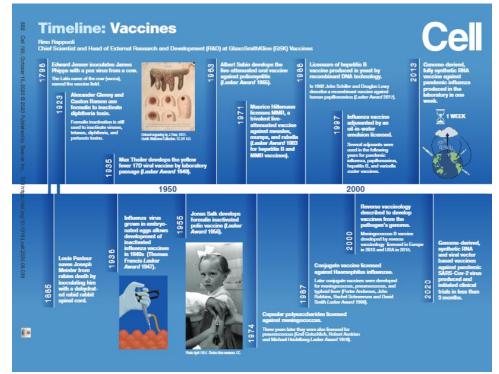
*Note:* Adapted from Ripperger *et al.* Assessment of anti-S2 as secondary confirmation of seropositivity. Pan anti-S2 levels (IgA, IgG and IgM) expressed as an optical density (OD) measurement. The **blue region** indicates overlap between negative (naïve) and positive controls (immune) and % indicates frequency of negative control values in this range. Permission request in process.

## In Brief

#### Vaccines

- Goodman *et al*. <u>Answering key questions about COVID-19 vaccines</u>. JAMA. Authors answer frequent questions about safety, efficacy and other issues concerning potential SARS-CoV-2 vaccines.
- Warren *et al.* <u>Trustworthiness before trust COVID-19 vaccine trials and the Black community</u>. NEJM.
  Overview of historic reasons why some in the black community are skeptical of the medical establishment and that trust will not be built before these institutions prove themselves to be trustworthy.
- Krause & Gruber. Emergency use authorization of COVID vaccines Safety and efficacy follow-up considerations. NEJM. Authors argue that long-term assessment of COVID-19 vaccines safety and efficacy will require continued data gathering under FDA Emergency Use Authorization after vaccines are made available.
- Lee *et al*. Post approval vaccine safety surveillance for COVID-19 vaccines in the US. JAMA. Authors argue a combination of passive, enhanced-passive, active and novel approach to surveillance and harmonized safety endpoints will be necessary to monitor safety of COVID-19 vaccines.
- Rappuoli, R. <u>Timeline: Vaccines.</u> Cell. Infographic of timeline of important vaccine events.

#### Figure:



Note: From Rappuoli, R. Timeline of vaccine development from 1796 to 2020. Permission request in process.

#### Travel

- Freedman & Wilder-Smith. In-flight transmission of SARS-CoV-2: A review of the attack rates and available data on the efficacy of face masks. Journal of Travel Medicine. Review summarizing all peer-reviewed or public health publications of flights with likely, possible or unproven in-flight SARS-CoV-2 transmission.
- Brewster et al. <u>Lessons learned for COVID-19 in the cruise ship industry</u>. Toxicology and Industrial Health. An overview of the US government and cruise ship industry's COVID-19 response with lessons learned and recommendations.

#### Miscellaneous

Goldstein, J. <u>The Spanish 1918 flu and the COVID-19 disease: The art of remembering and foreshadowing pandemics.</u> Cell. Author looks back on how the 1918 influenza pandemic affected the mood, tone and themes of art in the early-mid 20<sup>th</sup> century and contemplates how art will be affected by COVID-19.

#### Figure:



Note: From Goldstein, J. John Singer Sargent. Interior of a Hospital Tent. 1918. Permission request in process.

- Glenn *et al*. <u>Refusals after prehospital administration of naloxone during the COVID-19 pandemic</u>.
  Prehospital Emergency Care. Naloxone refusal after non-fatal opioid overdose in a pre-hospital system, before and during the pandemic.
- Atlani-Duault *et al.* COVID-19: France grapples with the pragmatics of isolation. Lancet Public Health. Author summarizes France's COVID-19 Scientific Council recommendations to reduce the mandatory quarantine period to 7 days and to offer incentives to promote adherence to COVID-19 regulations.
- Van Vinh Chau et al. Superspreading event of SARS-CoV-2 infection at a bar, Ho Chi Minh City, Vietnam.
  Emerging Infectious Diseases. Report of a SARS-CoV-2 superspreading event initiated at a bar in Vietnam with evidence of symptomatic and asymptomatic transmission.

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