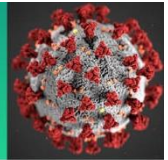


COVID-19 Science Update



From the Office of the Chief Medical Officer, CDC COVID-19 Response, and the CDC Library, Atlanta, GA.
Intended for use by public health professionals responding to the COVID-19 pandemic.

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Section headings in the COVID-19 Science Update align with the [CDC Science Agenda for COVID-19](#).

Prevention, Mitigation and Intervention Strategies

PEER-REVIEWED

[Vaccination and non-pharmaceutical interventions for COVID-19: a mathematical modelling study.](#)

Moore *et al.* The Lancet Infectious Diseases (March 18, 2021).

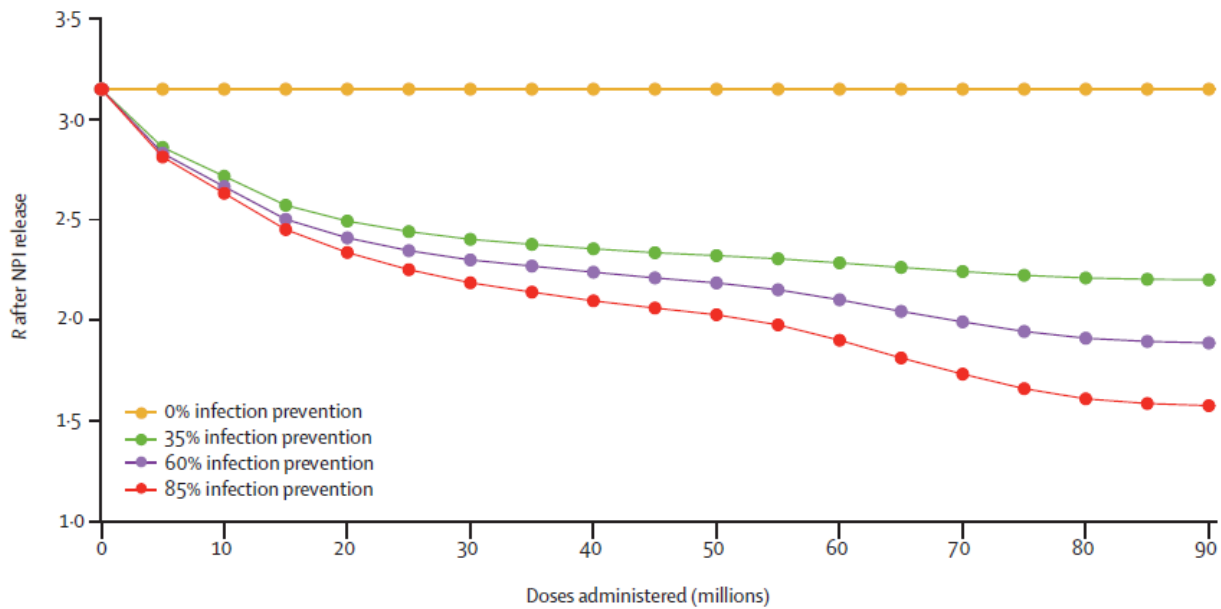
Key findings:

- R is projected to remain >1 under all scenarios of vaccine efficacy scenarios (Figure 1):
 - With the rollback of NPIs and most optimistic (85%) efficacy against infection, $R = 1.58$ (95% credibility interval [CI] 1.36-1.83).
- Projected COVID-19 deaths under default uptake scenarios and removal of NPIs once all adults have received 2 vaccine doses:
 - 21,400 deaths (95% CI 1,400-55,100) for a vaccine that prevents 85% of infections.
 - 96,700 deaths (95% CI 51,800-173,200) for a vaccine that prevents 60% of infections.

Methods: A “susceptible-exposed-infected-recovered” (SEIR) model was fitted to UK epidemiological data to evaluate the effect of the UK vaccine rollout combined with lifting non-pharmaceutical interventions (NPI) to predict the reproduction number (R), COVID-19 daily deaths and hospital admissions between January 2021 and January 2024. Default assumptions for vaccine efficacy for symptomatic disease was 88% and vaccine uptake by age ranged from 75%–95%. The model also considered vaccine efficacy against infection which was varied from 0 to 85% and the spread of B.1.1.7. **Limitations:** Not considered: effects of waning immunity; variants of concern (VOCs) that escape immune response; varying vaccine efficacy by age.

Implications: Vaccination alone is unlikely to contain SARS-CoV-2. Gradual easing of non-pharmaceutical interventions in addition to high population uptake of a high-efficacy vaccine are necessary to prevent subsequent waves of infection. Monitoring of VOCs such as those that escape immune response (e.g., E484K mutation) will be necessary.

Figure:



Note: Adapted from Moore *et al.* Estimated reproduction number (R) after NPI release for a given number of administered doses for 4 vaccine scenarios with varying infection prevention efficacy: 0%, 35%, 60%, and 85%. Model excludes any additional increase in immunity from natural infection (after 1/29/2021) and any effect on contact patterns resulting from NPIs. Licensed under CC-BY-NC-ND.

[Impact of the COVID-19 vaccine on asymptomatic infection among patients undergoing pre-procedural COVID-19 molecular screening.](#) Tande *et al.* Clinical Infectious Diseases (March 10, 2021).

Key findings:

- Vaccinated persons had a 65% reduction in risk for asymptomatic SARS-CoV-2 infection during a pre-procedure screening compared to unvaccinated patients (adjusted relative risk [aRR] = 0.35, 95% CI 0.26-0.47).
- Vaccinated persons had an 80% reduction in risk for asymptomatic SARS-CoV-2 infection after either (1) testing >10 days post first dose (aRR = 0.21, 95% CI 0.12-0.37) or (2) testing after 2 doses (aRR = 0.20, 95% CI 0.09-0.44) of mRNA vaccine, compared to unvaccinated persons.

Methods: Retrospective cohort study of consecutive, adult patients (N = 39,156) asymptomatic for COVID-19 within a large US healthcare system who underwent pre-procedural SARS-CoV-2 screening between December 17, 2020, and February 8, 2021. Primary exposure was vaccination with at least one dose of Pfizer-BioNTech or Moderna vaccine prior to screening (median time from first dose to screening = 16 days). Adjusted relative risk (aRR) of positive SARS-CoV-2 molecular test was calculated adjusting for age, sex, race/ethnicity, and patient residence in Health Referral Region (local vs. non-local). **Limitations:** Unmeasured confounding among vaccinated individuals; generalizability may be limited as study participants were largely non-Hispanic white and <65 years; no longitudinal follow-up on symptom status post-procedure.

Implications: This study provides real-world evidence of a decrease in asymptomatic infection after vaccination with a mRNA vaccine and should be considered in developing post-vaccination policy recommendations.

[Efficacy of the ChAdOx1 nCoV-19 Covid-19 vaccine against the B.1.351 variant.](#) Madhi *et al.* NEJM (March 16, 2021).

Key findings:

- Primary end-point analysis: Overall vaccine efficacy against mild-to-moderate COVID-19 was 21.9% (95% CI -49.9%-59.8%).
- Secondary end-point analysis among participants who developed mild to moderate COVID-19, 39 (92.9%) were infected with B.1.351:
 - Efficacy of a 2-dose ChAdOx1 nCoV-19 vaccine regimen against the B.1.351 variant was not evident (efficacy = 10.4%, 95% CI: -76.8%-54.8%).
- The vaccine induced strong neutralizing antibody levels against original D614G virus on pseudovirus neutralization assay 14 days after second vaccine dose.

Methods: Double-blind, multicenter RCT in South Africa (between June 24 and November 9, 2020) was conducted to assess ChAdOx1 nCoV-19 (AstraZeneca-Oxford), primary efficacy analysis for vaccine efficacy (vaccine n = 750, placebo n = 717). Efficacy against B.1.351 analyzed in secondary endpoint analysis among 42 participants who developed COVID-19. Serum samples collected from 25 persons after having received the second vaccine dose were tested for neutralizing activity. **Limitations:** Lack of severe COVID-19 cases prevents conclusions around severe illness; limited generalizability.

Implications: The lack of efficacy of ChAdOx1 nCoV-19 against mild to moderate COVID-19 associated with the B.1.351 variant suggests that second generation vaccinations or boosters may be needed to address emerging variants of concern.

Detection, Burden, and Impact

Increased Mortality Associated with B.1.1.7 Variant

PEER-REVIEWED

The SARS-CoV-2 variant of concern B.1.1.7 that was first identified in the UK in the fall of 2020 has become the dominant strain in the UK and parts of Europe and is increasing in prevalence across the US. The B.1.1.7 variant has been associated with increased transmission compared to the wild type lineage. The following two studies present findings regarding increased mortality of B.1.1.7.

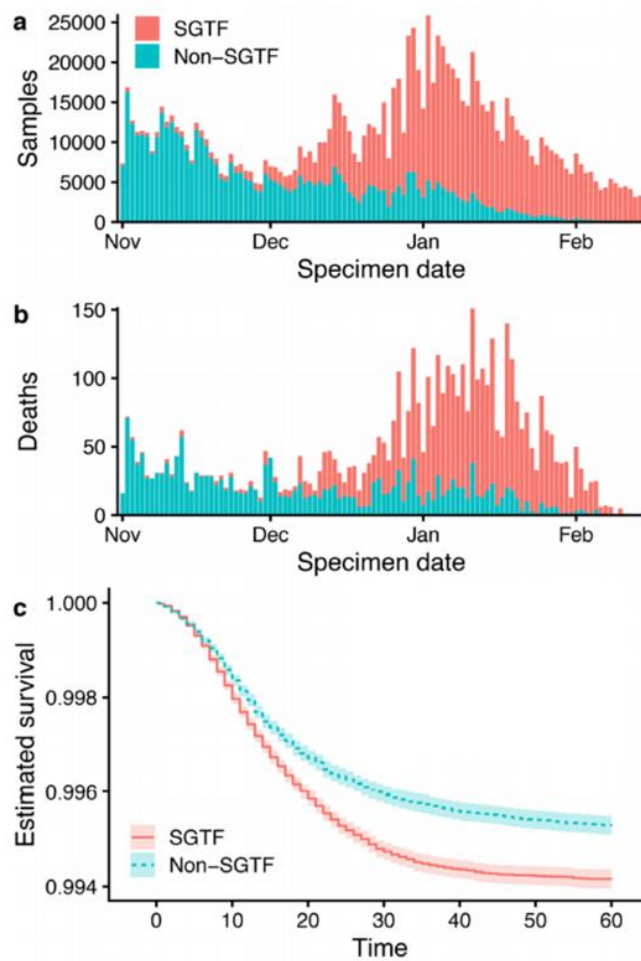
A. [Increased mortality in community-tested cases of SARS-CoV-2 lineage B.1.1.7.](#) Davies *et al.* Nature (March 15, 2021).

Key findings:

- Prevalence of spike gene target failure (SGTF), associated with B.1.1.7 infection, increased steeply over time, from 5.8% in November 2020 to 94.3% in February 2021 (Figure panel a).
- B.1.1.7 is associated with increased mortality compared to other SARS-CoV-2 variants (hazard ratio = 1.61, 95% CI 1.42-1.82), after correcting for missing data/misclassification of SGTF weighting). (Figure panels b, c)

Methods: Analysis of a dataset containing 2,245,263 positive SARS-CoV-2 PCR tests and 17,642 COVID-19 deaths from community-based testing in England between September 1, 2020 and February 14, 2021. Identification of the B.1.1.7 variant in infected individuals was confirmed by spike gene target failure status (SGTF). Absolute mortality risks and hazard of death were calculated after confirmation of SGTF status in numerous demographic subsets. **Limitations:** Could not completely assess SGTF status within study population; non-random sample.

Figure:



Note: Adapted from Davies *et al.* a) The number of samples **with SGTF** and **without SGTF** by day from November 1, 2020–February 14, 2021; b) Number of deaths within 28 days of positive test by specimen date **with SGTF** and **without SGTF**; and c) Kaplan-Meier plot showing survival (95% confidence intervals) among individuals who were community-tested **with SGTF** and **without SGTF**. Permission request in process.

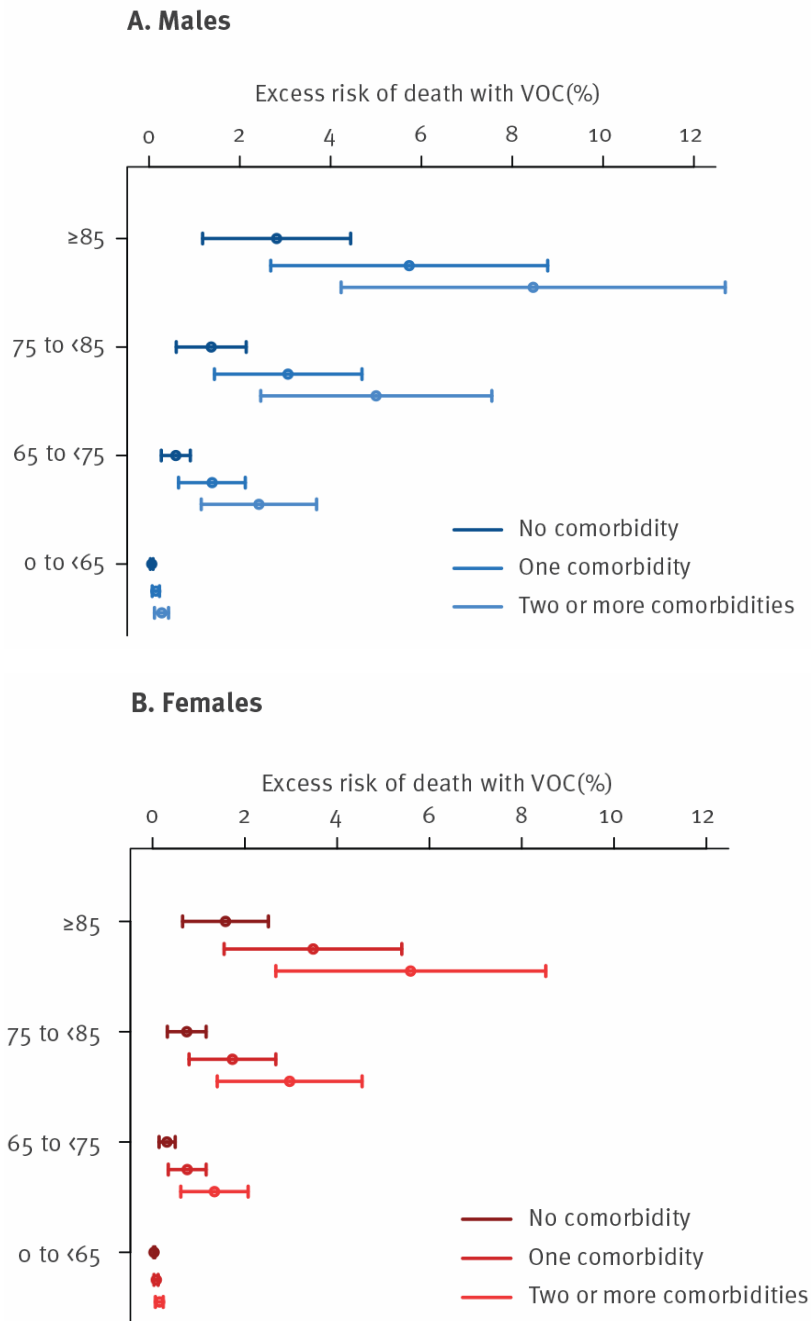
B. [Case fatality risk of the SARS-CoV-2 variant of concern B.1.1.7 in England, 16 November to 5 February.](#) Grint *et al.* Eurosurveillance (March 18, 2021).

Key findings:

- Risk of death was greater (adjusted hazard ratio 1.67, 95% CI 1.34-2.09) among individuals with confirmed B.1.1.7 variant of concern compared with individuals with non-B.1.1.7 SARS-CoV-2.
- 28 days after a SARS-CoV-2-positive test, individuals with B.1.1.7 had a higher absolute risk of death compared with non-B.1.1.7 SARS-CoV-2 in all groups stratified by sex, age, and presence of comorbidities (Figure):
 - Risk of death was higher for males and increased with age and comorbidities.
 - Those ≥85 years with ≥2 comorbidities had the highest risk of death.

Methods: Cohort study among (n = 184,786) unvaccinated persons testing positive for SARS-CoV-2 between November 16, 2020, and January 11, 2021, in England. Spike gene target failure was used as a proxy for B.1.1.7 identification. **Limitations:** Selection bias might overestimate absolute mortality risks (if people with mild or asymptomatic infections were less likely to be tested); lead-time bias might underestimate relative mortality associated with B.1.1.7 given this variant was more prevalent later in the study period.

Figure:



Note: Adapted from Grint *et al.* Excess risk of death by 28 days after positive test comparing SARS-CoV-2 VOC infection with non-VOC infection among **males** (A); and among **females** (B). Licensed under CC BY 4.0.

Implications for both studies (Davies *et al.* and Grint *et al.*): Both studies were consistent with [Challen *et al.*](#), regarding the magnitude (~60%–70%) of the increased risk of mortality associated with the B.1.1.7 variant

compared with other SARS-CoV-2 lineages such as the wild type. Other analyses indicating increased transmissibility of B.1.1.7 as well as the increasing spread of B.1.1.7 within the US highlight the need for rapid implementation of vaccination and continued implementation of non-pharmaceutical mitigation measures.

PREPRINTS (NOT PEER-REVIEWED)

[A potential SARS-CoV-2 variant of interest \(VOI\) harboring mutation E484K in the spike protein was identified within lineage B.1.1.33 circulating in Brazil.](#) Resende *et al.* bioRxiv (March 13, 2021).

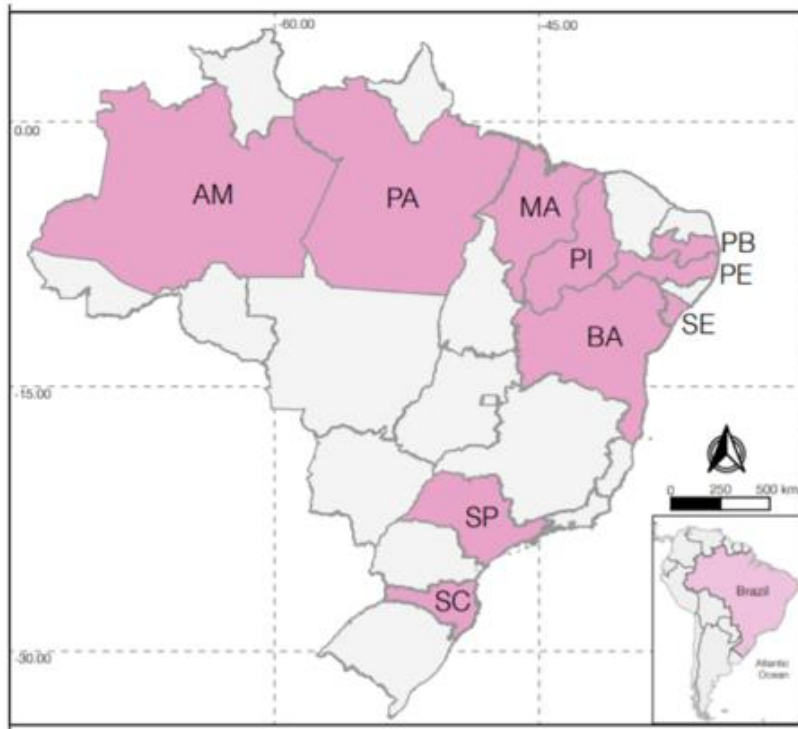
Key findings:

- A new SARS-CoV-2 variant of interest (VOI) N.9, within lineage B.1.1.33, with 4 non-synonymous lineage-defining mutations (NSP3:A1711V, NSP6:F36L, S:E484K, and NS7b:E33A), was detected in Brazil between November 2020 and February 2021.
- N.9 probably emerged in the Summer of 2020 (estimated to be August 15, 2020; 95% High Posterior Density June 16–September 22, 2020), and has been identified in 10 different Brazilian states (Figure).

Methods: The [nextclade tool](#) was used to identify B.1.1.33 lineage mutations among SARS-CoV-2 samples from Brazil sequenced by the Fiocruz COVID-19 Genomic Surveillance Network between March 12, 2020, and January 27, 2021; or that were available in [Global Initiative on Sharing All Influenza Data](#) as of March 1, 2021. Used Bayesian reconstruction to estimate timing of VOI N.9 emergence. **Limitations:** Effects of VOI N.9 on transmission, severity, diagnosis, and treatment of SARS-CoV-2 are unknown.

Implications: The E484K mutation has been associated with resistance to monoclonal antibodies and reduced neutralization potency of sera from convalescent and vaccinated individuals. The rapid dispersion of VOI N.9 across Brazil and the presence of the E484K mutation warrant monitoring for evidence of impact on effectiveness of treatments and vaccines, and surveillance for further spread, including in the US.

Figure:



Note: Adapted from Resende *et al.* Geographic distribution of the VOI N.9 identified in Brazil (states are abbreviated per the ISO standard). Licensed under CC-BY-ND 4.0.

Natural History of SARS-CoV-2 Infection

PEER-REVIEWED

[Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study.](#) Hansen *et al.* The Lancet (March 17, 2021).

Key findings:

- Overall protection against repeat infection for those previously infected was 78.8% (95% CI 74.9-82.1%).
 - Protection was 47.1% (95% CI 24.7-62.8) among those aged ≥65 years, 81.3% (95% CI 72.6-87.3) among those aged 50–64 years, 80.1% (95% CI 71.8-85.9) among those aged 35–49 years, and 82.7% (95% CI 77.1-86.9) among those aged 0-34 years.
 - There were no differences in estimated protection against repeat infection by sex or evidence of waning protection over time (3–6 vs. ≥7 months of follow-up).

Methods: Analysis of Danish population-level cohort (n = 2,432,509) tested for SARS-CoV-2 by RT-PCR between February 26 and December 31, 2020. Calculated rate ratios (RRs) for persons testing positive among those with a positive or negative test ≥3 months earlier, adjusted for potential confounders. Estimated protection against repeat infection (1-RR). Findings pertain to the alternative cohort analysis that includes data from both surges.

Limitations: Potential selection bias in obtaining testing based on presumed risk; misclassification based on imperfect sensitivity and specificity of RT-PCR tests or on persistent infections counted as reinfections; unknown applicability of findings to reinfections with new SARS-CoV-2 variants.

Implications: Findings support vaccination of previously infected individuals because natural protection is robust but not absolute. Persons ≥65 years, even if previously infected, should receive enhanced protective measures including vaccination.

Transmission

PEER-REVIEWED

[Household SARS-CoV-2 transmission and children: a network prospective study.](#) Soriano-Arandes *et al.* Clinical Infectious Diseases (March 12, 2021).

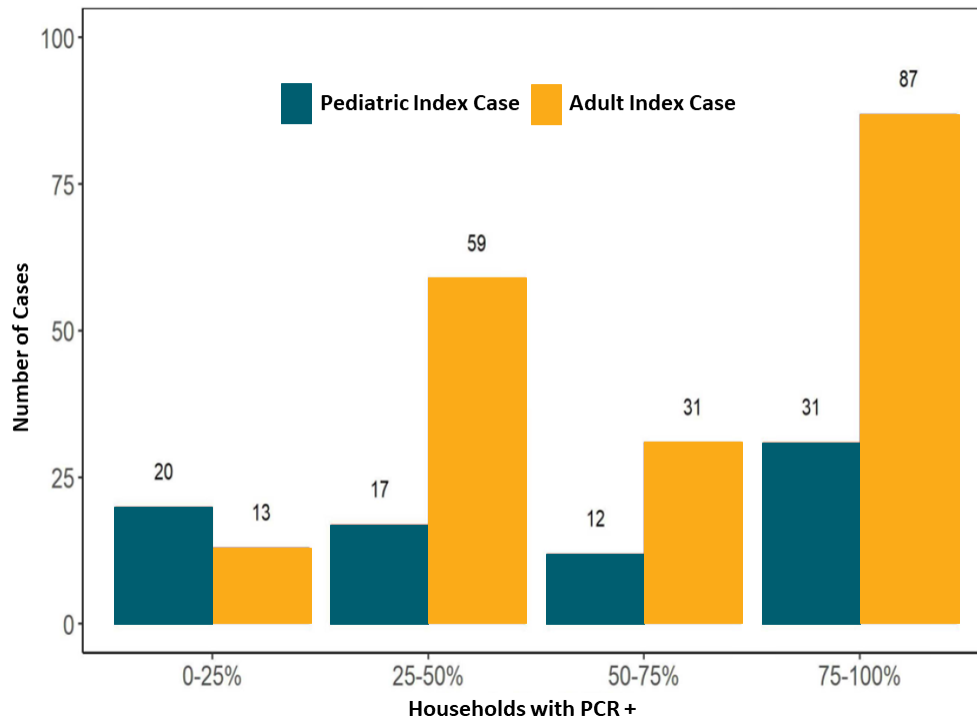
Key findings:

- SARS-CoV-2 transmission occurred in 62% of household contacts.
 - 80 (7.7%) children were household index cases (Figure).
 - 756 (72%) pediatric COVID-19 cases were secondary to an adult case.
- Secondary attack rate (SAR) was significantly lower in households with pediatric vs. adult index cases (59.0% vs. 67.6%, p = 0.006).
 - Among pediatric index cases, SAR was lower during the school period vs. the summer period (53.0% vs. 64.4%, p = 0.02).

Methods: Spanish prospective observational study of SARS-CoV-2 household transmission in children (<16 years) with COVID-19 (n = 1,040) and household contacts (n = 3,392); data were collected between July 1 and October 31, 2020. Index case was defined as first member of the household to develop symptoms or test positive for SARS-CoV-2. Two study periods were established, summertime (July 1–September 15) and school time (September 16–October 31). **Limitations:** Pediatric cases did not include children ≥16 years; index case definition may lead to underestimation of contribution of asymptomatic individuals; findings may be dependent of variant distribution at time of study.

Implications: Children, whether symptomatic or not, do not greatly contribute to household clusters of infection and are unlikely to be major drivers of the pandemic even if attending school.

Figure:



Note: Adapted from Soriano-Arandes *et al.* Percentage of positive SARS-CoV-2 RT-PCRs (pediatric vs. adult) in household by the age of the index cases. Permission request in process.

PREPRINTS (NOT PEER-REVIEWED)

[An observational cohort study on the incidence of SARS-CoV-2 infection and B.1.1.7 variant infection in healthcare workers by antibody and vaccination status.](#) Lumley *et al.* medRxiv (March 12, 2021).

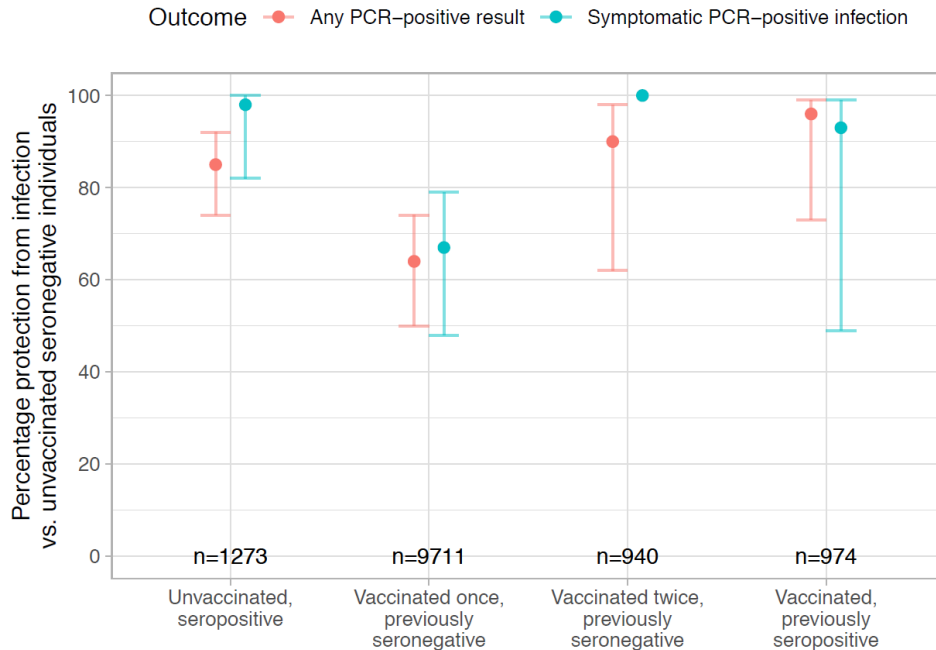
Key findings:

- Either 2 vaccine doses or natural infection provided $\geq 85\%$ protection against symptomatic and asymptomatic SARS-CoV-2 infection in healthcare workers (Figure):
 - 2 vaccine doses: 90% lower incidence (0.10 adjusted incident rate ratio [aIRR], 95% CI 0.02-0.38); natural infection: 85% lower incidence (aIRR 0.15, 95% CI 0.08-0.26).
- Single-dose vaccination reduced the incidence of symptomatic infection by 67% (aIRR 0.33, 95% CI 0.21-0.52) and any PCR-positive result by 64% (aIRR 0.36, 95% CI 0.26-0.50).
- No evidence of differences in immunity induced by natural infection and vaccination for infections with S-gene target failure and the circulating variant, B.1.1.7.

Methods: Longitudinal cohort study of 1 versus 2 dose vaccine effectiveness among healthcare workers in England ($n = 13,109$) between April 23, 2020, and February 28, 2021. Vaccines include BNT162b2 (Pfizer-BioNTech; $n = 8,285$) and ChAdOx1 nCoV-19 (Oxford AstraZeneca; $n = 2,738$). The Thermo Fisher TaqPath PCR diagnostic assay was used to determine gene target failure, indicative of B.1.1.7. Incident rate calculated using Poisson regression model, adjusting for age, sex, occupational role, and temporal changes in incidence. **Limitations:** Findings might not be generalizable to the population; priority was given to staff who were at greater risk of SARS-CoV-2 infection; limited power to detect differences between vaccines.

Implications: Natural infection resulting in detectable antibodies and two vaccine doses provide protection against SARS-CoV-2 (re)infection, including against the B.1.1.7 variant. These findings could help inform post vaccination policies.

Figure:



Note: Adapted from Lumley *et al.* Protection from infection by antibody and vaccination status, compared with seronegative individuals. Outcomes were either **any PCR positive result** or **symptomatic PCR positive infection**. The number of healthcare workers in each follow up group is shown. 95% confidence intervals are plotted, except for previously seronegative HCWs vaccinated twice who had no symptomatic PCR confirmed infections. Licensed under CC-BY 4.0.

In Brief

Detection, Burden, and Impact

- Haage *et al.* [Impaired performance of SARS-CoV-2 antigen-detecting rapid tests at elevated and low temperatures](#). Journal of Clinical Virology (March 16, 2021). When exposed to elevated temperatures, even short term, the sensitivity of currently available SARS-CoV-2 rapid antigen-detecting tests (Ag- RDT) is comprised, while exposure to low temperatures limits specificity. Recommended temperatures should always be maintained.
- Gershengorn *et al.* [Association of race and ethnicity with COVID-19 test positivity and hospitalization is mediated by socioeconomic factors](#). Annals of the American Thoracic Society (March 15, 2021). In a retrospective cohort study in Miami (March–July 2020), racial and ethnic disparities in COVID-19 incidence and outcomes were found to be mediated by socioeconomic factors, including population density at the patient’s home address, median income, and household size.

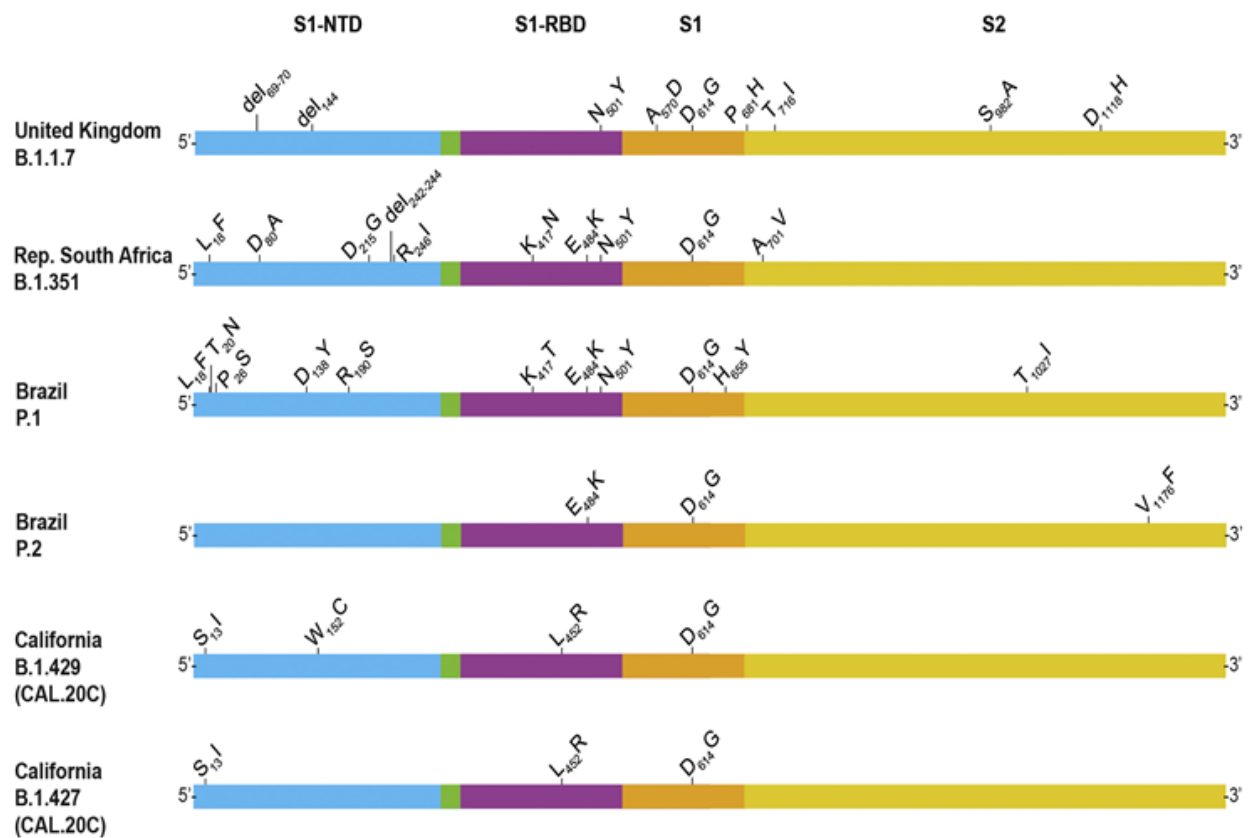
Natural History of SARS-CoV-2 Infection

- Sandberg *et al.* [Longitudinal characterization of humoral and cellular immunity in hospitalized COVID-19 patients reveal immune persistence up to 9 months after infection](#). bioRxiv (Preprint, March 17, 2021). In

both moderate and severe COVID-19 patients, neutralizing antibody titer, memory B cell response, and polyfunctional T cell responses were present 5 and 9 months after symptom onset, potentially providing long-term protection against reinfection.

- Long *et al.* [Sequence analysis of 20,453 SARS-CoV-2 genomes from the Houston metropolitan area identifies the emergence and widespread distribution of multiple isolates of all major variants of concern](#). The American Journal of Pathology (March 16, 2021). Multiple variants of concern, including the UK (B.1.1.7), South African (B.1.351), and Brazil (P.1) variants, contain large numbers of spike protein region mutations (Figure). These mutations have been associated with increased transmissibility, and in some cases may be associated with increased hospitalization and mortality (B.1.1.7).

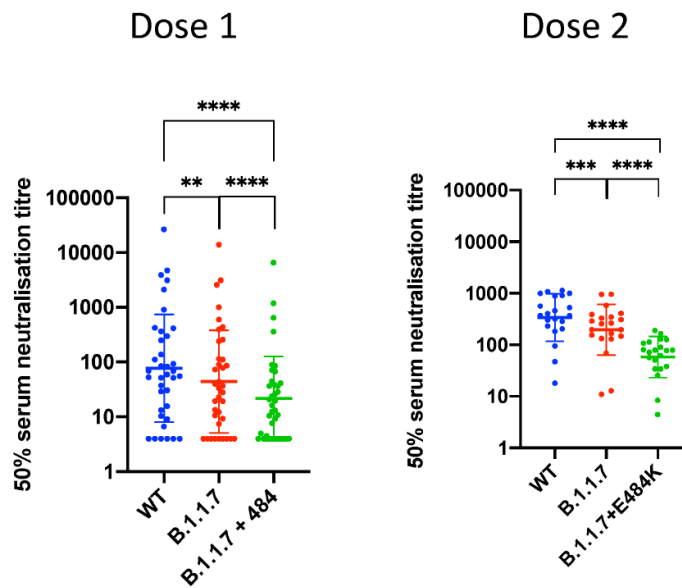
Figure:



Note: Adapted from Long *et al.* Schematic showing structural changes present in the spike protein domains of major SARS-CoV-2 variants (S1-NTD, S1-RBD, S1, and S2). Reprinted from The American Journal of Pathology, online ahead of print. Long *et al.*, Sequence analysis of 20,453 SARS-CoV-2 genomes from the Houston metropolitan area identifies the emergence and widespread distribution of multiple isolates of all major variants of concern. Copyright ©2021, with permission from Elsevier Inc. on behalf of the American Society for Investigative Pathology.

- Collier *et al.* [Sensitivity of SARS-CoV-2 B.1.1.7 to mRNA vaccine-elicited antibodies](#). Nature (March 11, 2021). Modest decreases in vaccine-elicited antibodies against the B.1.1.7 variant were observed compared to the wild type; when the E484K mutation was introduced in B.1.1.7, there was a greater loss of neutralizing activity (Figure).

Figure:

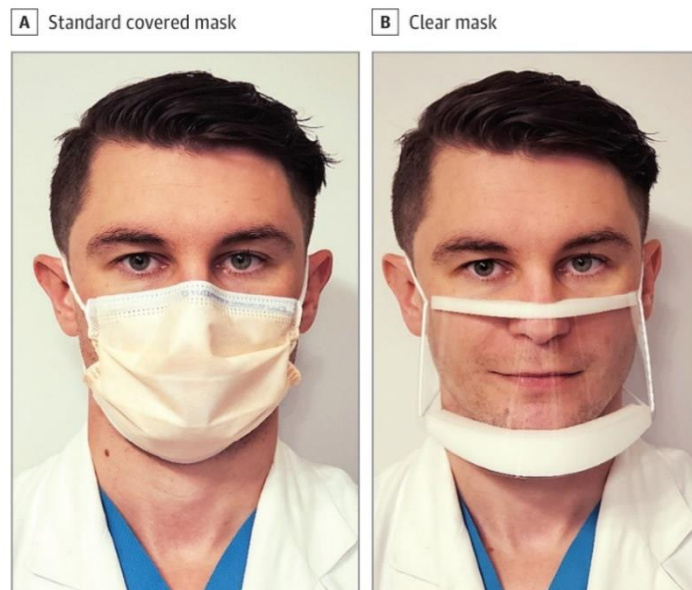


Note: Adapted from Collier *et al.* Neutralization potency of mRNA vaccine sera (pre-SARS-CoV-2 B.1.1.7) against pseudovirus bearing spike mutation in the **B.1.1.7 lineage** and **B.1.1.7 lineage with E484K mutation** in the receptor binding domain. Vaccine dose 1 (n = 37) and vaccine dose 2 (n = 21) compared to **wild-type**. Wilcoxon matched pairs signed rank test p-values: **<.01, ***<.0001, ****<.00001). Permission request in process.

Protection in Healthcare and Non-Healthcare Work Settings

- Kratzke *et al.* [Effect of clear vs standard covered masks on communication with patients during surgical clinic encounters: A randomized clinical trial.](#) JAMA Surgery (March 11, 2021). In a randomized clinical trial of 200 patients, surgeons wearing clear masks, rather than standard covered masks, were rated significantly higher in empathy, trust, and in providing understandable explanations (Figure).

Figure:



Note: Adapted from Kratzke *et al.* Reproduced with permission from JAMA Surgery. 2021. Published online March 11, 2021. doi:10.1001/jamasurg.2021.0836. Copyright©2021 American Medical Association. All rights reserved.

- Sheehan *et al.* [Reinfection rates among patients who previously tested positive for COVID-19: a retrospective cohort study](#). *Clinical Infectious Diseases* (March 15, 2021). In a retrospective cohort of 150,000 patients from a multi-hospital system in Ohio and Florida, prior SARS-CoV-2 was 82% protective against asymptomatic infection and 85% protective against symptomatic infection, increasing over time.

Prevention, Mitigation, and Intervention Strategies

- Arnold *et al.* [Are vaccines safe in patients with Long COVID? A prospective observational study](#). medRxiv (Preprint, March 14, 2021). Many patients with long COVID have expressed vaccine hesitancy due to concerns that vaccine might worsen associated symptoms; in this matched observational cohort study among previously hospitalized patients with persistent symptoms, vaccination was not associated with worsening of symptoms, quality of life, or mental well-being.
- Rottenstreich *et al.* [Efficient maternofetal transplacental transfer of anti-SARS-CoV-2 spike antibodies after antenatal SARS-CoV-2 BNT162b2 mRNA vaccination](#). medRxiv (Preprint, March 12, 2021). SARS-CoV-2 mRNA vaccination administered to a cohort of 20 women during pregnancy induced adequate serologic response with subsequent transplacental transfer.

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