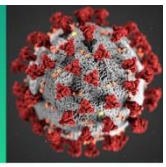
COVID-19 Science Update



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Intended for use by public health professionals responding to the COVID-19 pandemic.

***** Available on-line at https://www.cdc.gov/library/covid19 *****

Section headings in the COVID-19 Science Update align with the CDC Science Agenda for COVID-19.

Detection, Burden, and Impact

PEER-REVIEWED

Farmer and farm worker illnesses and deaths from COVID-19 and impacts on agricultural output. Lusk *et al.* PLoS One (April 28, 2021).

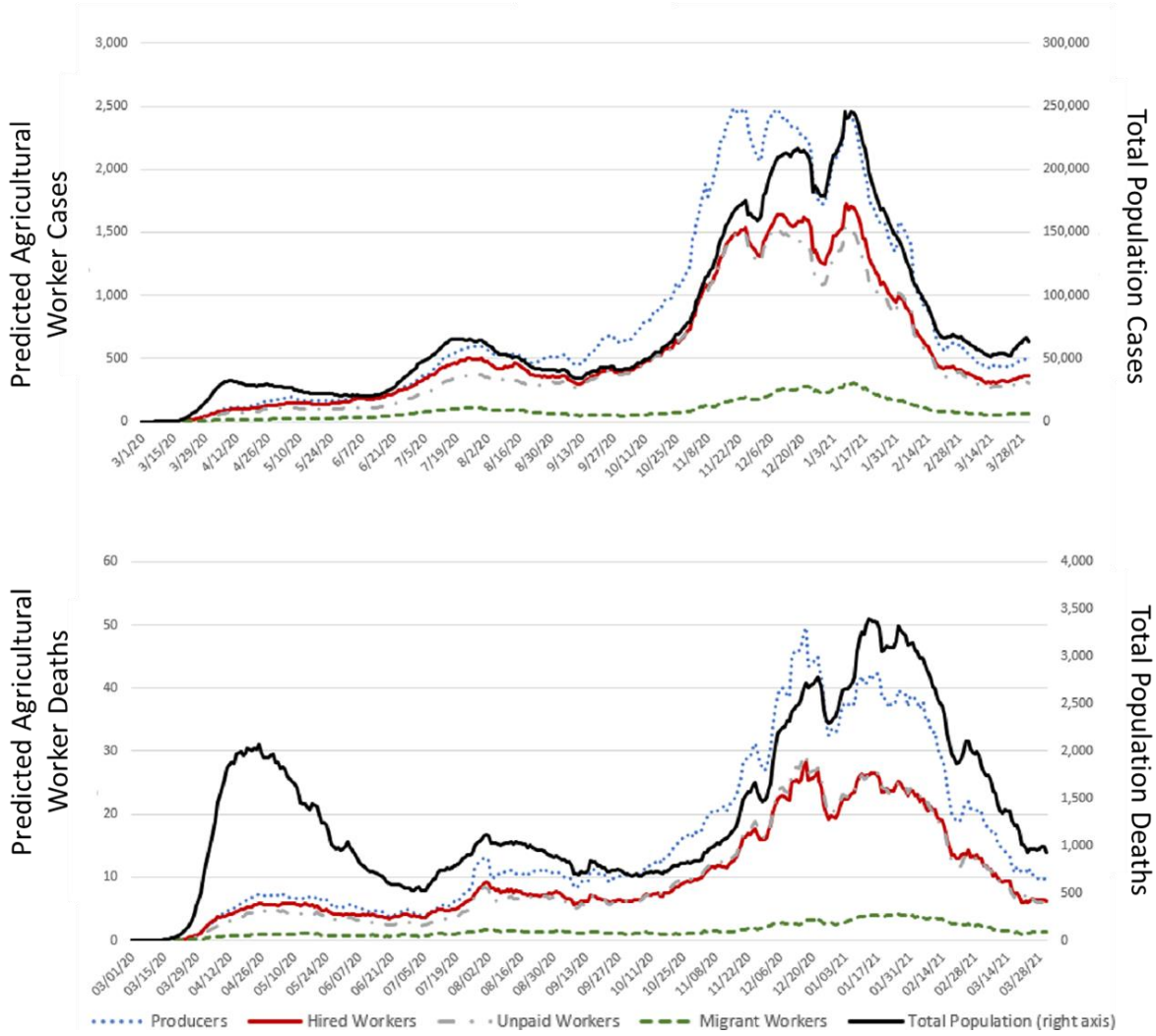
Key findings:

- COVID-19 incidence and death rates among all agricultural workers were approximately 9% and 0.2%, respectively.
    - Incidence and death rates were similar among agricultural producers (farmers), agricultural workers, unpaid agricultural workers and migrant agricultural workers.
    - Trends in the number of cases and deaths for agricultural workers were similar to the surrounding communities (Figure).
- Reduction in worker availability resulted in an estimated loss of $309 million in agricultural output.

Methods: Estimates of COVID-19 cases and deaths among agricultural workers (between March 1, 2020 and March 31, 2021) were calculated using county-level data from the Johns Hopkins' coronavirus dashboard, the U.S. Census Bureau 2017 county population counts and U.S. Department of Agriculture's (USDA) 2017 Census of Agriculture. Economic impact of reduction in agricultural labor was determined using USDA Economic Research Service data. *Limitations*: Potential for double counting workers who worked on more than one farm.

Implications: COVID-19 has negatively affected agricultural workers, a highly vulnerable population. Reductions in agricultural labor have the potential to adversely affect food supply.

Figure:



Note: adapted from Lusk *et al*. Predicted number of cases (top) and deaths (bottom) in **producers (farmers)**, **hired workers**, **unpaid workers**, and **migrant workers** in the agricultural sector (left y-axis) compared with the **total population cases and deaths** (right y-axis). Licensed under CC BY.

Association between income inequality and county-level COVID-19 cases and deaths in the US. Tan *et al.* JAMA Network Open (May 3, 2021).

Key findings:

- County-level income inequality was weakly positively associated with COVID-19 cases (Spearman $\rho = 0.052$; $p < 0.001$) and deaths (Spearman $\rho = 0.134$; $p < 0.001$) over the period between March 2020 and February 2021.

Methods: Ecological analysis of cases and deaths adjusted for county-level factors, with income inequality measured by Gini coefficient (where 0 represents all income equally shared and 1 represents all income going to 1 individual). Cases and deaths were obtained from the Johns Hopkins University COVID-19 data repository. County level data were obtained from the U.S. Census Bureau's American Community Survey (2014-2018). *Limitations*: No individual-level data.

Implications: Interventions targeted to areas with high inequality could help flatten the curve and lessen the COVID-19 burden driven by inequality.

PREPRINTS (NOT PEER-REVIEWED)

Racial and ethnic disparities for SARS-CoV-2 positivity in the United States: A generalizing pandemic.
Ferguson *et al.* medRxiv (May 2, 2021).

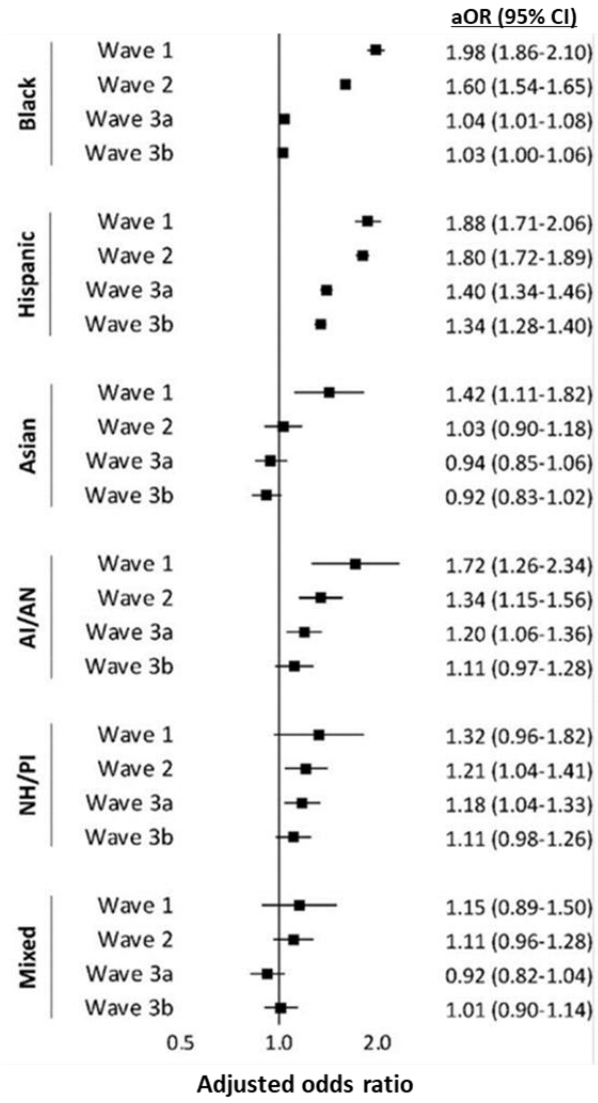
Key findings:

- From February 2020 to February 2021, disparities in SARS-CoV-2 test positivity decreased for all racial/ethnic minority groups compared with White individuals (Figure).

Methods: Nationwide retrospective cohort study using electronic health record data from 951,408 Veteran's Affairs patients tested for SARS-CoV-2 between February 12, 2020 and February 12, 2021, estimating SARS-CoV-2 positivity by racial/ethnic group over time and by region. Models adjusted for characteristics including rural/urban residence, comorbidities, substance use, and medication history. *Limitations*: Results may not be generalizable; did not evaluate social determinants of health.

Implications: The decreased racial and ethnic disparities in the odds of a positive SARS-CoV-2 test in later waves of the pandemic may indicate improvements in addressing disparities identified early in the pandemic.

Figure:



Note: Adapted from Ferguson *et al.* Adjusted odds ratio for test positivity by race (non-Hispanic, White as reference) and by wave between February 12, 2020 and February 12, 2021. Wave 1 (February 12–May 31, 2020); Wave 2 (June 1–September 30, 2020); Wave 3a (October 1–December 11, 2020); and Wave 3b (December 12, 2020–February 12, 2021). CI-confidence interval.

Natural History of SARS-CoV-2 Infection

PEER-REVIEWED

SARS-CoV-2 worldwide replication drives rapid rise and selection of mutations across the viral genome: A time-course study - potential challenge for vaccines and therapies. Weber *et al.* EBMO Molecular Medicine (May 1, 2021).

Key findings:

- Novel SARS-CoV-2 mutations increased from about 10 in April 2020 to approximately 180 in March 2021.

- While most mutations were found in the well-characterized spike and nucleocapsid proteins, some were found in sequences for predicated proteins whose functions are not known.
- By March 2021, prevalence of variants of concern B 1.1.7, B 1.351, and P.1 and P.2 had increased in multiple countries.

Methods: Complete SARS-CoV-2 RNA sequences (n = 383,570) within the Global Initiative of Sharing All Influenza Data (GISAID) database January 2020 thru March 2021, from 4 continents, were compared to the reference genome of wildtype SARS-CoV-2 and evaluated for mutations. *Limitations*: Analysis was limited to 10 countries and was subject to selection bias; sequences included in GISAID may not be representative of predominant circulating virus strains.

Implications: The rapid evolution of SARS-CoV-2 mutations and variants raises concerns about increased transmissibility, immune escape, and efficacy of existing vaccines.

Antibody response to 2-dose SARS-CoV-2 mRNA vaccine series in solid organ transplant recipients. Boyarsky *et al.* JAMA (May 5, 2021).

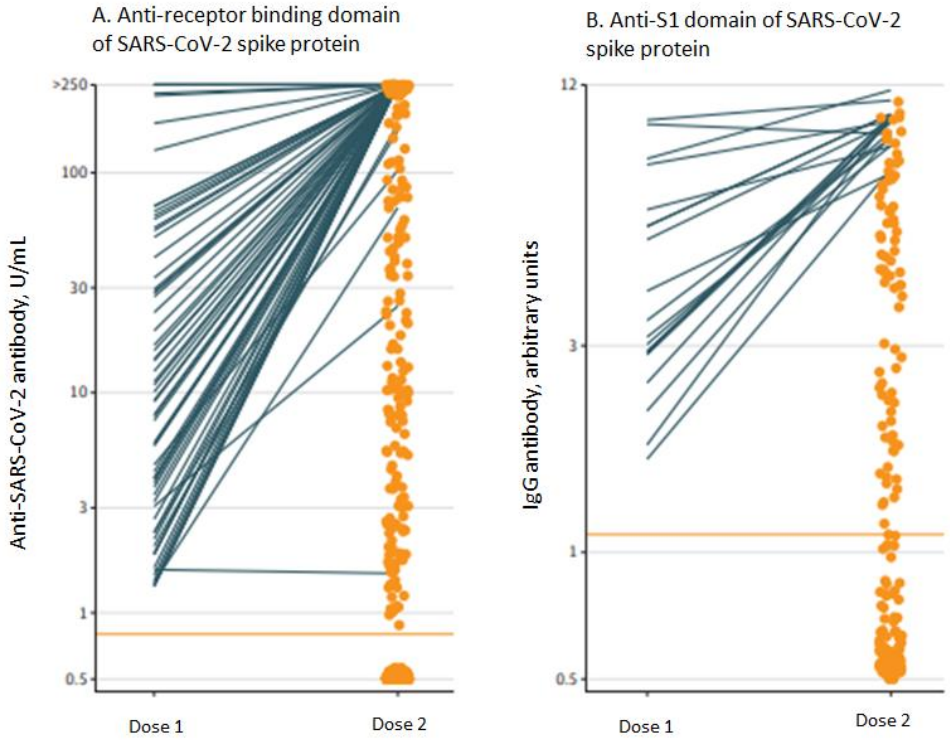
Key findings:

- Only 357 of 658 (54%, 95% CI 50%-58%) transplant recipients had a measurable antibody response to 2 doses (median 29 days after dose 2) of mRNA vaccines (Figure).
    - At a median of 21 days after dose 1, antibody was detectable in 98 participants (15%, 95% CI 12%-18%).
- Only 43% (205/473) of transplant recipients receiving anti-metabolite maintenance immunosuppression therapy had an antibody response after 2 doses compared with 82% (152/185) of transplant recipients not receiving antimetabolites.

Methods: Prospective cohort study of transplant recipients who received 2 doses of either Pfizer/BioNTech or Moderna SARS-CoV-2 mRNA vaccines between December 16, 2020 and March 13, 2021. Antibodies to the spike protein and the receptor binding domain were measured by Roche Elecsys or EURIMMUNE immunoassays, respectively. *Limitations*: No immunocompetent control group; did not measure post-vaccination SARS-CoV-2 infection; did not measure memory B-cell or T-cell responses.

Implications: While more transplant recipients developed detectable antibodies following a 2nd dose of mRNA vaccines compared with dose 1, a substantial proportion likely remain at risk for SARS-CoV-2 infection even after vaccination.

Figure:



Note: Adapted from Boyarsky *et al*. Antibodies to spike protein. A) Total antibodies to the receptor-binding domain (n = 470) or B) IgG to the S1 domain (n = 188). **Lines** show **the antibody trajectory of participants with detectable antibody after dose 1**. **Dots** show **antibody levels after dose 2** for participants who had undetectable antibody after dose 1. Horizontal **orange** lines show manufacturer limits of detection. Reproduced with permission from JAMA, 2021. Published online May 5, 2021. doi:10.1001/jama.2021.7489.

PREPRINTS (NOT PEER-REVIEWED)

Preliminary analysis of safety and immunogenicity of a SARS-CoV-2 variant vaccine booster. Wu *et al.* medRxiv (May 6, 2021).

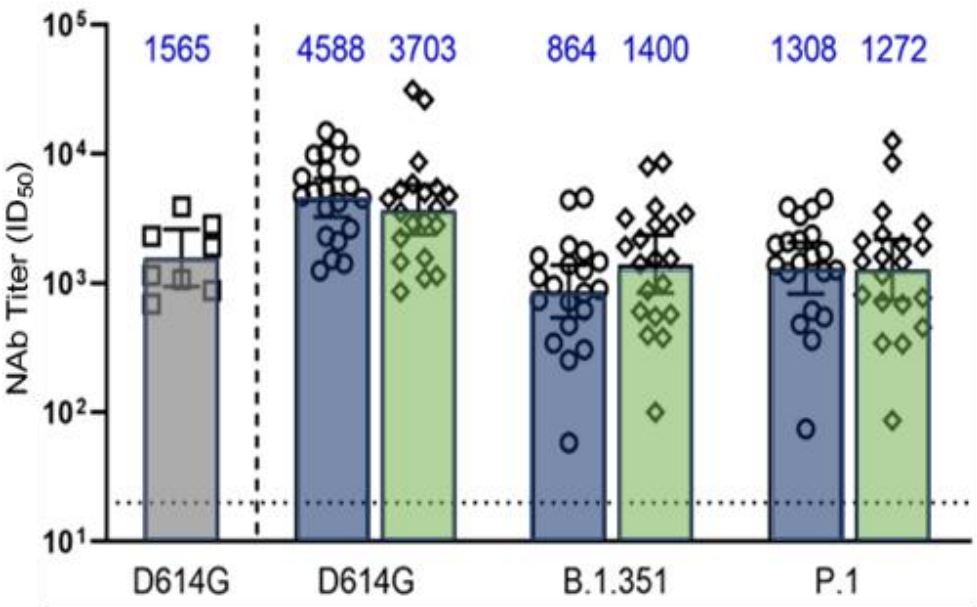
Key findings:

- Participants receiving a 3rd "booster" dose of the Moderna vaccine had high neutralizing antibody titers similar to that seen after the initial vaccine series (Figure).
    - Similar neutralizing antibody titers were seen after boosting with the Moderna mRNA prototype vaccine compared to a booster dose of the Moderna mRNA-1273.351 vaccine modified to encode for the B.1.351 variant spike protein.
    - There were approximately 2-fold higher neutralizing antibody titers against B.1.351 after boosting with the variant vaccine (1400) compared with the prototype vaccine (864) (Figure).
- Similar safety profiles were seen with either the prototype or variant booster vaccine.

Methods: Between 169 and 198 days after the second dose of the Moderna vaccine, a cohort 20 participants received a booster dose of either 50 µg of mRNA-1273 vaccine or 50 µg of mRNA-1273.351. Sera taken from participants on days 1, 8, 15, 29, 57 and 181 were analyzed for neutralizing antibody against SARS-CoV-2 pseudoviruses using the D614G, B.1.351, and P.1 variant sequences of the spike protein. Participants were contacted by phone every 4 weeks to assess safety. *Limitations:* Small sample size; only data for day 1 and day 15 samples are included in this early report.

Implications: Booster vaccines increased waning neutralizing antibody titers to levels similar to or higher than peak titers after the primary series vaccinations.

Figure:



Note: Adapted from Wu *et al*. Reference titers for neutralizing antibody (NAb) of D614G by sera from participants **1 week after primary 2-dose mRNA-1273 series** vs. titers for neutralization of D614G, B.1.351, and P.1 SARS-CoV-2 pseudoviruses by sera taken 2 weeks post-booster dose with **mRNA-1273** or **mRNA-1273.351**, given 6-8 months after primary mRNA-1273 2-dose series. Bars and numbers above bars show geometric mean titers. Horizontal dotted line = NAb titer lower limit of quantitation. Used by permission of authors.

SARS-CoV-2 antibodies remain detectable 12 months after infection and antibody magnitude is associated with age and COVID-19 severity. Laing *et al.* medRxiv (May 2, 2021).

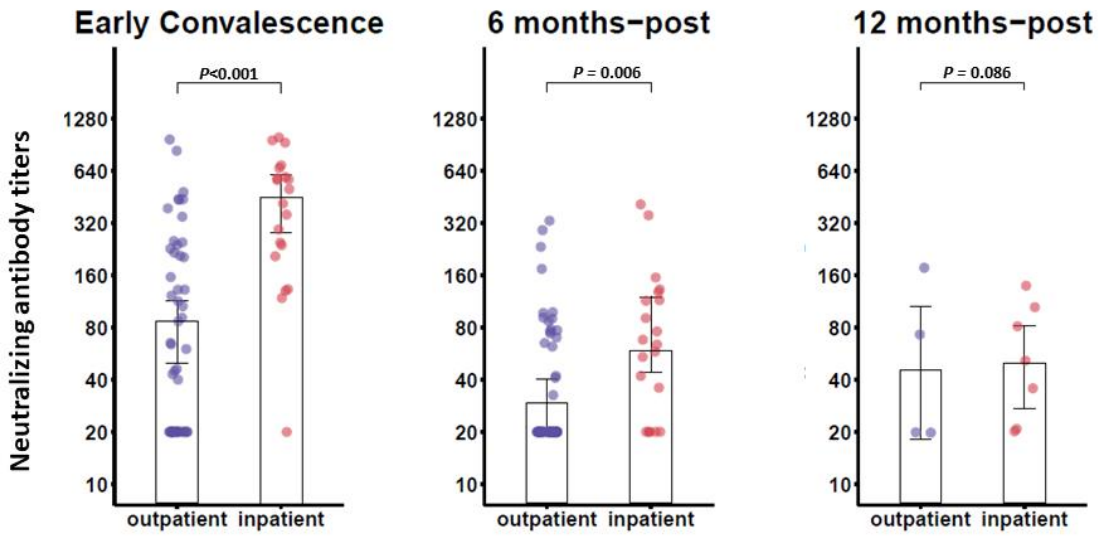
Key findings:

- After 6 months, 4.7% of patients were no longer seropositive for SARS-CoV-2 antibodies and at 12 months 18.2% were seronegative.
    - All patients that became seronegative were outpatients.
- Compared with outpatients, the geometric mean neutralizing antibody titer (GMT) for inpatients was (Figure):
    - Higher during early convalescence, 378 [95% CI 246-580] vs 83 [95% CI 59-116] (P <0.001)
    - Higher after six months, 65 [95% CI 43-98] vs 33 [95% CI 26-40] (P = 0.006),
    - Similar after 12 months.

Methods: Prospective cohort study of SARS-CoV-2 positive participants who sought medical treatment at US military hospitals between March 2020 and March 2021. Participants had blood drawn for neutralizing antibody titers at approximately 6 and 12 months after symptom onset but prior to vaccination (outpatient n = 192, inpatient n = 58 at baseline for total antibody; for combined inpatients and outpatients, n = 72 at 6 months and n = 11 at 12 months). *Limitation*: Small sample size for inpatient group; high loss to follow-up at 12 months.

Implications: Antibodies against SARS-CoV-2 are still present in the majority of COVID-19 patients after 12 months of follow-up, but the reversion of almost one-fifth of patients to seronegative emphasizes the importance of vaccination in all populations including individuals who have recovered from natural infection.

Figure:



Note: Adapted from Laing *et al*. Evaluation of the magnitude and duration of antibody response and COVID-19 clinical phenotype. Early convalescence, 6 months-post SARS-CoV-2, and 12 months post SARS-CoV-2 S-pseudovirus neutralization test (SNT) neutralizing antibodies were compared by hospitalization status (**outpatient** vs. **inpatient**). P-values were determined by unpaired t-test with Welch's correction; error bars indicate the geometric mean and 95% CI. U.S. Government work not subject to copyright.

Prevention, Mitigation and Intervention Strategies

PEER-REVIEWED

Effectiveness of the BNT162b2 COVID-19 vaccine against the B.1.1.7 and B.1.351 variants. Abu-Raddad *et al.* NEJM (May 5, 2021).

Key findings:

- The effectiveness of the Pfizer/BioNTech vaccine was:
  - 89.5% (95% CI 85.9%-92.3%) for PCR-confirmed SARS-CoV-2 B.1.1.7 infections (n = 32,808).
  - 75.0% (95% CI 70.5%-78.9%) for PCR-confirmed SARS-CoV-2 B.1.351 infections (n = 43,012).
  - 97.4% (95% CI 92.2%-99.5%) against severe, critical, or fatal COVID-19 disease (n = 1,695).
- Breakthrough infections (n = 1,616) and deaths (n = 2) after the second dose were rare.

Methods: Test-negative, case-control study of effectiveness >=14 days after the second dose of vaccine in Qatar using a national COVID-19 database with data between December 21, 2020 and March 31, 2021. *Limitations*: Vaccine effectiveness was not assessed by age group or underlying conditions.

Implications: These findings provide real-world evidence of BNT162b2 vaccine effectiveness against mild to severe COVID-19 associated with the B.1.1.7 and B.1.351 variants.

Social, Behavioral, and Communication Science

PEER-REVIEWED

Lives versus livelihoods? Perceived economic risk has a stronger association with support for COVID-19 preventive measures than perceived health risk. Nisa *et al.* Nature Scientific Reports (May 6, 2021).

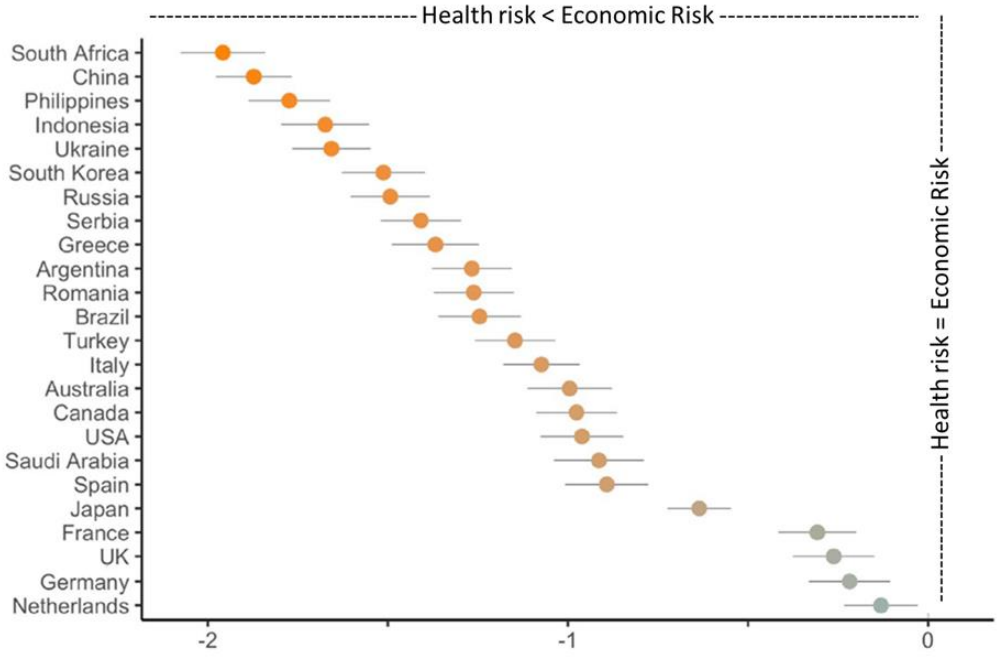
Key findings:

- Respondents in countries surveyed early in the COVID-19 pandemic expected economic risks to be greater than health risks (all paired t tests: p <0.01) (Figure).
    - This pattern was consistent across all age, sex, education, employment, financial, and political subgroups.
- Perceived economic risk was inversely associated with practicing risk mitigation and supporting strict containment policies.
    - Perceived health risk associated with support for mandatory vaccination and quarantine only.

Methods: Online cross-sectional surveys with national proportional (by sex and age) quota sampling from 24 countries (N = 22,561), April 10, 2020 to May 11, 2020. *Limitations*: Internet convenience panels; data from early in pandemic.

Implications: Public messaging may be more effective if delivering the message that COVID-19 mitigation measures will reduce (further) economic and job losses.

Figure:



Note: Adapted from Nisa *et al*. Standardized mean difference between perceived economic and health risks on 8-point scales by country. Intensity of **orange** shading and negativity indicate degree to which economic risk outweighs health risk; error bars indicate 95% CI. Licensed under CC BY 4.0.

In Brief

Detection, Burden, and Impact

- Pottegård *et al*. **Arterial events, venous thromboembolism, thrombocytopenia, and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population based cohort study.** BMJ (May 5, 2021). The morbidity ratio of observed to expected events was 1.97 (95% CI 1.50-2.54) for thromboembolism, 1.23 (95% CI 0.97-1.55) for bleeding, and 0.34 (95% CI 0.19-0.57) for deaths, based on data from 28-days of follow-up after receiving the Oxford-AstraZeneca ChAdOx1-S vaccine in 206,894 adults aged 18–65 years; the absolute risk for venous thromboembolic events was low.

- Pollock *et al*. **Implementation of SARS-CoV2 screening in K-12 schools using in-school pooled molecular testing and deconvolution by rapid antigen test.** medRxiv (Preprint, May 5, 2021). Between January 4 and April 9, 2021, 0.8% of school-based pooled tests using nasal swabs (50,636 pools with an average 7 swabs per pool) were RT-PCR-positive; of 80 positive pools for which each individual in the pool was tested, 74 (92.5%) had an individual positive using the BinaxNow antigen test.

Transmission of SARS-CoV-2

- Carter *et al*. **Widespread SARS-CoV-2 transmission among attendees at a large motorcycle rally and their contacts, 30 US jurisdictions, August-September, 2020.** Clinical Infectious Diseases (April 29, 2021). 463 primary cases and 186 secondary and tertiary cases of COVID-19 associated with the Sturgis, South Dakota, motorcycle rally were identified in 30 jurisdictions. Of the primary cases, 17 (3.7%) were hospitalized and 1 died.

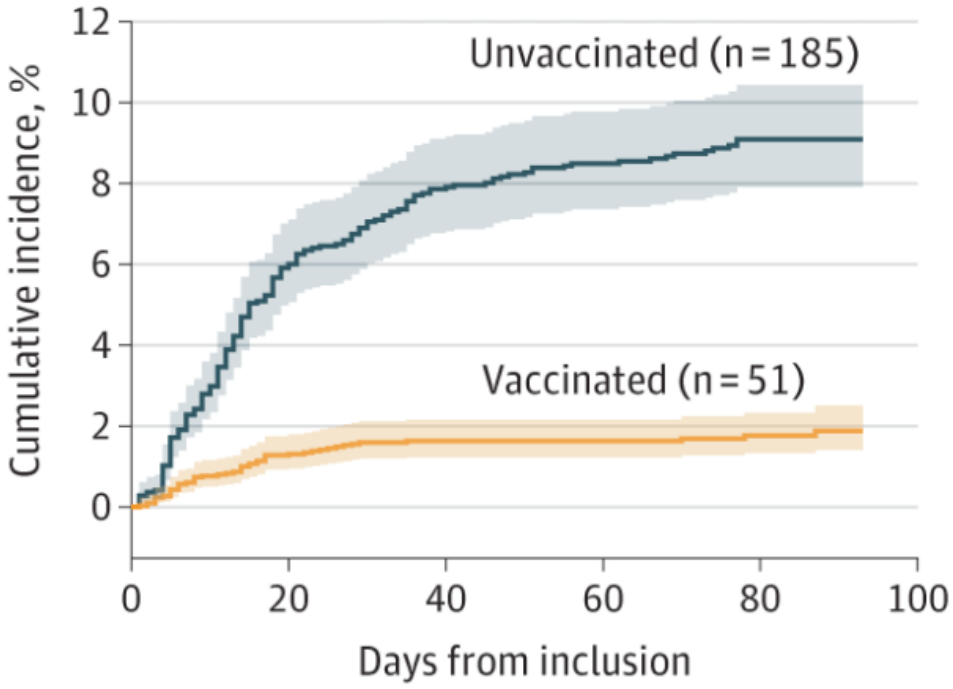
Natural History of SARS-CoV-2 Infection

- Gravagnuolo *et al*. **High throughput diagnostics and dynamic risk assessment of variants of concern.** Lancet (Preprint, May 3, 2021). In November 2020, a laboratory in England using real-time RT-PCR tests, began detecting virus strains (or variants) that were positive for nucleocapised (N) and Orf1b but negative for spike (S). The high throughput (80,000 tests per day) quickly identified this variant, B.1.1.7, that soon became the dominant strain in the UK.

Prevention, Mitigation, and Intervention Strategies

- Haas *et al.* **Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: An observational study using national surveillance data.** The Lancet (May 5, 2021). Based on Israeli national data between January 24 and April 3, 2021, vaccine effectiveness 7 days after the 2nd dose of the Pfizer/BioNTech BNT162b2 vaccine was 95.3% (95% CI 94.9%-95.7%) against infection, 91.5% (95% CI 90.7%-92.2%) against asymptomatic infection, 97.2% (95% CI 96.8%-97.5%) against hospitalization, and 96.7% (95% CI 96.0%-97.3%) against death; during this time frame, the dominant SARS-CoV-2 strain was B.1.1.7.

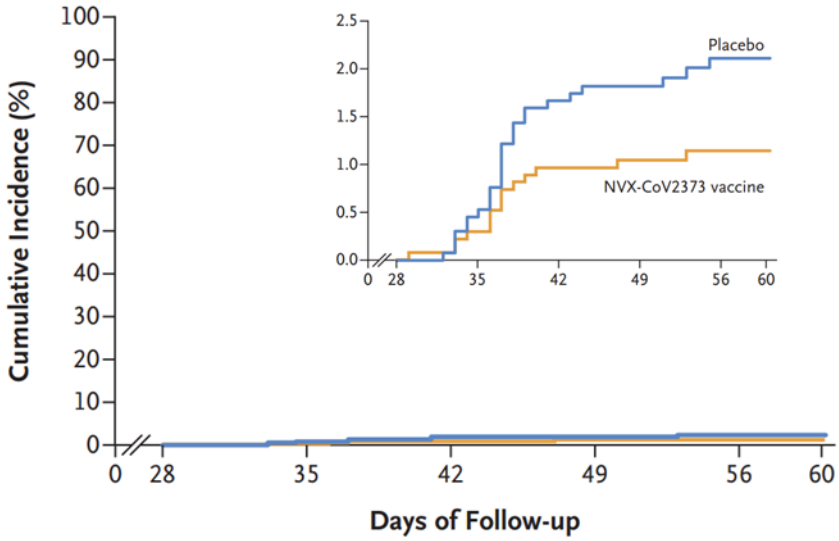
- Tang *et al*. **Asymptomatic and symptomatic SARS-CoV-2 infections after BNT162b2 vaccination in a routinely screened workforce**. JAMA (May 6, 2021). Among employees at St Jude Children's Research Hospital, the incidence rate ratio comparing Pfizer/BioNTech vaccinated and unvaccinated employees was 0.21 (95% CI 0.15-0.28) for any SARS-CoV-2 infection, 0.28 (95% CI 0.18-0.42) for asymptomatic screening results, and 0.16 (95% CI 0.10-0.25) for symptomatic or known exposure cases.



Note: Adapted from Tang *et al*. Cumulative incidence of any SARS-CoV-2 positive test by days since study began or first asymptomatic test results for unvaccinated employees or days since vaccination for vaccinated employees, among 2,165 **unvaccinated** and 3,053 **vaccinated** (2,776 received 2 doses) employees December 17, 2020 through March 20, 2021.. Reproduced with permission from JAMA, 2021. Published online May 6, 2021. doi:10.1001/jama.2021.6564. Copyright© 2021 American Medical Association. All rights reserved.

- Angel *et al*. **Association between vaccination with BNT162b2 and incidence of symptomatic and asymptomatic SARS-CoV-2 infections among health care workers**. JAMA (May 6, 2021). Among a cohort of 6,274 health care workers (HCW), the adjusted incidence rate ratio for HCWs fully vaccinated with the Pfizer/BioNTech vaccine was 0.14 (95% CI 0.07-0.31) for asymptomatic SARS-CoV-2 infection and 0.03 (95% CI, 0.01-0.06) for symptomatic SARS-CoV-2 infection.

- Shinde *et al*. **Efficacy of NVX-CoV2373 COVID-19 vaccine against the B.1.351 variant**. NEJM (May 5, 2021). In a randomized clinical trial conducted in South Africa when the predominant circulating variant was B.1.351, the efficacy of the Novavax NVX-CoV2373 vaccine was 49.4% (95% CI 6.1%-72.8%) against symptomatic COVID-19 among HIV-negative and medically stable HIV-positive adults seronegative for SARS-CoV-2 at baseline. Of HIV-positive participants who were SARS-CoV-2 seronegative at baseline, 4/76 in the vaccine group and 2/72 in the placebo group developed symptoms of COVID-19.



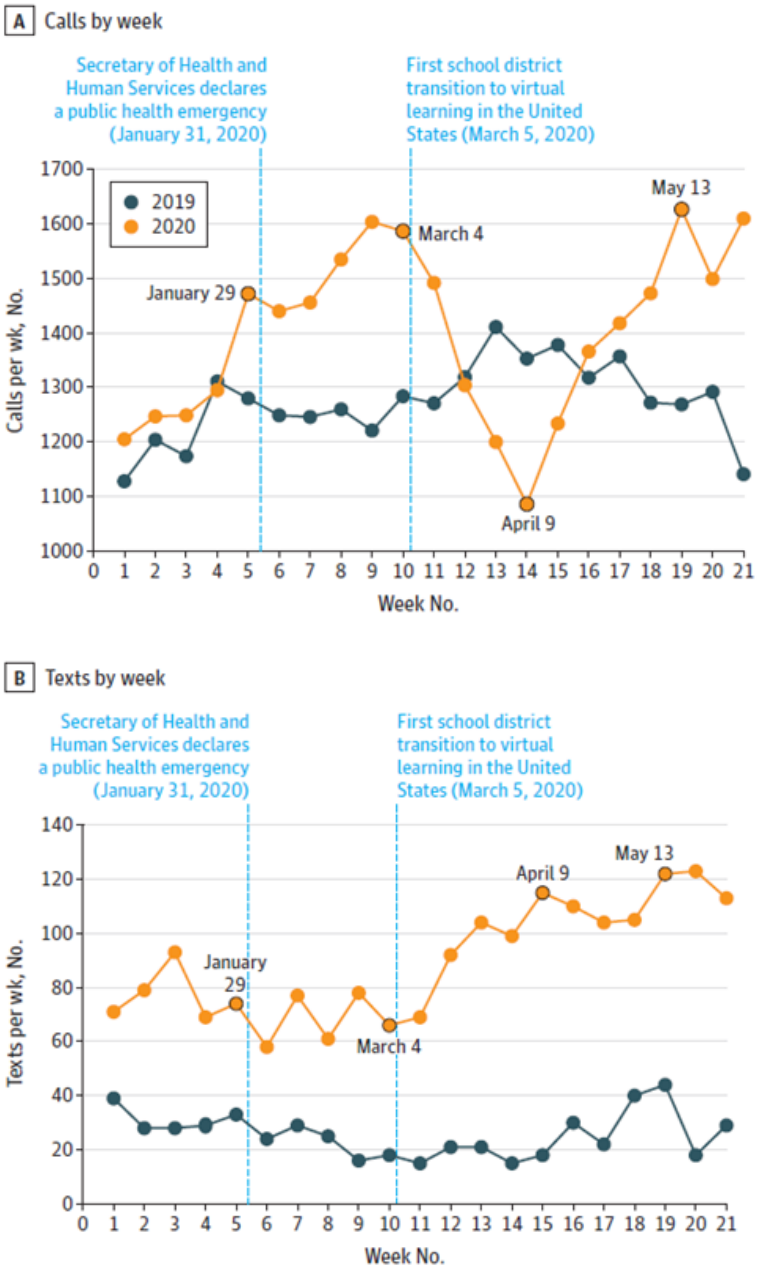
Note: Adapted from Shinde *et al.* Cumulative incidence of symptomatic COVID-19 among SARS-CoV-2 seronegative participants at baseline 7 days after second dose of **NVX-CoV2373 vaccine** or **placebo** (i.e., day 28) (n = 2,684). From the New England Journal of Medicine, Shinde *et al.*, Efficacy of NVX-CoV2373 COVID-19 vaccine against the B.1.351 variant. May 5, 2021, online ahead of print. Copyright © 2021 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

- Corchado-Garcia *et al*. **Real-world effectiveness of Ad26.COV2.S adenoviral vector vaccine for COVID-19.** medRxiv (Preprint, April 30, 2021). Effectiveness of the Janssen (Johnson & Johnson) vaccine measured 14 days after vaccination was 76.7% (95% CI 30.3%-95.3%) in preventing SARS-CoV-2 infection among adult patients (vaccinated n = 2,195, unvaccinated matched cohort n = 21,950) in the multi-state Mayo Clinic Health System between February 27 and April 14, 2021.

Social, Behavioral, and Communication Science

- Ortiz *et al*. **Assessing child abuse hotline inquiries in the wake of COVID-19.** JAMA Pediatrics (May 3, 2021). Calls to a national child abuse and neglect hotline increased in early 2020, dropped briefly but dramatically following school closures, then rebounded to levels higher than 2019. Text inquiries, primarily from individuals <18 years old, increased after March 2020 and remained higher than 2019 levels, suggesting a possible higher rate of child-related distress and maltreatment in early stages of the pandemic compared with the previous year.

Figures:



Note: Child abuse hotline Childhelp A) phone and B) text inquiries per week **March 1–May 27, 2019** (16,599 inquiries) compared with **March 1–May 26, 2020** (18,881 inquiries). Vertical dashed lines indicate HHS's health emergency declaration on January 31, 2020 and school closure initiation on March 5, 2020. Licensed under CC BY.

cdc.gov/coronavirus