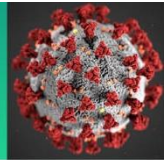


COVID-19 Science Update



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.

*** 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](#).

Prevention, Mitigation and Intervention Strategies

PEER-REVIEWED

[SARS-CoV-2 incidence and vaccine escape](#). Thompson *et al.* The Lancet Infectious Diseases (April 13, 2021).

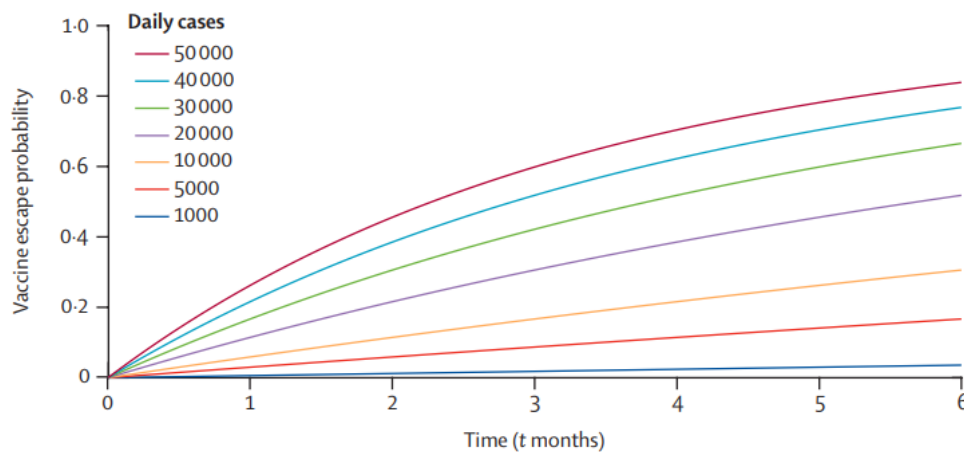
Key findings:

- The risk of a SARS CoV-2 escape variant appearing is a function of incidence and time (Figure).
- A reduction in cases leads to both a reduction in the risk of escape variants appearing and a reduction in their subsequent establishment in the population.

Methods: A model illustrating the relationship between incidence of SARS-CoV-2 cases and the probability of developing a vaccine escape variant. Assuming a fixed vaccine escape mutation probability per infection (p), the risk of a vaccine escape variant arising in a specified time period is $1 - (1 - p)^N$, where N represents the number of cases in that period. **Limitations:** Model does not consider potential of vaccine escape variants in vaccinated hosts, nor the escape variant's fitness.

Implications: Strategies to mitigate vaccine escape risk, including non-pharmaceutical interventions and vaccination, should be fully implemented.

Figure:



Note: Adapted from Thompson *et al.* Risk that at least one vaccine escape variant arises in a time period of length t , for different daily number of cases. The per-infection probability of vaccine escape is $p = 2 \times 10^{-7}$. Reprinted from The Lancet Infectious Diseases, Thompson *et al.*, SARS-CoV-2 incidence and vaccine escape, Copyright 2021, with permission from Elsevier.

[Pathologic antibodies to platelet factor 4 after ChAdOx1 nCoV-19 vaccination.](#) Scully *et al.* NEJM (April 16, 2021).

Key findings:

- 23 patients (14 female, ages 21-77 years), presented with acute thrombocytopenia and thrombosis 6 to 24 days after ChAdOx1 nCoV-19 vaccination.
 - Fibrinogen levels were low or normal and D-dimer levels were elevated at presentation.
 - 7 died.
- Antibodies to platelet factor 4 (PF4) were positive in 22 patients and negative in 1 patient.

Methods: Patients with suspected vaccine-induced thrombosis and thrombocytopenia in the UK underwent antibody assays, including those for PF4 and functional heparin-induced thrombocytopenia. *Limitations:* Case series.

Implications: Some patients receiving the ChAdOx1 nCoV-19 (Oxford-AstraZeneca) vaccine may develop a pathogenic PF4-dependent syndrome. These findings are consistent with other reports of [pulmonary embolism and thrombocytopenia](#), [ophthalmic vein thrombosis and ischemic stroke](#), and [intracranial venous sinus thrombosis](#) after the administration of ChAdOx1 nCoV-19, and [thrombotic thrombocytopenia](#) after administration of Ad26.COVS.2 (Johnson & Johnson/Janssen) vaccine. Clinicians should avoid platelet transfusions in suspected vaccine-induced thrombosis and thrombocytopenia and should consider administering a non-heparin anticoagulant and intravenous immune globulin.

[The effect of eviction moratoria on the transmission of SARS-CoV-2.](#) Nande *et al.* Nature Communications (April 15, 2021).

Key findings:

- Across a range of modeled scenarios, increased evictions led to significant increases in SARS-CoV-2 infections.
 - Increased infections occurred not only among households of evicted persons but also among other city residents, including those living in neighborhoods with relatively few evictions.
- Based on this model, the September 4, 2020 [CDC order](#) prohibiting evictions due to inability to pay rent may have prevented thousands of infections for every million metropolitan residents.

Methods: Simulations of hypothetical American cities with population of 1 million using COVID-19 case and death data from approximately 50 US cities to evaluate impact of evictions on infection counts; eviction rates varied between none and 0.1%-2.0%. Model assumes evictions begin September 1, 2020, evictees will join an existing household or become homeless, and household transmission rate is 30%. *Limitations:* Model depends on accuracy of assumptions about transmission probability and background trajectory of the epidemic in cities.

Implications: Policies to stem evictions might reduce SARS CoV-2 infections.

[Fitted filtration efficiency of double masking during the COVID-19 pandemic.](#) Sickbert-Bennett *et al.* JAMA Internal Medicine. (April 16, 2021).

Key findings:

- Across 3 cloth masks (cotton ear loop, cotton bandana, polyester gaiter), fitted filtration efficiency (FFE) ranged from 41% to 44%.
- A procedure mask under a cloth mask improved FFE (range: 66% to 81%).
- FFE for a procedure mask over a cloth mask (range: 55% to 60%) was similar to a procedure mask alone (55%).

Methods: A quality improvement study comparing the FFE of single-worn and doubling of disposable medical procedure masks and cloth face coverings among 3 volunteers. FFE is the concentration of particles behind the

mask as a percentage of the particle concentration in a sodium chloride particle-enriched chamber atmosphere, measured during a series of repeated movements as outlined by the OSHA Quantitative Fit Testing protocol.

Limitations: Only one type of disposable medical procedure mask was tested.

Implications: Double masking, with a medical procedure mask under a cloth mask, improves filtration of respiratory particles.

Detection, Burden, and Impact

PEER-REVIEWED

[6-month neurological and psychiatric outcomes in 236,379 survivors of COVID-19: a retrospective cohort study using electronic health records.](#) Taquet *et al.* *Lancet Psychiatry* (April 6, 2021).

Key findings:

- Incidence of neurological or psychiatric diagnoses among COVID-19 survivors was 33.62% (95% CI 33.17–34.07).
- Neurological and psychiatric comorbidities were more common in COVID-19 patients than in those who had influenza (HR 1.44, 95% CI 1.40–1.47) or respiratory infections (HR 1.16, 95% CI 1.14–1.17).

Methods: Retrospective, time-to-event cohort study using electronic health records 6-months post COVID-19 diagnosis. Primary cohort of 236,379 COVID-19 patients older than 10 years matched with a control cohort of patients with influenza or respiratory infections in the same period. Cohorts assessed for differences in neurological and psychiatric sequelae. **Limitations:** Unknown completeness of electronic health records; no validation of diagnosis; sparse information on demographic and lifestyle factors.

Implications: This study provides evidence of substantial neurological and psychiatric morbidity in the 6-months after COVID-19 infection.

[Genomic characteristics and clinical effect of the emergent SARS-CoV-2 B.1.1.7 lineage in London, UK: a whole-genome sequencing and hospital-based cohort study.](#) Frampton *et al.* *Lancet Infectious Diseases* (April 12, 2021).

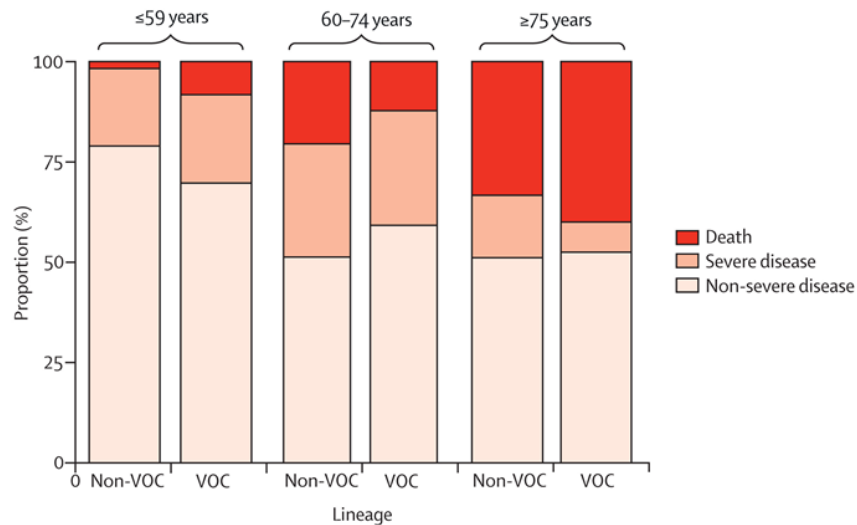
Key findings:

- No evidence of association between severe disease or death and SARS-CoV-2 lineage (B.1.1.7 vs non-B.1.1.7, adjusted prevalence ratio 1.02 [0.76–1.38]) (Figure).
- Viral load was higher in B.1.1.7 samples than in non-B.1.1.7 samples, as measured by Ct value (mean 28.8 [SD 4.7] vs 32.0 [4.8]; $p = 0.0085$) and genomic read depth (1280 [1004] vs 831 [682]; $p = 0.0011$).
- No B.1.1.7 variant of concern (VOC) defining mutations were found in samples from 32 patients treated with a 5-day course of remdesivir.

Methods: Among 496 patients admitted to two UK hospital centers between November 9, 2020 and December 20, 2020, 341 had PCR positive SARS-CoV-2 samples that could be sequenced. Association between B.1.1.7 infection and clinical severity, death and viral load was investigated. **Limitations:** Ct analyses were limited by data availability; sequences for 155 of 496 patients could not be used.

Implications: B.1.1.7 may not cause greater illness severity or death among hospitalized patients than other variants, despite being more infectious.

Figure:



Note: Adapted from Frampton *et al.* Severity of illness across patient age groups and by presence of VOC or non-VOC SARS-CoV-2 infection. VOC, variant of concern B.1.1.7. Licensed under CC-BY-NC-ND 4.0.

Natural History of SARS-CoV-2 Infection

PEER-REVIEWED

Reinfection Among Healthcare Workers

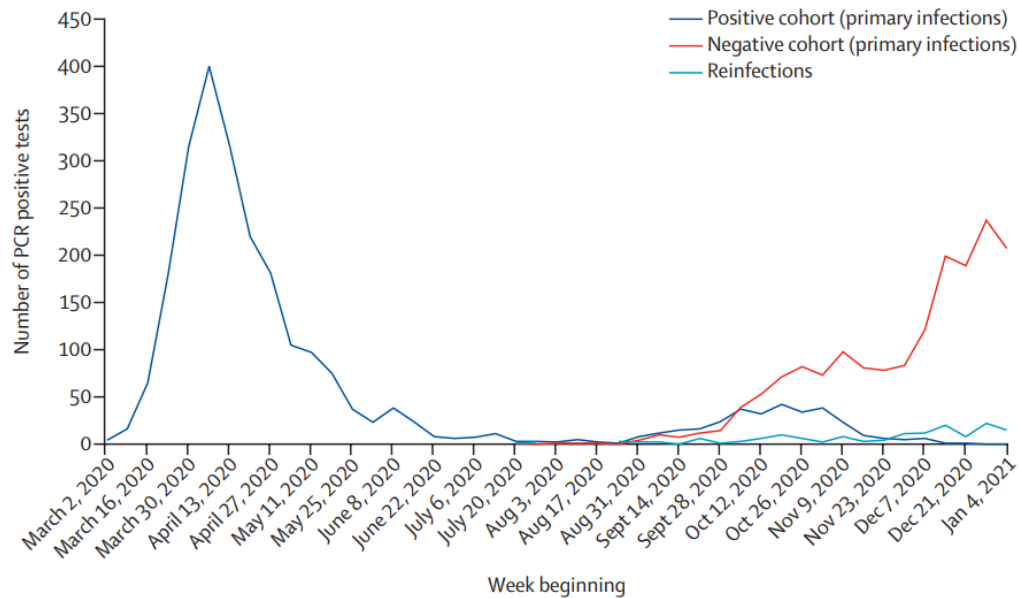
Reinfection with any strain of SARS CoV-2 following a previous infection or vaccination may be possible, and the risk may differ among variants of concern. Few cases of reinfection have been reported to date: the following studies present cases of confirmed, probable, or possible reinfection among healthcare workers.

A. SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN). Hall *et al.* The Lancet (April 9, 2021).

Key findings:

- Reinfection occurred at a lower rate in the cohort with prior SARS-CoV-2 infection (7.6 reinfections per 100,000 person-days) than did primary infection in a cohort without prior infection (57.3 primary infections per 100,000 person-days) (adjusted incidence rate ratio 0.159 [95% CI 0.13-0.19]) (Figure).
- Median interval between primary infection and reinfection was >200 days.

Methods: Between June 18, 2020 and January 11, 2021, 25,661 UK healthcare workers underwent regular SARS-CoV-2 PCR and antibody testing. Of these, 13,401 were vaccinated between December 8, 2020 and January 11, 2021. Reinfection was defined as possible (two positive PCRs >90 days apart or antibody positive with a new PCR >4 weeks later), probable (requiring supportive serologic or genomic data), or confirmed (confirmed SARS CoV-2 negative between episodes). **Limitations:** Seroconversions were not included; results may not be generalizable to other communities due to varying SARS CoV-2 strain distributions.

Figure:

Note: Adapted from Hall *et al.* Weekly frequency of positive PCR tests of healthcare workers with primary infection in the **positive** and **negative** cohorts, and **reinfections**. Reprinted from The Lancet, Hall *et al.*, SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN), Copyright 2021, with permission from Elsevier.

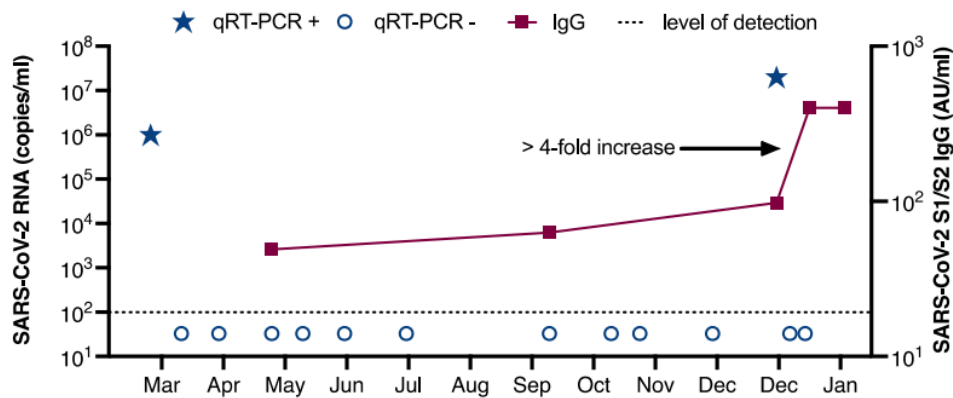
B. SARS-CoV-2 reinfection in a healthcare worker despite the presence of detectable neutralizing antibodies. Brehm *et al.* *Viruses* (April 12, 2021).

Key findings:

- An immunocompetent healthcare worker (27-year-old female nurse) developed mild illness upon SARS-CoV-2 reinfection 282 days after primary infection with a >4-fold increase in S1/S2 antibody levels (Figure).
 - A genetically distinct SARS-CoV-2 variant was isolated on reinfection.
 - There were no escape mutations noted in the reinfecting virus.
- A moderate immune response was described after primary infection.
 - Despite the presence of neutralizing antibodies, viral shedding occurred during reinfection.

Methods: Viral properties and immune response were characterized using aRT-PCR, cell culture, antibody assays and genome analysis. **Limitations:** Single case.

Figure:



Note: Adapted from Brehm *et al.* Quantitative SARS CoV-2 RNA copies and S1/S2 IgG antibody levels from primary infection (March 2020) through reinfection (December 2020) in an immunocompetent healthcare worker. Licensed under CC BY 4.0.

Implications for both studies (Hall *et al.* and Brehm *et al.*): Individuals with prior SARS-CoV-2 infection may have a lower risk of future infections compared to individuals without prior infections. Reinfections have been reported, however, including a recent [case in Brazil](#). Humoral response after primary infection may play an important role in determining viral neutralization upon reinfection.

Social, Behavioral, and Communication Science

PEER-REVIEWED

[Trends in drug overdose mortality in Ohio during the first 7 months of the COVID-19 pandemic](#). Currie *et al.* JAMA Network Open (April 14, 2021).

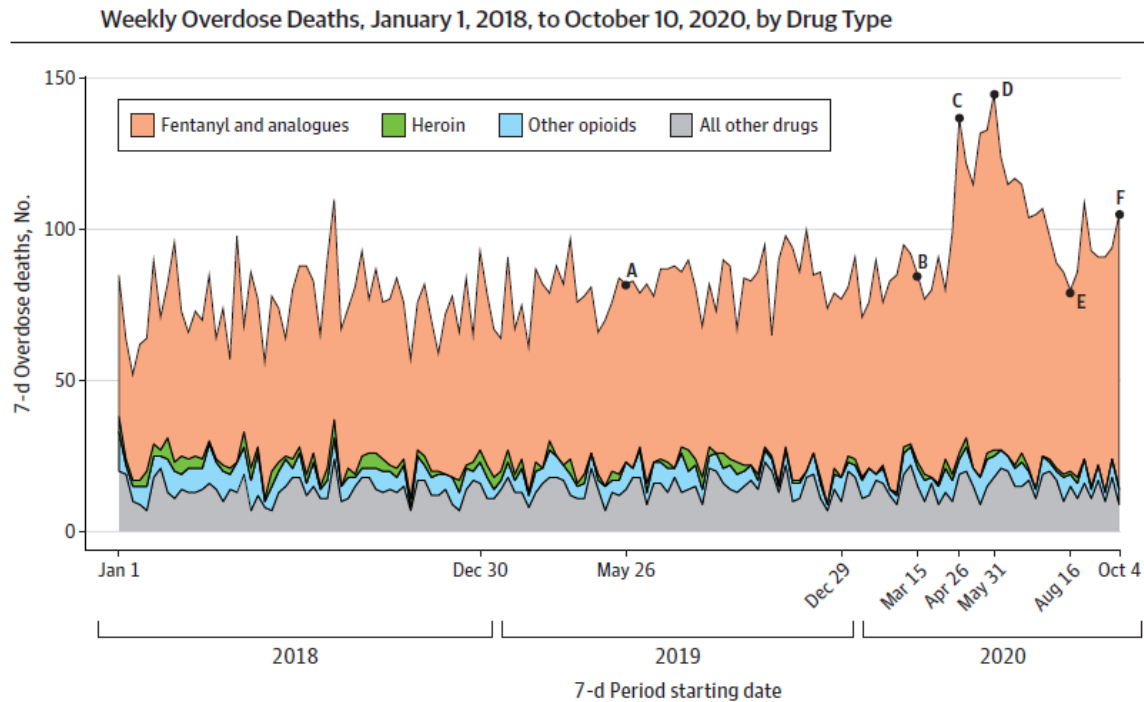
Key findings:

- Fatal weekly overdoses increased 70.6% (from 85 the week of March 15, 2020 to 145 the week of May 31, 2020) following the declaration of a national emergency for the COVID-19 pandemic (Figure).
 - Overdoses peaked the week of May 31, 2020, representing a relative increase of 76.8% (from 82 to 145) in drug overdoses from the year before.
- Fentanyl-related deaths represented 73.6% of total fatal overdoses and were the only drug category that spiked during the January to October, 2020 period of the COVID-19 pandemic (Figure).

Methods: A cross-sectional study of 12,195 overdose deaths using publicly available health department data between January 1, 2018 and October 10, 2020. Fatal overdoses were classified by drug type. Overdose deaths were compared with number of deaths in 2018 and 2019. **Limitations:** Findings may not be generalizable; cause of death is pending for some individuals who may have had an overdose.

Implications: The association between timing of the COVID-19 pandemic and increases in fatal overdoses is not yet understood. Possible contributing factors include disruptions to opioid use disorder treatment services, social patterns in drug usage, and [interruptions to/changes in the illicit drug supply](#).

Figure:



Note: Adapted from Currie *et al.* Weekly drug overdose deaths shown for all Ohio counties, documented by drug type in 2018, 2019, and 2020: **fentanyl and analogues overdoses**; **heroin**; **opioids**; and all other drugs (nonfentanyl, nonheroin opioids). Point A is a reference to overdoses a year before the pandemic. Points B-F follow the temporal pattern of overdoses after the implementation of COVID-19 mitigation strategies (i.e. lockdowns) and the lifting of those restrictions. Licensed under CC BY.

In Brief

Prevention, Mitigation, and Intervention Strategies

- Wolf *et al.* [Thrombocytopenia and intracranial venous sinus thrombosis after “COVID-19 vaccine AstraZeneca” exposure](#). Journal of Clinical Medicine (April 9, 2021). Three women age 22-46 who presented with neurologic signs and symptoms 7-17 days after their 1st vaccination with ChAdOx1 were found to have intracranial venous sinus thrombosis (IVST) which improved with treatment. These and other recent cases, e.g., in [Scully](#), [Bayas](#), and [Muster](#), indicate that thrombocytopenia and IVST may occur following ChAdOx1 nCoV-19 exposure. Triggering and predisposing factors are unknown. The formation of antibodies against PF4 may cause platelet consumption with low platelet counts and thrombus formation.
- Cho *et al.* [Physical activity and the risk of COVID-19 infection and mortality: a nationwide population-based case-control study](#). Journal of Clinical Medicine (April 6, 2021). A study of COVID-19 patients (N = 6,288) and matched controls showed that higher levels of physical activity were associated with a lower risk of SARS CoV-2 infection and COVID-19 disease morbidity and mortality.
- Lacson *et al.* [Immunogenicity of SARS-CoV-2 vaccine in dialysis](#). medRxiv (Preprint; April 13, 2021). [Published in the Journal of the American Society of Nephrology \(November 2021\)](#). The majority of dialysis patients (165/186; 88.7%) developed detectable antibodies to the SARS-CoV-2 spike antigen after completing vaccination, suggesting this population is responsive to vaccination.
- Andrejko *et al.* [Early evidence of COVID-19 vaccine effectiveness within the general population of California](#). medRxiv (Preprint; April 10, 2021). A study (N = 645) in a population where 69% of SARS-CoV-2 isolates

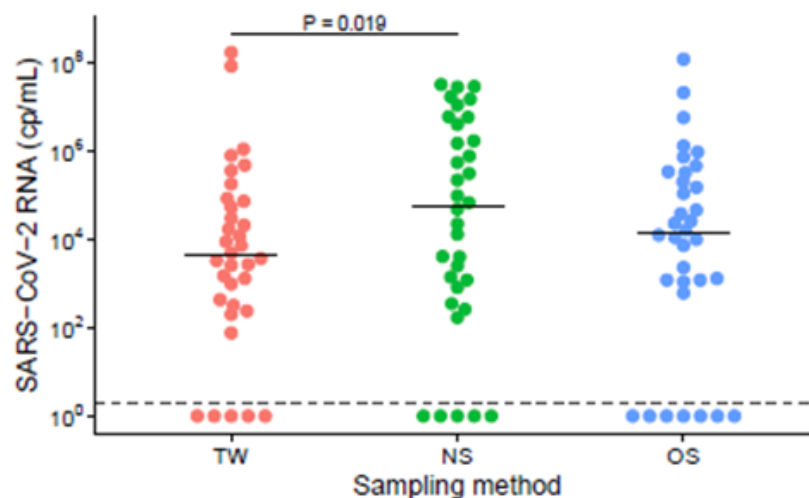
sequenced were variants of concern found that vaccine effectiveness was 86% among fully vaccinated persons; however, vaccine hesitancy was high (133/415; 32%) among unvaccinated persons.

- Self *et al.* [Shelter characteristics, infection prevention practices, and universal testing for SARS-CoV-2 at homeless shelters in 7 US urban areas](#). *AJPH* (April 7, 2021). In a study including 63 shelters, those that implemented head-to-toe sleeping, excluded symptomatic staff from work, and offered on-site medical services were less likely to have high infection prevalence.

Detection, Burden, and Impact

- Buonsenso *et al.* [Preliminary evidence on long COVID in children](#). *Acta Paediatrica* (April 9, 2021). In one hospital in Italy, 42.6% of children and adolescents ≤ 18 years diagnosed with COVID-19 (N = 129) reported at least one symptom >60 days after infection.
- Hitzenbichler *et al.* [Comparison of throat washings, nasopharyngeal swabs and oropharyngeal swabs for detection of SARS-CoV-2](#). *Viruses* (April 10, 2021). RT-qPCR analysis of 102 samples from 34 adult patients with confirmed SARS-CoV-2 infection found that the median concentration (copies/mL) was significantly higher for nasopharyngeal swabs (NS) than for throat washings (TW), suggesting TW and oropharyngeal swabs (OS) could be considered for testing.

Figure:



Note: Adapted from Hitzenbichler *et al.* SARS-CoV-2 RNA concentrations in 34 study participants by sampling site (TW, throat washing; NS, nasopharyngeal swab; OS, oropharyngeal swab). Median concentrations are shown as horizontal lines. A statistically significant difference between the groups is indicated by a horizontal line on top of the data panels. Licensed under CC BY 4.0.

Social, Behavioral, and Communication Science

- Dai *et al.* [Behavioral nudges increase COVID-19 vaccinations: two randomized controlled trials](#). medRxiv (Preprint; April 14, 2021). [Published in Nature as Behavioural nudges increase COVID-19 vaccinations \(August 2, 2021\)](#). Among $>100,000$ vaccine-eligible patients (>65 years or qualifying conditions) receiving a text-based motivational reminder message, vaccine appointment scheduling increased by 86% within 6 days, and vaccination increased by 26% within 4 weeks of the message, compared to eligibility notification alone, although overall vaccination rates were below 15%.

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