



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Avoidance of COVID-19 for Children and Adolescents and Isolation Precautions



Shipra Gupta, MD^{a,*}, Layne Smith, PharmD^b, Adriana Diakiw, MD^a

KEYWORDS

• COVID-19 transmission • Prevention • Children • Household transmission

KEY POINTS

- Infections caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) are spread mainly by person-to-person transmission via respiratory droplets.
- Household transmission has been well documented, and spread from presymptomatic and symptomatic individuals is a key driver for transmission.
- SARS-CoV-2–related illness has usually been mild in children, with rare complications leading to mortality.
- Various investigations and published experiences have shown that schools and day care centers have been safely opened with implementation of guidance of mask wearing, maintaining distance, and hand hygiene.
- Vaccination against SARS-CoV-2 offers a way to reduce rates of severe illness and mortality from the disease.

INTRODUCTION

Prevention is better than cure has been the dictum driving the public health response to the novel coronavirus, which was first reported in China toward the end of 2019.¹ Full-length genomic sequencing from virus identified from infected patients was 96% identical to a bat coronavirus. The novel coronavirus shared 79.6% sequence identity with the severe acute respiratory syndrome (SARS) coronavirus and, therefore, was named SARS coronavirus-2 (SARS-CoV-2).² The virus has since spread worldwide and was declared a pandemic by the World Health Organization (WHO) on March 11, 2020.^{3,4}

Initial emphasis had been on containment measures to curb community spread, with widespread lockdowns, school closures, and nonpharmaceutical interventions

^a West Virginia University School of Medicine, One Medical Center Drive, HSC 9214, Morgantown, WV 26506, USA; ^b West Virginia University School of Pharmacy, One Medical Center Drive, Morgantown, WV 26506, USA

* Corresponding author.

E-mail address: Shipra.gupta@hsc.wvu.edu

such as masking and social distancing. There have been multiple reports of familial clusters and studies on household transmission.^{5–14} However, there is limited guidance on prevention measures once a household member is diagnosed with or exposed to the virus. This article highlights available data on transmission of SARS-CoV-2 and reviews preventive measures to reduce transmission of the virus both in the community and the household setting.

Epidemiology

Transmission and incubation period

The acquisition of SARS-CoV-2 occurs when a susceptible host comes in contact with respiratory secretions from an infected individual. Most transmission occurs through large droplets and occasionally small droplets via airborne spread.^{15–18} Airborne transmission can occur in enclosed spaces, poorly ventilated areas with improper air handling and prolonged or higher exposure dose of respiratory particles, as with expiratory exertion during exercise or singing.^{19–22} Theoretically, transmission can occur through contaminated surfaces; however, this is infrequent. Virus has been detected in stool specimens; however, viable virus has not been isolated from stool samples.²³ The incubation period for SARS-CoV-2 is up to 14 days from the time of exposure, and about 50% of people exposed have symptoms by day 4 or 5 and 98% by day 12 from exposure.^{24–29}

The window of contagiousness for a symptomatic individual starts about 2 to 3 days before onset of symptoms, peaks at symptoms onset, and declines over the following 7 days in most cases.^{30–33} Therefore, presymptomatic transmission seems to be a significant driver of spread of infection in the community and households. Early on during the pandemic, asymptomatic carriers were thought to be significant spreaders, especially in the household setting.^{34,35} However, recent data from Wuhan, China, showed that there was no SARS-CoV-2 detected by polymerase chain reaction (PCR) in 1174 close household contacts of the 300 asymptomatic persons.³⁶ The role of asymptomatic spreaders remains controversial, with recent modeling data suggesting that 50% of new infections were estimated to have been acquired from asymptomatic spreaders.³⁷ The period of contagiousness for asymptomatic individuals is not clearly understood and, for purposes of contact tracing, the cutoff is 48 hours before the positive test date is applied for identification of individuals who had potential exposure.

Secondary Attack Rates and Household Transmission

Secondary attack rate (SAR) is defined as the proportion of infections that occur among susceptible individuals following contact with an infected person within the incubation period.³⁸ The SAR for SARS-CoV-2 varies in different contact and exposure settings. Recent meta-analysis showed a pooled SAR for SARS-CoV-2 in diverse contact settings of 7% (95% confidence interval [CI], 3%–12%).³⁹ This study also highlighted low SAR in health care facilities, public transport, and work settings compared with the high SAR in households and exposures in social gatherings.

Crowded indoor environments and close contact among household members are high-risk settings for transmission of SARS-CoV-2. Initial reports out of China described SAR of 12.4% among household contacts when defined by close relatives and 17.1% when they shared the same residential address.⁸ Recent systemic review and meta-analysis estimated household SAR of 16.6% (95% CI, 14.0%–19.3%).⁴⁰ Most published literature reports increased SAR from symptomatic index cases compared with asymptomatic index cases as well as in spouses compared with other family contacts.^{40,41}

Lewis and colleagues⁹ reported that 31 out of the 58 households from Utah and Wisconsin had secondary transmission and 52 of 188 household contacts tested positive by either polymerase chain reaction (PCR) assay or serologic testing, giving a secondary infection rate of 28%. This study was done during March to April 2020 when there was low community prevalence at the study sites to reduce risk of additional community exposure. A higher secondary infection rate of 53% (95% CI, 46%–60%) was detected in households in a study done in Tennessee and Wisconsin in April to September 2020.⁶

Various retrospective studies have identified black ethnicity, male gender, smoking, and obesity as risk factors associated with higher risk of infection.^{42–44} Higher rates of infection have been reported in older household contacts (age \geq 60 years) compared with younger contacts.^{5,8} Multiple reports described lower SAR for children compared with adults.^{5,8–10,40,41} Hu and colleagues⁴⁵ performed a retrospective review of secondary cases and reported that secondary cases had less severe symptoms such as fever, cough, sore throat, and myalgia compared with the index cases.

Transmission from Children

Prolonged shedding of respiratory viruses after viral illness has been described in children younger than 5 years compared with older participants.⁴⁶ With most children having no symptoms or mild symptoms, it was thought that children could serve as a silent reservoir for SARS-CoV-2. However, multiple studies of outbreaks in familial clusters have shown that children are rarely the index case and are often identified after an adult has tested positive. Similar findings were confirmed from outbreaks at childcare facilities that were linked to index cases in adults.⁴⁷ In a large, multicenter, cross-sectional investigation in Germany, the estimated SARS-CoV-2 seroprevalence was low in parents and 3-fold lower in children.⁴⁸ Follow-up interviews with families of children who were hospitalized for coronavirus disease 2019 (COVID-19) illness were performed 6 weeks after the child became ill and showed there were no reported illnesses in the households and 1 case of child-to-child transmission.⁴⁹

School and Day Care Attendance

Schools across the United States were preemptively closed to in-person classes and transitioned to virtual learning early during the pandemic to mitigate spread of SARS-CoV-2. However, as months passed, certain states allowed in-person learning options along with the remote option. With the help of the local health department and guidance from Centers for Disease Control and Prevention (CDC), there have been multiple reports published for safe reopening of schools. A recent study showed that attending school or childcare 2 weeks before the testing date was not associated with an increased probability of a positive SARS-CoV-2 test.⁴⁷ Parents of cases and controls reported 64% and 76% consistent mask use respectively for both children and staff at schools or childcare facilities. Most of the children (<18 years old) who tested positive for SARS-CoV-2 were more likely to have attended gatherings with people outside their households 14 days before testing positive. Similar results were reported from North Carolina schools over a period of 9 weeks with extensive contact tracing where there was limited secondary transmission and zero child-to-adult transmission noted within the school.⁵⁰ These studies highlight that in-person teaching at schools can be achieved with consistent mask wearing, hand hygiene, and maintaining a distance of 2 m (6 feet) as well as screening and early detection of infection.

Nonpharmaceutical Interventions for Prevention of Severe Acute Respiratory Syndrome Coronavirus-2

Nonpharmaceutical interventions recommended to reduce transmission of SARS-CoV-2 include mask wearing, social distancing, hand hygiene, disinfection of frequently touched surfaces, improved ventilation, self-isolation, and quarantine.

Mask Wearing

Face masks are thought to reduce viral transmission from both the source and target of infection; they reduce the exhalation of respiratory particles by an infected person^{51,52} and reduce the inhalation of these particles by a susceptible host.^{52,53} Evidence supporting face mask use comes from epidemiologic data, observational studies, mathematical models, and laboratory studies.

Like SARS and Middle Eastern Respiratory Syndrome (MERS) Coronavirus, SARS-CoV-2 is a member of the Betacoronavirus genus, but it resembles the 2009 H1N1 influenza virus in its high degree of upper respiratory tract shedding, its propensity for asymptomatic and presymptomatic transmission, and the scope of its global spread.⁵⁴ The WHO sponsored a systematic review and meta-analysis that concluded that face mask use could significantly decrease the risk of SARS-CoV-2 infection.⁵⁵ In their systematic review and meta-analysis, Li and colleagues found that mask wearing significantly reduced the risk of COVID-19 infection, with a pooled odds ratio of 0.38 and 95% CI of 0.21 to 0.69.⁵⁶ A retrospective cohort study of households in Beijing, China, showed a 79% reduction in transmission if both the index case and family contacts wore masks before onset of symptoms in the index case.⁵⁷

Epidemiologic studies support the widespread use of face masks to prevent community transmission of SARS-CoV-2. Early in the course of the pandemic, Cheng and colleagues⁵⁸ compared the epidemiology of SARS-CoV-2 in the Hong Kong Special Administrative Region (HKSAR), where community-wide compliance with face mask use was 96.6%, with selected countries in North America, Europe, and Asia having similar population density but without universal masking. The incidence of SARS-CoV-2 was significantly lower in HSKAR.⁵⁸ A cross-sectional population-level study in the United States showed that self-reported face mask use was correlated with increased odds of transmission control, and that the effect of mask use was higher with increased levels of physical distancing.⁵⁹

Laboratory studies of airborne transmission provide additional evidence for the role of mask wearing in preventing the spread of COVID-19. Ueki and colleagues⁵² examined the efficacy of cotton, surgical, and N95 masks in blocking the transmission of infectious droplets and aerosols of SARS-CoV-2 using an airborne transmission simulator. All types of masks were protective against transmission of infectious particles, with a stronger effect noted when the mask was worn by the source of the virus.⁵² A study of the aerosol filtration efficiency of cloth masks showed that snugly fitted masks could provide good protection from a range of aerosol particle sizes. Filtration efficiency was significantly higher in masks made from multiple layers of tightly woven fabric, particularly when different types of fabric were combined in the same mask. Of note, filtration efficiency in poorly fitted masks was found to decrease by more than 60%, highlighting the importance of proper mask fitting to reduce transmission of respiratory particles.⁵³

Current evidence-based guidelines from the CDC emphasize the importance of consistent and correct face mask use to decrease transmission of SARS-CoV-2 in the community. The CDC recommends using fabric masks made with 2 or 3 layers of tightly woven, breathable fabric (such as cotton), or disposable, single-use

nonmedical masks. Regardless of the type of mask used, it should be snugly fitted around the nose and chin, without large gaps at the sides or top. Masks with exhalation valves or vents should not be used, because they may allow passage of respiratory particles. In order to prevent critical supply shortages, surgical masks and respirators should be avoided in the community setting. Outside the home, face masks should be worn while indoors in public places, and in crowded outdoor areas where interpersonal distance is less than 2 m.⁶⁰

Physical Distancing

Studies of COVID-19 outbreaks occurring in community settings outside the home have shown that increased infection risk is associated with close contact with other members of the community, particularly in enclosed spaces.⁶⁰ A contact tracing study of train passengers in China found that risk of SARS-CoV-2 transmission increased with spatial proximity to the index case, as well as increased duration of shared travel time.⁶¹

Epidemiologic studies lend support to public health guidance on physical distancing to slow the spread of the pandemic. The WHO's systematic review and meta-analysis of nonpharmaceutical measures to prevent SARS-CoV-2 transmission found that the risk of viral infection decreased as interpersonal distancing increased, and concluded that physical separation of at least 1 m was beneficial, but separation of 2 m might be more effective in decreasing the risk of infection.⁵⁵

The COVID-19 Pandemic Pulse Study evaluated self-reported movement patterns and nonpharmaceutical intervention use with SARS-CoV-2 positivity in Maryland in June of 2020. Although this study failed to show a statistically significant effect for indoor mask use, it did show a significant association between strict social distancing and decreased risk of SARS-CoV-2 infection. Of note, after adjusting for social distancing and demographic variables, the types of movement that significantly correlated with increased infection risk were use of public transportation and visiting a place of worship within the previous 2 weeks.⁶²

Physical distancing to reduce the spread of SARS-CoV-2 has reduced the incidence of other respiratory viruses. A Mayo Clinic study that reviewed community transmission of respiratory viruses in Arizona found that enactment of distancing policies coincided with a marked reduction in both the overall number of respiratory panel tests and the percentage of positive test results for common respiratory viruses during April through July of 2020, compared with the equivalent time frame in 2017 through 2019.⁶³

Based on the available evidence regarding transmission patterns, unnecessary interactions with persons outside the household should be limited while SARS-CoV-2 is circulating in the community.⁶⁰ When outside the home, physical distance of at least 2 m should be maintained from nonhousehold members. Unnecessary exposure to indoor environments should be avoided, particularly those associated with increased transmission risk, such as indoor restaurant dining, worship services, and exercise classes. Nonessential use of public transportation should be avoided whenever possible. Because there is emerging evidence of SARS-CoV-2 transmission occurring in large outdoor gatherings, exposure to crowded outdoor venues should also be avoided.^{60,64} Limiting contact with other members of the community is especially important for persons at high risk for severe COVID-19 illness, and those who share a household with someone at high risk. With the advent of widespread immunization for COVID-19, the CDC has issued revised guidelines for indoor visits or small gatherings in private residences. Fully vaccinated people do not need to wear masks or maintain physical distancing during indoor visits with other fully vaccinated people,

or with unvaccinated people from a single household who are at low risk for severe COVID-19. If any of the unvaccinated people or their household members are at increased risk of severe COVID-19, or if the unvaccinated people come from multiple households, fully vaccinated people should continue to wear masks, maintain physical distance of at least 2 m, and visit outdoors or in a well-ventilated indoor space.⁶⁵ Unvaccinated individuals should continue to limit the number of unvaccinated visitors allowed inside the home, ensure that masks are worn by unvaccinated visitors and members of the household alike, maintain at least 2 m of separation from unvaccinated visitors at all times, and limit the amount of time spent visiting indoors.⁶⁶ All people, regardless of their immunization status, should continue to avoid medium-sized or large gatherings, regardless of their immunization status.⁶⁵

The CDC recommends that people postpone travel while SARS-CoV-2 is prevalent in the community. Those who do travel should be tested for SARS-CoV-2 from 1 to 3 days before departure and retested 3 to 5 days after arrival. On return, travelers should self-isolate and monitor for symptoms at home for 7 days if tested, even if test results are negative, and for 10 days if not tested. If other members of the household did not accompany the traveler, both the traveler and other members of the household should wear masks in shared household spaces for 14 days.⁶⁷

Hand Hygiene

Although there are several case reports of suspected transmission of SARS-CoV-2 via contact with contaminated surfaces, there is currently no definitive evidence of transmission via direct contact or fomites.⁶⁸ Studies of nonpharmaceutical interventions to prevent the spread of respiratory viruses have shown mixed results on the efficacy of hand washing alone. A systematic review and meta-analysis of influenza virus transmission in the community found that frequent hand hygiene plus mask wearing significantly decreased transmission of influenza, but hand hygiene alone did not.⁶⁹ However, these reviews considered the impact of hand hygiene on transmission of respiratory viruses but not SARS-CoV-2. These results may not correspond with the real-world transmission dynamics of SARS-CoV-2, which is significantly more stable than influenza virus.⁷⁰ A modeling study by Przekwas and Chen⁷¹ described how SARS-CoV-2 might be inoculated onto respiratory epithelium via deposition of viral particles on the face by contaminated hands, and concluded that washing of the face and hands might prevent infection.

Because SARS-CoV-2 is a lipid-enveloped RNA virus, it is susceptible to inactivation by agents that disrupt the integrity of its lipid envelope, such as alcohol and hand soap.⁷² A review of commonly used hand sanitizers found that most alcohol-based hand sanitizers were successful at inactivating enveloped viruses, including coronavirus, but that washing with soap and water was superior to sanitizers in removing pathogens and debris from hands.⁷³ A laboratory study by Hirose and colleagues⁷⁰ determined that hand sanitizer containing 80% ethanol completely inactivated SARS-CoV-2 on skin within 15 seconds of exposure.

Disinfection of Frequently Touched Surfaces

Although less likely, transmission by fomites remains a possibility, and disinfection of frequently touched surfaces may help to decrease the risk of infection. A retrospective cohort study of households in Beijing, China, found that daily use of a disinfectant containing chlorine or ethanol was 77% effective in decreasing household transmission of SARS-CoV-2.⁵⁷

A literature review that examined the effectiveness of various cleaning products in disinfecting surfaces contaminated by human coronaviruses concluded that the virus was

successfully inactivated by solutions of 62% to 71% ethanol, 0.5% hydrogen peroxide, or 0.1% sodium hypochlorite within 1 minute. For household disinfection, the investigators recommend a 1:50 dilution of standard household bleach; alternatively, a solution of 62% to 70% ethanol may be used for disinfection of small surfaces.⁷⁴ Current guidance for prevention of COVID-19 from WHO recommends the use of 0.1% sodium hypochlorite solution or 70% to 90% ethanol for household disinfection.⁷⁵

Ventilation

Respiratory particles emitted by humans span a continuum of sizes, from large droplets to tiny aerosols. Conventional wisdom holds that droplets more than 5 μm in diameter fall to the ground within 1 to 2 m of the source, whereas smaller aerosols remain suspended in the air; however, this is now understood to be a false dichotomy. The duration of time that a particle remains suspended in the air depends not only on its diameter but also on the velocity at which it is emitted, and a host of environmental factors, including the temperature, humidity, speed, and direction of ambient airflow.⁷⁶ Therefore, both proximity and ventilation have emerged as key determinants of transmission risk for SARS-CoV-2.⁶⁸ A mathematical model of indoor transmission found that increasing ventilation rate was correlated with decreasing infection probability. Of note, the model also predicted that mask wearing indoors significantly decreased infection probability, even at lower rates of air exchange.⁷⁷ Using the principles of fluid mechanics, Bhagat and colleagues⁷⁸ assessed the impact of ventilation on the movement of infectious particles in an enclosed space, and concluded that displacement ventilation was most effective in removing contaminated air and decreasing the exposure risk. Displacement ventilation consists of exhaust fans or vents installed on or near the ceiling of the room, as can be found in the kitchens and bathrooms of most modern homes.

Preventive Measures When Household Member Has Been Diagnosed with COVID-19 and Is at Home

Given the high secondary attack rate of SARS-CoV-2 in households, special care must be taken to reduce the risk of transmission to household contacts when an infected person is quarantined at home. The CDC provides detailed recommendations for preventive measures when a member of the household is symptomatic with COVID-19 and is cared for at home. The same recommendations apply when a household member has tested positive for the virus but remains asymptomatic or presymptomatic. Affected persons should be isolated from other members of the household and, if possible, should use a separate bedroom and bathroom, and eat meals in their rooms. Caregivers should limit exposure to the individual and try to maintain at least 2 m of interpersonal distance. The affected persons and their household contacts should wear masks whenever they are near each other; however, masks should not be worn by children less than 2 years of age, people who are unable to remove them without assistance, or anyone with respiratory distress.⁷⁹ Prevention of airborne transmission is particularly important in household settings. Current CDC guidance emphasizes the importance of good ventilation to decrease the concentration of potentially infectious airborne particles in shared indoor spaces. Recommendations for improving household ventilation include the following⁸⁰:

- Open doors and windows as much as possible to introduce fresh air from outside.
- Increase air circulation in the home using portable fans, ceiling fans, or central heating, ventilation, and air conditioning fan setting.

- Install high-efficiency pleated filters in central heating, ventilation, and air conditioning systems. Filter indoor air using a portable air cleaner or high-efficiency particulate air filter.
- Turn on exhaust fans in kitchen and bathroom, or place portable fans blowing outward near open doors and windows, to move stale air outdoors.

To decrease transmission through direct contact and fomites, the CDC advises that household members wash their hands frequently with soap and water for at least 20 seconds, or use hand sanitizer containing at least 60% alcohol, and avoid touching the eyes, nose, or mouth with unwashed hands. Frequently touched surfaces, such as light switches, doorknobs, desks, tables, electronics, sinks, faucets, and toilets, should be cleaned and disinfected daily. If the affected person uses a shared bathroom, the person should clean and disinfect it after use if are able to do so; if not, the caregiver should wait as long as possible before entering the bathroom to clean and disinfect it. Caregivers should wear gloves to prevent contact with the affected person's secretions, bodily fluids, or stool. Gloves should also be worn when handling contaminated items, washing dishes, or doing laundry. Dishes should be washed with soap and hot water, or in a dishwasher. Dirty laundry may be combined with laundry from other household members but should be washed and dried on the hottest settings possible. Used gloves, masks, and other contaminated items should be discarded in a trash can with a disposable liner, preferably one set aside for use by the affected person, and gloves should be worn when handling and disposing of contaminated trash. Caregivers should wash their hands after removing gloves.⁷⁹

Because the estimated incubation period of SARS-CoV-2 can last up to 14 days, the CDC recommends that caregivers and close household contacts of the affected person quarantine at home for 14 days after their last exposure to the affected person, or 14 days after the affected person meets criteria to end isolation. Close contact is defined as being within 2 m of the infected person for a total of 15 minutes or more, direct physical contact such as hugging or kissing, sharing the same utensils for eating or drinking, or direct exposure to respiratory droplets from coughing or sneezing. Caregivers and close household contacts with a history of laboratory-confirmed COVID-19 infection and recovery within the past 3 months or fully vaccinated contacts are exempted from the quarantine requirement, and do not require repeat testing unless they become symptomatic.⁸¹ Public health departments establish quarantine guidelines within their jurisdictions based on local circumstances and resources, and may recommend alternative guidelines to shorten the duration of quarantine.⁸¹

Pharmaceutical Interventions

Throughout the pandemic, there have been ongoing efforts to evaluate the antiviral properties of medications that could prevent SARS-CoV-2 infection following exposure. Examples include antiparasitic drugs such as ivermectin, antimalarials such as hydroxychloroquine, antiviral medications such as amantadine, and antiretroviral medications.⁸² None of the therapeutics have shown a clear benefit and none have been approved/recommended for early prevention of COVID-19 infection.

In addition, there are various ongoing clinical studies to understand the role of early therapeutic interventions to prevent progression of disease in the early phase of illness. Anti-SARS-CoV-2 monoclonal antibodies such as bamlanivimab and the combination of casirivimab and imdevimab received an emergency use authorization (EUA) by the US Food and Drug Administration (FDA) as preventive management for nonhospitalized patients at high risk of disease progression who have mild to moderate illness. The interim results of a phase 2, randomized, placebo-controlled trial

showed that a single infusion of bamlanivimab increased the viral RNA clearance and decreased rates of hospitalization compared with a placebo group.⁸³ The current EUAs for both bamlanivimab and the combination of casirivimab and imdevimab include pediatric patients at least 12 years of age who weigh at least 40 kg.

Vitamin D and vitamin C have been studied as potential immunomodulatory agents to prevent infection with SARS-CoV-2. However, data on prevention of COVID-19 with supplements containing vitamin D and vitamin C are limited to observational studies. Vitamin D increases innate immunity by secretion of antiviral peptides, which improve mucosal defenses. Various systematic reviews and meta-analyses of observational data have shown that low levels of serum vitamin D are associated with increase in respiratory tract infections, including influenza and pneumonia. A recent study evaluated the association between average levels of vitamin D and mortality caused by COVID-19 and number of cases of COVID-19. This study was limited to European countries and found a negative correlation between levels of vitamin D and number of cases of COVID-19 as well as mortality caused by COVID-19, showing that low vitamin D level may be associated with COVID-19 infection and complications.⁸⁴ Another study of patients in European countries found a significant negative correlation between average vitamin D levels and COVID-19 cases, but not with death.⁸⁵ Because of the limited ability to generalize from these trials and lack of studies in pediatric patients, supplementation with vitamin D to prevent SARS-CoV-2 infection is currently not recommended. However, vitamin D supplementation may be warranted in pediatric patients with known vitamin D deficiency.

Ascorbic acid, or Vitamin C, has been studied as potential immunomodulatory agent. Vitamin C has been evaluated in patients with serious infections and sepsis with inconsistent results.^{86,87} Although there are many ongoing clinical trials evaluating its place in therapy, it is currently not routinely recommended for prevention of SARS-CoV-2 in pediatric patients.

Zinc supplementation has also been studied as a preventive as well as for management of COVID-19 in ongoing clinical trials. In vitro studies have shown that increased intracellular zinc concentrations decrease replication in RNA viruses such as rhinoviruses and coronaviruses.^{88,89}

Topical Agents

The nose and mouth are significant entry portals for the virus, because infection is primarily transmitted by inhalation of, or contact with, infected droplets. In addition, the nasal cavity and nasopharynx contains the highest viral load. Therefore, topical nasal irrigations and oral rinses have been identified as potential options to prevent SARS-CoV-2 infection.

There is currently limited evidence regarding the use of topical therapies in the prevention of SARS-CoV-2 infection specifically. However, available data to support these agents in other viral illnesses may help guide preventive measures for SARS-CoV-2.⁹⁰ Regular use of saline nasal irrigation in children has been shown to prevent symptoms of rhinitis and associated complications.⁹¹ In addition, use of hypertonic saline nasal irrigation and gargling was associated with decreased duration of illness, over-the-counter medication use, transmission within household contacts, and viral load of many viruses, including rhinovirus, enterovirus, influenza A virus, and coronavirus (not SARS-CoV-2).⁹²

Povidone-iodine (PVP-1) is another topical agent identified for potential use in the prevention of SARS-CoV-2 infections. PVP-1 is a solution that disrupts microbial metabolic pathways, destabilizes structural components of cell membranes, and leads to irreversible damage to pathogens. PVP-1 has been shown to achieve almost

100% virucidal activity against SARS-CoV-2 within 30 seconds of contact in the laboratory.⁹³ Another in vitro study found that PVP-1 at diluted concentrations of 0.5%, 1.25%, and 2.5% completely inactivated SARS-CoV-2 within 15 seconds of contact.⁹⁴ Although neither of these studies was done in humans, a review of PVP-1 use in sinonasal and oral cavities found that PVP-1 is safe to use in the nose up to a strength of 1.25% for 5 months and in the mouth up to a strength of 5% for 6 months.⁹⁵ However, the over-the-counter product is commercially available at a strength of 10%, so this product should not be used in the nose or mouth. Until a commercially available diluted solution is available and clinical trials have been completed, PVP-1 should not be used to prevent SARS-CoV-2 infections in children.

There is currently insufficient evidence to support the use of topical therapies to prevent COVID-19 in children. Risks associated with these therapies include irritation, loss of smell, and destruction of microorganisms in the nose or mouth that are useful in preventing infection. In addition, if nasal spray solutions are used on multiple children without sterilizing the bottle or product, spread of disease may increase. There are currently multiple trials underway to determine the safety and efficacy of topical agents in prevention of COVID-19 infection and transmission.

Vaccines

Vaccines offer the best preventive strategy to contain the SARS-CoV-2 pandemic. Several vaccines using different methodologies are being developed across the world. Recently, 2 nucleoside-modified RNA vaccines encoding the SARS-CoV-2 spike protein were shown to be efficacious in preventing COVID-19 illness, including severe disease.^{96,97} These 2 vaccines received an EUA by the FDA and are being used across the United States to vaccinate health care workers and people at high risk of severe disease. The Pfizer-BioNTech COVID-19 vaccine and MODERNA COVID-19 vaccine also received an interim recommendation for immunization of individuals greater than or equal to 16 years and greater than or equal to 18 years of age respectively.^{98,99} However, there are clinical trials being done to evaluate safety and efficacy in younger children.

There are limited data on the effect of vaccine on asymptomatic transmission, and therefore the current recommendation is to continue practicing masking and social distancing until most the population is immunized.

SUMMARY

Prevention of exposure to SARS-CoV-2 and, most recently, vaccination against the virus have been the mainstay of efforts to control the spread of the virus. Children have been reported to have mild illness, with few developing complications and having poor outcomes. Children have also been noted to not spread or acquire the virus as much as adults. Childcare settings and schools have been safely reopened with minimal transmission noted among children with safety measures of masking, maintaining distance, and hand washing. Transmission in outdoor settings is low and indoor transmission can be reduced in the household setting by increasing ventilation along with other mitigation strategies. Pharmaceutical interventions other than vaccination have not been shown to prevent infection with SARS-CoV-2.

CLINICS CARE POINTS

- Nonpharmaceutical interventions such as social distancing, masking, and hand hygiene have been the primary preventive strategies to avoid infection with SARS-CoV-2.

- Early and rapid identification of infected individuals and tracing of contacts, as well as isolation and quarantine, are effective measures to curb the spread of infection.
- Systematic development of effective vaccines to prevent severe illness caused by COVID-19 offer a path forward to containing the pandemic and reducing the burden of severe disease. Other pharmaceutical interventions are still under investigation and so far have not shown benefit in preventing COVID-19.

DISCLOSURE

The authors have no commercial or financial conflicts of interest or funding sources.

REFERENCES

1. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med* 2020;382(8):727–33.
2. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020;579(7798):270–3.
3. Director-General's opening remarks at the media briefing on COVID19. World Health Organization WHO; 2020.
4. Coronavirus disease 2019 (COVID-19) Situation report - 3.11.2020. World Health Organization WHO. Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200302-sitrep-42-covid-19.pdf?sfvrsn=224c1add_2. Accessed June 4, 2021.
5. Fung HF, Martinez L, Alarid-Escudero F, et al. The household secondary attack rate of SARS-CoV-2: A rapid review. *Clin Infect Dis* 2020. <https://doi.org/10.1093/cid/ciaa1558>.
6. Grijalva CG, Rolfes MA, Zhu Y, et al. Transmission of SARS-COV-2 Infections in Households - Tennessee and Wisconsin, April-September 2020. *MMWR Morb Mortal Wkly Rep* 2020;69(44):1631–4.
7. Jing QL, Liu MJ, Yuan J, et al. Household Secondary Attack Rate of COVID-19 and Associated Determinants. *medRxiv* 2020. <https://doi.org/10.1101/2020.04.11.20056010>.
8. Jing QL, Liu MJ, Zhang ZB, et al. Household secondary attack rate of COVID-19 and associated determinants in Guangzhou, China: a retrospective cohort study. *Lancet Infect Dis* 2020;20(10):1141–50.
9. Lewis NM, Chu VT, Ye D, et al. Household Transmission of SARS-CoV-2 in the United States. *Clin Infect Dis* 2020. <https://doi.org/10.1093/cid/ciaa1166>.
10. Li W, Zhang B, Lu J, et al. Characteristics of Household Transmission of COVID-19. *Clin Infect Dis* 2020;71(8):1943–6.
11. Wang Z, Ma W, Zheng X, et al. Household transmission of SARS-CoV-2. *J Infect* 2020;81(1):179–82.
12. Xu X, Liu X, Wang L, et al. Household transmissions of SARS-CoV-2 in the time of unprecedented travel lockdown in China. *medRxiv* 2020. <https://doi.org/10.1101/2020.03.02.20029868>.
13. Yang MC, Hung PP, Wu YK, et al. A three-generation family cluster with COVID-19 infection: should quarantine be prolonged? *Public Health* 2020;185:31–3.
14. Yung CF, Kam KQ, Chong CY, et al. Household Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 from Adults to Children. *J Pediatr* 2020; 225:249–51.
15. Kang M, Wei J, Yuan J, et al. Probable Evidence of Fecal Aerosol Transmission of SARS-CoV-2 in a High-Rise Building. *Ann Intern Med* 2020;173(12):974–80.

16. Miller SL, Nazaroff WW, Jimenez JL, et al. Transmission of SARS-CoV-2 by inhalation of respiratory aerosol in the Skagit Valley Chorale superspreading event. *Indoor Air* 2020. <https://doi.org/10.1111/ina.12751>.
17. Yu IT, Li Y, Wong TW, et al. Evidence of airborne transmission of the severe acute respiratory syndrome virus. *N Engl J Med* 2004;350(17):1731–9.
18. WHO. WHO. Transmission of SARS-CoV-2: implications for infection prevention precautions. Available at: <https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions>. Accessed June 6,2021.
19. Bae S, Kim H, Jung TY, et al. Epidemiological Characteristics of COVID-19 Outbreak at Fitness Centers in Cheonan, Korea. *J Korean Med Sci* 2020; 35(31):e288.
20. Brlek A, Vidovič Š, Vuzem S, et al. Possible indirect transmission of COVID-19 at a squash court, Slovenia, March 2020: case report. *Epidemiol Infect* 2020;148: e120.
21. Lu J, Gu J, Li K, et al. COVID-19 Outbreak Associated with Air Conditioning in Restaurant, Guangzhou, China, 2020. *Emerg Infect Dis* 2020;26(7):1628–31.
22. Li Y, Leung GM, Tang JW, et al. Role of ventilation in airborne transmission of infectious agents in the built environment - a multidisciplinary systematic review. *Indoor Air* 2007;17(1):2–18.
23. Xu Y, Li X, Zhu B, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat Med* 2020;26(4):502–5.
24. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020;382(18):1708–20.
25. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med* 2020;382(13):1199–207.
26. Lauer SA, Grantz KH, Bi Q, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann Intern Med* 2020;172(9):577–82.
27. He X, Lau EHY, Wu P, et al. Author Correction: Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med* 2020;26(9):1491–3.
28. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med* 2020;26(5):672–5.
29. Team C-I. Clinical and virologic characteristics of the first 12 patients with coronavirus disease 2019 (COVID-19) in the United States. *Nat Med* 2020;26(6): 861–8.
30. Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. *N Engl J Med* 2020;382(12):1177–9.
31. To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis* 2020;20(5): 565–74.
32. Wölfel R, Corman VM, Guggemos W, et al. Author Correction: Virological assessment of hospitalized patients with COVID-2019. *Nature* 2020;588(7839):E35.
33. Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature* 2020;581(7809):465–9.
34. Jiang XL, Zhang XL, Zhao XN, et al. Transmission Potential of Asymptomatic and Paucisymptomatic Severe Acute Respiratory Syndrome Coronavirus 2 Infections: A 3-Family Cluster Study in China. *J Infect Dis* 2020;221(12):1948–52.
35. Ye F, Xu S, Rong Z, et al. Delivery of infection from asymptomatic carriers of COVID-19 in a familial cluster. *Int J Infect Dis* 2020;94:133–8.

36. Cao S, Gan Y, Wang C, et al. Post-lockdown SARS-CoV-2 nucleic acid screening in nearly ten million residents of Wuhan, China. *Nat Commun* 2020;11(1):5917.
37. Johansson MA, Quandelacy TM, Kada S, et al. SARS-CoV-2 Transmission From People Without COVID-19 Symptoms. *JAMA Netw Open* 2021;4(1):e2035057.
38. Palmer CR. Encyclopedia of biostatistics. *BMJ* 1999;318(7182):542.
39. Tian T, Huo X. Secondary attack rates of COVID-19 in diverse contact settings, a meta-analysis. *J Infect Dev Ctries* 2020;14(12):1361–7.
40. Madewell ZJ, Yang Y, Longini IM, et al. Household Transmission of SARS-CoV-2: A Systematic Review and Meta-analysis. *JAMA Netw Open* 2020;3(12):e2031756.
41. Koh WC, Naing L, Chaw L, et al. What do we know about SARS-CoV-2 transmission? A systematic review and meta-analysis of the secondary attack rate and associated risk factors. *PLoS One* 2020;15(10):e0240205.
42. Niedzwiedz CL, O'Donnell CA, Jani BD, et al. Ethnic and socioeconomic differences in SARS-CoV-2 infection: prospective cohort study using UK Biobank. *BMC Med* 2020;18(1):160.
43. Sattar N, Ho FK, Gill JM, et al. BMI and future risk for COVID-19 infection and death across sex, age and ethnicity: Preliminary findings from UK biobank. *Diabetes Metab Syndr* 2020;14(5):1149–51.
44. Engin AB, Engin ED, Engin A. Two important controversial risk factors in SARS-CoV-2 infection: Obesity and smoking. *Environ Toxicol Pharmacol* 2020;78:103411.
45. Hu P, Ma M, Jing Q, et al. Retrospective study identifies infection related risk factors in close contacts during COVID-19 epidemic. *Int J Infect Dis* 2020. <https://doi.org/10.1016/j.ijid.2020.12.011>.
46. Byington CL, Ampofo K, Stockmann C, et al. Community Surveillance of Respiratory Viruses Among Families in the Utah Better Identification of Germs-Longitudinal Viral Epidemiology (BIG-LoVE) Study. *Clin Infect Dis* 2015;61(8):1217–24.
47. Lopez AS, Hill M, Antezano J, et al. Transmission Dynamics of COVID-19 Outbreaks Associated with Child Care Facilities — Salt Lake City, Utah, April–July 2020. *MMWR Morb Mortal Wkly Rep* 2020;1319–23.
48. Tönshoff B, Müller B, Elling R, et al. Prevalence of SARS-CoV-2 Infection in Children and Their Parents in Southwest Germany. *JAMA Pediatr* 2021. <https://doi.org/10.1001/jamapediatrics.2021.0001>.
49. Pitman-Hunt C, Leja J, Jiwani ZM, et al. SARS-CoV-2 Transmission in an Urban Community: The Role of Children and Household Contacts. *J Pediatr Infect Dis Soc* 2020. <https://doi.org/10.1093/jpids/piaa158>.
50. Zimmerman KO, Akinboyo IC, Brookhart MA, et al. Incidence and Secondary Transmission of SARS-CoV-2 Infections in Schools. *Pediatrics* 2021. <https://doi.org/10.1542/peds.2020-048090>.
51. Leung NHL, Chu DKW, Shiu EYC, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nat Med* 2020;26(5):676–80.
52. Ueki H, Furusawa Y, Iwatsuki-Horimoto K, et al. Effectiveness of Face Masks in Preventing Airborne Transmission of SARS-CoV-2. *mSphere* 2020;5(5). <https://doi.org/10.1128/mSphere.00637-20>.
53. Konda A, Prakash A, Moss GA, et al. Aerosol Filtration Efficiency of Common Fabrics Used in Respiratory Cloth Masks. *ACS Nano* 2020;14(5):6339–47.
54. Wu Z, Harrich D, Li Z, et al. The unique features of SARS-CoV-2 transmission: Comparison with SARS-CoV, MERS-CoV and 2009 H1N1 pandemic influenza virus. *Rev Med Virol* 2020;e2171.

55. Chu DK, Akl EA, Duda S, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. *Lancet* 2020;395(10242):1973–87.
56. Li Y, Liang M, Gao L, et al. Face masks to prevent transmission of COVID-19: A systematic review and meta-analysis. *Am J Infect Control* 2020. <https://doi.org/10.1016/j.ajic.2020.12.007>.
57. Wang Y, Tian H, Zhang L, et al. Reduction of secondary transmission of SARS-CoV-2 in households by face mask use, disinfection and social distancing: a cohort study in Beijing, China. *BMJ Glob Health* 2020;5(5). <https://doi.org/10.1136/bmjgh-2020-002794>.
58. Cheng VC, Wong SC, Chuang VW, et al. The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2. *J Infect* 2020;81(1):107–14.
59. Rader B, White LF, Burns MR, et al. Mask-wearing and control of SARS-CoV-2 transmission in the USA: a cross-sectional study. *Lancet Digit Health* 2021. [https://doi.org/10.1016/S2589-7500\(20\)30293-4](https://doi.org/10.1016/S2589-7500(20)30293-4).
60. Honein MA, Christie A, Rose DA, et al. Summary of Guidance for Public Health Strategies to Address High Levels of Community Transmission of SARS-CoV-2 and Related Deaths, December 2020. *MMWR Morb Mortal Wkly Rep* 2020; 69(49):1860–7.
61. Hu M, Lin H, Wang J, et al. The risk of COVID-19 transmission in train passengers: an epidemiological and modelling study. *Clin Infect Dis* 2020. <https://doi.org/10.1093/cid/ciaa1057>.
62. Clipman SJ, Wesolowski AP, Gibson DG, et al. Rapid real-time tracking of non-pharmaceutical interventions and their association with SARS-CoV-2 positivity: The COVID-19 Pandemic Pulse Study. *Clin Infect Dis* 2020. <https://doi.org/10.1093/cid/ciaa1313>.
63. Freeman CM, Rank MA, Bolster LaSalle CM, et al. Effectiveness of Physical Distancing: Staying 6 Feet Over to Put Respiratory Viruses 6 Feet Under. *Mayo Clin Proc* 2021;96(1):148–51.
64. Bulfone TC, Malekinejad M, Rutherford GW, et al. Outdoor Transmission of SARS-CoV-2 and Other Respiratory Viruses, a Systematic Review. *J Infect Dis* 2020;29. <https://doi.org/10.1093/infdis/jiaa742>.
65. Prevention CfDca. Interim public health recommendations for fully vaccinated people 2021. Available at: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html#anchor_1615143393075. Accessed March 23, 2021.
66. Prevention CfDca. Personal and Social Activities. 2021. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/personal-social-activities.html>. Accessed March 24, 2021.
67. Prevention CfDca. Travel During COVID-19. 2021. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/travelers/travel-during-covid19.html>. Accessed February 6, 2021.
68. Meyerowitz EA, Richterman A, Gandhi RT, et al. Transmission of SARS-CoV-2: A Review of Viral, Host, and Environmental Factors. *Ann Intern Med* 2021;174(1): 69–79.
69. Wong VW, Cowling BJ, Aiello AE. Hand hygiene and risk of influenza virus infections in the community: a systematic review and meta-analysis. *Epidemiol Infect* 2014;142(5):922–32.

70. Hirose R, Ikegaya H, Naito Y, et al. Survival of SARS-CoV-2 and influenza virus on the human skin: Importance of hand hygiene in COVID-19. *Clin Infect Dis* 2020. <https://doi.org/10.1093/cid/ciaa1517>.
71. Przekwas A, Chen Z. Washing hands and the face may reduce COVID-19 infection. *Med Hypotheses* 2020;144:110261.
72. Rundle CW, Presley CL, Militello M, et al. Hand hygiene during COVID-19: Recommendations from the American Contact Dermatitis Society. *J Am Acad Dermatol* 2020;83(6):1730–7.
73. Golin AP, Choi D, Ghahary A. Hand sanitizers: A review of ingredients, mechanisms of action, modes of delivery, and efficacy against coronaviruses. *Am J Infect Control* 2020;48(9):1062–7.
74. Kampf G, Todt D, Pfaender S, et al. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *J Hosp Infect* 2020;104(3):246–51.
75. Organization WH. Cleaning and disinfection of environmental surfaces in the context of COVID-19: Interim guidance. 2020. Available at: <https://www.who.int/publications/i/item/cleaning-and-disinfection-of-environmental-surfaces-in-the-context-of-covid-19>. Accessed February 10, 2021.
76. Tang JW, Bahnfleth WP, Bluysen PM, et al. Dismantling myths on the airborne transmission of severe acute respiratory syndrome coronavirus (SARS-CoV-2). *J Hosp Infect* 2021. <https://doi.org/10.1016/j.jhin.2020.12.022>.
77. Dai H, Zhao B. Association of the infection probability of COVID-19 with ventilation rates in confined spaces. *Build Simul* 2020;4:1–7.
78. Bhagat R, Davies Wykes M, Dalziel S, et al. Effects of ventilation on the indoor spread of COVID-19. *J Fluid Mech* 2020;903:F1.
79. Prevention CfDca. Caring for someone Sick at home: Advice for caregivers in non-healthcare settings. 2021. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/care-for-someone.html>. Accessed March 24, 2021.
80. Prevention CfDca. Improving ventilation in Your home. 2021. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/Improving-Ventilation-Home.html>. Accessed January 26, 2021.
81. Prevention CfDca. When to Quarantine: Stay home if you might have been exposed to COVID-19 2020. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html>. Accessed January 27, 2021.
82. Andrade BS, Rangel FS, Santos NO, et al. Repurposing Approved Drugs for Guiding COVID-19 Prophylaxis: A Systematic Review. *Front Pharmacol* 2020;11:590598.
83. Chen P, Nirula A, Heller B, et al. SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19. *N Engl J Med* 2021;384(3):229–37.
84. Ilie PC, Stefanescu S, Smith L. The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality. *Aging Clin Exp Res* 2020;32(7):1195–8.
85. Ali N. Role of vitamin D in preventing of COVID-19 infection, progression and severity. *J Infect Public Health* 2020;13(10):1373–80.
86. Aranow C. Vitamin D and the immune system. *J Investig Med* 2011;59(6):881–6.
87. Wei XB, Wang ZH, Liao XL, et al. Efficacy of vitamin C in patients with sepsis: An updated meta-analysis. *Eur J Pharmacol* 2020;868:172889.
88. Korant BD, Kauer JC, Butterworth BE. Zinc ions inhibit replication of rhinoviruses. *Nat* 1974;248(449):588–90.

89. te Velhuis AJ, van den Worm SH, Sims AC, et al. Zn(2+) inhibits coronavirus and arterivirus RNA polymerase activity in vitro and zinc ionophores block the replication of these viruses in cell culture. *PLoS Pathog* 2010;6(11):e1001176.
90. Casale M, Rinaldi V, Sabatino L, et al. Could nasal irrigation and oral rinse reduce the risk for COVID-19 infection? *Int J Immunopathol Pharmacol* 2020;34:2058738420941757.
91. Slapak I, Skoupá J, Strnad P, et al. Efficacy of isotonic nasal wash (seawater) in the treatment and prevention of rhinitis in children. *Arch Otolaryngol Head Neck Surg* 2008;134(1):67–74.
92. Ramalingam S, Graham C, Dove J, et al. A pilot, open labelled, randomised controlled trial of hypertonic saline nasal irrigation and gargling for the common cold. *Sci Rep* 2019;9(1):1015.
93. Anderson DE, Sivalingam V, Kang AEZ, et al. Povidone-Iodine Demonstrates Rapid In Vitro Virucidal Activity Against SARS-CoV-2, The Virus Causing COVID-19 Disease. *Infect Dis Ther* 2020;9(3):669–75.
94. Frank S, Brown SM, Capriotti JA, et al. In Vitro Efficacy of a Povidone-Iodine Nasal Antiseptic for Rapid Inactivation of SARS-CoV-2. *JAMA Otolaryngol Head Neck Surg* 2020. <https://doi.org/10.1001/jamaoto.2020.3053>.
95. Frank S, Capriotti J, Brown SM, et al. Povidone-Iodine Use in Sinonasal and Oral Cavities: A Review of Safety in the COVID-19 Era. *Ear Nose Throat J* 2020;99(9):586–93.
96. Polack FP, Thomas SJ, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med* 2020;383(27):2603–15.
97. Baden LR, El Sahly HM, Essink B, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med* 2020. <https://doi.org/10.1056/NEJMoa2035389>.
98. Oliver SE, Gargano JW, Marin M, et al. The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine - United States, December 2020. *MMWR Morb Mortal Wkly Rep* 2020;69(50):1922–4.
99. Oliver SE, Gargano JW, Marin M, et al. The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Moderna COVID-19 Vaccine - United States, December 2020. *MMWR Morb Mortal Wkly Rep* 2021;69(5152):1653–6.