2020 is finally behind us, but we have much to do in first half of 2021. I hope you and your family had a joyous and safe New Year.

Today under COVID-19 News I report on the new variant B.1.1.7. Next, my review on vaccination updates.

Under Journal Reviews I included two articles from the AIM-their fourth update of masks. The next article is the science behind the Moderna vaccine. This article and the article reviewed on the Pfizer vaccine in the Daily Briefing several weeks ago [also on the NEJM] have many similarities. The last article is a large review on the prevalence and characteristics of taste disorders in COVID-19.

Ed

COVID-19 News

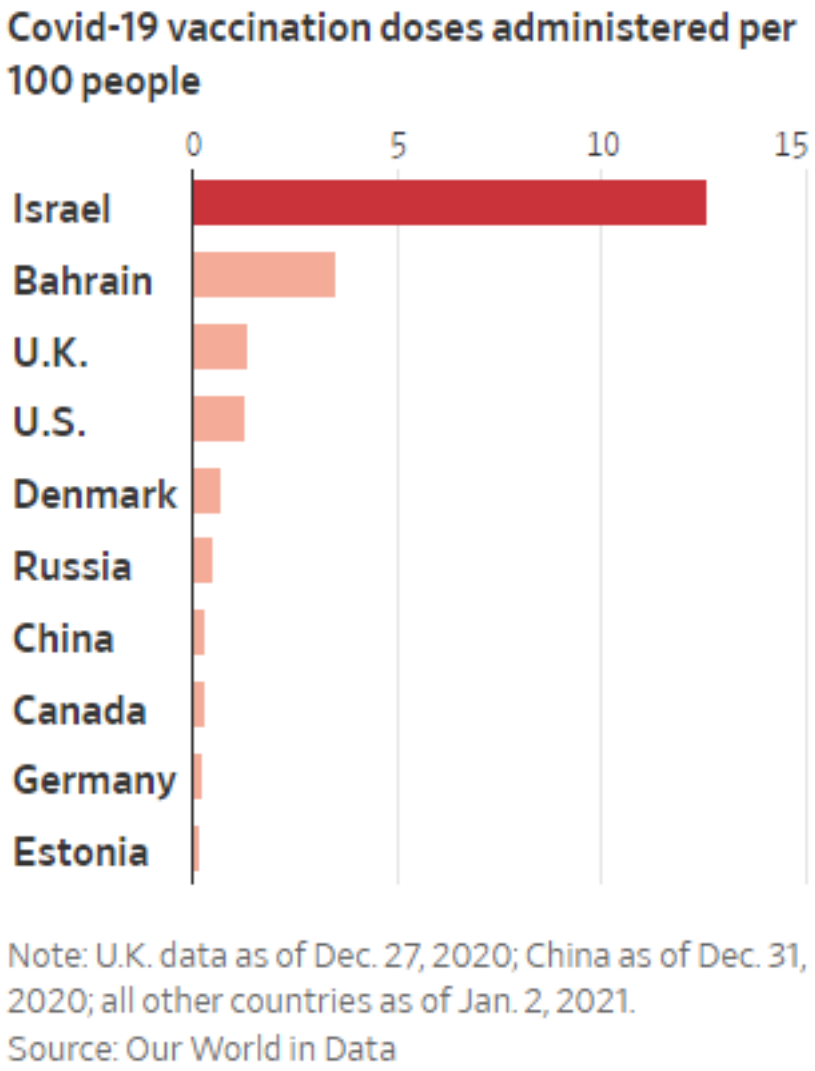
B.1.1.7
3 states have now reported the B.1.1.7 variant. The list of countries that have identified infections with the variant has been growing rapidly and includes the United States, UK, Turkey, Australia, Belgium, Brazil, Canada, Chile, China, Denmark, Finland, France, Germany, Iceland, India, Ireland, Israel, Italy, Japan, Jordan, Lebanon, Malta, the Netherlands, Norway, Pakistan, Portugal, Singapore, South Korea, Spain, Sweden, Switzerland, Taiwan, and the United Arab Emirates. The variant does not lead to more severe cases of COVID-19, but its presence may lead to more infections and hospitalizations.

Comment: I am not surprised that we have identified more cases of B.1.1.7. Last fall we reported that most cases in the US were now G614 a variant from D614 which like B.1.1.7 seemed more contagious but not more virulent. This new variant (B.1.1.7) comes at a time when many states are already battling surges in caseloads and anticipating more from holiday gatherings and travel. Our genomic surveillance is extremely limited compared to the UK. This is another wake up call for further investment in public health which has been underfunded for decades.

Vaccination Update
The goal was to have 20+ million people get their first shot by the end of this year. However, only 14 million doses of the Pfizer and Moderna vaccines have been sent out across the US as of December 28th. The feds are holding back ~50% of doses to make sure there is vaccine available to give everyone a second dose. In addition, only 2.8 million people have received their first dose, though that number may increase since reporting may lag due in part to reporting data using new tools. Health officials and hospitals are struggling with a lack of resources. The holiday season has meant that people may be off work and clinics have reduced hours, slowing the pace of vaccine administration. In addition, saving doses for nursing homes has also contributed to delays. There is still a reluctance by some to take the vaccine. In addition the federal government has left it to states to determine what to do with the vaccines it ships to them, and with some states pushing decision-making to local health departments and hospitals. The distribution system needs improvement. The best option to speed up vaccine distribution may be through national pharmaceutical chains. It is estimated they could deliver up to 100 million doses per month. Bottom line, the process has gone far from smooth. [some states have done a good job] This contrasts with Israel which has vaccinated more than 10 percent of population who have now received a first dose of vaccine, a rate that has far outstripped the rest of the world. (see below) By contrast, only ~2 percent of the population of the United States and only small fractions of the

population in many European countries received a vaccine dose by the end of 2020, though China, the United States and Britain have each distributed more doses overall.

Options under discussion is to delay second dose (UK has adopted this strategy) or give two half doses. In regulatory documents in the UK, Astra Zeneca claims their vaccine was 73% effective in clinical trials three weeks after first dose. Many researchers are concerned this delayed approach could be detrimental and some people would not receive a second dose even if delayed. The second dose is to optimize protection against disease reported to be 95% after second dose. [may be important in increasing memory cells for longer duration of effect] There is little data to support delaying second dose at present. How long would protection last after only one dose? Another approach is to administer half the dose. In trials people between 18 and 55 who received two half-doses had identical immune responses with the Moderna vaccine.



Comment: I do believe vaccinations will accelerate in January and February. We must continue to encourage high-risk groups to take the vaccine and improve the distribution system.

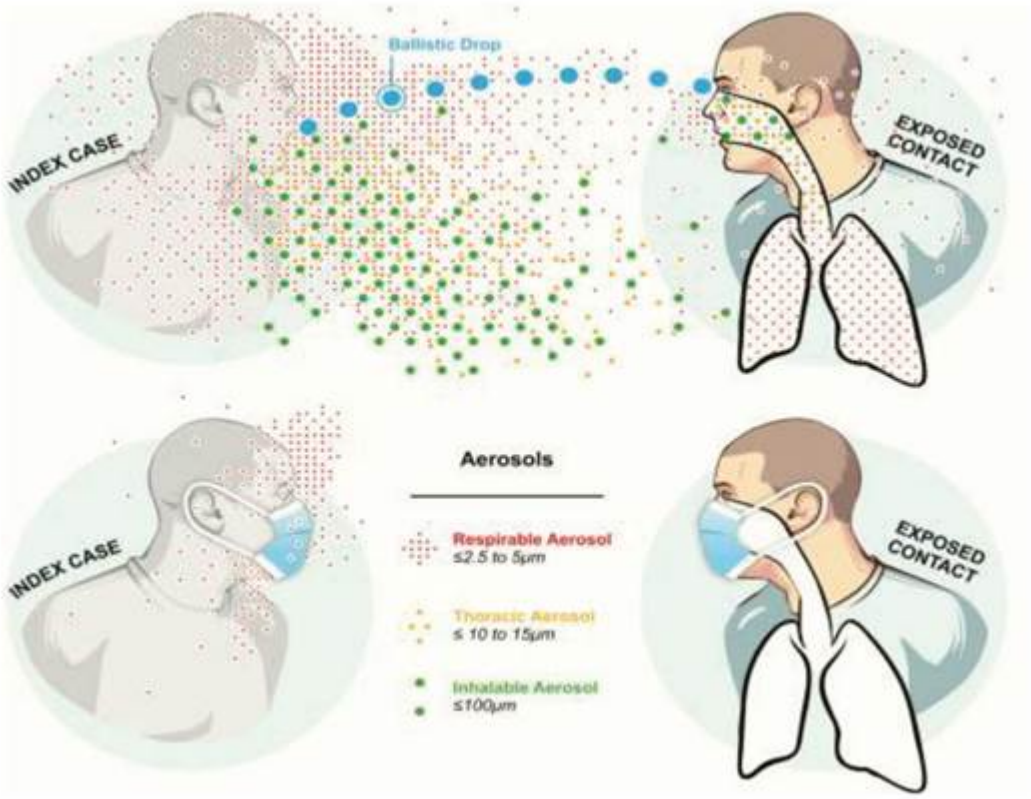
Journal Review

Masks and Face Coverings for the Lay Public
Ann Intern Med published online December 28, 2020
doi:10.7326/M20-6625

Update Alert 4: Masks for Prevention of Respiratory Virus Infections, Including SARS-CoV-2, in Health Care and Community Settings
Ann Intern Med published online December 28, 2020
doi:10.7326/L20-1429

The first paper analyzed the impact of masking by the general public on the spread of the virus. The authors reviewed over 100 research articles and concluded that masking could substantially reduce the spread of viruses, including SARS-CoV-2, without risks to the wearer. This review clearly shows that masks and face coverings worn by members of the public are highly effective in reducing the spread of SARS-CoV-2. A growing body of evidence suggests that the virus is transmitted primarily by droplets in close contact situations [< 6 feet] and through aerosols or small particles hovering in the air for extended periods of time that accumulate especially in closed and crowded spaces. [this is why crowding, and ventilation is so important in addition to masks] Masks trap the particles exhaled. (see below) There is also laboratory evidence that they may protect the wearer as well. Therefore, masks can reduce transmission and save lives. Filtration properties and comfort vary widely across mask types. Masks should be at least 2 ply and fit well.

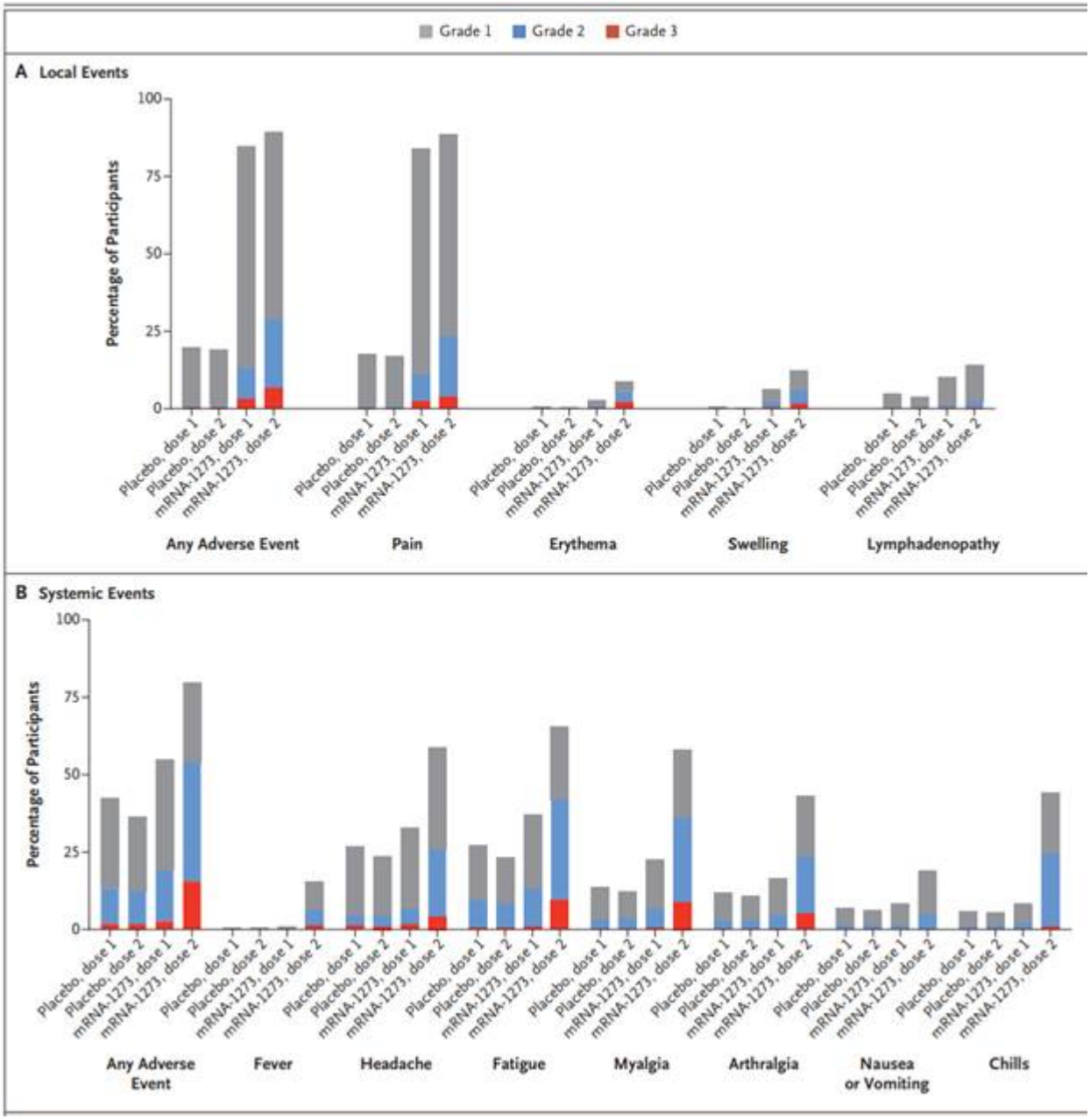
The second report is the fourth update to a "living review" of data on mask use by the general public and by health care workers -- focused mainly on three studies: one study of masking and the prevention of SARS-CoV-2 in a community setting [the DANMASK trial already reviewed in the Daily Briefing] and two additional studies of mask use in healthcare settings. The DANMASK open label trial, which included 6,024 community dwelling adults in Denmark, found that the incidence of SARS-CoV-2 infection among participants was 2%. Surgical mask use, as compared to no mask use, was associated with a small reduction in risk for infection, but the finding was not statistically significant, the researchers noted. The study suggests that masks may have small benefits in reducing the risk of infection in the wearer. Unfortunately, Denmark is a place where it would be harder to show benefits because the infection rate there is low and people have been good about following guidelines, such as social distancing and handwashing. An important reason to wear masks is to prevent those who do not realize they are infected [asymptomatic] or have mild symptoms from infecting others. But the DANMASK study was not designed to evaluate that. In interpreting the results of the DANMASK study, it is essential to remember that it was not a study of source control, and therefore does not tell us about the ability of community mask wearing to reduce overall transmission in the pandemic. Of the two other studies, one, which included 16,397 health care workers and first responders, found that use of an N95 or surgical mask all of the time versus not all of the time was associated with a decreased risk for infection. The second study, which included 20,614 asymptomatic health care workers, found that the risk for infection was reduced with any mask use versus no mask use. The two additional observational studies on mask wearing are consistent with the expected degree of protection based on the authors' previous work and the meta-analysis on the effects of masks in the transmission of non-COVID coronaviruses.



Comment: Both articles continue to show that the science of universal community masking has been associated with fewer new cases and lower mortality in every study to examine this question. Masking plus social distancing and avoiding crowds especially in poorly ventilated spaces can reduce community spread.

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine
N Engl J Med published online December 30, 2020
DOI: 10.1056/NEJMoa2035389
This phase 3 randomized, observer-blinded, placebo-controlled trial was conducted at 99 centers across the United States. Persons at high risk for SARS-CoV-2 infection or its complications were randomly assigned in a 1:1 ratio to receive two intramuscular injections of mRNA-1273 (100 μg) or placebo 28 days apart. The primary end point was prevention of Covid-19 illness with onset at least 14 days after the second injection in participants who had not previously been infected with SARS-CoV-2. The mRNA-1273 vaccine is a lipid nanoparticle–encapsulated mRNA-based vaccine that encodes the prefusion stabilized full-length spike protein of the SARS-CoV-2. [Moderna vaccine] The trial enrolled 30,420 volunteers who were randomly assigned in a 1:1 ratio to receive either vaccine or placebo (15,210 participants in each group). Symptomatic Covid-19 illness was confirmed in 185 participants in the placebo group (56.5 per 1000 person years; 95% confidence interval [CI], 48.7 to 65.3) and in 11 participants in the mRNA-1273 group (3.3 per 1000 person-years; 95% CI, 1.7 to 6.0); vaccine efficacy was 94.1% (95% CI, 89.3 to 96.8%; P<0.001). Efficacy was similar across key secondary analyses, including assessment 14 days after the first dose, analyses that included participants who had evidence of SARS-CoV-2 infection at baseline, and analyses in participants 65 years of age or older. Severe Covid-19 occurred in 30 participants, with one fatality; all 30 were in the placebo group.

Solicited adverse events at the injection site occurred more frequently in the mRNA-1273 group than in the placebo group after both the first dose (84.2%, vs. 19.8%) and the second dose (88.6%, vs. 18.8%). Solicited systemic adverse events occurred more often in the mRNA-1273 group than in the placebo group after both the first dose (54.9%, vs. 42.2%) and the second dose (79.4%, vs. 36.5%). The severity of the solicited systemic events increased after the second dose in the mRNA-1273 group, with an increase in proportions of grade 2 events (from 16.5% after the first dose to 38.1% after the second dose) and grade 3 events (from 2.9% to 15.8%). Solicited systemic adverse events in the mRNA-1273 group lasted a mean of 2.6 days and 3.1 days after the first and second doses, respectively. Both solicited injection-site and systemic adverse events were more common among younger participants (18 to <65 years of age) than among older participants (≥65 years of age) similar to the Pfizer vaccine.



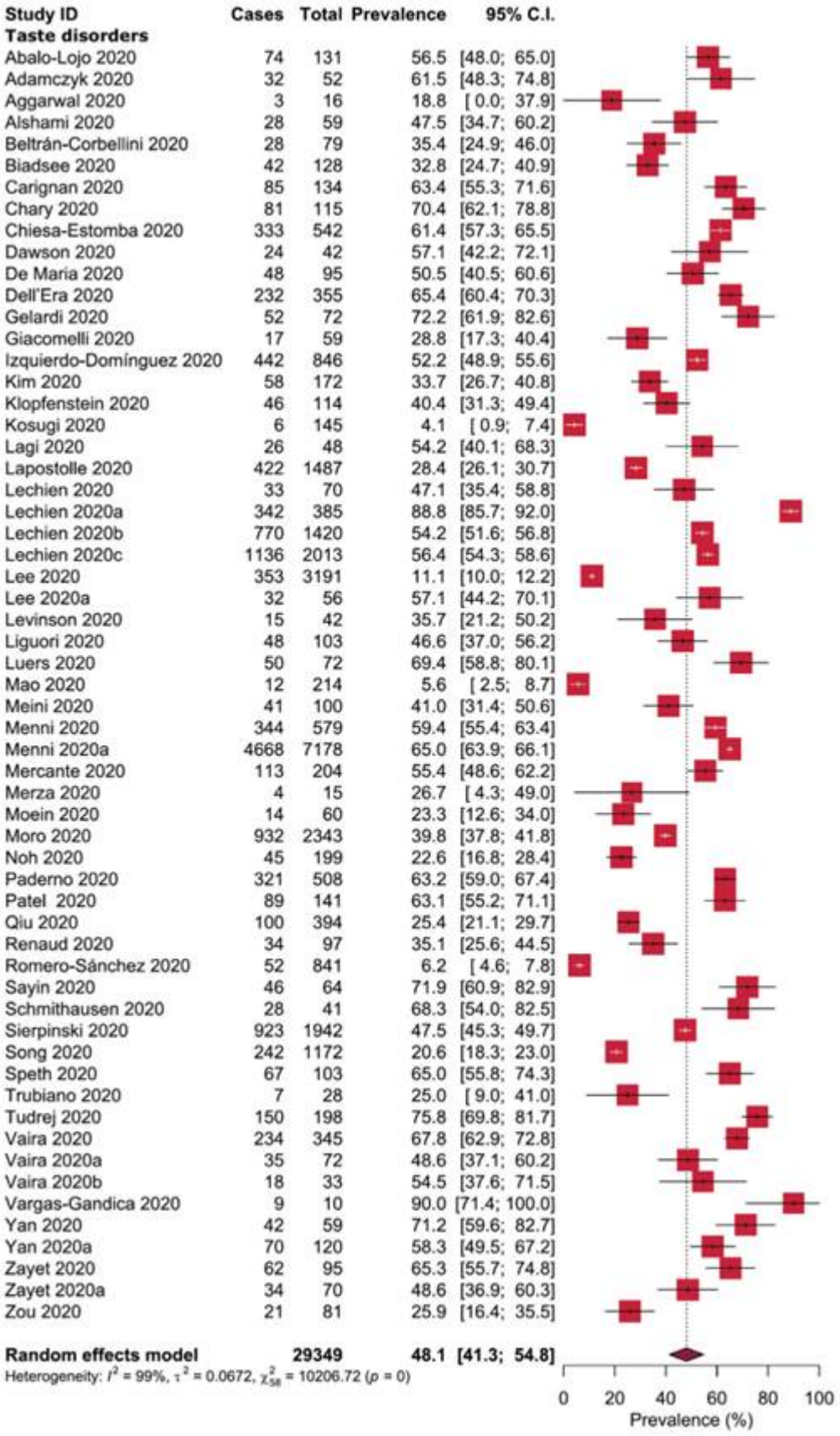
Comment: The mRNA-1273 vaccine showed 94.1% efficacy at preventing Covid-19 illness, including severe disease. [in fact, 100% efficacy for severe disease] Aside from transient local and systemic reactions, no safety concerns were identified. Since both the Moderna and Pfizer vaccine has been administered 11 anaphylactic reactions have been documented. PEG is being investigated as the potential ingredient.

Prevalence and Characteristics of Taste Disorders in Cases of COVID-19: A Meta-analysis of 29,349 Patients

Otolaryngology–Head and Neck Surgery published online December 2020
DOI: 10.1177/0194599820981018

PubMed, Scopus, Web of Science, Embase, and Google Scholar databases were searched to identify studies published between December 1, 2019, and June 23, 2020. Observational studies, clinical trials, and case series were included. In addition, preprints were considered if data of interest were reported. Two authors independently screened articles for eligibility. A random effects model was used to estimate the pooled prevalence with 95% CIs. Quality assessment was done with critical appraisal tools of the Joanna Briggs Institute. The robustness of the pooled estimates was checked by subgroup and sensitivity analyses.

Fifty-nine studies were included (N = 29,349 patients, 64.4% female). The pooled prevalence of taste disorders in patients with COVID-19 was 48.1% (95% CI, 41.3%-54.8%). The prevalence of taste disorders in studies with objective assessments was higher as compared with subjective assessments (59.2% vs 47.3%). The disorders were observed in 55.2% of European patients; 61.0%, North American; 27.1%, Asian; 29.5%, South American; and 25.0%, Australian. Ageusia, hypogeusia, and dysgeusia were detected in 28.0%, 33.5%, and 41.3% of patients with COVID-19. We identified 91.5% of the included studies as high quality.


Study ID
Cases
Total
Prevalence
95% C.I.
Taste disorders
Abalo-Lojo 2020 74 131 56.5 [48.0; 65.0]
Adamczyk 2020 32 52 61.5 [48.3; 74.8]
Aggarwal 2020 3 16 18.8 [0.0; 37.9]
Alshami 2020 28 59 47.5 [34.7; 60.2]
Beltrán-Corbellini 2020 28 79 35.4 [24.9; 46.0]
Biadsee 2020 42 128 32.8 [24.7; 40.9]
Carignan 2020 85 134 63.4 [55.3; 71.6]
Chary 2020 81 115 70.4 [62.1; 78.8]
Chiesa-Estomba 2020 333 542 61.4 [57.3; 65.5]
Dawson 2020 24 42 57.1 [42.2; 72.1]
De Maria 2020 48 95 50.5 [40.5; 60.6]
Dell'Era 2020 232 355 65.4 [60.4; 70.3]
Gelardi 2020 52 72 72.2 [61.9; 82.6]
Giacomelli 2020 17 59 28.8 [17.3; 40.4]
Izquierdo-Domínguez 2020 442 846 52.2 [48.9; 55.6]
Kim 2020 58 172 33.7 [26.7; 40.8]
Klopfenstein 2020 46 114 40.4 [31.3; 49.4]
Kosugi 2020 6 145 4.1 [0.9; 7.4]
Lagi 2020 26 48 54.2 [40.1; 68.3]
Lapostolle 2020 422 1487 28.4 [26.1; 30.7]
Lechien 2020 33 70 47.1 [35.4; 58.8]
Lechien 2020a 342 385 88.8 [85.7; 92.0]
Lechien 2020b 770 1420 54.2 [51.6; 56.8]
Lechien 2020c 1136 2013 56.4 [54.3; 58.6]
Lee 2020 353 3191 11.1 [10.0; 12.2]
Lee 2020a 32 56 57.1 [44.2; 70.1]
Levinson 2020 15 42 35.7 [21.2; 50.2]
Liguori 2020 48 103 46.6 [37.0; 56.2]
Luers 2020 50 72 69.4 [58.8; 80.1]
Mao 2020 12 214 5.6 [2.5; 8.7]
Meini 2020 41 100 41.0 [31.4; 50.6]
Menni 2020 344 579 59.4 [55.4; 63.4]
Menni 2020a 4668 7178 65.0 [63.9; 66.1]
Mercante 2020 113 204 55.4 [48.6; 62.2]
Merza 2020 4 15 26.7 [4.3; 49.0]
Moein 2020 14 60 23.3 [12.6; 34.0]
Moro 2020 932 2343 39.8 [37.8; 41.8]
Noh 2020 45 199 22.6 [16.8; 28.4]
Paderno 2020 321 508 63.2 [59.0; 67.4]
Patel 2020 89 141 63.1 [55.2; 71.1]
Qiu 2020 100 394 25.4 [21.1; 29.7]
Renaud 2020 34 97 35.1 [25.6; 44.5]
Romero-Sánchez 2020 52 841 6.2 [4.6; 7.8]
Sayin 2020 46 64 71.9 [60.9; 82.9]
Schmithausen 2020 28 41 68.3 [54.0; 82.5]
Sierpinski 2020 923 1942 47.5 [45.3; 49.7]
Song 2020 242 1172 20.6 [18.3; 23.0]
Speth 2020 67 103 65.0 [55.8; 74.3]
Trubiano 2020 7 28 25.0 [9.0; 41.0]
Tudrej 2020 150 198 75.8 [69.8; 81.7]
Vaira 2020 234 345 67.8 [62.9; 72.8]
Vaira 2020a 35 72 48.6 [37.1; 60.2]
Vaira 2020b 18 33 54.5 [37.6; 71.5]
Vargas-Gandica 2020 9 10 90.0 [71.4; 100.0]
Yan 2020 42 59 71.2 [59.6; 82.7]
Yan 2020a 70 120 58.3 [49.5; 67.2]
Zayet 2020 62 95 65.3 [55.7; 74.8]
Zayet 2020a 34 70 48.6 [36.9; 60.3]
Zou 2020 21 81 25.9 [16.4; 35.5]
Random effects model 29349 48.1 [41.3; 54.8]
Heterogeneity: I^2 = 99%, τ^2 = 0.0672, χ^2_{58} = 10206.72 (p = 0)
0
20
40
60
80
100
Prevalence (%)

Comment: New onset of taste disorders has been described as a potential early symptom of COVID-19 infection. It represents involvement of the olfactory nerve [brain involvement] and can be an isolated symptom along with loss of smell. The prevalence of taste disorders in patients with COVID-19 was surprisingly high at 48.1%. Dysgeusia is the most common subtype, followed by ageusia and hypogeusia.