SAFE HEALTHCARE FOR ALL
COVID-19 Updates: What We Know Now

Newest Episodes:
• To Mask or Not to Mask as Part of Standard Precautions?
TUNE IN TO THE SHEA JOURNALS PODCASTS

Available on:
- iHeartRadio
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Safe healthcare for all
With funding from the Centers for Disease Control and Prevention, IDSA has launched the COVID-19 Real Time Learning Network, an online community that brings together information and opportunities for discussion on latest research, guidelines, tools and resources from a variety of medical subspecialties around the world.

www.COVID19LearningNetwork.org
@RealTimeCOVID19 | #RealTimeCOVID19
Prevention

An online learning module designed with frontline healthcare personnel in mind.

PreventionCHKC.org
ICHE Journal – Fast Tracking COVID Article Submissions

*Infection Control & Hospital Epidemiology* publishes scientifically authoritative, clinically applicable, peer-reviewed research on control and evaluation of the transmission of pathogens in healthcare institutions and on the use of epidemiological principles and methods to evaluate and improve the delivery of care. Major topics covered include infection control practices, surveillance, antimicrobial stewardship, cost-benefit analyses, resource use, occupational health, and regulatory issues.

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SHEA Webinar

COVID-19 Town Hall
Round 89
House Keeping Items

• Technical difficulties? Visit: https://support.zoom.us
• Webinar recording, PowerPoint presentation, and references available LearningCE’s Rapid Response Program
• Streaming Live on SHEA's Facebook page
• Zoom Q&A and Chat
SHEA Town Hall 89
Overview
SARS-CoV-2 Variants, US, CDC

Weighted and Nowcast Estimates in United States for 2-Week Periods in 3/19/2023 – 7/8/2023

Hover over (or tap in mobile) any lineage of interest to see the amount of uncertainty in that lineage’s estimate.

USA

Nowcast: Model-based projected estimates of variant proportions

WHO label | Lineage # | %Total | 95%CI
---|---|---|---
Omicron | XBB.2.3 | 13.4% | 11.3-15.8%
 | XBB.1.9.2 | 5.6% | 4.0-7.7%
 | XBB.1.9.1 | 9.4% | 8.1-10.9%
 | XBB.1.5.68 | 1.0% | 0.6-1.9%
 | XBB.1.5.59 | 1.6% | 1.0-2.6%
 | XBB.1.5.10 | 0.8% | 0.4-1.5%
 | XBB.1.5.1 | 0.7% | 0.5-1.0%
 | XBB.1.5 | 16.1% | 13.8-18.6%
 | XBB.1.16 | 4.1% | 2.0-7.9%
 | XBB.1.16.1 | 10.4% | 8.4-12.8%
 | XBB.1.16.6 | 17.5% | 15.2-20.0%
 | XBB | 3.6% | 2.5-5.1%
 | FE.1.1 | 1.3% | 0.6-2.7%
 | FD.2 | 0.1% | 0.1-0.3%
 | EU.1.1 | 1.1% | 0.6-1.7%
 | EG.5 | 13.0% | 7.5-21.1%
 | CH.1.1 | 0.2% | 0.1-0.4%
 | BG.1.1 | 0.0% | 0.0-0.0%
 | BG.1 | 0.0% | 0.0-0.0%
 | BN.1 | 0.0% | 0.0-0.0%
 | BF.7 | 0.0% | 0.0-0.0%
 | BA.5 | 0.0% | 0.0-0.0%
 | BA.2.75 | 0.0% | 0.0-0.0%
 | BA.2 | 0.0% | 0.0-0.0%
 | Other | 0.0% | 0.0-0.1%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally at least one 2-week period. “Other” represents the aggregation of lineages which are circulating <1% nationally during all 2-week periods displayed.

https://covid.cdc.gov/covid-data-tracker/#variant-proportions
US COVID-19 HOTSPOTS

February 6, 2022

February 12, 2023

June 23, 2023

July 22, 2023

Average daily cases per 100,000 people in past week

Hospitalizations decreased 9.9% from our last Town Hall
ICU admissions increased 2.4% from our last Town Hall

Source: New York Times –
COVID-19 Daily Hospital Admissions in the United States, by Age

Daily hospitalizations decreased 9.4% from our last Town Hall

Source: New York Times 7-22-2023
COVID-19 DEATHS IN THE UNITED STATES

Cumulative Deaths – 1,132,206

84.8% decrease from our last Town Hall

INFLUENZA ACTIVITY BY STATE IN THE UNITED STATES

January 8, 2023

May 6, 2023

June 23, 2023

July 22, 2023

Source: CDC https://www.cdc.gov/flu/weekly/usmap.htm 7-22-23
PERCENTAGE OF OUTPATIENT VISITS FOR INFLUENZA-LIKE ILLNESS

This system monitors visits for ILI (fever and cough or sore throat), not laboratory confirmed influenza and may capture patient visits due to other respiratory pathogens that cause similar symptoms.

This Month’s Emerging Infectious Disease News

1. A *JAMA* study of extended care facilities between May and December 2021 found that more than 40% of the facilities never administered either monoclonal antibodies or antiviral agents and also found evidence that structural barriers likely contributed to underuse and disparities.

2. A *JAMA* study from England found no evidence of an increased risk of stroke in the 21 days immediately after vaccination with either of the 2 mRNA COVID-19 bivalent BA.1 vaccines.

3. Another *JAMA* study found that time to recovery from COVID-19 pneumonia among hospitalized participants was not significantly affected by administration of abatacept, cenicriviroc, or infliximab when compared with standard care.

4. A *JAMA Pediatrics* study reported significant developmental delay in children exposed to the pandemic.

5. A *JAMA Network Open* paper found that, despite having better chronic risk factor profiles, patients admitted during the pandemic for heart failure, COPD, or asthma in Ontario and Alberta exhibited poorer outcomes (more required ICU admission and more died).

6. Another *JAMA Network Open* paper found that mRNA vaccines administered in pregnancy provoked an IgG response for the mother-infant dyad for 6 months after birth; post-vaccination systemic symptoms may indicate a more robust immune response, without adverse outcomes.

7. Another *JAMA Network Open* study performed a secondary analysis of placebo recipients in four randomized vaccine trials, finding that exposure history and demographic factors had the strongest outcome associations.

8. A scholarly article in *The Annals of Internal Medicine* addresses approaches to the societal management of viral medical rumors and false or misleading information.

References available in the chat
9. A series of letters to the editor [and the Editor-in-Chief’s response] in the July issue of *The Annals of Internal Medicine* address the limitations of a recently published study comparing masks and n95 respirators during care of COVID-19 patients.

10. Two opinion pieces published online together in *Clinical Infectious Diseases* provide point and counterpoint for routine COVID screening at admission.

11. A Brazilian study published in *Infection Control and Hospital Epidemiology* described the adverse effects on the pandemic on a national initiative to decrease healthcare-associated infections in ICUs.

12. An opinion piece published in *Infection Control and Hospital Epidemiology* makes the case that to address vaccine hesitancy effectively, one has to have cultural competencies.


14. A *Lancet* paper just published online found that early initiation of Paxlovid was associated with a significantly reduced risk of all-cause mortality by day 28 when compared to molnupiravir, both in the overall population and in patient subgroups, including those fully vaccinated with the booster dose.

15. A *Nature* paper identified a common HLA allele associated with rapid clearance of SAR-CoV-2 (and therefore is associated with asymptomatic infection).

16. Two pieces in the past month in the *New York Times* provide outgoing CDC Director, Rochelle Walensky’s, insights about the Nation’s pandemic response as well her view of what needs to be done to prepare us for the next pandemic.

References available in the chat
Panelists:

Dr. David Henderson  
NIH Consultant

Dr. Sarah Haessler  
Baystate Health

Dr. Kristina Bryant  
University of Louisville

Dr. David Weber  
UNC School of Medicine
COVID-19 UPDATE
FOCUS ON LONG COVID-19: PREVENTION AND THERAPIES

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Disclosures: Consultancy; Pfizer, Merck, PDI, BD, Germitec, Wellair
All drugs/vaccines issues discussed consistent with FDA approvals or authorizations
LONG COVID-19

Zadeth FH, et al
Arch Microbiol Immunol
2023;7:36-61
CONSEQUENCES OF COVID-19

Fig. 2 | SARS-CoV-2 infection, COVID-19 and long COVID increases the risk of several medical conditions. Because diagnosis-specific data on large populations with long COVID are sparse, outcomes from general infections are included and a large proportion of medical conditions are expected to result from long COVID, although the precise proportion cannot be determined. One year after the initial infection, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections increased the risk of cardiac arrest, death, diabetes, heart failure, pulmonary embolism and stroke, as studied with use of US Department of Veterans Affairs databases. Additionally, there is clear increased risk of developing myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and dysautonomia. Six months after breakthrough infection, increased risks were observed for cardiovascular conditions, coagulation and haematological conditions, death, fatigue, neurological conditions and pulmonary conditions in the same cohort. The hazard ratio is the ratio of how often an event occurs in one group relative to another; in this case people who have had COVID-19 compared with those who have not. Data sources are as follows: diabetes⁹, cardiovascular outcomes⁸, dysautonomia¹⁰,¹⁰¹, ME/CFS¹⁰,¹⁰² and breakthrough infections¹.
Systematic Review of the Prevalence of Long COVID

**Methods.** We searched key registers and databases from 1/1/20-11/2/21, limited to publications in English and studies with at least 100 participants

**Results.** One hundred twenty studies in 130 publications were included. Length of follow-up varied between 12 weeks and 12 months. Few studies had low risk of bias. All complete and subgroup analyses except 1 had I² ≥90%, with prevalence of persistent symptoms range of 0%–93% (pooled estimate [PE], 42.1%; 95% prediction interval [PI], 6.8% to 87.9%). Studies using routine healthcare records tended to report lower prevalence (PE, 13.6%; PI, 1.2% to 68%) of persistent symptoms/pathology than self report (PE, 43.9%; PI, 8.2% to 87.2%). However, studies systematically investigating pathology in all participants at follow up tended to report the highest estimates of all 3 (PE, 51.7%; PI, 12.3% to 89.1%). Studies of hospitalized cases had generally higher estimates than community-based studies.

**Conclusions.** The way in which Long COVID is defined and measured affects prevalence estimation. Given the widespread nature of SARS-CoV-2 infection globally, the burden of chronic illness is likely to be substantial even using the most conservative estimates.
Prevalence and risk factors of long COVID 6–12 months after infection with the Omicron variant among non-hospitalized patients in Hong Kong

Long COVID has been reported among patients with COVID-19, but little is known about the prevalence and risk factors associated with long COVID 6–12 months after infection with the Omicron variant. This is a large-scale retrospective study. A total of 6242 out of 12 950 non-hospitalized subjects of all ages with SARS-CoV-2 infection (confirmed by polymerase chain reaction/rapid antigen test) during the Omicron dominant outbreak (December 31, 2021–May 6, 2022) in Hong Kong were included. Prevalence of long COVID, frequencies of symptoms, and risk factors were analyzed. Three thousand four hundred and thirty (55.0%) subjects reported at least one long COVID symptom. The most reported symptom was fatigue (1241, 36.2%). Female gender, middle age, obesity, comorbidities, vaccination after infection, having more symptoms, and presenting fatigue/chest tightness/headache/diarrhea in the acute stage of illness were identified as associated risk factors for long COVID. Patients who had received three or more doses of vaccine were not associated with a lower risk of long COVID (adjusted odds ratio 1.105, 95% confidence interval 0.985–1.239, p=0.088). Among patients with at least three doses of vaccine, there was no significant difference in the risk of long COVID between the CoronaVac vaccine and BNT162b2 vaccine (p > 0.05). Omicron infection can lead to long COVID in a significant proportion of non-hospitalized patients 6–12 months after infection. Further investigation is needed to uncover the mechanisms underlying the development of long COVID and determine the impact of various risk factors such as vaccines.

Post COVID-19 symptoms are common, also among young adults in the general population

Post coronavirus disease-19 (post COVID-19) is mainly studied in clinical populations and less is about post COVID-19 in a young general population. The aim of the study is to investigate the prevalence and symptoms of post COVID-19 and its potential risk factors in young adults. Participants from the Swedish population-based birth cohort BAMSE were included (n = 2022, mean age 26.5 years). Post COVID-19 was assessed through a questionnaire and defined as symptoms after confirmed COVID-19 (registry-based or self-reported positive test) lasting for ≥ 2 months. In total, 681 participants had had confirmed COVID-19. Among them, 112 (16.5%) fulfilled the definition of post COVID-19 (17.8% in females, 14.5% in males, p = 0.26). The most common post COVID-19 symptoms were altered smell and taste (68.8%), dyspnea (33.7%) and fatigue (30.4%). Overall, no major risk factors for post COVID-19 were identified except for being bedbound during COVID-19. However, asthma and rhinitis were associated with the post COVID-19 symptom dyspnea, migraine with altered smell and taste, and lower self-rated health with fatigue. In conclusion, post COVID-19 symptoms are common, also among young adults in the general population. Although not life-threatening, it could have a considerable impact on public health due to the high prevalence and long-term symptoms.

EFFECTIVENESS OF ANTIVIRALS TO REDUCE RISK OF SEVERE COVID-19
Randomized Trial of **Metformin**, Ivermectin, and Fluvoxamine for Covid-19

**METHODS:** In this phase 3, double-blind, randomized, placebo-controlled trial, we used a 2-by-3 factorial design to test the effectiveness of three repurposed drugs — metformin, ivermectin, and fluvoxamine — in preventing serious SARS-CoV-2 infection in non-hospitalized adults who had been enrolled within 3 days after a confirmed diagnosis of infection and less than 7 days after the onset of symptoms.

**RESULTS:** The adjusted odds ratio for a primary event was 0.84 (95% confidence interval [CI], 0.66 to 1.09; P = 0.19) with metformin, 1.05 (95% CI, 0.76 to 1.45; P = 0.78) with ivermectin, and 0.94 (95% CI, 0.66 to 1.36; P = 0.75) with fluvoxamine. In prespecified secondary analyses, the adjusted odds ratio for emergency department visit, hospitalization, or death was 0.58 (95% CI, 0.35 to 0.94) with metformin, 1.39 (95% CI, 0.72 to 2.69) with ivermectin, and 1.17 (95% CI, 0.57 to 2.40) with fluvoxamine. The adjusted odds ratio for hospitalization or death was 0.47 (95% CI, 0.20 to 1.11) with metformin, 0.73 (95% CI, 0.19 to 2.77) with ivermectin, and 1.11 (95% CI, 0.33 to 3.76) with fluvoxamine.

**CONCLUSIONS:** None of the three medications that were evaluated prevented the occurrence of hypoxemia, an emergency department visit, hospitalization, or death associated with Covid-19.

Bramante CT, et al. NEJM 2022;387:599
Real-world effectiveness of molnupiravir and Paxlovid against mortality, hospitalization, and in-hospital outcomes among community-dwelling, ambulatory patients with confirmed SARS-CoV-2 infection during the omicron wave in Hong Kong: an observational study

Methods: Observational study, 2/26/22-7/26/22; period when Omicron BA.2.2. dominant. Retrospective cohort design as primary analysis, and a case-control design.

Results: Molnupiravir use was associated with lower risks of death (HR 0.76 [95% CI 0.61–0.95]) and in-hospital disease progression (0.57 [0.43–0.76]) than non-use was, where a risk of hospitalization was similar in both groups (0.98 [0.89–1.06]). Nirmatrelvir plus ritonavir use was associated with lower risks of death (0.34 [0.22–0.52]), hospitalization (0.76 [0.67–0.86]), and in-hospital disease progression (0.57 [0.38–0.87]) than non-use was. We consistently found reduced risks of mortality and hospitalization associated with early oral antiviral use among older patients.

Conclusions: Early initiation of novel oral antivirals was associated with reduced risks of mortality and in-hospital disease progression. Nirmatrelvir plus ritonavir use was additionally associated with a reduced risk of hospitalization.

Wong CKH, et al. Lancet 2022;400:1213
Methods: This modeling study used person-level data from the California Department of Public Health on COVID-19 cases, hospitalizations, deaths, and vaccine administration from July 23, 2022 to January 23, 2023.

Results: For both bivalent vaccines and nirmatrelvir-ritonavir, the most efficient strategy (based on NNT) for averting severe COVID-19 was targeting the 75+ years group. We predicted that perfect coverage of bivalent boosters in the 75+ years group would avert 3,920 hospitalizations (95% UI: 2,491-4,882; 7.8% total averted; NNT 387) and 1,074 deaths (95% UI: 774-1,355; 16.2% total averted; NNT 1,410). Perfect uptake of nirmatrelvir-ritonavir in the 75+ years group would avert 5,644 hospitalizations (95% UI: 3,947-6,826; 11.2% total averted; NNT 11) and 1,669 deaths (95% UI: 1,053-2,038; 25.2% total averted; NNT 35).

Table 2: Public health impact and number needed to treat to avert COVID-19 cases, hospitalizations, and deaths with bivalent COVID-19 vaccine strategies.

<table>
<thead>
<tr>
<th>Age group-based strategy</th>
<th>COVID-19 cases</th>
<th>COVID-19 hospitalizations</th>
<th>COVID-19 deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Everyone</td>
<td>NNT</td>
<td>Total Averted</td>
<td>% Averted</td>
</tr>
<tr>
<td>Strategy 1</td>
<td>100 (83-136)</td>
<td>326,111 (240,338-393,041)</td>
<td>28.3%, (21.7-34.2)</td>
</tr>
<tr>
<td>Strategy 2</td>
<td>128 (97-205)</td>
<td>209,888 (126,016-264,472)</td>
<td>17.9%, (10.9-23.0)</td>
</tr>
<tr>
<td>Strategy 3</td>
<td>52</td>
<td>125,254 (113,298-136,562)</td>
<td>10.9%, (8.8-12.7)</td>
</tr>
<tr>
<td>Strategy 4</td>
<td>107 (80-214)</td>
<td>51,829 (45,151-111,943)</td>
<td>7.0%, (4.7-9.7)</td>
</tr>
<tr>
<td>Age group-based strategies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>75+ years</td>
<td>NNT</td>
<td>Total Averted</td>
<td>% Averted</td>
</tr>
<tr>
<td>Strategy 5</td>
<td>51</td>
<td>14,318 (12,070-16,677)</td>
<td>1.2%, (1.0-1.4)</td>
</tr>
<tr>
<td>Strategy 6</td>
<td>103 (88-217)</td>
<td>29,100 (25,321-32,884)</td>
<td>2.5%, (2.1-3.0)</td>
</tr>
<tr>
<td>Strategy 7</td>
<td>103 (88-217)</td>
<td>29,100 (25,321-32,884)</td>
<td>2.5%, (2.1-3.0)</td>
</tr>
</tbody>
</table>

*For unvaccinated persons, we assumed the vaccine administered was a monovalent dose following current clinical guidance for the primary series.
All analyses compared perfect vaccine uptake to baseline coverage of bivalent vaccines.
All age group-based strategies (Strategies 3-7) excluded the unvaccinated population when targeting vaccines to older age groups.
NNT, number needed to treat.

Table 3: Public health impact and number needed to treat for nirmatrelvir-ritonavir during COVID-19 infection to avert hospitalizations and deaths.

<table>
<thead>
<tr>
<th>Age group-based strategies</th>
<th>COVID-19 hospitalizations</th>
<th>COVID-19 deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNT</td>
<td>Total averted</td>
<td>% Averted</td>
</tr>
<tr>
<td>Strategy 1 75+ years</td>
<td>19 (16-27)</td>
<td>9,699 (6,882-11,711)</td>
</tr>
<tr>
<td>Strategy 2 85+ years</td>
<td>15 (12-21)</td>
<td>8,218 (5,705-10,961)</td>
</tr>
<tr>
<td>Strategy 3 75+ years</td>
<td>11 (9-15)</td>
<td>5,644 (3,907-8,282)</td>
</tr>
</tbody>
</table>

All analyses compared current uptake (50% in eligible COVID-19 cases without medical contraindications) to 100%.

Park HJ, et al.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10246024/pdf/nihpp-2023.05.18.23289533v1.pdf
THERAPEUTICS DEMONSTRATED TO REDUCE RISK OF POST-COVID-19 SEQUELAE

COVID-19 Vaccine
Paxlovid
Munupiravir
POST COVID-19 SEQUELAE

Nomenclature of post-COVID-19 conditions

- Post-COVID condition (WHO, CDC)
- Long COVID syndrome Long COVID
- Long-haul COVID Post-acute COVID-19
- Long-term effects of COVID Chronic COVID
- Post-acute sequelae of SARS-CoV-2 infection (PASC)
- Post-COVID Neurological Syndrome (PCNS)
Molnupiravir and risk of post-acute sequelae of covid-19: cohort study

WHAT IS ALREADY KNOWN ON THIS TOPIC
Among people with SARS-CoV-2 infection, molnupiravir use within five days of symptom onset has been shown to reduce the risk of hospital admission or death in people at risk of progression to severe covid-19.

WHAT THIS STUDY ADDS
In people with SARS-CoV-2 infection and at least one risk factor for progression to severe covid-19, compared with no treatment, molnupiravir use during the first five days after a positive SARS-CoV-2 test result was associated with reduced risk of post-acute sequelae of SARS-CoV-2.

The reduced risk in the molnupiravir group was evident in those who had not received a covid-19 vaccine, received at least one vaccine dose, and had received a booster dose, and in those with primary SARS-CoV-2 infection and reinfection.

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Xie Y, et al. BMJ 2023;381:e074572
Molnupiravir and risk of post-acute sequelae of covid-19: cohort study

Methods: Cohort study in US VA. 229286 participants who tested positive for SARS-CoV-2 between 1/5/22-1/15/23, had at least one risk factor for progression to severe covid-19, and survived the first 30 days after testing positive were enrolled.

Results: Compared with no treatment, molnupiravir use within five days of a positive SARS-CoV-2 test result was associated with reduced risk of PASC (relative risk 0.86 (95% confidence interval 0.83 to 0.89); absolute risk reduction at 180 days 2.97% (95% confidence interval 2.31% to 3.60%)), post-acute death (hazard ratio 0.62 (0.52 to 0.74); 0.87% (0.62% to 1.13%), and post-acute hospital admission (0.86 (0.80 to 0.93); 1.32% (0.72% to 1.92%)). Molnupiravir was associated with reduced risk of eight of the 13 postacute sequelae: dysrhythmia, pulmonary embolism, deep vein thrombosis, fatigue and malaise, liver disease, acute kidney injury, muscle pain, and neurocognitive impairment. Molnupiravir was also associated with reduced risk of PASC in people who had not received a covid-19 vaccine, had received one or two vaccine doses, and had received a booster dose, and in people with primary SARS-CoV-2 infection and reinfection.

Xie Y, et al. BMJ 2023;381:e074572

Methods: This was a decentralized, remotely delivered trial in the US of 1,125 adults age 30 to 85 with overweight or obesity, fewer than 7 days of symptoms, and enrolled within 3 days of a documented SARS-CoV-2 infection. Multi-site, phase 3, randomized, quadruple-blinded placebo-controlled clinical trial.

Result: The median age was 45 years (IQR 37 to 54), 56% female of whom 7% were pregnant. Two percent identified as Native American; 7.4% as Black/African American; 82.8% as white; and 12.7% as Hispanic/Latino. The median BMI was 29.8 kg/m² (IQR 27 to 34); 51% had a BMI >30 kg/m². Overall, 8.4% reported having received a diagnosis of Long Covid from a medical provider: 6.3% in the metformin group and 10.6% in the metformin control; 8.0% in the ivermectin group and 8.1% in the ivermectin control; and 10.1% in the fluvoxamine group and 7.5% in the fluvoxamine control. The Hazard Ratio (HR) for Long Covid in the metformin group versus control was 0.58 (95% CI 0.38 to 0.88); 0.99 (95% CI 0.592 to 1.643) in the ivermectin group; and 1.36 in the fluvoxamine group (95% CI 0.785 to 2.385).

Conclusions: There was a 42% relative decrease in the incidence of Long Covid in the metformin group compared to its blinded control in a secondary outcome of this randomized phase 3 trial.


Results: Overall, 93 (8·3%) of 1126 participants reported receipt of a long COVID diagnosis by day 300. The cumulative incidence of long COVID by day 300 was 6·3% (95% CI 4·2–8·2) in participants who received metformin and 10·4% (7·8–12·9) in those who received identical metformin placebo (hazard ratio [HR] 0·59, 95% CI 0·39–0·89; p=0·012). The metformin beneficial effect was consistent across prespecified subgroups. When metformin was started within 3 days of symptom onset, the HR was 0·37 (95% CI 0·15–0·95). There was no effect on cumulative incidence of long COVID with ivermectin (HR 0·99, 95% CI 0·59–1·64) or fluvoxamine (1·36, 0·78–2·34) compared with placebo.

Conclusion: Outpatient treatment with metformin reduced long COVID incidence by about 41%, with an absolute reduction of 4·1%, compared with placebo. Metformin has clinical benefits when used as outpatient treatment for COVID-19 and is globally available, low-cost, and safe.

Bramante CT, et al. Lancet ID 2023;June 8
CONCLUSIONS

• COVID-19 vaccination demonstrated to reduce risk of severe COVID-19 and post-acute sequelae of COVID-19. Caveats:
  • Bivalent vaccine more effective than ancestral vaccine. However, effectiveness against XBB variants reduced.
  • Impact of vaccine lower at present due to waning of vaccine induced immunity, lower virulence of XBB variants, and high prevalence of natural immunity
  • XBB univalent booster will be available in the Fall
• Paxlovid effective in reducing risk of severe COVID-19 in all subgroups (e.g., vaccinated, older, immunocompromised) and effective in reducing risk of long COVID-19. Paxlovid now FDA approved
  • Major limitation is use is drug interactions. Cost may also be a factor
• Metformin likely effective in reducing risk of long COVID-19
  • Effectiveness in reducing risk of severe COVID-19 not defined – likely major limitation in use compared to Paxlovid and Mulnupiravir
• Oral antivirals need to be administered within 5 days of onset of symptoms.
• At the present, best protection offered by being up-to-date with COVID-19 vaccines (i.e., receipt of bivalent vaccine) plus use of Paxlovid for patients at high risk for severe COVID-19 and/or PASC.
• No proven therapies for Long COVID-19 (need RCTs). Novel therapies for long COVID-19 should be explored