

The BMI

mlooi@bmj.com Cite this as: *BMJ* 2022;379:o2516 http://dx.doi.org/10.1136/bmj.o2516 Published: 27 October 2022

COVID UNANSWERED QUESTIONS

Has covid-19 become milder?

Deaths and hospital admissions are falling, so does this mean that the virus is less severe? **The BMJ** asks the experts

Mun-Keat Looi, Elisabeth Mahase

Is covid-19 really getting milder?

The short answer is no. Covid-19 is still a deadly disease, having killed almost 1.1 million people in 2022 at the time of writing. There remains a high risk of hospital admission and death for anyone without prior immunity. With some populations still largely unexposed to the virus, such as in China, and variation in the types of vaccines used in different places, it would be cavalier to call covid-19 anything but serious.

"It's really hard to compare the severe disease aspects of [variants] because the immunity of our population is so different," says Steve Griffin, associate professor at the University of Leeds. "When people call omicron mild, yes, there's probably a lesser tendency for it to go deep in the lungs. But if you think about the clinical impact of it, because of its massive prevalence, even though it's got a lower chance of causing the sorts of severe disease we're talking about with acute covid-19, the actual clinical impact is still very, very marked."

David Strain, senior clinical lecturer at the University of Exeter Medical School, points out that covid-19 tends to make other diseases worse. "It doesn't matter what those other diseases are," he told *The BMJ* in August 2022. "Patients who've got longstanding Crohn's disease are coming in with exacerbations of their Crohn's or their coeliac or their arthritis."

Monica Verduzco Gutierrez, professor and chair of the Department of Rehabilitation Medicine at the Long School of Medicine in San Antonio, Texas, also emphasises that even mild covid-19 could cause long covid, with lingering symptoms and debility.

She adds that we've yet to fully understand the impact of reinfections. A study of the health records of six million people held by the US Department of Veteran Affairs, released as a preprint in June, suggested that people who had a second or third covid-19 infection had considerably higher rates of heart disease, kidney disorders, and other health problems during the first 30 days of infection, as well as in the months that followed, than people who had been infected only once.

Why does it appear to be getting milder?

The evolution of the virus, as well as the increased immunity of general populations, means that presented symptoms and the frequency of symptoms in many places are shifting, with deaths and hospital admissions falling in countries such as the UK over the course of 2022.

Gutierrez says, "The original strain had more disabling impacts in regard to post-covid conditions because so many more people had severe disease." It's understandable why, to some people, acute covid appears to have become milder in its effects, especially in vaccinated people. But, as detailed above, that doesn't mean that the disease itself is getting any milder.

A paper published in *The BMJ* in August² showed that disease caused by the early omicron variants (BA.1 and BA.2) seemed to be less severe in these terms than delta. And the World Health Organization has suggested that the omicron variants' tendency to target the upper part of the body—which also helps its transmissibility—could correlate with fewer cases of severe pneumonia, since it isn't infecting cells deeper in the lungs.³

Do different variants cause different severity of disease?

Emma Thomson, professor of infectious diseases at the University of Glasgow, told a Royal Society of Medicine event in August, "Alpha was more severe than the original lineages that entered the UK, and then delta was more severe than alpha. Omicron has taken a dive in severity, but we know that it doesn't take much for the virus to change. By random mutation, it may well be the situation that we get a variant which is more severe."

Eric Topol, professor of molecular medicine at the Scripps Research Institute in California, says that there's a tension between the virus becoming more transmissible and fitter and our immune response getting slightly stronger, but "overall, the virus is winning."

Griffin is similarly worried about the virus's ability to change at a dramatic rate. "You've got a really well adapted virus, and it has [decided], 'That's not good enough.' So it's jumping up to what we might call another fitness peak. These are exquisitely antibody evasive viruses, and they are changing at a tremendous rate."

Strain says that, with the early omicron variant BA.2, "the [acute] covid itself wasn't that bad. But the long covid was much worse." Anecdotally, he says, about 15-20% of his hospital's staff were left with fatigue after infection with BA.2, and many were still on phased return months later. This has reduced since BA.4 and BA.5 have dominated infections.

Is long covid the real worry?

Yes, says Griffin, describing the still high levels of virus circulating as "a real worry." He adds, "I don't think we should just pretend that prevalence doesn't matter. And that's why I really quite strongly disagree with the 'living with covid' strategy. I think it's fundamentally wrong. It's disregarding vulnerable people. It's disregarding long covid."

A report issued in July by the UK's Institute for Fiscal Studies estimates that one in 10 people who develop long covid stop working, generally going on sick leave rather than losing their jobs altogether. The report suggests that, as long as the prevalence and severity of covid remain at current levels, the aggregate impact is equivalent to 110 000 workers being off sick. 4 Griffin adds, "If you look at the risk groups in terms of profession, things like teachers, social workers, healthcare workers, bus drivers—these are the people more likely to develop long covid because they're obviously in person facing roles."

"We're breeding long covid with all of this," says Topol. "It's really unfortunate that we've seen this response, which is to just let it rip. It's not acceptable. In my view, too many have given up the fight, and that's sad because we know of really good measures that are innovative, that we have the foundation for, which we're not advocating and we're not putting priority and resources.

"We're decreasing funding when in fact we should be investing, because it's a very wise investment. The ability to get ahead of the virus will save us inordinate amounts of cost later."

Do you have a "Covid Unanswered Question"? Post a Rapid Response to this article using the link at the top right, or email mlooi@bmj.com, and we'll try to cover it in this series.

Competing interests: None.

Provenance and peer review: Commissioned; externally peer reviewed.

- 1 Al-Aly Z, Bowe B, Xie Y, et al. Outcomes of SARS-CoV-2 reinfection. Res Square 2022 [preprint]. doi: 10.21203/rs.3.rs-1749502/v1
- Ward IL, Bermingham C, Ayoubkhani D, etal. Risk of covid-19 related deaths for SARS-CoV-2 omicron (B.1.1.529) compared with delta (B.1.617.2): retrospective cohort study. BMJ 2022;378:e070695. doi: 10.1136/bmj-2022-070695 pmid: 35918098
- Farge E, Roy M. WHO sees more evidence that Omicron causes milder symptoms. Reuters. 4 Jan 2022. https://www.reuters.com/business/healthcare-pharmaceuticals/who-sees-more-evidence-that-omicron-affects-upper-respiratory-tract-2022-01-04/
- Cominetti N, Henehan K, Slaughter H, Thwaites G. Long covid in the labour market. Health Foundation, Resolution Foundation. Feb 2021. https://www.resolutionfoundation.org/app/up-loads/2021/02/Long-covid-in-the-labour-market.pdf

This article is made freely available for personal use in accordance with BMJ's website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.