# Are Repeat Coronavirus Infections Really More Dangerous Than the First?

— No, but a recent study has been misinterpreted by some as saying that

by Jeremy Faust, MD
November 29, 2022

**What happens to people who get reinfected with SARS-CoV-2, the virus that causes COVID-19?** A recent paper in *Nature Medicine* has been misinterpreted by some as providing evidence that repeat infections are somehow worse than first-time infections.

Here's the actual situation: second infections are far less dangerous than first infections, with respect to severe, critical, and fatal COVID-19. This is true regardless of vaccination status.

**Here's what we know.** Hybrid immunity provides the best overall protection, and the safest way to achieve that is to get vaccinated *before* a first-time infection occurs, so that a person has a better chance to survive long enough to even *have* the reinfection question become relevant.

> A study in JAMA showed that surviving a coronavirus infection was highly protective ("effectiveness %") against death and hospitalization, with little waning. Protection against repeat infection was also good, though that wanted to around 60% by 15 months. (Lin et al).

If second infections were somehow more dangerous than primary infections, the "effectiveness" of the first infection against death and hospitalization would literally be negative in the graph above (annotated by me from a massive paper in *JAMA* using data from North Carolina). Instead, we see sustained protection against death and hospitalization, even 15 months after infection. Prior infection also protects against repeat infections, albeit not as well, and with faster waning.

**Medical News from Around the Web**

DNA identifies remains of Florida teen who disappeared in 1972. Detectives now say she may have been killed by a serial killer cop.

More reassuring data come from Qatar, a nation which has emerged as a powerhouse for real-world vaccine effectiveness data. Researchers matched and compared people with similar characteristics who had been infected twice to those who had been infected once. The results (published in the *New England Journal of Medicine*) should come as a relief. Even among unvaccinated people, only 1 in 325 people who were reinfected had severe disease, meaning that oxygen levels were below 94% (95-100% being normal). Among reinfected patients, critical or fatal disease *never occurred*. Now, this was a fairly healthy cohort of people -- a group whose rate of critical disease (marked by respiratory failure requiring intensive care) COVID-related fatality rate with initial infection was 0.5% and 0.1% respectively. While those rates sound low, we see rates like that in younger and healthy people. Overall, the findings are crystal clear. When researchers compared similar people who had either one or two infections, outcomes were *far* worse after the first one.

**So what's this we keep hearing about repeat infections being worse than primary ones?** A new paper of Veterans Administration data authored by a small group of respected researchers went absolutely viral this month. (For you research nerds out there, the paper already has an Altmetric score of nearly 9,898 as of November 22, 2022, which is basically a supernova).

**What half of Twitter (and the media) incorrectly thinks the paper says:** Second infections are associated with higher rates of all-cause mortality and other adverse outcomes than primary infections were.

**What the paper actually says:** Getting repeat infections is not benign. For a subset of patients sick enough to seek medical attention upon reinfection, more bad things happened compared to patients who *either* did not have reinfections, or who *did* but did not need to seek medical attention.

The authors anticipated that people would make the mistake being made, which is why they wrote in the paper, "Our analyses should not be interpreted as an assessment of severity of a second infection versus that of a first infection, nor should they be interpreted as an examination of the risks of adverse health outcomes after a second infection compared to risks incurred after a first infection." That's pretty definitive.

Epidemiologist Gideon Meyerowitz-Katz has a nice explanation on Twitter that goes into all of this.

It all boils down to who was included in the study dataset. As Meyerowitz-Katz says, the paper *did not* compare people with reinfection to those without reinfection, as many seem to think. Instead, it explicitly compared reinfected people who *sought medical attention* to those who either were not reinfected, *or* who were reinfected but who were tested outside of the medical system (if at all) and who never felt the need to seek out medical care (thus, the database doesn't "know" about their infections). Failing to realize

this could easily cause someone to interpret the study's data (incorrectly) as saying that vaccination added no protection against future bad outcomes. That would be an obviously incorrect reading.

**What does this paper say?** Basically, all we can draw from this paper is that repeat coronavirus infections are not good, especially for older people who are likely to have existing medical problems (i.e., Veterans Administration patients). This is not exactly breaking news.

Of course, the best way to avoid a repeated infection is to not get infected in the first place. That said, if you do get a repeat infection, I hope it is reassuring to know that it's likely to be less dangerous than the first go-round -- especially with a vaccine on board.

*Jeremy Faust, MD, is editor-in-chief of* MedPage Today, *and an emergency medicine physician at Brigham and Women's Hospital. This post originally appeared in* Inside Medicine*.*