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## CORONAVIRUS

# How similar is covid-19 to the flu?

**Chris Stokel-Walker** asks whether what we've learnt about covid-19 makes the comparison to influenza fair and correct

Chris Stokel-Walker,

### How have people compared covid-19 and influenza?

For those who sought to downplay the severity of the disease caused by SARS-CoV-2, “just like the flu” was a way to express how they thought that lockdown measures were over the top.

As the pandemic progressed, groups of experts<sup>1</sup> began talking about the possible evolution of SARS-CoV-2 into something more “flu-like”—the natural extension, as some virologists thought, of a virus getting less deadly so that it could continue to propagate in the population. By killing fewer hosts, there is a higher chance that the virus will be transmitted to others. Emma Thomson, professor in infectious diseases at the MRC-University of Glasgow Centre for Virus Research, told *The BMJ* in a video, “I learnt at medical school that viruses generally get less severe. But I think that’s probably one of those statements that’s made with very little evidence behind it. We’ve never watched evolution like [SARS-CoV-2] on such a large scale and with so much sequencing of the [viral genome being done]. So we now have much better evidence to show that there’s a real heterogeneity [in the way that viruses evolve].”<sup>2</sup>

Finally, there’s the disease covid-19 itself and the way that we are coming to “live with the virus” in the same way that each year we live with influenza, which kills 290 000 to 650 000 people globally each year, according to the World Health Organization.

### What do the viruses target?

Both SARS-CoV-2 and the influenza virus target the respiratory epithelium, so in that respect the target cells they’re infecting are quite similar, says Wendy Barclay, head of the Department of Infectious Disease and chair in influenza virology at Imperial College London. There are differences in what each virus requires, however, to infect people. Influenza requires haemagglutinin and neuraminidase, whereas SARS-CoV-2 uses protein S to infect humans, a 2020 study found.<sup>3</sup>

### How do their symptoms differ?

There are similarities when it comes to acute infection, says Cheryl Walter, a virologist and lecturer in biomedical science at the University of Hull—people generally get a sore throat, a runny nose, and perhaps a general sense of fever and achiness. But, as is well documented, covid-19 has caused a range of symptoms not usually seen with the flu. We’re still trying to understand why people lose their sense of smell and taste, she says.

One difference between the two is that SARS-CoV-2 seems to sometimes trigger a more substantial immune response, which makes some people very ill. “The immune response can be different from one person to the next, and we see that can mean the difference between life and death,” says Walter.

### How does mortality compare?

In the early days of the pandemic, covid-19’s infection fatality ratio (IFR)—the proportion of people who died after contracting the disease—was much higher than the flu’s. How to calculate covid’s IFR has been the subject of academic debate,<sup>4</sup> with estimates varying from 0.49% to 2.53% in one study.

Factors that affect the IFR of covid are thought to include a person’s age, location, and ethnic background, as well as where they live and work. In one study that analysed disease mortality across 190 countries, IFRs for the same disease varied by a factor of more than 30, showing how variable mortality can be.<sup>5</sup>

Another important variable that affects IFR is the extent to which people are vaccinated. As the vaccine rollout has progressed, covid-19 has become less fatal. Likewise, the rise of new covid variants<sup>6</sup> has helped reduce covid’s IFR. One non-academic analysis indicated that covid-19’s IFR has now become equal to or less than flu’s (around 0.04%), whereas in mid-2020 covid-19 was 20 times more likely to kill people than the flu.<sup>7</sup>

### What about variants?

As we now well know, SARS-CoV-2 mutates and evolves, forming new variants that have been fuelling fresh waves. This pattern of behaviour is similar to what happens each year with new variants of influenza, which is why the flu vaccine must be reformulated each year, based on variants that emerge in the southern hemisphere’s earlier winter months.

A big difference with SARS-CoV-2 is that it has evolved much faster—this year alone has seen at least four omicron “subvariants under monitoring” as the World Health Organization calls them, including BA.4 and BA.5 that are currently responsible for most of the world’s infections. Unlike influenza, this has continued even through warmer months, posing a challenge for vaccination efforts to keep up.

### How is vaccination handled?

The pandemic is now centred around new variants and waning immunity, with an emphasis on regular

booster jabs, particularly tweaked to the new variants, to top up immunity.<sup>8</sup> This is not dissimilar to the yearly flu jab, although the speed at which new covid variants are emerging is a problem for the development of new booster vaccine formulations.

In terms of rollout, covid booster jabs are being tied in with the well established annual flu vaccination effort. The UK's NHS is running two vaccination schemes in parallel this autumn and winter, just as it did last year. The annual winter flu jab season will coincide with this autumn's seasonal covid booster campaign, which will see 26 million people in England eligible for the jab.<sup>9</sup> The NHS is encouraging hospital hubs and general practices to try and vaccinate patients against both covid-19 and the flu simultaneously "where possible."

For covid, as with the flu, it is the most vulnerable people (older or immunocompromised people and those with certain conditions such as severe asthma) that are prioritised. In the early stages of the covid-19 vaccine rollout, it was given to those most in need of the jab ("priority groups") before being offered to people of all ages. This is different from the flu jab campaign, which targets vulnerable and older people. But the UK Joint Committee on Vaccination and Immunisation's latest advice indicates that most people under the age of 50 will not be offered an autumn booster this year, unless they are vulnerable, in line with how the flu jab is rolled out.<sup>10</sup>

The increasing similarity with the flu jab campaign is likely to continue, says Paul Hunter, a virologist and professor in medicine at the University of East Anglia. "I suspect that the current over 60s might well continue to be vaccinated pretty much forever, whereas younger people probably won't," he says, much like the flu. Unlike the flu, we are not yet at the stage where vaccination is available or recommended for everyone. But that could, of course, change depending on whether a more potent variant arises.

### What about treatments?

Besides vaccines, we now have a range of treatments for covid-19, including antivirals.<sup>11</sup> In large part, the knowledge we now have about how to treat covid-19 comes from the Recovery trial,<sup>12</sup> which tested various interventions and their efficacy. But, says Barclay, although many of these treatments have been "tried here and there with the flu, it's not really ever been used." The much prophesied influenza pandemic has yet to arrive—instead we've had covid-19. As such, it's difficult to compare the rapid rise and use of covid-19 interventions with flu treatments that are rarely used.

Steroids like dexamethasone, for example, are now a core first line therapy for covid-19. But if a patient comes into hospital with severe flu, we don't give them steroids in the UK, says Barclay. "People have not been convinced with flu that this intervention was helpful." There doesn't seem to be much of an appetite to change that either, even though such interventions proved to be positive with covid. The Recovery trial proposed an extension to its remit to explore treatments for severe influenza, but this was rejected.<sup>13</sup>

This is a missed opportunity, says Barclay. "There are lots of things we can learn about what to do with flu from SARS, and what some people have been thinking about is using these small molecules more like prophylactics, getting them into people very quickly," she says; for example, monoclonal antibodies could be used to treat flu just as we have with covid-19.

### Are there similarities in the way the two diseases are perceived?

Before the pandemic, England and Wales, along with other countries, would "accept" between 10 000 and 25 000 deaths a year

caused by influenza.<sup>14</sup> And it's arguable that countries opening up and living largely as if the pandemic is not ongoing signals a similar acceptance of the still high numbers of deaths from covid-19—as of 23 September 2022, 44 341 deaths in England and Wales in 2022 were marked as caused by or involving covid-19.<sup>15</sup>

Whether this is acceptable or abhorrent is a matter of debate. But given what the world has gone through in the past two years, we must take lessons, says Deepti Gurdasani, a clinical epidemiologist and senior lecturer in machine learning at Queen Mary University of London. She says that the pandemic experience should make us less tolerant of the toll of airborne diseases "because now we've learned that things like ventilation can massively reduce the mortality associated with all airborne diseases,<sup>16</sup> not just covid." In other words, we know we can save lives with simple interventions, so why don't we?

Barclay, who sits on various UK government advisory bodies, is less certain that public perception—and the perception of those in charge of mitigating risks—will change. "I think we live with deaths from seasonal flu," she says. "And I think we will live with deaths from covid as well. I don't think there's any alternative to that."

"I think we will continue to try and strike the balance between the numbers, and how uncomfortable those numbers feel, and how uncomfortable the hospital situation is. Basically, everything will be predicated on whether the NHS can cope."

"What people forgot is that when SARS-CoV-2 first emerged into the human population, it was a brand new animal virus, which humans had not seen before," Barclay says. That lack of precedence, and the lack of immunological priming for the effects of the virus in humans, is what caused such severity of disease in the pandemic's early days. "The whole world was completely susceptible. A proportion of those people were going to get really quite ill because they had no immune backup whatsoever to rely on."

That's not the situation many populations are in now. Though more frequent than flu, encounters with covid are becoming common, with some degree of immunity from exposure to prior variants, vaccination, or both helping to lessen their severity—so far.

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