

# XE, XD & XF: what to know about the Omicron hybrid variants

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Canada recently reported its first cases of the Omicron subvariant XE, one of several hybrid variants of SARS-CoV-2 that have emerged since the beginning of this year.

First detected in the United Kingdom in January, XE has genetic material from the Omicron subvariants BA.1 and BA.2, along with three new mutations that are not present in either pre-existing strain.

## Hybrid versus mutant

Hybrid or “recombinant” subvariants like XE occur when two different strains of a virus infect the same cell at the same time and blend their genetic material to produce a new variant.

Compared with the slower process of a virus mutating through errors in the replication of its genetic code, recombination can allow for major, rapid changes in transmissibility, severity, and resistance to vaccines and treatments.

According to Susan Hopkins of the UK Health Security Agency, “Recombinant variants are not an unusual occurrence, particularly when there are several variants in circulation, and several have been identified over the course of the pandemic to date.”

Like variants that occur via mutation, most hybrid strains die off relatively quickly, and some may not differ noticeably from their parent variants.

At least two recombinant subvariants in which Delta and Omicron lineages combine — XD and XF — have emerged in Europe in recent months. So far, there is no evidence to suggest that these so-called “Deltacron” strains are more transmissible or cause worse outcomes.

However, the World Health Organization (WHO) has listed XD as a “variant

under monitoring” — a label given to SARS-CoV-2 strains with genetic changes that may pose a future risk, but whose epidemiological impact is still unclear.

Community transmission of XE in England has raised concerns that it may have some staying power, too.

## Is Omicron XE more transmissible?

XE appears to be roughly 10% more transmissible than its parent variant BA.2, previously the most infectious strain of SARS-CoV-2, according to Maria Van Kerkhove of the WHO.

And in recent weeks, the UK has reported growth rates for XE as much as 20% higher than for BA.2 — albeit with large fluctuations. As of April 5, more than 1000 cases of XE had been reported in England, almost double the number reported on March 25.

Besides the UK and Canada, other countries, including Japan, India, Thailand and Israel, have also identified XE cases, mostly linked with international travel.

The WHO is encouraging public health authorities to monitor Omicron subvariants as distinct lineages. However, the organization will not classify XE as a variant of concern separate from Omicron until it observes major differences in disease transmission or severity.

Canadian officials are actively monitoring Omicron subvariants, including XE, according to Mark Johnson of the Public Health Agency of Canada.

“While preliminary international reports have shown that XE has modestly increased transmissibility compared to BA.2, more data are needed to confirm this finding,” Johnson stated.

## Is XE more severe than other strains?

It is too early to know if XE or the other hybrid variants cause more severe disease than other SARS-CoV-2 strains.

According to Grace Roberts, a virologist and research fellow at Queen’s University Belfast, XE likely shares similar characteristics with BA.2 because most of its makeup, including its spike protein, comes from that strain. That means that vaccinations (which target the spike protein) may offer similar levels of protection against XE as for BA.2.

And although both BA.1 and BA.2 appear to be more transmissible than earlier strains of SARS-CoV-2, neither has proven to cause more severe disease.

“It is the devil we know, so to speak,” according to Mark Cameron, an immunologist and associate professor at Case Western Reserve University. “Essentially, a reshuffling of the same deck of cards.”

Tom Peacock, a virologist at Imperial College London, told CNBC that other recombinants that contain spike and structural proteins from different virus families, like XD does, are a “little more concerning.”

## How do hybrids complicate pandemic response?

Every time the virus changes there is a risk that current vaccines, which were designed to target the original strain of SARS-CoV-2, will be less effective, according to Horacio Bach, an infectious disease expert at the University of British Columbia.

Lifting public health restrictions also increases the risk of multiple strains of SARS-CoV-2 cocirculating and

recombining, Bach told Global News. “As long as you have everything open now — no mask on and nothing — the potential that you generate new mutants, variants or new recombinants is always open.”

Meanwhile, declines in testing for SARS-CoV-2 in many countries have meant that available data on new variants are “progressively less representative, less timely,” wrote Ranjan Mohapatra and colleagues in a letter in the *Journal of Medical Virology*. “This is hindering real-time tracking of the presence of the virus, [and] how the virus and its variants are spreading and evolving.”

The WHO is urging continued public health precautions, including physical distancing, wearing masks and staying home when sick.

“All of these tools continue to work against reducing the spread,” said Van Kerkhove. Meanwhile, “Vaccinations remain critically important and are incredibly effective at preventing severe disease and death, so get vaccinated when it’s your turn.”

**Greg Basky**, Saskatoon, Sask., with files from **Lauren Vogel**, *CMAJ*

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