

# The emergence of JN.1 is an evolutionary 'step change' in the COVID pandemic: Why this is significant

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Since it was detected in <u>August 2023</u>, the JN.1 variant of COVID has



spread widely. It has become dominant in Australia and <u>around the world</u>, driving the <u>biggest COVID wave</u> seen in many jurisdictions for at least the past year.

The World Health Organization (WHO) <u>classified</u> JN.1 as a "<u>variant</u> of interest" in December 2023 and in January <u>strongly stated</u> COVID was a continuing global health threat causing "far too much" preventable disease with worrying potential for long-term health consequences.

JN.1 is significant. First as a pathogen—it's a surprisingly new-look version of SARS-CoV-2 (the virus that causes COVID) and is rapidly displacing other circulating strains (omicron XBB).

It's also significant because of what it says about COVID's evolution. Normally, SARS-CoV-2 variants look quite similar to what was there before, accumulating just a few mutations at a time that give the virus a meaningful advantage over its parent.

However, occasionally, as was the case when omicron (B.1.1.529) arose two years ago, variants emerge seemingly out of the blue that have markedly different characteristics to what was there before. This has significant implications for disease and transmission.

Until now, it wasn't clear this "step-change" evolution would happen again, especially given the ongoing success of the steadily evolving omicron variants.

JN.1 is so distinct and causing such a wave of new infections that many are wondering whether the <u>WHO</u> will recognize JN.1 as the next variant of concern with its own Greek letter. In any case, with JN.1 we've entered a new phase of the pandemic.

# Where did JN.1 come from?



The JN.1 (or BA.2.86.1.1) story begins with the emergence of its <u>parent</u> <u>lineage</u> BA.2.86 around mid 2023, which originated from a much earlier (2022) omicron sub-variant BA.2.

<u>Chronic infections</u> that may linger unresolved for months (if not years, in some people) likely play a role in the emergence of these step-change variants.

In chronically infected people, the virus silently tests and eventually retains many mutations that help it avoid immunity and survive in that person. For BA.2.86, this resulted in more than 30 mutations of the spike protein (a protein on the surface of SARS-CoV-2 that allows it to attach to our cells).

The sheer volume of infections occurring globally sets the scene for major viral evolution. SARS-CoV-2 continues to have a <u>very high rate of mutation</u>. Accordingly, JN.1 itself is already <u>mutating and evolving</u> quickly.

### How is JN.1 different to other variants?

BA.2.86 and now JN.1 are behaving in a manner that looks unique in laboratory studies in two ways.

The first relates to how the virus evades immunity. JN.1 has inherited more than 30 mutations in its spike protein. It also acquired a new mutation, <u>L455S</u>, which further decreases the ability of antibodies (one part of the <u>immune system</u>'s protective response) to bind to the virus and prevent infection.

The second involves changes to the way JN.1 <u>enters</u> and replicates in our cells. Without delving in to the molecular details, recent high-profile lab-



based research from the <u>United States</u> and <u>Europe</u> observed BA.2.86 to enter cells from the lung in a similar way to pre-omicron variants like delta. However, in contrast, preliminary work by Australia's Kirby Institute <u>using different techniques</u> finds replication characteristics that are aligned better with omicron lineages.

Further research to resolve these different cell entry findings is important because it has implications for where the virus may prefer to replicate in the body, which could affect disease severity and transmission.

Whatever the case, these findings show JN.1 (and SARS-CoV-2 in general) can not only navigate its way around our immune system, but is finding new ways to infect cells and transmit effectively. We need to further study how this plays out in people and how it affects clinical outcomes.

# Is JN.1 more severe?

The step-change evolution of BA.2.86, combined with the immuneevading features in JN.1, has given the virus a <u>global growth advantage</u> well beyond the XBB.1-based lineages we faced in 2023.

Despite these features, evidence suggests our <u>adaptive immune system</u> could still recognize and respond to BA.286 and JN.1 effectively. Updated monovalent vaccines, tests and treatments <u>remain effective</u> against JN.1.

There are two elements to "severity": first if it is more "intrinsically" severe (worse illness with an infection in the absence of any immunity) and second if the virus has greater transmission, causing greater illness and deaths, simply because it infects more people. The latter is certainly the case with JN.1.



### What next?

We simply don't know if this <u>virus</u> is on an evolutionary track to becoming the "next common cold" or not, nor have any idea of what that timeframe might be. While <u>examining the trajectories</u> of four historic coronaviruses could give us a glimpse of where we may be heading, this should be considered as just one possible path. The emergence of JN.1 underlines that we are experiencing a continuing epidemic with COVID and that looks like the way forward for the foreseeable future.

We are now in a new pandemic phase: post-emergency. Yet COVID remains the major infectious disease causing harm globally, from both acute infections and long COVID. At a societal and an individual level we need to re-think the risks of accepting wave after wave of infection.

Altogether, this underscores the importance of <u>comprehensive strategies</u> to reduce COVID transmission and impacts, with the least imposition (such as <u>clean indoor air interventions</u>).

People are <u>advised</u> to continue to take active steps to protect themselves and those around them.

For better pandemic preparedness for emerging threats and an improved response to the current one it is crucial we <u>continue global surveillance</u>. The low representation of low- and middle- income countries is a concerning blind-spot. Intensified research is also crucial.

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