IS OMICRON MILD?
by Alessandra Mezzetti, PhD

Omicron is a much more rapidly spreading variant of SARS-CoV-2 that is causing a tsunami of cases in several countries, threatening health care systems and livelihoods. This variant has more mutations than any previous variant of concern and shows significant immune escape from both prior infection and vaccination, including in people who have received three doses of vaccine.[1] [2]

This has been confirmed by the Imperial College (UK) Covid-19 Response Team (Report 49) that found 5.41 times higher risk of reinfection from Omicron than for Delta from previous natural infection (this suggests very low levels of immunity remaining from prior infection), low protection afforded by two doses of the Pfizer vaccine, and 55-80% vaccine efficacy for symptomatic infection in people boosted (dose 3) with a mRNA vaccine.[3]

Since it was first identified in South Africa, Omicron has been said to be “mild.”[4] Here, we consider what we know so far of this variant and describe common misuses of the word “mild” in connection with Omicron.

The use of the term “mild” in relation to Omicron occurs in three contexts:

1. **Misrepresentation of language:** The word “mild” may be misrepresented or misconstrued in three ways: (**1.1**) Substantial differences between expectations of laypersons and current clinical definitions of “mild” acute COVID (**1.2**), “mild” long-term sequelae (**1.3**) and “mild” disease in children
2. **Misunderstanding of population level effects:** Otherwise “mild” cases can unnecessarily become severe when individuals are unable to access care during situations of high incidence rates when resources and capacities are limited or unavailable
3. **Faulty comparisons to previous variants:** Caveats in the assertion of relative “mildness” compared with other variants

[1] Increased risk of SARS-CoV-2 reinfection associated with emergence of the Omicron variant in South Africa | medRxiv
[2] SARS-CoV-2 Omicron strain exhibits potent capabilities for immune evasion and viral entrance | Signal Transduction and Targeted Therapy
[3] Report 49: Growth, population distribution and immune escape of Omicron in England
[4] South Africa accuses UK and others of 'knee-jerk' reaction to new variant | Coronavirus | The Guardian

1. Misrepresentation of Language

1.1 What is “mild” Covid?

The current definitions of infection/illness due to SARS-CoV-2 are focused on the clinical manifestation of symptoms during the acute phase of the infection, and disregard possible long-term, chronic effects. According to US National Institutes of Health (NIH) guidelines, mild Covid pertains to "[i]ndividuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea (difficult or labored breathing), or abnormal chest imaging."[5]

The NIH indicates that “[m]ost mildly ill patients can be managed in an ambulatory setting or at home.” Additionally, no imaging or other laboratory tests are carried out on “otherwise healthy patients with mild COVID-19.”

When hearing the term “mild disease,” a layperson usually does not think of the clinical definition given by the NIH, but likely has in mind a headache, maybe a few days of fever, i.e., something that a couple of aspirins may quickly take care of, and certainly not something with possible chronic disabling outcomes.

The following are testimonials of what “mild Covid” may be like. From them, it is apparent that the clinical definition of “mild” given by the NIH does not match that of ordinary people. Furthermore, many who have experienced clinically “mild” SARS-CoV-2 infections are now facing a series of chronic symptoms generally known as Long Covid (see 1.2):

- “It was a miserable five days. My legs and arms ached, my fever crept up to 103 and every few hours of sleep would leave my sheets drenched in sweat. I'd drop into bed exhausted after a quick trip down to the kitchen. To sum it up, I'd put my breakthrough case of COVID-19 right up there with my worst bouts of flu. Even after my fever cleared up, I spent the next few weeks feeling low.”[6]

- “The Covid I have is "mild". The pain? Worse than broken bones, kidney stones, pancreatitis, and unmedicated childbirth. Not "just a cold". Mild like a mild bear attack. Literally feels like a bear is gnawing my bones. OTC pain meds = NO relief. Worst time I've ever had”[7]

[5] Clinical Spectrum of SARS-CoV-2 Infection
[6] What A 'Mild' Breakthrough COVID Case Feels Like : Shots - Health News : NPR
[7] https://twitter.com/catladyactivist/status/1479314930822225920

- “Breakthrough case 8/5/21. 102 degree fever for 5 days, migraine level headache + exhaustion so bad I couldn't get out of bed alone. Only have about 60% of smell + taste back, more chronic fatigue, + I now loose words mid sentence.”[8]

- “My "mild" case of COVID has resulted in Postural Orthostatic Tachycardia Syndrome #POTS, pericarditis, & #MyalgicEncephalomyelitis type symptoms including crushing fatigue, #PEM & brain fog.
  I've been unable to work for 7+ months & be an active mom to my busy 3 year old.”[9]

- “Got sick w/ breakthrough Covid on 7/28/2021. 7 days later couldn’t stop coughing. Lost 10 pounds. Still can’t remember words. Vision impaired. Decreased lung function.”[10]

- “I'm such a "mild case". Unable to work for 1.5 years now. My autonomic nervous system is not working properly. The simplest tasks give me a heart rate of 160. Sometimes I can’t even sit or stand up. I am 34 years old. #longcovid didn’t kill me, but I am not living either”[11]

1.2 Long Covid

The term “Long Covid” refers to the sequelae of SARS-CoV-2 infection that persist several weeks, oftentimes months, past the acute phase of the disease, regardless of initial severity. The UK Office for National Statistics (ONS) estimates that, as of 6 December 2021, 1.3 million people in the UK, 2% of the UK population, suffer from Long Covid[12] with symptoms including[13]

- extreme tiredness (fatigue)
- shortness of breath
- chest pain or tightness
- problems with memory and concentration ("brain fog")
- difficulty sleeping (insomnia)
- heart palpitations
- dizziness
- pins and needles
- joint pain
- depression and anxiety
- tinnitus, earaches

[8] https://twitter.com/the_blue_gypsy/status/1478799431814324226
[9] https://twitter.com/Carrie_McGinn/status/1423364598112083975
[10] https://twitter.com/ItsInTheDNA/status/1478764407219965960
[11] https://twitter.com/JetRoz/status/1423021909189480452
[12] Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK - Office for National Statistics
[13] Long-term effects of coronavirus (long COVID) - NHS

- feeling sick, diarrhea, stomach aches, loss of appetite
- a high temperature, cough, headaches, sore throat, changes to sense of smell or taste
- rashes.

A Finnish expert panel's summary of over 4,000 international studies showed that one in two adults and about 2% of children who have been infected with SARS-CoV-2 may experience Long Covid.[14]

Dr. Emilia Liana Falcone, the director of the post-COVID-19 Research Clinic at the Institut de recherches cliniques de Montréal (IRCM), considers the long-term sequelae of Covid infections extremely alarming: "Several who were very high functioning, very healthy now find themselves in a situation where they just cannot go back to work. They're more than a year out. And they're basically taking early retirement in some cases."[15]

Petersen et al.[16] assessed the pulmonary, cardiac, vascular, renal, and neurological status of a cohort of patients at ~10 months after Covid infection and observed multiple markers of disease persistence compared to matched controls. Specific markers included lower lung volume and significantly higher airway resistance, lower ventricular function, more concentrated cardiac biomarkers, evidence suggestive of deep vein thrombosis, and lower glomerular filtration rate. The authors did not find signs of cognitive impairment, in contrast to other assessments that have found substantially reduced cognitive performance and persistent neurological symptoms following Covid infection.[17]

1.3 Omicron and Children

One of the most common narratives of this pandemic has been that pediatric infections are thought to be generally less severe. However, there is a sharp increase in pediatric hospitalizations during the Omicron wave, especially among the 0-4Y age group, for whom there is no approved vaccine yet.

A recent report from the South African National Institute for Communicable Diseases[18] shows that cases under 18 years of age account for both a large proportion of Covid infections and an increasingly high hospital admission rate, which may suggest that the young are more impacted by Omicron in contrast to the adult population, although the authors caution that more research is needed.

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[14] Long COVID could become Finland's largest chronic disease, warns minister | Reuters
[15] Omicron 'isn't a regular cold,' Quebec doctor says, urging people to avoid infection and risk of long-COVID | CTV News
[16] Multi-organ assessment in mainly non-hospitalized individuals after SARS-CoV-2 infection: The Hamburg City Health Study COVID programme | European Heart Journal | Oxford Academic
[17] Persistent neurologic symptoms and cognitive dysfunction in non-hospitalized Covid-19 "long haulers" - Graham - 2021 - Annals of Clinical and Translational Neurology - Wiley Online Library
[18] SPECIAL PUBLIC HEALTH SURVEILLANCE BULLETIN

In contrast, when Wang et al.[19] studied the severity of Covid due to the Omicron variant in comparison to the Delta variant, during a 3-day-window following infection, they observed a 29% reduction in emergency department visits, 67% reduction in hospitalizations, 68% reduction in ICU admissions, and 71% reduction in mechanical ventilation in children under 5 years old.

Although there are conflicting indications on whether the Omicron variant may cause less severe outcomes in children compared to Delta, the rapid exponential growth of infections in the younger population is resulting in a concerning higher number of hospitalizations in this age group compared to what was seen in previous waves.

2. Reasons for and Consequences of Omicron's Higher Transmissibility

The Omicron variant infects and multiplies at a much faster pace than Delta and the original strain (roughly 70 times faster) in the upper respiratory tract, which explains the higher transmission rate compared to previous variants. While its localization on the bronchi may be suggestive of mild symptoms, Dr. Chan (University of Hong Kong) points out that individuals respond differently to infection and by infecting more people, the overall result of a potentially milder variant may still be a large number of severe outcomes and deaths.[20] Critical staffing and resource shortages exacerbate the problem by raising the probability of milder infections turning more severe as apt and timely care cannot be guaranteed.[21]

3. Severity Compared to Other Variants

Concerning the risk of hospitalization, the Imperial College (UK) Covid-19 Response Team found an overall reduction of the risk of hospitalization in Omicron, compared to Delta. However, they caution that this reduced risk must be balanced against the risk of reinfection with Omicron, which is higher.[22]

A clinical trial of the Janssen (J&J) vaccine in South Africa showed that, of the patients hospitalized, 16% required oxygen supplementation and 0.2% required mechanical ventilation

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[19] COVID infection severity in children under 5 years old before and after Omicron emergence in the US | medRxiv
[20] HKUMed finds Omicron SARS-CoV-2 can infect faster and better than Delta in human bronchus but with less severe infection in lung
[21] Coronavirus US: Nearly a quarter of hospitals are reporting a critical staff shortage as Omicron drives a rise in Covid-19 cases - CNN
[22] Report 50: Hospitalisation risk for Omicron cases in England

during the Omicron wave, versus 43% and 7-8%, respectively, during the Beta and Delta waves.[23]

Davies et al.[24] observed a lower risk of death during the Omicron wave than in waves one, two and three (Delta), with the latter being the most severe. However, they noted that prior infection or vaccination was the main factor in the observation of less severe outcomes due to the Omicron variant, while the intrinsically reduced virulence of Omicron may be responsible for only 25%[25] of the reduced risk of hospitalization compared to Delta. Given that Delta was found to have twice the risk of hospitalization than Alpha,[26] whose risk, in turn, was assessed as roughly 50% higher than the original strain,[27] people who have not been infected or vaccinated are at more than double the risk for hospitalization after an Omicron infection compared to an infection with the original strain.

Public Health Ontario[28] cautions that, although the available data appear to point to a lower severity of the Omicron variant compared to Delta, one limitation is that jurisdictions may use different metrics to report hospitalizations. Additionally, the data is insufficient to assess hospitalization outcomes, mortality and Long Covid, while the high transmissibility of Omicron is such that it threatens the health systems of many jurisdictions.

Conclusion

The exceptionally high number of infections by the highly transmissible Omicron variant has resulted in an exponential increase in hospitalizations and is threatening health care systems in many countries despite the lower risk of hospitalization compared to Delta. Record hospitalizations have also been observed among children, including the 0-4Y age group. Furthermore, potential long-term sequelae such as Long Covid cannot be ruled out for the Omicron variant.

Therefore, it is inadequate to conclude that Omicron is “mild,” regardless of whether one considers the clinical definition of this term or the layman’s idea of what may constitute a mild infection. Furthermore, Omicron's increased characteristic delay between infection and death may have led to underestimates of this variant's severity.[29] And, as the Director General of the WHO, Dr. Tedros Adhanom Ghebreyesus, has pointed out, because the tsunami of Omicron cases is such that health systems around the world are being overwhelmed, people are being

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[23] Milder disease with Omicron: is it the virus or the pre-existing immunity? | Nature Reviews Immunology
[24] Outcomes of laboratory-confirmed SARS-CoV-2 infection in the Omicron-driven fourth wave compared with previous waves in the Western Cape Province, South Africa | medRxiv
[25] Matching the estimate from the Imperial College Covid-19 Response Team (Report 50)
[26] Increased risk of hospitalisation and death with the delta variant in the USA - The Lancet Infectious Diseases
[27] Risk of hospital admission for patients with SARS-CoV-2 variant B.1.1.7: cohort analysis | The BMJ
[28] COVID-19 Variant of Concern Omicron (B.1.1.529): Risk Assessment, January 19, 2022
[29] The Fallacy of “Mild” Omicron. There is a limit to the speed at which… | by Dr. David Glassman | Jan, 2022 | Medium

hospitalized and dying in record numbers and as excess deaths, this variant should not be called “mild.”[30]

Finally, this variant’s immune evasion ability is such that allowing it to circulate in the population - or the spread of any other variant - under the pretext of it being “mild,” may result in the generation of new, more immune evasive ones in the future, with no guarantee of them being milder.

[30] Covid: Deadly Omicron should not be called mild, warns WHO - BBC News