Editorial: World Health Organization (WHO) Variants of Concern Lineages Under Monitoring (VOC-LUM) in Response to the Global Spread of Lineages and Sublineages of Omicron, or B.1.1.529, SARS-CoV-2

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Conflict of interest: None declared

Abstract
On 26 November 2021, the World Health Organization (WHO) identified the B.1.1.529 variant, or Omicron variant, as the fifth variant of concern (VOC) of SARS-CoV-2. The B.1.1.529 Omicron variant of SARS-CoV-2 includes five lineages, BA.1, BA.2, BA.3, BA.4, and BA.5. During the past six months, several identified sublineages of B.1.1.529 have rapidly spread globally. Although the lineages BA.1 and BA.2 initially predominated, BA.4, BA.5, and sublineage BA.2.12.1 are now dominant in Europe and the USA. On 12 May 2022, the European Centre for Disease Prevention and Control (ECDC) reclassified BA.4 and BA.5 from variants of interest (VOI) to variants of concern (VOC). BA.2.12.1, BA.4, and BA.5 have shown higher transmissibility and increased neutralization evasion compared with BA.2 when tested against plasma from patients with triple-vaccination and following infection with BA.1. On 7 June 2022, the World Health Organization (WHO) added a new category to its SARS-CoV-2 variant tracking system, the VOC Lineages Under Monitoring (VOC-LUM), which aims to inform global public health authorities of the VOC lineages and sublineages that may require prioritized attention and monitoring. This Editorial aims to present an update on the lineages and sublineages of the Omicron variant of SARS-CoV-2 and the VOC-LUM initiative from the WHO.

Keywords: COVID-19 • SARS-CoV-2 • Viral Variant • Variant of Concern • Editorial
Recent population and laboratory studies support the concerns regarding the potential threat of the new SARS-CoV-2 Omicron lineages and sublineages [7,8]. On 17 June 2022, in the journal *Nature*, Cai and colleagues reported that BA.2.12.1, BA.4, and BA.5 showed higher transmissibility than BA.2 [7]. Structural comparisons of the spike (S) protein showed that BA.2.12.1 and BA.4/BA.5 had comparable angiotensin-converting enzyme 2 (ACE2)-binding affinities to BA.2 [7]. Also, BA.2.12.1, BA.4, and BA.5 showed increased neutralization evasion compared with BA.2 when tested against plasma from patients with triple-vaccination and following infection with BA.1 [7]. Studies on epitope distribution and Omicron neutralization efficacy of neutralizing antibodies indicated that Omicron might evolve mutations to evade the humoral immune response following BA.1 infection [7]. Therefore, BA.1-derived vaccine boosters may not achieve adequate immune protection against the new Omicron lineages [7]. Laboratory studies have shown that antibodies generated following vaccination are less effective at blocking the BA.4 and BA.5 viruses than earlier Omicron variants, including BA.1 and BA.2, possibly due to L452R and F486V spike mutations in BA.4 and BA.5 [8].

Therefore, due to the increasing global transmission of the Omicron VOCs and the subsequent expected increased viral diversity, on 7 June 2022, the WHO added a new category to its SARS-CoV-2 variant tracking system [9]. The VOC Lineages Under Monitoring (VOC-LUM) initiative aims to inform global public health authorities of the VOC lineages that may require prioritized attention and monitoring (*Table 2*) [9]. The main objective of the VOC-LUM is to investigate whether these lineages pose an additional threat to global public health [9]. If any lineages show distinct characteristics that may increase

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**Table 1.** The five (Pango) lineages of the B.1.1.529 or Omicron variant of SARS-CoV-2 include BA.1, BA.2, BA.3, BA.4, and BA.5.

| Omicron lineage | Geographic region of first detection | Date first detected | Date of designation | WHO status |
|-----------------|--------------------------------------|---------------------|---------------------|------------|
| B.1.1.529       | South Africa                         | 24 November 2021    | Designated as a VOC on 26 Nov 2021 | VOC        |
| BA.1*           | South Africa                         | January 2022        | Re-designated as a VOC on 22 Feb 2022 | VOC        |
| BA.2*           | South Africa                         | January 2022        | Re-designated as a VOC on 22 Feb 2022 | VOC        |
| BA.3            | South Africa                         | January 2022        | Non-designated – detected worldwide but with few cases | Non-designated |
| BA.4*           | South Africa                         | January 2022        | Designated as a VOC-LUM on 7 June 2022 | VOC-LUM    |
| BA.5*           | South Africa                         | January 2022        | Designated as a VOC-LUM on 7 June 2022 | VOC-LUM    |

* The WHO recommends that these descendant lineages of B.1.1.529 should be monitored as distinct lineages by public health authorities with comparative assessments of their viral characteristics. VOC-LUM – variant of concern lineage under monitoring. Adapted from: World Health Organization (WHO). SARS-CoV-2 Variants. 7th June 2022 [9].

**Table 2.** The Omicron lineages included in the World Health Organization (WHO) variants of concern lineages under monitoring (VOC-LUM), as of 7 June 2022.

| Pango lineage designation | Relationship to the Omicron VOC | Geographic region and date first detected |
|---------------------------|--------------------------------|----------------------------------------|
| BA.4*                     | Sister lineage of BA.1 and BA.2 | Jan 2022; South Africa                 |
| BA.5*                     | Sister lineage of BA.1 and BA.2 | Jan 2022; South Africa                 |
| BA.2.12.1                 | Sublineage of BA.2              | Dec 2021; USA                          |
| BA.2.9.1                  | Sublineage of BA.2              | Feb 2022; Multiple countries           |
| BA.2.11                   | Sublineage of BA.2              | March 2022; Multiple countries         |
| BA.2.13                   | Sublineage of BA.2              | Feb 2022; Multiple countries           |

* On 12 May, 2022, the European Centre for Disease Prevention and Control (ECDC) reclassified sublineages BA.4 and BA.5 from variants of interest (VOI) to variants of concern (VOC) [6]. Adapted from: World Health Organization (WHO). SARS-CoV-2 Variants. 7th June 2022 [9].

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disease incidence or severity compared to the original VOC, the TAG-VE and WHO may identify the virus as a VOC-LUM [9].

The B.1.1.529, or Omicron variant, of SARS-CoV-2 is currently the dominant variant circulating globally [9]. Some sublineages of Omicron show transmission advantage compared to other circulating VOC lineages and mutational changes that confer a transmission or infection advantage [9]. For example, some countries, including the UK, have made public health authorities aware that Omicron BA.2 may have a transmissibility advantage that explains its increasing prevalence, including in care homes [10].

The primary roles of the VOC-LUM initiative from the WHO include: a review of the global epidemiology of the viruses; tracking worldwide spread; sharing virus isolates via the WHO Biohub; submission of the complete genome sequences to a publicly available database; improving the understanding of any potential impacts of the VOC-LUM on the epidemiology of COVID-19; and laboratory assessments on the impact of the VOC-LUM on relevant virus characteristics [9].

Conclusions

The new WHO VOC-LUM initiative has been established to recognize the importance of new lineages and sublineages of the Omicron, or B.1.1.529, variant of SARS-CoV-2. The emergence of new lineages and sublineages of the Omicron, or B.1.1.529, variant of SARS-CoV-2, is likely to continue due to high mutation rates. The concern is that with reduced SARS-CoV-2 testing in populations, the epidemiological landscape of emerging viruses may become unclear due to the lack of viral genomic data.

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