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## Letter to the Editor

**SARS CoV-2 genetic jump to a new SARS CoV-3 pandemic: Let's be prepared**

Dear Editor,

I read with great interest the recent reassuring correspondence: Genetic and structural genome-based survey reveals the low potential for epidemiological expansion of the SARS-CoV-2 XBB.1.5 sublineage by Scarpa et al.<sup>1</sup> It added a very valuable genetic and structural insight to my prior correspondence calling the world to follow the African approach in dealing with COVID-19<sup>2</sup> and both letters might reasonably encourage the global health care authorities to consider relaxation and/or abortion of the remaining COVID restrictions.

However, the emergence of a new global SARS CoV-2 Omicron subvariant, remains always a possibility that can't be excluded for any of the current variants, including XBB.1.5, as also wisely admitted by Scarpa et al.<sup>1</sup> Interestingly, influenza viruses showed a potential for significant evolutionary "antigenic jumps" even after extended periods of apparent stasis<sup>3</sup> and we could consider the period elapsed from 2003 when SARS CoV-1 emerged to 2019 when SARS CoV-2 showed approximately 20% genetic nucleotide sequence identity difference from its ancestor as such a period. Therefore, I suggest that whenever the world would reach the highly anticipated SARS CoV-2 stasis, we should prepare ourselves for a most probably inevitable SARS CoV-3 pandemic that could emerge in less than 16 years of apparent stasis and we should learn from our previous mistakes at all aspects to avoid wasting more millions of lives.

Notably, our African call to adopt early immune-modulatory treatment using generic drugs<sup>4</sup> and to abandon all COVID restrictions<sup>2</sup> is totally independent from the evolutionary status of SARS-CoV-2. In Africa, and in my clinical practice since April 2020 and onwards, we adopted early treatment, avoided almost all COVID restrictions and escaped its vaccine mandates.<sup>2</sup> With time, we witnessed how science proved us right to eventually admit that natural infection is as protective as, if not superior to, mRNA vaccination.<sup>5</sup> Moreover, we insist that upon proper early treatment, natural infection is much safer and unpaid.<sup>6</sup>

Importantly, we argue that though SARS CoV-2, due to its proofreading exoribonuclease participating in genome error correction, has less mutation error rates than influenza A and B viruses,<sup>7</sup> it has evolved and is still evolving much faster in terms of transmissibility and immune evasion, and the causes might include the first ever global mass vaccination,<sup>6,8</sup> the wide use of mutagenic drugs as

molnupiravir and favipiravir,<sup>9</sup> as well as the added adaptive evolutionary pressure caused by the protease inhibitor nirmatrelvir boosted by ritonavir.<sup>10</sup>

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None.

**Conflict of interests**

None.

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