Review of: "Evolution of new variants of SARS-CoV-2 during the pandemic: mutation-limited or selection-limited?"

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Potential competing interests: No potential competing interests to declare.

This is an interesting study that is nicely presented.

The one aspect of SARS-CoV-2 dynamics that is not currently treated in any of the three hypotheses is the role of chronic infections in variant emergence. Variants emerge with many mutations, perhaps in part due to the fact that more immune-escape mutations in different epitopes enables larger fitness gains (e.g. Omicron BA.1 emergence). This could suggest a role for mutation-limitation in finding the “right” combinations that maximize fitness in light of existing population immunity. More generally, the role of chronic infections in variant emergence creates decoupling between peaks of a prior variant that are likely to kick-start the largest numbers of chronic infections, versus the emergence of the variants that evolve out from this wave which might emergence many months after the initial infection/wave.