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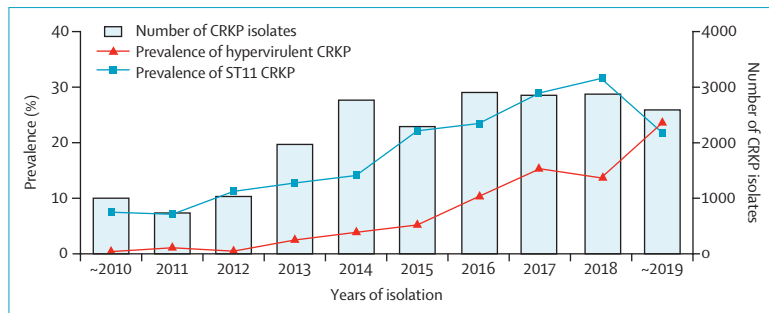


Figure: Presence of global CRKP, ST11 CRKP, and hypervirulent CRKP isolates from 1980 to 2022
The numbers of CRKP isolates were retrieved from the National Center for Biotechnology Information GenBank database. ST=sequence type. CRKP=carbapenem-resistant *Klebsiella pneumoniae*.

of hypervirulent *K pneumoniae* associated with dominant CRKP clones in China.^{2,3} These data show that the classic isolates of CRKP have already evolved into hypervirulent isolates and that a considerable proportion of CRKP strains should now be designated as hypervirulent CRKP. Highly pathogenic hypervirulent CRKP has been spreading rapidly worldwide, and requires increased clinical attention (figure). Accordingly, we developed the Bacterial Whole Genome Sequence Typing Database (BacWGSTdb), a freely accessible public repository for bacterial WGS typing and source tracking, to provide a one-stop solution to detecting highly pathogenic clones during their early stages of expansion.⁴ To prevent future transmission, real-time surveillance powered by WGS and stringent infection-control measures should be implemented.

Rapid and cost-effective WGS is crucial for diagnosing and monitoring the outbreaks and transmission dynamics of bacterial infections.⁵ The genomic features and antimicrobial resistance of bacterial pathogens in low-income and middle-income countries might be underestimated due to the paucity of genomic data. Overall, our data highlight the global evolution and geographical variations of hypervirulent CRKP, advocate for active WGS-based surveillance of CRKP, and emphasise the pressing need for further prospective, multicentre, intercontinental studies. These efforts would aid in the

development of appropriate infection-control measures to prevent further transmission of hypervirulent CRKP.

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Additional considerations for assessing COVID-19 impact on dengue transmission

In their multi-continent assessment of the impact of COVID-19-related restrictions on dengue incidence, Yuyang Chen and colleagues reported an astounding drop in dengue risk in 2020 attributable to public health and social measures during the pandemic (relative risk 0.01–0.17; $p < 0.01$).¹ Taking population immunity into account, the authors acknowledged how the unprecedented dengue burden of 2019 might have driven high immunity to dengue in 2020. Chen and colleagues also mentioned idiosyncrasies in the model that could not be explained. We would like to add possible considerations of (1) administrative delays and (2) genotype-replacement events driving the 2019 epidemics affecting conclusions drawn from the model.

On a much smaller, regional scale, we assessed how COVID-19 might have impacted dengue transmission in southeast Asia.² Administrative delays from the COVID-19 burden resulted in under-reporting, delayed reporting, and no reporting from some areas given how taxed health-care systems were during this time. This fact alone might not complicate the model's conclusions, but if the case fatality rate is being used as a surrogate measure of under-reporting, 2020 would vary greatly from previous years, leading to an inflated interpretation of COVID-19 restrictions.

Second, the complicated interplay of dengue serotype-specific immunity contributes to the difficulty of predicting dengue virus outbreaks at local, subnational, or national levels. A recent study of data from Thailand revealed that as dengue virus evolves to evade host immunity, major epidemics result

when a serotype strain becomes more antigenically similar to other serotypes than its own.³ The force of the invading strain can result in a selective sweep, reducing viral diversity with a subsequent drop in cases. Chen and colleagues added spatial random effects to account for the introduction of new dengue serotypes, and population immunity was labelled annual anomaly in the model. However, we would like to suggest to the authors that the greatest dengue year on record in 2019, in terms of incidence, be treated as unique in that it was probably fuelled by viral evolutionary events resulting in genotype replacements and might falsely augment the differential dengue virus burden between a higher-than-usual 6-year mean dengue incidence (inclusive of 2019) versus the comparison year of 2020. From an academic standpoint, we would be curious to see how the model would perform if the outlier year of 2019 were removed.

We appreciate the authors' timely contribution to understand the multifaceted disease ecology of dengue coupled with human movement data in the context of COVID-19.

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Authors' reply

Christina Yek and colleagues raise two additional considerations when interpreting our recent findings that COVID-19 interventions reduced dengue incidence in 2020.¹ First, whether administrative delays might be an additional, unconsidered dimension to under-reporting and, second, whether the inclusion of abnormal data from 2019 might bias our predictions of cases averted.

Disruption-induced administrative delays in reporting are plausible and would have led to fewer dengue cases being reported in 2020. To minimise this, we restricted our analysis to January–December, 2020, despite more recent data being available from 2021. Searches for data were last updated on Feb 2, 2022, and no delay-related changes were identified compared with the original searches from Feb 23, 2021. If administrative delays did occur in 2020, they were probably quickly rectified before early 2021. Furthermore, our case fatality-based under-reporting analysis would probably have detected under-reporting due to administrative delays if they had occurred. Many countries with dengue endemics (eg, Sri Lanka) have separate reporting procedures for suspected dengue deaths that involve distinct, rapid reporting channels that are regularly audited.² Delays in reporting dengue cases but not deaths would result in higher case fatality rates, which we did not detect for any country.

We also agree that 2019 was an abnormally high incidence year for dengue and this would have resulted in below average incidence in 2020, similar to previous post-outbreak years (eg, 2017 in Brazil), even in the absence of COVID-19 interventions. These post-outbreak reductions are probably due to a combination of viral (eg, genotype replacement, as suggested), mosquito (eg, successful vector control), and host (eg, rising immunity to circulating viruses) factors that might differ between

outbreaks but have a consistent effect of suppression.^{3,4} The annual anomaly term in our model estimates this expected post-outbreak reduction. Although 2019 was an unprecedented year for dengue globally, many countries have had similar outbreaks previously (see the appendix [p 31] in our Article¹), allowing annual anomaly effects to be appropriately estimated. Inclusion of this term decreases predicted cases in 2020 and, thus, cases averted by COVID-19 interventions. Therefore, removing 2019 dengue data from the historical model-fitting dataset, as suggested, marginally increases our estimate of dengue cases averted by COVID-19 interventions but also substantially increases prediction uncertainty (0.76 million [95% credible interval 0.00–2.23] vs 0.72 million [0.12–1.47]). We therefore believe the original estimates we presented¹ offer the best overall estimate of the protective effects of COVID-19 interventions against dengue.

We declare no competing interests.

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