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## COVID-19 vaccine effectiveness against the omicron (BA.2) variant in England



The omicron (B.1.1.529) variant, first detected in the UK on Nov 27, 2021, rapidly became the dominant strain, due in part to reduced vaccine effectiveness.<sup>1</sup> An increase in sequenced cases of the omicron sub-lineage BA.2 was observed in the week beginning on Jan 3, 2022.<sup>2</sup> BA.2 has a growth advantage over BA.1<sup>3,4</sup> and has become the dominant strain in the UK at the time of writing. Neutralisation assays using monoclonal antibodies have suggested a small antigenic difference between BA.1 and BA.2, although sera from individuals with booster vaccinations neutralise both variants similarly.<sup>3</sup>

The UK COVID-19 vaccination programme has been in place since Dec 8, 2020, with primary courses of two doses of either BNT162b2 (Comirnaty, Pfizer–BioNTech), ChAdOx1-S (Vaxzevria, Oxford/AstraZeneca), or mRNA-1273 (Spikevax, Moderna). Booster vaccination with either BNT162b2 or a half dose (50 µg) of mRNA-1273 was introduced on Sept 14, 2021, to adults older than 50 years and those in risk groups, and on Nov 29, 2021, to all adults.

In this Comment, we estimate vaccine effectiveness against symptomatic disease and hospitalisation with BA.1 and BA.2 after one or two doses of BNT162b2,

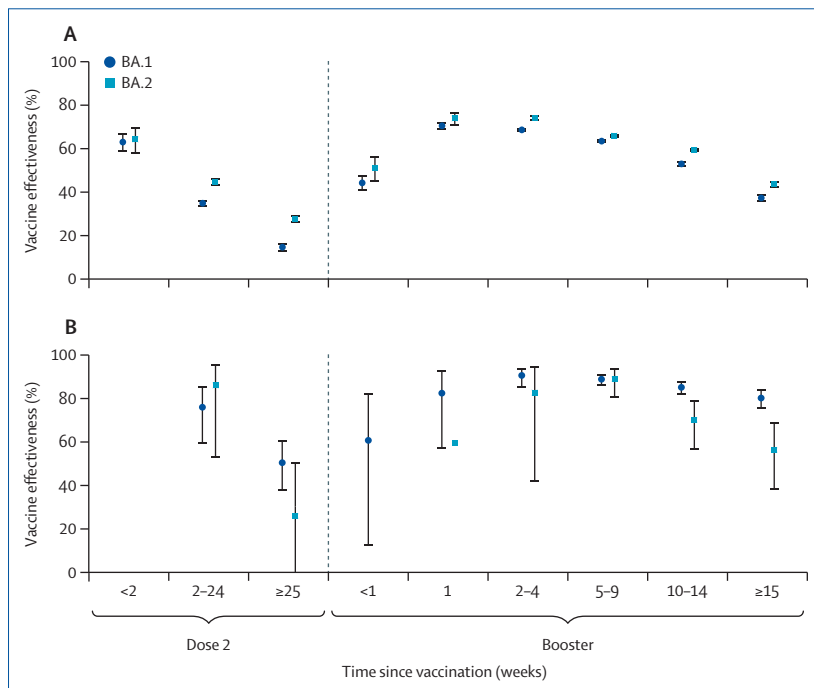
ChAdOx1-S, or mRNA-1273, and after booster doses of BNT162b2 or mRNA-1273 during a period of co-circulation. We used a test-negative case-control study design.<sup>5–8</sup> Our analysis included all vaccines used in the UK. Vaccination status was included as an independent variable and effectiveness defined as 1 minus the odds of vaccination in cases, divided by the odds of vaccination in controls (appendix pp 1–3).

Between Jan 17 and March 31, 2022, there were 1127517 eligible tests from symptomatic individuals, of which 265820 were positive for BA.1, 246069 were positive for BA.2, and 615628 were negative (controls). The hospitalisation analysis included 15043 eligible tests, of which 1662 were positive for BA.1, 623 were positive for BA.2, and 12758 were controls (appendix pp 4–7).

There was no evidence of reduced vaccine effectiveness against symptomatic disease with BA.2 compared with BA.1 (figure; appendix p 9). 25 weeks or more after two doses, vaccine effectiveness was 14.8% (95% CI 12.9–16.7 against BA.1 and 27.8% (25.9–29.7) against BA.2. Booster immunisation increased protection after a week to 70.6% (68.9–72.2)

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See Online for appendix



**Figure:** Vaccine effectiveness against symptomatic disease (A) and hospitalisation (B) following infection with the omicron sub-lineages BA.1 and BA.2 in adults aged 18 years and older in England

against BA.1 and 74.0% (70.8–76.9) against BA.2, waning to 37.4% (35.8–39.0) against BA.1 and 43.7% (42.3–45.1) against BA.2 at 15 or more weeks after receiving the booster dose. Protection against hospitalisation was lower in people with BA.2 than in people with BA.1 in some periods but higher for others (figure); the CIs overlapped in most periods. After a booster dose, vaccine effectiveness against hospitalisation peaked at 90.8% (85.1–94.3) against BA.1 and 89.1% (80.5–94.0) against BA.2 before decreasing to 80.4% (75.6–84.3) and 56.5% (38.4–69.3), respectively, after 15 or more weeks. Due to the small number of individuals involved, there was greater uncertainty around the vaccine effectiveness estimates against hospitalisation than around those against symptomatic disease.

Overall, we found no reduction in vaccine effectiveness against symptomatic disease with BA.2 compared with BA.1. As previously observed, we found that vaccine effectiveness wanes over time,<sup>1,7,9,10</sup> but there was no difference in the rate of decline between the two sub-lineages. Due to the small number of people with BA.2, we were not able to stratify by manufacturer in these analyses; however, we found little difference according to vaccine after a third dose in previous analyses of the

omicron variant.<sup>1</sup> These findings are consistent with neutralisation assays,<sup>3</sup> but there is discrepancy with a Danish household transmission study, which found that BA.2 was associated with increased susceptibility to infection for vaccinated individuals.<sup>4</sup> Differences between the UK and Denmark studies might be explained by different vaccination and infection histories in the respective countries, or by methodological differences, and need further exploration.

Vaccine effectiveness against severe disease is higher and retained for longer than effectiveness against mild disease.<sup>9</sup> Since the omicron variant became dominant, people are increasingly likely to have COVID-19 as an incidental finding rather than as the primary reason for admission.<sup>8</sup> Using specific definitions to identify admissions with severe respiratory disease gives higher vaccine effectiveness estimates than using broader definitions, and these estimates probably reflect the true vaccine effectiveness against hospitalisation.<sup>8</sup> Vaccine effectiveness against hospitalisation was similar for BA.1 and BA.2 after booster vaccination, although vaccine effectiveness might wane faster for BA.2 than for BA.1. The BA.2 analysis might be more susceptible to misclassification bias, because of cases incidentally hospitalised with COVID-19 due to the higher infection rates during the periods after the booster when BA.2 predominated (appendix p 4); this bias might explain the lower vaccine effectiveness estimates for BA.2 than for BA.1 in these periods.

We declare no competing interests. The UK Health Security Agency has legal permission, provided by Regulation 3 of The Health Service (Control of Patient Information) Regulations 2002, to process patient confidential information for national surveillance of communicable diseases and, as such, individual patient consent is not required to access records.

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## Antimicrobial resistance data, frugal sequencing, and low-income countries in Africa



Antimicrobial resistance is most prevalent in Africa's low-income countries (LICs). Furthermore, Africa's LICs have the highest overall death rate due to antimicrobial resistance-related causes globally; regrettably, these conclusions about Africa are the result of statistical modelling.<sup>1</sup> Several recent papers have highlighted data gaps on antimicrobial resistance in Africa's LICs.<sup>2</sup> Collecting comprehensive antimicrobial resistance data in Africa's LICs has been problematic due to a paucity of laboratory-based antimicrobial-resistance surveillance.<sup>3</sup> Most clinical microbiology labs, which would ordinarily be in charge of antimicrobial-resistance surveillance, by performing routine antimicrobial susceptibility testing, do not have the requisite resources.<sup>3,4</sup>

In contrast with high-income countries, where antimicrobial resistance sequencing is common, sequencing in Africa's LICs remains mostly unexplored. Yet, it provides real-time data streaming for immediate and actionable results. Since the debut of the Sanger sequencer (Applied Biosystems, USA), numerous sequencing platforms have been developed.<sup>5</sup> More portable sequencers, such as MinION and SmidgION systems (Oxford Nanopore Technologies, UK), have been released in recent years and are continually being improved.<sup>6</sup> These sequencers have markedly reduced the costs associated with sequencing. Regardless, Africa's LICs have not adopted this frugal sequencing strategy and older sequencing platforms, even when donated or purchased and installed, go unused.

The drawbacks of older sequencing platforms, including expensive initial purchase, operating and

maintenance costs and the poor bioinformatics capacity in African LICs which made these platforms unappealing compared with traditional microbial techniques (ie, culture and antimicrobial susceptibility testings), are less preset with newer machines. Platforms, such as MinION, have low initial purchase, operating, and maintenance costs; while the portability and ability to be powered by laptop or smartphone, with minimal hardware and simple configuration via a standard USB port and inbuilt real-time analysis software, allows sequencing from any location.

Antimicrobial resistance diagnosis and monitoring with standardised sequencing and timely data sharing can make it possible to know the potential origins and transmission patterns of antimicrobial resistance.<sup>7</sup> Regardless of the breakthroughs in sequencing, sequencers will be unable to lead the way in redefining how antimicrobial resistance is diagnosed and monitored in Africa's LICs without considerable cooperation from the most essential policymakers. Key policymakers in Africa's LICs must be persuaded to modify their mindsets and adopt sequencing in order to improve antimicrobial resistance diagnosis and monitoring, which could assist to fill the gap in antimicrobial resistance data in Africa.

To leverage sequencing for diagnosis and monitoring, a consensus sample needs to be considered. However, antimicrobial resistance diagnosis and monitoring continues to be hampered by an absence of consensus on the best clinical sample for detecting microorganisms in the most frequent infectious diseases.<sup>8</sup> Nonetheless, research has suggested that the consensus sample



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