Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

RSV-specific IgG from 2020 to 2021 (n=9) and those who did not (n=549).

Post-fusion F IgG antibody concentrations declined from 2020 to 2021 (p<0·001) and increased with age (p<0·001; figure 1B). The decrease was greatest for the 1-year interval between timepoints 1 and 3 (p<0·001) when compared with the decrease between timepoints 1 and 2 (p<0·001) and between timepoints 2 and 3 (p=0·182). The decrease in antibodies was significant in all age groups, except for participants aged 31–40 years. Across the 3 timepoints, the age group of 71 years and older had higher antibody concentrations than participants aged 1–10 years (p=0·019), 21–30 years (p<0·001), 31–40 years (p=0·021), 41–50 years (p<0·001), and 51–60 years (p=0·034). In our analysis, we did not find evidence of differences in decay rates between age groups. We found 9 individuals (1·6%) with antibody boosting of at least two-fold during this period, indicative of exposure to the virus (figure 1C). These individuals were all adults of at least 30 years of age, and since two adults showed elevated IgG before the increase in clinical reports of RSV infections, these findings might indicate that circulation initiated in the adult population. On average, these individuals had lower IgG concentrations in 2020 (p=0·028) than those not showing a rise in IgG concentrations (figure 1D).

These data support the assumption that RSV-specific antibody concentrations declined during the COVID-19 pandemic in all age groups and are in line with a previous report showing decay of antibodies to RSV.[5] We do not have data on RSV-specific antibody kinetics in our cohort before the pandemic and there are relatively large variations between individuals, so the effect on susceptibility to RSV is not clear yet. Antibodies to the F protein, especially in pre-fusion confirmation, have an important role in the neutralisation of RSV and were previously shown to correlate well with virus neutralisation.[7] However, the degree to which virus neutralisation is affected and the exact correlation with immune protection are yet to be determined.[8] Following this preliminary analysis, additional timepoints, including follow-up samples, are being investigated to support and extend these findings. In conclusion, monitoring changes in antibody concentrations could identify populations susceptible to RSV infection.

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Effect of hybrid immunity and bivalent booster vaccination on omicron sublineage neutralisation

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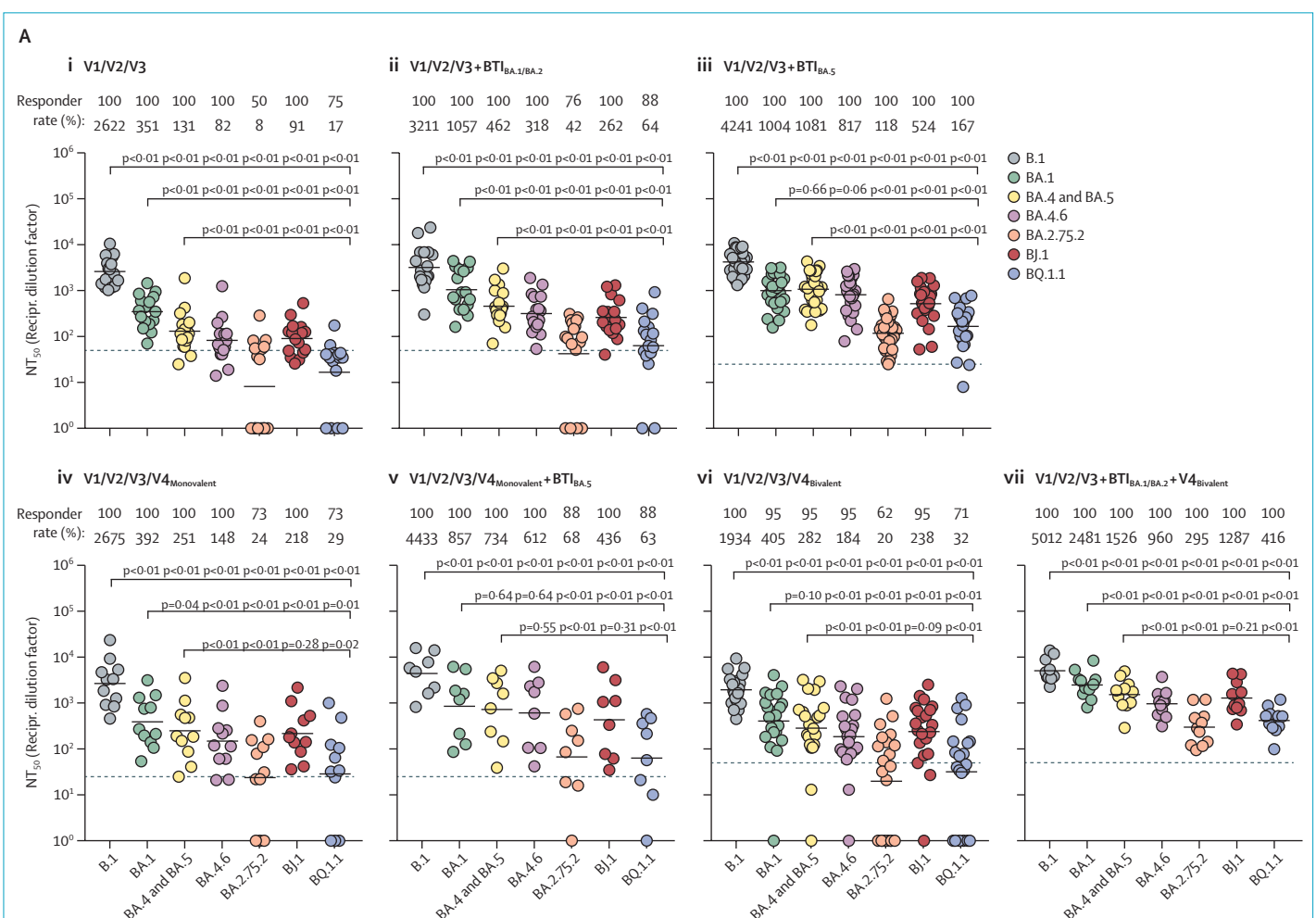
Vaccination is the central strategy to control the COVID-19 pandemic. Vaccination-induced antibodies that target the viral spike (S) protein and neutralise SARS-CoV-2 are crucial for protection against infection and disease. However, most vaccines encode for the S protein of the virus that circulated early in the pandemic (eg, the B.1 lineage), and emerging SARS-CoV-2 variants have mutations in the S protein that reduce neutralisation sensitivity. In particular, the omicron variant (B.1.1.529 lineage and sublineages) is highly mutated and efficiently evades antibodies.[1–3] Therefore, bivalent mRNA vaccines have been developed that include the genetic information for S proteins of the B.1 lineage and the currently dominating omicron BA.5 lineage. These vaccines have shown increased immunogenicity and protection in mice,[4] but information on potential differences in the effectiveness of monovalent and bivalent vaccine boosters in humans is scarce.[5–7]

We compared neutralisation of BA.1, BA.4 and BA.5 (identical S proteins, BA.4-5), BA.4.6, and the emerging omicron sublineages

BA.2.75.2 (circulating mainly in India), BJ.1 (parental lineage of the currently expanding XBB recombinant), and BQ.1.1 (the incidence of which is increasing in the USA and Europe). We tested neutralisation by antibodies that were induced upon triple vaccination, vaccination and breakthrough infection during the BA.1 and BA.2 wave or BA.5 wave in Germany, triple vaccination plus monovalent or bivalent mRNA booster vaccination, or triple vaccination plus breakthrough infection (BA.1 and BA.2 wave) and a bivalent mRNA booster vaccination. For this, we used S protein bearing pseudotypes, which adequately model antibody-mediated neutralisation of SARS-CoV-2.[8] We found that neutralisation of particles pseudotyped with the B.1 S protein ($B.1_{pp}$) was highest for all cohorts, followed by neutralisation of $BA.1_{pp}$ and $BA.4\text{-}5_{pp}$, which is in line with expectations (figure; appendix p 17).[1,2] Compared with $BA.4\text{-}5_{pp}$, neutralisation of $BA.4.6_{pp}$ and $BJ.1_{pp}$ was moderately reduced (up to 2·2 times lower), whereas neutralisation of $BA.2.75.2_{pp}$ and $BQ.1.1_{pp}$ was strongly reduced (up to 15·5 times lower; figure; appendix p 8). These results suggest that omicron sublineages BA.2.75.2 and BQ.1.1 possess high potential to evade neutralising antibodies elicited upon diverse immunisation histories. We observed that BA.1 and BA.2 breakthrough infections and BA.5 breakthrough infections in individuals who had been triple vaccinated induced higher omicron sublineage neutralisation (on average 3·7–8·5 times higher compared with triple vaccinated individuals without breakthrough infection) than monovalent or bivalent booster vaccination (on average 1·9–2·2 times higher compared with triple vaccinated individuals without breakthrough infection; appendix p 17). Furthermore, the highest omicron sublineage neutralisation was obtained for individuals who were triple vaccinated and also had a BA.1 or BA.2 breakthrough



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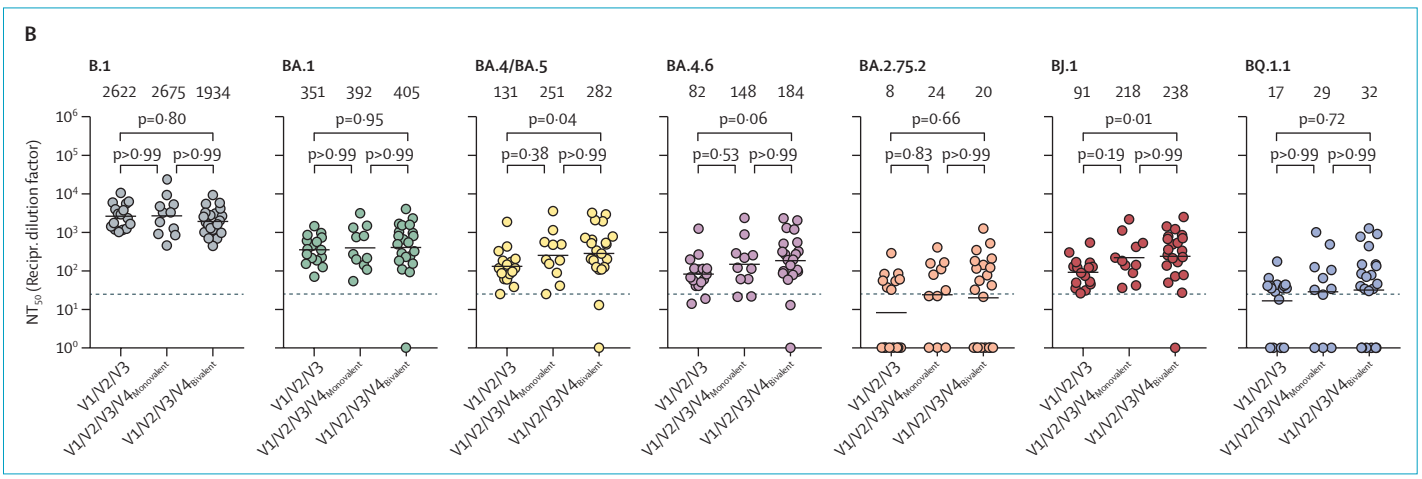

***Figure*: Omicron sublineage-specific neutralisation activity elicited upon triple vaccination, breakthrough infection, and monovalent or bivalent vaccine boosters.**
(A) Neutralising activity in patient plasma. Plasma samples were analysed from individuals who were (i) triple vaccinated (n=16), (ii) triple vaccinated with a BTI during the BA.1 and BA.2 wave in Germany (n=17), (iii) triple vaccinated with a BTI during the BA.5 wave in Germany (n=27), (iv) triple vaccinated that received the monovalent BNT162b2 (Pfizer–BioNTech) vaccine booster (n=11), (v) triple vaccinated with a subsequent monovalent BNT162b2 vaccine booster and a BTI during the BA.5 wave in Germany (n=8), (vi) triple vaccinated individuals with a subsequent bivalent BNT162b2 original and omicron BA.4-5 vaccine booster (n=21), (vii) or triple vaccinated with a BTI during the BA.1 and BA.2 wave in Germany and a subsequent bivalent BNT162b2 original and omicron BA.4-5 vaccine booster (n=11). Information on the methods and statistical analysis are reported in the appendix (pp 10–12). (B) Individual analysis of vaccinated cohorts without BTI. Information on the methods and statistical analysis are reported in the appendix (pp 10–12). Dashed lines indicate the lowest plasma dilution tested. Of note, all samples yielding an NT_{50} value of less than 6·25 (starting dilution of 1:25) or 12·5 (starting dilution of 1:50) were considered negative and were assigned an NT_{50} value of 1. BTI=breakthrough infection. NT_{50}=neutralising titre 50. Recipr. dilution factor=reciprocal dilution factor. V=vaccination.

infection plus a subsequent bivalent booster vaccination (on average 17·6 times higher compared with triple vaccinated individuals without breakthrough infection; appendix p 17). No notable differences were detected between the neutralisation activity induced upon monovalent or bivalent vaccine boosters (on average 2·0 times higher following monovalent vaccination and 2·1 times higher following bivalent vaccination compared with triple vaccinated individuals without breakthrough infection).

Collectively, our results show that the emerging omicron sublineages BQ.1.1 and particularly BA.2.75.2 efficiently evade neutralisation independent of the immunisation history. Although monovalent and bivalent vaccine boosters both induce high neutralising activity and increase neutralisation breadth, BA.2.75.2-specific and BQ.1.1-specific neutralisation activity remained relatively low. This finding is in keeping with the concept of immune imprinting by initial immunisation with vaccines targeting the ancestral SARS-CoV-2 B.1 lineage.[9,10] Furthermore, the observation that neutralisation of $BA.2.75.2_{pp}$ and $BQ.1.1_{pp}$ was most efficient in the cohort that had a breakthrough infection during the BA.1 and BA.2 wave and later received a bivalent booster vaccination, but was still less efficient than neutralisation of $B.1_{pp}$, implies that affinity maturation of antibodies and two-time stimulation with different omicron antigens might still not be sufficient to overcome immune imprinting. As a consequence, novel vaccination strategies have to be developed to overcome immune imprinting by ancestral SARS-CoV-2 antigen.

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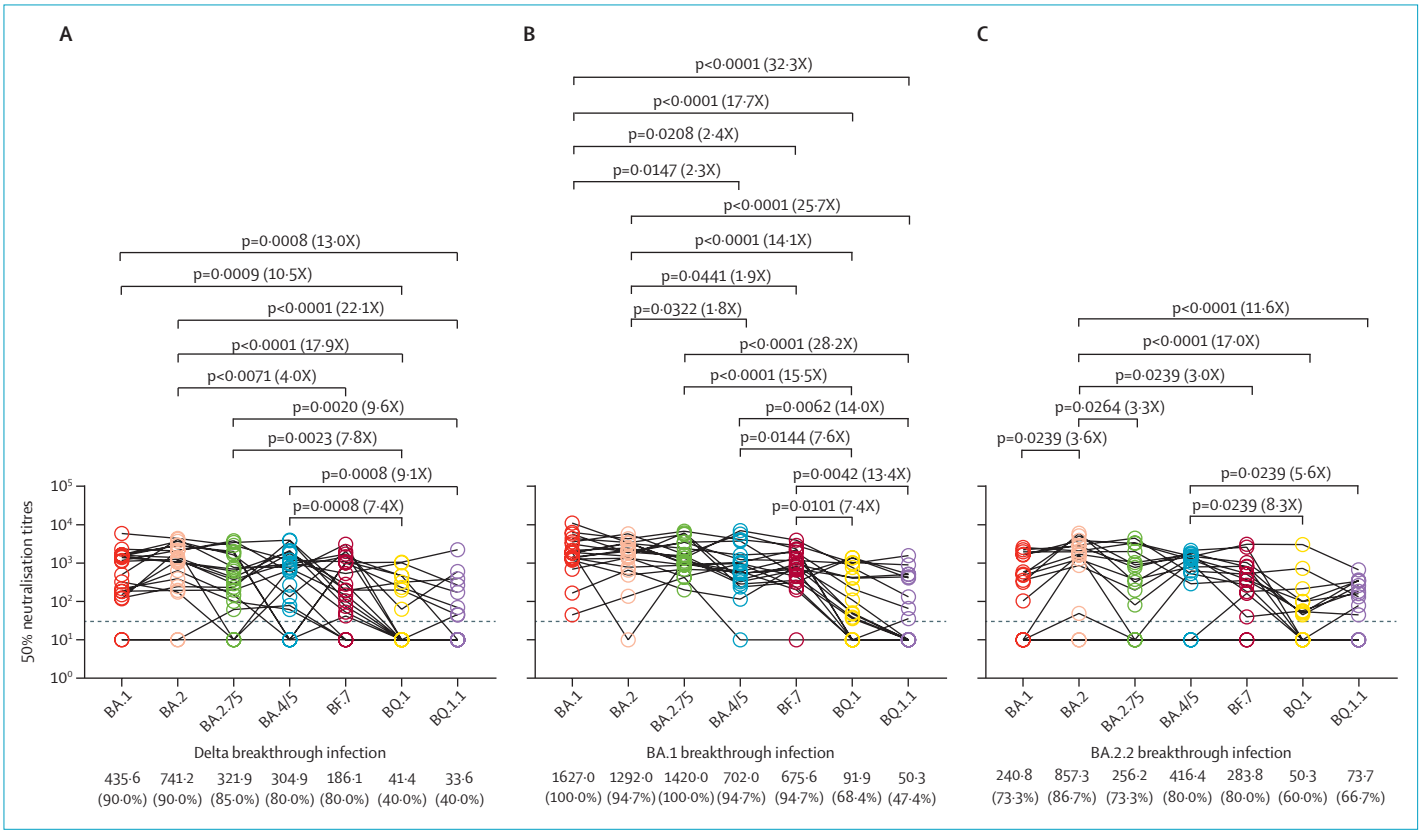
Omicron BQ.1 and BQ.1.1 escape neutralisation by omicron subvariant breakthrough infection

See Online for appendix

Although the SARS-CoV-2 omicron (BA.1 or B.1.1.529) subvariant BA.5 is dominant worldwide, several new subvariants, including BQ.1, BQ.1.1, BF.7, and BA.4.6, are appearing more frequently in sequenced SARS-CoV-2 infections,[1,2] raising the concern of additional escape neutralisation by antibodies elicited by vaccination or infection. We examined the degree of neutralising antibody escape by omicron subvariants BQ.1, BQ.1.1, BF.7, BA.1, BA.2, BA.2.75, and BA.4 and BA.5 (hereafter referred to as BA.4/5), using 50% neutralisation titres of six serum panels from individuals who had previously had delta BA.1 and BA.2.2 breakthrough infections and more recently had BA.5.1.2, BA.2.76, and BF.7 breakthrough infections (appendix p 2–4, 6).

We first examined the resistance of these omicron subvariants to serum samples from 20 individuals with delta breakthrough infections (appendix p 6). We observed a similar neutralisation activity between BQ.1 and BQ.1.1 but a significantly higher neutralisation resistance compared with BA.1, BA.2, BA.2.75, and BA.4/5; and only 40% of serum samples neutralised BQ.1 and BQ.1.1 (figure A). Specifically, BQ.1 showed a substantially lower neutralisation sensitivity compared with BA.1 (10·5 fold), BA.2 (17·9 fold), BA.2.75 (7·8 fold), and BA.4/5 (7·4 fold); and BQ1.1 showed a lower neutralisation sensitivity compared with BA.1 (13·0 fold), BA.2 (22·1 fold), BA.2.75 (9·6 fold), and BA.4/5 (9·1 fold) (figure A). The serum neutralisation activity was similar against BA.1, BA.2, BA.2.75, BA.4/5, and BF.7, and more than 80% of serum samples neutralised these subvariants (figure A). In addition, BF.7 showed a neutralisation sensitivity 4·0 fold lower than BA.2 (figure A).

Next, we examined the resistance of omicron subvariants to neutralisation by serum samples from individuals



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