Background

Early evidence suggests that the effectiveness of coronavirus (COVID-19) vaccines against mild disease with the Omicron variant is lower than effectiveness against the previous variant (Delta). However, after 3 doses, high levels of protection are seen against hospitalisation with the Omicron variant. Further doses of vaccine are being considered for the most vulnerable groups. In this updated analysis we estimate effectiveness of 3 doses of COVID-19 vaccines against mild and severe disease in adults aged 65 years or older.

Methods

A test negative case control design was used to estimate vaccine effectiveness (VE) against symptomatic COVID-19 with the Omicron variant compared to the Delta variant. Vaccination rates in PCR positive cases are compared to vaccination rates in those who test negative. Individuals who reported symptoms and tested in Pillar 2 (community testing) between 27 November and 31 December 2021 were included in the analysis. Cases were defined as the Omicron variant or Delta variant based on whole genome sequencing, genotyping, or S-gene target status on PCR testing. VE against symptomatic disease was estimated by period after receipt of a vaccine. Pillar 2 symptomatic confirmed cases were linked to the Emergency Care Dataset (ECDS) to identify admissions via emergency care 0 to 14 days after the positive test (excluding admissions due to injuries). Cox survival analysis was then used to estimate the risk of hospital admission by vaccination status. Due to small numbers all vaccine brands are considered together. Adjustments were made for age, gender, previous positive test, region, ethnicity, clinically extremely vulnerable status, risk group status, recent travel and period. To estimate VE against hospitalisation the odds ratios (OR) for symptomatic disease were multiplied by the hazard ratios (HR) for hospitalisation among symptomatic cases: $VE_{hospitalisation} = 1 - (OR_{symptomatic\ disease} \times HR_{hospitalisation})$.

Results

VE against symptomatic disease for cases aged 65 years or older is shown in Figure 1 for those who received a primary course of the ChAdOx1-S (AstraZeneca) (Figure 1a) and BNT162b2 (Pfizer) (Figure 1b) vaccine. In all periods, effectiveness was lower for Omicron compared to Delta. There was minimal or no effect against mild disease with the Omicron variant from 20 weeks after the second dose of either a ChAdOx1-S or BNT162b2 primary course. Among those who had received 2 doses of ChAdOx1-S, at 2 to 4 weeks after a booster dose (either BNT162b2 or mRNA-1273 (Moderna)), VE ranged from around 62% to 65%, dropping to 48% and 56% at 5-9 weeks for the BNT162b2 and mRNA-1273 booster, respectively. For the BNT162b2 booster, VE dropped further to 32% at 10+ weeks. Among those who had received 2 doses of BNT162b2 followed by a BNT162b2 booster, VE was 65% at 2 to 4 weeks post the booster, dropping to 49% at 5 to 9 weeks and 31% at 10+ weeks. For those who had received 2 doses of BNT162b2 followed by a mRNA-1273 booster, VE was 70% at 2 to 4 weeks post the booster, dropping to 57% at 5 to 9 weeks.

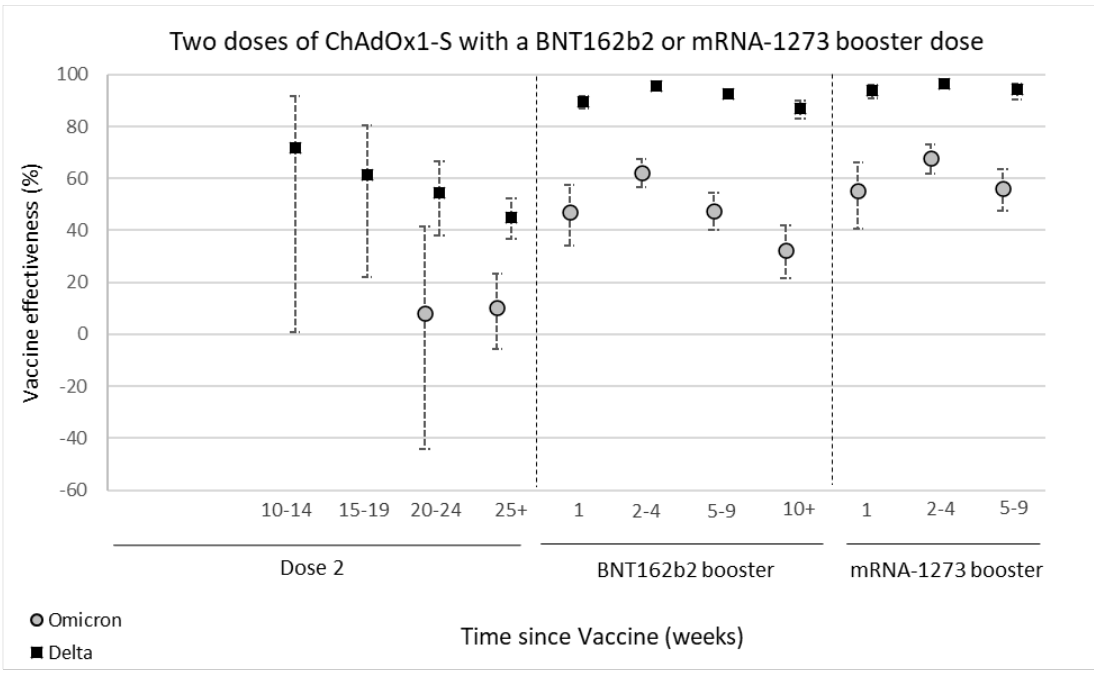
There were 98 hospitalisations after 3 doses included in the analysis. Results for hospitalisations for cases aged 65 years or older are shown in Table 1. At 2 to 9 weeks post the third dose, receiving 3 doses of a vaccine was associated with an 89% reduced risk of hospitalisation among symptomatic cases with the Omicron variant. This dropped slightly but remained high at an 85% reduced risk of hospitalisation at 10+ weeks post receipt the third dose. This dropped slightly but remained high at an 85% reduced risk of hospitalisation at 10+ weeks post receipt of the third dose. When combined with VE against symptomatic disease this was equivalent to VE against hospitalisation of 94% 2 to 9 weeks after the booster dose and 89% at 10 weeks post the booster dose in those aged 65 years or older.

These estimates suggest that VE against symptomatic disease with the Omicron variant is significantly lower than compared to the Delta variant and wanes rapidly in those aged 65 years or older. Nevertheless, protection against hospitalisation is much greater than that against symptomatic disease, in particular after a booster dose, where estimated VE against hospitalisation is around 90 to 95%.

These results should be interpreted with caution due to the low numbers and the possible biases related to differences in vaccine coverage and exposure to Omicron in different population groups.

Figure 1. Vaccine effectiveness for those aged 65 years or older against symptomatic diseases by period after dose 2 and a booster dose for Delta (black squares) and Omicron (grey circles) for (a) recipients of 2 doses of ChAdOx1-S (AstraZeneca) vaccine as the primary course and BNT162b2 (Pfizer) or mRNA-1273 (Moderna) as a booster; (b) recipients of 2 doses of BNT162b2 (Pfizer) vaccine as the primary course and BNT162b2 (Pfizer) or mRNA-1273 (Moderna) as a booster.

a)



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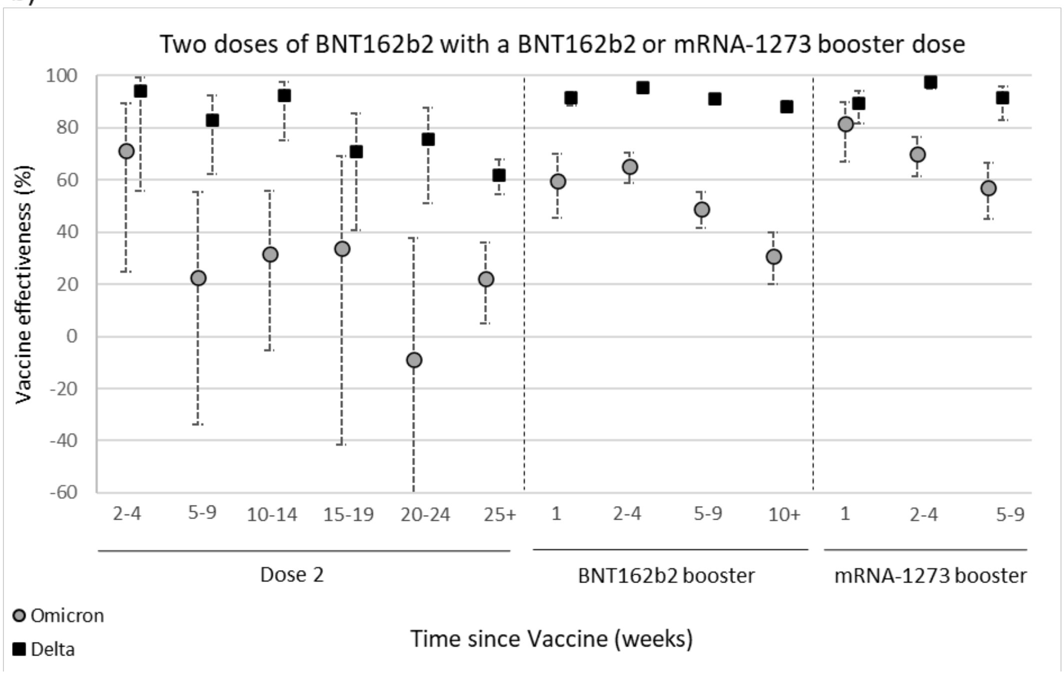

Table 1. Vaccine effectiveness against hospitalisation for Omicron (all vaccine brands combined). OR = odds ratio, HR = hazard ratio, VE = vaccine effectiveness, (CI=Confidence interval).

Interval after dose	OR against symptomatic disease (95% CI)	HR against hospitalisation (95% CI)	VE against hospitalisation (95% CI)
2 to 9 weeks	0.51 (0.43-0.6)	0.11 (0.06-0.21)	94% (89-97)
10+ weeks	0.72 (0.61-0.85)	0.15 (0.08-0.27)	89% (80-95)