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The relative effectiveness of three and four doses of COVID-19 vaccine in Victoria, Australia: A data linkage study

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ABSTRACT

Background: The Coronavirus Disease 2019 (COVID-19) pandemic led to extensive vaccination campaigns worldwide, including in Australia. Immunity waning and the emergence of new viral variants pose challenges to the effectiveness of vaccines. Our study aimed to assess the relative effectiveness (rVE) of 3 and 4 compared with 2 doses of COVID-19 vaccine. The study focuses on the Victorian population, a majority of whom had no prior exposure to the virus before vaccination.

Methods: We used routinely collected data for the state of Victoria, Australia, to assess rVE during an Omicron-dominant period, 1 June 2022 to 1 March 2023. Immunisation, notifications, hospitalisations and mortality data for residents aged 65 years and older were linked for analysis. Cox proportional hazard regression was used to estimate the rVE against COVID-19 hospitalisation or death, accounting for key confounders with vaccination as a time-varying covariate.

Results: In 1,070,113 people 65 years or older who had received their second dose, a third and fourth dose of a COVID-19 vaccine significantly reduced the hazard of hospitalisation or death compared to two doses. rVE was highest within two weeks from administration at 40 % (95 % CI: 0 % to 64 %) and 66 % (95 % CI: 60 % to 71 %) for a third and fourth dose, respectively. Additional protection conferred by third and fourth doses waned over time from administration.

Conclusions: Our findings underscore the need for additional vaccine doses and updated vaccine strategies. These findings have implications for public health advice and COVID-19 vaccine strategies. Further research and monitoring of vaccine effectiveness in real-world settings are warranted to inform ongoing pandemic response efforts.

1. Introduction

The emergence in 2019 of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) – the pathogen causing Coronavirus Disease 2019 (COVID-19) – led to the rapid development of COVID-19 vaccines. It is now well-established that the duration of protection afforded by COVID-19 vaccines is limited; thus ongoing post-marketing evaluation of these vaccines is needed to inform public health decision making. Antibodies induced by both SARS-CoV-2 infection [1] and vaccination [2] wane over time. Moreover, evolution and diversification of SARS-CoV-2 viruses has led to the emergence of a number of variants that have exhibited reduced sensitivity to vaccine-induced antibodies

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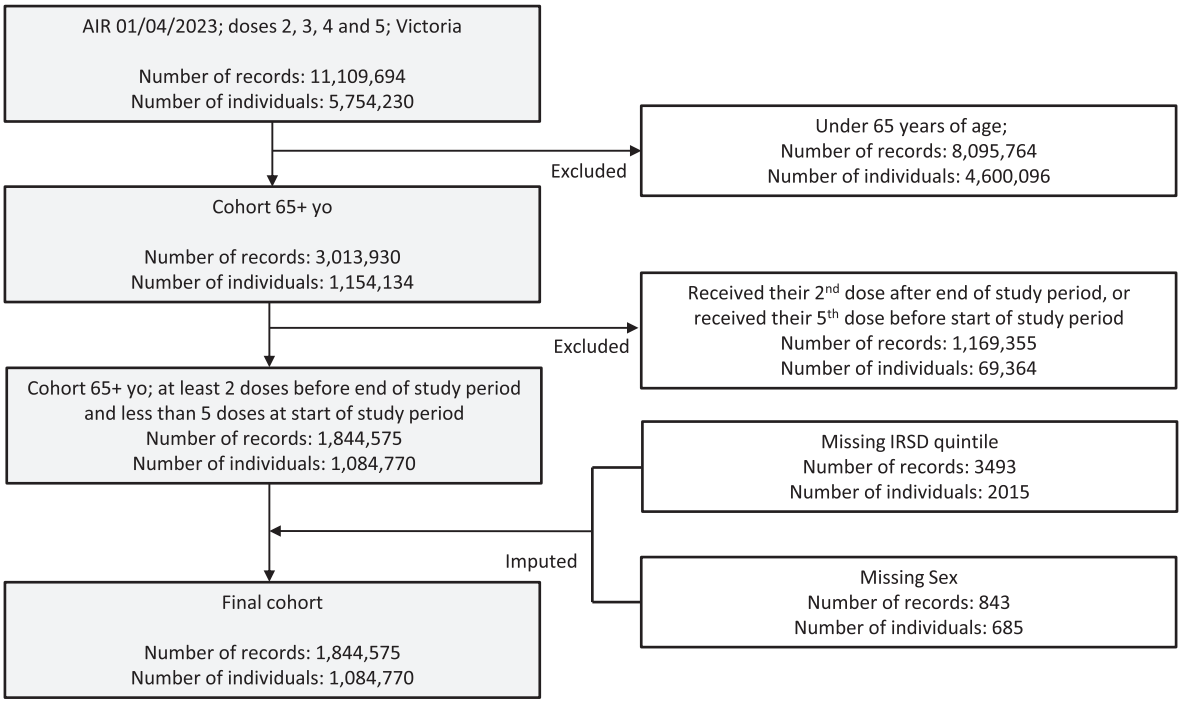

Fig. 1. STROBE diagram showing the cohort selection. Inclusion criteria was to be 65 years and over at the start of the study period, having received a second dose of a COVID-19 vaccine before the end of the study period, and having less than five doses at the start of the study period. Missing sex (n = 690) and IRSD (n = 1853) was imputed as per described in the methods section. Note that in AIR, each vaccination event creates a record, allowing individuals to contribute more than one record.

[3–5], and reduced vaccine effectiveness (VE) against infection and to a lesser degree, against severe disease [6–8].

The compounding effects of antibody waning and antigenic drift have required continued provision of subsequent doses of COVID-19 vaccines, and, more recently, the development of bivalent vaccines [9]. With each additional dose there is a period of improved immunity, followed by a period of waning effectiveness. For example, in Israel, initial gains from the third dose program were followed by observations of waning immunity soon after [10]. In Australia, Liu et al. reported a reduction in the effectiveness of a second dose as time from administration increased [11]. The UK Health Security Agency (UKHSA) found also that with each additional dose there was a temporary increase in protection against hospitalisation that waned over time [12].

Understanding patterns of waning immunity is key to supporting public health advice and COVID-19 vaccine rollout strategies, and these effects may differ in populations that were first exposed to the virus through infection (e.g. the UK), versus vaccination (e.g. Australia). Thus, we aimed to estimate the additional protection against hospitalisation or death provided by a third and fourth dose of a COVID-19 vaccine relative to two doses in the Victorian population, the majority of whom were infection-naïve prior to vaccine rollout, which occurred during an Omicron-dominant period.

2. Methods

2.1. Study population and data sources

We used routinely collected public health data for the state of Victoria, Australia, to assess the relative effectiveness of three and four doses of a COVID-19 vaccine versus two doses at preventing hospitalisation or death during an Omicron (BA.2 and BA.4/BA.5) dominant period. Victoria is Australia's second largest state, with a population of 6.5 million, a majority of whom (4.9 million) reside in Melbourne [13]. The eligible population was all Victorian residents registered with the Australian Immunisation Register (AIR), aged 65 years and older on 1 June 2022 who had at least two doses and less than five doses on this date. The study was restricted to adults aged 65 years and older to avoid the influence of differential vaccination eligibility across age groups over time, and because people in this age group are at highest risk of severe COVID-19 outcomes [14]. Reporting all COVID-19 vaccine doses to the AIR is mandatory [15]. These data were used to obtain demographic information (age, sex, residential address), and date and brand of vaccination for each dose received.

Details of COVID-19 hospitalisations and deaths are recorded in the Victorian Healthcare Associated Infection Surveillance System (VICNISS) [16] and the Victorian Death Index (VDI) [17], respectively. A hospital admission was considered COVID-19 related if the patient had a positive SARS-CoV-2 test before admission and was infectious at the time of admission or tested positive during their hospital stay. A death is coded as a COVID-19 death if it occurred within 35 days of a COVID-19 diagnosis and/or if COVID-19 is listed as a cause of death on the death certificate. VICNISS and VDI data are routinely linked to COVID-19 case notifications data held in the state's COVID-19 surveillance database, Transmission and Response Epidemiology Victoria (TREVI), for ongoing monitoring of severe COVID-19 outcomes. Linkage between the AIR and TREVI was conducted using a multistage deterministic approach, using combinations of first name, surname, date of birth, and address as the linkage keys.

Hospitalisations occurring before the study period, which may indicate potential comorbidities and chronic conditions, were retrieved from the Victoria Admitted Episodes Database (VAED) – an administrative dataset comprising demographic, administrative, and limited clinical data for all patients admitted to public and private Victorian health services. Linkage between AIR and VAED was performed using a single-stage deterministic approach, using name, surname, and date of birth as linkage keys. Residential address (statistical area 1 [18] was used to approximate the socioeconomic position of individuals in the AIR using the index of relative social disadvantage (IRSD) derived from 2016 Australian Census data [19]. More disadvantaged areas have a lower IRSD score. Missing sex and IRSD quintile records were imputed by randomly sampling values from the observed levels of the respective variables. Specifically, for individuals with missing sex data, we

Table 1
Characteristics of the study population at the start of the study period.

	Dose 2 N = 111,960	Dose 3 N = 591,920	Dose 4 N = 364,732	Overall N = 1,068,612
Age group				
65–69	34,124 (30 %)	153,841 (26 %)	65,683 (18 %)	253,648 (24 %)
70–74	30,353 (27 %)	154,330 (26 %)	94,268 (26 %)	278,951 (26 %)
75–79	20,218 (18 %)	118,383 (20 %)	88,261 (24 %)	226,862 (21 %)
80+	27,265 (24 %)	165,366 (28 %)	116,520 (32 %)	309,151 (29 %)
IRSD[1] quintile				
1	29,315 (26 %)	129,812 (22 %)	61,105 (17 %)	220,232 (21 %)
2	24,519 (22 %)	128,293 (22 %)	69,289 (19 %)	222,101 (21 %)
3	22,806 (20 %)	121,723 (21 %)	72,445 (20 %)	216,974 (20 %)
4	20,121 (18 %)	112,557 (19 %)	75,746 (21 %)	208,424 (20 %)
5	15,199 (14 %)	99,535 (17 %)	86,147 (24 %)	200,881 (19 %)
≥2 hospital admissions[2]	49,168 (44 %)	314,861 (53 %)	224,870 (62 %)	588,899 (55 %)
Sex				
Female	60,772 (54 %)	316,865 (54 %)	195,552 (54 %)	573,189 (54 %)
Male	51,188 (46 %)	275,055 (46 %)	169,180 (46 %)	495,423 (46 %)
Vaccine brand				
Vaxzevria (ChAdOx1 nCoV-19)	69,275 (62 %)	9,572 (1.6 %)	1,257 (0.3 %)	80,104 (7.5 %)
BioNTech (BNT162b2)	32,775 (29 %)	477,019 (81 %)	304,276 (83 %)	814,070 (76 %)
Spikevax (mRNA-1273)	8,162 (7.3 %)	102,783 (17 %)	57,413 (16 %)	168,358 (16 %)
Other	1,748 (1.6 %)	2,546 (0.4 %)	1,786 (0.5 %)	6,080 (0.6 %)

[1] Index of Relative Socioeconomic Disadvantage. A higher quintile indicates less disadvantage.
[2] In five-year period up to 1 June 2022.

randomly assigned a sex (male or female) based on the observed sex distribution in the dataset. Similarly, we assigned IRSD quintile values (1 to 5) to those with missing IRSD data by randomly sampling from the observed IRSD quintile distribution among individuals with available data. This approach was considered appropriate as the missingness was random and not systematically related to other variables in the dataset. The method of random sampling for imputation preserves the overall distribution of the variables, thus maintaining the integrity of the dataset. Additionally, an assessment conducted on the exclusion of individuals with missing records found that the difference in estimates was negligible. This negligible difference is attributable to the very small proportion of subjects with missing records relative to the overall study population.

2.2. Study period

The study period was 1 June 2022 to 1 March 2023 and was chosen to start two months after the rollout of fourth doses for people aged 65 years and older (and other risk groups [20] and extended to six weeks prior to the data extraction date to account for the expected lag in reporting of COVID-19 deaths. During the study period, Victoria experienced three waves of SARS-CoV-2 transmission dominated by Omicron BA.2 between April and July, BA.4 and BA.5 between July and November, and polyclonal variants including BA.2.75, BQ.1 and XBB between December 2022 and March 2023 (see Supplementary Fig. 1).

During the study period, a fourth dose was approved in March 2022 for very high-risk adults [21]. This was extended to high-risk adults in May 2022 [21], then made available for all adults > 30 years in July 2022 [22]. By December 2022 over 75 % of Australians aged 30 years and older had received their third dose of vaccine, while 33 % had received a fourth dose [23]. Fifth doses became available to severely immunocompromised adults in late 2022 and in February 2023 were recommended to all at risk adults aged 18 years and older whose last vaccine was > 6 months prior [24]. Available vaccines included Comirnaty (BNT162b2; Pfizer/BioNTech), Vaxzevria (ChAdOx1 nCoV-19; AstraZeneca), and Spikevax (mRNA-1273; Moderna), and later Nuvaxovid (Novavax), Spikevax Biv BA.1 (Moderna) and Comirnaty Biv BA.1 (Pfizer).

2.3. Estimation of relative vaccine effectiveness (rVE)

We used Cox proportional hazards regression models to estimate the hazard of severe COVID-19-related outcomes (i.e. hospitalisation or death) in subjects with third and fourth doses of a COVID-19 vaccine relative to two doses. Relative VE (rVE) was calculated as (1–aHR) * 100 %. Observation time started on 1 June 2022 or the date of administration of a second dose, whichever occurred later. Observation time ended on the date of COVID-19 hospitalisation or death, or censored to the earliest of date of receipt of a fifth dose or the census date, 1 March 2023. Vaccination status was modelled as a time-varying covariate with four levels according to time since vaccination for dose 3 and dose 4: 0–2 weeks; 3 to 16 weeks; 17 to 24 weeks; and 25 weeks and over. These intervals were chosen to represent meaningful medium- and long-term phases, aligned with the observed patterns of waning immunity reported in the literature. The reference category was 2 doses, regardless of time from administration. Effectiveness of dose 4 was also estimated relative to 3 doses between 3 and 16 weeks from administration. Other variables were included as fixed covariates and included age [5–38], sex (male/female), IRSD quintile, and history of hospitalisation (≥2 / ≤1 previous admissions in previous 5 years). All analysis were performed using R Software version 4.1.2 [25].

2.4. Ethics

Approval from a Human Research Ethics Committee was not applicable as this analysis was conducted by the Victorian Department of Health as part of its public health function pursuant to the Public Health and Wellbeing Act 2008 (Vic) [26] and the Health Records Act 2001 (Vic) [27]. Permission for data linkage from relevant data custodians in the Victorian and Australian Government was obtained.

3. Results

There were 1,070,113 individuals 65 years of age and over registered on the AIR who received their second dose before the end of the study period and had less than five doses at the start of the study period. These individuals were linked to 11,130 events of hospitalisation and/or death due to COVID-19. Of these events, 9,265 were hospitalisations, and 1,865 were deaths. It should be noted that in instances where death occurred on the same day as hospital admission, the event was classified as a death. Sex and IRSD quintile were imputed for 690 (0.06 %) and 1853 (0.17 %) subjects (see STROBE flowchart, Fig. 1).

Table 1 shows the demographic characteristics and vaccination status of the study population at the start of the follow up period. The median age of the study population was 75 years, and there was a total of 779,038 person years of follow up. At the start of the study period, 10 % (n = 111,960) had received two doses of vaccine, 55 % (n = 591,920) had received three doses and 34 % (n = 364,732) had received 4 doses of vaccine. At the end of the study period, 2 dose vaccine coverage was 9 % (91,880), three dose coverage was 24 % (n = 233,291) and 4 dose coverage was 67 % (n = 660,741). The median time from administration at the start of the study period for dose 2 was 157 days, with 90 % of the

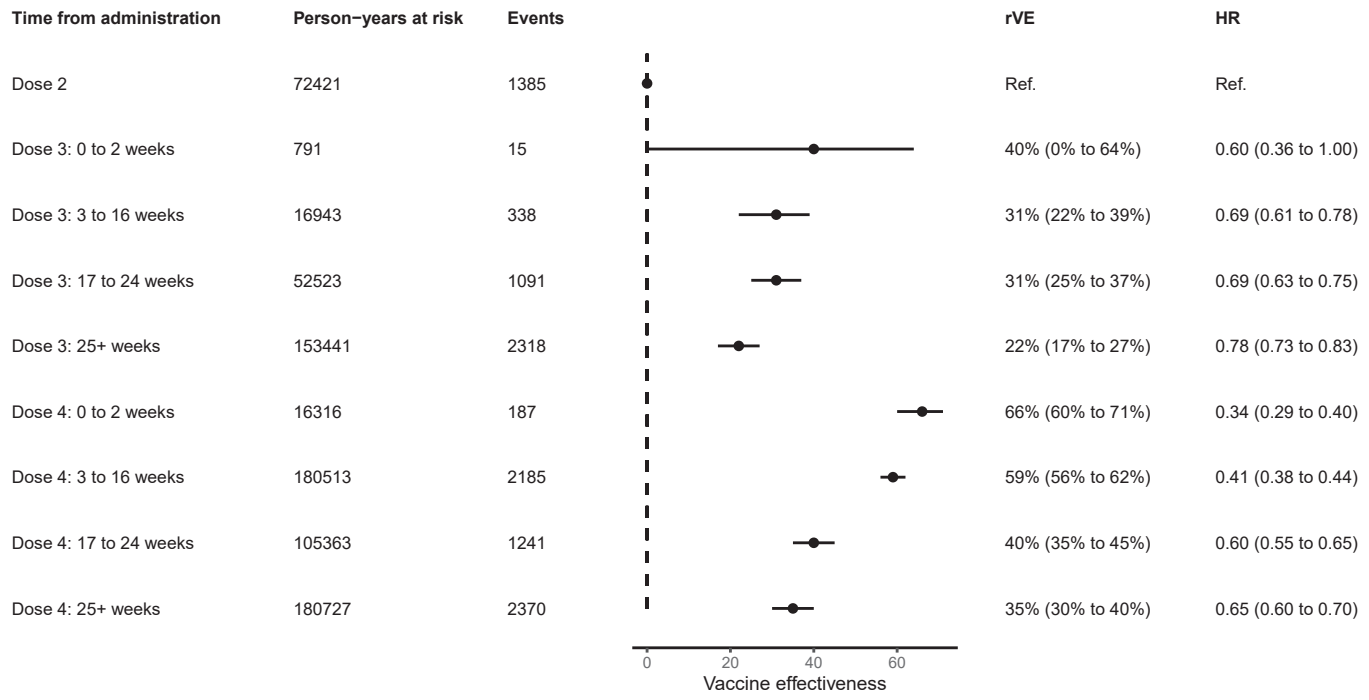

Fig. 2. COVID-19 relative vaccine effectiveness in preventing severe COVID-19 outcomes (i.e., hospitalisation or death) relative to a second dose. Adjusted for age, sex socioeconomic status and recent history of hospitalisation. Victoria, 1 June 2022 to 1 March 2023.

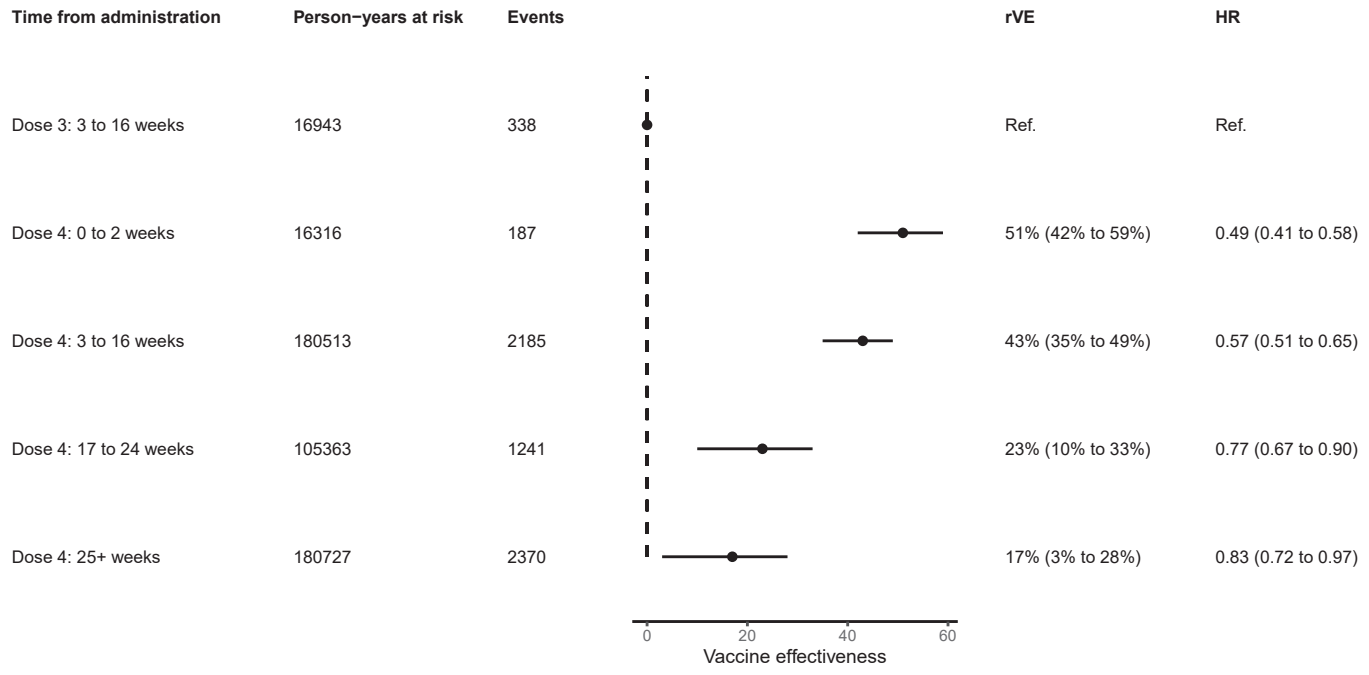

Fig. 3. COVID-19 relative vaccine effectiveness in preventing severe COVID-19 outcomes (i.e., hospitalisation/death) relative to a third dose administered from 3 to 16 weeks. Adjusted for age, sex socioeconomic status and recent history of hospitalisation. Victoria, 1 June 2022 to 1 March 2023.

distribution of time from administration between 127 days and 224 days.

Comirnaty (BNT162b2; Pfizer/BioNTech), Vaxzevria (ChAdOx1 nCoV-19; AstraZeneca) vaccines accounted for a majority of second doses in the study population. For third and subsequent doses, Comirnaty was the most common vaccine. The distribution of study subjects across IRSD levels was relatively homogeneous. Women were slightly over-represented for all vaccine doses. Around half of study subjects

with two doses at the start of the study period had been hospitalised two or more times within the five years prior to the start of the study period. This number went up to two thirds for those with four doses at the start of the study period.

Fig. 2 shows the number of events (i.e., hospitalisation or death), the person-years at risk and the relative vaccine effectiveness (rVE) for the different vaccine exposure groups assessed. Results are adjusted for age, sex, IRSD and recent history of hospitalisation. The hazard of severe outcomes was significantly lower in individuals that had received a third or fourth dose of a COVID-19 vaccine relative to those that had had only 2 doses. Protection against severe disease was highest 0 to 2 weeks for both dose 3 and 4, and progressively waned as time from administration passed. Protection reached relatively low levels in individuals for whom 24 weeks or more had passed since the most recent dose was administered (Fig. 2).

When the effectiveness of dose 4 was assessed using as reference category dose 3 between 3 and 16 weeks from administration, regression model coefficients followed a similar pattern to those obtained using dose 2 as reference category (Fig. 3). Effectiveness of a fourth dose peaked early after administration and subsequently waned as time from administration passed. However, the absolute value of coefficients was lower than when using dose 2 as the reference category. For example, whereas the maximum VE using dose 2 as reference category was within 2 weeks from administration at 66 %, when the reference category was dose 3 this value was 51 %.

4. Discussion

In this study, we found that in a period during which the Omicron variant (including subvariants BA.2 and BA.4/5) was dominant, a third and fourth dose of vaccine provided additional protection against hospitalisation or death when compared to two doses in people >= 65 years. There was evidence that protection against severe disease waned over several months. The peak of protection relative to time from administration was observed within the first two weeks of receipt of each dose. The highest level of protection was observed within 2 weeks of receiving dose 4, with a relative VE compared to a second dose of 66 % (95 % CI: 60 % to 71 %). The highest estimate for dose 3 was also within 2 weeks of receipt, but confidence intervals were wide due to the low number of observations in this category.

Our findings are consistent with a study from New South Wales which found that VE for a third dose relative to a second dose (within 90 days of administration) was 65 % [11]. UKHSA vaccine surveillance reports have estimated the vaccine effectiveness (compared with unvaccinated individuals) at over 85 % depending on definition, but with some evidence of waning to levels similar to 2 dose effectiveness after > 3–4 months [12]. A Swedish study found higher VE against severe disease, with similar VE against delta and omicron [28]. A third dose was also found to provide additional protection against hospitalisation or death in other studies [29–31].

Our analysis used data from over one million individuals and linkage to multiple databases allowed control for health and demographic confounders. However, we were unable to control for indication for vaccination—based on residential aged care status, presence of severely immunocompromising conditions or occupation group—which may have confounded the analyses of waning protection because those considered at higher risk became eligible for third and fourth doses earlier than other groups. We were also unable to distinguish third primary series doses in immunocompromised people from booster doses. Since vaccination uptake tends to increase during periods of relatively high COVID-19 incidence, and higher-risk groups are more likely to be vaccinated earlier, it is possible that a disproportionately high number of data points close to the time of administration originated from high-risk groups, potentially exaggerating the waning effect. Adjusting for history of hospitalisation was unlikely to fully account for the confounding effect of conditions that are associated with vaccination and severe COVID-19 outcomes but do not result in hospitalisation, nor modified schedules for particular patient groups.

Misclassification of the exposure and the outcome from inaccuracies in data linkage are also possible [32]. We anticipate this misclassification bias to be non-differential, but note that our use of multiple vaccination categories means the bias produced is not guaranteed to be toward the null [33]. Moreover, linkage errors may be more likely for certain age groups, and the direction of the bias caused by these dependent errors is difficult to predict [34]. Our study also did not adjust for previous COVID-19 infection, which may modify the risk of severe disease outcomes [35] and confound VE estimates [8,36]. Case ascertainment was known to be low and variable over the study period, so any attempt to adjust for prior infection would have been imperfect. Furthermore, the misclassification of previous infection is likely to be imbalanced between different severe disease risk profiles, with groups at a higher risk of severe disease being more likely to report infection, as they are more frequently in contact with health services (either primary or secondary care), which increases the chances of a case being reported.

Our results support the advice from the Australian Technical Advisory Group on Immunisation (ATAGI) made on 8 February 2023 which advised adults 65 years and over or people aged 18 and over with comorbidities to be revaccinated if they had not been infected or vaccinated with the last 6 months [24]. Our data suggest that a shorter time period (<16 weeks) between vaccinations could be considered, consistent with US recommendations of 4 months [37] and the UK and Israel, which permit revaccination among older adults every 3 months [38]. The protection that additional doses confer against severe disease makes them a valuable public health tool to protect the most vulnerable populations. Evidence on the decline over time of this protection suggests periodical revaccination is required to sustain high levels of protection.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Sheena Sullivan reports a relationship with Pfizer Inc that includes: consulting or advisory. Sheena Sullivan reports a relationship with Moderna Inc that includes: consulting or advisory. Sheena Sullivan reports a relationship with Seqirus Australia Pty Ltd that includes: consulting or advisory.

Data availability

The authors do not have permission to share data.

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Data availability statement

The authors do not have permission to share these data. However, data can be requested through the Centre for Victorian Data Linkage, https://www.health.vic.gov.au/reporting-planning-data/applying-for-data-linkage.

R scripts used to construct the cohort and estimate vaccine effectiveness can be made available upon request to José Canevari jtcanevari@gmail.com.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2023.11.047.

References

[1] Ibarrondo FJ, Fulcher JA, Goodman-Meza D, Elliott J, Hofmann C, Hausner MA, et al. Rapid decay of anti-SARS-CoV-2 antibodies in persons with mild Covid-19. N Engl J Med 2020;383(11):1085–7.

[2] Perez-Alos L, Armenteros JJA, Madsen JR, Hansen CB, Jarlhelt I, Hamm SR, et al. Modeling of waning immunity after SARS-CoV-2 vaccination and influencing factors. Nat Commun 2022;13(1):1614.

[3] World Health Organization. Statement on the update of WHO's working definitions and tracking system for SARS-CoV-2 variants of concern and variants of interest. Geneva: World Health Organization; 2023 [Available from: https://www.who.int/news/item/16-03-2023-statement-on-the-update-of-who-s-working-definitions-and-tracking-system-for-sars-cov-2-variants-of-concern-and-variants-of-interest].

[4] Davis C, Logan N, Tyson G, Orton R, Harvey WT, Perkins JS, et al. Reduced neutralisation of the Delta (B.1.617.2) SARS-CoV-2 variant of concern following vaccination. PLoS Pathog 2021;17(12):e1010022.

[5] Planas D, Veyer D, Baidaliuk A, Staropoli I, Guivel-Benhassine F, Rajah MM, et al. Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization. Nature 2021;596(7871):276–80.

[6] Bernal JL, Andrews N, Gower C, Gallagher E, Simmons R, Thelwall S, et al. Effectiveness of COVID-19 vaccines against the B.1.617.2 variant. New Engl J Med 2021;385:585–94. https://doi.org/10.1056/NEJMoa2108891.

[7] Tenforde MW, Self WH, Zhu Y, Naioti EA, Gaglani M, Ginde AA, et al. Protection of messenger RNA vaccines against hospitalized coronavirus disease 2019 in adults over the first year following authorization in the United States. Clin Infect Dis 2023;76(3):e460–8.

[8] Tsang TK, Sullivan SG, Huang X, Wang C, Wang Y, Nealon J, et al. Prior infections and effectiveness of SARS-CoV-2 vaccine in test-negative study: a systematic review and meta-analysis. medRxiv 2022. 2022.11.03.22281925.

[9] Offit PA. Bivalent Covid-19 vaccines – a cautionary tale. N Engl J Med 2023;388(6):481–3.

[10] Bar-On YM, Goldberg Y, Mandel M, Bodenheimer O, Freedman L, Kalkstein N, et al. Protection of BNT162b2 vaccine booster against Covid-19 in Israel. N Engl J Med 2021;385(15):1393–400.

[11] Liu B, Gidding H, Stepien S, Cretikos M, Macartney K. Relative effectiveness of COVID-19 vaccination with 3 compared to 2 doses against SARS-CoV-2 B.1.1.529 (Omicron) among an Australian population with low prior rates of SARS-CoV-2 infection. Vaccine 2022;40(43):6288–94.

[12] UK Health Security Agency. COVID-19 vaccine surveillance report - Week 24; 2022 [Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1083443/Vaccine-surveillance-report-week-24.pdf].

[13] Australian Bureau of Statistics (ABS). Greater Melbourne 2021 Census All persons QuickStats Canberra: ABS; 2022 [updated 2022; cited 2022 18 October]. Available from: https://www.abs.gov.au/census/find-census-data/quickstats/2021/2GMEL.

[14] Pijls BG, Jolani S, Atherley A, Derckx RT, Dijkstra JIR, Franssen GHL, et al. Demographic risk factors for COVID-19 infection, severity, ICU admission and death: a meta-analysis of 59 studies. BMJ Open 2021;11(1):e044640.

[15] Australian Government. Australian Immunisation Register Canberra: Australian Government; 2023 [Available from: https://www.servicesaustralia.gov.au/australian-immunisation-register].

[16] Curtis SJ, Cutcher Z, Brett JA, Burrell S, Richards MJ, Hennessy D, et al. An evaluation of enhanced surveillance of hospitalised COVID-19 patients to inform the public health response in Victoria. Commun Dis Intell 2018;2020:44.

[17] Victorian Department of Health. Datasets available in the Centre for Victorian Data Linkage's Integrated Data Resource Melbourne: Government of Victoria; 2023 [Available from: https://www.health.vic.gov.au/sites/default/files/migrated/files/collections/factsheets/c/cvdl-datasets-available-in-integrated-data-resource.docx].

[18] Australian Bureau of Statistics. Statistical Area Level 1 Canberra: Australian Bureau of Statistics; 2021 [Available from: https://www.abs.gov.au/statistics/standards/australian-statistical-geography-standard-asgs-edition-3/jul2021-jun2026/main-structure-and-greater-capital-city-statistical-areas/statistical-area-level-1].

[19] Australian Bureau of Statistics. Socio-Economic Advantage and Disadvantage. In: Australian Bureau of Statistics, editor. Canberra: Government of Australia; 2018.

[20] ABC News. Fourth COVID-19 vaccine shots are available, but only for certain groups of people. Here's who is eligible: Australian Broadcasting Corporation; 2022 [Available from: https://www.abc.net.au/news/2022-04-04/covid-19-vaccine-fourth-dose-booster-shot-australian-eligible/100963788].

[21] Australian Government Department of Health. Expanded ATAGI recommendations on winter COVID-19 booster doses for people at increased risk of severe COVID-19 2022 [updated 25 May 2022 Available from: https://www.health.gov.au/news/expanded-atagi-recommendations-on-winter-covid-19-booster-doses-for-people-at-increased-risk-of-severe-covid-19].

[22] Australian Government Department of Health and Aged Care. Expanded eligibility for fourth COVID-19 vaccine dose 2022 [updated 7 July 2022 Available from: https://www.health.gov.au/ministers/the-hon-mark-butler-mp/media/expanded-eligibility-for-fourth-covid-19-vaccine-dose].

[23] Operation COVID Shield. COVID-19 Vaccine Roll-out update - 22 December 2022 Canberra: Government of Australia; 2022 [updated 22 Dec 2022. Available from: https://www.health.gov.au/sites/default/files/2022-12/covid-19-vaccine-rollout-update-22-december-2022.pdf].

[24] Australian Government. ATAGI 2023 booster advice Canberra: Australian Government; 2023 [updated 8 Feb 2023. Available from: https://www.health.gov.au/news/atagi-2023-booster-advice].

[25] Team RC. R: A language and environment for statistical computing. R Foundation for Statistical Computing. Vienna, Austria. URL: https://www.R-project.org/.4.2.3ed2022.

[26] Government of Victoria. Public Health and Wellbeing Act 2008 (Act Number 46/2008). Authorised version incorporating amendments as at 30 Aug 2022 Melbourne: Government of Victoria; 2023 [Available from: https://www.legislation.vic.gov.au/in-force/acts/public-health-and-wellbeing-act-2008/061.

[27] Government of Victoria. Health Records Act 2001 Melbourne: Department of Health; 2023 [Available from: https://www.health.vic.gov.au/legislation/health-records-act].

[28] Kahn F, Bonander C, Moghaddassi M, Rasmussen M, Malmqvist U, Inghammar M, et al. Risk of severe COVID-19 from the Delta and Omicron variants in relation to vaccination status, sex, age and comorbidities - surveillance results from southern Sweden, July 2021 to January 2022. Euro Surveill 2022;27(9):2200121.

[29] Buchan SA, Chung H, Brown KA, Austin PC, Fell DB, Gubbay JB, et al. Estimated effectiveness of COVID-19 vaccines against omicron or delta symptomatic infection and severe outcomes. JAMANetw Open 2022;5(9):e2232760.

[30] Nyberg T, Ferguson NM, Nash SG, Webster HH, Flaxman S, Andrews N, et al. Comparative analysis of the risks of hospitalisation and death associated with SARS-CoV-2 omicron (B.1.1.529) and delta (B.1.617.2) variants in England: a cohort study. Lancet 2022;399(10332):1303–12.

[31] Thompson MG, Natarajan K, Irving SA, Rowley EA, Griggs EP, Gaglani M, et al. Effectiveness of a third dose of mRNA vaccines against COVID-19-associated emergency department and urgent care encounters and hospitalizations among adults during periods of delta and omicron variant predominance - VISION Network, 10 States, August 2021-January 2022. MMWR Morb Mortal Wkly Rep 2022;71(4):139–45.

[32] Doidge JC, Harron KL. Reflections on modern methods: linkage error bias. Int J Epidemiol 2019;48(6):2050–60.

[33] Greenland S, Gustafson P. Accounting for independent nondifferential misclassification does not increase certainty that an observed association is in the correct direction. Am J Epidemiol 2006;164(1):63–8.

[34] Kristensen P. Bias from nondifferential but dependent misclassification of exposure and outcome. Epidemiology 1992;3(3):210–5.

[35] Reynolds CJ, Pade C, Gibbons JM, Butler DK, Otter AD, Menacho K, et al. Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose. Science 2021;372(6549):1418–23. https://doi.org/10.1126/science.abh1282.

[36] Monge S, Pastor-Barriuso R, Hernán MA. The imprinting effect of covid-19 vaccines: an expected selection bias in observational studies. BMJ 2023;381:e074404.

[37] Food and Drug Administration. Coronavirus (COVID-19) Update: FDA Authorizes Changes to Simplify Use of Bivalent mRNA COVID-19 Vaccines Washington DC: Government of the United States of America; 2023 [Available from: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-changes-simplify-use-bivalent-mrna-covid-19-vaccines].

[38] Ministry of Health. Vaccines Tel Aviv: Government of Israel; 2023 [Available from: https://corona.health.gov.il/en/vaccine-for-covid/].