Effectiveness of COVID-19 vaccines over 13 months covering the period of the emergence of the Omicron variant in the Swedish population

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Abstract

Background: True population-based estimates of vaccine effectiveness (VE) against COVID-19 remain scarce, and VE against the SARS-CoV-2 Omicron variant is not well characterized. In this study, we estimated real-world VE against infection, hospitalization, and more severe outcomes (ICU admission and death) up to 13 months after vaccination among individuals without prior COVID-19. VE before and after the emergence of the Omicron was investigated.

Methods: We used data from the entire Swedish population above age 12 (n=9,153,456) from multiple national registers. Cox regression with time-varying exposure was used to estimate weekly/monthly VE against COVID-19 outcomes from December 27, 2020, to January 31, 2022. The analyses were stratified by age, sex, and vaccine type (BNT162b2, mRNA-1273 and AZD1222).

Findings: Two vaccine doses showed long-lasting good protection against infection before Omicron (VE were above 85% for all time intervals), but less protection against Omicron infection (dropped to 43% by week four and no protection by week 14). Similarly, VE against hospitalization was high and stable before Omicron, but showed clear waning during the Omicron period, although VE estimates were substantially higher (above 80% to week 25, dropping to 40% by week 40) than against infection. For severe COVID-19 outcomes, higher VE were observed during the entire follow-up period. The mRNA vaccines showed better VE against infection than AZD1222 among individuals above age 65 but similar high VE against hospitalization. The vaccines were generally equally effective regardless of age and sex.

Interpretation: Two vaccine doses offered long-lasting protection against infection before Omicron but waned rapidly during Omicron period. Regarding severe COVID-19 outcomes, good long-term protection during a 13-month follow-up was observed.

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Keywords: SARS-CoV-2; COVID-19 vaccines; vaccine effectiveness; Omicron

Research in context

Evidence before this study

The study was proposed in November 2021 and a study protocol was drafted on 1 December 2021. We searched regularly in PubMed and Google Scholar for the entire duration of designing and performing the study between Nov 2021 and August 2022. We used different search terms, e.g., 'COVID-19 vaccine effectiveness', 'COVID vaccine efficacy', 'COVID vaccine real-world effectiveness' in the databases. We also reviewed pre-print studies but considered them of lower quality than published studies and in the end, we did not include them as references in the manuscript. Therefore, only studies that appeared in PubMed and/or Google Scholar during the search period were included and discussed. We mainly focused on the observational studies of real-world effectiveness, although phase-3 trials were also reviewed since they provide the vaccine efficacy background. We did not limit to publications in English, but only abstracts for publications in non-English language were reviewed. The non-English publications we reviewed were also eventually excluded in the comparison and discussion since information, especially the details in statistics, were not sufficient.

The randomized clinical trials showed better vaccine protection than the ones observed from real-world setting. There were considerable differences in the duration of protection and its magnitude reported in different studies, and there was especially limited and inconsistent evidence on long-lasting protection. A lower vaccine effectiveness against Omicron was suggested and described in relatively few studies but data are still inconsistent and limited, and data from Sweden is still extremely limited (one regional study).

Added value of this study

This study showed two doses of vaccine had progressively waning effectiveness against infection in a 13-month follow-up period. The waning effect was more pronounced after the emergence of Omicron, which dropped to 43% by week four and no protection by week 14 after the second dose. The protection against hospitalization and more severe COVID-19 (ICU admission and death) was reassuring, both in the pre-Omicron period and Omicron period. Our study was performed in the whole Swedish population, which means our findings not subject to selection bias as such. Additionally, we used shorter time-intervals than previous reports in our analysis in order to capture potential rapid changes in the pattern of effectiveness after each dose. In all, our findings add more detailed long-term data on time-varying vaccine effectiveness against COVID-19, as observed in a complete general Swedish population, especially the data on effectiveness against Omicron infection, which has not previously been shown in published Swedish studies.

Implications of all the available evidence

Although a booster dose (3rd or even 4th dose) has been introduced in Sweden, many persons appear to still consider a basic vaccination sufficient protection, and the coverage of people with 3 or more doses is still not ideal. Our study showed that even with two doses, the vaccine effectiveness against Omicron infection was poor and only short-lasting. Similar results were shown in other studies in UK, Qatar and Malaysia, but not in Sweden. Our findings strengthen the existing evidence and on a clinical level strongly suggest that more effort is needed to encourage people to get a booster dose. For future research, there is a need to investigate the effectiveness of the booster dose and VE against reinfection in similar detail to our analysis and to follow up with analyses against the latest emerging virus variants. Our group, among others, will continue with such work.

Introduction

With the rapid evolution of SARS-CoV-2 and vaccine approvals, [1,2] concerns remain about long-term vaccine effectiveness (VE) against new variants and for newly approved vaccines. A meta-analysis of 18 studies until November 2021 reported waning VE against COVID-19 infection from 83% in the first month to 22% at five months or longer. Effectiveness against hospitalization or more severe outcomes was higher. [3] However, the meta-analysis did not include the period with Omicron, which was first detected in November 2021 and quickly became the dominant variant globally. [4,5] A rapid increase in COVID-19 infections even in vaccinated populations was seen in many countries and triggered concerns about the effectiveness of approved vaccines against Omicron. Early laboratory data also reported lower antibody response to Omicron than other strains of SARS-CoV-2. [6,7] Several early studies with real-world setting further revealed lower VE and faster waning against Omicron infection in the UK, Qatar and Malaysia. [8–10]

In Sweden, vaccination was initiated in the elderly population on December 27, 2020, and reached larger and younger populations during 2021 and 2022. [11] We used comprehensive Swedish register data to estimate the time-varying VE in reducing the risks of COVID-19 infection, hospitalization, intensive care unit (ICU) admission and death in a 13-month follow-up and compared the pattern of time-varying VE before and after the emergence of Omicron.

Material and Methods

Study design and population

This study is part of the RECOVAC (Register-based large-scale national population study to monitor COVID-19 vaccination effectiveness and safety) study within the larger SCIFI-PEARL (Swedish Covid-19 Investigation for Future Insights – a Population Epidemiology Approach using Register Linkage) project with regularly updated data from various National Registers.[12] The current study included the whole Swedish population ≥12 years old (born in 2009 or earlier), representing the approved population for COVID-19 vaccination in Sweden. We followed the cohort from January 1, 2020 (before the start of the pandemic) to January 31, 2022, with vaccines being introduced as the cohort is being followed (the first vaccination was on 27 December, 2020). The end of follow-up coincides with the termination of large-scale COVID-19 polymerase chain reactions (PCR) testing in Sweden (February 9, 2022). For COVID-19 ICU admission, the end of follow-up was December 31, 2021, due to data availability. The first Omicron case was diagnosed on November 29, 2021, in Sweden and quickly became the dominating variant (Figure S1).[13] Therefore, we also subdivided the follow-up period into before and after December 1, 2021, representing before and after the emergence of Omicron. This study focused on two doses of vaccine, which was the original recommended COVID-19 vaccination strategy.

This study extends previous vaccine investigations by modelling exposure over time with high granularity (first weekly, then monthly after vaccination) and was approved by the Swedish Ethical Review Authority.

Data sources

We obtained data from multiple National Registers. Vaccination data was from the National Vaccination Register (NVR), held by the Public Health Agency of Sweden. All individuals with their first positive SARS-CoV-2 PCR test were identified from SmiNet, the national register of notifiable communicable diseases managed by the same Agency. PCR testing was introduced from the beginning 2020 and large-scale testing was started in mid-2020. All individuals with symptoms of COVID-19 were then encouraged to get tested, free of cost, until February 2022. COVID-19 diagnoses from both out-patient specialist visits and in-patient care records were obtained from the Swedish National Patient Registry (NPR). COVID-19 related ICU data was obtained from the Swedish Intensive care Register (SIR). Date and cause of death data was obtained from the Register of total population (RTB) and National Cause-of-Death Register (NCDR).

A complete medical history from 2015 was obtained from NPR, and drug history for prescription drugs from 2018 was obtained from the National Prescribed Drug Register (NPDR). Sociodemographic data including education, family situation, income, and occupation data from 2015 were obtained from Statistics Sweden (SCB). Information on elderly subjects living at special care facilities and/or receiving home care services was obtained from the National Social Service Register.

Exposure and Outcomes

The exposure variables were vaccination status (unvaccinated, dose one, dose two), time intervals after each vaccination and different vaccines (BNT162b2, mRNA-1273 and AZD1222), based on data from NVR. The first dose was defined as each individual's first record in NVR. The second and third dose were defined as the following records in NVR with a predefined minimum time gap between doses (details see Section S1 in Supplementary Appendix).

Four different COVID-19 outcomes were investigated: COVID-19 infection; hospitalization; ICU admission; and death. COVID-19 infection was defined as the first of: a positive PCR test, a COVID-19 diagnosis code (ICD10: U07·1/U07·2) from NPR, an ICU admission from SIR, or death due to COVID-19 (underlying or contributing cause of death) from NCDR. Most COVID-19 infection cases (98·4%) were defined by positive PCR tests. The onset date of infection was defined as two days before the registered date for any component events, based on an estimated minimum incubation time. [14] For hospitalization and severe COVID-19 outcomes (ICU admission and death), the actual registered date was used as the event date.

We studied the first occurrence of each outcome during the pandemic (after which an individual would be censored). Thus, the VE estimates apply to the first occurrence of an outcome event after vaccination, compared to unvaccinated individuals, in individuals previously free of this event.

Covariates

The procedure of covariate selection was performed in 10% random samples of the data due to computational challenges related to the large population and dataset (Details see Section S3 in Appendix, Table S2). We included the following covariates in the final models: age (modelled by restricted cubic spline with four knots), sex, country of birth (Sweden/other countries), health care workers (yes/no), income (tertiles of the study populations), education (primary, secondary, tertiary, unknown), marital status (married, unmarried, unknown), living at special housing and/or receiving home services for the elderly (yes/no), and prior comorbidities and treatments (yes/no). Prior comorbidities, including cardiovascular diseases, stroke, hypertension, diabetes, obstructive respiratory diseases, chronic kidney diseases, obesity, autoimmune diseases, dementia, psychiatric conditions, and cancer, were defined based on five-year prior medical history from NPR, and prior treatments based on one-year prior prescription drug history from NPDR. Other covariates were defined with information retrieved from Statistics Sweden (see Section S2 in Appendix for details).

Statistical analysis

Cox proportional hazard models with time-varying exposure were used. [15] In the model, each individual's follow-up time was first divided according to vaccination status (unvaccinated, first dose and second dose) and then the vaccination exposure periods were further divided into time intervals after each dose until transition to the next dose (see Section S3 in Appendix). Since the fine division of follow-up time was computationally challenging, some modelling steps were performed in 10% random samples of the data to support the final full-scale analyses (Section S3 in Appendix, Table S1 and S2).

This study estimated VE for COVID-19 outcomes for time intervals after one and two doses. In the analysis of VE for one dose on an outcome, subjects were censored at the earliest of: event, second dose, emigration, death, or end of follow-up. In the analysis of VE for two doses, the time period under the first dose was treated as a loss to follow-up (neither exposed nor unexposed), and subjects were again observed when receiving their second dose and censored at the earliest of: event, third dose, emigration, death, or end of follow-up. Furthermore, we used a restricted cubic spline with five knots in extended Cox regression to flexibly model the VE for each dose and illustrate effectiveness trends by smooth curves in addition to time interval estimates.

We estimated time-varying VE for the entire follow-up, for the period before Omicron (end of follow-up on November 30, 2021) and for the Omicron period, respectively. For analysis of the Omicron period after December 1, 2021, we modelled the entire follow-up period, but only events after December 1, 2021, were considered as incident cases for estimation, and individuals with earlier events were censored at their event.

Additionally, stratified analyses were performed for COVID-19 infection and hospitalization by sex or age group (12-17, 18-39, 40-59, 60-64, 65-79 and 80+), as well as in subjects with two doses of homologous BNT162b2, mRNA-1273 or AZD1222. Since AZD1222 was mainly used in older individuals, stratified analyses for vaccine types were restricted to individuals ≥65 years.

From the estimated hazard ratios (HR), results were presented as VE with 95% confidence intervals (CI), with VE calculated as 100*(1-HR). All analyses were performed in StataMP 17.

Results

Study population

Among 9,153,456 study individuals, 15% remained unvaccinated during the entire study period, and 85% had at least one dose of vaccine, 82% had two doses, and 45% had ≥ three doses on January 31, 2022 (Table 1). Most individuals received two doses of BNT162b2 (78%) or mRNA-1273 (12%). Only 8% had two doses of AZD1222, and most (86%) were ≥65 years (Table 2). The average intervals between the first and second and the second and third dose were seven and 28 weeks, respectively. For homologous AZD1222, the interval between the first and second dose was slightly longer (ten weeks) and between the second and third dose slightly shorter (25 weeks) (Table S3). The trends of vaccine uptake are presented in Figure S2 and S3.

There were 2,002,024 first-time COVID-19 infection cases between January 1, 2020, and January 31, 2022 (Table 1), representing 22% of the cohort. For hospitalization, ICU admission and death, the corresponding figures were 0·9%, 0·1% and 0·2%, respectively.

VE during a 13-month follow-up period

The initial analysis was performed for the entire follow-up (13 months). VE against COVID-19 infection after two doses of any vaccine peaked at week three with 72·0% (95%CI 71·0%-73·0%) but then dropped quickly to 19·5% (18·8%-20·2%) by weeks 14-17 and showed no protection from week 18 (Figure 1a, Table S4). VE against hospitalization was >82% from weeks one to 25 and peaked above 90% at weeks five to six (Figure 1b, Table S4). VE after two doses against severe COVID-19 outcomes was even higher and more durable (Figures 1c-d, Table S5). Figure 2 shows spline curves illustrating smoothed trends for all COVID-19 outcomes. Some discrepancies were observed between the smoothed trends (Figure 2) and time interval estimates (Figure 1), especially during the later time points. This is mainly because restricted cubic spline assumes a linear association in the tails. Additionally, there are fewer cases at later time points which can influence the accuracy of estimations.

As expected, the VE after one dose was generally lower than after two doses. Peak VE was <50% against infection and protection was lost from week 30. For severe COVID-19 outcomes, there was a transient decline in VE from week one to week two with an increase again in the following weeks. Overall, the VE rarely reached 80% (Figure S4 and Table S6 and S7).

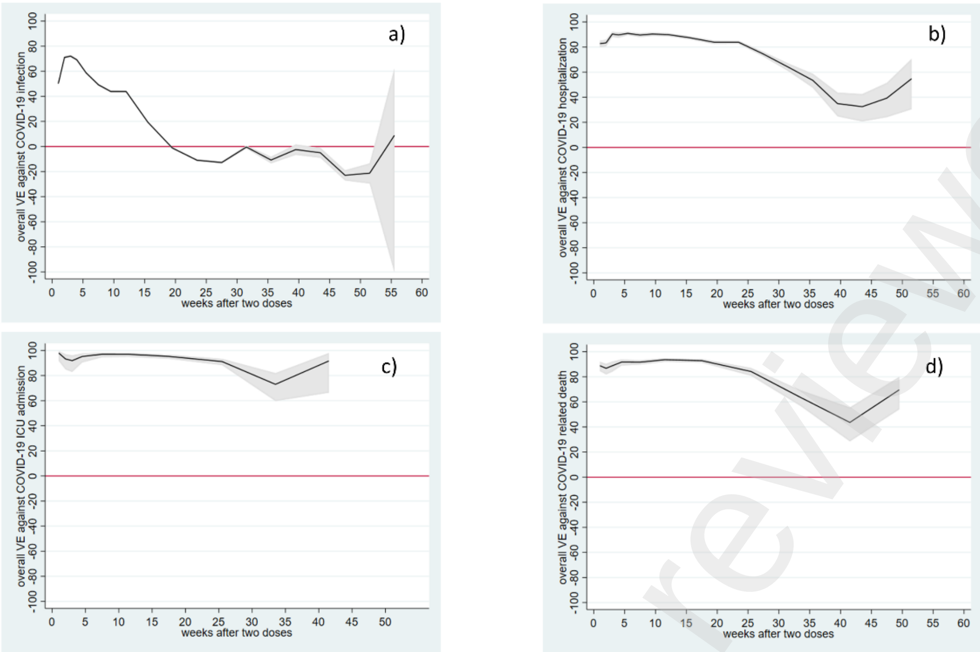

Figure 1. Overall vaccine effectiveness against COVID-19 infection (a) and severe outcomes [hospitalization (b), ICU admission (c), death (d)] after two doses. Legend: VE denotes vaccine effectiveness. Gray area indicates 95% confidence intervals. Red line indicate VE=0.

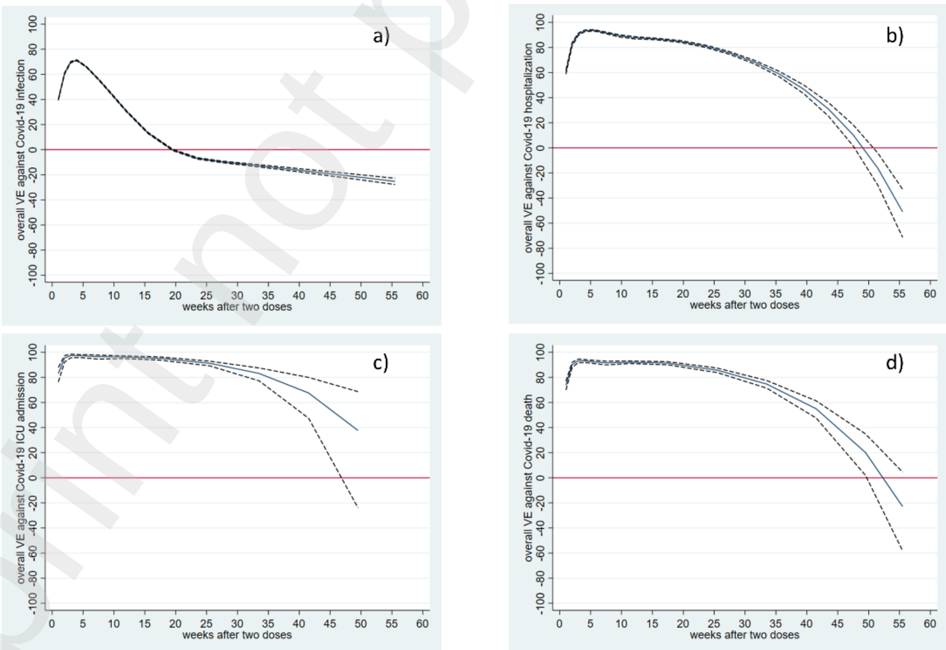

Figure 2. Restrict cubic spline of overall vaccine effectiveness against COVID-19 infection (a) and severe outcomes [hospitalization (b), ICU admission (c), death (d)] after two doses.

Legend: VE denotes vaccine effectiveness. Area within dotted line indicates 95% confidence intervals. Red line indicate VE=0.

VE after two doses before and after the emergence of the Omicron

The more fast-waning VE that we observed for the entire follow-up than in other earlier published data appeared likely to be related to the emergence of Omicron. Therefore, the analyses for the pre-Omicron and Omicron periods separately are particularly important. There was a large difference in VE against infection before and after the emergence of Omicron. Before Omicron, VE was above 85% for most time intervals (Figure 3a, Table S8), whereas VE was lower and decreased quickly for infection caused by Omicron and two doses of vaccine showed no protection against infection by week 14 (Figure 3b, Table S8).

A difference in VE from pre-Omicron and Omicron period was also observed for hospitalization, but it was not as large as for infection (Figure 3c and 3d, Table S9). Before Omicron, VE was stable, durable, and high (above 85%), while VE against hospitalization caused by Omicron was about 80% up to week 25 and then decreased but showed some protection against hospitalization during the entire follow-up.

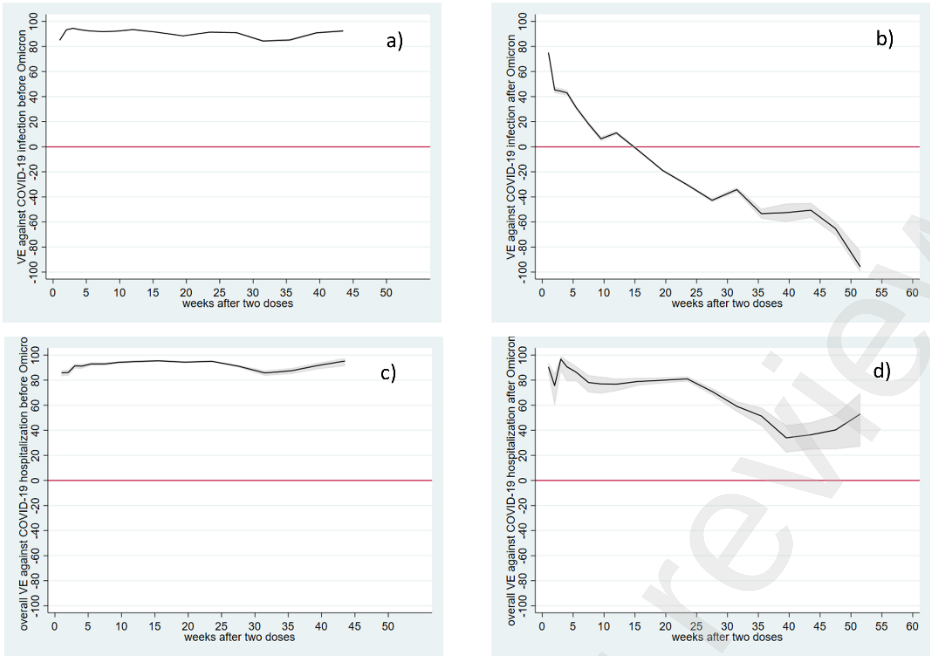

Figure 3. Two doses vaccine effectiveness before and after omicron, against COVID-19 infection (a,b) and hospitalization (c,d). Legend: VE denotes vaccine effectiveness. Gray area indicates 95% confidence intervals. Red line indicate VE=0.

VE after two doses by age, sex, and vaccine type

The overall VE trends against infection were relatively similar across age groups, although VE against infection was possibly somewhat higher among the elderly (>60 years, Figure S5). A slight potential sex difference was suggested (Figure S6), with lower VE in males. AZD1222 showed lower VE against infection than the mRNA vaccines (Figure S7). Regarding hospitalization, the three vaccines showed similar higher VE in the early weeks, with a slightly faster decrease for AZD1222.

Discussion

This study examined the time-varying VE against infection, hospitalization, and severe COVID-19 outcomes over 13 months including the emergence of the Omicron variant in Sweden. The most important finding was a difference in the pattern of VE during the pre-Omicron period and Omicron period. We found high and stable VE (in the range 85%-95%) when restricting to the pre-Omicron period, which was similar to a US study with >10 million North Carolina residents and a 9-month follow-up until September 2021. They estimated monthly VE after two doses of the two mRNA vaccines, with peak VE of about 95% at two months after the first dose, decreasing to 70-80% at seven months.[16] However, in another Swedish study performed before Omicron, more progressively waning was observed. [17] That study included in total 1,685,948 individuals with 1:1 matched of vaccinated and unvaccinated status, and estimated a peak (92%) at 15–30 days, declining to no effect after eight months after two doses of vaccine. [17] The difference between our study and the previous Swedish study is likely due to the different target population, as our study is based on the full population, while Nordström et al. studied only 30% of vaccinated individuals that could be matched. [17]

Unlike the high and stable VE against infection before Omicron, we observed very rapidly waning effectiveness during Omicron period, which dropped to zero protection by week 14. Several studies have also reported lower and more rapidly waning VE with Omicron. [8–10,18,19] These studies all used a test-negative case-control study design with potential limitations such as being sensitive to the test sensitivity and specificity. [20] In a UK study, [9] with two doses of mRNA vaccines, the VE dropped from 65-70% to 10% by 25 weeks after the second dose. The VE with two doses of AZD1222 was even lower and less durable (from 45-50% to no effect by 20 weeks). Our results were similar to the UK study, albeit with even more rapidly waning effectiveness. Somewhat implausibly, we even observed a negative VE against Omicron infection from week 14, indicating that vaccinated individuals experienced a higher risk of infection than those unvaccinated. This may relate to harvesting bias in this analysis of the first event of a common outcome (as infection with Omicron is getting close to ubiquitous in many areas now). More unvaccinated individuals had already been infected, leaving a larger pool of vaccinated individuals susceptible to their first infection later by Omicron. As a result, a higher risk among vaccinated individuals might be observed for a limited time period.

Largely due to the long follow-up period covering the emergence of Omicron and the difference in VE during pre-Omicron and Omicron periods, our analysis for the entire follow-up revealed a general lower peak VE than in previous studies, including phase-three trials and observational studies. As expected, previous trials with shorter follow-up (e.g., five or six months after vaccination) showed very high vaccine efficacy against infection after BNT162b2 [21,22] or mRNA-1273 vaccine, [23,24] with average efficacy above 90%, and around 70%, for AZD1222, [25,26] while observational studies focusing on real-life population effectiveness and using longer follow-up (e.g., seven to nine months) reported slightly lower levels. [16,17]

More importantly, a higher and longer protection was seen against hospitalization and severe COVID-19 (ICU admission and death) than against COVID-19 infection in this study, as previously reported in other studies. [16,17,27] Even for hospitalization by Omicron, the effectiveness remained high, as observed in other studies. [8,28]

In line with previous trials and real-world observational studies showing lower VE of AZD1222 than mRNA-1273 or BNT162b2, [17,27,29] we observed lower VE after two doses of homologous AZD1222 than the two mRNA vaccines among individuals ≥65 years. We restricted the age range in this analysis based on the vaccine strategy in Sweden, where AZD1222 was offered to the older population and stopped in mid-2021 (Figure S3). For COVID-19 hospitalization, the three vaccines showed similar VE in the early period, with homologous AZD1222 waning faster from week 20.

We restricted our analysis up to two doses, as this was originally recommended basic vaccination schedule. Though a booster dose (dose three) was introduced, some individuals and groups have considered themselves adequately covered by two doses and the coverage of three vaccine doses to date is not ideal, providing a substantially smaller number of cases and shorter follow-up that precludes a detailed time-related analysis as we have conducted here for doses one and two. Although two doses of vaccine are required for basic vaccination, some persons remain on one dose for different reasons. There is a need to estimate the VE and evaluate time for VE build-up and durability of single-dose vaccine responses. As anticipated, our results showed overall lower VE against infection with only one dose than with two, although the initial ramping-up period for protection against infection seemed relatively short, reaching an average effectiveness of 50% at week three. For severe COVID-19 outcomes, we observed a paradoxical high VE immediately after the first dose, followed by a dip and then an expected rise. This effect was previously described, [30] and attributed to vaccinated patients being less likely to seek care after vaccination, especially for milder COVID-19-type symptoms and COVID-19 exposure.

This population-based study renders our results not subject to selection bias. Additionally, we used Cox regression considering both time-varying exposure (from unvaccinated to one dose and then two doses) and time-varying effects (period effects for each dose). This approach avoided any assumptions about the interval between doses as in the mentioned US study. [16] However, our study cannot entirely avoid common limitations of observational VE studies, for instance, potential bias due to residual and unmeasured confounders. Of greater importance may be the human behaviors related to vaccination. Those who chose to be vaccinated later, or not at all, may differ in behaviors from those who chose to be vaccinated earlier, a potential bias that is difficult to quantify or address. Additionally, with increased proportion of home-based testing and antigen testing, there is a risk of missing COVID-19 infection cases. However, suboptimal sensitivity of outcome assessment is relevant for all observational studies, including COVID-19 studies, and difficult to fully address. The Swedish register data system nonetheless remains one of the best in the world and captures a broad range of outcomes, including COVID-19, with high accuracy.

Conclusion

This study provides more detailed long-term data on time-varying VE against COVID-19 in a complete general population. The progressively waning protection against Omicron infection after two doses of vaccine underscores the need of additional efforts to encourage people to get a booster dose to ensure a better population level protection. With respect to hospitalization and severe COVID-19, two doses of vaccine provided good and long-lasting protection, albeit waning more clearly during Omicron than pre-Omicron period.

Authors contribution

All authors participated in literature search, conceived, and designed the study. FN acquired the funding. HL, FN and BK collected and verified the underlying data. YX performed analysis and drafted the original draft. FN supervised the work. All authors interpreted the results, critically reviewed and edited the manuscript. All authors gave final approval of the version to be published and had final responsibility for the decision to submit for publication.

Declaration of interests

Dr. Gisslén reports personal fees (DSMB) from AstraZeneca, Gilead, GSK/ViiV, MSD, Biogen, Novocure, Amgen, Novo Nordisk, outside the submitted work. Dr Leach reports consulting for Scandinavian Biopharma. Dr. Vanfleteren has received grants and personal fees from

AstraZeneca and personal fees from GSK, Novartis, Boehringer-Ingelheim, Menarini, Resmed, Chiesi, AGA Linde, Zambon and Pulmonx. Dr. Nyberg reports prior employment at AstraZeneca until 2019, and ownership of some AstraZeneca shares. Mr. Kirui, Dr. Wettermark, Dr. Santosa, Dr. Li, and Dr. Xu have nothing to disclose.

Data sharing statements

The data in this study are pseudonymized individual-level data from Swedish healthcare registers and are not publicly available according to Swedish legislation. They can be obtained from the respective Swedish public data holders on the basis of ethics approval for the research in question, subject to relevant legislation, processes and data protection.

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Table 1. Sociodemographic and comorbidity characteristics of the study cohort (Swedish population ≥12 years of age in 2021) according to vaccine dose received and COVID-19 clinical outcomes by January 31, 2022.

	entire population	Vaccine uptake						COVID-19 outcome events			
		vaccinated with at least one dose		vaccinated with at least two doses		vaccinated with more than two doses		Infection	Hospitalization	ICU	Death
Characteristics	count	count	%	count	%	count	%	count	count	count	count
All residents ≥12 yrs	9153456	7750175	84·7	7492231	81·9	4069838	44·5	2002024	81488	8167	17408
Age group											
12-17y	729379	524970	72·0	451781	61·9	462	0·1	172493	476	26	1
18-39y	2919192	2317509	79·4	2201250	75·4	487513	16·7	827836	9388	601	76
40-59y	2636496	2304475	87·4	2262200	85·8	1289901	48·9	719142	20626	2432	563
60-64y	576885	526344	91·2	521098	90·3	430858	74·7	98341	7226	1147	460
65-79y	1613620	1496463	92·7	1483929	92·0	1352311	83·8	126937	23392	3355	4309
≥80y	677884	580414	85·6	571973	84·4	508793	75·1	57275	20380	606	11999
Sex											
Males	4593274	3827301	83·3	3689578	80·3	1914129	41·7	955270	45558	5704	9538
Females	4560182	3922874	86·0	3802653	83·4	2155709	47·3	1046754	35930	2463	7870
Country of birth											
Sweden	7173976	6375825	88·9	6201225	86·4	3557726	49·6	1561900	53760	4941	13810
Other countries	1979480	1374350	69·4	1291006	65·2	512112	25·9	440124	27728	3226	3598
Health care workers											
Yes	1765714	1548251	87·7	1504469	85·2	806464	45·7	540620	12198	1304	414
No	7387742	6201924	83·9	5987762	81·0	3263374	44·2	1461404	69290	6863	16994
Education											
Primary	1624747	1330160	81·9	1276567	78·6	711662	43·8	292496	23732	2288	7389
Secondary	3515542	3037726	86·4	2961176	84·2	1729812	49·2	771477	33412	3545	6450
Tertiary	3033764	2728483	89·9	2684092	88·5	1586958	52·3	731879	21109	2037	2978
Unknown	979403	653806	66·8	570396	58·2	41406	4·2	206172	3235	297	591

Income [a]											
Low	2843443	2151668	75·7	2055470	72·3	1067553	37·5	1377828	101658	7885	13811
Medium	2843745	2512100	88·3	2452190	86·2	1317623	46·3	2079536	68123	6560	5159
High	2872082	2653320	92·4	2617388	91·1	1684159	58·6	2171200	61814	6675	2617
Unknown	624186	433087	69·4	367183	58·8	503	0·1	330659	794	51	3
Marital status											
Married	3408329	3054335	89·6	3005911	88·2	2096079	61·5	738892	37793	4355	6123
Unmarried	5732710	4693822	81·9	4484570	78·2	1973458	34·4	1262593	43666	3810	11284
Unknown	12417	2018	16·3	1750	14·1	301	2·4	539	29	2	1
Special care facilities											
No	9065928	7693339	84·9	7437607	82·0	4028541	44·4	1983797	78662	8135	11832
Yes	87528	56836	64·9	54624	62·4	41297	47·2	18227	2826	32	5576
Home care service											
No	8903449	7559894	84·9	7307304	82·1	3922014	44·1	1964729	68803	7824	8818
Yes	250007	190281	76·1	184927	74·0	147824	59·1	37295	12685	343	8590
Prior comorbidities and treatments [b]											
Cardiovascular disease											
No	8478793	7162241	84·5	6914482	81·6	3594586	42·4	1911159	61569	6762	9537
Yes	674663	587934	87·1	577749	85·6	475252	70·4	90865	19919	1405	7871
Stroke											
No	9058839	7670273	84·7	7413794	81·8	4004535	44·2	1989901	78182	7987	15800
Yes	94617	79902	84·4	78437	82·9	65303	69·0	12123	3306	180	1608
Hypertension											
No	7113536	5892738	82·8	5657425	79·5	2513924	35·3	1743515	38670	3918	4184
Yes	2039920	1857437	91·1	1834806	89·9	1555914	76·3	258509	42818	4249	13224
Diabetes											
No	8610137	7266301	84·4	7015964	81·5	3684709	42·8	1923342	64901	6204	12690
Yes	543319	483874	89·1	476267	87·7	385129	70·9	78682	16587	1963	4718
Obstructive respiratory diseases											
No	8314536	7006607	84·3	6769169	81·4	3601311	43·3	1824514	65536	6648	13652

Yes	838920	743568	88·6	723062	86·2	468527	55·8	177510	15952	1519	3756
Chronic kidney diseases											
No	9055450	7671976	84·7	7415874	81·9	4008312	44·3	1987063	75642	7731	14937
Yes	98006	78199	79·8	76357	77·9	61526	62·8	14961	5846	436	2471
Obesity											
No	8981258	7604699	84·7	7352735	81·9	3992828	44·5	1957435	77704	7678	16835
Yes	172198	145476	84·5	139496	81·0	77010	44·7	44589	3784	489	573
Autoimmune diseases											
No	8943975	7564864	84·6	7310314	81·7	3927986	43·9	1967287	75473	7635	15460
Yes	209481	185311	88·5	181971	86·9	141852	67·7	34737	6015	532	1948
Dementia											
No	9097600	7710590	84·8	7453854	81·9	4039271	44·4	1991197	79069	8149	14309
Yes	55856	39585	70·9	38377	68·7	30567	54·7	10827	2419	18	3099
Psychiatric conditions											
No	7411418	6240821	84·2	6025166	81·3	3120897	42·1	1666204	53403	5898	7771
Yes	1742038	1509354	86·6	1467065	84·2	948941	54·5	335820	28085	2269	9637
Cancer											
No	8705114	7352319	84·5	7099348	81·6	3732517	42·9	1948418	71208	7429	13814
Yes	448342	397856	88·7	392883	87·6	337321	75·2	53606	10280	738	3594

a) Low/medium/high income categorized using tertiles of the study populations

b) Prior comorbidities and treatments were defined using information of 2-year prior medical history and 1-year prior prescription drugs history (Section S2 in Appendix)

Table 2. Sociodemographic and comorbidity characteristics of people receiving two doses according to vaccine type.

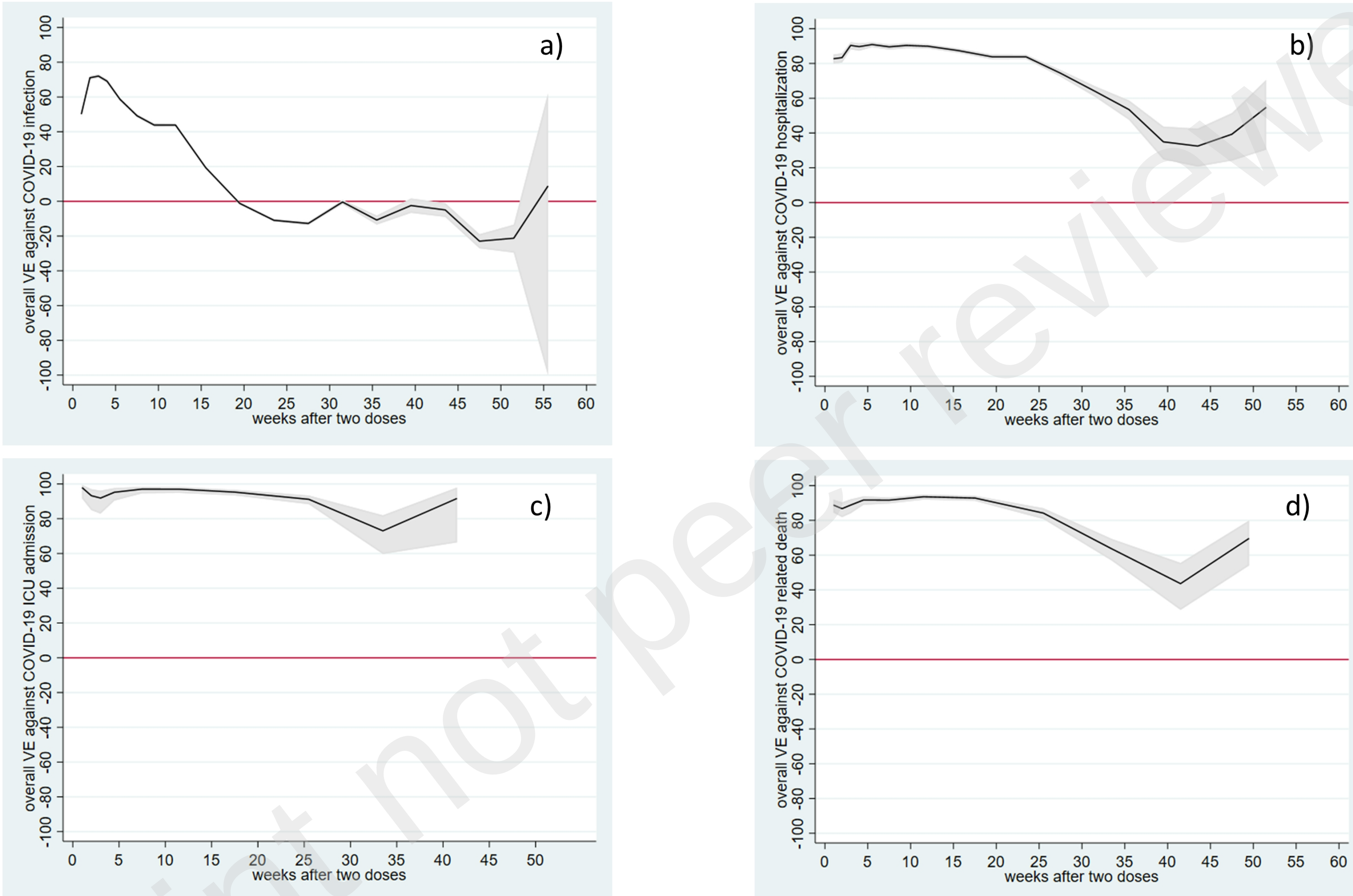
	vaccine uptake	**vaccine type**					
	two doses	**Homologous BNT162b2**		**Homologous mRNA-1273**		**Homologous AZD1222**	
Characteristics	count	count	%	count	%	count	%
All residents >=12 yr	7492231	5858168	78·2	894487	11·9	595039	7·9
Age group							
12-17y	451781	446576	7·6	30129	3·4	1	0·0
18-39y	2201250	1739396	29·7	356327	39·8	29772	5·0
40-59y	2262200	1859436	31·7	298996	33·4	41381	7·0
60-64y	521098	456742	7·8	38203	4·3	12063	2·0
65-79y	1483929	883888	15·1	106293	11·9	478493	80·4
>=80y	571973	472130	8·1	64539	7·2	33329	5·6
Sex							
Males	3689578	2910935	49·7	455604	50·9	281162	47·3
Females	3802653	2947233	50·3	438883	49·1	313877	52·7
Country of birth							
Sweden	6201225	4827821	82·4	724205	81·0	524892	88·2
Other countries	1291006	1030347	17·6	170282	19·0	70147	11·8
Health care workers							
Yes	1504469	1112637	19·0	179500	20·1	119297	20·0
No	5987762	4745531	81·0	714987	79·9	475742	80·0
Education							
Primary	1276567	971760	16·6	162404	18·2	121539	20·4
Secondary	2961176	2270684	38·8	357753	40·0	261433	43·9
Tertiary	2684092	2075266	35·4	326770	36·5	207945	34·9
Unknown	570396	540458	9·2	47560	5·3	4122	0·7
Income [a)]							

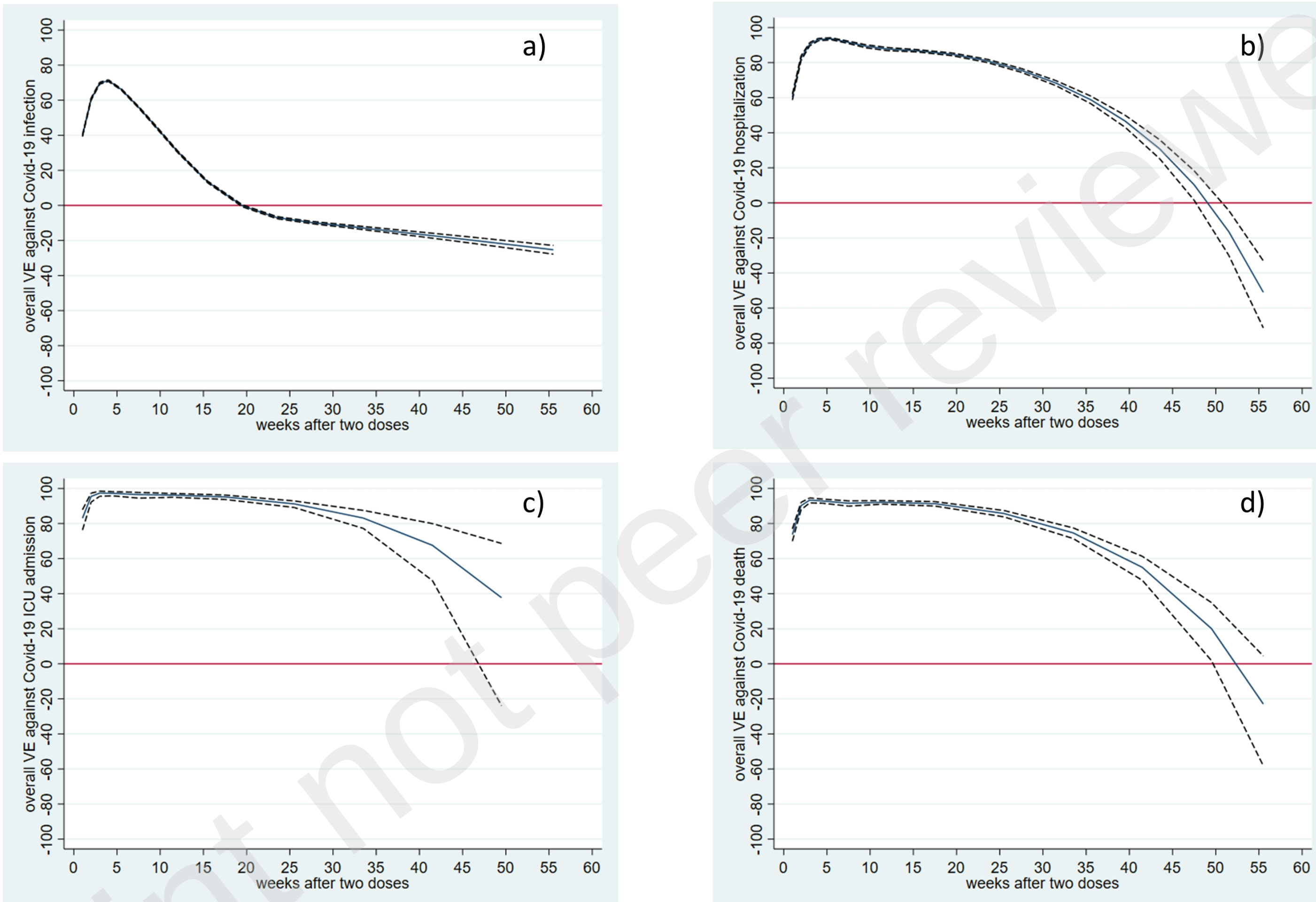
Low	2055470	1583045	27·0	266250	29·8	166084	27·9
Medium	2452190	1865049	31·8	313698	35·1	203912	34·3
High	2617388	2026669	34·6	300081	33·5	225007	37·8
Unknown	367183	383405	6·5	14458	1·6	36	0·0
Marital status							
Married	3005911	2276394	38·9	330761	37·0	339868	57·1
Unmarried	4484570	3580270	61·1	563482	63·0	255135	42·9
Unknown	1750	1504	0·0	244	0·0	36	0·0
Special care facilities							
No	7437607	5804580	99·1	893989	99·9	594881	100·0
Yes	54624	53588	0·9	498	0·1	158	0·0
Home care service							
No	7307304	5692424	97·2	880716	98·5	590566	99·2
Yes	184927	165744	2·8	13771	1·5	4473	0·8
Prior comorbidities and treatments [b)]							
Cardiovascular disease							
No	6914482	5428674	92·7	837515	93·6	510530	85·8
Yes	577749	429494	7·3	56972	6·4	84509	14·2
Stroke							
No	7413794	5797064	99·0	887348	99·2	585524	98·4
Yes	78437	61104	1·0	7139	0·8	9515	1·6
Hypertension							
No	5657425	4526433	77·3	719071	80·4	293171	49·3
Yes	1834806	1331735	22·7	175416	19·6	301868	50·7
Diabetes							
No	7015964	5509183	94·0	846257	94·6	522451	87·8
Yes	476267	348985	6·0	48230	5·4	72588	12·2
Obstructive respiratory diseases							
No	6769169	5302461	90·5	814549	91·1	521747	87·7

Yes	723062	555707	9·5	79938	8·9	73292	12·3
Chronic kidney diseases							
No	7415874	5799854	99·0	885461	99·0	586798	98·6
Yes	76357	58314	1·0	9026	1·0	8241	1·4
Obesity							
No	7352735	5748820	98·1	877508	98·1	585194	98·3
Yes	139496	109348	1·9	16979	1·9	9845	1·7
Autoimmune diseases							
No	7310314	5721375	97·7	875715	97·9	571667	96·1
Yes	181971	136793	2·3	18772	2·1	23372	3·9
Dementia							
No	7453854	5823453	99·4	892704	99·8	593332	99·7
Yes	38377	34715	0·6	1783	0·2	1707	0·3
Psychiatric conditions							
No	6025166	4729802	80·7	727596	81·3	460745	77·4
Yes	1467065	1128366	19·3	166891	18·7	134294	22·6
Cancer							
No	7099348	5576635	95·2	856102	95·7	527112	88·6
Yes	392883	281533	4·8	38385	4·3	67927	11·4

a) Low/medium/high income categorized using tertiles of the study populations

b) Prior comorbidities and treatments were defined using information of 2-year prior medical history and 1-year prior prescription drugs history (Section S2 in Appendix)


a)
overall VE against COVID-19 infection
weeks after two doses
b)
overall VE against COVID-19 hospitalization
weeks after two doses
c)
overall VE against COVID-19 ICU admission
weeks after two doses
d)
overall VE against COVID-19 related death
weeks after two doses


a)
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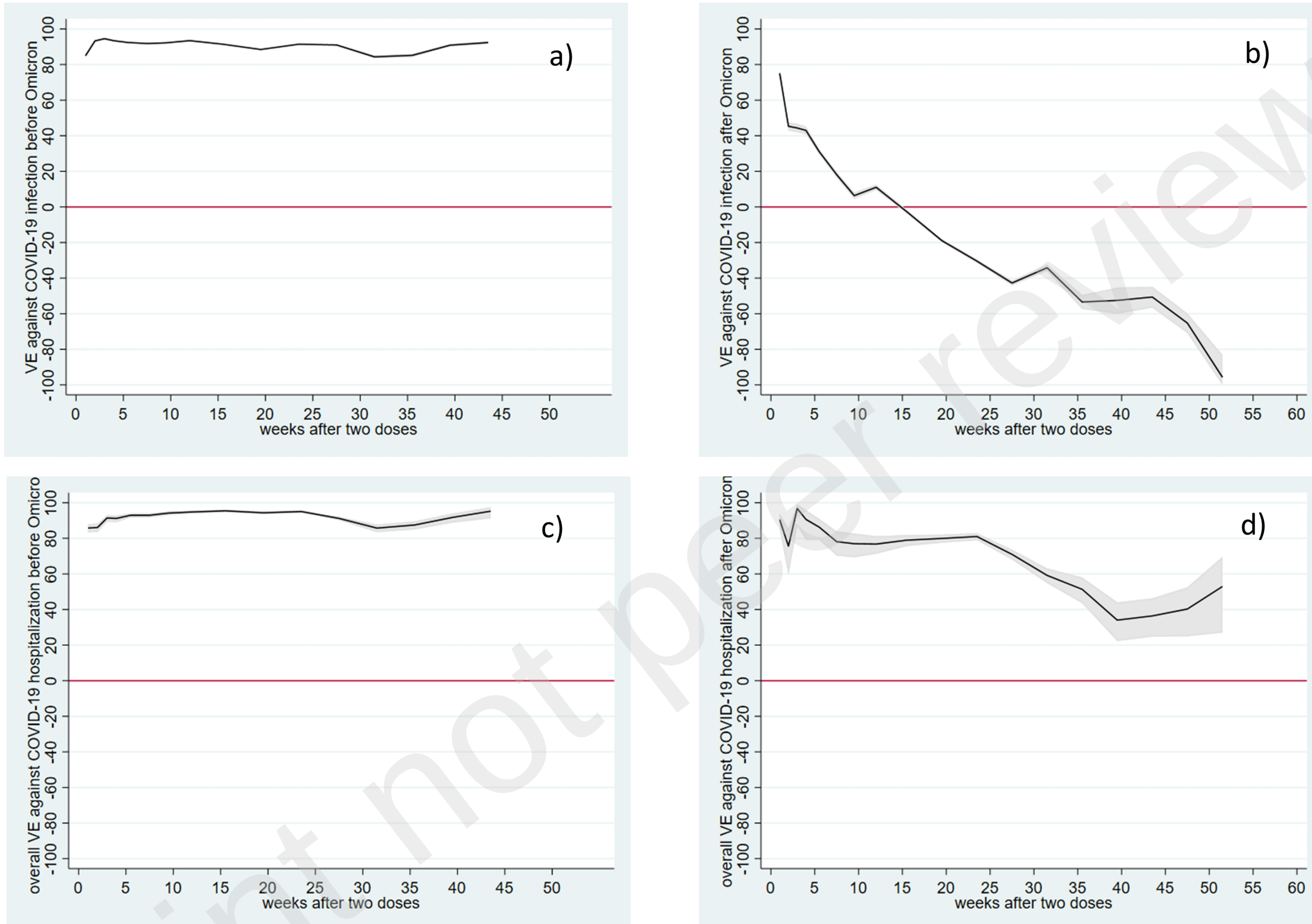
overall VE against Covid-19 infection
overall VE against Covid-19 hospitalization
overall VE against Covid-19 ICU admission
overall VE against Covid-19 death
weeks after two doses


a)
VE against COVID-19 infection before Omicron
weeks after two doses
b)
VE against COVID-19 infection after Omicron
weeks after two doses
c)
overall VE against COVID-19 hospitalization before Omicro
weeks after two doses
d)
overall VE against COVID-19 hospitalization after Omicron
weeks after two doses