

**Number of COVID-19 hospitalisations averted by vaccination: estimates for the Netherlands, January 6, 2021 through August 30, 2022**

van Iersel, Senna C.J.L.; McDonald, Scott A.; de Gier, Brechje; Knol, Mirjam J.; de Melker, Hester E.; Henri van Werkhoven, C. H.; Hahné, Susan J.M.; RIVM COVID-19 epidemiology and surveillance team

*Published in:*  
Vaccine

*DOI:*  
[10.1016/j.vaccine.2023.05.018](https://doi.org/10.1016/j.vaccine.2023.05.018)

*Publication date:*  
2023

*Document Version*  
Publisher's PDF, also known as Version of record

[Link to publication in ResearchOnline](#)

*Citation for published version (Harvard):*

van Iersel, SCJL, McDonald, SA, de Gier, B, Knol, MJ, de Melker, HE, Henri van Werkhoven, CH, Hahné, SJM & RIVM COVID-19 epidemiology and surveillance team 2023, 'Number of COVID-19 hospitalisations averted by vaccination: estimates for the Netherlands, January 6, 2021 through August 30, 2022', *Vaccine*, vol. 41, no. 26, pp. 3847-3854. <https://doi.org/10.1016/j.vaccine.2023.05.018>

**General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

**Take down policy**

If you believe that this document breaches copyright please view our takedown policy at <https://edshare.gcu.ac.uk/id/eprint/5179> for details of how to contact us.



# Number of COVID-19 hospitalisations averted by vaccination: Estimates for the Netherlands, January 6, 2021 through August 30, 2022



Senna C.J.L. van Iersel<sup>a,\*</sup>, Scott A. McDonald<sup>a</sup>, Brechje de Gier<sup>a</sup>, Mirjam J. Knol<sup>a</sup>, Hester E. de Melker<sup>a</sup>, C.H. Henri van Werkhoven<sup>a,b</sup>, Susan J.M. Hahné<sup>a</sup>, the RIVM COVID-19 epidemiology and surveillance team

<sup>a</sup>Center for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands

<sup>b</sup>Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

## ARTICLE INFO

### Article history:

Received 6 March 2023

Received in revised form 1 May 2023

Accepted 4 May 2023

Available online 10 May 2023

### Keywords:

COVID-19

SARS-CoV-2

Vaccination

Vaccine effectiveness

## ABSTRACT

**Background:** Vaccines against COVID-19 have proven effective in preventing COVID-19 hospitalisation. In this study, we aimed to quantify part of the public health impact of COVID-19 vaccination by estimating the number of averted hospitalisations. We present results from the beginning of the vaccination campaign ('entire period', January 6, 2021) and a subperiod starting at August 2, 2021 ('subperiod') when all adults had the opportunity to complete their primary series, both until August 30, 2022.

**Methods:** Using calendar-time specific vaccine effectiveness (VE) estimates and vaccine coverage (VC) by round (primary series, first booster and second booster) and the observed number of COVID-19 associated hospitalisations, we estimated the number of averted hospitalisations per age group for the two study periods. From January 25, 2022, when registration of the indication of hospitalisation started, hospitalisations not causally related to COVID-19 were excluded.

**Results:** In the entire period, an estimated 98,170 (95 % confidence interval (CI) 96,123–99,928) hospitalisations were averted, of which 90,753 (95 % CI 88,790–92,531) were in the subperiod, representing 57.0 % and 67.9 % of all estimated hospital admissions. Estimated averted hospitalisations were lowest for 12–49-year-olds and highest for 70–79-year-olds. More admissions were averted in the Delta period (72.3 %) than in the Omicron period (63.4 %).

**Conclusion:** COVID-19 vaccination prevented a large number of hospitalisations. Although the counterfactual of having had no vaccinations while maintaining the same public health measures is unrealistic, these findings underline the public health importance of the vaccination campaign to policy makers and the public.

© 2023 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Background

The COVID-19 pandemic has had an enormous negative impact on health and wellbeing worldwide. COVID-19 has directly affected public health with over 600 million confirmed cases to date, and more than 6.5 million deaths [1]. In the Netherlands, with a total population of 17.7 million individuals, approximately 8.5 million COVID-19 cases have been confirmed by surveillance monitoring from February 27, 2020, up to August 30, 2022, of which approximately 113,000 have resulted in hospitalisation and more than 22,000 in death [2]. Several times during the pandemic, the intensive care units (ICU) were overwhelmed. This imposed pressure on hospital staff, causing a shortage of staff and delaying surgical procedures [3]. Also, this pressure increased the need to

introduce drastic infection control measures in the community. Although they were believed to be effective in controlling the pandemic by decreasing transmission [4,5], these control measures also had a negative impact on other aspects of society; for instance, psychological problems in children and adolescents due to social isolation [6,7], increased prevalence of mental health indicators such as loneliness, anxiety, depression and stress [8,9], and increased numbers of people facing economic difficulties.

Large-scale COVID-19 vaccination has positively affected several public health indicators and reduced the need for restrictions. COVID-19 vaccination has been found effective in limiting infection [10,11], the transmission of infection [12,13], the number of hospitalisations and intensive care unit (ICU) admissions [14], and deaths [15,16]. In the Netherlands, the vaccination campaign against COVID-19 started on January 6, 2021 [17]. Since then, over 36 million vaccine doses have been administered. The vaccination planning strategy aimed to reduce severe disease. In general, older

\* Corresponding author.

E-mail address: [senna.van.iersel@rivm.nl](mailto:senna.van.iersel@rivm.nl) (S.C.J.L. van Iersel).

age groups were eligible before younger age groups, with some exceptions, such as healthcare workers, residents of nursing homes, people living in an institution, and individuals with specific underlying comorbidities [18]. All children aged 12–17 were eligible from the beginning of July 2021 [19].

As of today, five types of vaccines have been administered in the Netherlands, Comirnaty (COM), Spikevax (MOD), Vaxzevria (VAX), Jcovden (JANSS) and Nuvaxovid (NVXD). Two doses are needed to complete the primary vaccination schedule or one dose when an individual had a prior SARS-CoV-2 infection, except for JANSS, where one dose is sufficient, independent of a prior infection. From November 18, 2021 [20], booster doses of COM or MOD and from March 25, 2022 [21] booster doses of JANSS have been administered starting with the oldest age groups. A second booster dose of COM or MOD was offered to people over 70 years and some vulnerable health groups from the week of February 28, 2022 [22] and for 60-year-olds from March 26, 2022 [23].

Previous research estimated the substantial beneficial impact of vaccination on health outcomes. By using a mathematical susceptible-exposed-infectious-recovered-susceptible (SEIRS) model, an estimated 14.4 million deaths (79 %) were prevented in the first year of COVID-19 vaccination when fitting the model to official reported deaths in 185 countries and territories, or 19.8 million deaths (63 %) when the model was fitted to excess deaths [24]. A study used an agent-based model to estimate that in New York City 8,508 (48.6 %) deaths and 48,076 (52.9 %) hospitalisations were averted between December 14, 2020 and July 15, 2021 [25]. The percentage of expected deaths in people aged 60 years and older that were averted by vaccination in 33 European countries between December 2020 and November 2021 ranged per country from 6 % to 93 % with in total for all 33 countries a median of 469,186 deaths [26]. For these estimates, methods were adapted from an ecological study to estimate the number of averted individuals with influenza that needed medical attention by the influenza vaccination programme [27]. A similar study in Italy estimated 79,152 averted hospitalisations (32 %) during the roll-out of the vaccination campaign between January and September 2021 [28].

Quantifying the impact of the vaccination campaign against COVID-19 on hospitalisations helps policy makers and the public to assess the importance of vaccination. With this study we aimed to estimate the number of COVID-19 related hospitalisations averted by the COVID-19 vaccination campaign in the Netherlands.

## 2. Data & methods

### 2.1. Data

We estimated the number of COVID-19 related hospitalisations averted by the COVID-19 vaccination campaign from January 6, 2021 through August 30, 2022. We analysed this study period together with a second study subperiod in which all adults had the opportunity to complete their primary series and children aged 12 to 17 were eligible for vaccination, from August 2, 2021 through August 30, 2022. This allowed the impact of the whole vaccination campaign to be differentiated from the impact when all adults had the opportunity to complete the primary series. We present estimates per age group to evaluate the variation in impact of the vaccination campaign.

Vaccine coverage (VC) was determined by registrations in the Dutch COVID-vaccine Information and Monitoring System (CIMS), supplemented with anonymized registrations by the Municipal Health Services (MHS) for those individuals who did not give consent to be registered in CIMS [29]. The administered doses, dates of vaccination and vaccine types are registered on individual level. A

completed primary series includes one dose of JANSS, two doses of COM, MOD, NVXD or VAX, or one dose (other than JANSS) following a previous SARS-CoV-2 infection within three months before the dose was administered. Population data per age group is taken from the Dutch population register. Age was calculated as 2021 – birth year. Individuals with missing birth year were excluded (<0.01 %).

All confirmed COVID-19 hospital registrations by the foundation National Intensive Care Evaluation (NICE) were used. Admission date and age of all hospitalised persons in the Netherlands, including ICU admissions, with a positive SARS-CoV-2 test or CT-confirmed COVID-19 are included in this database. With the rise of Omicron, clinicians increasingly encountered positive SARS-CoV-2 tests in patients hospitalised for reasons that were not directly or indirectly related to COVID-19. Therefore, from January 25, 2022, NICE distinguishes the indication for admission, with four possible indications:

Indication	Description	% of all hospitalised patients with SARS-CoV-2 (January 25, 2022 through August 30, 2022)
1	Because of COVID-19; COVID-19 is the indication for admission and the patient is treated for it.	28.1 %
2	A combination with COVID-19; COVID-19 is one of the indications for admission; without COVID-19 the patient would not have been hospitalised.	12.7 %
3	Different primary reason for admission than COVID-19; the patient has COVID-19 but is hospitalised for an unrelated indication.	21.0 %
4	Patient has SARS-CoV-2 infection but it is unknown whether this is the reason for admission.	11.2 %
Missing		27.0 %

Hospital admissions for an indication other than COVID-19 (i.e., indication 3) were excluded from the data. We retained all SARS-CoV-2 positive admitted patients with unknown (i.e., indication 4) or missing indication because otherwise we would potentially exclude 38.2 % of COVID-19 caused admissions from January 25, 2022. Before January 25, 2022, all hospitalisations were included, since the indication was not recorded. For hospitalisations, age at date of disease onset was estimated as:

$$Age_{date\_of\_disease\_onset} = year(month(AdmissionDate - 7 days) - 6 months) - BirthYear$$

Here, *AdmissionDate* is the hospital admission date and the date of disease onset is estimated by extracting seven days from the admission date, with the assumption that the median time between date of disease onset and hospitalisation is one week,

based on national COVID-19 surveillance data. Because only birth year is known, we extract six months from the date of disease onset, given that approximately half of the persons have aged a year by the middle of the year. We then subtract the birth year to get the estimate of the age at disease onset.

Data from CIMS and NICE, linked by citizen service number, were used to estimate calendar-time specific vaccine effectiveness (VE) estimates. These were based on the incidence rate ratio (IRR), modelled using a negative binomial regression model, including a natural cubic spline for calendar date and adjusting for birth year in 5-year bands [14]. From this model, VE is calculated as  $(1 - \text{IRR}) * 100\%$ . Potential waning and differences in VE between SARS-CoV-2 variants is implicitly included in these VE estimates since the differences in hospitalisation risk associated with vaccination status are modelled over calendar time by including an interaction spline for calendar time and vaccination status. We used the same lag time of seven days to calculate the date of disease onset. To determine age at the date of disease onset for VE estimates, we used the same formula as for hospitalisations that is described above. Hospital admissions for an indication other than COVID-19 were also excluded from the data for estimating the VE.

## 2.2. Methods

All analyses were done in R [30]. We used a study design similar to [26,27], with some modifications to include primary series (p), first and second boosters (b1 and b2) vaccine coverage. In addition, in contrast to [26], we use calendar-time specific VE estimates instead of a static base VE. In short, the method expresses the ratio of averted to observed hospitalisations in terms of VE and VC. We multiply this ratio with the number of observed hospitalisations to get an estimate of the daily number of averted hospital admissions. Specifically, we used the following formulas to estimate the number of averted hospitalisations for each vaccination series, each day  $t$ , and per age group  $a$ :

$$\text{Nr\_averted}_{\text{primary\_series},t,a} = \text{Nr\_observed\_hospitalisations}_{t,a} * \frac{\text{VE}_{p,t,a} * (\text{VC}_{p,t-21,a} - \text{VC}_{b1,t-14,a})}{1 - (\text{VE}_{p,t,a} * (\text{VC}_{p,t-21,a} - \text{VC}_{b1,t-14,a})) - (\text{VE}_{b1,t,a} * (\text{VC}_{b1,t-14,a} - \text{VC}_{b2,t-14,a})) - (\text{VE}_{b2,t,a} * \text{VC}_{b2,t-14,a})}$$

$$\text{Nr\_averted}_{\text{first\_booster},t,a} = \text{Nr\_observed\_hospitalisations}_{t,a} * \frac{\text{VE}_{b1,t,a} * (\text{VC}_{b1,t-14,a} - \text{VC}_{b2,t-14,a})}{1 - (\text{VE}_{p,t,a} * (\text{VC}_{p,t-21,a} - \text{VC}_{b1,t-14,a})) - (\text{VE}_{b1,t,a} * (\text{VC}_{b1,t-14,a} - \text{VC}_{b2,t-14,a})) - (\text{VE}_{b2,t,a} * \text{VC}_{b2,t-14,a})}$$

$$\text{Nr\_averted}_{\text{second\_booster},t,a} = \text{Nr\_observed\_hospitalisations}_{t,a} * \frac{\text{VE}_{b2,t,a} * \text{VC}_{b2,t-14,a}}{1 - (\text{VE}_{p,t,a} * (\text{VC}_{p,t-21,a} - \text{VC}_{b1,t-14,a})) - (\text{VE}_{b1,t,a} * (\text{VC}_{b1,t-14,a} - \text{VC}_{b2,t-14,a})) - (\text{VE}_{b2,t,a} * \text{VC}_{b2,t-14,a})}$$

Here, VE stands for the vaccine effectiveness against hospitalisation and VC for the cumulative vaccine coverage.  $\text{VC}_p$  includes every individual with a completed primary series (including those with a first and or second booster),  $\text{VC}_{b1}$  consists of all individuals with at least a first booster (including those with a second booster) and  $\text{VC}_{b2}$  comprises individuals with a second booster.  $\text{VC}_p - \text{VC}_{b1}$  thus contains only those individuals with a primary series but not a first (or implicitly second) booster, and  $\text{VC}_{b1} - \text{VC}_{b2}$  consists of only those individuals with a first booster but not a second booster. In Appendix 1, a more intuitive explanation of the formula is provided. The time delay on day  $t$  is shown as  $t-x$  with  $x$  in days and  $a$  represents age group (12–49, 50–59, 60–69, 70–79 and 80+). The delay accounts for the time to immune response after vaccination and median time to hospitalisation after infection. Individuals aged under 12 and individuals whose age is unknown are excluded. We assume a full immune response after 14 days for the primary series and after 7 days for the first and second booster, and a time of 7 days between disease onset and disease onset, based on the

median delay of reported date of disease onset to hospital admission of confirmed COVID-19 cases, as registered by the Dutch Municipal Health Services. Monte Carlo simulations based on the regression coefficients and variance–covariance matrix of the negative binomial model were used to calculate the 95 % CIs for averted admissions to ensure that the uncertainty in the VE estimates are correctly reflected in the estimations. For each day of the study period, the variance–covariance matrix was computed and the 95 % CIs around VE was estimated; per day, 1.000 draws from this distribution were used to estimate the number of averted admissions, and the 95 % CI was constructed accordingly.

The number of averted hospitalisations was estimated per age group from the start of the vaccination campaign in the Netherlands (January 6, 2021) to August 30, 2022 ('entire period'). The same analysis was carried out for the subperiod between August 2, 2021 and August 30, 2022 ('subperiod'). In the subperiod, all adults in the Netherlands were eligible for COVID-19 vaccination and had the opportunity to complete the primary series. For this period, observed hospitalisations were used from August 2, 2021 onwards, meaning that the first averted hospitalisations were estimated three weeks later, starting from August 23, 2021, due to the vaccine coverage delay present in the formulas. Because observed hospitalised individuals can be admitted to hospital more than once, we did not remove them from the risk set. We thus also retained averted hospitalised persons in the population at risk for future hospitalisations.

We estimated the absolute and relative number of averted hospitalisations per period in which a virus variant was dominant. We define the start of a dominant period as the time that a variant comprises at least 50 % of all test samples of infected individuals that are sequenced by the pathogen surveillance in the Netherlands [31]. The periods we use are:

- Wildtype: From the start until February 14, 2021
- Alpha: February 15 until June 27, 2021
- Delta: June 28 until December 26, 2021
- Omicron: December 27, 2021 until August 30, 2022

For hospitalisations we use the estimated date of disease onset (date of hospitalisation – 7 days) to determine the dominant virus variant period.

## 3. Results

Vaccine coverage of the primary series on August 30, 2022, ranged from 73 % for age group 12–49 to 94 % for 70–79-year-olds (Fig. 1.A). At the start of the subperiod on August 2, 2021, when all adults in the Netherlands had the opportunity to complete their primary series, coverage varied from 41 % (age group 12–49) to 92 % (age group 70–79). In general, the coverage in older age groups was higher compared to younger age groups for primary, first and second booster vaccination (Fig. 1.A–C). Daily VE estimates for all ages (12 years and older) and per age group are shown in Appendices I and II.

In total, 74,074 observed hospitalisations of individuals of 12 years and older were included in the entire period and 42,930 in the subperiod. Fig. 2 illustrates the weekly number of observed and estimated averted hospitalisations for individuals aged 12 years and older. From the start of the vaccination campaign, an estimated 98,170 hospitalisations (95 %CI 96,123–99,928) have been averted, with most of them in the subperiod (90,753; 95 %CI 88,790–92,531). These numbers equal 57.0 % (95 %CI 56.5 %–57.4 %) and 67.9 % (95 %CI 67.4 %–68.3 %) of all hospital admissions for respectively the entire period and the subperiod.

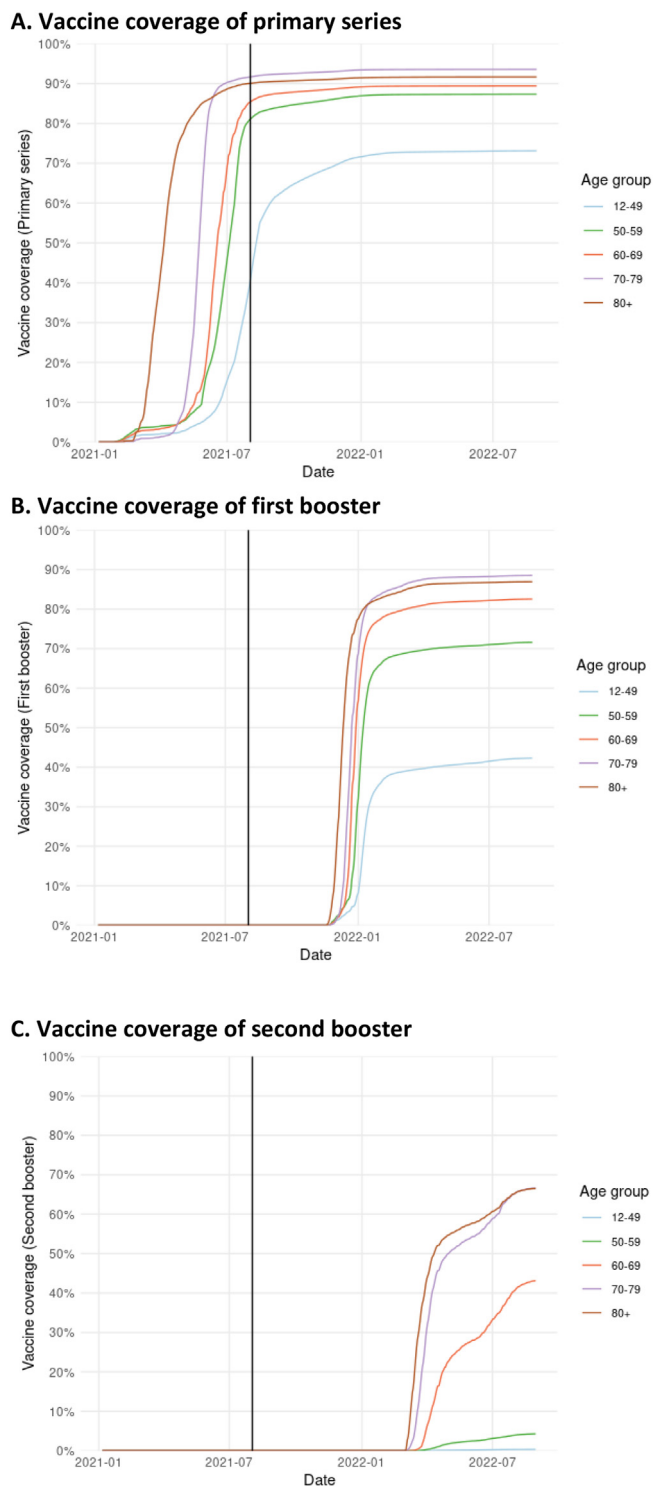


Fig. 1. Daily vaccine coverage per age group. The vertical line marks the start of the subperiod (August 2, 2021).

Fig. 3 summarises the observed and estimated averted hospitalisations per age group for the entire period from January 6, 2021 through August 30, 2022, and for the subperiod from August 2, 2021 through August 30, 2022. The number of estimated averted hospitalisations was highest for age group 70–79 years, both absolute (32,483, of which 30,268 in the subperiod) and relative to observed hospitalisations (63.5 % in the entire period and 73.3 % in the subperiod). The lowest numbers were observed for age

group 12–49 years: 7,607 (37.3 %) estimated averted hospitalisations, of which 7,255 (49.9 %) in the subperiod.

During the Alpha period, an estimated 1,826 (8.1 %; 95 %CI 1,767–1,876; 7.8 %–8.3 %) hospitalisations were averted by vaccination (Fig. 4). The largest number of hospitalisations was averted during the Delta period, both in absolute (57,395; 95 %CI 55,918–58,723) as well as relative (72.3 %, 71.8 %–72.8 %) terms. In the Omicron period, an estimated 38,949 (63.4 %) admissions were averted (95 %CI 37,749–40,152, 62.7 %–64.1 %).

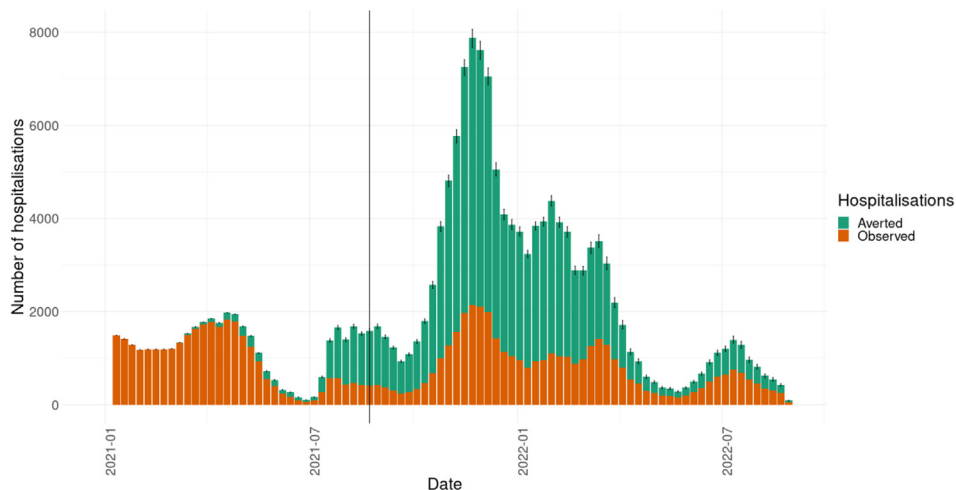
#### 4. Discussion

We aimed to quantify the impact of COVID-19 vaccination in the Netherlands in terms of averted hospitalisations. Results show that the vaccination campaign has had a considerable, positive impact on an important indicator of COVID-19 health burden – admission to hospital – which reinforces the investment in the vaccination programme for preventing serious disease at the patient level, reducing the associated burden on the healthcare system, and retaining capacity to admit non-COVID-19 patients. An estimated 98,170 (57.0 %) admissions have been averted from the start of the vaccination campaign, of which 90,753 (67.9 %) in the period where all adults had the opportunity to complete the primary series and children aged 12–17 were eligible for vaccination (subperiod).

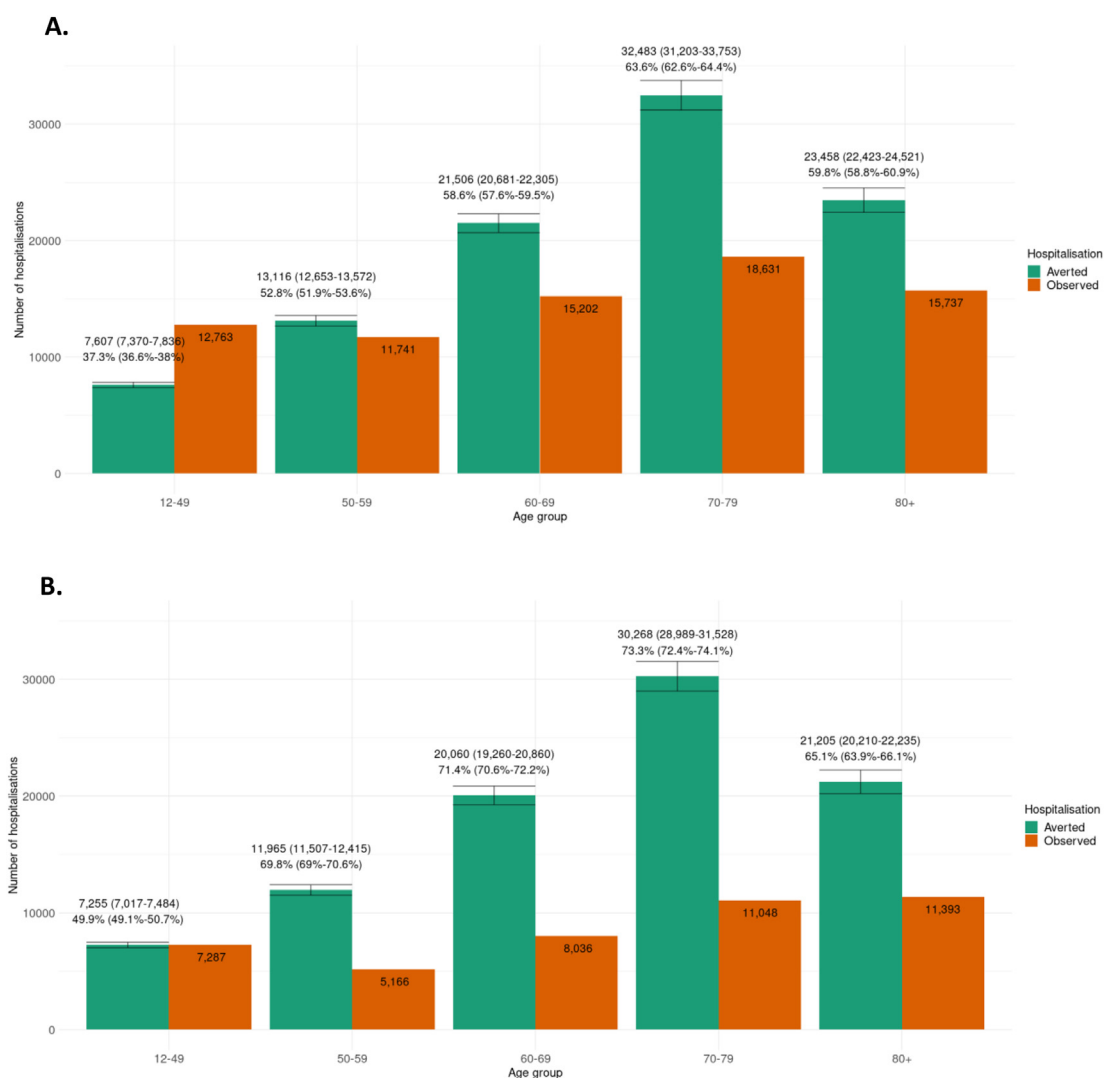
An upward trend can be seen in the fraction of averted hospitalisations from younger to older age groups, with a peak for age group 70–79. This age trend is similar to the vaccine coverage, which is higher for older age groups, and highest for age group 70–79. They are also in line with the number of observed hospitalisations, which is generally higher for older age groups. The greatest percentage of hospital admissions was averted in the Delta period, and the number of averted admissions was highest in the same period because Delta infection was more likely to lead to hospitalisation than Omicron. VE decreased significantly with the emergence of Omicron. While VE against hospitalisation remained much higher than against infection, a drop in VE was still observed around the start of 2022.

The difference in the percentage averted admissions between the period from the start of the vaccination campaign (entire period) and the period in which all adults in the Netherlands had the opportunity to complete the primary series (subperiod) is substantial, with over 10 % more averted hospitalisations in the subperiod compared to the entire period. This underlines the need for a rapid roll-out of the vaccination campaign, especially in times when the number of observed hospital admissions is high. The very large difference in the relative number of averted hospitalisations between the Alpha period (8.1 %) and the Delta and Omicron periods (72.3 % and 63.4 %), with the Alpha period comprising a large part of initial roll-out, highlights the importance of a rapid roll-out.

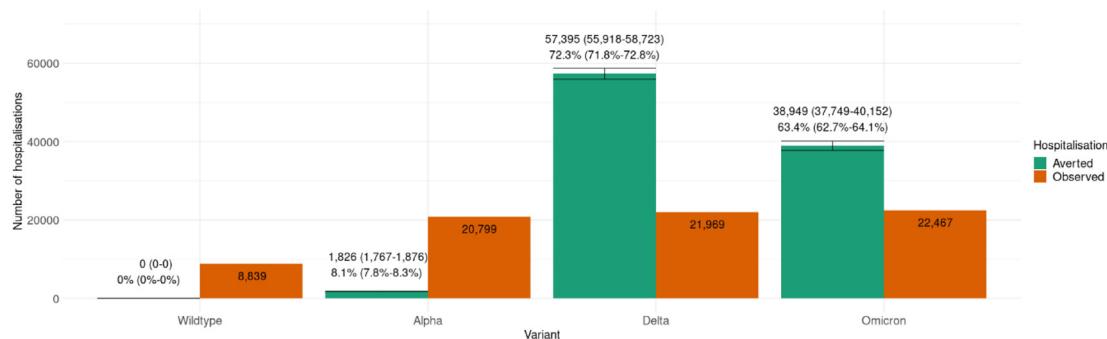
Comparing our relative estimates to relative estimates of averted hospitalisations or deaths in previous research is not straightforward, because the calculations depend on several factors. Firstly, outcomes are affected by the VE estimates used. The VE against death is higher than the VE against hospitalisation, which leads to a lower expected percentage averted hospitalisations compared to averted deaths. Secondly, a higher vaccine coverage leads to a higher estimated percentage of averted admissions. In the Netherlands, coverage is relatively high, thus we would expect a higher estimate. Lastly, the number of observed hospitalisations, the timing of peaks in observed hospitalisations, and the length of the study period affect the relative estimates. Nevertheless, our estimate in the entire period (57.0 %) is similar to the estimate of 52.9 % averted hospitalisations for New York [25]. However, it is much higher than the estimated 32 % averted



**Fig. 2.** Total weekly number of observed and estimated averted hospitalisations for individuals aged 12 years and older. The vertical line marks the cut-off for estimated averted hospitalisations in the subperiod (August 23, 2021, 3 weeks after the start of the study period, accounting for the delay in the time to immune response following completion of the primary vaccination series and the median time to hospitalisation following infection).



**Fig. 3.** Percentage and absolute number of estimated averted hospitalisations with 95 % CI bounds, and the number of observed hospitalisations, per age group. A. Entire period (January 6, 2021 until August 30, 2022) B. Subperiod (August 2, 2021 until August 30, 2022).



**Fig. 4.** Number and percentage of estimated averted hospitalisations and number of observed hospitalisations per dominant variant, from the start of the vaccination campaign (January 6, 2021) until August 30, 2022.

hospitalisations for Italy [28], which can be explained by differences in study period; in this study, the study period consisted of mainly the roll-out period of the vaccination campaign (January 2021 to September 2021).

The current study has several limitations. The CIMS data, from which calendar-time specific VE estimates were derived, did not contain vaccination records for individuals who did not consent to share their data (in total around 6.2 % of all administered doses). This will have resulted in misclassification of some vaccinated individuals as unvaccinated, leading to an underestimation of VE estimates [14]. Secondly, the VE estimates were not adjusted for comorbidities, as this information could not be individually linked to the hospital and vaccination data. Presumably, this has also resulted in conservative VE estimates, assuming that individuals with a higher risk of severe illness from COVID-19 were invited for vaccination earlier and were more likely to accept vaccination.

Similarly, because previous infections could not be individually linked to the hospital and vaccination data, it was not possible to adjust for previous infections in the VE analyses. The acquisition of infection-induced immunity will have led to underestimation of VE since unvaccinated individuals likely acquired it earlier and at higher rates [32]. This is the most plausible explanation for the negative VE estimates for some age groups during part of 2022 (Appendices II and III). Another limitation is that we do not consider indirect effects of vaccination in our analyses. Vaccination not only protects against severe COVID-19, but also reduces the probability of infecting other individuals [13,33]. This leads to fewer hospitalisations, and therefore not taking this into account makes the estimate more conservative.

Additional limitations may have resulted in an overestimation of averted hospitalisations. Firstly, we did not remove once-hospitalised persons (either observed or averted) from the population at risk for future hospitalisations, thus allowing for individuals to be admitted to the hospital more than once. In practice, the probability of being hospitalised after a prior hospital admission is likely lower than without a prior hospital admission. Secondly, the indication for COVID-19 hospitalisation was unknown until January 25, 2022. Hospitalisations with a positive SARS-CoV-2 test – but not due to COVID-19 – could thus not be excluded before this date. Because clinicians increasingly saw patients being hospitalised with a positive SARS-CoV-2 test, but whose indication for admission was not because of COVID-19, once the Omicron variant became dominant, registration of the indication of admission was added not long afterwards. Therefore, we assumed the impact on our estimates was limited. In addition, for the VE estimates the indication was unknown until January 25, 2022. Under the assumption that vaccination has no effect on the incidence of hospitalisations with – but not due to COVID-19 – VE would be underestimated. We therefore expect that this limitation has more impact on the

relative number of estimated averted hospitalisations, leading to underestimation, than on the absolute number, possibly leading to minor overestimation. The same applies to hospital admissions after January 25, 2022 with an unknown indication for admission.

Determining the impact of the COVID-19 vaccination campaign is challenging, since the counterfactual is unknown; we do not know what would have happened in the absence of the vaccination campaign. In practice, hospitals would not have been capable of admitting the enormous estimated number of patients needing hospital care, since their capacity would then have been exceeded. It is likely that stricter control measures would have been required to limit the total number of COVID-19 hospitalisations and/or spread admissions out over a longer time period. In our study, however, we estimated the impact under the assumption that public health measures and compliance to these measures would have been identical to the actual measures that had been imposed, and we assumed that there was no limit in hospital bed and staff capacity. Nevertheless, quantification of the effect of the vaccination campaign in terms of averted hospitalisations demonstrates its considerable positive impact on public health.

## 5. Conclusion

From January 6, 2021 until August 30, 2022 an estimated 98,170 (95 % CI 96,123–99,928) COVID-19 hospitalisations were averted by the SARS-CoV-2 vaccination campaigns, relative to 74,074 observed hospitalisations. The relative and absolute number of averted hospitalisations was most pronounced for age group 70–79 and during the Delta period. COVID-19 vaccination prevented a considerable burden of morbidity by reducing the number of COVID-19 hospitalisations. By doing so, it helped to improve access to healthcare for both COVID-19 patients as well as non-COVID-19 patients, due to less pressure on hospitals and healthcare workers.

## Ethics approval and consent to participate

The Centre for Clinical Expertise at the RIVM assessed the above-mentioned research proposal. They verified whether the work complies with the specific conditions as stated in the law for medical research involving human subjects (WMO). They are of the opinion that the research does not fulfill one or both of these conditions and therefore conclude it is exempted for further approval by the ethical research committee.

## Consent for publication

Not applicable.

## Authors' contributions

Study design: Senna van Iersel, Scott McDonald, Brechje de Gier, Mirjam Knol, Hester de Melker, Henri van Werkhoven, Susan Hahné. Data collection, management and quality control: Senna van Iersel, Scott McDonald, Brechje de Gier, Henri van Werkhoven, the RIVM COVID-19 epidemiology and surveillance team. Data analysis: Senna van Iersel, Scott McDonald, Henri van Werkhoven. Interpretation of the data: Senna van Iersel, Scott McDonald, Brechje de Gier, Mirjam Knol, Hester de Melker, Henri van Werkhoven, Susan Hahné. Manuscript draft: Senna van Iersel. All authors critically revised the manuscript and approved the final manuscript.

## Funding

This work was funded by the Dutch Ministry of Health, Welfare and Sports.

## Data availability

The datasets generated and/or analysed during the current study are not publicly available due to privacy reasons but are available from the corresponding author on reasonable request.

## Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Senna van Iersel reports financial support was provided by Netherlands Ministry of Health Welfare and Sport.

## Acknowledgements

### Members of the RIVM COVID-19 surveillance and epidemiology team:

Albert Jan van Hoek, Agnetha Hofhuis, Amber Maxwell, Annabel Niessen, Anne Teirlinck, Anne-Wil Valk, Carolien Verstraten, Claudia Laarman, Danytza Berry, Daphne van Wees, Dimphey van Meijeren, Don Klinkenberg, Eric Vos, Femke Jongenotter, Fleur Petit, Frederika Dijkstra, Guido Willekens, Irene Veldhuijzen, Jacco Wallinga, Jan van de Kastelee, Janneke van Heereveld, Janneke Heijne, Jantien Backer, Jeanet Kemmeren, Kirsten Bulsink, Kylie Ainslie, Liselotte van Asten, Liz Jenniskens, Lieke Wielders, Loes Soetens, Maarten Mulder, Maarten Schipper, Manon Haverkate, Marit de Lange, Marit Middeldorp, Naomi Smorenburg, Nienke Neppelenbroek, Patrick van den Berg, Pieter de Boer, Priscila de Oliveira Bressane Lima, Rianne van Gageldonk-Lafeber, Rolina van Gaalen, Steven Nijman, Stijn Andeweg, Susan Lanooij, Susan van den Hof, Tara Smit, Thomas Dalhuisen, Tjarda Boere

## Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2023.05.018>.

## References

- [1] World Health Organization. WHO Coronavirus (COVID-19) Dashboard: World Health Organization; 2022. Available from: <https://covid19.who.int/>.
- [2] Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis* 2020;20(5):533–4.
- [3] de Wit GA, Oosterhoff M, Kouwenberg LHJA, Rotteveel AH, van Vliet ED, Janssen K, et al. De gezondheidsgevolgen van uitgestelde operaties tijdens de

- corona-pandemie. Schattingen voor 2020 en 2021. National Institute for Public Health and the Environment; 2022.
- [4] Flaxman S, Mishra S, Gandy A, Unwin HJT, Mellan TA, Coupland H, et al. Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. *Nature* 2020;584(7820):257–61.
- [5] Haug N, Geyrhofer L, Londei A, Dervic E, Desvars-Larrive A, Loreto V, et al. Ranking the effectiveness of worldwide COVID-19 government interventions. *Nat Hum Behav* 2020;4(12):1303–12.
- [6] Racine N, McArthur BA, Cooke JE, Eirich R, Zhu J, Madigan S. Global prevalence of depressive and anxiety symptoms in children and adolescents during COVID-19: a meta-analysis. *JAMA Pediatr* 2021;175(11):1142–50.
- [7] Luijten MAJ, van Muilekom MM, Teela L, Polderman TJC, Terwee CB, Zijlmans J, et al. The impact of lockdown during the COVID-19 pandemic on mental and social health of children and adolescents. *Qual Life Res* 2021;30(10):2795–804.
- [8] Daly M, Robinson E. Psychological distress and adaptation to the COVID-19 crisis in the United States. *J Psychiatric Res* 2021;136:603–9.
- [9] van Tilburg TG, Steinmetz S, Stolte E, van der Roest H, de Vries DH. Loneliness and mental health during the COVID-19 pandemic: a study among Dutch older adults. *J Gerontol: Ser B* 2020;76(7):e249–55.
- [10] Lopez Bernal J, Andrews N, Gower C, Gallagher E, Simmons R, Thelwall S, et al. Effectiveness of Covid-19 vaccines against the B.1.617.2 (Delta) variant. *N Engl J Med* 2021;385(7):585–94.
- [11] Andeweg SP, de Gier B, Eggink D, van den Ende C, van Maarseveen N, Ali L, et al. Protection of COVID-19 vaccination and previous infection against Omicron BA.1, BA.2 and Delta SARS-CoV-2 infections. *Nat Commun* 2022;13(1):4738.
- [12] de Gier B, Andeweg S, Joosten R, ter Schegget R, Smorenburg N, van de Kasstelee J, et al. Vaccine effectiveness against SARS-CoV-2 transmission and infections among household and other close contacts of confirmed cases, the Netherlands, February to May 2021. *Eurosurveillance* 2021;26(31):2100640.
- [13] de Gier B, Andeweg S, RIVM COVID-19 surveillance epidemiology team, Hahné SJM, van den Hof S, et al. Vaccine effectiveness against SARS-CoV-2 transmission to household contacts during dominance of Delta variant (B.1.617.2), the Netherlands, August to September 2021. *Eurosurveillance* 2021;26(44):2100977.
- [14] de Gier B, Kooijman M, Kemmeren J, de Keizer N, Dongelmans D, van Iersel SCJL, et al. COVID-19 vaccine effectiveness against hospitalizations and ICU admissions in the Netherlands, April–August 2021. *medRxiv*. 2021:2021.09.15.21263613.
- [15] Sheikh A, Robertson C, Taylor B. BNT162b2 and ChAdOx1 nCoV-19 vaccine effectiveness against death from the Delta variant. *New Engl J Med* 2021;385(23):2195–7.
- [16] de Gier B, van Asten L, Boere T, van Werkhoven H, van Roon A, van den Ende C, et al. COVID-19 vaccine effectiveness against mortality and risk of death from other causes after COVID-19 vaccination, the Netherlands, January 2021–January 2022. *medRxiv*. 2022:2022.07.21.22277831.
- [17] Valk A, van Meijeren DL, Smorenburg N, Neppelenbroek NJM, van Iersel SCJL, de Bruijn S, et al. Vaccinatiegraad COVID-19 vaccinatie Nederland, 2021. National Institute for Public Health and the Environment; 2022.
- [18] Pluijmaekers AJM, de Melker HE. The national immunisation programme in the Netherlands. Surveillance and developments in 2021–2022. National Institute for Public Health and the Environment; 2022.
- [19] Jongeren van 12 tot en met 17 jaar kunnen zich vanaf begin juli laten vaccineren 2021 [Available from: <https://www.rijksoverheid.nl/actueel/nieuws/2021/06/30/jongeren-van-12-tot-en-met-17-jaar-kunnen-zich-vanaf-begin-juli-laten-vaccineren>].
- [20] Boosterprik versneld van start 2021 [Available from: <https://www.rijksoverheid.nl/actueel/nieuws/2021/11/12/boosterprik-voor-60-plussers-versneld-van-start>].
- [21] Janssen booster possible as of 25 March 2022 [Available from: <https://www.rivm.nl/en/news/janssen-booster-possible-as-of-25-march>].
- [22] Extra coronaprik voor 70-plussers, bewoners van verpleeghuizen en mensen met een ernstig verminderde weerstand 2022 [Available from: <https://www.rijksoverheid.nl/actueel/nieuws/2022/02/24/extra-coronaprik-voor-70-plussers-bewoners-van-verpleeghuizen-en-mensen-met-een-ernstig-verminderde-weerstand>].
- [23] Extra coronaprik nu ook voor 60-plussers 2022 [Available from: <https://www.rijksoverheid.nl/actueel/nieuws/2022/03/25/extra-coronaprik-nu-ook-voor-60-plussers>].
- [24] Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. *Lancet Infect Dis* 2022;22(9):1293–302.
- [25] Shoukat A, Vilches TN, Moghadas SM, Sah P, Schneider EC, Shaff J, et al. Lives saved and hospitalizations averted by COVID-19 vaccination in New York City: a modeling study. *Lancet Reg Health - Am* 2022;5:100085.
- [26] Meslé MM, Brown J, Mook P, Hagan J, Pastore R, Bundle N, et al. Estimated number of deaths directly averted in people 60 years and older as a result of COVID-19 vaccination in the WHO European Region, December 2020 to November 2021. *Eurosurveillance* 2021;26(47):2101021.
- [27] Machado A, Mazagatos C, Dijkstra F, Kislaya I, Gherasim A, McDonald SA, et al. Impact of influenza vaccination programmes among the elderly population on primary care, Portugal, Spain and the Netherlands: 2015/16 to 2017/18 influenza seasons. *Eurosurveillance* 2019;24(45):1900268.



- [28] Sacco C, Mateo-Urdiales A, Petrone D, Spuri M, Fabiani M, Vescio MF, et al. Estimating averted COVID-19 cases, hospitalisations, intensive care unit admissions and deaths by COVID-19 vaccination, Italy, January–September 2021. *Eurosurveillance* 2021;26(47):2101001.
- [29] Wekelijkse update deelname COVID-19 vaccinatie in Nederland 2023 [Available from: <https://www.rivm.nl/covid-19-vaccinatie/wekelijkse-update-deelname-covid-19-vaccinatie-in-nederland>].
- [30] R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2022.
- [31] Covid-19 rapportage van SARS-CoV-2 varianten in Nederland via de aselecte steekproef van RT-PCR positieve monsters in de nationale kiemsurveillance; 2022.
- [32] Kahn R, Schrag SJ, Verani JR, Lipsitch M. Identifying and alleviating bias due to differential depletion of susceptible people in postmarketing evaluations of COVID-19 vaccines. *Am J Epidemiol* 2022;191(5):800–11.
- [33] Lyngse FP, Mortensen LH, Denwood MJ, Christiansen LE, Møller CH, Skov RL, et al. Household transmission of the SARS-CoV-2 Omicron variant in Denmark. *Nat Commun* 2022;13(1):5573.