Estimated number of lives directly saved by COVID-19 vaccination programmes in the WHO European Region from December, 2020, to March, 2023: a retrospective surveillance study

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Lancet Respir Med 2024; 12: 714–27

Published Online August 7, 2024 https://doi.org/10.1016/S2213-2600(24)00179-6

This online publication has been corrected. The corrected version first appeared at thelancet.com/respiratory on June 23, 2025

See Comment page 663

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Summary

Background By March, 2023, 54 countries, areas, and territories (hereafter CAT) in the WHO European Region had reported more than 2·2 million COVID-19-related deaths to the WHO Regional Office for Europe. Here, we estimated how many lives were directly saved by vaccinating adults in the WHO European Region from December, 2020, to March, 2023.

Methods In this retrospective surveillance study, we estimated the number of lives directly saved by age group, vaccine dose, and circulating variant-of-concern (VOC) period, regionally and nationally, using weekly data on COVID-19 mortality and infection, COVID-19 vaccination uptake, and SARS-CoV-2 virus characterisations by lineage downloaded from The European Surveillance System on June 11, 2023, as well as vaccine effectiveness data from the literature. We included data for six age groups (25–49 years, 50–59 years, ≥60 years, 60–69 years, 70–79 years, and ≥80 years). To be included in the analysis, CAT needed to have reported both COVID-19 vaccination and mortality data for at least one of the four older age groups. Only CAT that reported weekly data for both COVID-19 vaccination and mortality by age group for 90% of study weeks or more in the full study period were included. We calculated the percentage reduction in the number of expected and reported deaths.

Findings Between December, 2020, and March, 2023, in 34 of 54 CAT included in the analysis, COVID-19 vaccines reduced deaths by 59% overall (CAT range 17–82%), representing approximately 1·6 million lives saved (range 1·5–1·7 million) in those aged 25 years or older: 96% of lives saved were aged 60 years or older and 52% were aged 80 years or older; 51% of lives were saved among those who had received a first booster (three doses of vaccine: primary course plus one booster), and 60% were saved during the Omicron period.

Interpretation Over nearly 2·5 years, most lives saved by COVID-19 vaccination were in older adults who had received three doses and were during the Omicron period, reinforcing the importance of vaccination among the most at-risk individuals. Further modelling work should evaluate indirect effects of vaccination and public health and social measures.

Funding US Centers for Disease Control and Prevention.

Introduction

From the beginning of the COVID-19 pandemic to March, 2023, 2·2 million COVID-19 deaths were reported to the WHO Regional Office for Europe from the 54 countries, areas, and territories (CAT) in the WHO European Region.[1] The true number of deaths directly or indirectly linked to COVID-19 is estimated to be even greater.[2]

Throughout the COVID-19 pandemic, disproportionately higher mortality rates have been observed in older age groups. A global review of publicly available data from 2020 to 2022 found that persons aged 60 years or older accounted for over 80% of all COVID-19 fatalities,[3] a pattern that has been consistently observed in other studies.[4–6]

Since they were first introduced in late 2020, COVID-19 vaccines have been shown to be safe and highly effective

Research in context

Evidence before this study

Since it was first identified in late December, 2019, COVID-19 has caused disproportionately high mortality rates in older adults (aged ≥60 years). With the rapid development, licensing, and availability of novel COVID-19 vaccines, immunisation campaigns across the WHO European Region started in late 2020 and March, 2021, initially targeting the most vulnerable and exposed populations, including older adults, people with comorbidities, and health-care professionals. We searched PubMed, without language restrictions, for articles published between Dec 1, 2020, and July 31, 2024, using the search terms "(impact COVID-19 vaccin*)" NOT "(cancer)" NOT "(tb)" NOT "(tuberculosis)" NOT "(childhood immunization)" NOT "(liver)" NOT "(diabetes)" NOT "(ebola)". 82 identified studies have estimated the number of lives saved by COVID-19 vaccination, both at national level (n=71) and multi-country level (n=11), in the earlier stages of the COVID-19 pandemic. However, only one country-level study assessed the number of lives saved beyond January, 2022, when the Omicron variant of concern (VOC) circulated, a period when vaccination coverage was high in many countries, areas, and territories (CAT), but SARS-CoV-2 transmission was at its highest.

Added value of this study

To our knowledge, this is the first retrospective surveillance study to quantify the impact of COVID-19 vaccination in adults, according to age group and variant, for the entire pandemic period across multiple countries. We calculated the numbers of lives saved by age group, vaccine dose, and period of circulation of VOC, across diverse settings, using real-world data reported for 34 CAT in the WHO European Region between December, 2020, to April, 2023. For this period, we estimated that COVID-19 vaccination programmes were associated with an overall 59% reduction (CAT range 17–82%) in the number of deaths among people aged 25 years or older, representing over 1·6 million lives saved (range 1·5–1·7 million). Most lives saved (51%) were among those who received a first booster (three doses of vaccine: primary course plus one booster). Those aged 60 years or older accounted for 96% of the total lives saved whereas people aged 80 years or older represented 52% of the total lives saved, and 60% of all lives were saved during the Omicron period.

Implications of all the available evidence

Our results reinforce the importance of up-to-date COVID-19 vaccination, particularly among older age groups. Communication campaigns supporting COVID-19 vaccination should stress the value of COVID-19 vaccination in saving lives to ensure that vulnerable groups are vaccinated ahead of periods of potential increased transmission.

in protecting against severe COVID-19 infection.[7,8] In the WHO European Region since the first COVID-19 vaccines were administered,[7,8] WHO has recommended that older age groups (aged ≥60 years) be prioritised for COVID-19 vaccination.[9] As of March, 2023, 69% of people aged 60 years or older in 49 CAT across the European Region were reported to have received at least three doses of vaccine.[7]

Previous studies have estimated the number of lives saved by COVID-19 vaccination in individual countries at various stages after the introduction of COVID-19 vaccination programmes.[4,5,10–14] We previously estimated that vaccination directly saved 469 186 lives among people aged 60 years or older in 33 countries in the first year of the vaccination programme in Europe.[11] Another study[8] estimated the number of lives saved by vaccination during 2021 in 185 countries and territories. Only one study[3] has estimated the number of lives saved beyond 2021 (with the analysis carried out up to December, 2022), despite the continued circulation of SARS-CoV-2, and in particular the Omicron variant of concern (VOC) in the 2 years since. We aimed to expand on our previous work by estimating the number of lives saved by COVID-19 vaccination in adults aged 25 years or older in the WHO European Region, from the beginning of COVID-19 vaccine introduction to March, 2023—a period of 2·5 years. We stratified our results by age group, predominant circulating VOC, and vaccination dose, and considered waning protection and previous infection in our analysis. Lastly, we aimed to understand the varying impact of infections by age group.

Methods

Data sources

In this retrospective surveillance study, we estimated lives saved during the study period using CAT-level COVID-19 surveillance data and vaccination coverage data from week 50, 2020 (Dec 7, 2020), to week 12, 2023 (March 20, 2023)—hereafter, the full study period.

As part of COVID-19 routine surveillance reporting, which is jointly coordinated by the WHO Regional Office for Europe and the European Centre for Disease Prevention and Control (ECDC), every week CAT in the WHO European Region provided data on COVID-19 mortality and infection, COVID-19 vaccination uptake, and SARS-CoV-2 virus characterisations by lineage to The European Surveillance System (TESSy), which is curated by ECDC. On June 11, 2023, we downloaded COVID-19 data from TESSy for all 54 European CAT in the WHO European Region for the study period.

We conducted our analysis in two parts. For the first part, we analysed data from the full study period, for which a defined minimum COVID-19 mortality and vaccination dataset was available. We used data for people aged 60 years or older overall and narrower age

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For the **data from CoVariants** see https://covariants.org

See **Online** for appendix

groups (60–69 years, 70–79 years, and ≥80 years) because some CAT provided only data for people aged 60 years or older whereas others provided data for more discrete age groups (60–69 years, 70–79 years, and ≥80 years). Overall, data for six age groups (25–49 years, 50–59 years, ≥60 years, 60–69 years, 70–79 years, and ≥80 years) were included in both parts of the analysis. To be included in the analysis, CAT needed to have reported both mortality and vaccination data for either ≥60 years or more specific age groups (60–69 years, 70–79 years, and ≥80 years). Only CAT that reported weekly data for both vaccination and mortality by age group for 90% of study weeks or more in the full study period were included. These data were available for 34 of 54 CAT: Austria, Belgium, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, North Macedonia, Portugal, Moldova, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Ukraine, the UK (England), the UK (Scotland), and Kosovo (all references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 adopted in 1999). The following CAT reported mortality and vaccination data only for people aged 60 years or older for the full study period: Germany (data were collected but could not be made available), Moldova, and Ukraine. Israel and the UK (Scotland) reported data only for the following three age groups: 25–49 years, 50–59 years, and ≥60 years (appendix pp 7–17).

The second part of our analysis was restricted to the pre-Omicron period (week 50, 2020, to week 50, 2021; Dec 7, 2020, to Dec 13, 2021), which allowed us to include an additional five CAT (Albania, Montenegro, Norway, Poland, and UK [Wales]) that had consistently reported data only during the early part of the COVID-19 pandemic or had significant changes in reporting, such as a change in case definition, later in the pandemic.

To understand the differing impact of infection and mortality per age group, we also downloaded infection data from TESSy for the 34 CAT included in the full study period, for all age groups, and calculated the infection rate per 100 000 population for each age group.

We estimated periods of predominant circulation of VOC by CAT using virological data reported to TESSy. If data were unavailable in TESSy, we downloaded data from the Global Initiative on Sharing All Influenza Data (GISAID) obtained from CoVariants. A VOC was deemed predominant in the WHO European Region or in a CAT if 50% or more sequences per week were attributed to a given variant. Regionally and at CAT level, we defined the start of each VOC period (Alpha, Delta, and Omicron) as the first week of predominance, and the end of the VOC period as the week before the start of the subsequent predominant VOC period. For CAT where variant data were unavailable (Albania, Moldova, and Kosovo), we estimated the start and end weeks of variant periods as the median start and end week of geographically neighbouring CAT.

We downloaded population data for 2021 and 2022 from the United Nations[15] for non-EU or European Economic Area CAT and from Eurostat[16] for EU or EEA countries, except for the following CAT, where more detailed population denominators were available elsewhere: Estonia,[17] Italy,[18] Malta,[19] North Macedonia,[20] Poland,[21] Portugal,[22] Sweden,[23] Switzerland,[24] the UK (England, Scotland, and Wales),[25] and Kosovo.[26]

To identify studies that estimated COVID-19 vaccine effectiveness against mortality by age group and by VOC, we used the COVID-19 Study Explorer from International Vaccine Access Center.[27] We calculated mean vaccine effectiveness against death per dose and VOC (table 1) using inverse-variance weighting estimate to pool together estimates of the log risk ratio-based vaccine effectiveness estimates against death listed on the COVID-19 Study Explorer and in the appendix (pp 18–21). We included only vaccine effectiveness estimates against death from studies that met the following criteria: were conducted in adults from the general population; used unvaccinated individuals as the reference group; were conducted in the WHO European Region or other high-income countries, including the USA, Canada, Australia, and South Korea; and estimated vaccine effectiveness by VOC. We excluded vaccine effectiveness estimates from studies that included only people living in long-term care facilities, people with comorbidities, immunocompromised individuals, pregnant women, and children and health-care workers, or provided an estimated vaccine effectiveness against death in less than four weeks since vaccination.

	Alpha (B.1.1.7)	Delta (B.1.617.2)	Omicron (B.1.1.529)
d=1 (VE_1)	67% (66–69%)	83% (69–90%)	70% (65–75%)
d=2 (VE_2)	94% (93–95%)	83% (82–84%)	69% (67–70%)
d=3 (VE_3)	..	95% (95–95%)	78% (77–80%)
d=4 (VE_4)	..	..	84% (81–87%)
d=5 (VE_5)	..	..	84%* (81–87%)

The underlying literature from which the mean values were calculated are available in the appendix (pp 17–20). The ranges provided in brackets represent the values used for the sensitivity analyses. d=dose. VE=vaccine effectiveness. *Due to the absence of data relating the VE_5 Omicron in the general population, the values from VE_4 Omicron were used.

Table 1: **Estimated effectiveness of COVID-19 vaccination against mortality used in the analysis, according to circulating VOC and dose**

Data analysis

To estimate the number of lives saved as a result of COVID-19 vaccination in each CAT, we adapted methods previously developed by Machado and colleagues,[28] as described in another study.[11] We used the following parameter definitions: vaccine effectiveness against death (VE_d) for each respective

dose, where d is dose (first and second dose represent the primary series; third, fourth, and fifth doses represent the first, second, and third boosters), and proportion vaccinated ($PV_{d,t,w}$), with a given dose (including only those with no further doses) and given time since vaccination (t) in weeks in a specific calendar week (w). We calculated a separate vaccine effectiveness for each predominant VOC period (Alpha, Delta, or Omicron). Because there were no available vaccine effectiveness data for the fifth vaccine dose in the general population (studies were available for immunocompromised populations, which are not representative of our study population) during the Omicron period, we used the value of VE_4 Omicron as a proxy. We assumed, based on previous studies, that vaccine effectiveness declined by 0·25% every week since vaccination, regardless of dose.[29] Booster doses (denoted by VE_3 to VE_5) were administered from June, 2021. The formula we used to calculate the weekly number of lives saved by CAT, VOC period, dose, and age group is given in equations 1–4.

$$\text{Number lives saved}_{d,w} = \text{Deaths observed}_{w} \times \frac{\sum_{t=1}^{t_{max}} (1(t>\text{lag}_d)0{\cdot}9975^{t-\text{lag}_d-1} VE_d PV_{d,t,w} + 1(t\leq\text{lag}_d) VE_{d-1} PV_{d,t,w})}{1-\sum_{t=1}^{t_{max}}\sum_{d=1}^{5}(1(t>\text{lag}_d)0{\cdot}9975^{t-\text{lag}_d-1} VE_d PV_{d,t,w} + 1(t\leq\text{lag}_d) VE_{d-1} PV_{d,t,w})} \quad (1)$$

$$\text{Total number of lives saved}_{w} = \sum_{d=1}^{5} \text{Number of lives saved}_{d,w} \quad (2)$$

$$\text{Total expected deaths}_{w} = \text{Deaths observed}_{w} + \sum_{d=1}^{5} \text{Number of lives saved}_{d,w} \quad (3)$$

$$\text{Impact of vaccination programme} = \frac{\text{Total expected deaths} - \text{Total observed deaths}}{\text{Total expected deaths}} \quad (4)$$

To overcome the potential of unreported data in a certain week, we considered the number of deaths in a week as the rolling average (mean) number of deaths observed in the CAT over 3 consecutive weeks (the relevant week, the previous week, and the following week). For the 11 CAT that had no data on uptake for second or third boosters, we calculated an estimated weekly coverage using data from all other reporting CAT and assumed that the time to introduction of these doses was the mean time of the introduction of subsequent doses in all other CAT that reported data.

For each CAT, we estimated the cumulative expected COVID-19 mortality rate per 100 000 population had no vaccination occurred, as the sum of the observed deaths and of lives saved for each vaccine dose (equation 3). We estimated the impact of the vaccine programme on COVID-19 mortality, by age group and VOC, in each CAT, by calculating the percentage change (equation 4) between observed deaths and expected deaths.

We assumed the following time lags: reporting delay since death (1 week) and delay from vaccination to generation of immunoprotection against death of 2 weeks (first dose), 1 week (second dose),[30] and 1 week for each additional dose.[31]

Several simplifying assumptions were made when using these data parameters. First, we assumed that CAT used the same case definitions when reporting COVID-19 mortality to TESSy. We assumed that reporting delays were similar by time and place; and that vaccine effectiveness and waning immunity did not vary across vaccine brands, population groups, and previous infection status. We used the same vaccine effectiveness estimates across age groups. Lastly, to estimate the varying impact of age on the severity of infection, we also considered the case-fatality percentages per age group using the total number of reported infections and deaths.

We conducted our analyses in R (version 4.2.2) and the code to run the analysis is available on GitHub.

For the **code** see https://github.com/whocov/WHOEURO_COVID_lives_saved_by_vaccination

Sensitivity analyses

We performed eight sensitivity analyses to quantify uncertainty around the estimated number of lives saved. In the first two sensitivity analyses, we used the upper 95% CIs and lower 95% CIs from the inverse-variance weighted estimate pooling estimates as the vaccine effectiveness for sensitivity analysis 1 and sensitivity analysis 2, respectively. For sensitivity analysis 3 and sensitivity analysis 4, we increased the lag time by 1 week from receipt of vaccine dose to onset of immune protection (sensitivity analysis 3) and decreased the lag time by 1 week (sensitivity analysis 4). For sensitivity analysis 5, we decreased the weekly vaccine effectiveness waning to 0·1%, and for sensitivity analysis 6 we increased the weekly percentage waning to 0·7% using values described in Wu and colleagues.[29] For sensitivity analysis 7 and sensitivity analysis 8, we introduced an additional metric, previous infection, because this has been shown to reduce the risk of severe outcome after subsequent infection.[32] Previous infection could result in a reduction in vaccine effectiveness if vaccination uptake differs by previous infection. To take into account previous infection, we calculated weekly vaccine effectiveness as:

$$\text{Weighted mean of } (\alpha \times \text{seroprevalence} \times \text{VE}) + (1-\text{seroprevalence}) \times \text{VE}$$

where α represents the proportion decrease in vaccine effectiveness related to previous infection in the population, and seroprevalence represents seroprevalence estimates taken from published studies and updated over time when later seroprevalence estimates were available.[33,34] Both α (here a waning factor) and seroprevalence are proportions between zero and one. We used α values of 0·8 (sensitivity analysis 7) and 0·95 (sensitivity analysis 8).

Because these analyses used routinely reported anonymous data aggregated by broad age groups, ethical approval and informed consent were not required.

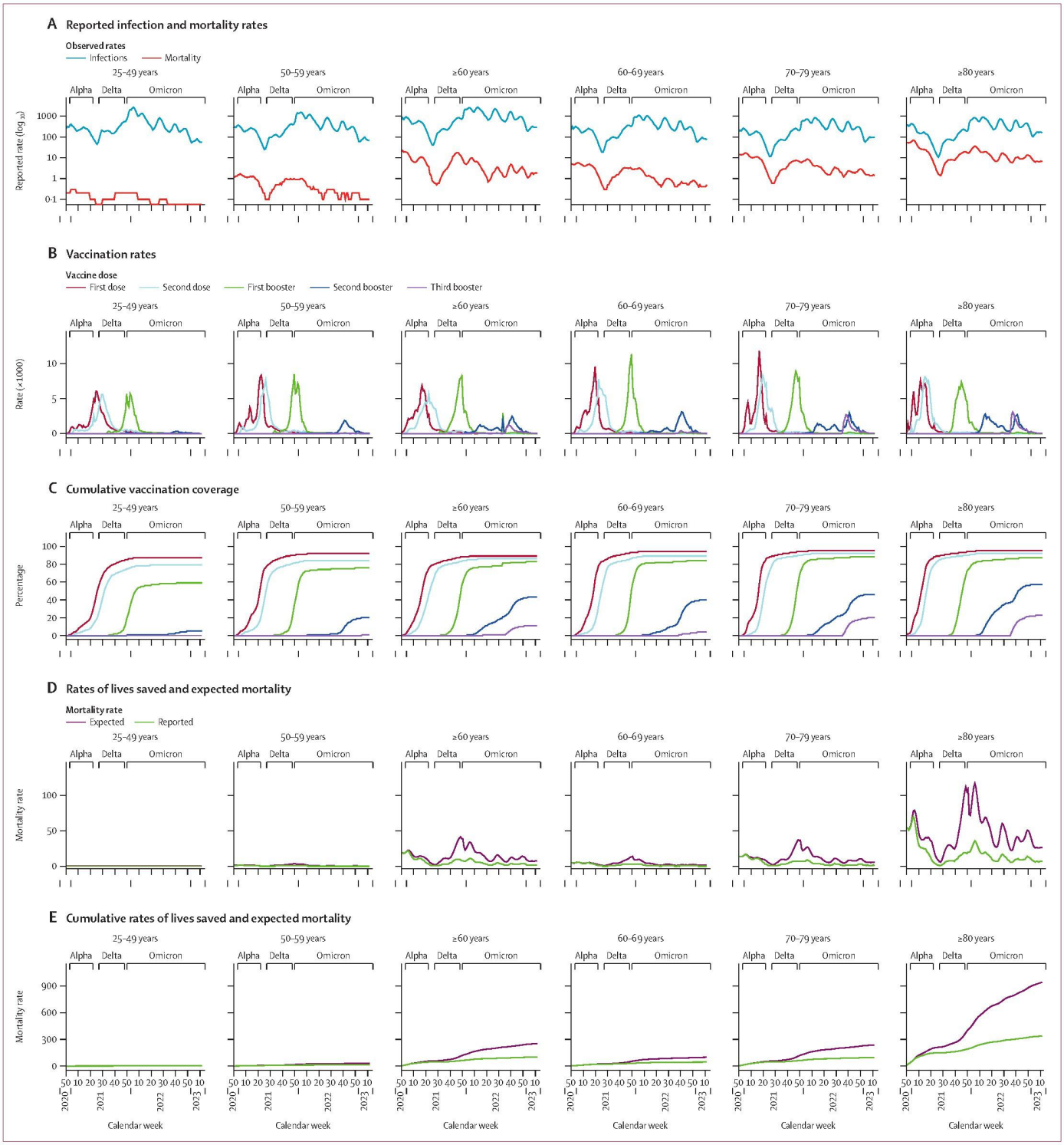

Figure 1: **Observed infection and mortality rates (A), vaccination rates (B), cumulative vaccination rates (C), rates of lives saved and expected mortality (D), and cumulative rates of lives saved and expected mortality (E), per age group and reporting week, from December, 2020, to March, 2023, in 34 CAT in the WHO European Region in the context of circulating variants of concern**

The ≥60 years group includes all countries reporting data for the 70–79 years and ≥80 years age groups, but also those countries reporting only ≥60 years data (Germany, Israel, Moldova, Ukraine, and the UK [Scotland]). All rates are per 100 000 general population and the age group ≥60 years includes data for 34 CAT. CAT=countries, areas, and territories.

	Index	Alpha	Delta	Omicron	Total
Aged 25–49 years (31 CAT)					
Reported mortality (rate per 100 000 general population)	3542 (3)	4218 (3)	5892 (4)	6179 (5)	19 831 (4)
Reported PVM	1771	603	982	386	..
Expected mortality (rate per 100 000 general population)	3542 (3)	4561 (3)	13 572 (10)	15 645 (12)	37 320 (7)
Expected PVM	1771	652	2262	978	..
Lives saved	0	343	7680	9466	17 489 (47%)*
Lives saved PVM	0	49	1280	592	..
Aged 50–59 years (31 CAT)					
Reported mortality (rate per 100 000 general population)	8326 (15)	10 285 (18)	9968 (18)	12 209 (21)	40 788 (18)
Reported PVM	4163	1469	1661	763	..
Expected mortality (rate per 100 000 general population)	8326 (15)	11 980 (21)	28 749 (51)	35 676 (63)	84 731 (38)
Expected PVM	4163	1711	4792	2230	..
Lives saved	0	1695	18 781	23 467	43 943 (52%)*
Lives saved PVM	0	242	3130	1467	..
Aged ≥60 years (34 CAT)					
Reported mortality (rate per 100 000 general population)	234 087 (396)	213 942 (362)	183 547 (310)	371 970 (625)	1 003 546 (424)
Reported PVM	117 044	30 563	30 591	23 248	..
Expected mortality (rate per 100 000 general population)	234 087 (396)	340 055 (575)	653 247 (1104)	1 275 386 (2144)	2 502 775 (1056)
Expected PVM	117 044	48 579	108 874	79 712	..
Lives saved	0	126 113	469 700	903 416	1 499 229 (60%)*
Lives saved PVM	0	18 016	78 283	56 464	..
Aged 60–69 years (29 CAT)					
Reported mortality (rate per 100 000 general population)	24 384 (53)	25 720 (56)	22 694 (49)	31 036 (66)	103 834 (56)
Reported PVM	12 192	3 674	3782	1940	..
Expected mortality (rate per 100 000 general population)	24 384 (53)	31 171 (68)	73 763 (160)	99 894 (214)	229 212 (124)
Expected PVM	12 192	4453	12 294	6243	..
Lives saved	0	5451	51 069	68 858	125 378 (55%)*
Lives saved PVM	0	779	8512	4304	..
Aged 70–79 years (29 CAT)					
Reported mortality (rate per 100 000 general population)	47 306 (136)	49 801 (143)	36 119 (104)	70 509 (199)	203 735 (146)
Reported PVM	23 653	7114	6020	4407	..
Expected mortality (rate per 100 000 general population)	47 306 (136)	69 209 (199)	140 140 (402)	244 224 (689)	500 879 (358)
Expected PVM	23 653	9887	23 357	15 264	..
Lives saved	0	19 408	104 021	173 715	297 144 (59%)*
Lives saved PVM	0	2773	17 337	10 857	..
Aged ≥80 years (29 CAT)					
Reported mortality (rate per 100 000 general population)	103 161 (461)	95 929 (427)	59 111 (263)	195 930 (873)	454 131 (506)
Reported PVM	51 580	13 704	9852	12 246	..
Expected mortality (rate per 100 000 general population)	103 161 (461)	180 120 (801)	265 994 (1184)	716 582 (3192)	1 265 857 (1410)
Expected PVM	51 580	25 731	44 332	44 786	..
Lives saved	0	84 191	206 883	520 652	811 726 (64%)*
Lives saved PVM	0	12 027	34 480	32 541	..

(Table 2 continues on next page)

Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Using COVID-19 variant data, we defined the VOC periods for the WHO European Region: the Index period (referring to the wild-type virus; up to Jan 2, 2021), the Alpha period (Jan 3 to June 6, 2021), the Delta period (July 11 to Dec 5, 2021), and the Omicron period (Dec 13, 2021, to March 26, 2023).

During the full study period, 29 CAT reported 1 064 165 COVID-19-related deaths in people aged 25 years or older to TESSy; of these deaths, 454 131 (43%) were in people aged 80 years or older. By contrast, 40 788 (4%) and 19 831 (2%) of COVID-19-related deaths were in people aged 50–59 years and 25–49 years, respectively. Of the 34 CAT that reported data for people

	Index	Alpha	Delta	Omicron	Total
(Continued from previous page)					
Total (34 CAT)					
Reported mortality (rate per 100 000 general population)	245 955 (100)	228 445 (93)	199 407 (81)	390 358 (158)	1 064 165 (108)
Reported PVM	122 978	32 635	33 234	24 397	34 328
Expected mortality (rate per 100 000 general population)	245 955 (100)	356 596 (144)	695 568 (282)	1 326 707 (538)	2 624 826 (266)
Expected PVM	122 978	50 942	115 928	82 919	..
Lives saved	0	128 151	496 161	936 349	1 560 661 (59%)*
Lives saved PVM	0	18 307	82 694	58 522	..

Data are by variant period and age group in CAT in the WHO European Region, during the Index period (referring to the wild-type virus; up to Jan 2, 2021), the Alpha period (Jan 3 to June 6, 2021), the Delta period (July 11 to Dec 5, 2021), the Omicron period (Dec 13, 2021, to March 26, 2023), and the full study period. The group aged ≥60 years includes data for all 34 CAT. Total was calculated as the sum of age groups 25–49 years, 50–59 years, and ≥60 years. The duration of each VOC dominance is 2 months for the Index period, 7 months for the Alpha period, 6 months for the Delta period, and 16 months for the Omicron period. PVM=per variant month. VOC=variant of concern. *Data in brackets are percentage change in lives saved. CAT=countries, areas, and territories.

Table 2: **Number of reported and expected deaths from SARS-CoV-2 infection, and lives saved, cumulatively and PVM**

aged 60 years or older, there were 1 003 546 COVID-19-related deaths (figure 1A, table 2).

The overall cumulative mortality rate for all people aged 25 years or older was 108 per 100 000 population and 424 per 100 000 for those aged 60 years or older. The cumulative mortality rate was 506 per 100 000 population for people aged 80 years or older, 146 per 100 000 for those aged 70–79 years, and 56 per 100 000 for those aged 60–69 years (table 2). For people aged 50–59 years and 25–49 years, cumulative mortality rates were 18 per 100 000 population and 4 per 100 000 population, respectively. By contrast, of 141 849 598 reported SARS-CoV-2 infections of any severity, the highest numbers occurred in people aged 25–49 years (76 493 868 [54%] infections), and the lowest in people aged 80 years or older (8 187 517 [6%] infections). Only 26% (37 554 313) of reported infections occurred among adults aged 60 years or older (figure 1A).

When considering each VOC mortality per variant month (PVM), regardless of age, most reported deaths were during the Omicron period (390 358 deaths); however, the Delta period had the highest number of reported deaths PVM (33 234 deaths; table 2). When considering each age group in turn, for people aged 25–49 years, the highest number of reported deaths PVM was during the Delta period (982 deaths), whereas for people aged 80 years or older, the highest number of reported deaths PVM was during the Alpha period (13 704 deaths; table 2).

Administration of the first booster doses started around week 30, 2021 (July, 2021). Initially, older age groups were prioritised. In most CAT, younger individuals became eligible shortly thereafter and second booster doses became available for people in older age groups in March, 2022, in most but not all CAT (figure 1B, C). By the end of the full study period (mid-March, 2023), in the 34 CAT overall, total coverage in all adults aged 25 years or older was 87% for the primary vaccine series, 82% for the second dose, 71% for the first booster, 24% for the second booster, and 5% for the third booster (table 3). Coverage for people aged 60 years or older was 89%, 86%, 83%, 43%, and 11% for each respective dose; for people aged 80 years or older, coverage was 95%, 92%, 87%, 57%, and 23% for each respective dose. Across all CAT included in this analysis, coverage was consistently higher in older age groups compared with younger age groups; this difference was even more pronounced for booster doses (figure 1C, table 3).

We estimated that, during the full study period, for the 34 CAT overall, COVID-19 vaccination reduced deaths by 59% (1 560 661 lives saved of 2 624 826 expected deaths; CAT range 17% [16 860 of 98 975] to 82% [41 465 of 50 862]) in adults aged 25 years or older. This reduction represents at least 1 560 661 lives saved and a mortality risk reduction of 158 per 100 000 population (table 2, table 4). Among all adults aged 60 years or older, vaccination reduced mortality by 60% (1 499 229 lives saved of 2 502 775 expected mortalities; figure 1D, E). The majority (52%; 811 726 lives saved of 1 560 661 expected deaths) of the lives saved were in people aged 80 years or older, equivalent to a mortality risk reduction of 904 per 100 000 population (table 2). We found that vaccination reduced mortality by 59% among those aged 70–79 years, 55% among those aged 60–69 years, 52% in those aged 50–59 years, and 47% in those aged 25–49 years (table 2). In all age groups, the biggest impact PVM was during the Delta period, followed by the Omicron and Alpha periods (table 2).

Among adults aged 25 years or older vaccinated with three doses, an estimated 798 376 lives (51% of 1 560 661 lives) were saved. Among people aged 80 years or older vaccinated with three doses, 403 453 lives (of 811 726 lives), representing a 50% reduction in expected mortality. Among people aged 60 years or older vaccinated with three doses, mortality was reduced by an estimated 51% (769 469 of 1 499 229 lives). In those aged 25–49 years, two doses reduced mortality by 47% (8268 of 17 489 lives; table 3, figure 2).

In the analysis of lives saved by predominant VOC, vaccination saved the most lives (60%; 936 349 of 1 560 661 lives) during the Omicron period, which lasted

	Vaccine uptake	Alpha	Delta	Omicron	Total
Aged 25–49 years (31 CAT)					
First dose	110 256 355 (85%)	114 (6%)	1130 (60%)	645 (34%)	1889
Second dose	99 416 586 (77%)	229 (3%)	5673 (69%)	2366 (29%)	8268
First booster	74 448 707 (57%)	0	851 (12%)	6197 (88%)	7048
Second booster	6 603 769 (5%)	0	26 (9%)	258 (91%)	284
Third booster	157 866 (0%)	NA	NA	NA	0
Total	290 883 283	343 (2%)	7680 (44%)	9466 (54%)	17 489
Aged 50–59 years (31 CAT)					
First dose	50 488 396 (89%)	689 (19%)	1704 (48%)	1152 (32%)	3545
Second dose	46 419 517 (82%)	1006 (6%)	13 259 (78%)	2653 (16%)	16 918
First booster	41 658 728 (74%)	0	3818 (17%)	18 041 (83%)	21 859
Second booster	11 011 072 (19%)	0	0	1621 (100%)	1621
Third booster	299 132 (1%)	NA	NA	NA	0
Total	149 876 845	1695 (4%)	18 781 (43%)	23 467 (53%)	43 943
Aged ≥60 years (34 CAT)					
First dose	125 250 761 (89%)	43 940 (60%)	14 586 (20%)	14 271 (20%)	72 797
Second dose	120 814 004 (86%)	82 157 (22%)	241 463 (65%)	48 964 (13%)	372 584
First booster	116 303 048 (83%)	16 (0%)	213 592 (28%)	555 861 (72%)	769 469
Second booster	60 615 440 (43%)	0	59 (<1%)	183 324 (100%)	183 383
Third booster	16 096 607 (11%)	0	0	100 996 (100%)	100 996
Total	439 079 860	126 113 (8%)	469 700 (31%)	903 416 (60%)	1 499 229
Aged 60–69 years (29 CAT)					
First dose	42 317 982 (91%)	3064 (38%)	3000 (38%)	1934 (24%)	7998
Second dose	40 072 892 (86%)	2387 (6%)	32 898 (82%)	4917 (12%)	40 202
First booster	37 800 945 (81%)	0	15 171 (23%)	51 853 (77%)	67 024
Second booster	17 940 191 (39%)	0	0	9915 (100%)	9915
Third booster	1 774 343 (4%)	0	0	239 (100%)	239
Total	139 906 353	5451 (4%)	51 069 (41%)	68 858 (55%)	125 378
Aged 70–79 years (29 CAT)					
First dose	32 649 123 (93%)	8675 (55%)	3579 (23%)	3531 (22%)	15 785
Second dose	31 633 138 (90%)	10 733 (15%)	54 204 (75%)	7761 (11%)	72 698
First booster	30 445 716 (86%)	0	46 234 (28%)	117 347 (72%)	163 581
Second booster	15 971 781 (45%)	0	4 (<1%)	22 599 (100%)	22 603
Third booster	6 852 090 (19%)	0	0	22 477 (100%)	22 477
Total	117 551 848	19 408 (7%)	104 021 (35%)	173 715 (58%)	297 144
Aged ≥80 years (29 CAT)					
First dose	20 919 657 (95%)	29 327 (70%)	4816 (12%)	7461 (18%)	41 604
Second dose	20 369 102 (92%)	54 848 (31%)	94 761 (54%)	25 929 (15%)	175 538
First booster	19 255 453 (87%)	16 (<1%)	107 251 (27%)	296 186 (73%)	403 453
Second booster	12 680 841 (57%)	0	55 (<1%)	119 509 (100%)	119 564
Third booster	5 027 196 (23%)	0	0	71 567 (100%)	71 567
Total	78 252 249	84 191 (10%)	206 883 (25%)	520 652 (64%)	811 726
Total (34 CAT)					
First dose	285 995 512 (87%)	44 743 (57%)	17 420 (22%)	16 068 (21%)	78 231
Second dose	266 650 107 (82%)	83 392 (21%)	260 395 (65%)	53 983 (14%)	397 770
First booster	232 410 483 (71%)	16 (<1%)	218 261 (27%)	580 099 (73%)	798 376
Second booster	78 230 281 (24%)	0	85 (<1%)	185 203 (100%)	185 288
Third booster	16 553 605 (5%)	0	0	100 996 (100%)	100 996
Total	879 839 988	128 151 (8%)	496 161 (32%)	936 349 (60%)	1 560 661

Data are n or n (%). Vaccine uptake percentage was calculated as the number of doses administered (shown) divided by the population number of that age group (not shown). The ≥60 years age group includes data for all 34 CAT. The total is calculated as the sum of age groups 25–49 years, 50–59 years, and ≥60 years. CAT=countries, areas, and territories. NA=not applicable.

Table 3: **Total vaccine uptake and number of lives saved by COVID-19 vaccine dose, variant, and age group**

	Vaccine uptake, %				Number of lives							Mortality rate per 100 000		
	VU_2	VU_3	VU_4	VU_5	Reported deaths	Saved after d_1	Saved after d_2	Saved after d_3	Saved after d_4	Saved after d_5	Total saved	Reported	Total expected	Percentage change
Israel*	95	78	19	<1	9397	330	13 810	20 611	6689	25	41 465	195	1053	82%
UK (England)*†	93	82	41	25	174 800	30 977	75 495	191 013	68 116	83 640	449 241	325	1159	72%
Finland	91	77	41	18	8508	199	2389	8603	7449	2196	20 836	149	513	71%
Malta	90	84	23	3	504	2	319	668	237	0	1226	96	331	71%
UK (Scotland)	94	84	50	13	10 527	629	5180	13 377	4484	1716	25 386	262	895	71%
Denmark	93	84	56	1	7119	3	1689	11 288	3927	91	16 998	124	419	70%
Iceland	79	88	35	10	235	0	4	395	139	4	542	70	232	70%
Belgium	88	82	51	8	15 921	1192	7975	22 881	3030	1226	36 304	140	459	69%
Austria	82	74	30	1	17 218	1529	9107	19 238	2196	36	32 106	189	542	65%
Cyprus	84	73	15	3	1490	106	1058	1462	181	17	2824	175	506	65%
Spain	84	76	35	<1	70 258	3719	42 521	73 075	7758	13	127 086	145	407	64%
Luxembourg	77	72	23	<1	754	37	294	797	150	0	1278	125	337	63%
Netherlands	81	76	44	25	12 990	842	11 817	6840	1842	631	21 972	75	201	63%
Ireland	94	84	45	18	6002	210	2055	4285	2000	1021	9571	135	350	61%
Italy	88	88	19	2	131 583	11 423	43 723	124 296	22 572	1012	203 026	206	524	61%
Greece	81	72	17	3	33 445	2765	16 000	28 204	3393	411	50 773	303	762	60%
Portugal	84	85	48	7	21 347	2050	4937	17 421	4234	1766	30 408	190	462	59%
Germany*	90	85	39	8	135 420	4247	52 769	101 677	19 323	4972	182 988	554	1303	57%
France	90	78	27	6	98 828	5299	29 493	74 626	14 473	1841	125 732	149	339	56%
Sweden*	87	74	47	2	16 109	464	2833	7066	9415	203	19 981	158	353	55%
Switzerland*†	78	81	13	2	8681	366	3566	6307	336	91	10 666	99	222	55%
Estonia	69	49	13	<1	2633	182	1178	1363	128	0	2851	192	400	52%
Czechia	75	58	13	<1	33 292	2604	12 949	17 975	805	0	34 333	314	637	51%
Hungary	73	54	8	<1	41 228	1039	9313	24 436	1285	0	36 073	419	785	47%
Croatia*	68	39	3	1	18 469	1319	7771	5877	89	34	15 090	454	825	45%
Lithuania*	68	43	2	<1	8195	599	4141	2076	1	0	6817	283	518	45%
Slovenia*	63	44	6	1	7252	244	2135	3293	146	50	5868	333	602	45%
Latvia*	62	39	6	1	5659	828	1985	1242	6	0	4061	294	505	42%
Slovakia	60	44	2	<1	17 768	548	4097	4763	0	0	9408	334	511	35%
North Macedonia	60	15	1	<1	7592	181	2800	525	0	0	3506	433	632	31%
Kosovo‡	65	11	0	<1	1699	55	460	33	0	0	548	129	170	24%
Moldova*†	39	22	2	<1	5983	293	1141	276	0	0	1710	844	1085	22
Romania*	39	12	0	<1	51 144	1859	9962	1306	0	0	13 127	271	340	20%
Ukraine*†	38	55	27	<1	82 115	2091	12 804	1081	884	0	16 860	897	1081	17%
Total	83	74	29	7	1 064 165	78 231	397 770	798 376	185 288	100 996	1 560 661	246	606	59%

CAT have been ordered according to the proportion of lives saved. d_1 refers to first vaccine dose, d_2 refers to second doses, d_3 refers to first booster, d_4 refers to second booster, and d_5 refers to third booster. Data presented for Germany, Moldova, and Ukraine consider only the groups aged ≥60 years. CAT=countries, areas, and territories. VU=vaccine uptake. *Booster doses were not reported by the CAT for at least one age group and so were calculated using the mean percentage change in vaccination coverage from CAT with booster 2 and booster 3 data. †It was not possible to differentiate booster doses 2 and 3 from booster 1. We calculate the mean percentage change in vaccination coverage for booster 3 using the mean from booster 1 and booster2. ‡All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 adopted in 1999.

Table 4: **Cumulative vaccine uptake, number of deaths reported and lives saved, and reported and expected mortality rates per 100 000 population aged ≥25 years, by CAT, for week 50, 2020, to week 12, 2023**

for 16 months (*vs* 6 months for the Delta period), a mortality risk reduction of 380 per 100 000 population. During the Omicron period, vaccination reduced mortality by 64% in people aged 80 years or older (520 652 of 811 726 lives), and by 60% for all adults aged 60 years or older (903 416 of 1 499 229 lives; table 3).

In the analysis of lives saved by CAT, among all adults aged 25 years or older, vaccination reduced mortality by the largest proportion in Israel (82%; 41 465 of 50 862 lives), the UK (England; 72%; 449 241 of 624 041 lives), Finland (71%; 20 836 of 29 344 lives), Malta (71%; 1226 of 1730 lives), and the UK (Scotland; 71%; 25 386 of 35 913 lives; table 4). In the CAT analysis by age group, among people aged 80 years or older, vaccination reduced mortality most in the UK (England; 74%; 290 610 of 392 844 lives), followed by Malta (72%; 704 of 978 lives), Denmark (71%; 10 377 of 14 670 lives), and Finland (71%; 13 900 of 19 483 lives). For adults aged

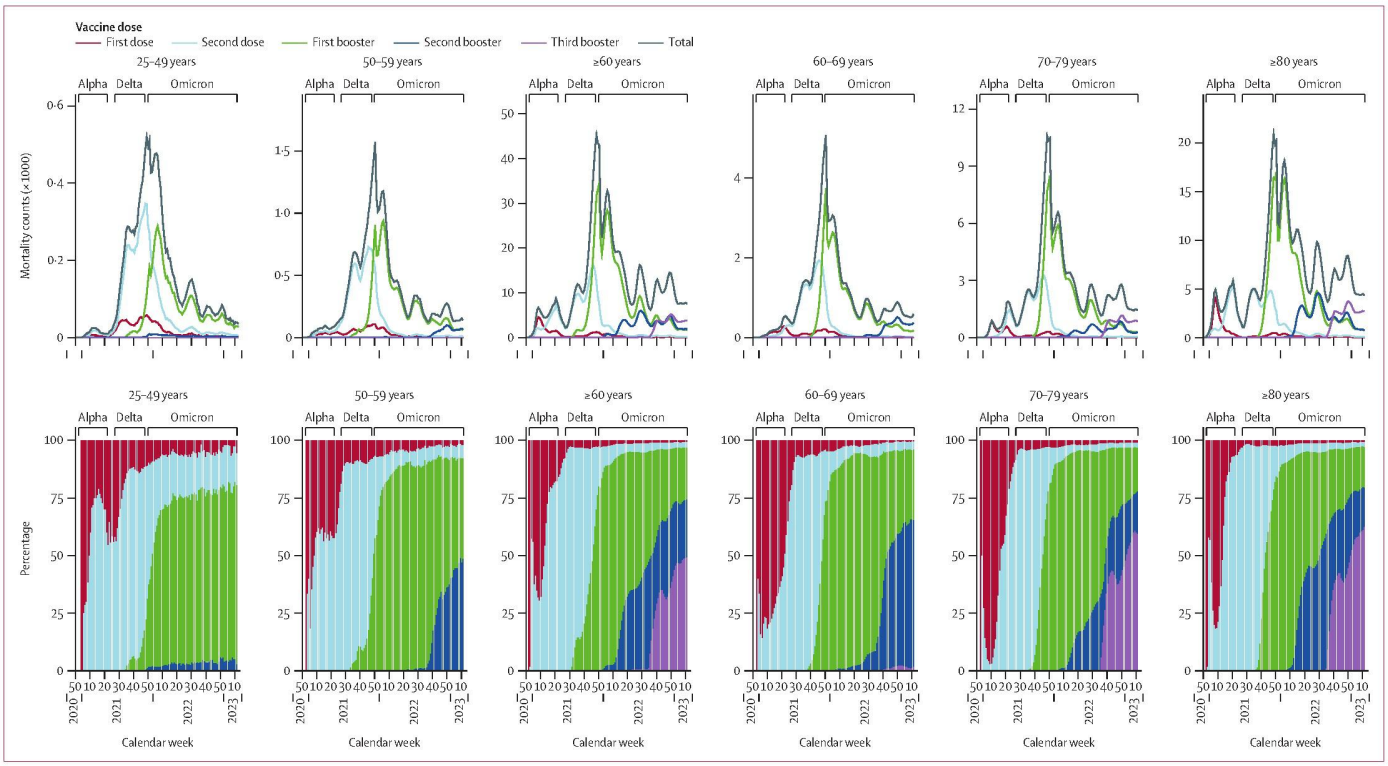

Figure 2: **Counts and percentage of estimated lives saved by number of vaccine doses received by age group, between week 50, 2020, and week 12, 2023, in 34 CAT in the WHO European Region**
Age groups 25–49 years and 50–59 years include data for 31 CAT, the ≥60 years age group includes data for 34 CAT, and the remaining age groups include data for 29 CAT. The ≥60 years group includes all countries reporting data for the 70–79 years and ≥80 years age groups, but also those countries reporting only ≥60 years data (Germany, Israel, Moldova, Ukraine, and the UK [Scotland]). CAT=countries, areas, and territories.

25–49 years, vaccination reduced mortality the most in Malta (67%; 28 of 42 lives), followed by Israel (66%; 513 of 783 lives), France (58%; 2393 of 4123 lives), and the UK (Scotland; 58%; 418 of 725 lives; appendix pp 19–26). Among adults aged 25–49 years, vaccination reduced mortality the least in Kosovo (13%; 18 of 103 lives), North Macedonia (22%; 110 of 506 lives), Romania (22%; 645 of 2928 lives), Slovakia (22%; 188 of 847 lives), and Slovenia (22%; 27 of 123 lives). Among people aged 80 years or older, the smallest reduction occurred in Romania (12%; 2148 of 17 341 lives), Kosovo (17%; 86 of 510 lives), and North Macedonia (28%; 727 of 2615 lives; appendix pp 22–30).

In CAT that reached at least 90% vaccine coverage in people aged 60 years or older by the early stages of the Delta period (Belgium, Denmark, Iceland, Ireland, Israel, Malta, the Netherlands, and the UK [England and Scotland]), the proportionate reduction in mortality was the highest. In these CAT, vaccination reduced deaths by more than 60% in people aged 25 years or older. Conversely, in CAT where vaccination coverage was lower than 50%, such as Romania, Moldova, and Kosovo, vaccination reduced deaths by 30% or less (appendix p 6).

In the subanalysis of the pre-Omicron period, which included 39 CAT, we estimated that 586 576 lives were saved among people aged 25 years or older (representing a 46% mortality risk reduction). For all adults aged 25 years or older, vaccination reduced mortality the most in Israel (84%; 28 309 of 33 583 lives), Norway (74%; 2729 of 3673), and Iceland (68%; 17 of 25 lives), whereas vaccination reduced mortality the least in Ukraine (13%; 10 002 of 76 213—among those aged ≥60 years only), Moldova (17%; 887 of 76 213 lives—among those aged ≥60 years only), and Romania (19%; 10 319 of 54 402 lives). In this analysis, among people aged 60 years or older 582 152 lives (99% of expected deaths) were saved, with 48% (277 144 lives) of all lives saved among people aged 80 years or older; of these lives, 68% were saved during the Delta period (190 272; appendix pp 31–46).

In the full analysis period, we estimated that 1 560 661 lives were saved by COVID-19 vaccination. When we used the highest vaccine effectiveness values (sensitivity analysis 1), we estimated that vaccination saved 1703 492 lives; when we used the lowest vaccine effectiveness values (sensitivity analysis 2), we estimated that vaccination saved 1456 357 lives. When we used shorter lag times (sensitivity analysis 3), we estimated that 1 517 019 lives were saved, whereas for longer lag times (sensitivity analysis 4), 1 587 960 lives were saved. When we used a longer vaccination waning time (sensitivity analysis 5), we estimated that 1 710 055 lives were saved, whereas a shorter vaccination waning time (sensitivity analysis 6) resulted in

1 223 641 lives saved. When we adjusted for a higher level of previous immunity (sensitivity analysis 7), we found that vaccination saved 1 127 226 lives (appendix p 59). When we assumed a lower level of previous immunity (sensitivity analysis 8), we estimated that vaccination saved 1 425 835 lives. Detailed results are presented in the appendix (pp 60–74).

Discussion

We found that, over nearly 2·5 years of the pandemic, COVID-19 vaccination programmes across 34 CAT of the WHO European Region reduced COVID-19 mortality by an estimated 59%, saving approximately 1·6 million lives. In the 34 CAT, the number of lives saved ranged from 542 to 449 241, and mortality was reduced from 17% to 82% by CAT. To our knowledge, our study is the first to estimate the number of lives saved from COVID-19 vaccination in the WHO European Region during a period that encompasses nearly the entire pandemic period, underscores the important role that COVID-19 vaccines have played in reducing mortality, and adds to previous studies in Europe[11] and globally[8] that have described the profound impact vaccination programmes have had in mitigating the effects of the COVID-19 pandemic.

Our study findings are consistent with those from other studies that have described lives saved from vaccination during the pandemic, including our previous article,[11] in which we estimated that COVID-19 vaccination reduced COVID-19 mortality in Europe by 51% in the first 12 months of the pandemic. A study of the global impact of the first year of vaccination found that vaccination had decreased mortality by 63% globally.[8,35] A modelling study of potential COVID-19-related averted deaths in low-income and lower-middle-income countries estimated that 1·5 million lives could have been saved in 2022, when Omicron started to circulate, were vaccination to be scaled up in these countries.[36] Another study considering 27 African countries showed that by vaccinating early, countries would have saved the most lives, showing the importance of vaccine availability and quick dissemination and administration, a key aim of the COVAX programme.[37]

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Our study findings highlight that even during the Omicron period, when the severity of infections decreased relative to earlier periods of previous VOC circulation,[9] COVID-19 vaccines still substantially reduced mortality. We found that most lives (60%) were saved during the Omicron period, the longest VOC period, when Omicron BA.1 and BA.2 began to circulate widely despite already high vaccination coverage. Widespread infections occurred during the Omicron period probably because of a combination of the scarcity of immunity, waning immunity against infection, and the highly transmissible nature of the virus. This high level of infection added to the level of population immunity to provide hybrid immunity, resulting in a reduction in infection severity.[38] Our findings reflect the ongoing effectiveness of COVID-19 vaccination in protecting against severe disease during this period of Omicron circulation when infection rates were extremely high, even with this reduction in infection severity.

We found the highest impact of vaccination was in adults aged 60 years or older, with 96% of all COVID-19-averted deaths by vaccine in 34 CAT shown in this age group, even though only 26% of reported infections in adults occurred in people in this age group. Similarly, adults aged 80 years or older accounted for 52% of all lives saved through vaccination, whereas only 6% of reported SARS-CoV-2 infections occurred in this age group. Other studies have found that COVID-19 vaccines have disproportionately saved the lives of older adults, with similar proportions of lives saved in those aged 60 years or older, ranging from 70% to 90%.[3,5,10,11]

In our analysis, the first three doses (primary course plus booster) had an important role in saving lives: the first two doses gave high protection against severe disease and the first booster addressed the issue of waning of protection as the 2021–22 winter period approached. Overall, within those who had received all three doses, an estimated 769 469 deaths in adults aged 60 years or older were prevented, which was the majority of lives saved during the period of this analysis. The latest Strategic Advisory Group of Experts (SAGE) recommendations for COVID-19 vaccination in the context of Omicron and high population immunity, recommends at least yearly vaccination in people aged 60 years or older.[39] This message is particularly urgent at a time when SARS-CoV-2 still continues to circulate and cause morbidity and mortality across the WHO European Region (as reported in the European Respiratory Virus Surveillance Summary) over 12 months after the declaration of the end of the Public Health Emergency of International Concern (PHEIC) by WHO,[40] with recent booster uptake concerningly low, particularly among high-risk groups.[7]

The strengths of this study include the availability of weekly, age-stratified data from the majority of CAT within the same geographical region. The temporal granularity of these data allowed us to understand the weekly evolution of the COVID-19 pandemic. CAT reported data to TESSy using a common reporting protocol with standardised definitions, allowing for comparisons between CAT, between age groups, and during different phases of the pandemic. Additionally, by using the number of reported deaths for our calculations, the indirect impact of the introduction of public health and social measures and measures to reduce transmission and mortality were already incorporated. Lastly, when comparing our vaccine effectiveness estimates against those from meta-analyses that considered severe events (such as hospitalisations and death),[29,41,42] for both primary series and booster doses, as well as when considering VOC in turn we found similar estimates of effectiveness against death.

As in our previous analysis,[11] our work has several limitations around complete adjustment for confounders, validity of the underlying data, and a few aspects of our methodology. First, regarding confounders, we were not able to adjust for the effects of health-care system capacities, sociodemographic variations such as deprivation and ethnicity, or the use of antivirals and other medication on mortality. Second, we were not able to stratify vaccine effectiveness by vaccine type, brand, age group, or infection status. We were also not able to differentiate the extent of waning immunity after vaccination disaggregated by dose. Moreover, we were not able to adjust for reporting biases (eg, under-reporting probably occurred early in the pandemic due to scarcity of tests available and later due to unreported self-testing). There was variability in the sensitivity of surveillance by CAT that we could not account for, and we could not account for any over-reporting because of potential misclassification of deaths later in the pandemic when vaccine escape became more widespread, although CAT were asked to report only deaths attributed to COVID-19 that were not otherwise explained. CAT in the Eastern part of the WHO European Region were more likely to have under-reported their COVID-19 mortality counts;[3] therefore, the true number of lives saved by vaccination in these CAT is probably higher than what we estimated. Furthermore, we attempted to address the role of previous infections in our sensitivity analysis by varying vaccine effectiveness against mortality (sensitivity analysis 1 and sensitivity analysis 2) and varying presumed levels of previous infection (sensitivity analysis 7 and sensitivity analysis 8), particularly to account for widespread vaccine escape that occurred during the Omicron period. These sensitivity analyses aimed to consider possible differential susceptibility linked to changes in vaccine uptake according to previous infection history and potentially less virulent VOC,[43] although we assumed that our base approach took this into account by using the observed mortality rates and vaccine effectiveness. Finally, we assumed that data reporting was limited among CAT both in terms of reporting delays and methodology (including whether deaths were caused by or with SARS-CoV-2 infection) and that vaccination intervals between doses were similar. Data for the fifth and the fourth vaccination doses were not always available and had to be calculated for some CAT. Based on meta-analyses estimating the vaccine effectiveness against severe disease for Omicron, the VE_3 for Omicron used in this analysis was probably low, thereby resulting in a conservative estimate of the number of lives saved. Variant periods were calculated differently in our methodology, with predominance determined by ≥50% of weekly sequences of a given VOC, compared with studies calculating predominance at 70% or higher of weekly sequences. We calculated vaccination coverage data using number of doses as reported to WHO by CAT, and this reporting method might have varied among CAT due to the diverse vaccines and dose regimens used across the WHO European Region.

In conclusion, over nearly 2·5 years, most lives saved by vaccination in the WHO European Region were in older adults (≥60 years), who had received three doses, and during the Omicron period, reinforcing the importance of up-to-date vaccination among the most at-risk individuals. Further modelling work should evaluate indirect effects of vaccination and public health and social measures.

Contributors

MMIM contributed to data curation, formal analysis, methodology, writing of the original draft, and reviewed and edited the manuscript. JB contributed to formal analysis, methodology, validation, writing of the original draft, and reviewed and edited the manuscript. PM contributed to methodology, writing of the original draft, and reviewed and edited the manuscript. MAK, JH, RPa, and DN contributed to methodology and reviewed and edited the manuscript. M-AW contributed to methodology, reviewed and edited the manuscript, and was involved in the decision to submit the manuscript. RPo contributed to conceptualisation, funding acquisition, methodology, validation, writing of the original draft, reviewed and edited the manuscript, and was involved in the decision to submit the manuscript. All other authors were involved in data curation and reviewed and edited the manuscript.

Declaration of interests

GD reports that the predecessor of the organisation he works for, Public Health England, received an unrestricted grant from GSK to undertake a study on the outcome of patients who received parenteral zanamavir. The funder received data and interim reports from Public Health England but did not influence analysis and reporting of the study. GD had no involvement in the GSK-funded study on parenteral zanamavir. Furthermore, the currently submitted work was part of the public health response activities to COVID-19 and had no relationship to GSK or the study on parenteral zanamivir. EP has received a personal grant from the Finnish Medical Foundation for PhD studies. JM declares that Public Health Scotland received funding from the EU Horizon 2020 programme for work in describing the epidemiology of COVID-19 and its impact on primary and secondary care as a partner in the IMOVE-COVID-19 project. MK declares having received consulting fees from Gilead Sciences for advising on development of a clinical module for collection of patient-reported outcome data from people living with HIV, and having received an honoraria from GESIDA for speaking at an annual conference on patient-reported outcome measures for people with HIV. All other authors declare no competing interests.

Data sharing

Data aggregated by week, age group, or country, area, or territory can be provided upon request to the corresponding author. Data from The European Surveillance System (TESSy) will be provided according to data access provisions laid out at https://www.ecdc.europa.eu/en/publications-data/european-surveillance-system-tessy.

Acknowledgments

The authors affiliated with WHO are alone responsible for the views expressed in this publication and they do not necessarily represent the decisions or policies of the WHO. This work was supported by a US Centers for Disease Control and Prevention cooperative agreement (grant number 6 NU511P000936–02–020). We gratefully acknowledge the input and feedback from colleagues at the European Centre for Disease Prevention and Control (ECDC)—namely, Nathalie Nicolay, Nick Bundle, Sabrina Bacci, and Edoardo Colzani—and the input of national public health staff involved in surveillance activities and data submission to TESSy. The authors would like to thank all the countries, areas, and territories for the provision of mortality and vaccination data, including: Czechia (Jiri Jarkovsky, Helena Jirincova, Pavel Slezak, Timotej Suri, Iva Vlckova, and Jan Zofka, of the National Institute of Public Health); France (Anna Maisa, of Santé Public France); Germany

(Felix Günther and Frank Sandmann, of the Robert Koch Institute, Berlin, Germany, for helpful discussions and comments); Israel (Rivka Rich and Noy Pardo, of the Israel Ministry of Health); Italy (Antonino Bella, Andrea Cannone, Martina Del Manso, Massimo Fabiani, Anna Teresa Palamara, Daniele Petrone, Patrizio Pezzotti, and Marco Tallon, of Istituto Superiore di Sanità); Luxembourg (Dritan Bejko, Bruno Consbruck, Corinna Ernst, and Guy Weber, of Ministère de la Santé et de la Sécurité Sociale); the Netherlands (Rijksinstituut voor Volksgezondheid en Milieu); Portugal (Maria Leonor Caleiro, Pedro Casaca, and Eugénia Fernandes, of Directorate-General of Health); Spain (Epidemiological Surveillance and Vaccination Departments of Autonomous Communities); Switzerland (Federal Office of Public Health, Bern); the UK (England: Colin Campbell, of the UK Health Security Agency); and the UK (Scotland; Ross Phillips, of Public Health Scotland).

References

1 WHO Regional Office for Europe. COVID-19 weekly epidemiological update (edition 147). 2023. https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---15-june-2023 (accessed June 21, 2023).

2 WHO. 14·9 million excess deaths associated with the COVID-19 pandemic in 2020 and 2021. 2022. https://www.who.int/news/item/05-05-2022-14.9-million-excess-deaths-were-associated-with-the-covid-19-pandemic-in-2020-and-2021 (accessed May 13, 2022).

3 Marron L, Mateo-Urdiales A, O'Donnell J, Robinson E, Domegan L. The impact of the COVID-19 vaccination programme on symptomatic and severe SARS-CoV-2 infection during a period of Omicron variant dominance in Ireland, December 2021 to March 2023. *Euro Surveill* 2024; **29:** 2300697.

4 Bonanad C, García-Blas S, Tarazona-Santabalbina F, et al. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. *J Am Med Dir Assoc* 2020; **21:** 915–18.

5 Umeh C, Watanabe K, Tuscher L, Ranchithan S, Gupta R. Comparison of clinical characteristics and outcomes of COVID-19 between young and older patients: a multicenter, retrospective cohort study. *Cureus* 2022; **14:** e21785.

6 Aburto JM, Schöley J, Kashnitsky I, et al. Quantifying impacts of the COVID-19 pandemic through life-expectancy losses: a population-level study of 29 countries. *Int J Epidemiol* 2022; **51:** 63–74.

7 WHO Regional Office for Europe. WHO/Europe COVID-19 vaccine programme monitor. 2023. https://worldhealthorg.shinyapps.io/EURO_COVID-19_vaccine_monitor (accessed June 26, 2023).

8 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:** 1293–302.

9 WHO Regional Office for Europe. Interim recommendations on COVID-19 vaccination in autumn 2022 for the WHO European Region: conclusions and recommendations of the European Technical Advisory Group of Experts on Immunization. Copenhagen: WHO Regional Office for Europe, 2022.

10 Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. *BMJ* 2021; **373:** n1088.

11 Meslé MM, Brown J, Mook P, 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. *Euro Surveill* 2021; **26:** 2101021.

12 Hauser A, Counotte MJ, Margossian CC, et al. Estimation of SARS-CoV-2 mortality during the early stages of an epidemic: a modeling study in Hubei, China, and six regions in Europe. *PLoS Med* 2020; **17:** e1003189.

13 Nyberg T, Ferguson NM, Nash SG, 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:** 1303–12.

14 Kislaya I, Machado A, Magalhães S, et al. COVID-19 mRNA vaccine effectiveness (second and first booster dose) against hospitalisation and death during Omicron BA.5 circulation: cohort study based on electronic health records, Portugal, May to July 2022. *Euro Surveill* 2022; **27:** 2200697.

15 United Nations Department of Economic and Social Affairs Population Division. World Population Prospects 2022, Online edition. 2022. https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/wpp2022_summary_of_results.pdf (accessed May 3, 2023).

16 Eurostat. Population on 1 January by age and sex. 2023. https://ec.europa.eu/eurostat/databrowser/product/view/demo_pjan (accessed May 2, 2023).

17 Statistics Estonia. RV021: population by sex and age group, 1 January. 2020. https://andmed.stat.ee/en/stat/rahvastik__rahvastikunaitajad-ja-koosseis__rahvaarv-ja-rahvastiku-koosseis/RV021 (accessed May 3, 2023).

18 Instituto Nazionale di Statistica. Resident population by gender, age and marital status as of 1 January 2022. 2023. https://demo.istat.it/ (accessed April 12, 2023).

19 National Statistics Office, Malta. Census of Population and Housing 2021: Final report: Population, migration and other social characteristics (volume 1). 2023. https://nso.gov.mt/wp-content/uploads/Census-of-Population-2021-volume1-final.pdf (accessed April 12, 2023).

20 State Statistical Office, North Macedonia. State Statistical Office, Census of Population, Households and Dwellings, 2021. 2022. https://www.stat.gov.mk/PrikaziSoopstenie_en.aspx?rbrtxt=146 (accessed April 12, 2023).

21 Statistics Poland. Population 2022. 2023. https://stat.gov.pl/en/topics/population/population/demographic-situation-in-poland-up-to-2022,13,3.html (accessed May 10, 2023).

22 Statistics Portugal. Annual average resident population (long series, start 1971 - no.) by sex and age; annual. 2023. https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_indicadores&indOcorrCod=0002721&contexto=bd&selTab=tab2&xlang=en (accessed April 28, 2023).

23 Official Statistics of Sweden. Population statistics 2022. 2023. https://www.statistikdatabasen.scb.se/pxweb/en/ssd/START__BE__BE0101__BE0101A/BefolkningR1860N/table/tableViewLayout1/ (accessed May 3, 2023).

24 Federal Statistical Office. Resident population by age group, 2021. 2023. https://www.bfs.admin.ch/bfs/en/home/statistics/catalogues-databases/tables.assetdetail.24885268.html (accessed April 27, 2023).

25 Office for National Statistics. Estimates of the population for the UK, England, Wales, Scotland and Northern Ireland. 2022. https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland (accessed May 16, 2023).

26 Kosovo Agency of Statistics. Kosovo Agency of Statistics. 2022. https://ask.rks-gov.net/ (accessed May 22, 2023).

27 International Vaccine Access Center (IVAC), Johns Hopkins Bloomberg School of Public Health. 2016. https://view-hub.org/vaccine/covid/effectiveness-studies (accessed May 31, 2023).

28 Machado A, Mazagatos C, Dijkstra F, 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. *Euro Surveill* 2019; **24:** 1900268.

29 Wu N, Joyal-Desmarais K, Ribeiro PAB, et al. Long-term effectiveness of COVID-19 vaccines against infections, hospitalisations, and mortality in adults: findings from a rapid living systematic evidence synthesis and meta-analysis up to December, 2022. *Lancet Respir Med* 2023; **11:** 439–52.

30 Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 Vaccine. *N Engl J Med* 2020; **383:** 2603–15.

31 Gilboa M, Regev-Yochay G, Mandelboim M, et al. Durability of immune response after COVID-19 booster vaccination and association with COVID-19 Omicron infection. *JAMA Netw Open* 2022; **5:** e2231778.

32 Silva ARD Jr, Villas-Boas LS, Tozetto-Mendoza TR, et al. Generation of neutralizing antibodies against Omicron, Gamma and Delta SARS-CoV-2 variants following CoronaVac vaccination. *Rev Inst Med Trop São Paulo* 2022; **64:** e19.

33 Bobrovitz N, Ware H, Ma X, et al. Protective effectiveness of previous SARS-CoV-2 infection and hybrid immunity against the omicron variant and severe disease: a systematic review and meta-regression. *Lancet Infect Dis* 2023; **23:** 556–67.

34 Bergeri I, Whelan MG, Ware H, et al. Global SARS-CoV-2 seroprevalence from January 2020 to April 2022: a systematic review and meta-analysis of standardized population-based studies. *PLoS Med* 2022; **19:** e1004107.

35 Yang J, Vaghela S, Yarnoff B, et al. (2022). Estimated global public health and economic impact of COVID-19 vaccines in the pre-omicron era using real-world empirical data. *Expert Rev Vaccines* 2023; **22:** 54–65.

36 Savinkina A, Bilinski A, Fitzpatrick M, et al. Estimating deaths averted and cost per life saved by scaling up mRNA COVID-19 vaccination in low-income and lower-middle-income countries in the COVID-19 Omicron variant era: a modelling study. *BMJ Open* 2022; **12:** e061752.

37 Liu Y, Procter SR, Pearson CAB, et al. Assessing the impacts of COVID-19 vaccination programme's timing and speed on health benefits, cost-effectiveness, and relative affordability in 27 African countries. *BMC Med* 2023; **21:** 85.

38 WHO Regional Office for Europe. Guidance on developing national COVID-19 vaccination policy and integrating COVID-19 vaccination into national immunization programmes and broader health care delivery mechanisms in the WHO European Region: August 2023. Copenhagen: WHO Regional Office for Europe, 2023.

39 WHO. WHO roadmap on uses of COVID-19 vaccines in the context of Omicron and high population immunity. Geneva: World Health Organization, 2023.

40 WHO. Statement on the fifteenth meeting of the IHR (2005) Emergency Committee on the COVID-19 pandemic. World Health Organization. 2023. https://www.who.int/news/item/05-05-2023-statement-on-the-fifteenth-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-coronavirus-disease-(covid-19)-pandemic (accessed July 26, 2024).

41 Pormohammad A, Zarei M, Ghorbani S, et al. Effectiveness of COVID-19 vaccines against Delta (B.1.617.2) variant: a systematic review and meta-analysis of clinical studies. *Vaccines (Basel)* 2022; **10:** 23.

42 Solante R, Alvarez-Moreno C, Burhan E, et al. Expert review of global real-world data on COVID-19 vaccine booster effectiveness and safety during the omicron-dominant phase of the pandemic. *Expert Rev Vaccines* 2023; **22:** 1–16.

43 Friis NU, Martin-Bertelsen T, Pedersen RK, et al. COVID-19 mortality attenuated during widespread Omicron transmission, Denmark, 2020 to 2022. *Euro Surveill* 2023; **28:** 2200547.