

# Estimated number of lives directly saved by COVID-19 vaccination programs in the WHO European Region, December 2020 to March 2023

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## 2 **Abstract**

3 **Background:** By March 2023, 54 countries, areas and territories (thereafter “CAT”) reported over 2.2  
4 million coronavirus disease 2019 (COVID-19) deaths to the World Health Organization (WHO) Regional  
5 Office for Europe (1). Here, we estimate how many lives were directly saved by vaccinating adults in the  
6 Region, from December 2020 through March 2023.

7 **Methods:** We estimated the number of lives directly saved by age-group, vaccine dose and circulating  
8 Variant of Concern (VOC) period, both regionally and nationally, using weekly data on COVID-19  
9 mortality and COVID-19 vaccine uptake reported by 34 CAT, and vaccine effectiveness (VE) data from  
10 the literature. We calculated the percentage reduction in the number of expected and reported deaths.

11 **Findings:** We found that vaccines reduced deaths by 57% overall (CAT range: 15% to 75%), representing  
12 ~1.4 million lives saved in those aged  $\geq 25$  years (range: 0.7 million to 2.6 million): 96% of lives saved  
13 were aged  $\geq 60$  years and 52% were aged  $\geq 80$  years; first boosters saved 51%, and 67% were saved  
14 during the Omicron period.

15 **Interpretation:** Over nearly 2.5 years, most lives saved by COVID-19 vaccination were in older adults by  
16 first booster dose and during the Omicron period, reinforcing the importance of up-to-date vaccination  
17 among these most at-risk individuals. Further modelling work should evaluate indirect effects of  
18 vaccination and public health and social measures.

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23 the WHO.

## 24 Research in context

### 25 Evidence before this study

26 Since first identified in late 2019, COVID-19 has caused disproportionately high mortality rates in older  
27 adults. With the rapid development and licensing of novel COVID-19 vaccines, immunization campaigns  
28 across the WHO European Region started in late 2020 and early 2021, initially targeting the most  
29 vulnerable and exposed populations, including older adults, people with comorbidities and healthcare  
30 professionals. Several studies have estimated the number of lives saved by COVID-19 vaccination, both  
31 at national and multi-country level in the earlier stages of the pandemic. However, only one multi-  
32 country study has assessed the number of lives saved beyond the first year of the pandemic, particularly  
33 when the Omicron variant of concern (VOC) circulated, a period when vaccination coverage was high in  
34 many countries, areas and territories (CAT), but COVID-19 transmission was at its highest.

### 35 Added value of this study

36 Here we quantified the impact of COVID-19 vaccination in adults by age-group, vaccine dose and period  
37 of circulation of VOC, across diverse settings, using real world data reported by 34 CAT in the WHO  
38 European Region for the period December 2020 to April 2023. We estimated that COVID-19 vaccination  
39 programs were associated with a 57% reduction (CAT range: 15% to 75%) in the number of deaths  
40 among the  $\geq 25$  years old, representing over 1.5 million lives saved (range: 0.7 million to 2.6 million) in 34  
41 European CAT during the first 2.5 years following vaccine introduction. The first booster saved the most  
42 lives (721,122 / 1,408,967, (57%) of all lives saved). The  $\geq 60$  years old age group accounted for 96% of  
43 the total lives saved (1,349,617 / 1,408,967) whereas the  $\geq 80$  years old age group represented 52% of  
44 the total lives saved (728,858 / 1,408,967 lives saved) and 67% of all lives were saved during the  
45 Omicron period (942,571 / 1,408,967).

### 46 Implications of all the available evidence

47 Our results reinforce the importance of up-to-date COVID-19 vaccination, particularly among older age-  
48 groups. Communication campaigns supporting COVID-19 vaccination should stress the value of COVID-  
49 19 vaccination in saving lives to ensure vulnerable groups are up-to-date with vaccination ahead of  
50 periods of potential increased transmission.

## 51 Main text

### 52 Introduction

53 From the beginning of the pandemic through March 2023, 2.2 million coronavirus disease 2019 (COVID-  
54 19) deaths were reported to the World Health Organization (WHO) Regional Office for Europe from the  
55 54 countries, areas and territories (CAT) in the WHO European Region (1). The true number of deaths  
56 directly or indirectly linked to COVID-19 is estimated to be even greater (2).

57 Throughout the COVID-19 pandemic, disproportionately higher mortality rates have been observed in  
58 older age-groups. Indeed a global review of publicly available data from 2020-2022 found that persons  
59 aged  $\geq 60$  years old accounted for over 80% of all COVID-19 fatalities (3), a pattern that has been  
60 consistently observed in other studies (4–6).

61 Since they were first introduced in late 2020, COVID-19 vaccines have been shown to be safe and highly  
62 effective in protecting against severe COVID-19 infection (7,8). In the European Region, since the first  
63 COVID-19 vaccines were administered (7,8), WHO has recommended that older age-groups be  
64 prioritized for COVID-19 vaccination (10). As of March 2023, 69% of people over  $\geq 60$  years in 49 CAT  
65 across the Region were reported to have received at least three doses of vaccine (7).

66 Previous studies have estimated the number of lives saved by COVID-19 vaccine in individual countries  
67 at various stages following the introduction of COVID-19 vaccination programs (4,5,11–15). We  
68 previously estimated that vaccination directly saved 469,186 lives among people  $\geq 60$  years old in 33  
69 countries in the first year of the vaccination program in Europe (12). Another study estimated the total  
70 number of lives saved by vaccine during 2021 in 185 countries and territories (8). Only one study (3), has  
71 estimated the number of lives saved beyond 2021 (analysis up to late 2022), despite the continued  
72 circulation of Severe Acute Respiratory Corona Virus 2 (SARS-CoV-2), and in particular the Variant of  
73 Concern (VOC), Omicron, in the two years since. We aimed to expand on our previous work by  
74 estimating the number of lives saved by COVID-19 vaccination in adults  $\geq 25$  years of age in the European  
75 Region from the beginning of vaccine introduction through March 2023, a period of 2.5 years. We  
76 stratified our results by age-group, predominant circulating VOC and vaccination dose and considered  
77 waning protection and prior infection in our analysis. Lastly, we aimed to understand the varying impact  
78 of infections by age group.

## 79        Methods

### 80        Data sources

81        We estimated lives saved during the study period using CAT-level COVID-19 surveillance data and  
82        vaccination coverage data from week 50/2020 (December 2020) to week 12/2023 (March 2023)  
83        (hereafter referred to as “the study period”).

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

90        We conducted our analysis in two parts. For the first part, we analyzed data from the full study period  
91        (week 50/2020 to week 12/2023, hereafter, the full study period) for which a defined minimum COVID-  
92        19 vaccination data set was available. We included data for six age groups (25-49, 50-59, ≥60, 60-69, 70-  
93        79 and ≥80 years) in both analyses. To be included in the analysis, CAT needed to have reported both  
94        mortality and vaccination data for at least one of the four older age-groups: ≥60, 60-69, 70-79 and ≥80.  
95        Only countries that reported weekly data for both vaccination and mortality by age-group for ≥90% of  
96        study weeks in the full study period were included. These data were available for 34/54 CAT <sup>1</sup>. The  
97        following CAT only reported mortality and vaccination data for people aged ≥60 years for the full study  
98        period: Germany (data were collected but could not be made available); the Republic of Moldova and  
99        Ukraine. Israel and United Kingdom (Scotland) were only able to report data by the following three age  
100        groups (25-49, 50-59 and ≥60 years) (Supplementary Table 1).

101        As a sub-analysis, we restricted our analysis to the pre-Omicron period (week 50/2020 to 50/2021),  
102        which allowed us to include an additional five CAT <sup>2</sup>) that had consistently reported data only during the

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<sup>1</sup> Austria, Belgium, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands (Kingdom of the), North Macedonia, Portugal, Republic of Moldova, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Ukraine, United Kingdom (England), United Kingdom (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 (1999)).

<sup>2</sup> Albania, Montenegro, Norway, Poland and United Kingdom (Wales).

103 early part of the pandemic or had experienced significant changes in reporting later in the course of the  
104 pandemic.

105 We estimated periods of VOC-predominant circulation by CAT using virological data reported to TESSy. If  
106 data were unavailable in TESSy, we downloaded data from the Global Initiative on Sharing All Influenza  
107 Data (GISAID) obtained from [CoVariants.org](https://covariants.org) (last accessed: November 2023). A VOC was deemed  
108 predominant in the Region or in a country if  $\geq 50\%$  of sequences per week were attributed to a given  
109 variant. Regionally and at a CAT level, we defined the start of each VOC period (Alpha, Delta and  
110 Omicron) as the first week of predominance, and the end of the VOC period as the week prior to the  
111 start of the following predominant VOC period. For CATs where variant data was unavailable (Albania,  
112 Republic of Moldova and Kosovo<sup>[1]</sup>), we estimated the start and end weeks of variant periods as the  
113 median start and end week of geographically neighboring CAT.

114 We downloaded population data for 2021 and 2022 from the United Nations (16) for non-EU/EEA CAT  
115 and from Eurostat (17) for EU/EEA countries, except for the following CATs, where more detailed  
116 population denominators were available: Estonia (18), Italy (19), Malta (20), North Macedonia (21),  
117 Poland (22), Portugal (23), Sweden (24), Switzerland (25), the United Kingdom (England, Scotland and  
118 Wales) (26) and Kosovo<sup>[1]</sup>(27).

119 To identify COVID-19 vaccine effectiveness (VE) studies that estimated VE against mortality by age-group  
120 and by VOC, we used the COVID-19 Study Explorer from International Vaccine Access Center (IVAC,  
121 <https://view-hub.org/vaccine/covid/effectiveness-studies>), Johns Hopkins Bloomberg School of Public  
122 Health (last accessed on 31<sup>st</sup> May 2023). We calculated an average VE against death per dose and VOC  
123 (summarized in Table 1), by calculating the average of VE estimates against death listed on the COVID-19  
124 Study Explorer. We only included VE estimates against death from studies that: were conducted in  
125 adults from the general population; used unvaccinated individuals as the reference group; were  
126 conducted in the WHO European Region or other high-income countries, including the United States,  
127 Canada, Australia and South Korea; and estimated VE by VOC. We excluded VE estimates from studies  
128 that only included people living in long-term care facilities, people with comorbidities,  
129 immunocompromised individuals, pregnant women, children and healthcare workers.

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[1] All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

130 Data analysis

131 To estimate the number of lives saved as a result of COVID-19 vaccination in each CAT, we adapted  
 132 methods previously developed by Machado *et al* (28), as described in Meslé *et al* (12). We used the  
 133 following parameter definitions: Vaccine Effectiveness against death ( $VE_{d,t}$ ) for each respective dose,  
 134 where d= dose (first dose, second dose, first booster dose, second booster dose and third booster dose)  
 135 and t= time since vaccination in weeks including a time lag from vaccination to immune protection  
 136 (described below); and Proportion Vaccinated ( $PV_{d,t}$ ) per week per dose (i.e. with no further doses by  
 137 that week). We calculated a separate VE for each predominant VOC period (Alpha, Delta or Omicron).  
 138 Because there were no available VE data for the first vaccine dose during the Omicron period, we used  
 139 the value  $VE_1$  Delta as a proxy. We assumed, based on previous studies, that VE declined by 0.25% every  
 140 week since vaccination, regardless of dose (29). Booster doses (denoted by  $VE_3$  to  $VE_5$ ) were  
 141 administered from June 2021. The formula we used to calculate the weekly number of lives saved by  
 142 VOC period, dose and age-group is given below (equations 1 – 3).

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

149

150 *Table 1: Summary of Vaccine Effectiveness (VE) values against mortality used in the analysis, according to circulating Variant of*  
 151 *Concern and dose. Please see Supplementary Table 6 regarding the underlying literature from which the average values below*  
 152 *were calculated. The ranges provided in brackets represent the values used for the sensitivity analyses. † Due to the absence of*  
 153 *data relating the  $VE_1$  (Omicron), the values from  $VE_1$  (Delta) were used. \*Due to the absence of data relating the  $VE_5$  (Omicron),*  
 154 *the values from  $VE_4$  (Omicron) were used*

Vaccine Effectiveness, after n doses:	Predominant circulating VOC		
	Alpha (B.1.1.7)	Delta (B.1.617.2)	Omicron (B.1.1.529)
N=1 ( $VE_1$ )	76% (min = 65%; max = 86%)	87% (min = 55%; max = 99%)	87%† (min = 55%; max = 99%)
N=2 ( $VE_2$ )	91% (min = 68%; max = 97%)	91% (min = 77%; max = 99%)	71% (min = 65%; max = 77%)
N=3 ( $VE_3$ )	-	95% (min = 89%; max = 98%)	81% (min = 59%; max = 95%)



N=4 (VE <sub>4</sub> )	-	-	83%
			(min = 74%; max = 91%)
N=5 (VE <sub>5</sub> )	-	-	83% *
			(min = 74%; max = 91%)

155

$$\text{Number lives saved}_{d,w} = \text{Deaths Observed}_w * \frac{\sum_{t=1}^{156} VE_{d,t} PV_{d,t}}{1 - \sum_{t=1}^{156} \sum_{d=1}^5 (VE_{d,t} PV_{d,t})} \quad (1)$$

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

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

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

156

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

162 We assumed the following time lags: reporting delay (one week); delay from vaccination to generation  
 163 of immunoprotection (four weeks (first dose), three weeks (second dose) (35), two weeks (first booster)  
 164 (30) and one week (for each additional booster) (31).

165 Several simplifying assumptions were made when using these data parameters. First, we assumed that  
 166 CATs used the same case definitions when reporting COVID-19 mortality to TESSy. We assumed that  
 167 reporting delays were similar by time and place; and that VE and waning immunity did not vary across  
 168 vaccine brands and population groups. Finally, we used the same VE estimates across age groups. Lastly,  
 169 we also considered the case-fatality percentages per age group using the total number of reported  
 170 infections and deaths.

171 We conducted our analyses in R version 4.2.2 (34); the code is available on GitHub.

## 172 Sensitivity analyses

173 We performed eight sensitivity analyses (SA) to quantify uncertainty around the estimated number of  
174 lives saved. In the first two sensitivity analyses, we used the maximum VE (SA1) and minimum VE (SA2)  
175 estimates identified through the results of the IVAC search. For the third and fourth SA, we increased  
176 the lag time by one week from receipt of vaccine dose to onset of immune protection (SA3) and  
177 decreased the lag time by one week (SA4). For the fifth SA (SA5), we decreased the weekly VE waning to  
178 0.1%, and for the sixth SA (SA6), we increased the weekly percent waning to 0.7%, using values  
179 described in Wu *et al* (29). Lastly, for SA7 and SA8, we introduced an additional metric – prior infection,  
180 since this has been shown to reduce the risk of severe outcome following subsequent infection (33).  
181 Prior infection could result in a reduction in VE if vaccination uptake differs by prior infection. To take  
182 into account prior infection, we calculated weekly VE as a weighted average of  
183  $(\alpha * \text{seroprevalence} * \text{VE}) + (1 - \text{seroprevalence}) * \text{VE}$  where alpha represents the proportion decrease in  
184 VE related to prior infection in the population, and Seroprevalence represents seroprevalence estimates  
185 taken from published studies and updated over time, when later seroprevalence estimates were  
186 available (34). Both alpha (here a waning factor) and seroprevalence are proportions between zero and  
187 one. We used Alpha values of 0.8 (SA7) and 0.95 (SA8).

## 188 Ethical considerations

189 Because this analysis utilized routinely reported anonymous data aggregated by broad age-groups, no  
190 ethical approval was required.

## 191 Results

### 192 Reported mortality

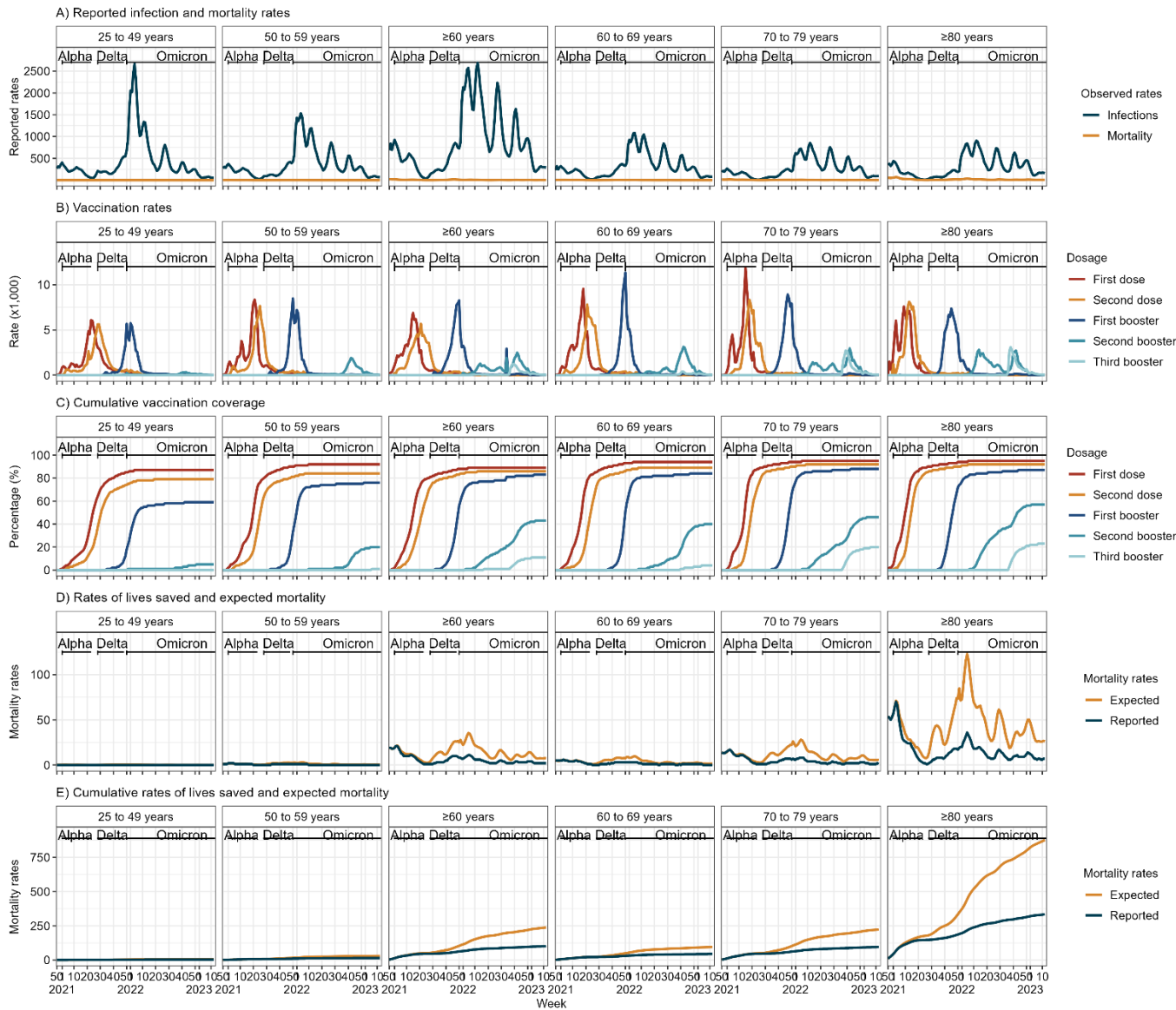
193 Using the variant data, we defined the following VOC periods for the Region: the Alpha period (3<sup>rd</sup>  
194 January to 6<sup>th</sup> June 2021, the Delta period (11<sup>th</sup> July to 5<sup>th</sup> December 2021) and lastly, the Omicron  
195 period (13<sup>th</sup> December 2021 to 26<sup>th</sup> March 2023).

196 Since the start of vaccination programs through March 2023, 29 CAT reported 1,050,501 COVID-19  
197 deaths in people aged  $\geq 25$  years to TESSy; of these deaths, 43% (n=447,600) were in people  $\geq 80$  years  
198 old. In contrast, only 4% and 2% of deaths were in people aged 50-59 and 25-49 years old, respectively.

199 Of the 34 CATs that reported data for people aged  $\geq 60$  years reported 990,881 deaths (Figure 1A, Table  
200 2).

201 The overall cumulative mortality rate for those aged  $\geq 25$  years was 109 per 100,000 population and 423  
202 per 100,000 for those aged  $\geq 60$  years. The cumulative mortality rate was 515 per 100,000 for people  
203 aged  $\geq 80$  years old, 147 per 100,000 population for 70-79 years old, 57 per 100,000 for 60-69 years old.  
204 For people aged 50-59 years and 25-49 years, cumulative mortality rates were 18 and 4 per 100,000  
205 population respectively. In contrast, reported infections of any severity were highest in people 25-49  
206 years old (9,355,861 / 153,978,991, 53%) and lowest in people aged  $\geq 80$  years old (9,355,861 /  
207 153,978,991, 6%). Only 27% (41,410,536 / 153,978,991) of reported infections occurred among adults  
208 aged  $\geq 60$  years (Figure 1A, Table 2).

209



210

211 *Figure 1: Summary of observed infection and mortality rates (A), vaccination rates (B), cumulative vaccination rates (C), rate of lives saved and expected mortality (D) and cumulative rate*  
 212 *of lives saved and expected mortality (E), per age-group in 34 CAT in the WHO European Region in context of circulating Variants of Concern (VOC) (black horizontal lines). Note: all rates*  
 213 *are per 100,000 general population and the ≥60 years age group includes data for 34 CAT.*

214 Table 2: Number of reported, expected deaths and lives saved, cumulatively and Per Variant Month (PVM) with number of countries, areas and territories (CAT) included in each  
 215 age group; from SARS-CoV-2 infection (rate per 100,000 general population) are shown in brackets, by variant-period and age-group, between weeks 50/2020 and 12/2023, in 34  
 216 CAT in the WHO European Region. Notes: the Index variant refers to the original circulating variant, or wild-type; the ≥60 years age group includes data for all 34 CAT; the Total is  
 217 calculated as the sum of 25-49, 50-59 and ≥60 years age groups. The duration of each VOC dominance is Index: 2 months; Alpha: 7 months; Delta: 6 months and Omicron: 16  
 218 months.

Age group in years (n CAT)	Mortality	Index	Alpha	Delta	Omicron	Total
25-49 (31 CAT)	Reported	3,482 (3)	4,157 (3)	5,763 (4)	6,148 (5)	19,550 (4)
	Reported PVM	1,741	594	960	384	
	Expected	3,482 (3)	4,321 (3)	12,563 (10)	15,914 (12)	36,280 (7)
	Expected PVM	1,741	617	2,094	995	
	Lives Saved	0	164	6,800	9,766	16,730
	Lives Saved PVM	0	23	1,133	610	
50-59 (31 CAT)	Reported	8,172 (15)	10,101 (18)	9,671 (17)	12,126 (21)	40,070 (18)
	Reported PVM	4,086	1,443	1,612	758	
	Expected	8,172 (15)	10,915 (19)	27,264 (48)	36,339 (64)	82,690 (37)
	Expected PVM	4,086	1,559	4,544	2,271	
	Lives Saved	0	814	17,593	24,213	42,620
	Lives Saved PVM	0	116	2,932	1,513	
≥60 (34 CAT)	Reported	231,295 (391)	211,184 (357)	179,111 (303)	369,291 (621)	990,881 (418)
	Reported PVM	115,648	30,169	29,852	23,081	
	Expected	231,295 (391)	266,882 (451)	564,438 (954)	1,277,883 (2,149)	2,340,498 (988)

<b>Age group in years (n CAT)</b>	<b>Mortality</b>	<b>Index</b>	<b>Alpha</b>	<b>Delta</b>	<b>Omicron</b>	<b>Total</b>
	Expected PVM	115,648	38,126	94,073	79,868	
	Lives Saved	0	55,698	385,327	908,592	1,349,617
	Lives Saved PVM	0	7,957	64,221	56,787	
	Reported	23,919 (52)	25,142 (54)	21,882 (47)	30,740 (66)	101,683 (55)
	Reported PVM	11,960	3,592	3,647	1,921	
60-69 (29 CAT)	Expected	23,919 (52)	27,535 (60)	67,142 (146)	101,544 (218)	220,140 (119)
	Expected PVM	11,960	3,934	11,190	6,346	
	Lives Saved	0	2,393	45,260	70,804	118,457
	Lives Saved PVM	0	342	7,543	4,425	
	Reported	46,408 (133)	48,858 (140)	34,692 (99)	69,794 (197)	199,752 (143)
	Reported PVM	23,204	6,980	5,782	4,362	
70-79 (29 CAT)	Expected	46,408 (133)	56,535 (162)	120,104 (344)	246,895 (697)	469,942 (336)
	Expected PVM	23,204	8,076	20,017	15,431	
	Lives Saved	0	7,677	85,412	177,101	270,190
	Lives Saved PVM	0	1,097	14,235	11,069	
	Reported	101,732 (454)	94,692 (421)	56,914 (253)	194,262 (865)	447,600 (498)
≥80 (29 CAT)	Reported PVM	50,866	13,527	9,486	12,141	
	Expected	101,732 (454)	133,231 (592)	229,979 (1,023)	711,516 (3,170)	1,176,458 (1,310)

<b>Age group in years (n CAT)</b>	<b>Mortality</b>	<b>Index</b>	<b>Alpha</b>	<b>Delta</b>	<b>Omicron</b>	<b>Total</b>
	Expected PVM	50,866	19,033	38,330	44,470	
	Lives Saved	0	38,539	173,065	517,254	728,858
	Lives Saved PVM	0	5,506	28,844	32,328	
	Reported	242,949 (98)	225,442 (91)	194,545 (79)	387,565 (157)	1,050,501 (106)
	Reported PVM	121,474	32,206	32,424	24,223	33,887
	Expected	242,949 (98)	282,118 (114)	604,265 (245)	1,330,136 (540)	2,459,468 (249)
	Expected PVM	121,474	40,303	100,711	83,134	
	Lives Saved	0	56,676	409,720	942,571	1,408,967
	Lives Saved PVM	0	8,097	68,287	58,911	
<b>Total (34 CAT)</b>						

220            **Vaccination roll-out**

221    Administration of the first booster doses started around week 30/2021 (July 2021). Initially, older age-  
222    groups were prioritized. In most CAT, younger individuals became eligible shortly thereafter and second  
223    booster doses became available for people in older age-groups in early 2022 (Figure 1Figure 1B, C). By  
224    the end of the analysis period (mid-March, 2023), in the 34 CAT overall, coverage in adults  $\geq 25$  years old  
225    was 87% for the primary vaccine series, 82% for the first booster, 71% for the first booster, 24% for the  
226    second booster and 5% for the third (Table 3)Table 2. Coverage for people aged  $\geq 60$  years was 89%,  
227    86%, 83%, 43% and 11% for each respective dose and for people aged  $\geq 80$  years was 95%, 92%, 87%,  
228    57% and 23% for each respective dose. Across all CATs included in this analysis, coverage was  
229    consistently higher in older age groups compared to younger age groups; this difference was even more  
230    pronounced for booster doses (Figure 1 and Table 2Table 2).

231



232 *Table 3: Total Vaccine Uptake (VU) and number of lives saved by COVID-19 vaccine dose, variant and age-group, and as percentage by Variant of Concern (VOC) period of total*  
 233 *lives saved in brackets, since the start of vaccinations in 34 countries, areas and territories (CAT) in the WHO European Region, with number of countries, areas and territories*  
 234 *(CAT) included in each age group. Notes: the ≥60 years age group includes data for all 34 CAT; the Total is calculated as the sum of 25-49, 50-59 and ≥60 years age groups.*

Age group in years (n CAT)	Dosage	VU (%)	Lives saved by variant and dose			
			Alpha	Delta	Omicron	Total
25-49 (31 CAT)	First dose	110,256,355 (85%)	59 (3%)	840 (49%)	829 (48%)	1,728
	Second dose	99,416,586 (77%)	105 (1%)	5,476 (69%)	2,374 (30%)	7,955
	First booster	74,448,707 (57%)	0 (0%)	469 (7%)	6,301 (93%)	6,770
	Second booster	6,603,769 (5%)	0 (0%)	15 (5%)	262 (95%)	277
	Third booster	157,866 (0%)	0 (-%)	0 (-%)	0 (-%)	0
	Total	290,883,283	164 (1%)	6,800 (41%)	9,766 (58%)	16,730
50-59 (31 CAT)	First dose	50,488,396 (89%)	321 (10%)	1,397 (44%)	1,430 (45%)	3,148
	Second dose	46,419,517 (82%)	493 (3%)	14,298 (82%)	2,542 (15%)	17,333
	First booster	41,658,728 (74%)	0 (0%)	1,898 (9%)	18,692 (91%)	20,590
	Second booster	11,011,072 (19%)	0 (0%)	0 (0%)	1,549 (100%)	1,549
	Third booster	299,132 (1%)	0 (-%)	0 (-%)	0 (-%)	0
	Total	149,876,845	814 (2%)	17,593 (41%)	24,213 (57%)	42,620
≥60 (34 CAT)	First dose	125,250,761 (89%)	21,973 (44%)	10,365 (21%)	17,316 (35%)	49,654
	Second dose	120,814,004 (86%)	33,716 (10%)	267,685 (76%)	48,754 (14%)	350,155
	First booster	116,303,048 (83%)	9 (0%)	107,243 (15%)	586,510 (85%)	693,762

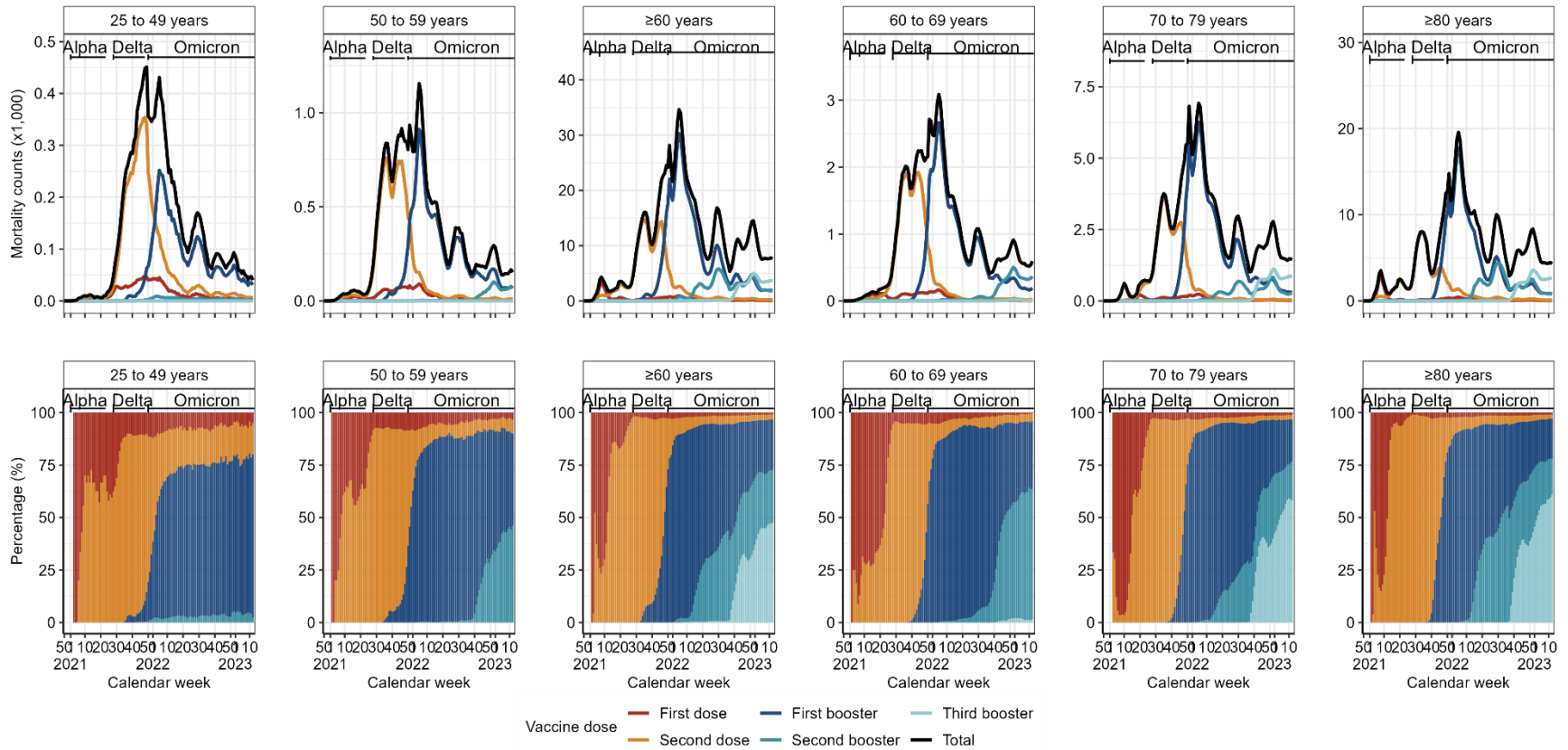
			Lives saved by variant and dose			
Age group in years (n CAT)	Dosage	VU (%)	Alpha	Delta	Omicron	Total
	Second booster	60,615,440 (43%)	0 (0%)	34 (0%)	166,379 (100%)	166,413
	Third booster	16,096,607 (11%)	0 (0%)	0 (0%)	89,633 (100%)	89,633
	Total	439,079,860	55,698 (4%)	385,327 (29%)	908,592 (67%)	1,349,617
60-69 (29 CAT)	First dose	42,317,982 (91%)	1,487 (24%)	2,397 (38%)	2,348 (38%)	6,232
	Second dose	40,072,892 (86%)	906 (2%)	36,206 (87%)	4,709 (11%)	41,821
	First booster	37,800,945 (81%)	0 (0%)	6,657 (11%)	54,266 (89%)	60,923
	Second booster	17,940,191 (39%)	0 (0%)	0 (0%)	9,265 (100%)	9,265
	Third booster	1,774,343 (4%)	0 (0%)	0 (0%)	216 (100%)	216
	Total	139,906,353	2,393 (2%)	45,260 (38%)	70,804 (60%)	118,457
70-79 (29 CAT)	First dose	32,649,123 (93%)	3,976 (36%)	2,762 (25%)	4,348 (39%)	11,086
	Second dose	31,633,138 (90%)	3,701 (5%)	60,621 (84%)	7,440 (10%)	71,762
	First booster	30,445,716 (86%)	0 (0%)	22,028 (15%)	123,937 (85%)	145,965
	Second booster	15,971,781 (45%)	0 (0%)	1 (0%)	21,341 (100%)	21,342
	Third booster	6,852,090 (19%)	0 (0%)	0 (0%)	20,035 (100%)	20,035
	Total	117,551,848	7,677 (3%)	85,412 (32%)	177,101 (66%)	270,190
≥80 (29 CAT)	First dose	20,919,657 (95%)	15,479 (55%)	3,660 (13%)	9,042 (32%)	28,181
	Second dose	20,369,102 (92%)	23,051 (14%)	112,698 (70%)	26,074 (16%)	161,823

			Lives saved by variant and dose			
Age group in years (n CAT)	Dosage	VU (%)	Alpha	Delta	Omicron	Total
	First booster	19,255,453 (87%)	9 (0%)	56,674 (15%)	313,385 (85%)	370,068
	Second booster	12,680,841 (57%)	0 (0%)	33 (0%)	105,763 (100%)	105,796
	Third booster	5,027,196 (23%)	0 (0%)	0 (0%)	62,990 (100%)	62,990
	Total	78,252,249	38,539 (5%)	173,065 (24%)	517,254 (71%)	728,858
	First dose	285,995,512 (87%)	22,353 (41%)	12,602 (23%)	19,575 (36%)	54,530
	Second dose	266,650,107 (82%)	34,314 (9%)	287,459 (77%)	53,670 (14%)	375,443
	First booster	232,410,483 (71%)	9 (0%)	109,610 (15%)	611,503 (85%)	721,122
	Second booster	78,230,281 (24%)	0 (0%)	49 (0%)	168,190 (100%)	168,239
	Third booster	16,553,605 (5%)	0 (0%)	0 (0%)	89,633 (100%)	89,633
	Total	879,839,988	56,676 (4%)	409,720 (29%)	942,571 (67%)	1,408,967

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239 *Figure 2: Counts (top row) and percentage (bottom row) of estimated lives saved per vaccine dose per age-groups, between weeks 50/2020 and 12/2023, in 34 countries, areas*  
 240 *and territories (CAT) in the WHO European Region. Note: age groups 25-49 and 50-59 years include data for 31 CATs, the ≥60 years age group includes data for 34 CATs and the*  
 241 *remaining age groups include data for 29 CATs.*

242 **Lives saved**

243 Analysis of full study period (December 2020 to March 2023)

244 We estimated that during the analysis period, for the 34 CAT overall, COVID-19 vaccination reduced  
245 deaths by 57% (CAT range: 15% to 75%) in adults aged  $\geq 25$  years. This reduction represents at least  
246 1,408,967 lives saved and a mortality risk reduction of 325 per 100,000 population (Table 2). Among all  
247 adults aged  $\geq 60$  years, vaccination reduced mortality by 58% (1,349,617 / 2,340,498 lives). The majority  
248 (728,858 / 1,408,967 lives, 52%) of the lives saved were in people aged  $\geq 80$  years, equivalent to a  
249 mortality risk reduction of 812 per 100,000 persons. We found that vaccination reduced mortality by  
250 57% among 70-79 years old, 54% among 60-69 years old, 52% in 50-59 years old and 46% for 25-49  
251 years old (Table 2).

252 Overall, the first booster saved an estimated 721,122 lives (from 1,408,967, 51%) in adults  $\geq 25$  years old.  
253 Among persons aged  $\geq 80$  years, the first booster saved 370,068 lives (from 728,858), representing a 51%  
254 reduction in expected mortality. Among people aged  $\geq 60$  years, the first booster reduced mortality by  
255 51% (693,762 / 1,349,617) whereas in those aged 25-49 years, the second dose reduced mortality by  
256 48% (7,955 / 16,730) (Table 3 and Figure 2).

257 In the analysis of lives saved by predominant VOC, vaccination saved the most lives (942,571 /  
258 1,408,967, 67%) during the Omicron period which lasted 16 months (compared to six months for the  
259 Delta period), when vaccination reduced mortality by 71% (mortality risk reduction of 383 per 100,000  
260 population). During the Omicron period, vaccination reduced mortality by 71% in people aged  $\geq 80$  years  
261 (517,254 / 728,858), and by 67% for all adults  $\geq 60$  years (908,592 / 1,349,617) (Table 3).

262 In the analysis of lives saved by CAT, among all adults  $\geq 25$  years old, vaccination reduced mortality by  
263 the largest proportion in Israel (75%), Malta (72%), Iceland (71%), Denmark and United Kingdom  
264 (Scotland) (both 70%) (Table 4). In the CAT analysis by age-group, among people  $\geq 80$  years old,  
265 vaccination reduced mortality most in Malta (72%), followed by United Kingdom (England) (71%) and  
266 Denmark and Iceland (both 70% reduction). For adults aged 25-49 years old, vaccination reduced  
267 mortality the most in Malta (68%), Iceland (67%) and Israel (60%) (Supplementary text and  
268 Supplementary Table 3). Among all adults, vaccination reduced mortality the least in Ukraine (15% -

269 where data were only available for people  $\geq 60$  years), Romania (20%) and Kosovo<sup>[1]</sup> (21%). Among  
270 individuals  $\geq 80$  years old, the smallest reduction occurred in Romania (12%), Kosovo<sup>[2]</sup> (17%) and  
271 Slovakia (27%) (Supplementary Table 3).

272 In CATs that reached  $\geq 90\%$  vaccine coverage in people  $\geq 60$  years old by the early stages of the Delta  
273 period (Belgium, Denmark, Iceland, Ireland, Israel, Malta, Netherlands (Kingdom of the), United Kingdom  
274 (England, Scotland)) the proportionate reduction in mortality was the highest. In these CATs, vaccination  
275 reduced deaths by  $>60\%$  in people aged  $\geq 25$  years. Conversely, in CAT where vaccination coverage was  
276 lower than 50%, such as Romania, Republic of Moldova and Kosovo<sup>[2]</sup> reduced deaths by  $\leq 30\%$   
277 (Supplementary Figure 1).

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<sup>[1]</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

<sup>[2]</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

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Table 4: Cumulative vaccination uptake, number of deaths reported and lives saved, reported and expected mortality rates per 100,000 population aged ≥25 years, by countries, areas and territories (CAT), for weeks 50/2020 to 12/2023. Notes: CATs have been ordered according to the proportion of lives saved; d<sub>1</sub> refers to first vaccine dose, d<sub>2</sub> refers to second doses, d<sub>3</sub> refers to first booster, d<sub>4</sub> refers to second booster and d<sub>5</sub> refers to third booster; data presented below for Germany, Republic of Moldova and Ukraine only considers the ≥60 years age group.

Countries, areas and territories	Vaccination uptake				Number of lives							Mortality rate per 100,000		
	VU <sub>2</sub>	VU <sub>3</sub>	VU <sub>4</sub>	VU <sub>5</sub>	Reported deaths	Saved after d <sub>1</sub>	Saved after d <sub>2</sub>	Saved after d <sub>3</sub>	Saved after d <sub>4</sub>	Saved after d <sub>5</sub>	Total Saved	Reported	Total Expected	% change
Israel <sup>1</sup>	95	78	19	<1%	9,397	63	6,383	15,691	6,470	24	28,631	195	787	75
Malta	90	84	23	3	504	1	352	708	205	0	1,266	96	338	72
Iceland	79	88	35	10	235	0	6	441	121	2	570	70	240	71
Denmark	93	84	56	1	7,119	0	1,808	11,440	3,440	78	16,766	124	415	70
United Kingdom (Scotland)	94	84	50	13	10,527	339	6,474	11,915	4,081	1,531	24,340	262	869	70
Finland	91	77	41	18	8,508	170	2,481	8,302	6,478	1,768	19,199	149	484	69
United Kingdom (England) <sup>1,2</sup>	93	82	41	25	174,800	19,839	80,578	164,580	57,638	73,897	396,532	325	1,061	69
Cyprus	84	73	15	3	1,490	92	1,105	1,472	173	16	2,858	175	510	66
Spain	84	76	35	<1%	70,258	3,017	48,581	76,636	7,085	11	135,330	145	424	66
Belgium	88	82	51	8	15,921	981	7,019	17,208	2,854	1,141	29,203	140	397	65
Ireland	94	84	45	18	6,002	134	2,420	4,191	1,737	878	9,360	135	345	61
Luxembourg	77	72	23	<1%	754	18	248	763	146	0	1,175	125	320	61
Austria	82	74	30	1	17,218	993	7,075	14,622	2,135	34	24,859	189	462	59
Italy	88	88	19	2	131,583	8,918	34,411	121,224	22,268	941	187,762	206	500	59

Vaccination uptake					Number of lives							Mortality rate per 100,000		
Countries, areas and territories	VU <sub>2</sub>	VU <sub>3</sub>	VU <sub>4</sub>	VU <sub>5</sub>	Reported deaths	Saved after d <sub>1</sub>	Saved after d <sub>2</sub>	Saved after d <sub>3</sub>	Saved after d <sub>4</sub>	Saved after d <sub>5</sub>	Total Saved	Reported	Total Expected	% change
Netherlands	81	76	44	25	12,990	360	13,068	3,540	1,492	477	18,937	75	183	59
Greece	81	72	17	3	33,445	2,250	14,540	26,391	3,385	399	46,965	303	728	58
Portugal	84	85	48	7	21,347	2,218	5,520	16,759	3,660	1,627	29,784	190	456	58
France	90	78	27	6	98,828	4,724	27,329	72,350	13,832	1,635	119,870	149	330	55
Germany <sup>1</sup>	90	85	39	8	135,420	2,790	50,738	89,400	18,661	4,837	166,426	554	1,236	55
Sweden <sup>1</sup>	87	74	47	2	16,109	152	2,440	6,954	8,821	187	18,554	158	339	53
Switzerland <sup>1,2</sup>	78	81	13	2	8,681	248	3,154	5,011	357	87	8,857	99	201	51
Estonia	69	49	13	<1%	2,633	123	1,103	1,280	123	0	2,629	192	384	50
Croatia <sup>1</sup>	68	39	3	1	4,805	235	1,513	1,990	55	17	3,810	118	212	44
Czechia	75	58	13	<1%	33,292	1,420	10,032	14,119	784	0	26,355	314	562	44
Hungary	73	54	8	<1%	41,228	992	9,202	21,623	1,218	0	33,035	419	754	44
Lithuania <sup>1</sup>	68	43	2	<1%	8,195	547	4,298	1,715	1	0	6,561	283	509	44
Slovenia <sup>1</sup>	63	44	6	1	7,252	218	2,003	3,130	144	46	5,541	333	587	43
Latvia <sup>1</sup>	62	39	6	1	5,659	770	1,855	1,173	5	0	3,803	294	491	40
North Macedonia	60	15	1	<1%	7,592	89	2,757	492	0	0	3,338	433	623	30
Slovakia	60	44	2	<1%	17,768	207	3,631	3,643	0	0	7,481	334	475	30



Countries, areas and territories	Vaccination uptake				Number of lives							Mortality rate per 100,000		
	VU <sub>2</sub>	VU <sub>3</sub>	VU <sub>4</sub>	VU <sub>5</sub>	Reported deaths	Saved after d <sub>1</sub>	Saved after d <sub>2</sub>	Saved after d <sub>3</sub>	Saved after d <sub>4</sub>	Saved after d <sub>5</sub>	Total Saved	Reported	Total Expected	% change
Republic of Moldova <sup>1,2</sup>	39	22	2	<1%	5,983	281	1,191	253	0	0	1,725	844	1,087	22
Kosovo <sup>[1]</sup>	65	11	0	<1%	1,699	10	407	33	0	0	450	129	163	21
Romania <sup>1</sup>	39	12	0	<1%	51,144	1,520	10,355	1,050	0	0	12,925	271	339	20
Ukraine <sup>1,2</sup>	38	55	27	<1%	82,115	811	11,366	1,023	870	0	14,070	897	1,051	15
Total	83	74	29	7	1,050,501	54,530	375,443	721,122	168,239	89,633	1,408,967	243	568	57

<sup>1</sup> Booster doses were not reported by the CAT for at least one age group and so were calculated using the average percentage change of vaccination coverage from CAT with booster 2 and 3 reporting.

<sup>2</sup> It was not possible to differentiate booster doses 2 and 3 from booster 1. The same method as above (1) was used for these CAT.

[1] All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

## 282 Sub-analysis of pre-Omicron period (weeks 50/2020 to 50/2021)

283 In the analysis of the pre-Omicron period, which included 39 CAT (listed in Methods), we estimated that  
284 443,041 lives were saved among people  $\geq 25$  years old (representing a 40% mortality risk reduction). For  
285 all adults  $\geq 25$  years, vaccination reduced mortality the most in Israel (75%), Iceland (71%) and Malta and  
286 Norway (both 65%), whereas vaccination reduced mortality the least in Ukraine (10% - among  $\geq 60$  years  
287 only), the Republic of Moldova and Kosovo<sup>[1]</sup> (both 17%). In this analysis, among people aged  $\geq 60$  years  
288 old a total of 418,354 lives (94% of expected deaths) were saved (a 40% reduction) nearly half of all lives  
289 saved (201,758 lives; 46%) were among people the  $\geq 80$  years old; of these, 80% were saved during the  
290 Delta period (Supplementary Table 3).

291

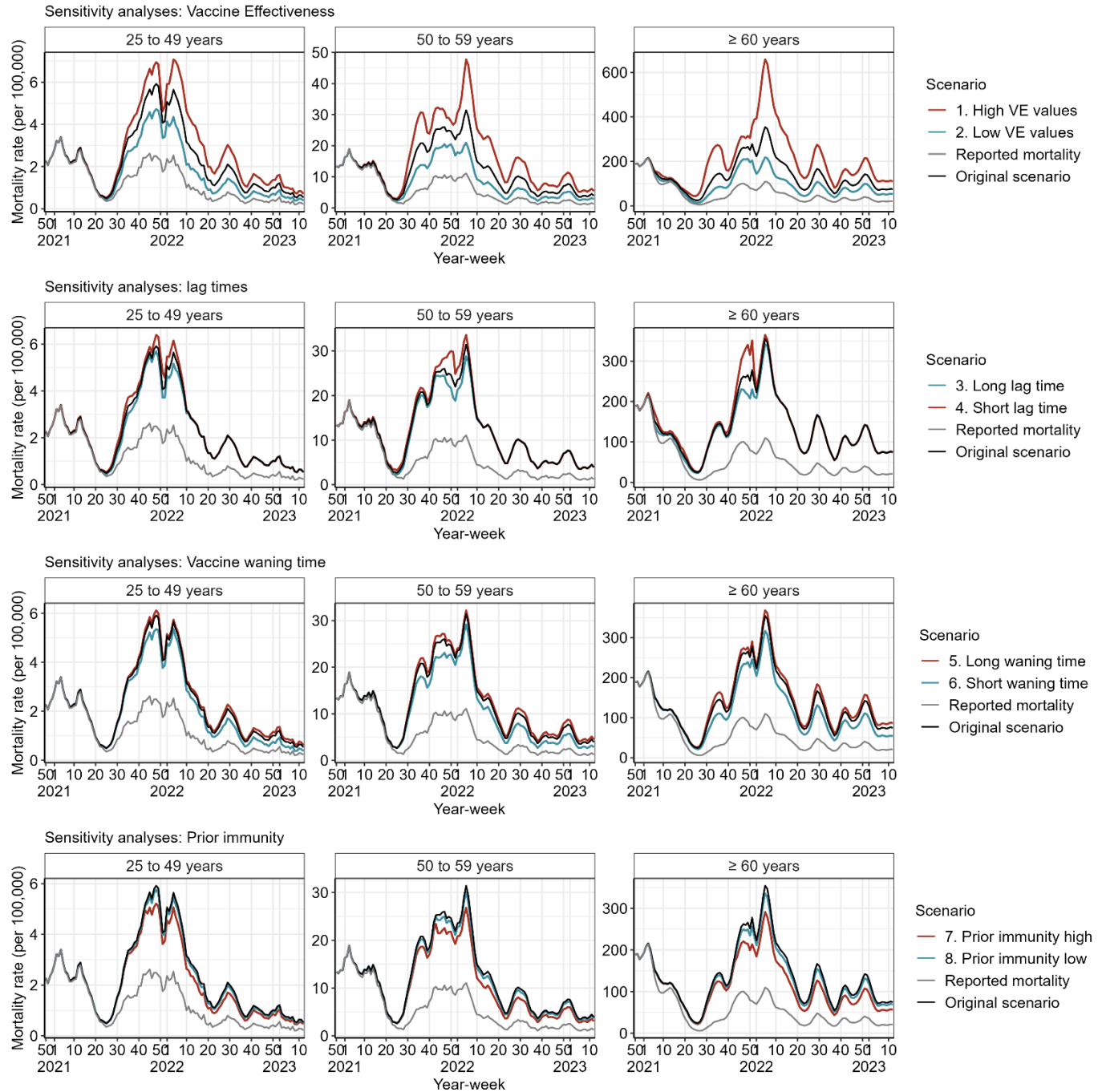
## 292 Sensitivity analyses

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294 When we used the highest VE values (SA1), we estimated that vaccination saved 2,618,085 lives; when  
295 we used the lowest VE values (SA2), we estimated that vaccination saved 747,248 lives. When we used  
296 shorter lag times (VE3), we estimated 1,323,593 lives were saved, whereas the longer lag times (SA4)  
297 saved 1,530,936 lives. When we used a longer vaccination waning time (SA5), we estimated 1,554,472  
298 lives saved whereas a shorter vaccination waning time (SA6 resulted in 1,091,492 lives saved (Figure 3).  
299 When we adjusted for a higher level of prior immunity (SA7), we found that vaccination saved 1,028,530  
300 lives. When we assumed a lower level of prior immunity (SA8), we estimated that vaccination saved  
301 1,294,035 lives. Detailed results can be found in Figure 3 Supplementary Table 5 and Supplementary  
302 Table 6.

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[1] All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).



303

304 *Figure 3: Summary of each sensitivity analysis compared to the original scenario and observed mortality, per age-group, in 34*  
 305 *countries, areas and territories (CAT) in the WHO European Region. Regional and country results are shown in Supplementary*  
 306 *Tables 4 and 5. Note: the ≥60 years age group includes CAT that have only reported ≥60 years data and those reporting by finer*  
 307 *age groups (namely, 50-59, 60-69 and ≥80 years).*

## 308 Discussion

309 We found that over nearly 2 ½ years of the pandemic, COVID-19 vaccination programs across 34 CAT of  
310 the WHO European Region reduced COVID-19 mortality by an estimated 57%, saving approximately 1.4  
311 million lives. In the 34 CAT, the number of lives saved ranged from 450 to 396,532, and mortality was  
312 reduced from 15% to 75% by CAT. Our study, the first to estimate the number of lives saved from  
313 COVID-19 vaccination in the WHO European Region during a period that encompasses nearly the  
314 majority of the pandemic period, underscores the important role COVID-19 vaccines have played in  
315 reducing mortality, and adds to previous studies in Europe (12) and globally (8) that have described the  
316 profound impact vaccination programs have had on mitigating the impact of the COVID-19 pandemic.

317 Our study findings are consistent with those from other studies have described lives saved from  
318 vaccination during the pandemic, including our previous article (12), where we estimated that COVID-19  
319 vaccination reduced COVID-19 mortality in Europe by 51% in the first 12 months of the pandemic. A  
320 study of the global impact of the first year of vaccination found that vaccination had decreased mortality  
321 by 63% globally (8). A modeling study of potential deaths averted in low-income and lower-middle-  
322 income countries estimated that 1.5 million lives could have been saved in 2022, when Omicron started  
323 to circulate, were vaccination to be scaled up in these countries (35).

324 Our study findings highlight that even during the Omicron period, when the severity of infections  
325 decreased relative to earlier periods of previous VOC circulation (10), COVID-19 vaccines still  
326 dramatically reduced mortality. We found that most lives were saved (67%) during the Omicron period,  
327 the longest VOC period, when Omicron BA.1 and BA.2 began to circulate widely despite already high  
328 vaccination coverage. Widespread infections occurred during the Omicron period likely due to a  
329 combination of lack of immunity, waning immunity against infection and a highly transmissible virus.  
330 This added to the level of population immunity to provide hybrid immunity resulting in a reduction in  
331 infection-severity (36). Our findings likely reflect the ongoing effectiveness of COVID-19 vaccine in  
332 protecting against severe disease during this period of Omicron circulation when infection rates were  
333 extremely high even with this reduction in infection severity.

334 We found the highest impact of vaccine was in adults ≥60 years-old, with 96% of all COVID-19 deaths  
335 averted by vaccine in 34 CAT occurred in this age group, even though only 27% of reported infections in  
336 adults occurred in people in this age group. Similarly, adults aged ≥80 years accounted for 52% of all  
337 lives saved through vaccination, only 6% of reported SARS-CoV-2 infections occurred in this age group.

338 Other studies have found that COVID-19 vaccine has disproportionately saved the lives of older adults;  
339 similar proportions of lives saved in those aged  $\geq 60$  years, ranging from 70% to 90% (3,5,11,12).

340 In our analysis, booster doses in older age-groups played an important role in saving lives: early  
341 introduction of the first booster dose, which was recommended because of concerns about waning  
342 protection against severe disease (8), prevented 1,349,617 deaths in adults  $\geq 60$  years old. Indeed, in  
343 adults  $\geq 60$  years old, the first booster dose was responsible for the majority of lives saved, highlighting  
344 the importance of up-to-date vaccination in this high-risk age group. Our results support the recently  
345 published Strategic Advisory Group of Experts (SAGE) recommendations for COVID-19 vaccination in the  
346 context of Omicron and high population immunity (37). This message is particularly urgent at a time  
347 when COVID continues to circulate, and cause morbidity and mortality, across the European Region (the  
348 European Respiratory Virus Surveillance Summary (ERVISS, <https://erviss.org/>)), with recent booster  
349 uptake concerningly low, particularly among high risk groups (7).

350 The strengths of this study include the availability of weekly, age stratified data from the majority of CAT  
351 within the same geographic region. The temporal granularity of these data allowed us to understand the  
352 weekly evolution of the pandemic. CAT reported data to TESSy using a common reporting protocol with  
353 standardized definitions, allowing for comparisons between countries, age-groups and during different  
354 phases of the pandemic. Additionally, by using the number of reported deaths for our calculations, the  
355 indirect impact of the introduction of PHSM and measures to reduce transmission and mortality were  
356 already incorporated.

357 As in our previous analysis (12), our work has several limitations, namely around complete adjustment  
358 for confounders, validity of the underlying data and a few aspects of our methodology. First, regarding  
359 confounders, we were not able to adjust for the effects of healthcare system capacities,  
360 sociodemographic variations such as deprivation and ethnicity, or the use of antivirals and other  
361 medication on mortality. Second, we were not able to stratify vaccine effectiveness by vaccine type,  
362 brand or age-group. We were also not able to differentiate the extent of waning immunity following  
363 vaccination disaggregated by dose. Moreover, we were not able to adjust for reporting biases - under-  
364 reporting likely occurred early in the pandemic due to lack of tests available and later due to unreported  
365 self-testing. There was likely variability in the sensitivity of surveillance by CAT which we could not  
366 account for, and we could not account for any overreporting because of potential misclassification of  
367 deaths later in the pandemic when vaccine escape became more widespread, though CAT were asked to

368 report only deaths where deaths were not otherwise explained by COVID-19. CAT in the Eastern part of  
369 the Region were more likely to have under-reported their COVID-19 mortality counts (3); therefore, the  
370 true number of lives saved by vaccination in these CAT is likely higher than what we estimated.  
371 Furthermore, we attempted to address the role of prior infections in our sensitivity analysis by varying  
372 VE against mortality (SA1 and SA2) and varying presumed levels of prior infection (SA7 and SA8),  
373 particular to account for widespread vaccine escape that occurred during the Omicron period. These SAs  
374 aimed to consider possible differential susceptibility linked to changes in vaccine uptake according to  
375 prior infection history and potentially less virulent VOCs (38), though we assumed that our base  
376 approach took this into account by using the observed mortality rates and VE. Finally, we assumed that  
377 data reporting was comparable among CAT both in terms of reporting delays and methodology  
378 (including whether deaths were caused by or with SARS-Cov-2 infection) and that vaccination intervals  
379 between doses were comparable. Data for the fifth and the fourth vaccination doses were not always  
380 available and had to be calculated for some CAT. Variant periods were calculated differently in our  
381 methodology (predominance determined by  $\geq 50\%$  of weekly sequences of a given VOC) compared to  
382 studies calculating predominance at  $\geq 70\%$  of weekly sequences. We calculated vaccination coverage  
383 data using number of doses as reported to WHO by CAT, and this reporting method may have varied  
384 among countries due to the diverse vaccines and dose regimens used across the Region.

385 In conclusion, over nearly 2.5 years, most lives saved by vaccination in Europe were in older adults (>60  
386 years), by first booster dose and during the Omicron period, reinforcing the importance of up-to-date  
387 vaccination among these most at-risk individuals. Further modelling work should evaluate indirect  
388 effects of vaccination and public health and social measures.

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414 **Disclaimer:** The authors alone are responsible for the views expressed in this article and they do not  
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416 The code for this analysis has been made publicly available and is hosted on the GitHub website at this  
417 address: [whocov/WHO EURO lives saved COVID vaccination: Repository relating to the publication](https://github.com/whocov/WHO_EURO_lives_saved_COVID_vaccination:Repository_relating_to_the_publication_entitled_Estimated_number_of_lives_directly_saved_by_COVID-19_vaccination_programs_in_the_WHO_European_Region,_December_2020_to_March_2023.)  
418 [entitled: Estimated number of lives directly saved by COVID-19 vaccination programs in the WHO](https://github.com/whocov/WHO_EURO_lives_saved_COVID_vaccination:Repository_relating_to_the_publication_entitled_Estimated_number_of_lives_directly_saved_by_COVID-19_vaccination_programs_in_the_WHO_European_Region,_December_2020_to_March_2023.)  
419 [European Region, December 2020 to March 2023. \(github.com\)](https://github.com/whocov/WHO_EURO_lives_saved_COVID_vaccination:Repository_relating_to_the_publication_entitled_Estimated_number_of_lives_directly_saved_by_COVID-19_vaccination_programs_in_the_WHO_European_Region,_December_2020_to_March_2023.)

## 420 421 Conflict of interest

422 Dr. Dabrera reports the predecessor of the organization he works for, Public Health England (PHE),  
423 received an unrestricted grant from GSK to undertake a study on the outcome of patients who received  
424 parenteral zanamavir. The funder received data and interim reports from PHE but did not influence  
425 analysis and reporting of the study. Gavin Dabrera had no involvement in the GSK-funded study on  
426 parenteral zanamavir. Furthermore, the currently submitted work was part of the public health  
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428  
429 None to declare otherwise

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