JAMA Health Forum™

Original Investigation

Global Estimates of Lives and Life-Years Saved by COVID-19 Vaccination During 2020-2024

John P. A. Ioannidis, MD, DSc; Angelo Maria Pezzullo, MD, MSc; Antonio Cristiano, MD; Stefania Boccia, MSc, DSc, PhD

Abstract

IMPORTANCE Estimating global lives and life-years saved is important to put into perspective the benefits of COVID-19 vaccination. Prior studies have focused mainly on the pre-Omicron period or only on specific regions, and lack crucial life-year calculations and often depend on strong modeling assumptions with unaccounted uncertainty.

OBJECTIVE To calculate the lives and life-years saved by COVID-19 vaccination worldwide from the onset of the vaccination campaigns and until October 1, 2024.

DESIGN, SETTING, AND PARTICIPANTS This comparative effectiveness study considered different strata of the worldwide population according to age, community-dwelling and long-term care residence status, pre-Omicron and Omicron periods, and vaccination before and after a SARS-CoV-2 infection.

EXPOSURES Any COVID-19 vaccination in any schedule and number of doses.

MAIN OUTCOME MEASURE Death.

RESULTS In the main analysis, more than 2.5 million deaths were averted (1 death averted per 5400 vaccine doses administered). Eighty-two percent were among people vaccinated before any infection, 57% were during the Omicron period, and 90% pertained to people 60 years or older. Sensitivity analyses suggested 1.4 to 4.0 million lives were saved. Some sensitivity analyses showed a preponderance of the benefit during the pre-Omicron period. An estimated 14.8 million life-years were saved (1 life-year saved per 900 vaccine doses administered). The sensitivity range was 7.4 to 23.6 million life-years. Most life-years saved (76%) were among people 60 years or older, but long-term care residents contributed only 2% of the total. Children and adolescents (0.01% of lives saved and 0.1% of life-years saved) and young adults aged 20 through 29 years (0.07% of lives saved and 0.3% of life-years saved) had very small contributions to the total benefit.

CONCLUSIONS AND RELEVANCE Estimates in this study are substantially more conservative than previous calculations focusing mostly on the first year of vaccination, but they still clearly demonstrate a major overall benefit from COVID-19 vaccination during the years 2020-2024. Most benefits in lives and life-years saved was secured for a portion of older persons, a minority of the global population.

JAMA Health Forum. 2025;6(7):e252223. doi:10.1001/jamahealthforum.2025.2223

Key Points

Question What was the global impact of COVID-19 vaccinations on deaths during the 2020-2024 period?

Findings This comparative effectiveness study found that COVID-19 vaccinations averted 2.5 million deaths during 2020-2024 (sensitivity range estimates, 1.4-4.0 million) and saved 15 million life-years (sensitivity range estimates, 7-24 million life-years). The estimated benefits had a steep age gradient.

Meaning COVID-19 vaccinations had a substantial benefit on global mortality during 2020-2024, but this benefit was mostly limited to a minority of the population of older individuals.

+ Invited Commentary

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Introduction

The development and wide implementation of COVID-19 vaccines are widely considered major successes for biomedical research and public health.[1,2] It is important to estimate the number of lives saved by COVID-19 vaccination worldwide since their introduction. Previous efforts to estimate deaths averted by COVID-19 vaccines used epidemic modeling or counterfactuals from surveillance data.[3-6] Models may give unreliable results, depending on assumptions.[7,8] Previous models attempted calculations with more limited, early evidence and therefore perhaps less plausible or uncertain assumptions, and they mostly addressed the pre-Omicron period.[3,4] The few that have included Omicron period data[5,6] focused on specific regions and have not calculated probable life-years saved. Life-year estimates are pivotal in decision-making.

Herein, lives and life-years saved worldwide among vaccinated individuals from the first licensing of vaccines in December 2020 until October 2024 were estimated. The number of deaths that might have occurred without vaccination and plausible reductions of mortality with diverse vaccines were estimated. Data were stratified by age, pre-Omicron and Omicron periods, vaccination before and after infection, and long-term care settings, using publicly available data.

Methods

The analysis compares the outcomes of global COVID-19 vaccination strategies with a scenario of no vaccination using best estimates on infection fatality rate (IFR), vaccination effectiveness (VE) for mortality, and proportion of population likely to have been infected before and after vaccination.

This is an analysis using public literature data, and no institutional review board approval was needed.

Outline of Calculations

The number of lives saved in each stratum the letter *i* is estimated as the product of the number who would have died absent vaccination and the VE for mortality. The number of people who would have died is estimated as the product of the total stratum population N_i, the proportion who would have been infected PI^*_i (absent vaccination), and the respective IFR:

$$L_i = N_i \times PI^*_i \times IFR_i \times VE_i$$

Total lives saved are estimated as

$$L = \Sigma L_i = \Sigma (N_i \times PI^*_i \times IFR_i \times VE_i)$$

Similarly, life-years saved (LY_i) are estimated as proportional to L_i, the stratum-specific life expectancy (LE) LE_i, and to a factor f_i that denotes how LE of those who died may have differed vs the general population LE; *f* takes smaller values when those who die are in worse health than the respective same-stratum general population. Thus

$$LY_i = L_i \times LE_i \times f_i$$

Total life-years saved are estimated as

$$LY = \Sigma LY_i = \Sigma (L_i \times LE_i \times f_i)$$

We first calculate the benefits for people vaccinated before any SARS-CoV-2 infection. For those first vaccinated after having at least 1 SARS-CoV-2 infection, we then assume that $PI^*_i \times IFR_i \times VE_i$ is lower by a certain *R* factor (mostly because of lower IFR in reinfection and lower PI*).

Values Used and Sensitivity Analyses

For details on values used, justification (with supporting references), and sensitivity analyses' ranges, see eMethods in eAppendix 1 of Supplement 1.[9-19] In brief, we use the 2021 world population

pyramid[9] age strata 0 through 19, 20 through 29, 30 through 39, 40 through 49, 50 through 59, 60 through 69, and 70 years or older, dividing the last stratum further in community-dwelling (97%) and long-term care residents (3%). Based on a systematic review of proportion infected before Omicron[13] and data on vaccination before Omicron,[12,14] we assume that 10% of those aged 0 through 19 years, 20% of those aged 20 through 29 years, and 46% of those in the higher age strata (overall 30% [sensitivity range, 25%-35%, retaining same age ratios]) had received at least 1 dose before any infection before Omicron. We assume that during Omicron, the remaining 56% of the global population who remained uninfected by November 2021 were infected at least once until October 2024. An additional 18% of the global population were first vaccinated during Omicron with slightly less than a third (5%) receiving at least 1 dose before being infected.

We assume that absent vaccination, all people would have been infected during the Omicron period. Before Omicron, we assume PI* to equal 20% for all age strata by November 2021 (sensitivity range, 10%-40%) and that 5% of the population were first infected in the pre-Omicron period after vaccination.

For IFR in unvaccinated people before Omicron, we use estimates from a systematic review for younger-age strata; from metaregressions for community-dwelling adults 70 years or older; and from a meta-analysis of case-fatality rates and studies estimating asymptomatic infection rates for long-term care residents. The sensitivity range is informed by the same sources. Omicron IFR among unvaccinated is assumed to be one-third of pre-Omicron values.

We assume VE equals 75% (sensitivity range, 40%-85%) before Omicron and 50% (sensitivity range, 30%-70%) during Omicron. For people vaccinated after at least 1 infection, we assume the rate (*R*) equals 5 (sensitivity range, 2.5-10).

For LE, the United Nations population division life table for 2021 (World, both sexes) is used taking the midpoint in each age bracket. For 70 years or older, LE at age 77 years is considered for community-dwelling individuals and 2 years for long-term care facility residents. The main analysis considers *f* equal to 0.5 for all strata (sensitivity range, 0.25-0.8).

Numbers Needed to Treat

We calculated the number of vaccine doses required to avert 1 death and to save 1 life-year by dividing estimated benefits by the total number of 13.64 billion vaccine doses administered worldwide.[20]

Results

Lives Saved

Table 1 shows characteristics of the different strata used in the calculations (eMethods in eAppendix 1 of Supplement 1).[9-19] In the main analysis (**Table 2**), more than 2.5 million lives were estimated to have been saved. They were mostly among people who were vaccinated before any infection (2.079 of 2.533 million [82%]). There were slightly more lives saved in the Omicron period (1.448 of 2.533 million [57%]). Of lives saved, 89.6% pertained to people 60 years or older due to their higher IFR and higher early vaccine coverage. Children and adolescents (0-19 years) accounted for only 0.01% of total lives saved and young adults (20-29 years), another 0.07%.

Sensitivity Analyses

Table 3 shows values ranging from 1.4 to 4.0 million lives saved in 1-way sensitivity analyses. Benefits tended to be larger for the Omicron period, but not when *R* values were low or when pre-Omicron PI* was assumed to be large. The widest range for 2-way sensitivity analyses was 1.0 to 6.0 million (considering lower and upper range for both VE and *R*).

Life-Years Saved

In the main analysis, there were 14.8 million life-years saved, with sensitivity analyses ranging between 7.4 and 23.6 million life-years (**Table 4**). People older than 60 years accounted for the most life-years saved (75.9%), but with very little contribution from long-term care residents (2% of the total). Those whose age ranged from 40 through 59 years also contributed a sizeable 20.5% of the total. Children and adolescents (0.1%) and young adults aged 20 through 29 years (0.3%) had negligible contributions.

Table 1. Characteristics of Strata Considered in the Calculations[a]

Age strata, y	World population[b]	Proportion vaccinated before infection in pre-Omicron period (sensitivity range)[c]	Infection fatality rate in the pre-Omicron period (sensitivity range)[d]
0-19	2 664 996 463	0.1 (0.083-0.117)	0.000003 (0-0.00002)
20-29	1 209 691 398	0.2 (0.167-0.233)	0.00002 (0-0.00007)
30-39	1 173 183 969	0.46 (0.383-0.537)	0.00011 (0.00005-0.00032)
40-49	975 497 948	0.46 (0.383-0.537)	0.00035 (0.00011-0.00077)
50-59	849 924 808	0.46 (0.383-0.537)	0.00123 (0.00047-0.00220)
60-69	597 651 319	0.46 (0.383-0.567)	0.00506 (0.00208-0.00860)
≥70			
Community dwellers	468 997 399	0.46 (0.383-0.567)	0.018 (0.013-0.023)
Long-term care residents[e]	14 505 074	0.46 (0.383-0.567)	0.12 (0.10-0.25)
All	7 954 498 378	0.30 (0.25-0.35)	NA

Abbreviation: NA, not applicable.

[a] Between December 2021 and October 2024, an additional 18% of the global population received a first dose.[12] Given the massive, rapid onslaught of the Omicron waves and the relatively slowing of vaccination of previously unvaccinated individuals after November 2021, only an additional 5% were considered to be first vaccinated with at least 1 dose before being infected and assumed no distortion of the relative vaccination rates across age strata. Other details on the justification of the assumptions and sensitivity analysis ranges can be found in the eMethods section of Supplement 1.

[b] Population pyramid data.[9]

[c] Proportion vaccinated before infection in pre-Omicron period makes assumptions that depend on data from the KFF,[12] the COVID-19 Cumulative Infection Collaborators,[13] and the Our World in Data website.[14]

[d] The infection fatality rates are based on Pezzullo et al,[15] Axfors et al,[16] Zhang et al,[17] Borras-Bermejo et al,[18] and Patel et al.[19]

[e] Long-term care residents are assumed to be 3% of the older stratum.[10,11]

Table 2. Lives Saved by COVID-19 Vaccination According to Time Period (Pre-Omicron, Omicron) and Whether Vaccination Was Given to Previously Uninfected or Previously Infected People

	Lives saved among those vaccinated, No.				
	Before Omicron		During Omicron		
Age strata, y	Previously uninfected	Previously infected	Previously uninfected	Previously infected	Total lives saved (% of total saved)
0-19	112	17	133	36	299 (0.01)
20-29	677	104	806	220	1808 (0.07)
30-39	8311	1274	9894	2704	22 183 (0.9)
40-49	21 988	3371	26 176	7155	58 690 (2.3)
50-59	67 324	10 323	80 148	21 907	179 702 (7.1)
60-69	194 753	29 862	231 849	63 372	519 836 (20.5)
≥70					
Community dwellers	543 662	83 361	647 216	176 906	1 451 145 (57.3)
Long-term care residents	112 095	17 188	133 447	36 475	299 205 (11.8)
All	948 922	145 501	1 129 669	308 776	2 532 869

Numbers Needed to Treat

The overall benefit corresponds to 1 death averted per 5400 vaccine doses (sensitivity range, 1 death averted per 3500 to 9300 vaccine doses) and 1 life-year saved per 900 (sensitivity range, 600 to 1800) vaccine doses.

Discussion

Using the best available empirical data on IFRs, VE, and proportion infected at various stages of the pandemic, we estimate that COVID-19 vaccination during the 2020-2024 period saved more than 2.5 million lives for 15 million life-years. The 2.5 million lives correspond to approximately 1% of total global mortality in that period. Sensitivity analyses suggested 1.4 to 4 million averted deaths with 7.4 to 24 million life-years saved. However, uncertainty is substantially wider in multiple-way sensitivity analyses. The overall benefit corresponds to 1 death averted per 5400 vaccine doses and 1 life-year

Table 3. Results of Sensitivity Analyses for Lives Saved by COVID-19 Vaccination

Previously infected	Lives saved, No. in millions				
	IFR sensitivity range[a]	D (≥1) before Omicron, 25%-35%[b]	PI* (10%-40% before Omicron)	VE (40%-85% before Omicron, 30%-70% during Omicron)[c]	*R*, 2.5-10[d]
Before omicron					
No	0.603-1.455	0.791-1.107	0.474-1.898	0.506-1.075	0.949
Yes	0.092-0.223	0.177-0.114	0.073-0.291	0.078-0.165	0.146
During omicron					
No	0.717-1.732	0.941-1.318	1.130	0.678-1.581	0.565-2.259
Yes	0.196-0.474	0.346-0.271	0.309	0.185-0.432	0.154-0.617
Total	1.608-3.884	2.256-2.810	1.986-3.628	1.447-3.254	1.814-3.971

Abbreviations: D (≥1), more than 1 dose; IFR, infection fatality rate; PI*, proportion of people vaccinated in the pre-Omicron period who would have been infected in the absence of vaccination; *R*, ratio for Omicron vs pre-Omicron; VE, vaccination effectiveness for death.

[a] For the IFR sensitivity range, see the eMethods section in Supplement 1.

[b] In the main analysis, in the pre-Omicron period, 30% and 23% of the global population are assumed to have been vaccinated with at least 1 dose before any infection and after previous infection, respectively.

[c] For the Omicron period, 30% and 41% of the global population are assumed to have received at least 1 dose before any infection and after being infected, respectively.

[d] *R* is the product of PI* × IFR × VE (eMethods Supplement 1).

Table 4. Estimates of Life-Years Saved From COVID-19 Vaccination

Age strata, y	Total lives saved, No.	Life expectancy, y	Life-years saved		
			f = 0.5 (%)[a]	*f* = 0.25	*f* = 0.8
0-19	299	64	9560 (0.1)	4780	15 297
20-29	1808	49.9	45 114 (0.3)	22 557	72 183
30-39	22 183	40.7	451 430 (3.0)	225 715	722 288
40-49	58 690	31.8	933 167 (6.3)	466 584	1 493 068
50-59	179 702	23.5	2 111 502 (14.2)	1 055 751	3 378 403
60-69	519 836	16.2	4 210 672 (28.6)	2 105 336	6 737 076
≥70					
Community dwellers	1 451 146	9.2	6 675 269 (45.3)	3 337 635	10 680 431
Long-term care residents	299 205	2	299 205 (2.0)	149 603	478 728
All	2 532 869	NA	14 735 921	7 367 961	23 577 474

Abbreviation: NA, not applicable.

[a] The *f* ratio of life expectancy in people dying from COVID-19 vs the total population in the same stratum. This is the main analysis.

saved per 900 vaccine doses. Numbers needed to treat vary widely across age groups, given the steep age-risk gradient of COVID-19 fatality rates.

Lives saved during the Omicron period appeared slightly higher than those saved during the pre-Omicron period. Estimated benefits during the Omicron period include both the benefits conferred by vaccination doses that were administered before Omicron (and maintained some protection during Omicron) and those conferred by vaccination first started or boosted in the Omicron period. Vaccinations late in the pandemic may have contributed relatively little mortality benefit. Postpandemic mortality benefits cannot be taken for granted; moving forward, optimizing vaccination recommendations would benefit from rigorous randomized trials.[21] Moreover, the estimated Omicron period benefits are low in some sensitivity analyses. The relatively low Omicron death burden is unlikely to reflect mostly higher vaccination benefits. Pre-Omicron PI* depended on exposure load and varied across countries. For example, there was hardly any pre-Omicron viral circulation in China or New Zealand. Therefore, in these countries hardly any lives were directly saved by COVID-19 vaccination before Omicron; any benefit materialized in the Omicron period.

We estimate that 9 of 10 deaths averted and 8 of 10 life-years saved were among people 60 years old or older. Although COVID-19 devastated long-term care facilities,[22] the proportion of life-years saved by vaccination was only 2% of the total, mostly because of the minimal LE of residents. This may nevertheless vary across countries and institutions, depending on resident population features (eg, palliative care vs relatively healthy retired older persons).

The relative contribution of children, adolescents, and young adults to lives and life-years saved appears minimal. Assessment of the absolute net benefits in these populations, if any, require careful consideration of potential additional benefits for nonlethal outcomes and adverse effects.[23,24] For young people, considerations for vaccination decision-making extend beyond the very rare mortality and may include shorter duration of symptoms and less severe illness. Cost-effectiveness ratios should be considered carefully in these age strata to document whether vaccination was worthwhile for them.[25] Those aged 0 through 29 years represent approximately half the global population. No worldwide data exist on how many vaccine doses were administered specifically in these age groups. However, if one-sixth of vaccine doses were given to these age groups, benefits would translate to 1 death averted per approximately 100 000 vaccine doses. One might argue that vaccination of younger individuals may have diminished transmission to older, vulnerable individuals. However, VE regarding infection risk was modest and rapidly waning. False messaging that vaccination will substantially avert transmission may even have backfired. Risk compensation with increased exposure due to false reassurance may even increase viral spread.[26]

Our estimates do not separate deaths averted from VE vs deaths caused from vaccination-related harms. Some may argue that, depending on risk aversion and regret considerations, a death caused because of harm may not carry the same weight as a death averted because of efficacy. Adverse events from COVID-19 vaccines remain a contentious topic. Randomized trial data are very limited.[27] Estimates of risk from registries and other observations carry substantial uncertainty. However, as shown in eAppendix 2 in Supplement 1, the number of deaths due to widely recognized and accepted adverse events (thrombosis, myocarditis, deaths in highly debilitated nursing home residents) are probably approximately 2 orders of magnitude smaller than the overall benefit. Still, these harms are important to weigh against benefits in specific subpopulations where there they have the highest frequency and where risk-benefit may change or even get reversed.

Our estimates include countries with different pandemic and vaccination experiences. There was large global vaccine inequity[28,29] and possibly many lost opportunities.[30] eAppendix 3 in Supplement 1 provides some tentative estimates of what might have been attainable under ideal circumstances.

Previous studies estimating lives saved by COVID-19 vaccination have focused on more limited periods or more restricted areas, countries, or regions. The most-cited study to date[3] used modeling to estimate 14.4 million COVID-19 deaths and 19.8 million excess deaths averted across 185 countries in the first year of vaccination alone, with very limited uncertainty (13.7-15.9 million and 19.1-20.4

million for 95% credible intervals, respectively). These results vary markedly from our pre-Omicron period estimates. We did not estimate total excess deaths averted globally because this is fraught with extreme uncertainties.[31] However, for COVID-19 deaths, our results suggest more than 10-fold lower deaths averted by COVID-19 vaccination in that early period. Differences may reflect unreliability of modeling in such complex circumstances[7] and high estimates of IFR (especially in older people) and VE (using short-term estimates available at that time) assumed in modeling.[3] Another modeling study estimated 620 000 averted deaths from vaccination in the pre-Omicron period, increasing to 2.1 million based on underreporting assumptions.[4] Our pre-Omicron estimates lie between these 2 estimates. Another study[5] covered 34 countries and territories in Europe and estimated 1.6 million lives saved until March 2023 with 96% of lives saved among those 60 years or older and 60% during the Omicron period. The analyzed countries include approximately half of the global population of high-income countries. Although we did not obtain estimates limited to these countries, our global estimates seem modestly more conservative. Differences may be due to implied IFR and VE estimates. However, we agree that most lives saved were among older persons with a slight preponderance of lives saved in the Omicron period. A study covering Latin America and the Caribbean until May 2022 estimated 1.18 million deaths averted (sensitivity range, 0.61-2.61 million) with 78% among those 60 years or older and 62% during the Omicron period.[32]

Limitations

Several caveats should be discussed. First, if one were to consider all factors in multiple-way sensitivity analyses, the range of possible estimates would spread further. Best-case and worst-case scenarios may have even more uncertainty if all involved parameters are allowed to vary, taking extreme values. Moreover, our IFR estimates are derived from national prevaccination seroprevalence studies. For unvaccinated individuals, IFR in the second pandemic year (2021, before Omicron) may have been lower with some effective treatments (eg, dexamethasone) becoming available, better organization of health care services, and more experience in managing severe COVID-19. Moreover, there is debate on whether the Delta variant was more or less lethal than the dominant variants of 2020.[33,34]

Second, for most factors considered, data informing their values come mostly from high-income countries. The picture is more uncertain in other countries. The 2 largest countries, China and India, have major uncertainty on estimates of COVID-19 disease burden,[35,36] let alone vaccine benefits.

Third, VE assumptions try to amalgamate many different vaccines (of variable effectiveness,[37,38] different doses, and different vaccination policies, along with waning effectiveness over time. Unavoidably, these assumptions simplify very complex backgrounds. Analyses of VE based on observational data carry substantial uncertainty and bias.[39,40] Healthy vaccine bias is often observed,[41] but it is difficult to adjust properly for its presence.

Fourth, life-year calculations are a contentious topic. A previous study that calculated adjusted LE in COVID-19 deaths based on comorbidities found small LE reduction vs the general population[42] but was limited by incomplete information on comorbidities and their severity. Thus, there was probably substantial underestimation of the LE difference between those who died of COVID-19 and those who were dying of all causes in the general population. Another study showed that if LE reduction is modeled through a standardized mortality ratio for COVID-19 deaths vs the general population, the mean LE at COVID-19 death in developed countries decreased from about 10 to 12 years to about 6 to 8 years with a standardized mortality ratio of 2,[42] close to what our main analysis anticipated for f equal to 0.5. That same study also estimated only 3.3 to 4.4 average discounted quality-adjusted life-years.[43] The standardized mortality ratio approach corresponds to higher f in young ages and larger f in deaths of older persons; however, the share of life-years saved accounted for by the older persons would be only slightly decreased.

In principle, if a disease, condition, or event kills anyone regardless of health status, eg, a nuclear bomb, then f is equal to 1; conversely, for a condition that appears exactly when a patient is dying from other coexisting ailments, f is equal to 0. The exact positioning of COVID-19 in that spectrum[44]

and the relative share of overcounting and undercounting of COVID-19 deaths[45] are still debated with substantial consequences for estimated disease burden and vaccination benefits. Regardless, taking LE at the age of death directly as a measure of anticipated life-years may lead to grossly misleading inferences.[46] For example, average LE at the age of death for all death causes in Western countries is approximately 9 to 12 years anyhow[46,47]—very close to the average unadjusted LE at the age of death for COVID-19 deaths. Interestingly, if many people avoided COVID-19 death by vaccination had indeed limited LE, postponement of death would be temporary. Such temporary postponement may explain in part why substantial excess deaths were seen[48] in several high-income countries in 2022-2023 despite high levels of vaccination. Of note, simple temporal correlations of excess deaths and vaccine use should not be used naively to infer vaccine effects. Vaccines may be used more extensively just before or during periods of higher viral circulation and death risk; this does not mean that they cause these deaths.

Finally, one may put COVID-19 vaccination benefits in perspective along with benefits from other available vaccinations. Comparisons should be cautious, given the different calculation methods used and acknowledging that mathematical models for other vaccinations may also not be fully reliable. Moreover, modeling the benefits of vaccination for a new pathogen with no previous immunity is different from modeling the benefits of vaccination for pathogens for which prior immunity has been achieved to a certain extent. However, one study[49] estimated that vaccination for 10 pathogens across 112 countries in 2000-2019 saved 50 million lives; another 47 million may be saved in the 2020-2030 years. Disability-adjusted life-years saved were 2700 million and 2300 million, respectively. If these calculations are sound, COVID-19 vaccination in 2020-2024 apparently saved fewer lives than measles or hepatitis B vaccination in the same period, but more than vaccination for each of the other 8 pathogens. However, life-years saved by COVID-19 vaccination for the same period were more than 30-fold lower than the life-years saved from measles vaccination, 10-fold lower than from hepatitis B vaccination, and substantially lower also than the life-years saved from human papillomavirus, yellow fever, *Haemophilus influenzae*, *Streptococcus pneumoniae*, and rubella vaccination.[49] Therefore, even though COVID-19 vaccines are clearly a major achievement, their benefits do not necessarily match the benefits of several other widely used vaccines. Decrease in trust and increased hesitancy for these vaccines may be devastating.[50,51] The COVID-19 pandemic and pandemic response created a more challenging landscape on how to overcome general vaccine hesitancy.[51-53]

Conclusion

This study found that COVID-19 vaccination offered major benefits during 2020-2024. However, our estimates are substantially more conservative than early modeling efforts to calculate lives saved based on the first year of vaccination alone and strong assumptions on IFR and VE.[3] Moreover, from our estimates the vaccination benefits seem to be largely limited to the portion of the global population that are older. Long-term outcomes in both vaccinated and unvaccinated people should also be examined with further follow-up.

ARTICLE INFORMATION

Accepted for Publication: February 25, 2025.

Published: July 25, 2025. doi:10.1001/jamahealthforum.2025.2223

Corresponding Author: John P. A. Ioannidis, MD, DSc, 3180 Porter Dr, Room A129, Stanford Research Park, Palo Alto, CA 94304 (jioannid@stanford.edu).

Author Affiliations: Department of Medicine, Stanford University School of Medicine, Stanford, California (Ioannidis); Department of Epidemiology and Population Health, Stanford University School of Medicine, Stanford, California (Ioannidis); Meta-Research Innovation Center at Stanford (METRICS), Stanford University, Stanford, California (Ioannidis, Pezzullo, Cristiano); Section of Hygiene, Department of Life Sciences and Public Health, Università Cattolica del Sacro Cuore, Rome, Italy (Pezzullo, Cristiano, Boccia); Department of Woman and Child Health and Public Health, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy (Boccia).

Author Contributions: Dr Ioannidis had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Ioannidis, Cristiano.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Ioannidis.

Critical review of the manuscript for important intellectual content: All authors.

Statistical analysis: Ioannidis.

Administrative, technical, or material support: Cristiano.

Supervision: Boccia.

Conflict of Interest Disclosures: None reported.

Funding/Support: The work of Dr Ioannidis is supported by an unrestricted gift from Sue and Bob O'Donnell to Stanford University. Antonio Cristiano has been supported by the European Network Staff Exchange for Integrating Precision Health in the Healthcare Systems project (Marie Skłodowska-Curie Research and Innovation Staff Exchange No. 823995). The work of Dr Pezzullo was supported by grant PE00000007 from the European Union within the NextGeneration EU-MUR PNRR Extended Partnership initiative (INF-ACT).

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: See Supplement 2.

REFERENCES

1. Fauci AS. The story behind COVID-19 vaccines. *Science*. 2021;372(6538):109. doi:10.1126/science.abi8397

2. Karikó K. Developing mRNA for therapy. *Keio J Med*. 2022;71(1):31. doi:10.2302/kjm.71-001-ABST

3. Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. *Lancet Infect Dis*. 2022;22(9):1293-1302. doi:10.1016/S1473-3099(22)00320-6

4. Yang J, Vaghela S, Yarnoff B, et al. 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(1):54-65. doi:10.1080/14760584.2023.2157817

5. Meslé MMI, Brown J, Mook P, et al; WHO European Respiratory Surveillance Network. 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. *Lancet Respir Med*. 2024;12(9):714-727. doi:10.1016/S2213-2600(24)00179-6

6. Steele MK, Couture A, Reed C, et al. Estimated number of COVID-19 infections, hospitalizations, and deaths prevented among vaccinated persons in the US, December 2020 to September 2021. *JAMA Netw Open*. 2022;5(7):e2220385. doi:10.1001/jamanetworkopen.2022.20385

7. Ioannidis JPA, Cripps S, Tanner MA. Forecasting for COVID-19 has failed. *Int J Forecast*. 2022;38(2):423-438. doi:10.1016/j.ijforecast.2020.08.004

8. Jewell NP, Lewnard JA, Jewell BL. Predictive mathematical models of the COVID-19 pandemic: underlying principles and value of projections. *JAMA*. 2020;323(19):1893-1894. doi:10.1001/jama.2020.6585

9. Popular pyramids of the world from 1950 to 2010. PopulationPyramid.net Accessed October 2, 2024. https://www.populationpyramid.net/world/2021

10. Percentage of older people receiving long-term care at a residential care facility and at home. World Health Organization. Accessed October 2, 2024. https://www.who.int/data/gho/indicator-metadata-registry/imr-details/percentage-of-older-people-receiving-long-term-care-at-a-residential-care-facility-and-at-home

11. Surveillance of COVID-19 in long-term care facilities in the EU/EEA. European Centre for Disease Prevention and Control. Accessed October 2, 2024. https://www.ecdc.europa.eu/en/publications-data/surveillance-COVID-19-long-term-care-facilities-EU-EEA

12. KFF global COVID-19 vaccine coverage tool: current and projected coverage. KFF. Published July 24, 2023. Accessed October 2, 2024. https://www.kff.org/interactive/kff-global-covid-19-vaccine-coverage-tool-current-and-projected-coverage/

13. COVID-19 Cumulative Infection Collaborators. Estimating global, regional, and national daily and cumulative infections with SARS-CoV-2 through Nov 14, 2021: a statistical analysis. *Lancet*. 2022;399(10344):2351-2380. doi:10.1016/S0140-6736(22)00484-6

14. Share of people with at least 1 dose of COVID-19 vaccine by age, France. Our World in Data. Accessed October 2, 2024. https://ourworldindata.org/grapher/covid-vaccine-by-age

15. Pezzullo AM, Axfors C, Contopoulos-Ioannidis DG, Apostolatos A, Ioannidis JPA. Age-stratified infection fatality rate of COVID-19 in the non-elderly population. *Environ Res*. 2023;216(Pt 3):114655. doi:10.1016/j.envres.2022.114655

16. Axfors C, Ioannidis JPA. Infection fatality rate of COVID-19 in community-dwelling elderly populations. *Eur J Epidemiol*. 2022;37(3):235-249. doi:10.1007/s10654-022-00853-w

17. Zhang J, Yu Y, Petrovic M, et al. Impact of the COVID-19 pandemic and corresponding control measures on long-term care facilities: a systematic review and meta-analysis. *Age Ageing*. 2023;52(1):afac308. doi:10.1093/ageing/afac308

18. Borras-Bermejo B, Martínez-Gómez X, San Miguel MG, et al. Asymptomatic SARS-CoV-2 infection in nursing homes, Barcelona, Spain, April 2020. *Emerg Infect Dis*. 2020;26(9):2281-2283. doi:10.3201/eid2609.202603

19. Patel MC, Chaisson LH, Borgetti S, et al. Asymptomatic SARS-CoV-2 infection and COVID-19 mortality during an outbreak investigation in a skilled nursing facility. *Clin Infect Dis*. 2020;71(11):2920-2926. doi:10.1093/cid/ciaa763

20. COVID-19 vaccination, world data. World Health Organization. Accessed June 26, 2025. https://data.who.int/dashboards/covid19/vaccines

21. Barosa M, Ioannidis JPA, Prasad V. Evidence base for yearly respiratory virus vaccines: current status and proposed improved strategies. *Eur J Clin Invest*. 2024;54(10):e14286. doi:10.1111/eci.14286

22. Country reports: COVID-19 and long-term care. International Long-Term Care Policy Network. Accessed October 2, 2024. https://ltccovid.org/country-reports-on-covid-19-and-long-term-care/

23. Cappelletti-Montano B, Demuru G, Laconi E, Musio M. A comparative analysis on serious adverse events reported for COVID-19 vaccines in adolescents and young adults. *Front Public Health*. 2023;11:1145645. doi:10.3389/fpubh.2023.1145645

24. Bardosh K, Krug A, Jamrozik E, et al. COVID-19 vaccine boosters for young adults: a risk benefit assessment and ethical analysis of mandate policies at universities. *J Med Ethics*. 2024;50(2):126-138. doi:10.1136/jme-2022-108449

25. Pilz S, Ioannidis JPA. Does natural and hybrid immunity obviate the need for frequent vaccine boosters against SARS-CoV-2 in the endemic phase? *Eur J Clin Invest*. 2023;53(2):e13906. doi:10.1111/eci.13906

26. Ioannidis JPA. Benefit of COVID-19 vaccination accounting for potential risk compensation. *NPJ Vaccines*. 2021;6(1):99. doi:10.1038/s41541-021-00362-z

27. Fraiman J, Erviti J, Jones M, et al. Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults. *Vaccine*. 2022;40(40):5798-5805. doi:10.1016/j.vaccine.2022.08.036

28. Carlson C, Becker D, Happi C, et al. Save lives in the next pandemic: ensure vaccine equity now. *Nature*. 2024;626(8001):952-953. doi:10.1038/d41586-024-00545-3

29. Nunes C, McKee M, Howard N. The role of global health partnerships in vaccine equity: a scoping review. *PLOS Glob Public Health*. 2024;4(2):e0002834. doi:10.1371/journal.pgph.0002834

30. 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(9):e061752. doi:10.1136/bmjopen-2022-061752

31. Ioannidis JPA, Zonta F, Levitt M. Flaws and uncertainties in pandemic global excess death calculations. *Eur J Clin Invest*. 2023;53(8):e14008. doi:10.1111/eci.14008

32. Savinkina A, Weinberger DM, Toscano CM, De Oliveira LH. Estimated deaths averted in adults by COVID-19 vaccination in select Latin American and Caribbean countries. *Open Forum Infect Dis*. 2024;11(10):ofae528. doi:10.1093/ofid/ofae528

33. Lin L, Liu Y, Tang X, He D. The disease severity and clinical outcomes of the SARS-CoV-2 variants of concern. *Front Public Health*. 2021;9:775224. doi:10.3389/fpubh.2021.775224

34. Ong SWX, Chiew CJ, Ang LW, et al. Clinical and virological features of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern: a retrospective cohort study comparing B.1.1.7 (Alpha), B.1.351 (Beta), and B.1.617.2 (Delta). *Clin Infect Dis*. 2022;75(1):e1128-e1136. doi:10.1093/cid/ciab721

35. Ioannidis JPA, Zonta F, Levitt M. Estimates of COVID-19 deaths in Mainland China after abandoning zero COVID policy. *Eur J Clin Invest*. 2023;53(4):e13956. doi:10.1111/eci.13956

36. Jha P, Deshmukh Y, Tumbe C, et al. COVID mortality in India: national survey data and health facility deaths. *Science*. 2022;375(6581):667-671. doi:10.1126/science.abm5154

37. Lin DY, Gu Y, Wheeler B, et al. Effectiveness of Covid-19 vaccines over a 9-month period in North Carolina. *N Engl J Med*. 2022;386(10):933-941. doi:10.1056/NEJMoa2117128

38. Korang SK, von Rohden E, Veroniki AA, et al. Vaccines to prevent COVID-19: a living systematic review with trial sequential analysis and network meta-analysis of randomized clinical trials. *PLoS One*. 2022;17(1):e0260733. doi:10.1371/journal.pone.0260733

39. Ioannidis JPA. Factors influencing estimated effectiveness of COVID-19 vaccines in non-randomised studies. *BMJ Evid Based Med*. 2022;27(6):324-329. doi:10.1136/bmjebm-2021-111901

40. Meester R, Bonte J. The test-negative design: opportunities, limitations and biases. *J Eval Clin Pract*. 2024;30 (1):68-72. doi:10.1111/jep.13888

41. Høeg TB, Duriseti R, Prasad V. Potential "healthy vaccinee bias" in a study of BNT162b2 vaccine against COVID-19. *N Engl J Med*. 2023;389(3):284-285. doi:10.1056/NEJMc2306683

42. Hanlon P, Chadwick F, Shah A, et al. COVID-19—exploring the implications of long-term condition type and extent of multimorbidity on years of life lost: a modelling study. *Wellcome Open Res*. 2021;5:75. doi:10.12688/wellcomeopenres.15849.3

43. Briggs AH, Goldstein DA, Kirwin E, et al. Estimating (quality-adjusted) life-year losses associated with deaths: with application to COVID-19. *Health Econ*. 2021;30(3):699-707. doi:10.1002/hec.4208

44. Rubo M, Czuppon P. How should we speak about years of life lost (YLL) values? *Eur J Epidemiol*. 2023;38(3): 345-347. doi:10.1007/s10654-023-00966-w

45. Ioannidis JPA. Over- and under-estimation of COVID-19 deaths. *Eur J Epidemiol*. 2021;36(6):581-588. doi:10.1007/s10654-021-00787-9

46. Marshall RJ. Standard expected years of life lost as a measure of mortality: norms and reference to New Zealand data. *Aust N Z J Public Health*. 2004;28(5):452-457. doi:10.1111/j.1467-842X.2004.tb00027.x

47. Wengler A, Rommel A, Plass D, et al; BURDEN 2020 Study Group. Years of life lost to death—a comprehensive analysis of mortality in Germany conducted as part of the BURDEN 2020 Project. *Dtsch Arztebl Int*. 2021;118(9): 137-144.

48. Ioannidis JPA, Zonta F, Levitt M. Variability in excess deaths across countries with different vulnerability during 2020-2023. *Proc Natl Acad Sci U S A*. 2023;120(49):e2309557120. doi:10.1073/pnas.2309557120

49. Toor J, Echeverria-Londono S, Li X, et al. Lives saved with vaccination for 10 pathogens across 112 countries in a pre-COVID-19 world. *Elife*. 2021;10:e67635. doi:10.7554/eLife.67635

50. Pandey A, Galvani AP. Exacerbation of measles mortality by vaccine hesitancy worldwide. *Lancet Glob Health*. 2023;11(4):e478-e479. doi:10.1016/S2214-109X(23)00063-3

51. Durrheim DN, Andrus JK, Tabassum S, Bashour H, Githanga D, Pfaff G. A dangerous measles future looms beyond the COVID-19 pandemic. *Nat Med*. 2021;27(3):360-361. doi:10.1038/s41591-021-01237-5

52. Pertwee E, Simas C, Larson HJ. An epidemic of uncertainty: rumors, conspiracy theories and vaccine hesitancy. *Nat Med*. 2022;28(3):456-459. doi:10.1038/s41591-022-01728-z

53. Kaufman J, Rak A, Vasiliadis S, et al. The case for assessing the drivers of measles vaccine uptake. *Vaccines (Basel)*. 2024;12(6):692. doi:10.3390/vaccines12060692

SUPPLEMENT 1.

eAppendix. Supplementary Methods
eAppendix 2. Deaths Due to Adverse Effects of Vaccines
eAppendix 3. Deaths Averted Under Ideal Circumstances
eReferences

SUPPLEMENT 2.

Data Sharing Statement