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COVID vaccination and age-stratified all-cause mortality risk

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Abstract

Accurate estimates of COVID vaccine-induced severe adverse event and death rates are critical for risk-benefit ratio analyses of vaccination and boosters against SARS-CoV-2 coronavirus in different age groups. However, existing surveillance studies are not designed to reliably estimate life-threatening event or vaccine-induced fatality rates (VFR). Here, regional variation in vaccination rates was used to predict all-cause mortality and non-COVID deaths in subsequent time periods using two independent, publicly available datasets from the US and Europe (month- and week-level resolutions, respectively). Vaccination correlated negatively with mortality 6-20 weeks post-injection, while vaccination predicted all-cause mortality 0-5 weeks post-injection in almost all age groups and with an age-related temporal pattern consistent with the US vaccine rollout. Results from fitted regression slopes ($p < 0.05$ FDR corrected) suggest a US national average VFR of 0.04% and higher VFR with age (lower bound estimates of VFR=0.004% in ages 0-17 increasing to 0.06% in ages >75 years), and 146K to 187K vaccine-associated US deaths between February and August, 2021. Notably, adult vaccination increased ulterior mortality of unvaccinated young (<18, US; <15, Europe). Comparing our estimate with the CDC-reported VFR (0.002%) suggests VAERS deaths are underreported by a factor of 20, consistent with known VAERS under-ascertainment bias. Comparing our age-stratified VFRs with published age-stratified coronavirus infection fatality rates (IFR) suggests the risks of COVID vaccines and boosters outweigh the benefits in children, young adults, and older adults with low occupational risk or previous coronavirus exposure. Our findings raise important questions about current COVID mass vaccination strategies and warrant further investigation and review.

Introduction

In June, 2021 the US FDA added a warning to Fact Sheets for Healthcare Providers Administering Vaccines, noting that “reports of adverse events suggest increased risks of myocarditis and pericarditis, particularly following the second dose and with onset of symptoms within a few days after vaccination (1).” Subclinical myocarditis may be a partial explanation for vaccine-induced deaths in men up to age 50 (2,3). A leading cause of immediate death following COVID vaccination may be thromboembolic events as all the vaccines have been associated with forms of venous and arterial thrombosis (4–9). Data-driven estimates of severe vaccine adverse event rates as well as all-cause mortality risk are critical for cost-benefit ratio analyses of COVID vaccination in various age groups.

The vaccine clinical trials (~15-20K participants in each arm) and safety surveillance studies (10) are either underpowered or did not include adequate safety assessments and follow-up with respect to vaccine-induced death (see Discussion for brief review). In the US, real-world vaccine safety signals have relied on the Center for Disease Control (CDC) Vaccine Adverse Events Reporting System (VAERS) database (11). The CDC has used VAERS data to report a vaccine fatality rate (VFR) of 0.002%¹, estimated by dividing the number of reported VAERS deaths by the total number of vaccine doses administered in the US. However, the VAERS has several limitations, including 1) reported incidents are not independently verified or confirmed to results from vaccination, and 2) it only receives, not collects, reports from individuals and/or health professionals and organizations and likely suffers from under-ascertainment/underreporting bias (12). A key limitation of the Vaccine Safety Datalink, a multisite vaccine safety dataset based on millions of US medical records (13), is that previous or raw versions of published datasets are not publicly available to outside researchers (14), limiting transparency, reproducibility, and reliability of published findings (10,15). This is

¹ <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html>

especially important given that previous VSD studies may have under- or misreported severe adverse events and mortality risk (10,15) (see Discussion for more details). A recent re-analysis of VSD data (subset from Kaiser Permanente) used more sensitive methods to detect myopericarditis cases following COVID vaccination and reported its risk may be one to two orders of magnitude higher than previously reported in the US (i.e. 195 cases per million second doses in males ages 12-39, or about 1 in 5K) (3).

Here, two independent, publicly available data sources from the US and Europe were used to test whether region-to-region variation in vaccination rates predicts or correlates with region-to-region variation in future (following weeks or month) mortality rates. We focused on mortality risk as data for severe adverse events such as myopericarditis and thromboembolism are neither readily or publicly available. Using the European data, we asked whether COVID vaccination correlates with deaths at short and long intervals post-injection stratified by 6 age groups (0-14, 15-44, 45-64, 65-74, 75-84, and 85+). With the US data, multiple linear regression was used to test whether we could observe similar short term effects seen in the European data. The US data was stratified by 8 age groups (0-17, 18-29, 30-39, 40-49, 50-64, 64-74, 75-84, and 85+). These models adjusted for COVID deaths as well as seasonality effects and interregional variation in mortality due to other factors by adjusting for same-month 2020 deaths. Using same month deaths from 2020 (as opposed to 2019 or earlier) also helped control for interregional differences in pandemic public health measures before the vaccination campaigns began.

Our second aim was to estimate a US national average VFR and age-stratified rates using significant regression slopes for the vaccination term in the regression model. The European data reports age-stratified mortality rates on a weekly basis and allows for higher temporal resolution analyses, but mortality rates are z-scored normalized and hence effect size estimates in real units are not possible. The units of the US data allow for such estimates since

it records raw numbers of administered vaccine doses and death counts in each jurisdiction, but at a lower (monthly) temporal resolution. Finally, we compared our estimates with previously published US national average and age-stratified SARS-CoV-2 infection fatality rates for risk-benefit ratio analysis of vaccination against COVID-19 stratified by age.

Results

Associations between weekly vaccination and mortality data from Europe and Israel

For each week since the start of 2021 for 22 European countries, weekly increases in percentages of the total population who received at least one injection were extracted from [Coronavirus \(COVID\) Vaccinations - Statistics and Research - Our World in Data](#), and correlated with varying time lags (0-28 weeks post vaccination) with weekly age-stratified mortality data extracted from euromomo.eu (see Supplementary Materials and Methods). The overall description of results requires distinguishing between the age group 0-14 which were unvaccinated during the time period analyzed, and ages above 14. For ages above 14, there is a positive association (correlation) between vaccination and mortality rates during the first few weeks of vaccination (Table 1, lags 0-5 and Figure 1 leftmost yellow peaks). Overall, mortality above age 14 associates near zero or negatively with vaccination for mortality later than 5-6 weeks after vaccination (Table 1, lags 5-20 and Figure 1 middle blue troughs). These results coincide with known clinical developments of vaccination, as found in the VAERS data: most deaths occur within the first weeks after vaccination, and vaccine protection occurs after the sixth week after first dose injection. For age groups 15-44 and 45-64, the overall tendency is that protective vaccine effects (meaning negative associations between mortality and vaccination) disappear about 20 weeks after first injection. After week 20, there might be a tendency for adverse effects of vaccination, meaning positive r values between mortality

beyond week 20 and vaccination at least 20 weeks before (Table 1, lags >20 and Figure 1 rightmost yellow peaks).

For the unvaccinated age group 0-14, most associations between mortality and vaccination in adults are positive (among 39 r values with unadjusted two-tailed $P < 0.05$, 32 are positive and 7 are negative r 's). This tendency for positive correlations increases from the week of vaccination until week 18 after vaccination, then disappears. It indicates indirect adverse effects of adult vaccination on mortality of children of ages 0-14 during the first 18 weeks after vaccination.

US results

The following analyses used publicly available US data on vaccination, mortality and age-stratified population size in each US state. The data were obtained from either the CDC or US Census Bureau (see Data Sources section in Supplementary Materials and Methods). Our analyses focused on whether we could replicate the higher mortality within the first 5 weeks of vaccination observed in the euromomo.eu data. Since US mortality data were limited to month-level resolution, we tested whether monthly vaccination rates predicted mortality during the same month or during the next month. Multiple linear regression was used to predict the total # of deaths among 8 age groups (0-17, 18-29, 30-39, 40-49, 50-64, 65-74, 75-84, >85 years) for 7 months (February, March April, May, June, July and August 2021). For each month and age group, the following equation was fitted:

$$\log(Y21_deaths) = \beta_0 + \beta_1 \log(Y20_deaths) + \beta_2 \log(Vax) + \varepsilon \quad (1)$$

Where $Y21_deaths$ and $Y20_deaths$ are the number of total deaths for that month in year 2021 and 2020, respectively, and Vax is the number of vaccine doses administered in

the previous month (or current month). See Supplementary Methods and Materials for more information and details about other analyses to rule out potential confounding factors such as COVID case rates and COVID deaths.

Prior month or current month vaccinations (# of administered doses) predicted monthly total deaths in most age groups. The beta coefficient for the vaccine term was significant in 15 regression models ($p < 0.05$ FDR corrected, see yellow boxes in Table 2). Most vaccination regression slopes terms were positive while no terms with negative slopes survived $p < 0.05$ corrected nor a more liberal threshold of $p < 0.05$ uncorrected. In older age groups (> 75 years) the beta weights were highest in the beginning of the year, while in younger ages th later in the year. This is the expected result since the vaccination campaign first targeted nursing homes and older age groups before younger age groups became eligible for vaccination. When using vaccination counts from the same month (instead of previous month) as deaths, 7 models survived the applied significance threshold where the original models did not, all in younger (< 50 years old) age groups (Table 3, light grey boxes). Using age-specific vaccination rates also increased detection of significant effects for 2 models (Table 3, dark gray boxes) where effects were not detected in the previous 2 models. Adjusting for the number of new COVID cases during the previous month did not significantly alter these results (see Supplementary Table 5). Moreover, the results were similar when predicting non-COVID associated deaths (Supplementary Table S6). Note that because COVID-associated deaths are rarer in younger age groups, the latter analyses had much less power because few states had available data to compute non-COVID deaths in ages 0-49 (see Supplementary Table S6). Scatter plots and best fit lines of significant vaccination terms ($p < 0.05$ FDR corrected, yellow boxes in Table 2 and cells with numbers in Table 3) for each month and age group are shown in Figure 3. Higher resolution versions of the same are shown in Supplementary Figure S1.

Cumulating the monthly model-estimated deaths across all significant results from the original models and from an additional 9 results from the two model variations mentioned above yielded a total of 146,988 deaths attributed to COVID vaccinations between February and August of 2021 (lower right cell of “Estimated Deaths” in Table 3). Applying the same procedure while thresholding the results at a more liberal threshold ($p < 0.05$ uncorrected) yielded an estimated 168,908 vaccine-related deaths (Supplementary Table S6). The same procedure applied using standard linear regression with a stringent threshold ($p < 0.05$ corrected) yielded 133,382 deaths attributed to vaccination (Supplementary Table S7), while thresholding these regression weights more liberally ($p < 0.05$ uncorrected) yielded 187,402 vaccine associated deaths (Supplementary Table S8).

Results from the *robustfit* regression models thresholded at $p < 0.05$ FDR corrected were used to estimate VFR (see Figure 4 and Supplementary Materials and Methods). Dividing the total number of model-estimated deaths by the total number of vaccine doses administered between January and August yielded an estimated US national average VFR of 0.04% (bottom of Table 2). Lower bound estimates of age-stratified VFRs were estimated by averaging the aVFR estimates (see eq 5 in Supplementary Materials and Methods) across all months and for all 3 models when thresholding regression slopes at $p < 0.05$ uncorrected (see methods). These yielded estimated aVFRs of 0.004% for ages 0-17 years, 0.005% for 18-29 years, 0.009% for 30-39, 0.017% for 40-49, 0.016% for 50-64, 0.036% for 65-74, 0.06% for 75-84, and 0.055% for 85-plus (see Table 3). Note we consider these to be lower bound estimates since the denominator (eq 5 in Supplementary Materials and Methods) is vaccine doses administered in a given month across all ages (vaccine doses stratified to the same age groups as the mortality data was not available, see limitations). Using age-stratified (vs. total population) vaccine doses as the independent variable would make the denominator smaller, but presumably leave the estimated regression slopes for vaccination unaffected (or they might

increase). Note that the results for age group 0-17 during are presumed to reflect vaccinations in ages >12 years (16) as well as indirect effects in ages <1 years (see Supplement for analyses restricted to ages <1 years) since no COVID vaccine was authorized in ages 0-11 over the time periods examined.

Discussion

In this study we find that regional variation in vaccination rates predicts mortality in subsequent time periods. The mortality data from euromomo.eu confirm previously known patterns in the vaccinated: a positive association with adverse events, including death, up to 5-6 weeks after the first injection, followed by a decrease in mortality associated with vaccination 6-20 weeks post-injection. The decrease is presumably due to the protective effect of vaccination, which is known to start 6 weeks after the first injection. The end of the protective vaccine period as observed in our data, about 20 weeks, corresponds approximately with the end of the protective vaccine period as generally accepted, 4-6 months (17). The euromomo.eu data also reveal an unexpected increase in mortality in children (which are unvaccinated) with adult vaccination rates in the previous period. It is notable that this indirect adverse vaccination effect was independently observed in both CDC and euromomo.eu datasets. The majority of deaths <18 years age occur in infants <1 years, and a significant effect of vaccination on infant mortality was detected when the US CDC data was restricted to that age group (see Supplementary Results). It is unclear to what extent the observed effects relate to abnormally high mortalities around delivery, and/or infants, and/or in older children and/or young adolescents. Note that several important concerns and errors have been raised in response to previously published studies supporting safety of vaccination in pregnant women (see Supplementary Discussion for a brief review).

The increased mortality in the first 0-6 weeks post-injection may be due in part to increased COVID infectivity before vaccine protection takes effect. A re-analysis of a large real world study of vaccine effectiveness (Dagan et al 2021 (18)) suggests infectivity in vaccinated persons increases 3-fold approximately 7 days following the 1st dose of the Pfizer vaccine (17). Figure 2 in (20) suggests a similar pattern with the CoronaVac vaccine. Likewise, the euromomo.eu data also suggest a tendency for adverse effects caused by the vaccine in those above age 14 beginning 20 weeks after first injection, potentially indicating that antibody-dependent enhancement (ADE) (21–23) or another related effect kicks in after protective vaccine effects dissipate. Alternatively, the increase in adverse effects observed after week 20 may instead be due to short term mortality arising from booster campaigns which began in late summer or fall. Further analyses are required to disentangle and understand the causes of this effect.

The US CDC data allowed for estimation of VFR and vaccine-induced deaths. Importantly, our calculations do not rely on VAERS and its associated limitations. Our estimated US national average VFR of 0.04% is 20-fold greater than the CDC reported VFR of 0.002%², suggesting vaccine-associated deaths are underreported by at least a factor of 20 in VAERS. The estimate is based only on significant effects detected in our analysis, and hence likely represents a lower bound on the actual underreporting factor.

Interestingly, our estimates of 133K to 187K vaccine-related deaths are very similar to recent, independent estimates based off of US VAERS data through August 28th, 2021 by Rose and Crawford (24). The authors report a range of estimates depending on different credible assumptions about the VAERS underreporting factor and percentages of VAERS deaths definitely caused by vaccination based on pathologists' autopsy findings. The authors compared a previously reported incidence rate of anaphylaxis in reaction to mRNA COVID

² <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html>

vaccine (~2.5 per 10,000 vaccinated) (25) to the number of events reported to VAERS to estimate an underreporting factor for anaphylaxis (41x). This factor, multiplied by the number of reported VAERS deaths and the percentage of VAERS deaths believed to be caused by vaccination based on pathologists' estimates, yields various estimates with an average around 180K deaths. Our estimate does not rely on VAERS data and uses independent and publicly available data, and thus contributes additional convergent evidence for the above estimate of vaccine-induced deaths.

The striking similarity of our estimates with those based on VAERS with data-driven estimates of its underascertainment bias (24) suggests our results evidence a causal, not just statistical association between vaccination and mortality. The combination of anecdotal evidence (see Supplementary Materials and Methods) and concerns and limitations with the vaccine safety trials (26) further lend credence to our interpretation. If such causal relation should exist, it would manifest itself as a statistically significant increase in all-cause mortality associated with time-lagged vaccination rates. We identify statistically significant associations between vaccination and increased mortality post-vaccination that do not appear to be explainable by other factors. See Supplementary Discussion for more reasons arguing why our results evidence a causal link (not just an association) between vaccination and death.

Death and severe adverse events to the COVID vaccines appear to be mediated in part by cytotoxicity of the spike protein and its (unintended) cleaving from transfected cells and biodistribution in organs outside the injection site (4,6,27–30). Vaccination may also contribute to higher COVID IFR before vaccination protection kicks in (and after full protection wears off) due to antibody dependent enhancement (ADE) (21,23,31). The effect may be related to enhanced respiratory disease observed in preclinical studies of SARS and MERS vaccines (32,33). An additional or alternative mechanism may stem from quality control issues related to production, handling and distribution of the vaccines. A recent analysis of VAERS data

suggests only ~5% of the vaccine batches account for the majority (>90%) of adverse reactions, those batches were the most widely distributed (more than 13 states), and reported adverse event rates appear to vary across jurisdictions an order of magnitude (34).

Existing safety and surveillance studies are not designed to reliably estimate COVID vaccine-induced death risk

A recent safety surveillance analysis of mRNA vaccines against COVID using the Vaccine Safety Datalink (13) found event rates for 23 serious health outcomes were not significantly higher for individuals 1 to 21 days after vaccination compared with similar individuals at 22 to 42 days after vaccination. This is not very informative as the main comparison of interest is the background rate of adverse events in the unvaccinated. If the severe adverse event rate is similar 1-21 days post-vaccination as it is 22-42 days post-vaccination, then no difference in risk (safety signal) will be detected. The authors include an analysis using an unvaccinated comparator group in Supplementary eTable 6. Surprisingly, the table reports significantly *reduced* risk of thrombosis with thrombocytopenia syndrome ($p=0.004$), hemorrhagic stroke ($p<0.001$), pulmonary embolism ($p<0.001$), and acute myocardial infarction ($p<0.001$) in the vaccinated 1-21 days post injection compared to the unvaccinated comparator group. This is intriguing because these adverse events are precisely the events known to be associated with both the viral vector-based and mRNA COVID vaccines based on CDC VAERS data (749 results for “acute myocardial infarction”, 4,579 results for “thrombosis” or “thrombocytopenia”, 98 results for “hemorrhagic stroke”, and 2,395 results for “pulmonary embolism” for mRNA vaccines as of Oct 22nd, 2021) and published case reports (4,7,35,36). The authors do not devote any discussion on how or why their results provide strong evidence that COVID vaccination appears to protect against the very adverse

events that were previously associated with vaccination. We speculate it is more likely the groups were mislabeled due to human or technical error.

A recent paper by Xu et al., also based on the Vaccine Safety Datalink (VSD) cohorts used in Klein et al., reported significantly reduced mortality risk in vaccinated vs. unvaccinated (15). As with Klein et al. that found significantly reduced risk for severe adverse events in vaccinated people (discussed above), the finding of reduced standardized mortality rates ($p < 0.001$) in the vaccinated compared with unvaccinated is unexpected, especially since the groups were matched for “similar characteristics” and standardized mortality rates were adjusted for age, sex, race and ethnicity. The authors suggest “This finding might be because of differences in risk factors, such as underlying health status and risk behaviors among recipients of mRNA and Janssen vaccines that might also be associated with mortality risk” (15). However, this does not comport with recent findings from a large survey study that found PhD-holders are among the most vaccine hesitant groups (37,38), as are women looking to become pregnant, religious people, and people who practice yoga/“wellness” culture (39). Given that the study is based on the same sites/cohorts used Klein et al. (10), which found significantly *reduced* risk in the vaccinated for the same severe adverse events that have associated with COVID vaccination in VAERS data and published case reports (see discussion above), we speculate their findings may be due to a technical or human error involving group labeling or coding. Note that the data used for their study is not publicly accessible (in contrast to our study), and two authors report receiving funding from Pfizer.

Vaccine cost-benefit ratio

According to a recent meta-analysis of IFR studies, up to 90% of the variation in population-wide coronavirus infection fatality rate (IFR) is explained by age composition and the extent to which older age groups are exposed to the virus (40). The study reports the IFR

for age 10 is 0.002%, age 18 years is 0.005%, 25 years is about 0.01%, 45 years 0.1%, 55 years 0.4%, 65 years 1.4%, 75 years 5%, and 15% >85 years (40). Calculations based on 61 studies (74 estimates) and eight preliminary national estimates by Ioannides suggest a median of 0.05% and upper bound IFR of 0.3% for ages <70 (41). This latter estimate is similar to an estimated US national average IFR of 0.35% based on a Bayesian evidence synthesis model that averaged age-specific IFRs weighted by the fraction of the population in each age group across US states (42). A comparison of previously published age-stratified IFR (40) with our age-stratified VFRs shows they are similar orders of magnitude below age 45, strongly suggesting the benefits of vaccination do not outweigh the risks in anyone ages 45 and younger (Figure 5).

An individual's overall risk of dying from COVID is also a function of infection risk, which varies based on lifestyle, location, time, occupation, and behavior (i.e. social distancing, effective masking with N95 etc.), as well as the presence of comorbidities. In the vaccine clinical trials (when social distancing and masking measures were in place), ~1-2% of the participants contracted symptomatic COVID in the placebo group over a period of a few months (33). Infection risk calculators allow someone to estimate their risk of infection based on attending an event of a certain size (43). For example, a 55 year old attending events over a given time period with a 10% infection risk has a $0.1 \times 0.4\% = 0.04\%$ chance of dying from COVID, which is similar to the odds of vaccine-induced death (VFR~0.01%).

In individuals with no previous exposure and natural immunity, the benefits of vaccination appear to outweigh the risks in age groups >75 years, where the IFR (>1%) is one or two orders of magnitude greater than the estimated VFR of 0.06% in this age group. The benefits may outweigh the risks in ages >45 with high COVID risk (several or more comorbidities and no previous coronavirus exposure) where the IFR of 0.1% is an order of magnitude higher than the estimated VFR of 0.01%. (30).

Implications for public health policy

There is little to no evidence that vaccines reduce community spread and transmission. The vaccine clinical trials used symptomatic, not asymptomatic COVID, as a clinical endpoint. Since they did not require weekly coronavirus testing in their participants, they were not designed to estimate vaccine efficacy in reducing infection and hence transmission of the virus in pre- and/or asymptomatic persons. Indeed a recent July CDC study in Barnstable, MA reported a majority (75%) of COVID infections were among fully vaccinated people in an area with 69% vaccination coverage, with similar viral loads between vaccinated and unvaccinated (44). Given that vaccines do not appear to reduce community spread and that the risks outweigh the benefits for most age groups, vaccine mandates in workplaces, colleges, schools and elsewhere are ill-advised. We do not see much benefit in vaccine mandates other than increasing serviceable obtainable market (SOM) share for the vaccine companies. See (26) and (30) for a more in-depth discussion and literature review on why the mandates are not based on sound science given the relatively low COVID risk in healthy middle-aged and young adults and growing evidence base for alternative prevention and early treatment options for COVID. See Supplemental Discussion for more resources where readers can learn about the nature and volume of life-altering COVID vaccine injuries.

Limitations and future directions

Future studies that include autopsies on VAERS-reported deaths are required to identify mechanisms of vaccine-induced death. Ideally, our analyses would use age-stratified vaccination to predict age-stratified mortality within the same age groups. However, the European and Israel vaccination data are not age-stratified, and the US vaccination data only provides some age-specific data starting in later months (i.e. vaccines administered to ages

>65, >18, and >12 years). In addition, while the US vaccination and COVID cases are updated daily, the age-stratified death counts are per-month, thus preventing analyses using shorter time windows. The additional information may have increased our sensitivity to detect significant effects in more age groups and time periods. Such a scenario would increase our mortality estimates, in which case the death estimates presented here based only on significant effects ($p < 0.05$ corrected) can be considered a lower bound on the estimated deaths attributed to COVID vaccination. The current study focused on vaccine-attributed deaths within 5-6 weeks of vaccination to estimate age-stratified VFR. Future work should examine later periods to estimate lives saved from vaccination and also potential vaccine associated mortality after protective effects wane.

Conclusions

In the European and Israeli data, we find that COVID vaccination correlates positively with mortality 0-5 weeks from vaccination, before associating with lower mortality 6-20 weeks from vaccination. The US data allowed us to estimate a US national average VFR of 0.04% and age-stratified vaccine-induced fatality rates within 1 month post-vaccination. Significant regression terms estimate 130K-180K US deaths can be attributed to vaccination between February and August of 2021. The estimate converges with independent estimates based on the Vaccine Adverse Events Reporting System (VAERS) and suggests VAERS deaths are underreported by a factor of 20. Comparison of our age-stratified VFR and with age-stratified IFR rates suggests the risks of COVID vaccination outweighs the benefits in children, young and middle age adults, and in older age groups with low COVID risk, previous coronavirus exposure, and access to alternative prophylaxis and early treatment options. Our findings raise important questions about mass COVID vaccinations strategies that warrant further

investigation and review.

Data and Resource Sharing

All data used in this study is publicly available. See Data Sources subsection in the Methods for links to the raw data. The extracted data (minimally preprocessed spreadsheets and intermediate results) for both European and US datasets is available in the provided Github repository which is publicly available. The repository also contains all MATLAB code used for the US dataset analyses. Readers who would like to inspect and replicate the results or reanalyze the data may find it easier to first double check the intermediate table files (in Table subfolder of the Github repo at <https://github.com/spiropan/CoVFR>) against the original CDC data and then work off of these tables with their software of choice.

Author Contributions

SPP analyzed US data and drafted the manuscript; HS analyzed European and Israeli data and drafted relevant text.

Conflict of interest

The authors have no relevant conflicts of interest to report.

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Table 1. Correlations between COVID vaccination rates and mortality as a function of lag (# weeks post-injection) and age group. Each cell summarizes the pearson correlation coefficients between weekly increase in percent vaccinated and weekly mortality in 23 European countries. Top header row: lag=weeks between mortality and injection, n=number of correlations summarized. Middle matrix (%) shows the percentage of positive correlations for that lag among n correlation. *=P < 0.05 corrected, sign test. Bottom matrix (P<0.05) shows the number of negative and positive correlation r's with P < 0.05 uncorrected. Blue: overall protective effect (more injections->lower mortality); yellow: overall adverse effect (more injections->higher mortality).

Lag	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
n	33	32	31	30	29	28	27	26	25	24	23	22	21	20	19	18	17	16	15	14	13	12	11	10	9	8	7	6	5
%																													
0-14	52	53	55	53	59	46	63	54	48	54	61	64	67	50	68	89*	65*	81*	67	57	54	42	55	50	44	38	29	33	40
15-44	61	47	42	47	45	50	44*	38*	28*	29*	26*	23*	29	45	32	39	41	56	67	71	46	67*	82*	70*	78*	88*	71*	67*	80*
45-64	67*	69*	55*	60	52	43	37	42	36	46	30	36	38	40	42	39	47	56	60	57	69	50	64	50	56	63	71	67	60
65-74	70*	66*	61*	53	62	46	41	31	44	25*	30*	27*	24*	30*	26*	33*	29*	25*	13*	21*	38*	25	36	40	56	38	29	33	40
75-84	73*	63*	58*	50	55	43	37*	42*	32*	33*	26*	14*	24*	20*	26*	17*	18*	31*	13*	14*	38*	33	27	40	44	38	43	67	60
85+	67*	72*	61*	63*	62*	64*	48	54	52	54	39	27*	14*	25*	26*	28*	41*	31*	27*	29*	31*	33	36	40	56	50	57	67	80
P<0.05																													
0-14, -	1	0	0	1	1	1	1	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0-14, +	1	2	2	3	1	1	0	2	1	1	2	1	1	1	1	2	1	0	3	1	1	1	1	1	0	1	0	0	0
15-44, -	1	1	1	0	1	0	2	0	0	1	1	0	0	2	2	2	1	1	1	1	1	1	1	0	0	0	0	0	1
15-44, +	2	3	2	1	2	0	1	1	0	0	0	0	0	0	1	0	0	0	3	1	0	1	0	1	0	0	0	0	0
45-64, -	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0
45-64, +	3	4	2	1	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	1	1	1	0	0	0	0	0	0
65-74, -	0	0	1	0	1	1	0	0	1	1	1	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
65-74, +	2	2	0	1	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
75-84, -	0	0	0	0	0	0	0	2	2	1	0	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
75-84, +	0	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
85+, -	0	0	0	0	0	0	0	1	0	0	1	0	0	0	1	1	1	2	1	0	0	0	0	0	0	0	0	0	0
85+, +	0	0	0	0	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0

Table 2. Regression weights and p-values for the vaccination term predicting same or next month deaths using US CDC data. For each month in 2021 and age group, beta weights and uncorrected p-values are listed for the vaccination term (β_2) in the fitted equation:

$$\log(Y_{21_deaths}) = \beta_0 + \beta_1 \log(Y_{20_deaths}) + \beta_2 \log(V_{ax}) + \varepsilon$$

where V_{ax} = vaccine doses administered previous or same month across all US states with available data for that month and age group (~42-52 states for each cell/regression, see Equation 1). Models were fitted using robust regression. Yellow indicates positive beta slopes with p-values < 0.05 FDR corrected. No negative slopes were significant.

Ages	February		March		April		May		June		July		August	
	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>
0-17	0.12	0.2145	0.01	0.9192	-0.03	0.7727	0.08	0.164	0.04	0.4979	0.25	0.0004	0.72	0.0015
18-29	0.12	0.282	0.07	0.4607	0.00	0.9828	0.24	0.0006	0.17	0.0017	0.42	0.0007	0.47	0.0187
30-39	0.11	0.1956	0.12	0.2716	0.06	0.5532	0.13	0.0613	0.15	0.0027	0.34	0.006	0.41	0
40-49	0.16	0.0832	0.09	0.146	0.10	0.2631	0.03	0.6951	0.05	0.2599	0.28	0.0004	0.40	0
50-64	0.07	0.2946	-0.03	0.5487	0.03	0.6703	-0.03	0.6104	0.03	0.5088	0.02	0.6669	0.06	0.726
65-74	0.05	0.5296	0.00	0.9752	0.03	0.7672	0.03	0.628	-0.03	0.4472	0.03	0.5518	0.13	0.3314
75-84	0.08	0.1995	0.04	0.3463	0.66	0	0.05	0.4973	-0.02	0.6506	0.08	0.2925	0.07	0.5904
85-plus	0.15	0.0001	0.18	0.0004	0.70	0	0.20	0.0037	-0.01	0.7658	0.06	0.4708	-0.04	0.7079

Table 3. Model-estimated deaths attributed to COVID vaccination for each age group and month using US CDC data. Significant beta weight coefficients (β_2) in Table 2 surviving $p < 0.05$ FDR corrected were used to estimate VFR and total deaths for each age group and month. If a model using same (not previous) month vaccinations was significant and the equivalent models using previous month was not, then death estimates from those models were used instead (light gray boxes). Similarly, if a model using age-specific vaccination (i.e. doses administered to people >65 yrs) was significant and the equivalent model using all vaccine doses administered was not, then death estimates from those models were used instead (dark gray boxes). See methods for VFR and aVFR definitions and calculations. ns=not significant at $p < 0.05$ FDR corrected. NA=Not available.

Model-estimated deaths										
Ages	Jan	Feb	March	April	May	June	July	Aug	Totals	aVFR (%)
0-17	NA	ns	ns	ns	ns	ns	648	1,227	1,875	0.004
18-29	NA	ns	ns	ns	1,355	861	2,139	ns	4,355	0.005
30-39	NA	ns	ns	ns	ns	1,101	2,422	2,567	6,090	0.009
40-49	NA	ns	ns	ns	ns	ns	3,067	3,979	7,046	0.017
50-64	NA	ns	ns	ns	ns	ns	ns	ns	0	0.016*
65-74	NA	ns	ns	ns	ns	ns	ns	ns	0	0.036*
75-84	NA	ns	ns	41,316	ns	ns	ns	ns	41,316	0.060
85-plus	NA	11,613	13,181	48,186	13,326	ns	ns	ns	86,306	0.055
								Total	146,988	
# Vaccine dose administered										
Vax all ages	2.65E+07	4.60E+07	7.63E+07	8.94E+07	5.25E+07	3.15E+07	1.82E+07	2.46E+07	364,881,402	
Vax >65 yrs	NA	NA	NA	1.40E+07	4.83E+06	3.05E+06	1.90E+06	2.83E+06	26,584,086	
Vax <65 yrs	NA	NA	NA	7.54E+07	4.77E+07	2.84E+07	1.63E+07	2.17E+07	189,500,231	
								VFR	0.04%	
Light gray indicates models estimated using same, not previous, month vaccinations										
Dark gray indicates models estimated using vaccines administered > ages 65										
Light blue indicates significant results when predicting deaths in ages <1 years. Model estimated 667 infant deaths (see Supplementary Results).										
*Robust regression did not yield significant results in these age groups. Thus these estimates were derived from results of standard least-squares regression.										

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Figure legends

Figure 1. Graphical representation of Table 1 European data results. Adverse effects in yellow, above horizontal line, protective effects in blue, below horizontal line. Results of correlation analyses for all age classes and all combinations of weeks, with mortality occurring the same week or after the injection week are plotted. In **a)** the percent positive correlations between vaccination rates and mortality is plotted against time since 1st injection for 6 age groups (A - 0-14 years, B 15-14 years, C 45-64 years, D 65-74 years, E 75-84 years, and F 85+ years). Percentages >50% are shaded yellow, <50% shaded blue. Asterisk indicates $p < 0.05$ corrected for the sign test (see methods). Pearson correlation coefficients r from these analyses are in Supplementary Table 3. In **b)** % positive correlations (left column) and numbers of negative and positive r with $p < 0.05$ uncorrected (middle and right columns).

Figure 2. Example correlation plots from the European dataset. Top: Z-score of weekly mortality for ages 15-44 in 23 countries on week 21 of 2021 as a function of increase in percent vaccinated in these countries, during week 13 of 2021. For this correlation, the time lag in weeks between injection and mortality is $21-13=8$ weeks. The association suggests beneficial injection effects at two months weeks after injection.

Bottom: Z-score of weekly mortality for ages 15-44 in 23 countries on week 14 of 2021 as a function of increase in percent vaccinated in these countries, during week 12 of 2021. For this correlation, the time lag in weeks between injection and mortality is $14-12=3$ weeks. The association suggests adverse injection effects during the first weeks after injection.

Figure 3. Scatter plots of monthly vaccination doses vs. subsequent month deaths with best fit regression lines from the US CDC dataset. The graph plots $\log(\text{administered vaccine doses})$ vs. $\log(\text{residual July 2021 deaths})$ after adjusting for $\log(\text{July, 2020 deaths})$ for

each month (top) and age group (right), for each regression model in which the β_2 term survived $p < 0.05$ FDR corrected (see Table 2 and methods) ns=not significant. For a higher resolution image see Supplementary Figure S1, and for the highest resolution plots viewable in a web browser see (45).

Figure 4. Method to estimate COVID vaccination mortality risk using publicly available US CDC data. The cartoon plot shows a schematic of the method to estimate COVID vaccine mortality risk using regional variation in vaccine doses administered and all-cause mortality. Vaccine-induced mortality risk is expressed as the ratio of model-predicted deaths over vaccine doses (i.e. “rise” over “run”). Predicted deaths are estimated as the difference between \hat{Y}_2 and \hat{Y}_1 for a given increase (i.e. 10%) in vaccine doses at \hat{Y}_1 . The approach is completely data-driven and does not rely on assumptions about reporting bias as with other methods.

Figure 5. Simple cost-benefit ratio analysis of COVID vaccination stratified by age. The lower bound estimates of age-stratified vaccine fatality rates from the current study (aVFR, right) have similar orders of magnitude as previously published coronavirus infection fatality rates (IFR). * Left panel is adapted from a meta-analysis of 27 studies to estimate age-stratified coronavirus infection fatality rates (IFR) (40).

Figure 1.

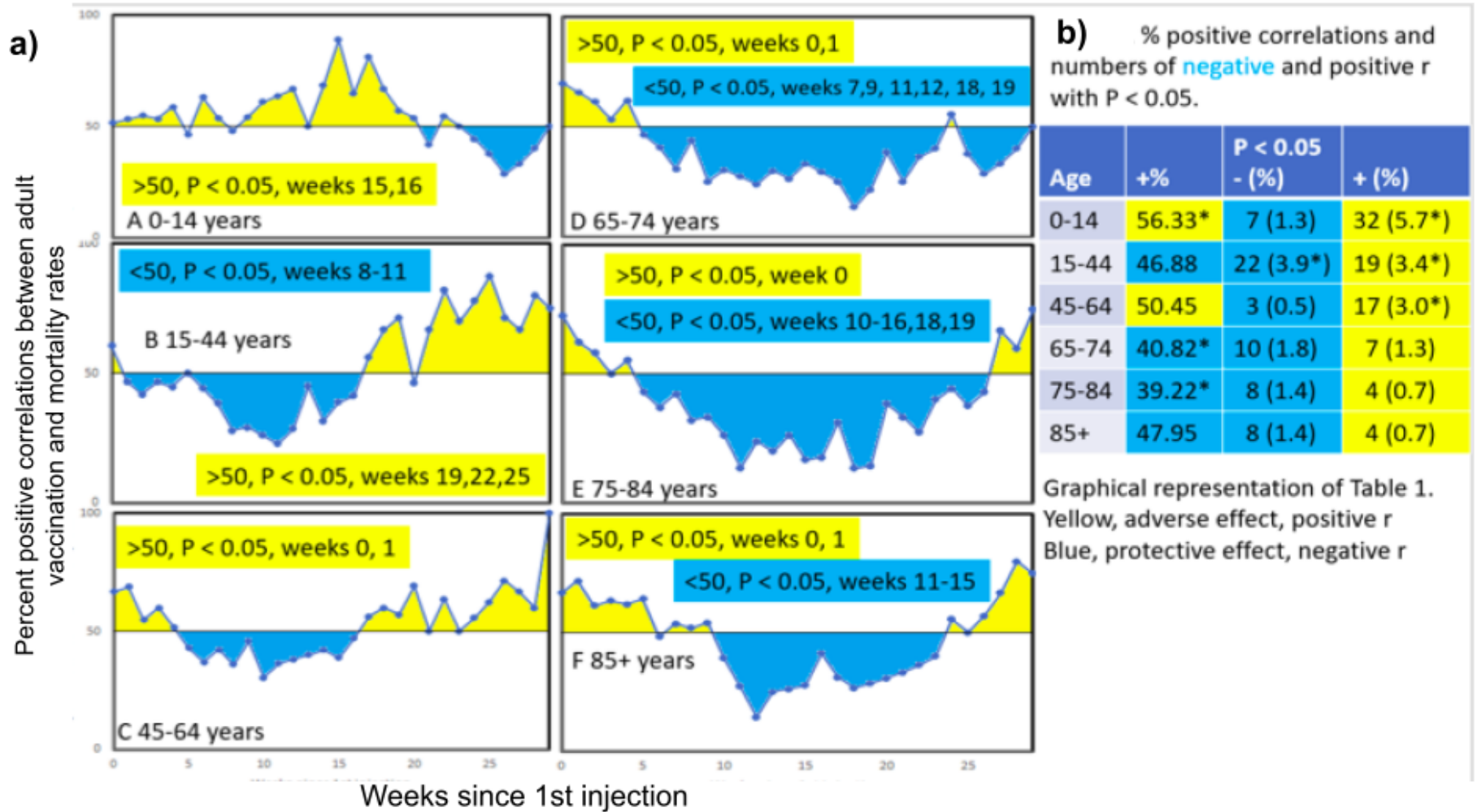


Figure 2.

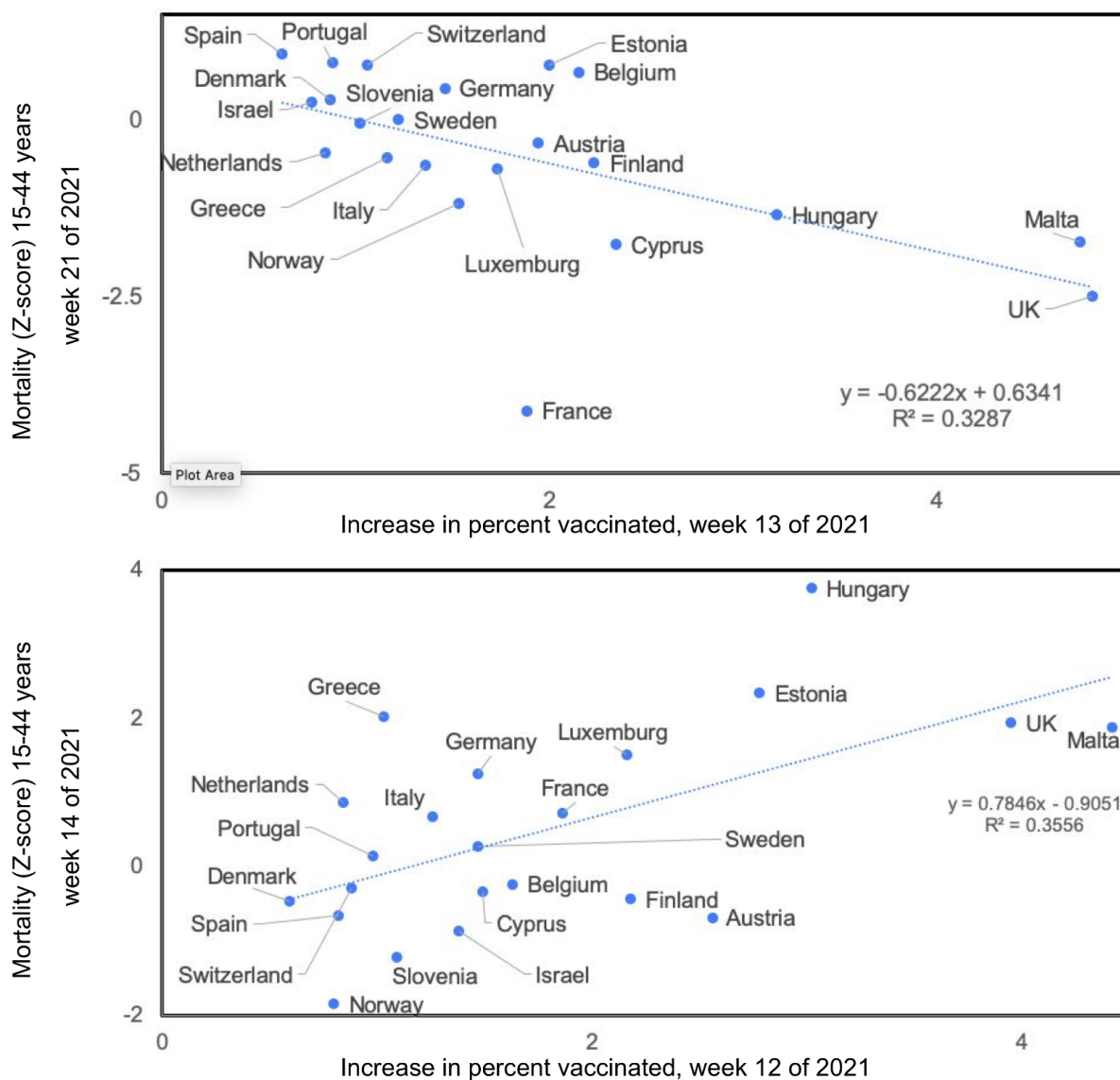


Figure 3

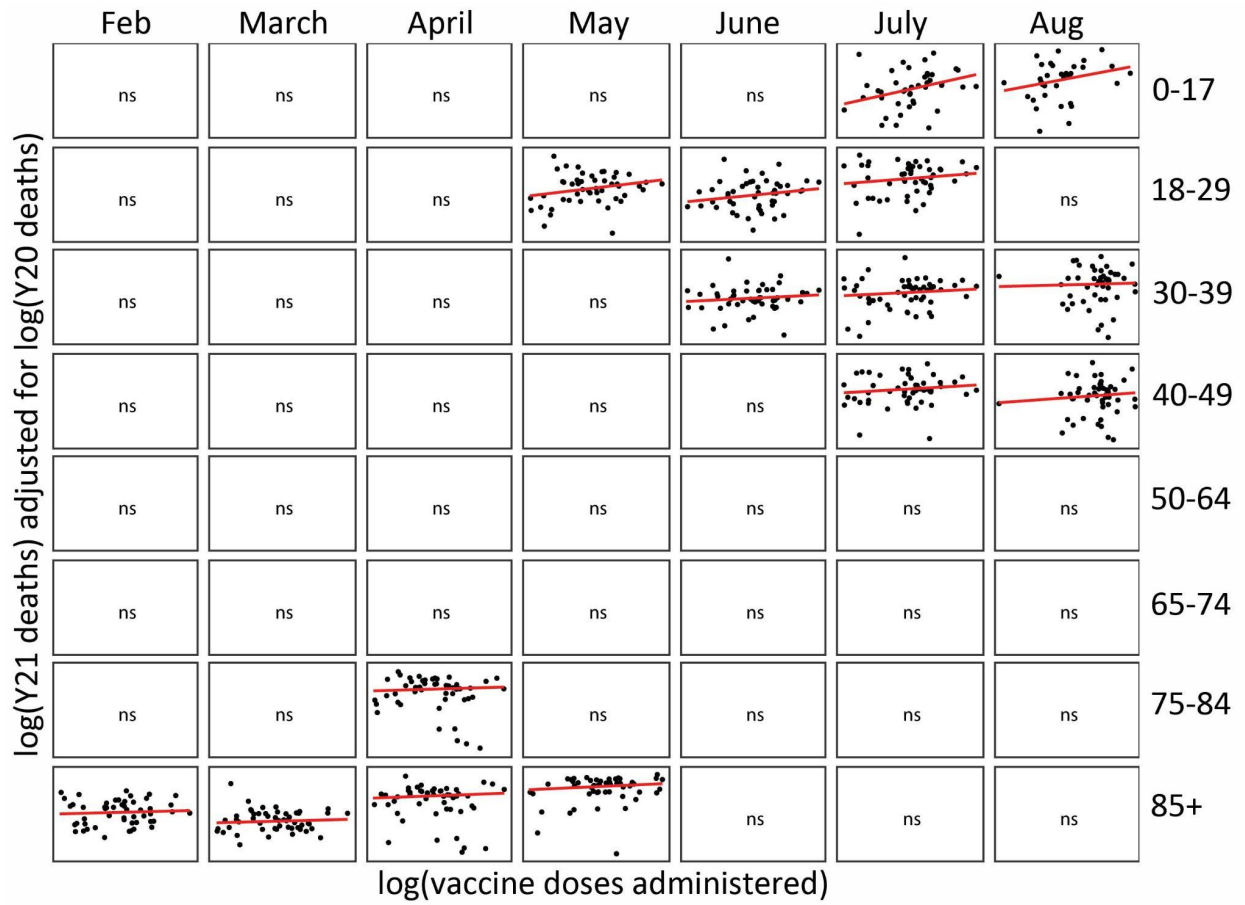


Figure 4

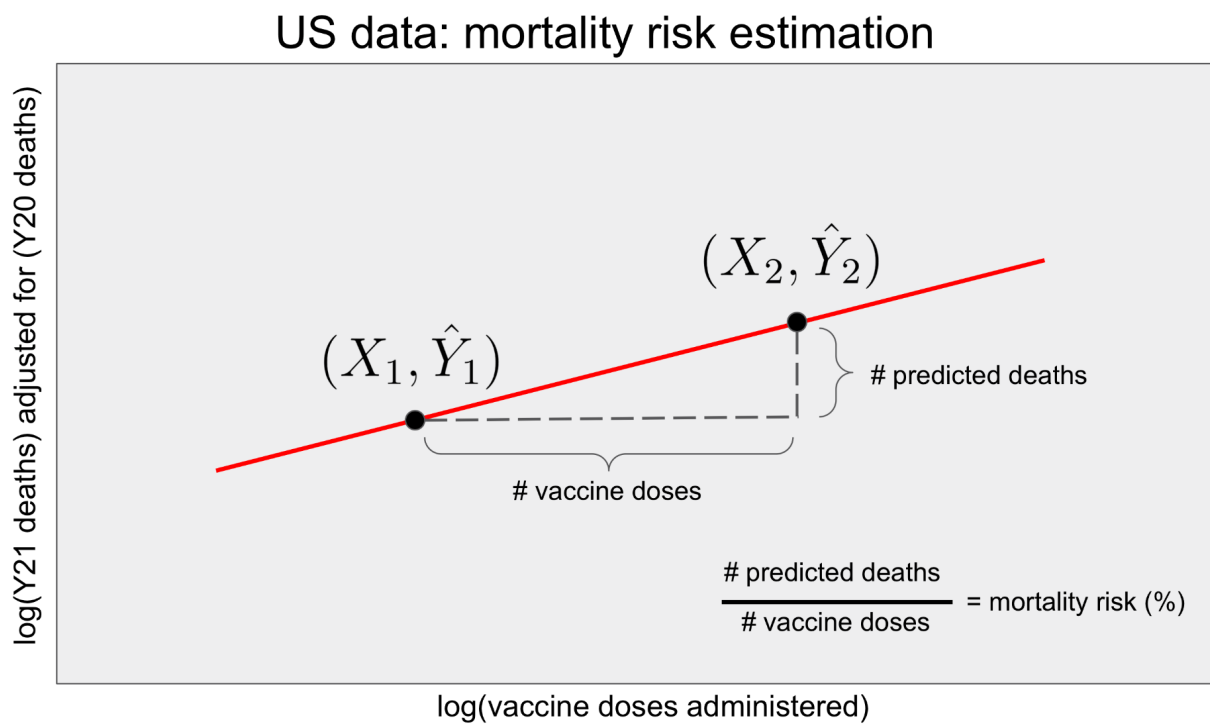


Figure 5

Comparing mortality risk of infection vs. vaccination

Age-stratified coronavirus infection fatality rates (previously published)*

Age group	COVID-19 IFR (95% CI)
0–34	0.004 (0.003–0.005)
35–44	0.068 (0.058–0.078)
45–54	0.23 (0.20–0.26)
55–64	0.75 (0.66–0.87)
65–74	2.5 (2.1–3.0)
75–84	8.5 (6.9–10.4)
85 +	28.3 (21.8–36.6)

Estimated age-stratified vaccine fatality rates (current study)

Ages	aVFR (%)
0-17	0.004
18-29	0.005
30-39	0.009
40-49	0.017
50-64	0.016*
65-74	0.036*
75-84	0.060
85-plus	0.055



* Levin AT, Hanage WP, Owusu-Boaitey N, Cochran KB, Walsh SP, Meyerowitz-Katz G. Assessing the age specificity of infection fatality rates for COVID-19: systematic review, meta-analysis, and public policy implications. *Eur J Epidemiol.* 2020 Dec;35(12):1123–38.

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This manuscript contains:

Supplementary Results

Supplementary Methods and Materials

Supplementary Discussion and References

8 Supplementary Tables S1-S8

1 Supplementary Figure S1

Running title: COVID-19 vaccination and age-stratified mortality

Keywords: Public health, medical ethics, risk-benefit ratio, COVID-19, SARS-CoV-2, vaccine adverse events

Supplementary Results

The 0-17 age group is peculiar in that it includes infants <1 years old. Infant deaths comprise the majority of deaths in this age group (1). Since infants are not vaccinated, we hypothesized this effect could be attributed to vaccinations in the mother given a July, 2021 report that found 2,346 VAERS-reported cases were pregnant mothers at time of vaccination, 36% of whom experienced some type of pregnancy disorder (2). To further test this possibility, an additional regression in the <1 years of age group was run, and results were significant for the August model ($p < 0.05$ corrected). The model estimated 667 infant deaths in the US during the month of August, 2021 may be attributed to vaccinations in July, 2021, while 1,227 deaths were estimated overall in the 0-17 age group (see light blue box, Table 2 of main text).

Methods and Materials

European dataset sources

Weekly age-stratified mortality data were extracted from euromomo.eu for each week since the start of 2021 for 22 countries covered by euromomo (21 european countries (Austria, Belgium, Cyprus, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Slovenia, Spain, Sweden, Switzerland, UK (England)) and Israel). These consist of weekly adjusted z-scores, for 6 age groups: 0-14, 15-44, 45-64, 65-74, 75-84 and 80+ years of age. Weekly increases in percentages of the total population who received at least one injection are extracted from [Coronavirus \(COVID\) Vaccinations - Statistics and Research - Our World in Data](https://ourworldindata.org/covid-vaccinations) (<https://ourworldindata.org/covid-vaccinations>). Supplementary Tables S1 and S2 contained the raw input mortality and vaccination data used in the analyses while Supplementary Table S3 contains the intermediate results (r correlations at each lag before statistical inference, see below).

US Dataset sources

All US data used in the analyses are publicly available and were obtained from either the CDC or US Census Bureau. Vaccination rates across time and US states were extracted from the “COVID Vaccinations in the United States, Jurisdiction” spreadsheet (3). Total deaths per month by age group and sex for each US state were extracted from “Provisional COVID Deaths by Sex and Age” spreadsheet (4). Number of COVID cases per month in each US state were extracted from “United States COVID Cases and Deaths by State over Time” (5). Age-stratified total populations per US state in 2019 were obtained from “NC-EST2019-AGESEX” spreadsheet (6). Spreadsheets were accessed during the first week of September 2021 and included data up through September 1st, 2021. To facilitate importing of data into MATLAB, spreadsheets were filtered (unused columns and rows were removed) and sorted by US State abbreviation. The proprocessed table for April is included as Supplementary Table S4. Similar tables for the other months are available on the Github repository in the subfolder InputFiles (see <https://github.com/spiropan/CoVFR>). The MATLAB script was used to extract relevant data and reorganize the data into tables for each month that list Y20 and Y21 deaths for each age group (columns) and for each state (rows) (see Github subfolder Tables).

Analyses of euromomo.eu data

These mortality data were analysed using Pearson’s correlation coefficient (Pearson’s r) between weekly increases in vaccination rates and mortality rates for the same week or subsequent weeks, from week 1 to week 33 of 2021, separately for each of the six age groups. This results in correlation matrices between vaccination rates and age-specific mortality, with lags between vaccination and mortality week ranging from lag 0 to lag 32 (see Supplementary Table 3). The r correlations were then combined into 9 sets of 3 or 4 week groupings as follows: lags [0,1,2], [3,4,5], [6,7,8], [9,10,11], [12,13,14], [15,16,17], [18,19,20], [21,22,23,24], and [25,26,27,28] for each age group. The last two sets contained 4 weeks to make up for the lower number of r correlations available at much longer lags. Each set of r correlations was then subjected to a sign test for a total of (9 time periods x 6 age-groups= 54) total sign tests and resulting p-values. These p-values were then

corrected for multiple comparisons correction using Benjamini-Hochberg False Discovery Rate (FDR) correction.

Analyses of US CDC data

Our analyses focused on whether we could replicate the higher mortality within the first 5 weeks of vaccination observed in the euromomo.eu data. Since US mortality data were limited to month-level resolution, we tested whether monthly vaccination rates predicted mortality during the same month or during the next month. All the raw data used in the following procedures are available as csv tables to facilitate reanalysis (see Resource and Data Sharing section). Multiple linear regression was used to predict the total # of deaths among 8 age groups (0-17, 18-29, 30-39, 40-49, 50-64, 65-74, 75-84, >85 years) for 7 months (February, March April, May, June, July and August 2021). For each month and age group, the following equation was fitted:

$$\log(Y21_deaths) = \beta_0 + \beta_1 \log(Y20_deaths) + \beta_2 \log(Vax) + \varepsilon \quad (1)$$

Where $Y21_deaths$ and $Y20_deaths$ are the number of total deaths for that month in year 2021 and 2020, respectively, and Vax is the number of vaccine doses administered in the previous month (or current month).

Our model is an ANCOVA model that adjusts for baseline outcomes (here Y20 monthly deaths) while predicting “post” intervention (i.e. vaccination) outcomes (here Y21 deaths). Such models have higher power compared to analyses applied to change scores or percent change looking at baseline (7–9). The models were fitted using robust regression using *robustfit* function in MATLAB 2014b. The algorithm uses iteratively reweighted least squares with the bisquare weighting function and helps ensure results are not driven by outliers by deweighting them during fitting. Standard least-squares linear regression using *glmfit* was also applied for comparison and for cases where results from robust regression could not be determined. The beta weights and associated p-values for

the term of interest (β_2) are reported for each regression in each set of models. Positive (negative) beta weights mean higher vaccinations predict higher (lower) mortality. Each set of models consisted of $8 \times 7 = 56$ regressions and resulting p-values, which were corrected for multiple comparisons using Benjamini-Hochberg False Discovery Rate (FDR) correction (10).

Since most (VAERS reported) vaccine-related deaths events occur within 1-2 weeks of vaccination, an additional set of models were estimated in which vaccinations were used to predict total deaths in the same month. Significant effects from these models replaced results when significant results using previous month vaccinations were not detected and were used instead when estimating deaths for that particular age group and month (Tables 2 and 3). To potentially improve sensitivity in detecting vaccination effects in older age groups, an additional model in which the number of vaccines administered to ages >65 years (instead of all ages) predicted deaths among ages >65 years was estimated. The significant results of these models replaced results from equivalent models with non-significant results and when estimating deaths attributed to vaccination. Since the number of vaccines administered by age is not recorded until the first week of March (Administered_65Plus column in (3)) these models employing age-specific vaccinations are estimated only for April-August.

Controlling for COVID-associated deaths

To control for deaths due to COVID in young adult, middle and older age groups, regressions were also run to predict non-COVID deaths (i.e. the number of total deaths minus deaths due to COVID, Influenza or Pneumonia which are provided in the same spreadsheet as total deaths). In addition, another set of models similar to Eq. 1 were estimated in which log # COVID cases in the previous month were included as an additional covariate.

Controlling for seasonality, population size, and mortality differences across states

Both the number of administered vaccine doses and number of deaths in a given time period is highly correlated with population size of each state. However, age-stratified population size was not adjusted for in the analyses. Rather, the analyses adjusted for the number of deaths in the same month during the previous year. This effectively controls for age-stratified population size differences across states while additionally controlling for seasonal effects on mortality and state-to-state variability in mortality due to other factors. In a post-hoc analysis, age-stratified populations were correlated with residual deaths (Y21 deaths after adjusting for Y20 deaths), which confirmed that controlling for Y20 deaths effectively removes variance due to age-stratified population difference (all p-values for Spearman rank correlation coefficients ranged between 0.15 and 0.9).

Estimating number of deaths attributed to COVID vaccination

The estimated beta (β_2) weights (regression slopes) that survived $p < 0.05$ FDR corrected were used to estimate death counts for that month and age group. Briefly, for each age group, the increase in deaths attributed to a small (i.e. 10%) increase in vaccinations across all states was used to estimate a vaccine mortality rate for each age group. The rate was then multiplied by the total count of administered vaccination for that month to arrive at an estimated number of deaths attributed to vaccination.

For each state with Y20 death data, increases in deaths due to 10% increase in vaccinations was estimated by solving a system of equations for \hat{Y}_1 and \hat{Y}_2 , where \hat{Y}_1 is the estimated Y21 deaths given the actual vaccine doses administered in that state, and \hat{Y}_2 is the predicted Y21 deaths given a 10% increase in the actual vaccine doses administered in that state:

$$\log(\hat{Y}_1) = \beta_0 + \beta_1 \log(\text{Y20_deaths}_1) + \beta_2 \log(\text{Vax}_1) + \varepsilon \quad (2)$$

$$\log(\hat{Y}_2) = \beta_0 + \beta_1 \log(\text{Y20_deaths}_1) + \beta_2 \log(\text{Vax}_1 \cdot 1.1) + \varepsilon \quad (3)$$

Solving for \hat{Y}_2 yields:

$$\hat{Y}_2 = \hat{Y}_1 * e^{\beta_2 \log(1.1)} \quad (4)$$

The differences between \hat{Y}_2 and \hat{Y}_1 were summed across all N states with available Y20 data, and then divided by 1/10th (10%) of the sum of vaccine doses administered across those states to estimate an age-specific vaccine-attributed fatality rate (aVFR) for that age group and month:

$$aVFR \approx \left(\frac{\sum_{k=1}^N \hat{Y}_2^k - \hat{Y}_1^k}{\sum_{k=1}^N 0.1 \cdot Vax_1^k} \right) \quad (5)$$

Finally, the aVFR was multiplied by the total number of vaccinations in the US during the month used in the regression model to arrive at an estimated death count attributed to vaccines for each month and age group that survived the applied significance threshold. The values are then used to populate the cells in Table 2.

Two approaches were used to estimate a US national average and age-stratified VFRs. The US national average VFR was estimated by dividing the death counts estimated above, summed over all age groups and months, by the total number of vaccine doses administered between January and August 21st. A second approach averaged across all monthly aVFRs (equation 5) within each age group, calculated based on thresholded regression weights ($p < 0.05$ uncorrected), resulting from the 3 model variations (i.e. the primary model using previous month vaccination, a second model using same month vaccinations, and a third using previous month vaccinations in ages > 65 years). A liberal threshold of $p < 0.05$ uncorrected was used to increase the sample size of rates used for the average. This yielded an estimated aVFR for each of the age groups analyzed in the study.

Supplementary Discussion

Errors and concerns raised with vaccines safety studies of pregnant women

Although vaccination during pregnancy is reported as safe by the US CDC (11), a number of issues and concerns have been raised with the studies supporting vaccine safety among pregnant women. Brock and Thornley (12) and McCullough et al. (13) point out several errors in an early safety

study among pregnant women by Shimabukuro et al. (14). The original Shimabukuro et al. study reported a spontaneous abortion rate <20 weeks gestation rate of 12.6% after vaccination, which is similar to previously published background rates. However, their denominator includes ~700 women who were vaccinated after the timeframe for recording the outcome had elapsed (up to 20 weeks of pregnancy). Excluding those participants results in a spontaneous abortion incidence rate that 7-8 times higher (82%-91%) than the originally report rate. Note that the rate seems high because the study only examined completed pregnancies and many participants were yet not followed up on at the time of the report (at early stages the majority of completed pregnancies are expected to be spontaneous abortions). Shimabukuro et al. has since issued correction which now states “No denominator was available to calculate a risk estimate for spontaneous abortions” in the Table footnotes. However, the article abstract, results and discussion still report and discuss the initial findings of the study, including the 12.6% spontaneous abortion rate in those exposed to vaccines before 20 weeks.

A related, more recent case-control study by Kharbanda et al. concluded “Among women with spontaneous abortions, the odds of COVID-19 vaccine exposure were not increased in the prior 28 days compared with women with ongoing pregnancies” (15). However, contrary to the authors’ conclusions, a comment on the article by Cosentino points out that a reanalysis of the frequencies reported in Table 1 shows the crude OR of vaccine exposure in women with spontaneous abortions is 1.07 (95% CI: 1.01-1.14, $p = 0.025$ by Fisher's exact test), a result that is apparently fully accounted for by the maternal age group 16-24 y, where the crude OR is 1.37 (95% CI: 1.07-1.75, $P = 0.017$). Cosentino also points out the arbitrariness of using 28 days as a window. Why not track and report spontaneous abortion rates across all participants up through week 19 gestation? The response by Kharbanda et al. to Cosentino states that their results differ because they controlled for confounding variables, but they do not report statistics for the nuisance terms, making it difficult to assess which nuisances variable accounted correlated with higher spontaneous abortions rates and why. Finally, we note that the authors’ original analysis DOES report trend level evidence for increased risk of

spontaneous abortion (see Table 2, gestation weeks 9-13, OR 1.07, 95% CI 0.99-1.17), but the result is not discussed by the authors elsewhere in the article.

Reasons arguing why our results evidence a causal link (not just an association) between vaccination and mortality:

1. Vaccination predicts mortality in future time periods. Thus results do not reflect increases in vaccination rates that are caused by increased mortality. Temporal precedence is a basis for inferring causality in i.e. Granger causality analysis.
2. Our estimates for total deaths due to vaccination are strikingly similar to independent estimates based on a fundamentally different dataset and approach based on the VAERS database that uses data-driven, credible assumptions about the VAERS underreporting bias (16). Our results provide independent, converging lines of evidence for vaccine-induced mortality risk, lending further credence to their accuracy and credibility.
3. We are aware of only one variable, COVID cases, that could potentially confound our results. This could happen IF more people get vaccinated as local COVID cases rise and COVID deaths comprise a majority of the deaths in subsequent time periods. Below are the main reasons why COVID case rates do NOT explain our findings:
 - a. An additional set of analyses that include COVID case numbers in previous month as a nuisance regressor yielded largely similar results (Supplementary Table S5).
 - b. A secondary set of analyses that use non-COVID, Influenza, and Pneumonia deaths (non-COVINFPNU) as the dependent variable yielded similar results to analyses that use total deaths, but with larger p-values because there are substantially fewer observations for each regression (Supplementary S6). Note that non-COVINFPNU deaths were not used as the primary outcome because the COVID death variable is missing for younger ages (sample size is cut in half for ages 40-49 and below 30 it is

about 10-25% of the full sample size when using Total Deaths), and for the younger age groups it is zero for most states that do report a value.

- c. Vaccination rates predict mortality in younger age groups (where COVID deaths are much rarer), providing further support that the effects seen here are not due to COVID.
4. The existing COVID vaccine surveillance studies supporting vaccine safety contain critical errors, issues and limitations (see Discussion, Supplementary Discussion and (17)).
5. Our results comport with the volume and nature of responses to social media posts, the FDA dockets for solicited public comments, and websites created to give voice to the vaccine-injured (see below section for sample links and URLs).
6. Our US results show an age-related temporal pattern that is consistent with the mass vaccination campaign that first targeted nursing homes and older age groups (i.e. vaccination predicts total deaths in ages older than 75 in early 2021, and then in younger ages later in the year). There appears to be no other explanation for this other than a causal link between vaccination and mortality risk.
7. Given items 1-6 and the absence of other potential confounding variables, the most logical and reasonable conclusion is that our results reflect a causal effect of COVID vaccination on mortality.

Life-altering COVID vaccine injuries: real-world evidence through personal testimonials

To help give a real-world sense of the risks and impact of COVID vaccines, readers are encouraged to browse through some of the testimonials on c19vaxreactions.com and nomoresilence.world, two websites dedicated to giving voice to those injured by COVID vaccines. Readers are also encouraged to sift through the over 100K solicited comments submitted to the public FDA advisory committee meeting held on Oct 26th, 2021 to discuss approval of the COVID vaccines for children ages 5-11 at <https://www.regulations.gov/document/FDA-2021-N-1088-0001>. Perusing through over 250K comments left on a Facebook post by WXZY-TV Channel 7 news

<https://www.facebook.com/wxyzdetroit/photos/a.461583946134/10158207966696135> is also

illuminating. The post asked people who had lost an unvaccinated loved one to COVID to contact them for a story, but instead received tens, if not hundreds, of thousands of stories of vaccine injuries or deaths instead. The post is telling of how injured patients, or those who have lost friends or family to vaccine-induced death, are often ignored by the same major news outlets that encouraged them to be vaccinated. This is understandable, as no one, especially those with good intentions and high hopes but who were misled by less-than-rigorous science, wants to acknowledge the possibility that the COVID vaccines and their boosters may be causing more harm than good overall. The sooner the taboo surrounding research and discussion of vaccine-induced injury and death is lifted, the sooner public health policy can be adjusted and resources can be mobilized to identify and develop therapies and interventions.

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Supplementary Table S1. Weekly increases in percent vaccinated in 23 European countries, Coronavirus (COVID-19) Vaccinations - Statistics and Research - Our World in Data. See [Supplementary Table 1 spreadsheet](#) (18).

Supplementary Table S2. Weekly total mortality data for 6 age classes for the first 33 weeks of 2021 from 23 European countries (<https://www.euromomo.eu/graphs-and-maps>). See [Supplementary Table 2 spreadsheet](#) (18).

Supplementary Table S3. Pearson correlation coefficient r between weekly injection percentage and weekly mortality for 6 age classes (appendices 1 and 2) for 23 European countries. See [Supplementary Table 3 spreadsheet](#) (18).

Supplementary Table S4. COVID Cases, prior month vaccinations and age-stratified mortality for April 2021. Cumulative number of vaccinations or COVID cases are as of April 1st, 2021. See [Supplementary Table 4 spreadsheet](#) (18). For the same tables for all other months see the Tables subfolder in the git repo (<https://github.com/spiropan/CoVFR>).

Supplementary Table S5. Same as main text Table 2, except models adjust for previous month COVID cases. For each month in 2021, beta weights and uncorrected p-values are listed for the vaccination (b3) term in the GLM equation: $\log(\text{Total Deaths Y21}) \sim b_0 + b_1 \cdot \log(\text{Total Deaths Y20}) + b_2 \cdot \log(\text{previous month COVID cases}) + b_3 \cdot \log(\text{vaccine doses administered previous month})$ across all US states with available data for that month and age group (~42-52 states for each regression). Yellow indicates positive slopes with p-values < 0.05 FDR corrected.

Ages	February		March		April		May		June		July		August	
	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>
0-17	0.20	0.0804	-0.04	0.788	-0.06	0.7097	0.08	0.3919	0.15	0.0781	0.25	0.0006	0.85	0.0002
18-29	0.05	0.67	0.02	0.8675	0.08	0.5718	0.35	0.0022	0.17	0.0087	0.43	0.001	0.48	0.0245
30-39	0.10	0.236	0.11	0.3307	0.12	0.3057	0.22	0.0246	0.06	0.2361	0.18	0.0338	0.43	0.0001
40-49	0.04	0.5992	0.10	0.1467	0.31	0.0066	0.04	0.6619	-0.01	0.8911	0.25	0.0011	0.33	0
50-64	0.01	0.8772	-0.05	0.3089	0.07	0.4449	-0.03	0.7569	-0.01	0.8857	0.00	0.9619	0.06	0.7524
65-74	-0.03	0.6456	-0.01	0.7956	0.55	0	0.06	0.5136	-0.06	0.2174	0.04	0.4281	0.14	0.3689
75-84	0.00	0.9792	0.03	0.5138	0.74	0	0.09	0.313	-0.04	0.4667	0.08	0.3745	0.10	0.4944
85-plus	0.08	0.0421	0.18	0.0011	0.80	0	0.20	0.0065	-0.02	0.6827	0.06	0.5826	0.09	0.5876

Supplementary Table S6. Same as main text Table 2, except the dependent variable is Non-COVID-Influenza-Pneumonia (COVINFPNU) Deaths. For each month in 2021, beta weights and uncorrected p-values are listed for the vaccination (b2) term in the GLM equation: $\log(\text{Non-COVID-Influenza-Pneumonia Deaths Y21}) \sim b_0 + b_1 \cdot \log(\text{Non-COVID-Influenza-Pneumonia Deaths Y20}) + b_2 \cdot \log(\text{vaccine doses administered previous month})$ across all US states with available data for that month and age group. Note that because COVID deaths are relatively rare among younger age groups, there are much fewer states with available data for Non-COVID-Influenza-Pneumonia deaths, particularly for the ages 0-49 (denoted with an asterisk). There were <9 data points for ages 0-17, <15 for 18-29, <18 for 30-39, and <28 for ages 40-49. Yellow (light peach) indicates positive slopes with p-values < 0.05 FDR corrected (p<0.05 uncorrected).

Ages	February		March		April		May		June		July		August	
	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>	<i>beta</i>	<i>pval</i>
0-17*	0.16	0.7765	0.12	0.884	0.02	0.9609	0.09	0.5649	0.17	0.2077	0.18	0.44	1.09	0.1555
18-29*	0.34	0.241	0.24	0.4753	-0.08	0.8776	0.34	0.0484	0.23	0.0492	0.17	0.4183	0.61	0.1516
30-39*	0.24	0.0403	0.13	0.6711	0.29	0.428	0.19	0.2136	0.32	0.0045	0.51	0.0009	0.52	0.1312
40-49*	0.14	0.097	0.09	0.3116	-0.08	0.5875	-0.03	0.6914	0.03	0.5984	0.22	0.0214	0.25	0.1238
50-64	0.13	0.0983	-0.04	0.4401	0.06	0.5302	-0.02	0.7485	0.04	0.4562	0.07	0.1317	0.10	0.5667
65-74	0.11	0.1673	-0.05	0.3438	0.23	0.0241	0.04	0.5858	-0.02	0.6384	0.05	0.3212	0.23	0.0173
75-84	0.05	0.5033	0.03	0.569	0.44	0.0004	0.07	0.4253	-0.01	0.9219	0.09	0.0637	0.16	0.1436
85-plus	0.17	0.0015	0.15	0.0531	0.79	0	0.19	0.0074	0.01	0.9093	0.09	0.1393	0.10	0.3665

Supplementary Table S7. Same as Table 3 of main text, except deaths were estimated based on robust regression results thresholded at $p < 0.05$ uncorrected.

Estimated Deaths									
Ages	Jan	Feb	March	April	May	June	July	Aug	Total
0-17	NA	NaN	NaN	NaN	NaN	NaN	647.76	1226.97	1874.73
18-29	NA	NaN	NaN	NaN	1354.55	563.56	1055.33	1832.9	4806.34
30-39	NA	NaN	NaN	NaN	NaN	691.16	1212.1	2176.17	4079.43
40-49	NA	NaN	NaN	NaN	NaN	NaN	1329.07	2673.17	4002.24
50-64	NA	NaN	NaN	NaN	NaN	NaN	NaN	7057.19	7057.19
65-74	NA	NaN	NaN	NaN	NaN	NaN	NaN	12208.21	12208.21
75-84	NA	NaN	NaN	41316.18	NaN	NaN	NaN	NaN	41316.18
85-plus	NA	11613.29	13180.95	55443.25	13326.06	NaN	NaN	NaN	93563.55
								Total	168,908

Supplementary Table S8. Model-estimated deaths attributed to COVID-19 vaccination for each age group and month. Same as Table 3 of main text, except deaths were estimated based on standard linear regression (glmfit MATLAB function) thresholded at $p < 0.05$ FDR corrected. Beta weight coefficients estimated from Equation 1 and surviving $p < 0.05$ FDR corrected were used to estimate VFR and total deaths for each age group and month. If a model using same (not previous) month vaccinations was significant and the equivalent models using previous month was not, then death counts from those models were used instead (light gray boxes). Similarly, if a model using age-specific (i.e. >65 yrs) vaccine dose administrations was significant and the equivalent models using total vaccine doses administered was not, then death counts from those models were used instead (dark gray boxes). See methods for VFR and aVFR definitions and calculations. ns=not significant at $p < 0.05$ FDR corrected. NA=Not available.

Estimated Deaths and aVFR										
Ages	Jan	Feb	March	April	May	June	July	Aug	Total	aVFRs (%)
0-17	NA	ns	ns	ns	ns	ns	576	1,311	1,887	0.0031
18-29	NA	ns	ns	ns	1,400	833	1,226	ns	3,459	0.0051
30-39	NA	ns	ns	ns	ns	ns	2,644	ns	2,644	0.0067
40-49	NA	ns	ns	ns	ns	1,905	3,412	ns	5,317	0.0087
50-64	NA	ns	ns	ns	ns	ns	ns	ns	0	0.0157
65-74	NA	ns	ns	23,813	ns	ns	ns	ns	23,813	0.0363
75-84	NA	ns	ns	26,679	ns	ns	ns	ns	26,679	0.0670
85-plus	NA	ns	13,136	39,101	17,346	ns	ns	ns	69,583	0.0529
								Total	133,382	

Supplementary Table S9. Model-estimated deaths attributed to COVID-19 vaccination for each age group and month. Same as Supplementary Table S5, except deaths were estimated based on standard linear regression (*glmfit* MATLAB function) thresholded at $p < 0.05$ uncorrected. Beta weight coefficients estimated from Equation 1 and surviving $p < 0.05$ uncorrected were used to estimate VFR and total deaths for each age group and month. If a model using same (not previous) month vaccinations was significant and the equivalent models using previous month was not, then death counts from those models were used instead (light gray boxes). Similarly, if a model using age-specific (i.e. >65 yrs) vaccine dose administrations was significant and the equivalent models using total vaccine doses administered was not, then death counts from those models were used instead (dark gray boxes). See methods for VFR and aVFR definitions and calculations. ns=not significant at $p < 0.05$ uncorrected. NA=Not available.

Estimated Deaths									
Ages	Jan	Feb	March	April	May	June	July	Aug	Total
0-17	NA	474 ns	ns	ns	306 ns	ns	576	1,311	2,667
18-29	NA	ns	ns	ns	1,400	544.24	1,226	2,093	5,263
30-39	NA	1,703 ns	ns	ns	ns	785	1,385	2,454	6,327
40-49	NA	ns	1,887 ns	ns	ns	1,905	1,347	2,764	7,902
50-64	NA	ns	ns	ns	ns	8,256 ns	ns	ns	8,256
65-74	NA	ns	ns	15,212	7577.31	ns	ns	ns	22,789
75-84	NA	ns	ns	26,679	11893.16	ns	26042	ns	64,614
85-plus	NA	ns	13,136	39,101	17346.48	ns	ns	ns	69,584
								Total	187,402

Supplementary Figure S1. Plots of log transformed vaccination vs. monthly Y21 deaths adjusted for Y20 deaths. Results are plotted for each model in which the vaccination terms was significant at $p < 0.05$ FDR corrected (see Table 2 and Table 3 of main text). ns=not significant. For higher resolution images [see Supplementary Figure S1](#) (18).

