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Understanding COVID-19 Vaccine Effectiveness Against Death Using a Novel Measure: COVID Excess Mortality Percentage

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Abstract

Background. While vaccines against COVID-19 have saved millions of lives, it is important to understand the remaining risk to the vaccinated and the incremental benefit of additional vaccine doses. Comparisons between more and less vaccinated groups can be misleading due to selection bias, because these groups can differ in underlying health and thus COVID-19 risk. The authors study by how much COVID-19 increased mortality from natural causes, controlling for underlying health.

Methods. They conduct a retrospective analysis of all deaths in Milwaukee County, Wisconsin, linked to vaccination records, and compare the percentage increase in deaths from natural causes due to COVID-19 between unvaccinated persons and those receiving 1, 2, or 3 vaccine doses, using an outcome measure that controls for non-COVID mortality and thus for population health, over April 1, 2021-March 31, 2022. We report how vaccination affects Relative Mortality Risk (RMR, defined as COVID-19 death as a fraction of other natural deaths for vaccinated persons, relative to this fraction for the unvaccinated) by age group and time period.

Findings. RMR was higher (vaccine effectiveness was lower) than in studies that did not address selection. RMR for two-dose vaccine recipients was 15.5% during April-June 2021, 19.0% during July–September 2021, 22.9% during October–December 2021 and 36.0% during January–March 2022, corresponding to Alpha, early Delta, later Delta, and Omicron-dominant periods. A booster dose reduced RMR to 8-9%. RMR was higher for ages 60+. Selection effects were large; unvaccinated persons had over twice the risk of non-COVID natural death than the vaccinated.

Interpretation. Studies of vaccine effectiveness against mortality that do not control for underlying health will overstate effectiveness. Using a measure that controls for population health, fully vaccinated older individuals have substantial RMR, but boosters provide important protection.

The Online Appendix can be downloaded from: http://ssrn.com/abstract=3706517.

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Panel: Research in Context

Evidence before this study

Prior studies of the effect of COVID-19 vaccination on death report high levels of vaccine effectiveness (VE), and correspondingly low levels of relative mortality risk (RMR = 1 – VE) for fully vaccinated versus unvaccinated persons; with some but limited waning of VE over time. However, these studies generally do not control for selection bias – the tendency for the vaccinated to be in better health than the unvaccinated, and thus to face lower COVID-19 mortality risk even if not vaccinated. Prior research is also limited to the period of Delta-variant dominance and does not address the value from a booster dose, or a single mRNA vaccine dose, in reducing mortality.

Added value of this study

We conducted a population-level analysis of all deaths in Milwaukee County, Wisconsin, linked to vaccination records, over April 1, 2021-March 31, 2022. We computed by age group and time period, for unvaccinated persons and those receiving 1, 2, or 3 vaccine doses, the COVID-19 Excess Mortality Percentage (CEMP), defined as deaths due to COVID-19 divided by deaths from other natural causes, converted to a percentage. The CEMP measure controls for population health through the denominator (deaths from other natural causes). We then measured relative mortality risk (RMR) as (CEMP for vaccinated persons divided by CEMP for unvaccinated persons). We report how vaccination and number of vaccine doses affects RMR over periods of Alpha, Delta, and Omicron dominance. We find larger RMR levels than prior studies, including stronger waning of effectiveness against death. For example, in the first quarter of 2022 (Omicron period), two-dose RMR versus the unvaccinated is 36%. RMRs are much higher for ages 60+ than ages 18-59. We also find large selection bias, which increases with the number of vaccine doses. For example, the two-dose vaccinated have less than half the risk of the unvaccinated of dying from other natural causes. These two findings are related: If we did not control for underlying health, we would find RMRs much closer to those from prior research. A third (booster) substantially reduced RMR. One vaccine dose (mRNA or J&J) provided moderate but apparently durable protection against death.

Implications of all the available evidence

Studies of vaccine effectiveness face substantial selection bias: The vaccinated are healthier than the unvaccinated. After controlling for selection effects, we find that VE against death is lower, and RMR is higher, than reported in prior studies. Booster doses provide important reductions in RMR, especially for persons aged 60+. One vaccine dose also provides meaningful, durable protection, although less than two doses.

Keywords: COVID-19; COVID-19 mortality; cause of death; COVID Excess Mortality

Percentage; vaccine effectiveness; vaccine efficacy; selection bias.

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Understanding COVID-19 Vaccine Effectiveness Against Death Using a Novel Measure: COVID Excess Mortality Percentage

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Introduction

It is important to understand the real-world effectiveness against mortality of the principal U.S.-approved COVID-19 vaccines. While randomized trials provided high quality evidence for vaccine efficacy in preventing infection, they were not powered to provide evidence on mortality. COVID-19 vaccines have saved millions of lives. However, it is important, especially given waning of the protective effect of vaccination over time and against newer variants, to understand the extent to which vaccination has reduced COVID-19 mortality, and the value of a booster dose.

Many studies have reported real-world evidence on vaccine effectiveness (VE) against infection, hospitalization, and death (for succinctness, we cite systematic reviews).[1,2] However, most studies assess VE with limited controls for individual characteristics, often only age and gender. These studies face selection bias. Suppose that health-conscious people are more likely to be vaccinated against COVID-19. Then lower COVID-19 mortality among the vaccinated would partly reflect their (unobserved) better health and thus lower risk even if not vaccinated.

We provide evidence on this selection effect, measure its magnitude, and address it by studying the impact of vaccination on COVID-19 mortality for the entire population of a large Midwestern city. We use natural, non-COVID mortality to proxy for underlying health. We calculate the COVID Excess Mortality Percentage (CEMP) – COVID deaths in a population as a fraction of all natural deaths in that population. In addition, we adjust for other variables available from death certificates that may be associated with mortality risk from COVID-19 and other natural causes.

Data and Methods

We obtain linked, de-identified mortality and vaccination records for Milwaukee adults aged 18+ (adult population 722,000), for January 1, 2021, through March 31, 2022, including 5-digit zip code of residence, age at death, gender, race/ethnicity, education, income, marital status, veteran status, manner of death, and text fields for primary cause of death, conditions contributing to death, and other significant conditions. We use text analysis to identify which natural deaths are due to COVID-19; this approach counts more COVID-19 deaths than relying on ICD-10 cause-of-death codes, prepared by the National Center for Health Statistics (NCHS) based on the text fields. We treat vaccine doses as effective against mortality beginning 14 days after receipt, and exclude immune-compromised decedents (see Appendix for details).

CEMP, VE, and RMR

We define the COVID-19 Excess Mortality Percentage (CEMP), as the percentage increase in natural deaths due to COVID-19:

$$CEMP = 100 \times \frac{COVID\text{-}19\ deaths}{Natural\ deaths - COVID19\ deaths} \quad (1)$$

The mRNA vaccines (Moderna, Pfizer) use two initial does; J&J uses one dose. We report results based on number of doses, thus treating one J&J dose as equivalent to one mRNA dose, but obtain similar results if we exclude J&J vaccinees.

We define VE and relative mortality risk after vaccination (RMR) in each time period as:

$$VE = \frac{(CEMP_{unvax} - CEMP_{vax})}{CEMP_{unvax}} \quad ; \quad RMR = 1 - VE = \frac{CEMP_{vax}}{CEMP_{unvax}} \qquad (2)$$

Below, we discuss principally RMR, which can be obtained directly from comparing mortality rates for both groups, or as an odds ratio for the effect of vaccination on death, from logistic regression for a population containing both groups. We use similar definitions to compute RMR and VE for two-versus-one-dose and three-versus-two-dose vaccinees. By using non-COVID natural deaths in the CEMP denominator, we treat the non-COVID natural mortality rate as a proxy for the overall health of a given group. Several risk factors for COVID mortality also predict non-COVID mortality. [3,4]

CEMP represents the odds, for a sample of natural-cause decedents, of dying from COVID-19 versus other natural causes. The ratio of CEMPs for two different groups, such as two-dose vaccinated versus unvaccinated, is an odds ratio, obtainable from logistic regression. We conduct multivariate logistic regression analysis of how vaccination affects RMR. The predictors are age, age^2, zip-code-level socio-economic status (zip-SES),[5] gender, race/ethnicity, education level, marital status, and military veteran status. We measure race/ethnicity as non-Hispanic White ("White"), Black, non-Black Hispanic ("Hispanic") and Other (including Asian, Native American, and mixed race).

Non-COVID-19 Natural Mortality Rate (NCNMR)

To assess whether vaccinated persons have different underlying health than the unvaccinated, proxied by their mortality rate from other natural causes, we need to estimate population. We use population estimates for 2020 from the American Community Survey. We measure the number of people receiving 1, 2, or 3 vaccine doses; and assume the remaining population is unvaccinated (see Appendix for details).

We define the NCNMR, and relative NCNMR for two groups with different numbers of vaccine doses *v* as of time of death, in each time period *t*, as:

$$NCNMR_t = \frac{(natural\ non{-}COVID{-}19\ deaths)_{vt}}{Population_{vt}} \ ; \ relative\ NCNMR_{v1t/v2t} = \frac{NCNMR_{v1t}}{NCNMR_{v2t}} \quad (3)$$

Results

Vaccination rates

Appendix Table App-1 provides summary information on vaccinated adults in Milwaukee, and which vaccine they received. Overall, around 74% of the adult population received at least one dose, 70% were fully vaccinated (one J&J dose or two mRNA doses), and of two-dose recipients, 56% received a third dose. These percentages are broadly in line with national averages.

Figure 1, Panel A, provides information on "full vaccination" rates (two mRNA doses or one J&J dose) by age range over time. Vaccine uptake was faster and more complete among those aged 60+, highest for ages 60-79, and slower and less complete at younger ages. Panel B provides information on receipt of a third dose, generally a booster dose following two-dose vaccination

with an mRNA vaccine. Three-dose percentages (conditional on receiving two doses) rise with age, but are similar for ages 60-79 and 80+.

CEMP and RMR by Quarter and Age Range: Overview

Table 1 reports the number of COVID-19 deaths, of natural deaths not due to COVID–19, and CEMP (the ratio of the two), in groups defined by age range and number of doses, for four periods: April-June 2021 (2Q-2021) with Alpha as the dominant virus variant; July-September 2021 (3Q-2021), Delta dominant, no boosters; October-December 2021 (4Q-2021), Delta dominant, boosters available; and January-March 2022 (1Q-2022), Omicron dominant. These periods correspond fairly well to when the respective variants accounted for a majority of infections (see Appendix)

Table 1 presents unadjusted results for COVID-19 deaths, other natural deaths, and CEMP by age group, time period, and vaccination status, and RMR for vaccinated versus unvaccinated groups. We present results by period, given evidence from other studies on waning vaccine effectiveness over time, differences in severity between the Delta and Omicron variants, and potential differences in RMR between variants. We also report full-sample RMRs for three-versus-two, three-versus-one, and two-versus-one dose. Many death counts in individual cells are small, and RMR estimates are therefore rough. Appendix Table App-2 reports 95% confidence intervals (CIs) for the RMRs.

CEMP levels for all groups were low in 2Q-2021 -- a relatively low period for COVID-19 infections and deaths -- but rose substantially in the 3Q-2021 (early Delta period) and further in 4Q-2021 (late Delta period). For the unvaccinated CEMP rose from 5.2% in 2Q-2021, to 17.5% in 3Q-2021, 34.8% in 4Q-2021, and 31.8% in 1Q-2022, with some variation by age. During the Omicron period (1Q-2022) CEMP levels fell substantially for persons under age 60 relative to 4Q-2021 (Delta period), but rose for ages 60+.

RMR for Two Doses Versus the Unvaccinated

Vaccine protection decreased during the study period, with two-dose RMR levels rising from 16% in 2Q-2021 to 19% in 3Q-2021, 23% in 4Q-2021, and 36% in 1Q-2022. However, we cannot separate the effects of waning over time from changes in the dominant virus variant.

We also find important differences in two-dose RMR for younger versus older persons. For persons aged 60+, protection is generally weaker than for younger persons, with progressive waning. RMR rises from 17% to 24% to 30% to 32% across calendar quarters. For persons aged 18-59, RMR is 0% (no deaths), 0%, and 3%, before rising in the Omicron period, to 63%, which may reflect small cell counts. RMR was nearly zero for ages 18-49, with only one death among two-dose recipients – a severely comorbid 35-year-old woman during 1Q-2022.

RMR for Booster Dose

Receipt of booster dose offered considerable additional protection. The RMR for booster recipients was 8.4% in 4Q-2021 and 8.7% in 1Q-2022. The protection offered by boosters varied considerably with age; for ages 18-59, RMR for a booster dose was 0% (99 COVID-19 deaths among unvaccinated persons versus none among three-dose recipients). Older persons, in contrast,

face meaningful risk even with a booster dose. For ages 60+, we found RMR of 14.5% for 4Q-2021 (Delta) and 10.3% for 1Q-2022 (Omicron).

RMR for One Dose

One-dose RMR has been rarely studied. RMR relative to the unvaccinated is substantial, at 54%, 58%, 32%, and 42% across our four time periods. One-dose RMR was similar in older and younger individuals and, unlike two-dose RMR, did not exhibit waning across our time periods.

Multivariate Estimates

In Table 2, we use a multivariate logistic model to predict RMRs for more versus less vaccinated groups, for the same sample as Table 1. The multivariate RMRs are consistent with the estimates presented in Table 1. For example, in 1Q-2022 (Omicron period), multivariate RMR for all two-dose recipients versus the unvaccinated is 35.4%, versus 36.0% from Table 2.

The similarity between unadjusted and multivariate estimates provides evidence that mortality risk from other natural causes does a good job of controlling for underlying health. Factors which predict COVID-19 mortality, including zip-SES, gender, race/ethnicity, and education,[6,7] have little effect on our estimates.

Robustness Checks

CEMP and RMR levels are slightly higher if we include the immune-compromised (Table App-5), but similar if we define immune-compromised more broadly (Table App-6), exclude J&J vaccine recipients (Table App-7), or use a 30-day between vaccination and assumed effectiveness (Table App-8). Results are similar across genders and for Whites versus non-Whites (Tables App-9, App-10).

Evidence for Selection Effects

Selection effects could explain why our RMR estimates are above those reported elsewhere. Table 3 provides evidence on selection effects. It reports mortality rates for non-COVID-19 natural causes (NCNMRs), by age group, vaccination status, and time period. NCNMRs vary strongly with vaccination status. For example, cumulative mortality for persons aged 18-59, over the four time periods, is 0.258% for the unvaccinated, versus 0.099% for the maximally vaccinated (two doses, plus a booster when available (ratio of 2.61:1). For ages 60+, the cumulative mortality rates are 5.15% for unvaccinated versus 2.18% for maximally vaccinated (for a ratio of 2.36:1). Related CIs are in Table App-11.

Selection effects are found across the spectrum of vaccine doses, with one-dose recipients having lower NCNMRs than the unvaccinated, two-dose recipients having lower NCNMRs than one-dose recipients, and three-dose recipients having lower NCNMRs than two-dose recipients.

In Appendix Figure App-1, we assess whether differences in NCNMRs could reflect either incomplete reporting of COVID-19 deaths or excess non-COVID mortality, related to prior COVID-19 infection. Neither can explain the apparent selection effects.

In Appendix Table App-12, we estimate RMRs using the COVID-19 mortality rate as the outcome. Consistent with the selection effects reported in Table 3, RMRs are substantially lower. For example, for ages 60+, two-dose RMR across sample quarters is (8%, 11%, 17%, 24%), versus our finding above (17%, 24%, 30%, 32%); three-dose RME across available quarters is (2%, 4%) versus (8%, 9%).

Discussion

Overview of Results

Our analysis provides a number of valuable insights. both for vaccine effectiveness against mortality and selection effects in who gets vaccinated. First, two-dose RMR estimates are substantially higher (and VE is correspondingly lower) than in other studies. For example, during 2H-2021, when the Delta variant was dominant, we estimate two-dose RMR versus the unvaccinated at 21% (average of 3Q-2021 and 4Q-2021). During 1Q-2022 (Omicron dominance), RMR for two doses versus unvaccinated is 36%. We believe that these higher estimates reflect our use of CEMP to measure COVID-19 mortality risk, which partly controls for otherwise unobservable health characteristics that affect COVID-19 risk.

Second, the vaccinated are healthier than the unvaccinated. Cumulative mortality from other natural causes for the unvaccinated is over twice that of the maximally vaccinated. Other studies do not control for these selection effects, and therefore severely overestimate the protective effect of vaccination. Although beyond the scope of this study, similar selection effects likely exist for studies of other severe-disease outcomes, such as hospitalization. Third, we find substantial waning of two-dose protection against mortality. We find RMR for two doses versus unvaccinated increases from 16% to 19%, 23%, and 36% over 2Q-2021 to 1Q-2022. This could reflect the impact of waning efficacy over time, lower efficacy against Delta and Omicron or some of both. Fully vaccinated (two doses) does not mean fully protected, particularly for the elderly. This also contrasts with prior studies, which typically report minimal evidence of waning against severe disease and death.[1,2]

Fourth, we find that a booster dose provides substantial additional protection, reducing RMR for all ages to 8.4% in 4Q-2021 and 8.7% in 1Q-2022, versus 23% and 36% for two-dose recipients. Nonetheless, our results suggest significantly more residual risk than prior booster studies, which did not control for selection effects. For example, a UK study found 1.3% RMR for boosted versus unvaccinated for ages 50+ (when this and other studies report VE, we convert to RMR).[8] One Israeli study finds 10% RMR for three-versus-two-doses for ages 50+;[9] a second reports three-versus-two-dose RMR of 6.8% for ages 60+;[10] a third reports three-versus-two-dose RMR of 19% across all ages.[11] All of these studies are during the Delta period.

Fifth, we find stronger protection from two or three doses for ages 18-59, compared to older persons, including zero deaths among younger three-dose recipients. These results support booster value for younger persons, many of whom may believe that two doses provide sufficient protection.

Finally, we find that a single dose provides only moderate protection, with RMR versus the unvaccinated around 50%, which appears to be long-lived. Similar results have been reported before for the single-dose J&J vaccine.[12,13] We find similar results for mRNA recipients.

We found only one other U.S. study that reports RMR after linking population-wide mortality and vaccination data. A study of Puerto Rico through mid-October 2021 (thus pre-Omicron and pre-booster), reports two-dose RMR after 144 days (longest period considered) of 14% for Pfizer and 7% for Moderna, versus 3% and 1% soon after vaccination.[14] This study does not control for selection effects.

The studies covered by systematic reviews report lower RMRs, from 6-12%.[1,2] One study reports RMRs similar to ours for U.S. veterans during 3Q-2021, of 18.3% for full vaccination (two mRNA or one J&J) for ages < 65 and 28.4% for ages 65+.[15] Likely not coincidentally, this study controls for an extensive set of comorbidities. We did not find other studies of VE or RMR against mortality during the Omicron period.

Public Reporting of COVID-19 Mortality: The Need for a Denominator

Many public websites, including the CDC website and state health department websites, report data on COVID-19 deaths. None reports a comparison to all other deaths, all natural deaths, or (as we propose) other natural deaths. Reporting CEMP, as well as COVID-19 deaths, would provide valuable information on the relative risks of death from COVID-19 versus other causes, and how they vary over time. Reporting CEMP would show substantial COVID-19 mortality risk for the unvaccinated relative to other natural causes at younger ages. This might make more salient the large reductions in mortality risk available from vaccination. Reporting COVID-19 mortality relative to other natural causes of death could lead to greater attention to selection effects, and their importance when estimating the true protection against death provided by different vaccination levels

The Avoidable Tragedy of the Unboosted

Evidence of vaccine waning first appeared in mid-2021, initially from Israel, for Pfizer. In response, Israel launched a booster campaign in late July 2021, which reached the whole population by the end of August. Israel encouraged receipt of a booster dose by generally limiting their "Green Pass," which allowed access to restaurants, theaters, etc., to persons who have received a booster shot within the last six months or had recently recovered from COVID infection.[16] Other countries soon followed. The U.S., however, hesitated. FDA scientists wrote publicly that the need for boosters was not sufficiently established.[17] Evidence of waning, which had persuaded other countries, plus Israeli evidence of booster value, was not enough for them, or an advisory committee to the Food and Drug Administration (FDA), which in September 2021 approved only a limited rollout to the elderly and persons at risk due to occupational exposure;[18] or an advisory committee to the Centers for Disease Control and Prevention (CDC), which supported boosters only for the elderly, although the CDC director overruled the committee's objections.[19]

Only two months later did the FDA and the CDC approve boosters for all adults; only at the end of November, 2021, did the CDC "recommend" boosters for all adults.[20] Even when boosters were approved, public health messaging was muddled, with the value of boosters "lost in the sea of changing recommendations and guidance," leading to low takeup.[21] Even today, U.S. booster takeup lags many other countries,[22,23] and knowledge of booster recommendations is spotty.[24]

Selection Effects and Behavioral Differences

We found important differences in background mortality risk between the vaccinated and the unvaccinated, and between one-dose, two-dose and three-dose recipients. They have different underlying health, which we imperfectly control by using CEMP as our principal outcome. They may behave differently in what infection risks they choose to take, when they get tested for possible infection, when they seek care if infected, which hospitals they go to, etc. For example, the unvaccinated, and to a lesser extent the one-dose vaccinated, may believe COVID is less severe than those who receive two or three doses. Conversely, vaccinated persons may accept greater risks of becoming infected, because they believe they are protected against serious illness.

Health and behavioral differences are major confounders both for this and for any other study of the effectiveness of the COVID-19 vaccines. Only the initial randomized trials can avoid this concern, but these trials focused on infection risk and were too small to study mortality.

Limitations

This study has important limitations. We study only mortality, not less-extreme outcomes such as hospitalization. Mortality from COVID-19 mortality is uncommon for younger persons, which limits statistical power. Our data is only for Milwaukee. Milwaukee is racially, ethnically, and economically diverse, but its COVID-19 experience may not be representative of other areas.

We do not observe, and thus cannot control for, individual health characteristics, except through the limited lens of death certificates. There could be health differences between the vaccinated and unvaccinated, that would affect COVID-19 mortality rates, not reflected in rates of natural non-COVID deaths. However, our control for non-COVID-19 natural mortality provides evidence of large selection effects, and thus improves on prior approaches. Similarly, we do not control for behavioral differences between the vaccinated and unvaccinated. However, neither do other real-world VE studies.

The CEMP measure implicitly assumes that COVID-19 infection does not meaningfully affect non-COVID mortality. This is not completely true; COVID infection predicts higher post-infection mortality from other causes, at least in the near term.[25] This will cause some downward bias in CEMP values. If this bias is similar for the vaccinated and unvaccinated, RMR and VE estimates should still be unbiased. However, the downward bias in CEMP will plausibly be larger for the unvaccinated, since COVID-19 will on average be more severe for the unvaccinated. If so, then RMR estimates based on CEMP will be somewhat *below* those we would estimate if we could attribute to COVID-19 the extra natural deaths among the previously infected. Any remaining bias appears to be small (Figure App-1).

COVID-19 deaths could be underreported, but we coded COVID-19 as the likely cause of death based on reading death certificates; this produced significantly larger counts than ICD-10 codes from the NCHS (See Appendix for details). Any remaining undercount appears small (Figure App-1). We lacked data on prior COVID-19 infection, which may differ across vaccination groups and will affect COVID-19 mortality risk. We thus cannot study whether or how RMR differs for the previously infected versus the uninfected.

V. Conclusion

We use a novel measure, CEMP, to study COVID-19 mortality risk after vaccination. This measure uses mortality from other natural causes to control for selection effects in who gets vaccinated. We find much higher relative mortality risk for vaccinated versus unvaccinated than prior studies, which lacked such a control. The vaccinated would thus face lower COVID-19 risk even if not vaccinated. We also find large differences in relative mortality risk between younger (age 18-59) and older (age 60+) people, and large benefits from a booster dose. It is important to confirm these findings regarding vaccine effectiveness in other larger populations, using this or another approach that adjusts for baseline mortality risk. The substantial mortality risk that remains after two-dose vaccination suggests that boosters are highly important in reducing mortality, and that non-vaccine mitigation strategies can substantially reduce mortality even in vaccinated populations, particularly among the elderly.

Data Sharing

The linked mortality and vaccination data on which this study relies was obtained under a data use agreement with the Wisconsin Department of Health Services, and cannot be publicly shared.

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Table 1. Vaccine Effectiveness (VE) by Age Group and Time Period

Table shows COVID deaths, natural non-COVID deaths, COVID Excess Mortality Percentage (CEMP), and relative mortality risk (RMR) for persons vaccinated with 1, 2, or 3 doses, versus the unvaccinated and those vaccinated with fewer doses. RMR for a given comparison of two groups by vaccination status is defined as the ratio of CEMP for group 1 to CEMP for group 2. Sample is adult decedents in Milwaukee County, Wisconsin, excluding immune-compromised persons. Due to the nature of the sample, CEMP ratios and RMRs for age ranges and for all persons are effectively weighted by mortality rates.

Age		**April-Jun 2021 (Alpha)**			**Jul-Sep 2021 (Delta no Booster)**			**Oct-Dec 2021 (Delta, With Booster)**				**Jan-Mar 2022 (Omicron)**			
Group	Measure	**0 doses**	**1 dose**	**2 doses**	**0 doses**	**1 dose**	**2 doses**	**0 doses**	**1 dose**	**2 doses**	**3 doses**	**0 doses**	**1 dose**	**2 doses**	**3 doses**
18-39	Covid deaths	2	0	0	7	0	0	16	0	0	0	3	0	1	0
	Other natural deaths	31	4	1	33	6	10	26	3	11	0	15	2	9	3
	CEMP	6.5%	0.0%	0.0%	21.2%	0.0%	0.0%	61.5%	0.0%	0.0%	NA	20.0%	0.0%	11.1%	0.0%
	RMR vs. Unvaccinated		0.0%	0.0%		0.0%	0.0%		0.0%	0.0%	NA		0.0%	55.6%	0.0%
40-59	Covid deaths	8	3	0	32	5	0	57	7	2	0	23	2	8	0
	Other natural deaths	148	31	36	114	30	57	103	41	93	7	93	33	50	32
	CEMP	5.4%	9.7%	0.0%	28.1%	16.7%	0.0%	55.3%	17.1%	2.2%	0.0%	24.7%	6.1%	16.0%	0.0%
	RMR vs. Unvaccinated		179.0%	0.0%		59.4%	0.0%		30.9%	3.9%	0.0%		24.5%	64.7%	0.0%
60-79	Covid deaths	27	1	3	48	7	14	96	7	33	1	90	7	24	7
	Other natural deaths	374	86	250	300	76	343	270	71	359	70	240	48	245	252
	CEMP	7.2%	1.2%	1.2%	16.0%	9.2%	4.1%	35.6%	9.9%	9.2%	1.4%	37.5%	14.6%	9.8%	2.8%
	RMR vs. Unvaccinated		16.1%	16.6%		57.6%	25.5%		27.7%	25.9%	4.0%		38.9%	26.1%	7.4%
80+	Covid deaths	6	1	2	27	5	14	49	6	36	4	53	7	26	11
	Other natural deaths	280	59	337	205	57	431	227	63	429	93	184	37	212	364
	CEMP	2.1%	1.7%	0.6%	13.2%	8.8%	3.2%	21.6%	9.5%	8.4%	4.3%	28.8%	18.9%	12.3%	3.0%
	RMR vs. Unvaccinated		79.1%	27.7%		66.6%	24.7%		44.1%	38.9%	19.9%		65.7%	42.6%	10.5%
Total	Covid deaths	10	3	0	39	5	0	73	7	2	0	26	2	9	0
18-59	CEMP	5.6%	8.6%	0.0%	26.5%	13.9%	0.0%	56.6%	15.9%	1.9%	0.0%	24.1%	5.7%	15.3%	0.0%
	RMR vs. Unvaccinated		153.4%	0.0%		52.4%	0.0%		28.1%	3.4%	0.0%		23.7%	63.4%	0.0%
Total	Covid deaths	33	2	5	75	12	28	145	13	69	5	143	14	50	18
60+	CEMP	5.0%	1.4%	0.9%	14.9%	9.0%	3.6%	29.2%	9.7%	8.8%	3.1%	33.7%	16.5%	10.9%	2.9%
	RMR vs. Unvaccinated		27.3%	16.9%		60.8%	24.4%		33.3%	30.0%	10.5%		48.8%	32.4%	8.7%
Total	**Covid deaths**	**43**	**5**	**5**	**114**	**17**	**28**	**218**	**20**	**71**	**5**	**169**	**16**	**59**	**18**
	CEMP	**5.2%**	**2.8%**	**0.8%**	**17.5%**	**10.1%**	**3.3%**	**34.8%**	**11.2%**	**8.0%**	**2.9%**	**31.8%**	**13.3%**	**11.4%**	**2.8%**
	RMR (versus unvax)		**53.8%**	**15.5%**		**57.5%**	**19.0%**		**32.3%**	**22.9%**	**8.4%**		**42.0%**	**36.0%**	**8.7%**
	RMR (versus 1 dose)			**28.8%**			**33.1%**			**70.8%**	**26.2%**			**85.8%**	**20.7%**
	RMR (versus 2 doses)										**37.0%**				**24.2%**

Table 2. COVID-19 Relative Mortality Risk (RMR) Calculated Using a Multivariate Logit Model

Table shows the odds ratios from logit regressions for persons who died of natural causes, for different numbers of vaccine doses by quarter over April 2021 – March 2022. These odds ratios directly measure RMR. Odds ratios are from logit model of Prob(Covid-19 Death) = f(doses received, baseline is 0 doses, 1 dose, or 2 doses depending on the RMR being estimated), with controls for age, age^2, zip-SES (measured in centiles), gender, race/ethnicity, education level, marital status, and military veteran status. 95% confidence intervals (CIs) are in parentheses. Sample excludes immune-compromised persons. Coefficients on covariates are suppressed. RMR equals the odds ratio on the respective vaccination status indicators relative to the baseline vaccination status.

			1 Dose		2 Doses		3 Doses	
Sample	Period	Remaining Risk	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
18-59	Apr-Jun 2021	Vs. unvaccinated	185.5%	[46.4%, 741.5%]	0%		No booster	
		Vs. 1 dose			0%		No booster	
	Jul-Sep 2021	Vs. unvaccinated	40.3%	[14.7%, 111.1%]	0%		No booster	
		Vs. 1 dose			0%		No booster	
	Oct-Dec 2021	Vs. unvaccinated	22.3%	[8.9%, 55.9%]	2.6%	[0.6%, 10.6%]	0%	
		Vs. 1 dose			6.1%	[1.1%, 33.1%]	0%	
		Vs. 2 doses					0%	
	Jan-Mar 2022	Vs. unvaccinated	23.3%	[4.6%, 118.2%]	62.8%	[25.3%, 156.2%]	0%	
		Vs. 1 dose			316.0%	[24.0%, 4162.8%]	0%	
		Vs. 2 doses					0%	
60+	Apr-Jun 2021	Vs. unvaccinated	23.8%	[4.6%, 122.9%]	18.4%	[7.1%, 47.6%]	No booster	
		Vs. 1 dose			55.9%	[9.7%, 321.3%]	No booster	
	Jul-Sep 2021	Vs. unvaccinated	58.2%	[30.0%, 112.8%]	25.6%	[16.0%, 41.0%]	No booster	
		Vs. 1 dose			39.9%	[18.5%, 86.1%]	No booster	
	Oct-Dec 2021	Vs. unvaccinated	30.4%	[16.4%, 56.5%]	30.6%	[22.1%, 42.2%]	10.9%	[4.4%, 27.2%]
		Vs. 1 dose			97.2%	[51.1%, 185.1%]	34.9%	[11.9%, 102.1%]
		Vs. 2 doses					14.5%	[89.7%, 0.0%]
	Jan-Mar 2022	Vs. unvaccinated	45.2%	[24.1%, 84.8%]	30.5%	[21.3%, 43.5%]	8.6%	[5.1%, 14.6%]
		Vs. 1 dose			66.2%	[34.3%, 128.1%]	18.4%	[8.6%, 39.7%]
		Vs. 2 doses					26.7%	[14.9%, 47.9%]
All (18+)	Apr-Jun 2021	Vs. unvaccinated	51.9%	[19.5%, 138.2%]	18.0%	[7.1%, 45.8%]	No booster	
		Vs. 1 dose			36.1%	[9.8%, 132.6%]	No booster	
	Jul-Sep 2021	Vs. unvaccinated	57.3%	[33.3%, 98.7%]	20.8%	[13.4%, 32.3%]	No booster	
		Vs. 1 dose			30.2%	[15.4%, 59.2%]	No booster	
	Oct-Dec 2021	Vs. unvaccinated	29.5%	[17.9%, 48.8%]	23.8%	[17.7%, 32.0%]	9.1%	[3.7%, 22.7%]
		Vs. 1 dose			69.2%	[40.5%, 118.3%]	25.4%	[9.2%, 69.7%]
		Vs. 2 doses					35.4%	[14.2%, 87.9%]
	Jan-Mar 2022	Vs. unvaccinated	40.1%	[22.7%, 70.7%]	34.0%	[24.5%, 47.3%]	8.2%	[4.8%, 13.7%]
		Vs. 1 dose			83.5%	[44.8%, 155.6%]	20.2%	[9.7%, 42.3%]
		Vs. 2 doses					23.7%	[13.5%, 41.8%]

* For ages 18-59, some cells for 2 or 3 doses have 0 deaths; for these we do not report a confidence interval.

Table 3. Non-Covid Natural Mortality Rate by Age Group and Time Period

Sample is same as Table 1. Table shows Non-COVID Natural Mortality Rate (NCNMR) and relative NCNMR versus the unvaccinated, for people vaccinated with 1 dose, 2 doses, or 3 doses. NCNMR is defined as the number of Non-COVID-19 natural deaths occurring among persons within the indicated age groups with the indicated vaccination status over the indicated period, divided by the estimated population of people in the same age group, vaccination status, and time period. The bottom two sets of rows sum results from the upper rows across broader age groups.

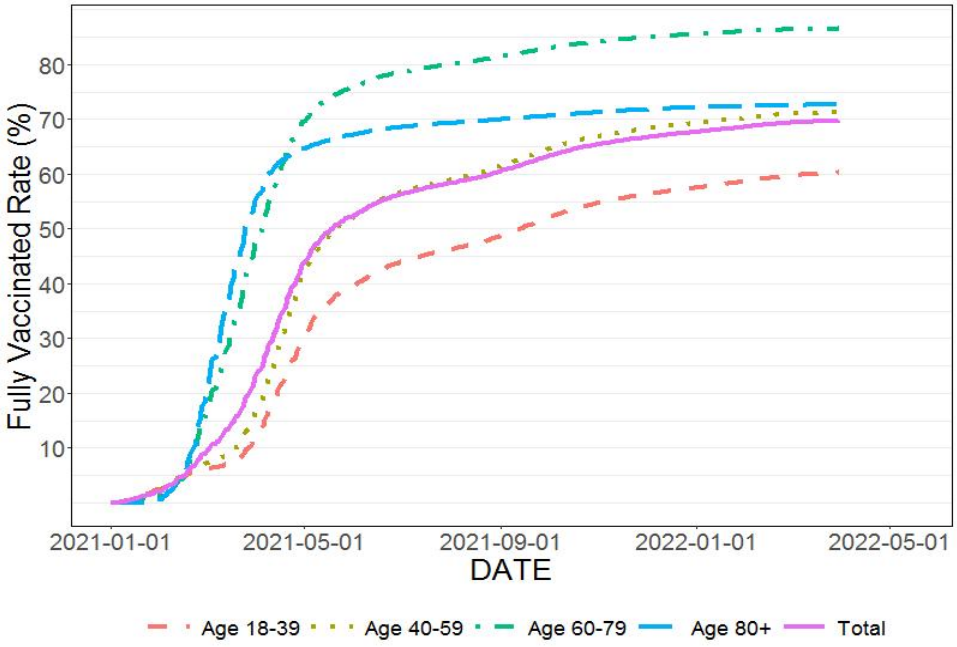
		April-Jun 2021 (Alpha)			**Jul-Sep 2021 (Delta no Booster)**			**Oct-Dec 2021 (Delta, With Booster)**				**Jan-Mar 2022 (Omicron)**			
Age	Measure	Unvax	1 dose	2 doses	Unvax	1 dose	2 doses	Unvax	1 dose	2 doses	3 doses	Unvax	1 dose	2 doses	3 doses
18-39	Non-Covid Natural MR	0.016%	0.011%	0.001%	0.022%	0.023%	0.007%	0.021%	0.010%	0.008%	0.000%	0.014%	0.007%	0.008%	0.004%
	NCNMR ratio to unvax		**70.4%**	**5.4%**		**101.7%**	**33.4%**		**49.5%**	**36.9%**	**0.0%**		**50.3%**	**60.1%**	**31.3%**
40-59	Non-Covid Natural MR	0.134%	0.103%	0.049%	0.139%	0.143%	0.047%	0.156%	0.189%	0.078%	0.056%	0.161%	0.187%	0.064%	0.044%
	NCNMR ratio to unvax		**76.6%**	**36.7%**		**102.5%**	**33.6%**		**120.8%**	**50.0%**	**36.0%**		**116.2%**	**39.9%**	**27.5%**
60-79	Non-Covid Natural MR	0.871%	0.520%	0.272%	0.939%	0.774%	0.300%	0.999%	0.717%	0.439%	0.195%	0.983%	0.580%	0.649%	0.286%
	NCNMR ratio to unvax		**59.7%**	**31.3%**		**82.3%**	**31.9%**		**71.8%**	**43.9%**	**19.5%**		**59.0%**	**66.1%**	**29.1%**
80+	Non-Covid Natural MR	2.644%	2.498%	1.581%	2.157%	3.643%	1.836%	2.561%	3.795%	2.559%	0.969%	2.295%	2.310%	2.972%	2.045%
	NCNMR ratio to unvax		**94.5%**	**59.8%**		**168.9%**	**85.1%**		**148.2%**	**99.9%**	**37.8%**		**100.6%**	**129.5%**	**89.1%**
Total	Non-Covid Natural MR	0.059%	0.054%	0.025%	0.063%	0.078%	0.026%	0.068%	0.087%	0.040%	0.010%	0.065%	0.076%	0.032%	0.026%
18-59	NCNMR ratio to unvax		**91.6%**	**41.4%**		**122.4%**	**41.2%**		**129.1%**	**58.5%**	**14.6%**		**117.5%**	**48.4%**	**39.5%**
Total	Non-Covid Natural MR	1.216%	0.748%	0.520%	1.219%	1.168%	0.561%	1.383%	1.154%	0.787%	0.326%	1.307%	0.863%	1.014%	0.581%
60+	NCNMR ratio to unvax		**61.5%**	**42.8%**		**95.8%**	**46.0%**		**83.4%**	**56.9%**	**23.6%**		**66.0%**	**77.5%**	**44.4%**

Figure 1: Vaccination Rates for Adults by Age Group in Milwaukee

Vaccination percentages over time for Milwaukee County residents, through March 31, 2022.

Panel A. Full-vaccination rates

Full vaccination is defined as 1 J&J dose, 2 mRNA doses, or more.



Panel B. Three Dose Vaccination Rates

Three dose vaccination rates, as percentage of people receiving two vaccine doses.