

Selection Effects and COVID-19 Mortality Risk After Pfizer vs. Moderna Vaccination: Evidence From Linked Mortality and Vaccination Records

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Abstract

Many studies report that the Pfizer-BioNTech (BNT162b2) and Moderna (mRNA1273) COVID-19 vaccines provide similar protection against mortality, with a modest edge for Moderna due to slower waning. However, most comparisons of Pfizer to Moderna, or of either vaccine to the unvaccinated, do not address selection effects for who gets vaccinated, with how many doses, when, and with which vaccine. The researchers report evidence on large selection effects and use a novel method to control for these effects. Instead of studying COVID-19 mortality, they study the COVID-19 Excess Mortality Percentage (CEMP), defined as COVID-19 deaths divided by non-COVID natural deaths for the same population. The CEMP measure uses non-COVID-19 natural deaths as a proxy for population health and thus controls, albeit imperfectly, for selection effects. The authors report mortality risk (RMR) for each vaccine relative to the unvaccinated and to the other vaccine, using linked mortality and vaccination records for all adults in Milwaukee County, Wisconsin, through June 30, 2022. Both vaccines provided similar protection for persons aged 18-59. However, for persons aged 60+, RMRs for two-dose Pfizer vaccinees were consistently over twice those for Moderna. Pfizer two-dose RMR for ages 60+ over April 2021–June 2022 was 248% of Moderna [95% CI=175%, 353%]. In the Omicron period, Pfizer RMR was 57% versus 23% for Moderna. Both vaccines demonstrated waning two-dose effectiveness over time, especially for ages 60+. A possible explanation for the Moderna advantage is a higher dose (100 µg versus 30 µg for Pfizer). For booster recipients, the Pfizer-Moderna gap is smaller and statistically insignificant. Younger persons (aged 18–59) were well-protected against death by two doses of either vaccine, and highly protected by three doses (no deaths among over 100,000 vaccinees). These results support booster importance for ages 60+, especially for Pfizer recipients. They suggest, but do not prove, that older persons may benefit from a larger vaccine dose.

The Online Appendix for this paper is available at <http://ssrn.com/abstract=4321773>.

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Introduction

COVID-19 vaccines have saved hundreds of thousands of lives in the United States (Steele 2022) and millions worldwide (Watson 2022). Conventional wisdom is that both mRNA vaccines, from Pfizer-BioNTech (BNT162b2) and Moderna (mRNA1273), provide strong and similar protection against severe disease and mortality, with perhaps a nod to Moderna, which wanes more slowly.

However, these studies rely on observational data, and are vulnerable to selection effects for who gets vaccinated, with how many doses, and with which vaccine. Failure to address selection effects can lead to biased estimates of vaccine effectiveness (VE) and relative mortality risk (RMR) for the vaccinated relative to the unvaccinated, and for Pfizer versus Moderna vaccinees.¹ In prior work, we provide evidence for strong selection effects in who gets vaccinated: two-dose vaccinees are healthier than the unvaccinated, and three-dose vaccinees are generally healthier than two-dose vaccinees.² Here, we extend that work and provide evidence for selection effects in which vaccine people receive.

Many studies have reported real-world evidence on vaccine effectiveness (VE) for the mRNA vaccines against infection, hospitalization, and death (for brevity, we cite principally systematic reviews).³⁻⁶ However, many studies, including those sponsored by the U.S. Centers for Disease Control (CDC), report results for both vaccines together.^{2,7-12} Studies that report vaccine-specific results have generally suggested a modest advantage for Moderna in effectiveness against hospitalization and death. However, most of these studies have limited controls for individual characteristics, often only age and gender; use research designs that are prone to selection effects, often a test-negative design, which compares people with positive COVID-19 tests to controls who test negative; and/or cover limited time periods or populations (e.g., US veterans).

Both vaccines use similar mRNA technology, but the initial two Moderna doses were 100 µg versus 30 µg for Pfizer (the booster doses are 50 µg for Moderna versus 30 µg for Pfizer). The differing doses reflect each company's decision on balancing the extra immune-system boost from a larger dose versus the risk of side effects. Yet we know from research on vaccines for other respiratory diseases (influenza, pneumonia) that VE declines with age among the elderly.^{13,14} There is also evidence for influenza, that the elderly benefit from a larger vaccine dose to compensate for their weaker immune systems.¹³⁻¹⁷ This pattern could plausibly hold for the COVID-19 vaccines.

In our prior work, we propose, validate, and use a novel approach for addressing selection when studying COVID-19 mortality risk.^{1,2,18} We use the non-COVID-19 natural mortality rate (Non-Covid-NMR) as a proxy for unobserved health and thus background mortality risk, within a population defined by age, gender, vaccination status, and other characteristics. We use a related measure, the COVID-19 Excess Mortality Percentage (CEMP) (defined as the COVID-19 mortality rate divided by Non-Covid-NMR) as an outcome for studying VE and RMR. This measure is available on a population wide basis and performs well in predicting COVID-19 mortality for unvaccinated populations. In this study, we use the CEMP measure to assess RMRs for Pfizer and Moderna vaccinees versus the unvaccinated, and the relative effectiveness of each vaccine.

Data and Methods

We study all deaths among adults age 18+ residing in Milwaukee County, Wisconsin (Milwaukee), a racially, ethnically and economically diverse county which includes 722,000 adults, of whom 19,895 died during the COVID-19 pandemic period from April 1, 2020, through June 30, 2022. We use death certificate data, which includes residence zip code, age at death, gender, race/ethnicity, education, income, manner of death, and text fields for cause of death and conditions leading to death. We use text analysis to identify deaths due to COVID-19. Our text analysis identifies substantially more COVID-19 deaths than do the cause-of-death codes assigned by the National Center for Health Statistics (NCHS) based on the text fields, and reduces misattribution of COVID-19 deaths as non-COVID deaths. See Appendix for details. We exclude J&J vaccinees, vaccinees who received only one dose, and vaccinees who received more than one type of vaccine. We treat vaccination as effective against mortality beginning 30 days after receipt, to allow for time from vaccination to full effectiveness, plus typical lags from infection to death.

We study over the vaccine-available period from April 1, 2021, through June 30, 2022, which includes the first half of 2022 (1H-2022), when Omicron was the dominant COVID-19 variant. We measure VE and RMR for two or three Pfizer or Moderna doses versus the unvaccinated, and for Pfizer versus Moderna vaccinees.

We define CEMP as COVID-19 deaths/non-COVID-19 natural deaths, converted to a percentage. We measure VE against death, and relative mortality risk ($RMR = 1 - VE$) versus the unvaccinated for combinations of vaccine type, number of doses, and time period. We report results for three time periods: pre-booster period (April 1-Sept. 30, 2021), Delta period (October 1-December 31, 2021, below “4Q-2021”), and Omicron period (January 1-June 30, 2022), but provide results by calendar quarter in the Appendix. We study two-dose vaccinees in each time period, and three-dose vaccinees beginning 4Q-2021, when booster doses became available. See Extended Methods in the Appendix for formal variable definitions.

CEMP, RMR, and the Pfizer/Moderna ratio are all ratios, so will be undefined if the denominator is zero; this issue did not affect our measures of CEMP and RMR versus the unvaccinated, but did prevent us from computing some Pfizer/Moderna ratios for younger persons, due to no deaths among Moderna vaccinees.

CEMP represents the odds, for a population of interest, of dying from COVID-19 versus other natural causes. The ratio of CEMPs for two groups, such as two-dose vaccinees versus unvaccinated, or Pfizer versus Moderna vaccinees, is the RMR for the two groups, and is also an odds ratio. These odds ratios can be either computed directly or obtained through logistic regression. We use both approaches. For multivariate logistic regression analysis of the association between vaccine type and RMR, the regression predictors are vaccine type; days since most-recent dose (minus 30 days); age, age², zip-code-level socio-economic status (zip-SES),¹⁹ gender, race/ethnicity (non-Hispanic White (“White”) versus other), and education (high-school or less versus some college or more).

CEMP treats non-Covid natural deaths as a proxy for the health of a given group, and thus the likelihood of COVID-19 mortality if not vaccinated. We assessed the validity of this approach by studying the correlation in Wisconsin between natural mortality in April-December 2019 (pre-COVID) and COVID-19 mortality over the same months in 2020 (Appendix Figure App-4).

Results

Study Population and Evidence on Selection Effects

In Table App-2 we provide information on the vaccination and natural mortality of Milwaukee adults during our sample period. Of 542,152 adult vaccinees, we excluded 94,221 because they did not receive 2 or 3 Pfizer or Moderna vaccines, and 5,843 immune-compromised persons. This left a sample of 442,088 Pfizer or Moderna vaccinees and 179,366 unvaccinated persons. Overall, through June 2022, around 74% of Milwaukee County adults received at least one dose, of whom 82% received two Pfizer or two Moderna doses; of these two-dose vaccinees, 57% received a third dose of the same vaccine. Among mRNA vaccine recipients, 66% received Pfizer. Only a small percentage of vaccinees received J&J or different vaccine types across doses.

Of the 10,140 deaths of adult Milwaukee County residents during our study period, we excluded 1,605 because they involve non-natural causes (e.g., suicide, homicide, accidental death), 1,064 because they received different vaccine regimens than 2 or 3 doses of Pfizer or Moderna, and 289 because they involved immune-compromised persons. This left a sample of 8,250 natural deaths. See Tables App-2 and Table 1.

Table 1 provides summary statistics for the sample of 8,250 natural deaths. There are large differences on various characteristics between the unvaccinated and vaccinated, between Pfizer and Moderna vaccinees, and between two-dose and three-dose vaccinees. Relative to two-dose recipients the unvaccinated are younger, much less likely to be White, more likely to be male, and less-educated. Relative to two-dose recipients, three-dose recipients are older, more likely to be White, and better educated. Moderna vaccinees are older than Pfizer vaccinees and more likely to be White. These differences provide evidence on selection effects.

Centrally for this project, for ages 60+, two-dose Pfizer vaccinees are substantially healthier (they have lower Non-Covid-NMR) than two-dose Moderna vaccinees, and three-dose Pfizer vaccinees are substantially healthier than three-dose Moderna vaccinees. The Pfizer vaccinees also have substantially higher CEMP levels. For younger two-dose vaccinees, age 18-59, selection effects are smaller. Three-dose Pfizer vaccinees are healthier than three-dose Moderna vaccinees, but there are no COVID-19 deaths in either group.

We confirm in Appendix Table App-10 the existence of large selection effects, controlling for age. For all ages, vaccinees are substantially healthier (less likely to die of other natural causes) than the unvaccinated, and three-dose recipients are healthier than two-dose recipients. For ages 60+, Pfizer vaccinees are much healthier than Moderna vaccinees. For two-dose vaccinees over the full sample period, Non-Covid-NMR for Pfizer vaccinees is 52.6% of that for Moderna; over the booster-available period. For three-dose vaccinees over the booster-available period, Non-Covid-NMR for Pfizer vaccinees is 56.0% of that for Moderna.

Two-Dose RMRs and Pfizer/Moderna Ratio

Table 2 reports the number of COVID-19 deaths, non-COVID-19 natural deaths, CEMP (the ratio of the two), Pfizer and Moderna RMRs versus the unvaccinated, and the Pfizer/Moderna ratio, in groups defined by age range (18-39, 40-59, 60-79, and 80+), number of doses, and vaccine type, for three time periods: pre-booster (April-September 2021) with Alpha and Delta as the

dominant virus variants; October-December 2021 (4Q-2021), with Delta dominant but boosters available; and January-June 2022 (1H-2022), with Omicron dominant.

We present results by period, given evidence from other studies on vaccine waning over time,^{4,20-22} differences in severity between the Delta and Omicron variants, and potential differences in RMR between variants. Some death counts in individual cells are small, so confidence intervals for RMRs and Pfizer/Moderna ratios are wide.

For ages 18-59, there were few vaccinee deaths and no evidence of a difference in effectiveness between vaccines. RMR versus unvaccinated persons was near zero for ages 18-39, with only one COVID-19 death among two-dose recipients. There were no COVID-19 deaths for ages 40-49 and 8 for ages 50-59 (4 Pfizer and 4 Moderna recipients).

For ages 60+, where most COVID-19 deaths occur, CEMP in the pre-booster period (2Q-3Q-2021), was 3.3% for two-dose Pfizer vaccinees versus 1.4% for two-dose Moderna vaccinees (Pfizer/Moderna ratio of 229%). In the Delta-and-booster period (4Q-2021), CEMP was 12.9% for two-dose Pfizer vaccinees versus 5.4% for two-dose Moderna vaccinees (Pfizer/Moderna ratio of 240%). In the Omicron-and-booster period (1H-2022)), CEMP was 11.2% for two-dose Pfizer vaccinees versus 4.4% for two-dose Moderna vaccinees (Pfizer/Moderna ratio of 254%). All ratios were significantly different from 100% at the 5% level or better.

For each vaccine, two-dose protection for ages 60+ waned during the study period, with RMRs for Pfizer two-dose vaccinees versus the unvaccinated rising from 34.9% in the pre-booster period to 44.1% in 4Q-2021; and 55.6% in the Omicron period. Two-dose RMRs for Moderna rose from 15.2% in the pre-booster period to 18.4% in 4Q-2021 and 21.8% in the Omicron period. However, we cannot separate the effects of waning over time from changes in the dominant virus variant or the increasing likelihood of previous infection.

Three-Dose RMRs and Pfizer/Moderna Ratio

For ages 18-59, the number of deaths among vaccinees, already small for two-dose recipients, is zero for our sample for recipients of three doses of either Pfizer or Moderna.

For ages 60+, a booster dose offered substantial additional protection against death, with broadly similar protection levels for Pfizer vs. Moderna vaccinees. The RMRs for booster recipients versus the unvaccinated were 13.4% (Moderna) vs. 6.3% (Pfizer) during 4Q-2021, and 8.7% (Moderna) versus 13.1% (Pfizer) in 1H-2022 (differences are not statistically significant).

Figure 1 summarizes in graphical form the principal RMR results for ages 60+. It shows RMRs points for two-dose Pfizer, two-dose Moderna, and during the booster period, three-dose Pfizer and three-dose Moderna, all versus the unvaccinated. The upward slopes for two-dose vaccinees illustrate waning. The gap between the Pfizer and Moderna lines shows the Moderna advantage. The solid lines for three dose recipients are well below the two-dose lines; the gap between the two-dose and three-dose lines illustrates the mortality risk reduction from a booster. That reduction is larger for Pfizer than for Moderna; reflecting higher Pfizer two-dose RMRs but similar three-dose RMRs.

Multivariate Estimates

In Table 3, we use a multivariate logistic model to predict the Pfizer/Moderna ratio for two- and three-dose recipients, for the same sample as in Table 2. Because of the small number of vaccinated decedents, especially for ages 18-59 and three-dose vaccinees, Table 3 reports results using limited covariates to preserve regression degrees of freedom: gender, age, age², and days since last vaccine dose (to allow for waning). However, point estimates are similar in regressions which also control for race/ethnicity, education, and zip-SES (Appendix Table App-4). For two-dose vaccinees aged 60+, the Pfizer/Moderna ratio and CI is 258% [CI=182%,366%] p < 0.001 for the full sample period. Subperiod estimates are similar. For three-dose vaccinees over the full booster period the Pfizer/Moderna ratio was 135% (not statistically different from 100%).

The similarity between the simpler estimates in Table 2 and the multivariate estimates provides further evidence that the CEMP denominator does a good job of controlling for population health and thus for COVID risk, even without additional covariates.

Robustness Checks

The Pfizer/Moderna ratio for ages 60+ is similar if we do not exclude the immune-compromised (Table App-5) or exclude the immune-compromised, defined more broadly than in the text (Table App-6). Results for this ratio are similar for men and women (Table App-7), and for Whites versus non-Whites (Table App-8).

Discussion

Prior Literature Comparing Pfizer to Moderna

Among other studies of VE against death, some study only a single vaccine type (e.g., Israeli studies of Pfizer; manufacturer-sponsored studies). Of those that study both vaccines, many report only combined results rather than vaccine-specific results.^{2,7-11,23} Among the studies which distinguish between vaccine types, some do not find substantial differences between Pfizer and Moderna. Others find differences, sometimes similar to those report, but do not highlight them. Only one study, limited to U.S. veterans, includes the Omicron-dominant period (only a short part of that period), or studies separately three-dose vaccinees.⁶ The only other U.S. study that reports RMR using linked population-wide mortality and vaccination data is Robles-Fontan et. al (2022), who study Puerto Rico through mid-October 2021 (pre-Omicron and pre-booster). They report two-dose RMR after 144 days (longest period considered) of 14% for Pfizer and 7% for Moderna, versus 3% and 1% soon after vaccination.²⁴ They thus find a Pfizer/Moderna ratio similar to ours, but their abstract states only that “[Both] vaccines were highly effective across all age groups.” The review by Black and Thaw (2022) reports a Moderna advantage after waning (at least 120 days after vaccination) during the Delta-dominant period, with midpoint RMR estimates from multiple studies of 13.3% for Pfizer vs. 9.2% for Moderna.⁴ Lytras et. al (2022) study Greece through year-end 2021, find a nearly 3:1 Moderna advantage against mortality, but this result must be extracted from a supplemental figure;²⁵ the text (at 5048) reports “[o]nly marginal differences [between vaccines] in effectiveness.” Mayr et. al (2022) report a Moderna advantage in reducing hospitalization risk, and an apparent advantage for a combined ICU-or-death outcome, but small sample size “precluded statistically significant comparisons.”²⁶ A study of Czechia through November 2021 reports two-dose RMR, 7-8 months after vaccination, of 17% for Pfizer vs. 12%

for Moderna (2022).²⁷ Other studies find smaller differences. Islam et al. (2022) study the pre-booster period; their outcome is hospitalization or death; report an insignificant Moderna advantage during the first 90 days after vaccination.²⁸ Several studies focus on U.S. veterans, and find no significant Pfizer-vs-Moderna differences.^{5,6,29,30}

Two-Dose Pfizer-vs-Moderna RMRs for Ages 60+

Our analysis can help to reconcile these disparate results. We study CEMP as the principal outcome, which controls for selection effects between Pfizer and Moderna vaccinees, and study a longer period, including the Omicron-dominant period through June 30, 2022. For ages 18-59, we find similar performance for both vaccines. In contrast, for ages 60+, we find substantially higher two-dose RMRs for Pfizer versus Moderna vaccinees. The Pfizer/Moderna ratio is at least 2:1 for ages 60+ in each of our three sample time periods.

A plausible explanation for Pfizer-vs-Moderna differences for older people, is that younger people benefit sufficiently from the boost to their immune system provided by two-doses of either vaccine. Beyond some threshold level, which both vaccines achieve, the magnitude of the boost appears to be less important. Older people may need a larger dose for full protection; similar to flu vaccine, for which the recommended dose is 4x higher for ages 60+.³¹

Results for Waning and Absolute RMR versus Unvaccinated

For ages 60+, where most vaccinee deaths occur, both vaccines showed waning over time, although the evidence on waning could be confounded by changes over time in the dominant virus variants, RMR levels versus the unvaccinated are higher for Pfizer, but the Pfizer/Moderna ratios are consistent over our time periods.

For two-dose recipients age 60+, we report substantially higher RMR estimates than most other studies, especially during the Omicron period. During this period, two-dose RMR versus the unvaccinated is 23% (Moderna) and 57% (Pfizer). These estimates likely reflect a combination of continued waning, a higher percentage of previously infected persons in the population, who have post-infection resistance even if unvaccinated, our use of CEMP to control for selection effects when measuring COVID-19 mortality risk, and perhaps changes over time in use of non-vaccine risk mitigation measures.

The Value of Boosters, Especially for Pfizer

For ages 60+, a booster dose provides substantial additional reduction in RMRs for both vaccines, especially during the Omicron period. A booster dose reduced Pfizer RMR from 57% to 13%. A booster dose also reduced RMR for Moderna vaccinees, from 23% to 9% in 1H-2022. For three-dose vaccinees, we did not find significant Pfizer vs. Moderna differences in RMR. In effect, the third dose allowed Pfizer to catch up to Moderna.

For ages 60+, our results imply much higher booster value than prior studies, especially for Pfizer. In effect, the higher two-dose RMRs that we find leave more room for boosters to reduce mortality. These large gains are found even though we also find higher three-dose RMRs than prior research. A UK study found 1.3% RMR for boosted versus unvaccinated for ages 50+ (when studies report VE, we convert to RMR).³² One Israeli study finds 10% RMR for three-

versus-two-doses for ages 50+;³³ a second reports three-versus-two-dose RMR of 6.8% for ages 60+;²¹ a third reports three-versus-two-dose RMR of 19% across all ages.³⁴

For ages 18-59, there are few deaths of two-dose vaccinees. A third dose is still valuable for ages 50-59. There was evidence for waning (higher two-dose RMR) in the Omicron period for both vaccines, and thus value from a booster dose. Zero deaths among booster recipients aged 18-59 through June 2022 is a striking result, which suggests value in a third dose, separated in time from the initial two doses. At the same time, at least through mid-2022, persons aged 18-49 are well protected against death after two doses.

Limitations

This study has important limitations. We study only mortality. Results could be different for other measures of severe disease, such as hospitalization or admission to the ICU. However, prior work has found that relative Pfizer vs. Moderna VE against hospitalization is similar to VE against mortality.^{1,3}

We have data only for Milwaukee County. Milwaukee County is racially, ethnically, and economically diverse, but may not be representative of other areas. However, the vaccination patterns in Milwaukee County (Appendix Table App-2, Figure App-3) are broadly similar to those seen nationally.

Third, we rely on non-COVID natural mortality as a surrogate for underlying risk of COVID death. This measure is theoretically attractive. It is conceptually similar to a “P-value” that is sometimes computed for all-cause excess mortality ($P = \text{excess mortality as a percentage of expected mortality}$).^{35,36} Non-COVID natural mortality rates in 2019, prior to COVID, strongly predict COVID mortality rates in 2020, when COVID vaccines were not available, for population groups defined by age, gender, and race/ethnicity (Appendix Figure App-4; Pearson correlation coefficient = 0.94).

Fourth, we lack data on prior COVID-19 infection. Especially in the Omicron era, when many people were already infected, comparison of unvaccinated to vaccinated persons could be affected by differences in the proportion of persons who have some natural resistance, due to prior infection. However, unless prior COVID infection is associated with choice of vaccine, which seems unlikely, estimates of the Pfizer/ Moderna ratio should still be unbiased.

Fifth, some deaths due primarily to COVID may be coded as non-COVID natural deaths. Moreover, COVID infection predicts higher near-term mortality from other causes.^{37,38} However, we coded COVID deaths based on text fields in death certificates to reduce miscoding (Appendix Table 1). The rate of non-COVID natural mortality during the study period was similar to that predicted by extrapolating natural mortality rates from the pre-pandemic period (Appendix Figure App-2). Any miscoding of COVID as non-COVID deaths will reduce CEMP estimates, but we have no reason to expect this to produce bias in the Pfizer/Moderna ratio.

Finally, our assessment of underlying health does not control for behavioral differences between the vaccinated and unvaccinated. However, we have no reason to expect behavioral differences between persons receiving Moderna versus Pfizer.

V. Conclusion

These results suggest several clinically important points. First, RMR estimates for persons aged 60+ are much higher, and therefore VE much less, than previously suggested. Moreover, two-dose RMRs for Pfizer recipients aged 60+ are more than double those for Moderna recipients. This difference is insignificant for younger persons, and becomes insignificant after a third dose, regardless of age.

We thus provide evidence that one COVID-19 vaccine does not fit all. The Moderna vaccine is preferable to Pfizer for ages 60+, at least until one gets to a booster dose. Conversely, younger persons are well protected by two-doses of either vaccine, and the lower Pfizer dose may have lower risk of side effects – in particular myocarditis, which is an important side effect for young men, with higher risk for Moderna than for Pfizer. Current U.S. public health messaging does not distinguish between vaccines, and promotes boosters for all. This guidance, our evidence suggests, is too crude. Also too crude is the apparent plan by the U.S. Food and Drug Administration to recommend, and perhaps only allow, a single vaccine schedule for all vaccines and all ages.

It will be important to monitor differences in effectiveness over time to determine if waning of booster protection differs between the two vaccines, to assess effectiveness against new variants, and to assess relative effectiveness against hospitalization.

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. Sample Summary Statistics

Table shows summary statistics for study sample: 621,454 adult residents of Milwaukee County, Wisconsin, who received two or three doses of the Pfizer or Moderna COVID-19 vaccines, or were unvaccinated, excluding immune-compromised persons and persons who died of non-natural causes. Higher SDI indicates lower area-SES. Monthly average population by vaccination status is average of beginning of month populations over April 1, 2021-June 1, 2022. Deaths are measured over April 1, 2021 – June 30, 2022. Non-Covid-NMR are based on average populations.

Variable	Vaccination Status									
	Unvaccinated		Moderna 2 doses		Pfizer 2 doses		Moderna 3 doses		Pfizer 3 doses	
Pop. at June 1, 2022	179,366		64,186		124,879		95,946		157,077	
Monthly average pop.	250,078		107,854		179,932		40,232		68,288	
Number of deaths	4,535		2,173		1,621		851		675	
Mean age at death	65		78		71		82		76	
Age at death n(%)										
18-39	614	13.5%	47	2.2%	77	4.8%	3	0.4%	12	1.8%
40-59,	977	21.5%	167	7.7%	257	15.9%	45	5.3%	60	8.9%
60-79	1,752	38.6%	795	36.6%	740	45.7%	271	31.8%	301	44.6%
80 +	1,192	26.3%	1,164	53.6%	547	33.7%	532	62.5%	302	44.7%
Female n(%)	1964	43.3%	1,226	56.4%	786	48.5%	524	61.6%	301	44.6%
Non-White	2180	48.1%	524	24.1%	604	37.3%	147	17.3%	184	27.3%
High school and below	3,122	68.8%	1,249	57.5%	977	60.3%	463	54.4%	380	56.3%
Mean SDI	78.3		67.1		73.7		63.8		67.4	
Age 18-59										
Covid Deaths	147	18.2%	4	3.3%	6	3.0%	0	0.0%	0	0.0%
Non-Covid Natural Deaths	660	81.8%	116	96.7%	197	97.0%	38	100.0%	45	100.0%
CEMP	22.27%		3.45%		3.05%		0.00%		0.00%	
Non-Covid NMR	0.31%		0.17%		0.15%		0.19%		0.11%	
Age 60+										
Covid Deaths	397	14.5%	58	3.2%	89	7.6%	14	1.9%	14	2.5%
Non-Covid Natural Deaths	2,341	85.5%	1,759	96.8%	1,088	92.4%	731	98.1%	546	97.5%
CEMP	16.96%		3.30%		8.18%		1.92%		2.56%	
Non-Covid NMR	5.95%		4.52%		2.31%		3.60%		1.88%	

Table 2. Relative Mortality Risks and Pfizer/Moderna Ratio by Age Group and Time Period

Sample is same as Table 1. Table shows COVID deaths, natural non-COVID deaths, COVID Excess Mortality Percentage (CEMP), RMR relative the unvaccinated for vaccinees with indicated vaccine types (Pfizer = P or Moderna = M) and number of doses. Vaccine doses are considered effective 14 days after receipt. 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, who were unvaccinated or received two or three Pfizer or Moderna doses. Due to the nature of the sample, CEMP ratios and RMRs are effectively weighted by natural mortality rates. *, **, *** indicates p < .05, .01, and .001, respectively; significant results (at p < .05 or better) in **boldface**.

Age Bracket	Death	Apr-Sep 2021			Oct-Dec 2021					Jan-Jun 2022				
		Unvax	M2	P2	Unvax	M2	P2	M3	P3	Unvax	M2	P2	M3	P3
18-39	Covid Deaths	9	0	0	16	0	0	0	0	4	0	1	0	0
	Non-Covid Natural Deaths	63	5	5	26	5	6	0	0	32	4	13	1	2
	CEMP	14.3%	0.0%	0.0%	61.5%	0.0%	0.0%	NA	NA	12.5%	0.0%	7.7%	0.0%	0.0%
	RMR to unvax		0.0%	0.0%		0.0%	0.0%	NA	NA		0.0%	61.5%	0.0%	0.0%
	Pfizer RMR to Moderna			NA			NA	NA	NA			NA	NA	NA
40-59	Covid Deaths	38	0	1	57	1	1	0	0	23	3	3	0	0
	Non-Covid Natural Deaths	260	28	52	102	31	63	1	2	177	43	58	36	41
	CEMP	14.6%	0.0%	1.9%	55.9%	3.2%	1.6%	0.0%	0.0%	13.0%	7.0%	5.2%	0.0%	0.0%
	RMR to unvax		0.0%	13.2%		5.8%	2.8%	0.0%	0.0%		53.7%	39.8%	0.0%	0.0%
	Pfizer RMR to Moderna			NA			49.2%	NA	NA			74.1%	NA	NA
60-79	Covid Deaths	75	4	9	95	13	17	1	0	90	7	18	3	6
	Non-Covid Natural Deaths	664	294	269	266	202	175	15	28	416	219	185	234	241
	CEMP	11.3%	1.4%	3.3%	35.7%	6.4%	9.7%	6.7%	0.0%	21.6%	3.2%	9.7%	1.3%	2.5%
	RMR to unvax		12.0%	29.6%		18.0%	27.2%	18.7%	0.0%		14.8%	45.0%*	5.9%	11.5%
	Pfizer RMR to Moderna			245.9%			150.9%		0.0%			304.4%*		194.2%
80+	Covid Deaths	32	8	7	49	15	22	1	1	56	11	16	9	7
	Non-Covid Natural Deaths	462	536	214	226	319	127	36	26	307	189	118	446	251
	CEMP	6.9%	1.5%	3.3%	21.7%	4.7%	17.3%	2.8%	3.8%	18.2%	5.8%	13.6%	2.0%	2.8%
	RMR to unvax		21.5%	47.2%		21.7%	79.9%	12.8%	17.7%		31.9%	74.3%	11.1%	15.3%
	Pfizer RMR to Moderna			219.2%			368.4%***		138.5%			233.0%*		138.2%
18-59	Covid Deaths	47	0	1	73	1	1	0	0	27	3	4	0	0
	Non-Covid Natural Deaths	323	33	57	128	36	69	1	2	209	47	71	37	43
	CEMP	14.6%	0.0%	1.8%	57.0%	2.8%	1.4%	0.0%	0.0%	12.9%	6.4%	5.6%	0.0%	0.0%
	RMR to unvax		0.0%	12.1%		4.9%	2.5%	0.0%	0.0%		49.4%	43.6%	0.0%	0.0%
	Pfizer RMR to Moderna			NA			52.2%		NA			88.3%		NA
60+	Covid Deaths	107	12	16	144	28	39	2	1	146	18	34	12	13
	Non-Covid Natural Deaths	1,126	830	483	492	521	302	51	54	723	408	303	680	492
	CEMP	9.5%	1.4%	3.3%	29.3%	5.4%	12.9%	3.9%	1.9%	20.2%	4.4%	11.2%	1.8%	2.6%
	RMR to unvax		15.2%	34.9%		18.4%	44.1%	13.4%	6.3%		21.8%	55.6%	8.7%	13.1%
	Pfizer RMR to Moderna			229.1%*			240.3%***		47.2%			254.3%**		149.7%

Table 3. Comparative RMR of Pfizer vs. Moderna from Multivariate Logit Model

Table shows odds ratio from logit estimation of COVID-19 mortality for samples of persons in Milwaukee County, aged 18-59 or aged 60+, who died of natural causes and received 2 or 3 doses of Pfizer or Moderna over indicated periods. Odds ratios are for Pfizer vaccinee mortality relative to Moderna vaccinees (P/M ratio), from logit model of Prob(Covid-19 Death) = f(received Pfizer (Moderna is baseline), with controls for age, age², gender, and (days since last vaccine dose - 30 days). Sample excludes immune-compromised persons and persons who received mixed Moderna and Pfizer doses. For NCNMR ratios, *, **, *** indicates p < .05, .01, and .001, respectively; significant results (at p < .05 or better) in **boldface**.

Age in years	Period	2-dose recipients			3-dose recipients		
		P/M ratio	p-value	95 CI	P/M ratio	p-value	95 CI
18-59	Apr-Sep 2021	No Covid deaths		NA	No deaths	NA	NA
	Oct-Dec 2021	130.6%	0.887	[3.3%, 5179.4%]	No deaths	NA	NA
	Jan-Jun 2022	97.2%	0.973	[19.3%, 489.8%]	No deaths	NA	NA
	Jan 2021-June 2022	103.3%	0.961	[28.5%, 374.4%]	No deaths	NA	NA
60+	Apr-Sep 2021	285.4%	0.010	[128.4%, 634.1%]			
	Oct-Dec 2021	254.2%	0.001	[149.5%, 432.2%]	36.1%	0.474	[2.2%, 585.8%]
	Jan-Jun 2022	238.9%	0.005	[130.6%, 437.1%]	152.6%	0.324	[65.9%, 353.5%]
	Jan 2021-June 2022	257.8%	< 0.001	[181.6%, 366.1%]	134.9%	0.454	[61.6%, 295.5%]

Figure 1. Summary of Two-Dose and Three-Dose RMRs for Pfizer and Moderna, Ages 60+

Figure summarizes RMRs from Table 2 for two-dose and three-dose Pfizer and Moderna vaccinees, relative to unvaccinated, for the indicated times periods. Figure shows increased RMRs during the Omicron period, and the reduction in RMR from a booster dose.

