Comparing the Efficacies of the Pfizer-BioNTech and the Moderna mRNA COVID-19 Vaccines

Firas Naber

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Abstract

The vaccine efficacy of the two COVID-19 vaccines BNT162b2 and mRNA-1273 from 2 months after the second dosage injections through 4 months is compared using data obtained from a clinical trial done on each vaccine. There were some differences in the procedures taken during the trials, such as the follow-up time, age of participants, and the number of participants. The efficacies of the vaccines were both greater than 90% soon after the second injection. However, the vaccine efficacy of the BNT162b2 after the second injection is expected to drop below 90% after more than 4 months have passed. The vaccine efficacy of the mRNA-1273 was at 94% at the 4 months mark, around 4% higher than the efficacy of BNT162b2.

Advisers and Key Words

- **Primary Adviser**: Jon Anderson
- **Secondary Adviser**: Jong-Min Kim
- **Key word 1**: Vaccine Efficacy
- **Key word 2**: COVID-19
- **Key word 3**: BNT162b2
- **Key word 4**: mRNA-1273

Introduction

The coronavirus disease 2019 (COVID-19) continues to spread across the globe since the virus first emerged, leading to many infections and deaths, with a current (growing) total of more than 80 million cases diagnosed and close to 1 million deaths in the United States alone (NYT, 2022). Several COVID-19 vaccines are available from different manufacturers based in different countries and can be used to reduce the number of infections, deaths, and the severity of illness as much as possible.

Vaccine efficacy (VE) is a rate used to measure the proportionate reduction in cases of an illness among vaccinated persons under ideal conditions, such as in vaccine clinical trials. VE is one of the important aspects considered when it comes to the approval, release, and distribution of a vaccine. However, VE is only a measure for releasing a considerably well-performing vaccine in a controlled environment, meaning that it would be tried on a private group of participants while medics constantly monitor their health, this is also known as a trial phase. After the trial phase(s) pass successfully and the vaccine is released, the illness reduction rate now has to be collected from the public (less controlled environment), to obtain the most reliable rate possible. This rate found in less controlled environments is known as vaccine effectiveness.

In this paper, two US-based COVID-19 vaccines, the BNT162b2 (also known as the Pfizer-BioNTech) mRNA COVID-19 vaccine and the mRNA-1273 (also known as the Moderna) mRNA COVID-19 vaccine will be compared when it comes to their VE rates, using data provided from 2 different vaccine trials (data resources). The resources used in this paper include VE records from the day the first dose of each vaccine was given to the trial participants, through about a 5-month follow-up period after receipt of the second vaccine injection. However, the focus of this paper will be on one time period reported in the data sources used which is between 2 and 4 months after receipt of the second injection.

Background and Computational Methods

	Developed Disease?		
	Infected	Non-case	Total
Vaccinated	a	b	$a+b$
Unvaccinated	c	d	$c+d$
Total	$a+c$	$b+d$	$a+b+c+d$

This table is one way to represent the data which will be used in the computation methods described later on in this section. It compares the the data in 2 groups, with group 1 being the data of the participants who were assigned a vaccine in a clinical study, where the number of people infected by some virus after vaccination (a) and the number of people who did not get infected by it (b) are input into the table. Group 2 is the data of the remaining participants in a study who were not assigned a vaccine, in other terms, the participants assigned a saline placebo injection. Again, the number of those participants who became infected by the virus while being unvaccinated (c) and the number of participants who did not get infected by the virus while being unvaccinated (d) are input into the table for further use to find the VE of the vaccine being studied.

Risk Ratio

Risk ratio (RR), also known as the relative risk compares the risk probability of a health event (e.g. disease or injury) in a primary group to the risk probability of a health event among a second group. The formula for measuring RR using the table above is

$$\widehat{\mathrm{RR}} = \frac{\text{The risk of disease (incidence proportion, attack rate) in group of primary interest}}{\text{The risk of disease (incidence proportion, attack rate) in comparison group}}$$

i.e.

$$\widehat{\mathrm{RR}} = \left(\frac{a/(a+b)}{c/(c+d)}\right)$$

Calculating RR requires the attack rate (also known as attack risk) to be found for both groups first. It is found by taking the number of people with the health event (e.g. sick or injured people) in a group and dividing that number by the total number of people in the same group.

If the risk ratio computed is 1.0, it would mean that both the group of primary interest and the comparison group have identical risk among them. A risk ratio greater than 1.0 indicates an increased risk for the group in the numerator, usually the exposed group. A risk ratio less than 1.0 (as in the example below) indicates a decreased risk for the exposed (vaccinated) group, possibly indicating that exposure protects against the disease.

Vaccine Efficacy

The VE mathematical formula was invented in 1915 by Greenwood and Yule, for the creation and testing of cholera and typhoid vaccines, and was first seen in their paper *The Statistics of Anti-typhoid and Anti-cholera Inoculations, and the Interpretation of such Statistics in general* (Greenwood and Yule, 1915).

VE is measured using the formula:

$$\mathrm{VE} = \frac{\text{Risk among unvaccinated group} - \text{Risk among vaccinated group}}{\text{Risk among unvaccinated group}}$$

Or,

$$\mathrm{VE} = 1 - \text{Risk Ratio}$$

(Doll and Hill, 1950)

The data sources used for this paper uses a different method to calculate the VE, using the total time (in 1000 person-years) instead of the risk of disease (number of individuals at risk) and the incidence rate ratio (IRR) instead of the RR. It is expected to obtain different results from the data sources used, however, the differences should be minor.

Standard Error of the Log Risk Ratio

After finding the risk ratio, the standard error of the log RR can then be calculated, which is then used to compute the 95% confidence interval (CI). The standard error of the log of the risk ratio is estimated using

$$\text{SE}\{ln(\widehat{\text{RR}})\} = \sqrt{\frac{1}{a} + \frac{1}{c} - \frac{1}{a+b} - \frac{1}{c+d}}$$

(Altman, 1991).

Confidence Interval Bounds of the Vaccine Efficacy

The 95% confidence interval bounds of the VE are found by taking 1 - the exponential of the bounds from the confidence interval of the log RR:

$$\text{CI} = \left(1 - e^{\left(ln(\widehat{\text{RR}}) - 1.96 \times \text{SE}\{ln(\widehat{\text{RR}})\}\right)} \text{to } 1 - e^{\left(ln(\widehat{\text{RR}}) + 1.96 \times \text{SE}\{ln(\widehat{\text{RR}})\}\right)}\right)$$

(Altman, 1991).

Numerical Example

Developed Chickenpox?			
	Chickenpox	Non-case	Total
Vaccinated	$a = 18$	$b = 134$	152
Unvaccinated	$c = 3$	$d = 4$	7
Total	21	138	159

(CDC, 2012a)

To find the risk ratio, the attack rate of each group needs to be found first. In this example, the two groups are the people exposed to chickenpox and the people who were not exposed. The attack rate for exposed equals:

$$a/a + b,$$

while the attack rate for unexposed equals

$$c/c + d.$$

Therefore, the risk of chickenpox among vaccinated participants would be equal to:

$$18/152 = 0.118 = 11.8\%.$$

The risk of chickenpox among unvaccinated participants is equal to:

$$3/7 = 0.429 = 42.9\%.$$

Using the attack risk values, we can find the VE for the chickenpox vaccine:

$$\text{VE} = (42.9 - 11.8)/42.9 = 31.1/42.9 = 0.72.$$

VE can also be found by using the risk ratio which is calculated by dividing the attack risk of the first group by that of the second group:

$$0.118/0.429 = 0.28,$$

meaning that the risk of a vaccinated individual getting infected by chickenpox is 0.28 times the risk of an unvaccinated person. From this risk ratio (less than 1.0), one could say that there is a decreased risk or protective effect for the vaccinated participants. After computing the risk ratio, the VE can also be obtained by subtracting the risk ratio from 1:

$$\text{VE} = 1 - \text{RR} = 1 - 0.28 = 0.72.$$

Concluding that the vaccinated group experienced 72% fewer chickenpox cases than they would have if they had not been vaccinated (CDC, 2012b).

Using the computational methods described earlier, the standard error of the logarithm of the risk ratio of chickenpox can be estimated using the attack rates, which are then used to compute the estimated VE and its 95% confidence interval bounds. The results of these computations are can be seen in the table below:

	Attack Rate	Risk Ratio	VE	95% CI
Vaccinated	0.118	0.28	72.0%	(25.7% - 89.5%)
Unvaccinated	0.429			

COVID-19 Efficacy Data

The Data

The data used for the comparison between the mRNA-1273 and BNT162b2 mRNA COVID-19 vaccines were obtained from two different studies (one for each of the vaccines). The data used in this paper for the BNT162b2 mRNA COVID-19 vaccine was obtained from the article Stephen J. Thomas, M.D., Edson D. Moreira *et al.*, with the use of the C4591001 clinical trial group data (Thomas *et al.*, 2021). The data used in this paper for the mRNA-1273 vaccine was obtained from Hana M. El Sahly, M.D., Lindsey R. Baden, M.D., *et al.*, with the use of the COVE study group data (El Sahly *et al.*, 2021).

BNT162b2 Vaccine Data

The BNT162b2 mRNA COVID-19 vaccine from Pfizer-BioNTech was granted emergency use authorization in the US in December 2020, at the time only 2 months of clinical trial data were available. The researchers in the paper by Thomas *et al.* reported the safety and efficacy data through 6 months of follow-up. The study reported in the paper was still ongoing at the time the paper was published. Some features of the C4591001 (BNT162b2 vaccine) clinical trial are that it is randomized, placebo-controlled, observer-blinded, and multinational.

The C4591001 trial started with 46,429 participants, which were randomly assigned for getting two injections of either the BNT162b2 vaccine or saline placebo, given 21 days apart, where 23,040 of the participants were randomly assigned to receive BNT162b2 and the 23,037 others were randomly assigned to receive the saline placebo. In the primary VE data source, reactogenicity to the vaccine through 7 days and adverse events through 6 months after vaccination were assessed in participants 16 or older. Efficacy of BNT162b2 against COVID-19 after receipt of the first dose (blinded follow-up period) was evaluated in participants 12 or older. The VE was found using the method described earlier on in the introduction section using the variables number at risk and the number of cases for the calculation. The BNT162b2 VE data used from the paper (EEP between 2 and 4 months after the second injection) can be seen in the table below, where the VE was calculated using data from 41,653 participants; the rest of the participants were excluded from the trial by this stage. From the participants remaining in the trial, 20,860 were randomly given the BNT162b2 vaccine and the 20,793 others were received the saline placebo. Refer to Thomas *et al.* for the entire VE study data (Thomas *et al.*, 2021).

Developed COVID-19?			
	COVID-19	Non-case	Total
Vaccinated	$a = 46$	$b = 20,814$	20,860
Placebo	$c = 449$	$d = 20,344$	20,793
Total	495	41,158	41,653

mRNA-1273 Vaccine Data

The mRNA-1273 COVID-19 vaccine by Moderna showed a good VE and safety profile after a median follow-up of 64 days in its clinical trial, which lead the FDA to authorize the vaccine's emergency use, however, the VE and safety beyond that period were not known. The study by El Sahly *et al.* reported the final results of the blinded analysis before place recipients could choose to receive the vaccine. Similar to the BNT162b2 trial, this study randomly assigned, at the beginning of the trial 30,415 participants into getting two injections of either the mRNA-1273 vaccine or saline placebo, given 28 days apart. 15,209 participants were assigned to receive mRNA-1273 and 15,206 to receive the placebo. The primary endpoint of this vaccine was the prevention of symptomatic infections with onset 14 or more days after the second injection at a median of 5.3 months. Efficacy of BNT162b2 against COVID-19 after receipt of the first dose was evaluated in adult participants 18 or older. VE was found using the method described earlier on in the introduction section using the variables the number at risk (estimated using the original data) and the number of cases for the calculation. The mRNA-1273 VE data used (EEP between 2 and 4 months after second injection) from the paper can be seen in the table below, where 25,797 participants remained in the study at that point, with 13,249 of those participants having the mRNA-1273 vaccine and the remaining 12,548 received the saline placebo (El Sahly *et al.*, 2021).

Developed COVID-19?			
	COVID-19	Non-case	Total
Vaccinated	$a = 28$	$b = 13,221$	13,249
Placebo	$c = 434$	$d = 12,114$	12,548
Total	462	25,335	25,797

COVID-19 Vaccine Efficacy Computations

The Standard Error and Confidence Interval Bounds

Using the data provided in the earlier sections, the standard error of the logarithm of the infection risk ratio can be estimated for both vaccines, where the BNT162b2 vaccine had an infection risk ratio:

$$\widehat{\text{RR}} = \left(\frac{46/(46 + 20,814)}{449/(449 + 20344)} \right) \simeq 0.10.$$

The standard error of the log of RR comes out to be approximately equal to 0.1545 for the BNT162b2 vaccine. The mRNA-1273 vaccine had an infection risk ratio:

$$\widehat{\text{RR}} = \left(\frac{28/(28 + 13,221)}{434/(434 + 12,114)} \right) \simeq 0.061.$$

The standard error of the log of the RR of the mRNA-1273 vaccine is found to be approximately equal to 0.1946.

The confidence intervals (CIs) for the VE of both vaccines can be estimated using the standard error values found in the earlier sections. The 95% CI for the BNT162b2 VE (between 2 and 4 months after the second injection) is estimated to be between 86.5% and 92.6%, while the 95% CI for the mRNA-1273 VE (between 2 and 4 months after second injection) is estimated to be between 91.1% and 95.8%. The final results are summarized in the table below:

Vaccine	Risk Ratio	SE{ln(RR)}	VE	VE 95% CI
BNT162b2	0.10	0.1545	90.0%	(86.5% - 92.6%)
mRNA-1273	0.061	0.1946	94.0%	(91.1% - 95.85%)

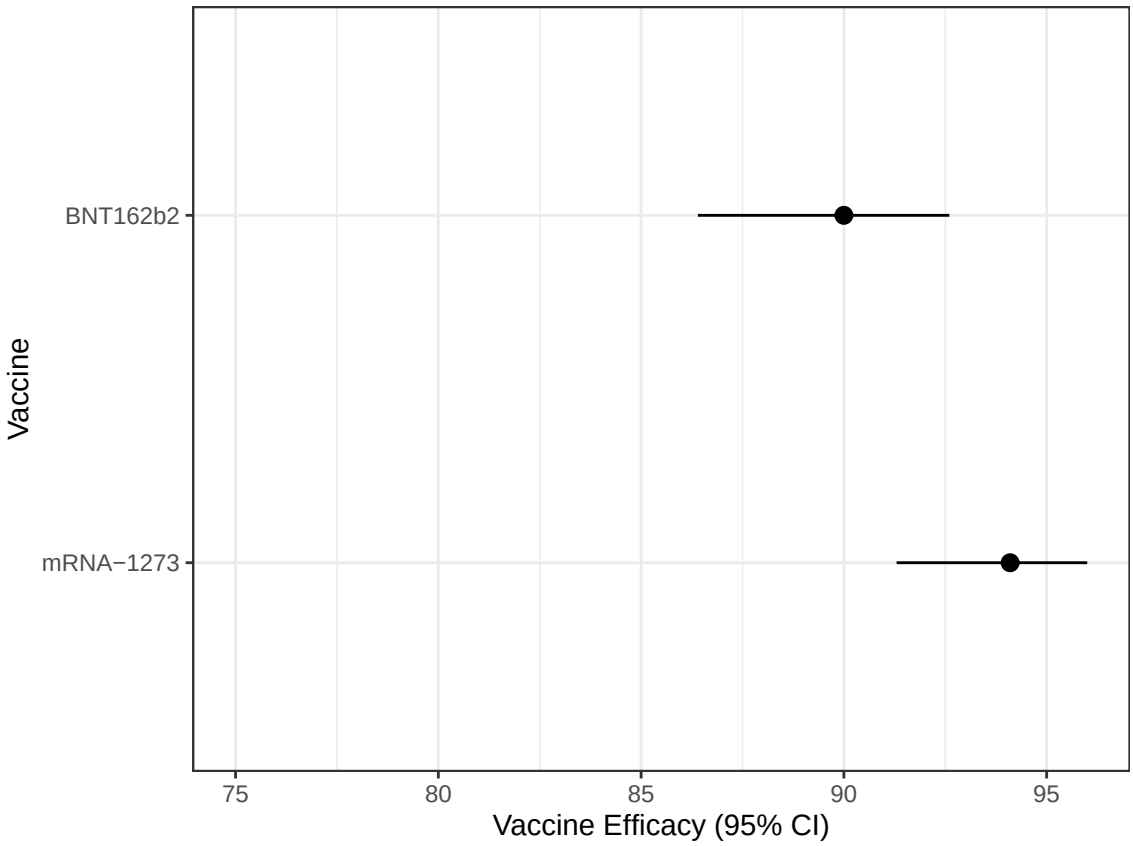

Figure 1: Visual Comparison of vaccine efficacy rates and 95% confidence interval bounds of the BNT162b2 and mRNA-1273 COVID-19 vaccines

Conclusion

In this paper, BNT162b2, also known as the Pfizer-BioNTech vaccine, and mRNA-1273, mostly known as the Moderna vaccine were compared in terms of their vaccine efficacy (VE). Both vaccines require two injects to fully function. VE refers to how well a vaccine performs under ideal conditions as in clinical trials where participants would have their health constantly monitored by medics.

The VE between 2 and 4 months after the second injection is given was compared in this paper, where the final VE result found for BNT162b2 was 90.0% with 95% confidence interval bounds from 86.5% to 92.6%. The VE result for mRNA-1273 found was 94.0% with 95% confidence interval bounds from 91.1% to 95.85%. in terms of those numbers, it can be concluded that mRNA-1273 has a higher VE than BNT162b2 from 2 months after the second injection throughout 4 months.

From the VE results found, it can be concluded that the VE of the mRNA-1273 COVID-19 vaccine is higher than that of the BNT162b2 vaccine between 2 and 4 months after the receipt of the second injection. However, these results do not determine that one vaccine is always better than the other, due to many other factors playing part when it comes to the differences between vaccines such as the VE after a longer period of time, because one VE might drop at a much stronger rate than the other after a 6 months or 1 year for instance. The VE of BNT162b2 is expected to drop below 90% after the 4 months mark, and the VE of mRNA-1273 is also to expected to drop after the 4 months mark below 94.0%.

Calculating VE for any vaccine is usually done over periods much longer than 2 to 4 months, and typically VE values drop with time as mentioned earlier, which is why booster vaccine injections are now available to be taken (after the vaccines have been approved by the FDA and distributed all around the world). Those booster injections usually improve the vaccine effectiveness (not efficacy), where the vaccine effectiveness is a measure of how well a vaccine protects against infection and severe illness after it has been released and used by the public. At this time, studies should focus on the vaccine effectiveness rather than their efficacy levels since many people around the world have already been vaccinated against COVID-19.

References

(2012a). "Principles of Epidemiology in Public Health Practice." URL https://www.cdc.gov/csels/dsepd/ss1978/lesson3/section5.html.

(2012b). "Principles of Epidemiology in Public Health Practice, Lesson 3, Section 6." URL https://www.cdc.gov/csels/dsepd/ss1978/lesson3/section6.html.

(2022). "Coronavirus in the U.S.: Latest Map and Case Count." URL https://www.nytimes.com/interactive/2021/us/covid-cases.html.

Altman D (1991). "Inter-rater agreement." *Practical statistics for medical research*, pp. 403–409.

Doll R, Hill AB (1950). "Smoking and carcinoma of the lung." *British medical journal*, **2**(4682), 739.

El Sahly HM, Baden LR, Essink B, Doblecki-Lewis S, Martin JM, Anderson EJ, Campbell TB, Clark J, Jackson LA, Fichtenbaum CJ, *et al.* (2021). "Efficacy of the mRNA-1273 SARS-CoV-2 Vaccine at Completion of Blinded Phase." *New England Journal of Medicine*, **385**(19), 1774–1785.

Greenwood M, Yule GU (1915). "The Statistics of Anti-typhoid and Anti-cholera Inoculations, and the Interpretation of such Statistics in general."

Thomas SJ, Moreira Jr ED, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL, Pérez Marc G, Polack FP, Zerbini C, *et al.* (2021). "Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine through 6 months." *New England Journal of Medicine*.