95% Effective? A Deep Dive into Pfizer's Vaccine Data Through Bayesian and Frequentist Lenses

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Abstract

This study reanalyzes the clinical trial data for Pfizer's COVID-19 vaccine, BNT162b2, using both Bayesian and Frequentist statistical methods. The original trial involved 34922 participants who were randomly assigned to either vaccine or placebo groups, reporting a vaccine efficacy rate of 95%. We employ a likelihood-based Frequentist approach alongside a Bayesian beta-binomial model to estimate vaccine efficacy and assess the uncertainties associated with these estimates through both confidence intervals and hypothesis tests. The results confirm a high vaccine efficacy that aligns with Pfizer's findings; however, each statistical methodology provides nuanced perspectives. Our comparative analysis highlights the strengths and limitations of each method, offering deeper insights into the interpretation of vaccine efficacy. This evaluation underscores the importance of utilizing diverse statistical techniques when making critical public health decisions.

Keywords

Bayesian analysis, *Likelihood inference*, *Vaccine efficacy*, *COVID-19*

Introduction / Background

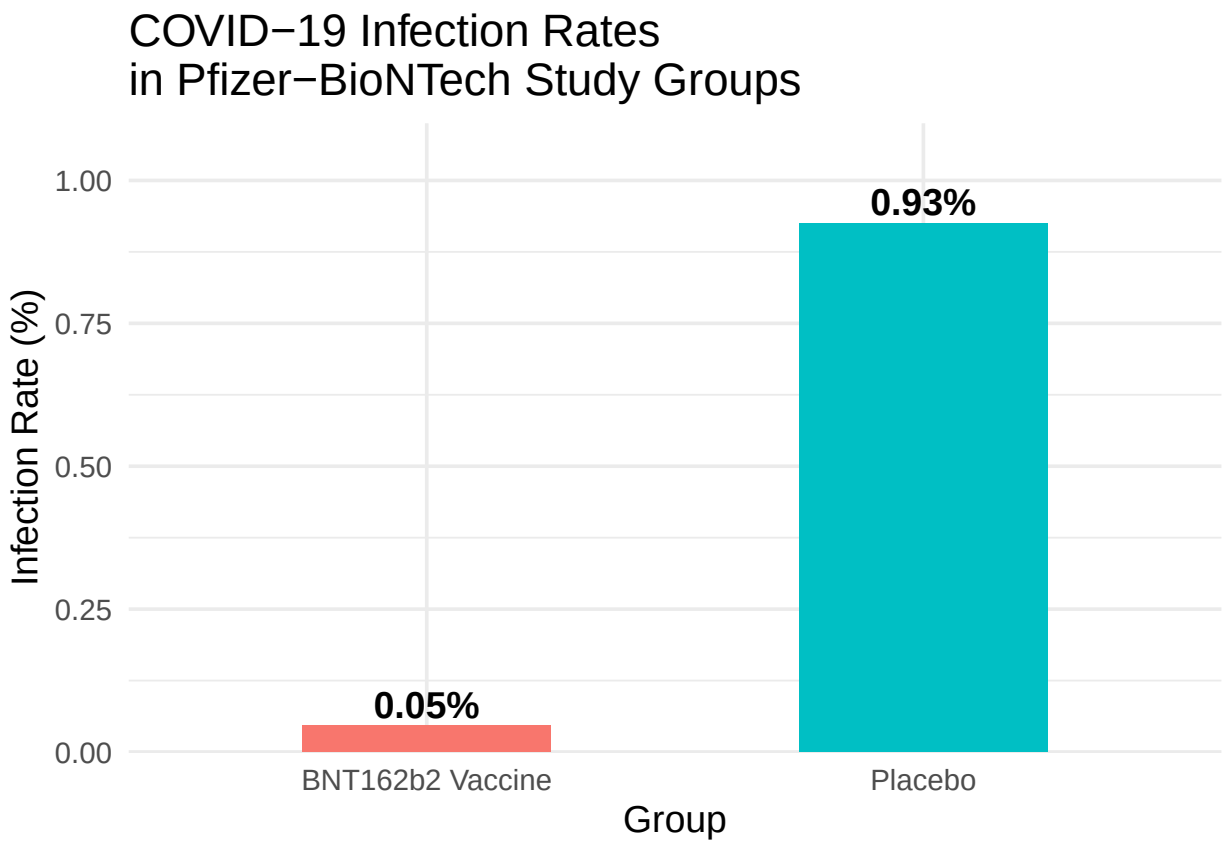
The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has created unprecedented global health challenges, leading to widespread illness and death. In response to this crisis, the rapid development and deployment of effective vaccines became a top priority. Among the vaccines developed, the BNT162b2 vaccine from Pfizer and BioNTech emerged as a key candidate, receiving Emergency Use Authorization (EUA) from the U.S. Food and Drug Administration (FDA) in December 2020. This vaccine utilizes innovative mRNA technology and was rigorously tested in a placebo-controlled, double-blinded trial to assess its effectiveness in preventing COVID-19 infections in individuals aged 16 and older.

Previous analyses reported by Polack et al. (2020) demonstrated a remarkably high vaccine efficacy of approximately 95%, with a Bayesian credible interval of [90.3%, 97.6%]. This finding was supported by strong statistical evidence indicating that the efficacy exceeded 30%. While these initial results were promising, thorough statistical examinations using multiple methodologies offer a more comprehensive validation of the vaccine's performance, thereby boosting confidence in public health recommendations.

In this paper, we re-evaluate the efficacy data of the Pfizer-BioNTech vaccine using both Bayesian and Frequentist statistical approaches. Our goal is to validate the robustness of the previously reported efficacy estimates and to identify any methodological discrepancies or consistencies between the two analytical frameworks. By employing these distinct yet complementary methodologies, we aim to provide comprehensive insights into the vaccine's effectiveness. Ultimately, this work will contribute to informed public health decisions and enhance the statistical integrity of vaccine efficacy evaluations.

Table 1: Vaccine Efficacy against COVID-19 at least 7 days after second dose in patients without evidence of infection

Group	Cases	Sample_Size
BNT162b2	8	17411
Placebo	162	17511
Total	170	34922



Statistical Methods

Model

Describe the statistical model used.

Likelihood Inference

For likelihood inference, we need to check CI using large number and bootstrap, for p-value, use chi square distribution and empirical p-value Assumption check:

1. Random Assignment:

   Each participant is randomly assigned to vaccine or placebo. Randomization should ensure that, on average, the two groups are comparable in all characteristics except for the vaccine itself.

2. No Major Differential Attrition:

   Over the course of the study, participants in vaccine and placebo arms remain under observation for approximately the same duration, with minimal difference in dropout between the groups.

3. Identical Probability Within Each group:

   All participants in the same group share the same probability of infection (π_v or π_p).

4. Independence of Infection Events:

   One participant becoming infected does not affect another participant's risk in any direct way that would violate the binomial assumption. Large and well-blinded trials in which participants have minimal contact (given), this is satisfied.

In this case, the number of infected individuals in each arm follows the binomial distribution $X \sim binom(n, \pi)$ which is:

$$L(\pi) = \binom{n}{x} \pi^x (1-\pi)^{n-x}$$

Since we are interested in efficacy of the vaccine ψ, we use the formula $\pi = \frac{1-\psi}{2-\psi} = g(\psi)$, n is the number of total case = 170, and x is the number of success of vaccine (got infected in vaccine group) = 8. Now we can set up the likelihood function:

$$\begin{aligned} L^*(\psi) &= L(g(\psi)) \\ &= \binom{170}{8} \left(\frac{1-\psi}{2-\psi}\right)^8 \left(1 - \frac{1-\psi}{2-\psi}\right)^{162} \\ &= \binom{170}{8} \left(\frac{1-\psi}{2-\psi}\right)^8 \left(\frac{1}{2-\psi}\right)^1 62 \\ &= \binom{170}{8} \left(\frac{1-\psi}{2-\psi}\right)^{8+162} \\ &= \binom{170}{8} \frac{(\psi^* - 1)^8}{(\psi^* - 2)^{170}} \end{aligned}$$

To get $\hat{\psi}_{mle}$, find the log likelehood function:

$$\ell^*(\psi) \;=\; \ln L^*(\psi) \;=\; \ln\big[(\psi-1)^8\big] \;-\; \ln\big[(\psi-2)^{170}\big] \;=\; 8\,\ln(\psi-1) \;-\; 170\,\ln(\psi-2).$$

Now find first derivative:

$$\frac{d}{d\psi}\,\ell^*(\psi) \;=\; 8\,\frac{1}{\psi-1} \;-\; 170\,\frac{1}{\psi-2}.$$

Set it equals to zero to get $\hat{\psi}_{mle}$:

$$8\,\frac{1}{\psi-1} \;-\; 170\,\frac{1}{\psi-2} \;=\; 0$$

Then solve the equation to find $\hat{\psi}_{mle}$.

To make sure this is a local maximum, find second derivative:

$$\ell''^{*}(\psi) \;=\; -\frac{8}{(\psi-1)^2} \;+\; \frac{170}{(\psi-2)^2}$$

1. Large sample CI:

To construct a large sample confidence interval estimate for ψ_0 at 95%, we still need to find standard error use $I(\hat{\psi})$.

$$I(\psi_0) = E_{\psi_0}\left[-\ell''^{*}(\psi)\right] = \frac{8}{(\psi_0-1)^2} - \frac{170}{(\psi_0-2)^2}$$

In the binomial likelihood view, we effectively have one observation from a Binomial(n, π)distribution, but that single binomial observation contains n underlying Bernoulli trials. In this case, SE is equal to:

$$\mathrm{SE}(\hat{\psi}) \;\approx\; \sqrt{\frac{1}{I(\hat{\psi})}}$$

Finally, we can find 95% large number CI by using CI formula:

$$\hat{\psi} \;\pm\; z_{0.975}\,\mathrm{SE}(\hat{\psi})$$

2. Bootstrap percentile interval:

   To make sure get the accurate conclusion, we choose to also include a bootstrap percentile interval.

3. P-value: chi square distribution:

To assess the significance of the estimated parameter ψ, we conduct a hypothesis test:

$$H_0 : \psi = 0.3 \quad \text{vs.} \quad H_1 : \psi \neq 0.3$$

Two extra standard test statistics are used, the likelihood ratio test statistic is:

$$\Lambda = \frac{L(\hat{\psi}_0^{mle})}{L(\hat{\psi}_0^{null})}$$

Under H_0, the larger the ratio, the stronger is the evidence against H_0.

The second statistic, Log likelihood ratio, follows a chi-square distribution with one degree of freedom under H_0. $W \sim \chi_1^2 = 2\ln(\Lambda)$.

After calculating those statistics, we compute the p-value as $P(\chi_1^2 \geq W)$, to observe if p value is less than 0.05.

4. Empirical P-value:

The second method to find p-value, using a simulation-based approach for a likelihood ratio test.
First we set parameters, set the total number of simulations B=1500, other parameters have already demonstrated in CI method.
Second, create a function that computes the log-likelihood $L(\psi)$ for a given ψ, which we will later use in simulation.
Third, simulate the W_{obs} for B times using random x observed in 170 cases with $\frac{1-\psi_0}{2-\psi_0}$.
Finally, compare W_{obs} and $\hat{W}$, if one $W_{obs} \geq \hat{W}$, return 1, others return 0, sum together than divide by B, which gives empirical p-value.

Bayesian Inference

Detail the Bayesian approach.

Random Variables

We have two groups in a clinical trial: Vaccine group (e.g., BNT162b2) of size n_v. Let X_v be the number of infected individuals in this group.

Placebo group of size n_p. Let X_p be the number of infected individuals in this group.

Hence, we assume

$$X_v \sim \text{Binomial}(n_v, p_v), \quad X_p \sim \text{Binomial}(n_p, p_p),$$

where p_v and p_p are the true (unknown) infection probabilities in the vaccine and placebo arms, respectively.

Statistical Model

Binomial Likelihoods: Each arm's number of infections is modeled with a Binomial distribution, reflecting the idea that each of the n_v or n_p individuals independently has some probability (p_v or p_p) of becoming infected. Parameter of Interest: The paper defines

$$\pi \;=\; \frac{p_v}{p_v + p_p}.$$

Equivalently, π can be interpreted as the fraction of all infections (across both arms) that occur in the vaccine arm. Vaccine Efficacy: Denoted by ψ, it is given by

$$\psi \;=\; \frac{1 - 2\pi}{1 - \pi}.$$

This transformation is chosen so that $\psi = 0$ if $p_v = p_p$, and it increases toward 1 as p_v becomes small relative to p_p.

Hypothesis of Interest

A common scientific question is whether the vaccine confers a certain minimum level of efficacy. For instance, "Is $\psi > 0.30$?'' That is, does vaccine efficacy exceed 30%? Formally, one might test:

$$H_0 : \psi \leq 0.30 \quad \text{vs.} \quad H_1 : \psi > 0.30.$$

In practice, the paper examines whether the 95% credible interval for ψ lies above 30%.

Binomial Likelihood

Let T be the number of infections in the vaccine arm. Then

$$T \mid \pi \ \sim \ \text{Binomial}(N, \pi),$$

where $N = 170$ is the total number of infected individuals. In the observed data, $T = 8$.

Beta Prior

We assume a prior $\pi \sim \text{Beta}(0.700102, 1)$. In the standard Beta form,

$$g(\pi) \ = \ \text{Beta}(\alpha, \beta) \ = \ \frac{\Gamma(\alpha+\beta)}{\Gamma(\alpha)\,\Gamma(\beta)}\,\pi^{\,\alpha-1}\,(1-\pi)^{\,\beta-1}, \quad 0 < \pi < 1.$$

Here, $\alpha = 0.700102$ and $\beta = 1$.

1. Posterior distribution of π:

$$h(\pi|t) = Beta(\alpha + 8, \beta + 170 - 8)$$

   We assmuse the posterior also follows Beta distribution based on the Theorem 13.2: Suppose $X \sim Binom(n, \pi)$ and we assume that π follows a Beta distribution with shape parameters α and β. Then the posterior distribution of π is also a Beta distribution with shape parameters $\alpha+x$ and $\beta+n-x$ where x is the observed value for X. Where x = 8, n = 170.

2.95% CI for ψ when asymmetric:

In Bayesian analysis, we use credible intervals (CIs) instead of traditional frequentist confidence intervals.

A $100(1-\alpha)\%$ credible interval for a parameter π is an interval [a,b] such that:

$$P(a \leq \pi \leq b|data) = 1 - \alpha$$

Using the beta posterior distribution, we could compute a 95% credible interval by extract the

2.5th and 97.5th percentiles

$$\pi_{lower} = Q_{0.025}(\pi)$$

$$\pi_{upper} = Q_{0.975}(\pi)$$

where $Q_p(\pi)$ is the quantile function.

We could use the function "quantile()" to compute a Bayesian credible interval by extracting the 2.5% and 97.5% quantiles if the distribution is not high skewed.

Then, since ψ is transformed from π using:

$$\psi_{samples} = \frac{1 - 2\pi_{samples}}{1 - \pi_{samples}}$$

We transform the credible interval bounds for ψ:

$$\psi_{lower} = \frac{1 - 2\pi_{upper}}{1 - \pi_{upper}}$$

$$\psi_{upper} = \frac{1 - 2\pi_{lower}}{1 - \pi_{lower}}$$

Due to the monotonicity and transformation properties of the function.

The highest Posterior Density Interval (HPDI) is an alternative to the quantile-based credible interval. It often preferred when the posterior distribution is asymmetric or skewed.

Given the posterior distribution $\mathrm{h}(\pi|t) = \mathrm{Beta}(\alpha+8,\, \beta+170-8)$, the HPDI is the shortest interval $[\alpha, \beta]$ such that:

$$P(\alpha \leq \pi \leq \beta|t) = credMass$$

Then, compute the 95% HPDI for π using "hdi()" function from the HDInterval.

Then, using the given transformation function from π to ψ to compute the 95% HPDI for ψ.

3. Bayesian P-value

   We need to compute the posterior probability that the vaccine efficacy ψ exceeds 30%:

   Null Hypothesis (H_0): $H_0 : \psi \leq 0.30$

   Alternative Hypothesis (H_1): $H_1 : \psi > 0.30$

We could using the p-value to test whether we can reject H_0 at a given significance level(0.05). We calculate:

$$P(\psi > 0.3)$$

Considering of transformation, we can get:

$$P(\psi > 0.3) = P(\frac{1-2\pi}{1-\pi} > 0.3)$$

we solve the inquality :

$$\frac{1-2\pi}{1-\pi} > 0.3$$

solving for π:

$$\pi < \frac{0.7}{1.7}$$

Thus:

$$P(\psi > 0.3) = P(\pi < \frac{0.7}{1.7})$$

Results

Present your findings.

For Likelihood Inference:

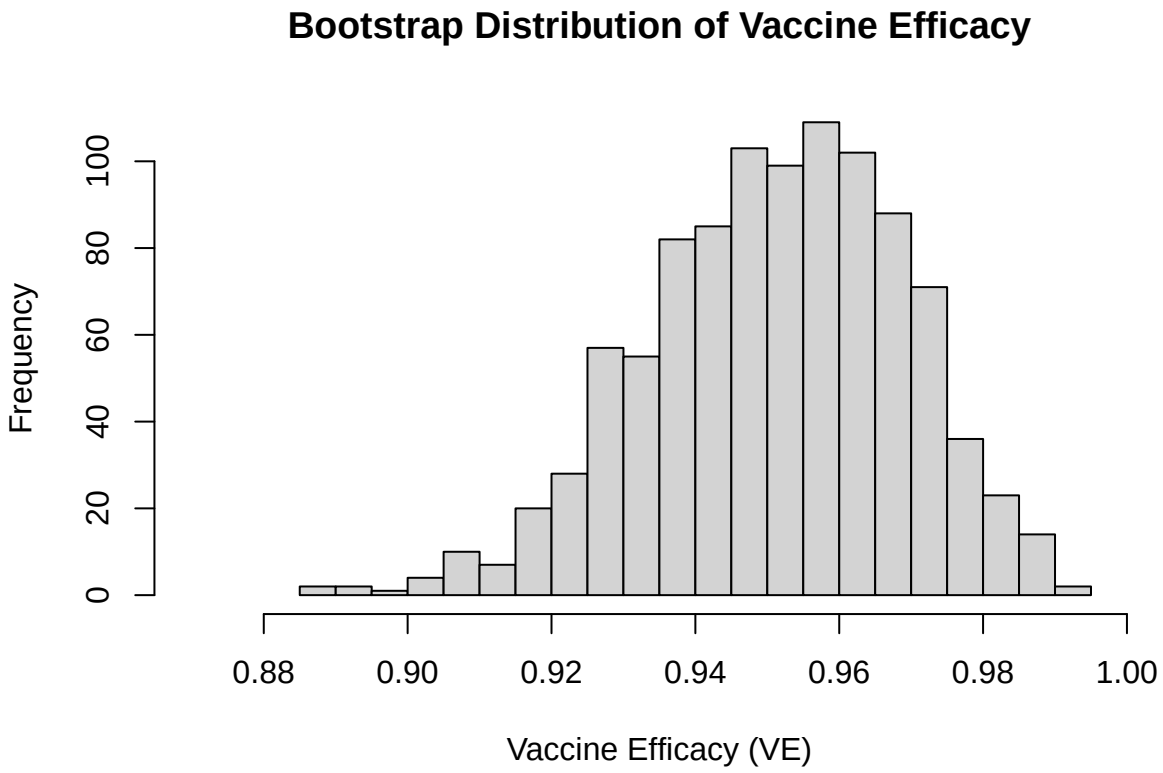
1. Large number CI Interval:

```
## [1] 0.01788533
```

We get [0.916, 0.986]. W are 95% confident that ψ_0 lies in the range (0.916,0.986) based on the observed data, the results are similar comparing to the 95% CI interval get in the article. This result strongly supports high efficacy and provides a precise estimate with a relatively low margin of error, thanks to the large sample size.

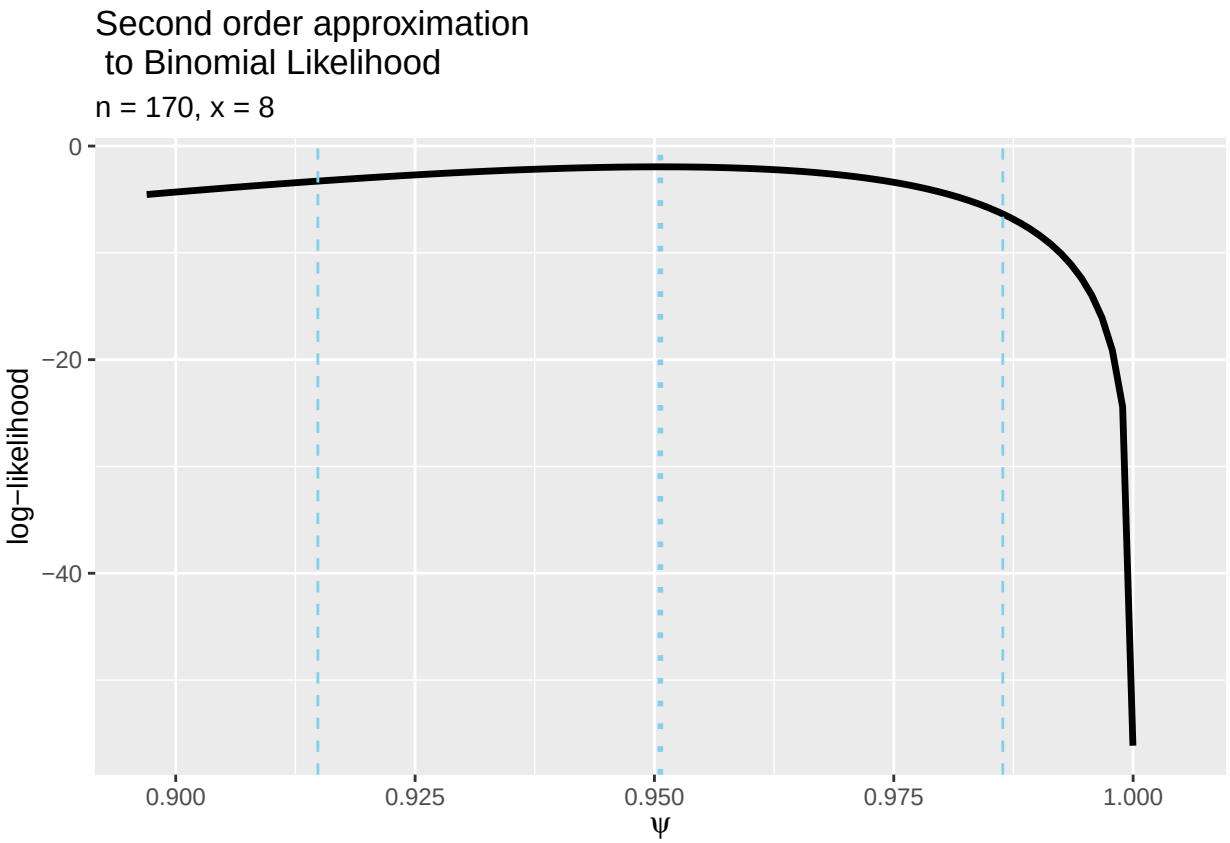
2. Bootstrap percentile interval:

```
##      2.5%     97.5%
## 0.9146612 0.9822516
```




```
## Warning: Removed 4 rows containing missing values or values outside the scale range
## (`geom_function()`).
```

```
## Warning: Removed 101 rows containing missing values or values outside the scale range
## (`geom_function()`).
```



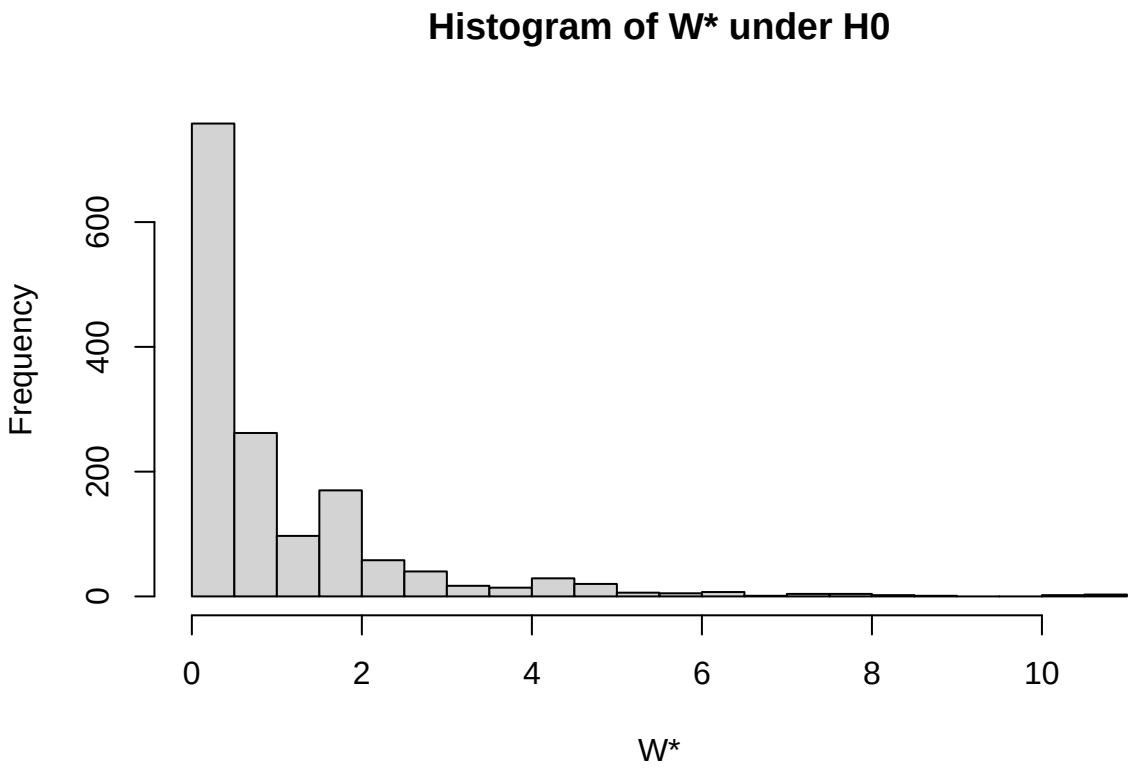
From the bootstrap distribution, the 95% confidence interval for vaccine efficacy runs approximately from 91.5% to 98.3%, indicating that most resampled estimates lie in this high-efficacy range. The histogram shows a fairly tight clustering around the mid-90% mark, with few bootstrap replicates suggesting efficacy below about 90% or above 99%. This suggests that, given the observed data, there is strong evidence that the vaccine's true efficacy is very likely above 90%. By conducting boosttrap

3. P-value (chi square distribution):

After calculation, p-value is $2.8222944 \times 10^{-28}$, which is extremely small compared to 0.05, in this case, we reject H_0 and claim that the true ψ_0 is significantly different from 0.3.

4. Empirical P-value:

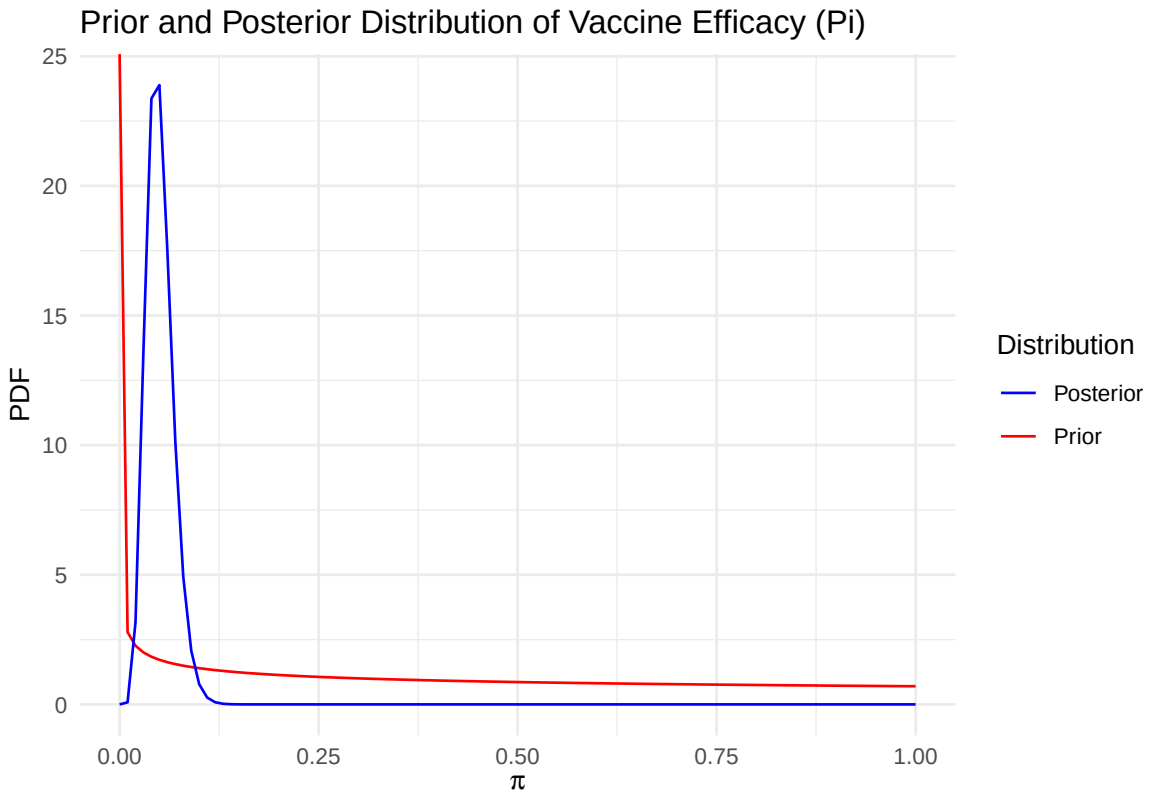
```
## Empirical P value 0
```



Both the chi-square based p-value and the empirical p-value are extremely small or essentially zero. This indicates that the observed data are highly inconsistent with the null hypothesis $\psi = 0.3$. In other words, the likelihood of obtaining such extreme test statistics under the assumption that $\psi = 0.3$ is approximately 0. Given that the maximum likelihood estimate of ψ is approximately 0.95, we conclude that the data provide extremely strong evidence against the null hypothesis, and strongly support that the true value of ψ is much higher than 0.3. This result suggests a very high efficacy compared to the 30% efficacy.

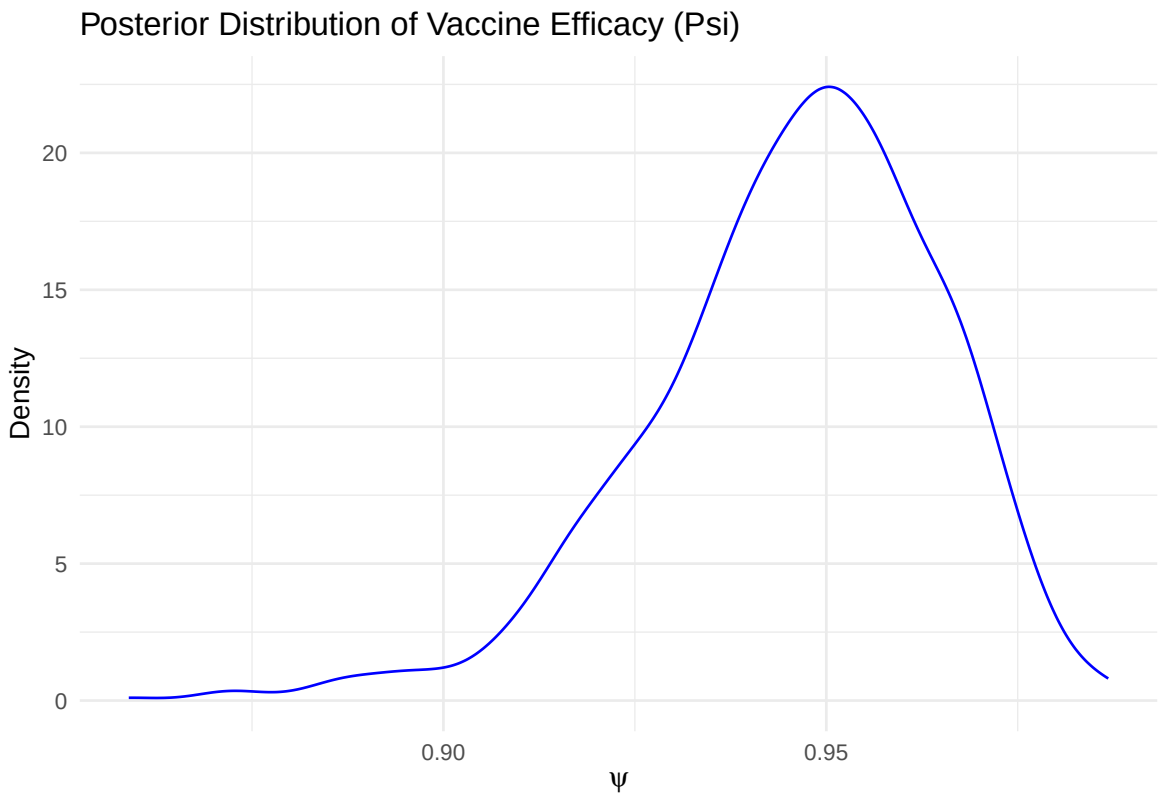
For Bayesian Inference:

1. Prior and Posterior Distribution of Vaccine Efficacy (Pi):



This graph shows the Prior and Posterior distribution of π in a Bayesian Model for vaccine efficacy. According to the graph, the red curve represents the prior distribution of π, it shows that the peak near $\pi = 0$, suggesting the prior assumnes a low infection probability and the long right tail indicates some uncertainty. The blue curve represents the posterior distribution of π. Since the posterior concentrates at small values of π, it implies that the infection probability is lower in the vaccinated group, which indirectly suggests high vaccine efficacy.

2. Posterior Distribution of Vaccine Efficacy (Psi):



This graph represents the posterior distribution of vaccine efficacy ψ. The posterior distribution is unimodel and the peak is occurs around $\psi \approx 0.95$, suggesting that the most probable vaccine efficacy is about 95%. This distribution is skewed to the left.

3. Quantile-Based Credible Interval:

```
##      2.5%     97.5%
## 0.9023418 0.9757407
```

Based on the output showing above, there is a 95% probability that the true vaccine BNT162b2 efficacy ψ lies within 90.2% to 97.6%, given the observed data and prior beliefs.

2. HPDI Credible Interval:

```
## Warning: package 'HDInterval' was built under R version 4.4.3
```

```
##     lower     upper
## 0.9090876 0.9788482
```

Based on the output showing above, the credible interval which was computed using HPDI stating that there is a 95% probability that the true vaccine BNT162b2 efficacy ψ lies within 90.9% to 97.9%, given the observed data and prior beliefs. The HPDI is slightly narrower than the quantile-based interval because it excludes low-density tail regions. For this question, we believe that HPDI is useful since the posterior distribution for ψ is skewed to the left, by viewing the graph "Posterior Distribution of Vaccine Efficacy (Psi)" graph above., it will provides a more precise credible interval.

3. P-value:

```
## [1] 1
```

Since $P(\psi > 0.30) \approx 1$, we strongly reject H_0. There is overwhelming evidence that the vaccine BNT162b2 is significantly more effective than 30%.

Discussion / Conclusion

Discuss / conclude here.

Bibliography

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Smith, A., & Johnson, C. (2023). *Title of the Online Article*. Retrieved from https://www.example.com.

Appendix

Code

Code to visualize the data using tables

```
pfizer_data <- data.frame(
  Group = c("BNT162b2", "Placebo", "Total"),
  Cases = c(8, 162, 170),
  Sample_Size = c(17411, 17511, 34922)
)

library(knitr)

kable(pfizer_data,
      caption = "Vaccine Efficacy against COVID-19 at least 7 days after second dose in patient
      align = "lcc")

data <- data.frame(
  Group = c("BNT162b2 Vaccine", "Placebo"),
  Cases = c(8, 162),
  Sample_Size = c(17411, 17511)
)

data$Infection_Rate <- (data$Cases / data$Sample_Size) * 100

# Plot with adjusted axis limits
ggplot(data, aes(x = Group, y = Infection_Rate, fill = Group)) +
  geom_bar(stat = "identity", width = 0.5) +
  geom_text(aes(label = sprintf("%.2f%%", Infection_Rate)),
```

```
            vjust = -0.3, size = 5, fontface = "bold") +
  scale_y_continuous(expand = c(0, 0), limits = c(0, 1.1)) +
  labs(title = "COVID-19 Infection Rates\nin Pfizer-BioNTech Study Groups",
       y = "Infection Rate (%)",
       x = "Group") +
  theme_minimal(base_size = 14) +
  theme(legend.position = "none")
```

Code to calculate large number CI

```
psi_0 = 0.3

n = 170

psi_mle = 154/162

CI_high = psi_mle + qnorm(0.975) * sqrt(1/(8/(psi_mle - 1)^2 - n/(psi_mle - 2)^2))

CI_low = psi_mle - 1.96 * sqrt(1/(8/(psi_mle - 1)^2 - n/(psi_mle - 2)^2))

sqrt(1/(8/(psi_mle - 1)^2 - n/(psi_mle - 2)^2))
```

Code to calculate bootstrap CI and visialize taylor approximation

```
x_v <- 8
n_v <- 17411

x_p <- 162
n_p <- 17511
```

```r
p_v <- x_v / n_v
p_p <- x_p / n_p

VE_hat <- 1 - (p_v / p_p)
# Construct the original 0/1 outcomes (vaccine + placebo)
data_v <- c(rep(1, x_v), rep(0, n_v - x_v))
data_p <- c(rep(1, x_p), rep(0, n_p - x_p))

B <- 1000
VE_boot <- numeric(B)

set.seed(123)  # reproducibility
for(b in 1:B){
  # sample with replacement from each arm
  samp_v <- sample(data_v, size=n_v, replace=TRUE)
  samp_p <- sample(data_p, size=n_p, replace=TRUE)

  p_v_star <- mean(samp_v)
  p_p_star <- mean(samp_p)
  # avoid division by zero if p_p_star is extremely small
  if(p_p_star == 0){
    VE_boot[b] <- NA
  } else{
    VE_boot[b] <- 1 - p_v_star / p_p_star
  }
}

# Remove any NAs (should be very rare)
VE_boot <- na.omit(VE_boot)
```

```r
# 95% percentile CI:
CI_boot <- quantile(VE_boot, c(0.025, 0.975))
CI_boot


hist(
  VE_boot, breaks = 30,
  main = "Bootstrap Distribution of Vaccine Efficacy",
  xlab = "Vaccine Efficacy (VE)",
  xlim = c(0.87, 1.0))


loglik.binom <- function(psi, x, n) {
  if(psi >= 1) return(NA_real_)
  pi <- (1 - psi) / (2 - psi)
  ll_val <- lchoose(n, x) + x*log(pi) + (n - x)*log(1 - pi)

  return(ll_val)
}


ml.binom <- maxLik2(
  loglik = loglik.binom,
  start  = 0.3,
  x      = 8,
  n      = 170
)


plot(ml.binom) +
  labs(
    title    = "Second order approximation\n to Binomial Likelihood",
    subtitle = "n = 170, x = 8",
```

```
    x         = expression(psi)
  )
```

Code to calculate p-value chi square distribution

```
peaky_head = ((psi_mle - 1)^8/(psi_mle - 2)^(170)) / ((psi_0 - 1)^8 / (psi_0 - 2)^(170))


w = 2*log(peaky_head)


p_chi = pchisq(w, 1, lower.tail =FALSE)
```

Code to calculate empirical p value (likelihood)

```
set.seed(414)


B <- 1500
psi0 = 0.3
x_obs <- 8
n     <- 170
pi0 <- (1 - psi0) / (2 - psi0)


loglik.binom <- function(psi, x, n) {
  if(psi >= 1) return(NA_real_)
  pi <- (1 - psi) / (2 - psi)
  ll_val <- lchoose(n, x) + x*log(pi) + (n - x)*log(1 - pi)


  return(ll_val)
}
```

```r
simulate_W <- function(i) {
  x_star <- rbinom(1, size = n, prob = (1 - psi0) / (2 - psi0))

  psi_star_hat <- (n - 2*x_star)/(n - x_star)

  ll_null  <- loglik.binom(psi0, x_star, n)
  ll_alt   <- loglik.binom(psi_star_hat, x_star, n)

  W_star <- 2*(ll_alt - ll_null)
  return(W_star)
}

null_sim <- lapply(1:B, simulate_W)
Wstar <- c(unlist(null_sim))

emp_p_value <- sum(Wstar >= w)/B
cat("Empirical P value", emp_p_value)

hist(Wstar, breaks=30, main="Histogram of W* under H0", xlab="W*")
abline(v = w, col="red", lwd=2)
```

Proofs

If applicable, include detailed mathematical derivations or additional theoretical explanations.