Prevented Fraction Assessment of Salmonella Enteritidis Vaccine Administered Subcutaneously and Intramuscularly for Chicken

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Our client, WeRChicken, Inc. has conducted a series of studies to evaluate the efficacy of the Salmonella Enteritidis fraction of a combination vaccine against Salmonella enteric serovar Enteritidis (SE) in Chickens. The objective of this study is to show that client's vaccine prevents SE regardless of whether it is administered subcutaneously (SC) or intramuscularly (IM). To implement this study, all chickens were vaccinated at 18 weeks of age. At 25 weeks of age, the chickens will be challenged with SE. At 26 weeks of age, the chickens will be examined for colonization of SE in the cecum. The response variable of the study is binary, positive (1) for colonization if the challenge strain of SE was re-isolated and negative (0) for colonization if not re-isolated. The variables that might influence the response variable are the vaccine administration method, SC and IM. The sample for this study is 157 commercial chickens in North America. They were randomly assigned to one of the following groups:

1. Treatment group A, vaccine administered SC.
2. Treatment group B, vaccine administered IM.
3. Control group C, placebo (some administered SC and some administered IM).

We will be using Prevented Fraction (PF) as our analysis method for this study. It is the proportion of incidents in the population that could be prevented by exposing the whole population (Prevented fraction of disease, 2020). We can test the client's vaccine prevents SE regardless of administration method by comparing the PFs between treatment group A vs. control group C and treatment group B vs. control group C.

Summary of Results

1. The results of the analyses comparing the PFs between treatment group A vs. control group C and treatment group B vs. control group C support the claim that WeRChicken, Inc.'s vaccine prevents SE regardless of whether it is administered SC or IM.
2. 56.86% is the proportion of incidents (positive for colonization if the challenge strain of SE was re-isolated) in the control group C that could be prevented by administer WeRChicken, Inc.'s vaccine SC.
3. 57.69% is the proportion of incidents (positive for colonization if the challenge strain of SE was re-isolated) in the control group C that could be prevented by administer WeRChicken, Inc.'s vaccine IM.

Statistical Methods

Study Design

The sample for this study is 157 commercial chickens in North America. Ideally, the sample selected for this study represents the target population, which is all commercial chickens around the world. However, we recognize that there are various types of commercial chickens around the world, and they may react differently to different vaccine administration methods. Hence, the eligibility restrictions for the sample selected in this study.

Analysis Variables

At 26 weeks of age, the chickens will be examined for colonization of SE in the cecum. The response variable of the study is binary, positive (1) for colonization if the challenge strain of SE was re-isolated and negative (0) for colonization if not re-isolated. The explanatory variables are vaccine administration methods. They are vaccine administered SC (treatment group), vaccine

administered IM (treatment group), and placebo administered SC or IM (placebo group). The sample for this study was randomly assigned to one of the placebo or treatment groups.

Analysis Method

PFs between treatment groups vs. control group were calculated using 1 minus Relative Risk (RR), with vaccine administration methods as explanatory variables. RR is a ratio of the probability of an event occurring in the exposed group versus the probability of the event occurring in the non-exposed group (Bilder & Loughin, 2015, p. 38) RR can be calculated through a 2*2 contingency table (Bilder & Loughin, 2015, p. 38). In this study, we will be required to build two 2*2 contingency tables, so that we can retrieve PFs for comparison. We will use R to transform the sample data into arrays and to perform the necessary calculations for RR[1].

Results and Conclusions

1. RR for group A vs. group C: the estimated probability of positive for colonization if the challenge strain of SE was re-isolated is only 43.14% (with a 95% confidence interval between 23.86% and 77.99%) as large for the treatment group A than for control group C.
2. RR for group B vs. group C: the estimated probability of positive for colonization if the challenge strain of SE was re-isolated is only 42.31% (with a 95% confidence interval between 23.37% and 76.59%) as large for the treatment group B than for control group C.

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[1] See Appendix: R Code for detailed R codes.

3. PF for group A vs. group C: 56.86% (with a 95% confidence interval between 22.01% and 76.14%) is the proportion of incidents (positive for colonization if the challenge strain of SE was re-isolated) in the control group C that could be prevented by administer WeRChicken, Inc.'s vaccine SC.
4. PF for group A vs. group C: 57.69% (with a 95% confidence interval between 23.41% and 76.63%) is the proportion of incidents (positive for colonization if the challenge strain of SE was re-isolated) in the control group C that could be prevented by administer WeRChicken, Inc.'s vaccine IM.
5. The results of the analyses comparing the PFs between treatment group A vs. control group C and treatment group B vs. control group C support the claim that WeRChicken, Inc.'s vaccine prevents SE regardless of whether it is administered SC or IM.
6. The effects of both administration methods (SC and IM) are very similar.

Appendix: R Code

```
###calculating the risk ratio by hand
salm <- read.table(file = "C:\\Users\\Moon\\Desktop\\Salmonella data.csv",
                   sep = ",", header = TRUE)


#extract counts from Cecum corresponding to each group
A1 <- sum(salm$Cecum == 1 & salm$Group == "A")
B1 <- sum(salm$Cecum == 1 & salm$Group == "B")
C1 <- sum(salm$Cecum == 1 & salm$Group == "C")
A0 <- sum(salm$Cecum == 0 & salm$Group == "A")
B0 <- sum(salm$Cecum == 0 & salm$Group == "B")
C0 <- sum(salm$Cecum == 0 & salm$Group == "C")


#Create 2*2 contingency table
AvsC<-array(data = c(A1, C1, A0, C0),
            dim = c(2,2),
            dimnames = list(First = c("Group A", "Group C"),
                            Second = c("Cecum = 1", "Cecum = 0")))
AvsC
```

```
##          Second
## First     Cecum = 1 Cecum = 0
##   Group A        11        40
##   Group C        25        25

BvsC<-array(data = c(B1, C1, B0, C0),
            dim = c(2,2),
            dimnames = list(First = c("Group B", "Group C"),
                            Second = c("Cecum = 1", "Cecum = 0")))
BvsC

##          Second
## First     Cecum = 1 Cecum = 0
##   Group B        11        41
##   Group C        25        25

#Function for Relative Risk and CI for Relative Risk
RR<-function(df){

  pi.hat.table<-df/rowSums(df)
  pi.hat.table

  pi.hat1<-pi.hat.table[1,1]
  pi.hat2<-pi.hat.table[2,1]

  # Relative risk where success is "Cecum = 1"
  RR<-round(pi.hat1/pi.hat2, 4)  #RR

  alpha<-0.05
  n1<-sum(df[1,])
  n2<-sum(df[2,])

  # Wald confidence interval
  var.log.rr<-(1-pi.hat1)/(n1*pi.hat1) + (1-pi.hat2)/(n2*pi.hat2)
  ci<-exp(log(pi.hat1/pi.hat2) + qnorm(p = c(alpha/2, 1-alpha/2)) * sqrt(var.
log.rr))
  RR.CI<-round(ci, 4)  #RR CI

  data.frame(RR, lowerCI=RR.CI[1], upperCI=RR.CI[2])

}

RR(AvsC)

##       RR lowerCI upperCI
## 1 0.4314  0.2386  0.7799

#The estimated probability of positive (1) for colonization if the challenge
strain of SE was re-isolated
 #is only 0.4314 times (or 43.14%) as large for the vaccinated group A than f
```

```
or control group C
1-RR(AvsC)#prevented fraction and its confidence interval
```

```
##       RR lowerCI upperCI
## 1 0.5686  0.7614  0.2201
```

```
#56.86% is the proportion of incidents in the control group C that could be p
revented by vaccinated group A
```

```
RR(BvsC)
```

```
##       RR lowerCI upperCI
## 1 0.4231  0.2337  0.7659
```

```
#The estimated probability of positive (1) for colonization if the challenge
strain of SE was re-isolated
 #is only 0.4231 times (or 42.31%) as large for the vaccinated group B than f
or control group C
1-RR(BvsC)#prevented fraction and its confidence interval
```

```
##       RR lowerCI upperCI
## 1 0.5769  0.7663  0.2341
```

```
#57.69% is the proportion of incidents in the control group C that could be p
revented by vaccinated group B
```

```
###calculating the risk ratio with riskratio()
#install.packages('fmsb')
library(fmsb)
fmsb::riskratio(11,25,51,50, conf.level=0.95, p.calc.by.independence=TRUE)#sa
me as AvsC
```

```
##            Disease Nondisease Total
## Exposed         11         40    51
## Nonexposed      25         25    50
```

```
##
##  Risk ratio estimate and its significance probability
##
## data:  11 25 51 50
## p-value = 0.002998
## 95 percent confidence interval:
##  0.2385902 0.7799242
## sample estimates:
## [1] 0.4313725
```

References

Bilder, C. R., & Loughin, T. M. (2015). *Analysis of categorical data with R*. Boca Raton: CRC Press, Taylor & Francis Group.

Prevented fraction of disease. (2020, August 14). Retrieved April 23, 2021, from https://med.libretexts.org/@go/page/13736