1 | SUPPLEMENTARY MATERIALS FOR: ESTIMATION OF VACCINE EFFICACY FOR VARIANTS THAT EMERGE AFTER THE PLACEBO GROUP IS VACCINATED

1.1 | Notation

Table 1 below provides a list of notation for the paper

TABLE 1 Notation

Symbol	Meaning
	General
strain	a unique collection of viral sequences, e.g. PANGO, WHO lineage, or any convenient group.
S	an index for a strain $= 0, 1, \ldots, M$ with $S = 0$ ancestral
A	Indicator of original arm, 1=vaccine 0=placebo
t	calendar time measured relative to start of study
Z(t)	Indicator of vaccination prior to t
V(s)	The mark e.g. neutralization assay value, associated with strain S
L	location or site
SSSA	Strain Specific Sieve Analysis (Cox model with baseline hazard $h_{0s}(t)$ for strain s)
SASA	Strain Anchored Sieve Analysis (Cox model with $h_{0s}(t) = h_0(t)P(t, s)$ with known $P(t, s)$
	Poisson Model
X_{AKS}	Case count for original arm A in Period $K = 1, 2$ for strain $S = 0, 1$
ω_{AKS}	$E(X_{AKS})$
p_{KS}	true community proportion of strain S in period $K = 1, 2$
θ_K	True mean number of cases on placebo in period K
θ_{KS}	True mean number of strain S cases on placebo in period K ($\theta_{KS} = \theta_K p_{KS}$)
VE_{KS}	1-ω_{1KS}/θ_{KS}. Vaccine efficacy over a single period for strain S for a person just vaccinated (K=1) or vaccinated 1 period ago (K=2).
	Cox Model
VE_s	$1 - \exp(\beta_s)$. True (time-constant) vaccine efficacy for strain s from Cox model
$P_L(t, s)$	True community proportion of s strains at time t in Location L
$p_L(k, s)$	Smoothed piecewise constant estimate of $P_L(t, s)$ for period k.
$h_0(t)$	baseline hazard for infection by any strain at calendar time t
$h_{0s}(t)$	baseline hazard for infection by strain s at calendar time t
β_{0s}	Maps to $\text{VE}_s = 1 - \exp(\beta_{0s})$
β_{1s}	coefficient for time since vaccination for strain s in Cox model
β_2	coefficient for $V(s)$ in the mark-based Cox model
$\mathcal{R}(t)$	Set of indices of subjects never infected before calendar time t
$\mathcal{S}$	Set of indices of strains observed in the trial

1.2 | GLM Analysis of Poisson Model

For ease of exposition, we have assumed that $n_0 = n_1 = n$ (i.e., that the trial was a 1:1 randomization, and ensuring that there are equal numbers in both arms). For this supplement we relax that assumption, and assume that $\gamma = n_1/n_0$. Under this generalization, this is a $\gamma : 1$ randomization and there are on average γ individual(s) in arm 1 for each individual in arm 0. Since vaccine efficacies measure proportions of events, we have

$$VE_{10} = 1 - \frac{\omega_{110}/n_1}{\omega_{010}/n_0} = 1 - \frac{\omega_{110}}{\gamma\omega_{010}},$$

and each individual in arm 0 is scaled to represent γ individuals (e.g., in a 2:1 randomization, there are twice as many individuals in the vaccine arm, and each individual in the placebo arm should be multiplied by 2 so the scaled mean for the placebos is twice as large, and the ratio will reduce to the proportions). We use Poisson regression to estimate the parameters of interest. In the generalized linear model in the Poisson family, we model the log of Poisson means as a linear combination of parameters. Let $\mathbf{Y}$ and β be a vector of responses and parameters, with the model of $E(\mathbf{Y})$ given by

$$\log\left\{E\begin{bmatrix}Y_1\\Y_2\\Y_3\\Y_4\\Y_5\\Y_6\\Y_7\\Y_8\end{bmatrix}\right\} = \mathbf{I}_8\begin{bmatrix}\beta_1\\\beta_2\\\beta_3\\\beta_4\\\beta_5\\\beta_6\\\beta_7\\\beta_8\end{bmatrix} + \begin{bmatrix}o_1\\o_2\\o_3\\o_4\\o_5\\o_6\\o_7\\o_8\end{bmatrix}, \tag{1}$$

where $\log(\cdot)$ and $E(\cdot)$ act componentwise (e.g., the log of the vector, is the vector of the log of each component), I_8 is an 8×8 identity matrix, and $o_1, \ldots, o_8$ are known constants called offsets. For our application, the responses, parameters and offsets are:

$$\log\left\{E\begin{bmatrix}X_{110}\\X_{010}\\X_{120}\\X_{020}\\X_{121}\\X_{120}\\U_{21}\\U_{20}\end{bmatrix}\right\} = \mathbf{I}_8\begin{bmatrix}\log(\omega_{110})\\\log(\omega_{010})\\\log(\omega_{120})\\\log(\omega_{020})\\\log(\omega_{121})\\\log(\omega_{021})\\\log(\phi_{21})\\\log(\phi_{20})\end{bmatrix} + \begin{bmatrix}\log(n_1)\\\log(n_0)\\\log(n_1)\\\log(n_0)\\\log(n_1)\\\log(n_0)\\0\\0\end{bmatrix}, \tag{2}$$

where U_{2S} are the counts for strain S from the unvaccinated community sample, and the offsets for the first 6 elements ensure that the parameters present rates not counts. Because all of the rates will be later used in ratios of the two arms, we can set $n_0 = 1$ and $n_1 = \gamma$. We are interested in the exponentiation of several linear combinations of parameters, specifically,

$$\begin{bmatrix}\rho_{10}\\\rho_{20}\\\rho_{11}\\\rho_{21}\\\Delta_0\\\Delta_1\\\sigma_1\\\sigma_2\end{bmatrix} = \exp(\mathbf{C}\beta) = \exp\left(\begin{bmatrix}1&-1&0&0&0&0&0&0\\1&-1&1&-1&0&0&0&0\\1&-1&0&-1&0&1&-1&1\\1&-1&0&-1&1&0&-1&1\\0&0&-1&1&0&0&0&0\\0&0&0&0&-1&1&0&0\\0&0&0&1&0&-1&1&-1\\0&0&1&0&-1&0&1&-1\end{bmatrix}\begin{bmatrix}\log(\omega_{110})\\\log(\omega_{010})\\\log(\omega_{120})\\\log(\omega_{020})\\\log(\omega_{121})\\\log(\omega_{021})\\\log(\phi_{21})\\\log(\phi_{20})\end{bmatrix}\right). \tag{3}$$

Standard Wald-type confidence intervals can be created assuming that the estimates of $\log(\omega_{AKS})$ and $\log(\phi_{IS})$ are asymptotically normal. Let $\hat{\beta}$ b the vector of those estimates, then we assume that approximately,

$$\mathbf{C}\hat{\beta} \dot{\sim} N\left(\mathbf{C}\beta, \mathbf{C}\hat{V}\mathbf{C}^\top\right)$$

```
#
# Computer code to reproduce Table 2
#
```

```
   C<- matrix( c(
     1,-1, 0, 0, 0, 0, 0, 0,
     1,-1, 1,-1, 0, 0, 0, 0,
     1,-1, 0,-1, 0, 1,-1, 1,
     1,-1, 0,-1, 1, 0,-1, 1,
     0, 0,-1, 1, 0, 0, 0, 0,
     0, 0, 0, 0,-1, 1, 0, 0,
     0, 0, 0, 1, 0,-1, 1,-1,
     0, 0, 1, 0,-1, 0, 1,-1),
     byrow=TRUE, nrow=8, ncol=8)

   trans<- function(B){ c(1-exp(B[1:4]), exp(B[5:8]) ) }


simData<-function(parms=c(theta10=1, theta20=1, theta21=1, VE10=.5, VE11=.5, VE20=.5,  VE21=.5,
                  phi20=1e3, phi21=1e3, gamma=1)){
  theta10<- parms["theta10"]
  theta20<- parms["theta20"]
  theta21<- parms["theta21"]
  VE10<- parms["VE10"]
  VE11<- parms["VE11"]
  VE20<-parms["VE20"]
  VE21<-parms["VE21"]
  phi20<-parms["phi20"]
  phi21<-parms["phi21"]
  gamma<- parms["gamma"]
  p20<-theta20/(theta21+theta20)
  p21<-theta21/(theta21+theta20)

  Y<-c(
    X110=rpois(1, theta10*(1-VE10)),
    X010=rpois(1, theta10),
    X120=rpois(1, theta20*(1-VE20)),
    X020=rpois(1, theta20*(1-VE10)),
    X121=rpois(1, theta21*(1-VE21)),
    X021=rpois(1, theta21*(1-VE11)),
    U21=rpois(1, phi21),
    U20=rpois(1, phi20) )

  # MU=true values, so replace N*p21,N*p20 for phi21,phi20
  # where N=phi20+phi21
  # N<- phi20+phi21
  N<-1
  MU<- c(theta10*(1-VE10),
         theta10,
         theta20*(1-VE20),
         theta20*(1-VE10),
         theta21*(1-VE21),
         theta21*(1-VE11),
         N*p21,
         N*p20)
```

```
  n0<- 1
  n1<-gamma
  Rate<-  MU/c(n1,n0,n1,n0,n1,n0,1,1)
  untrans.Parms<- C %*% matrix(log(Rate),8,1)
  Parms<- trans(untrans.Parms)
  names(Parms)<- c("VE10","VE20","VE11","VE21","Delta0","Delta1","Sigma1","Sigma2")
  list(Y=Y, Parms=Parms)
}



glmAnalysis<- function(Y,gamma=1, conf.level=0.95){
   I<- diag(8)
   I1<- I[,1]
   I2<- I[,2]
   I3<- I[,3]
   I4<- I[,4]
   I5<- I[,5]
   I6<- I[,6]
   I7<- I[,7]
   I8<- I[,8]
   OFFSET<- log(c(gamma,1,gamma,1,gamma,1,1,1))

   gout<- glm(Y~ -1 + I1+I2+I3+I4+I5+I6+I7+I8,offset=OFFSET, family="poisson")
   beta<- matrix(coef(gout),8,1)
   V<- vcov(gout)
   parms<- C %*% beta
   Vparms<- C %*% V %*% t(C)
   Za<- qnorm(1-(1-conf.level)/2)
   stdErr<- sqrt(diag(Vparms))
   parms<- as.vector(parms)
   lower<- parms - Za*stdErr
   upper<- parms + Za*stdErr
   # all null parameter values are zero, log(Ratios)=log(1)=0
   p.value<- 2*(1- pnorm(abs(parms/stdErr)))
   out<-matrix(NA,8,5)
   out[,1]<- parms
   out[,2]<- stdErr
   out[,3]<- lower
   out[,4]<- upper
   out[,5]<- p.value
   dimnames(out)<-list(c("logRho10","logRho20","logRho11","logRho21","logDelta0","logDelta1","logSigma1",
        c("Estimate","StdErr","lower CL","upper CL","two-sided p"))
   outVE<- matrix(NA,8,4)
   outVE[,1]<- trans(parms)
   # for VE, lower and upper switch because transformation is 1-exp(parm)
   # for other ratios they do not switch because transformation is exp(parm)
   outVE[,2]<- trans(c(upper[1:4],lower[5:8]) )
   outVE[,3]<- trans(c(lower[1:4],upper[5:8]) )
   outVE[,4]<- p.value
   dimnames(outVE)<-list(c("VE10","VE20","VE11","VE21","Delta0","Delta1","Sigma1","Sigma2"),
```

```
        c("Estimate","lower CL","upper CL","two-sided p"))
   list(out=out, outVE=outVE)
}


# Create parameters for all of the simulation Cases

nPHI<- 1e3
THETA2<- 500
parmNames<-c("theta10", "theta20", "theta21", "VE10", "VE11", "VE20",  "VE21", "phi20", "phi21", "gamma")

PARMS<-matrix(NA,5,length(parmNames),dimnames=list(paste("Case",1:5),parmNames))
PARMS[1,]<-c(1000,0.5*THETA2,0.5*THETA2,.9,.9,.9,.9,0.5*nPHI,0.5*nPHI,1)
PARMS[2,]<-c(1000,0.5*THETA2,0.5*THETA2,.9,.8,.8,.6,0.5*nPHI,0.5*nPHI,1)
PARMS[3,]<-c(1000,0.2*THETA2,0.8*THETA2,.9,.9,.9,.9,0.2*nPHI,0.8*nPHI,1)
PARMS[4,]<-c(1000,0.5*THETA2,0.5*THETA2,.9,.9,.9,.9,0.6*nPHI,0.4*nPHI,1)
PARMS[5,]<-c(1000,0.5*THETA2,0.5*THETA2,.9,.9,.9,.9,0.4*nPHI,0.6*nPHI,1)


dosim<-function(nsim=1e2,parms=Parms,...){
  knames<-as.character(1:nsim)
  DimNames<- c(dimnames(g$outVE),list(knames))
  out<- array(NA,dim=c(8,4,nsim),dimnames=DimNames)
  for (k in 1:nsim){
    Yk<- simData(parms)
    Gk<-glmAnalysis(Yk$Y,...)
    out[,,k]<- Gk$outVE
  }
  output<- list(out=out, parms=Yk$Parms)
  output
}



summarySim<-function(sout,alpha=0.05){
   Table<- matrix(NA,8,7,dimnames=list(dimnames(g$outVE)[[1]],c("true Value","mean","std","coverage","err
   Table[,"true Value"]<- sout$parms
   # create 8 X nsim matrix of estimates
   est<- sout$out[,"Estimate",]
   Table[,"mean"]<- apply(est,1,mean)
   Table[,"std"]<-  apply(est,1,sd)
   # create 8 X nsim matrices of lower and upper confidence limits
   lo<- sout$out[,"lower CL",]
   up<- sout$out[,"upper CL",]
   nsim<- dim(sout$out)[3]
   # create 8 X nsim true parameter matrix
   trueParm<- matrix(rep(sout$parms,nsim),8,nsim)
   # lower CL too high?
   errloMatrix<-  lo > trueParm
   # upper CL too low?
   errhiMatrix<-  up < trueParm
```

```
   # proportion errors lo=lower too high or hi=upper too low
   Table[,"errlo"]<- apply(errloMatrix,1,mean)
   Table[,"errhi"]<- apply(errhiMatrix,1,mean)
   # proportion with no errors = coverage
   Table[,"coverage"]<- 1 - Table[,"errlo"] - Table[,"errhi"]
   # proportion reject = power
   alphaMatrix<- matrix(alpha,8,nsim)
   pvalue<-  sout$out[,"two-sided p",]
   rejectMatrix<-  pvalue <= alphaMatrix
   Table[,"power"]<- apply(rejectMatrix,1,mean)
   Table
}

set.seed(1234)
NSIM<- 1e4



for (k in 1:5){
  set.seed(120*k + k)
  sout<-dosim(nsim=NSIM,parms=PARMS[k,])
  if (k==1){ sumSim<- list(summarySim(sout))
  } else {
    sumSim<- c(sumSim,list(summarySim(sout)) )
  }
}


getTable2<-function(sumSim){
  tab2<-matrix(NA,10,8,dimnames=list(c("Case 1","","Case 2","","Case 3","","Case 4","","Case 5",""),c("VE
  for (k in 1:5){
    mk<- sumSim[[k]]
    tab2[2*k-1,1:4]<- mk[1:4,"mean"]
    tab2[2*k,1:4]<- mk[1:4,"std"]
    tab2[2*k-1,5:8]<- mk[5:8,"power"]
  }
  tab2
}

tab2<-getTable2(sumSim)
library(xtable)
print(xtable(tab2,type="latex",digits=4),file="tab2.tex")
```

1.3 | Example Data Set and SAS code

Here we provide part of a dataset used in the example section. Volunteers can be infected with one of three strains S =st=0,1,2 which has mark $V(s)$ = v =0,1,2. There are 12 months or intervals within which p(k,s) is constant and a single site. Each volunteer generates up to 12 * 3 lines of data for the 12 months times the 3 strains. At the end of the dataset, we provide the

code that is used to estimate the SASA with strain specific time-varying vaccine efficacy

$$h_s(t) = h_{0s}(t)\exp(Z(t)\{\beta_{0s} + \beta_{12}(t - \tau^{(v)})\}),$$

where t is calendar time, $Z(t)$ is 1 following vaccination and 0 otherwise and $\tau^{(v)}$ is the time of vaccination.

1.3.1 | Variable names

```
id       - subject id
arm      - original arm
start    - begin of interval
stop     - end of interval
iev      - event indicator
vac      - 1 if vaccinated before the interval  0 otherwise
timevact - calendar day of vaccination (even if counterfactual to avoid .)
v        - value of the mark, missing if no event
st       - the strain specific dataset
off      - offset term for strain st and this start/stop interval
month    - period of time within which p(k,s) is constant
siteid   - clinical trial site
```

The $p(k, s)$ distribution is given as

```
Stratum 1  2   3    4  5   6   7   8   9   10  11  12
Left T  0  1   2    3  4  5    6   7   8   9   10  11
Strain  sep oct nov dec jan feb mar apr may jun jul aug
       --- --- --- --- --- --- --- --- --- --- --- ---
0 -wt   1.0 1.0 1.0  1.0 0.9 0.7 0.5 0.3 0.2 0.0 0.0 0.0
1-alpha 0.0 0.0 0.0  0.0 0.1 0.3 0.5 0.7 0.6 0.7 0.6 0.5
2-delta 0.0 0.0 0.0  0.0 0.0 0.0 0.0 0.0 0.2 0.3 0.4 0.5
```

1.3.2 | Data Set

ID 1 is a placebo volunteer who enrolls at time 0.0356 and is vaccinated at time 7.000 and is censored at time 12.00. ID 2 is a placebo volunteer who enrolls on 0.4381 and is vaccinated at time 7.000. ID 9 enrolls at time 0.4383 is randomized to vaccine and vaccinated. At time 8.8064 ID 9 becomes a disease case with strain S=1. The offsets were specified as log(p(k,s)) with values < -25 used for p(k,s)=0 to avoid logging zero. By construction, nonzero p(k,s) were always 0.10 or greater.

```
Obs ID ARM START iev STOP vac timevact V ST   off  month siteid
  1  1  0  0.0356 0 1.0000 0  7.00000  . 0  -0.0000 1      1
  2  1  0  0.0356 0 1.0000 0  7.00000  . 1 -26.0216 1      1
  3  1  0  0.0356 0 1.0000 0  7.00000  . 2 -26.0216 1      1
  4  1  0  1.0000 0 2.0000 0  7.00000  . 0  -0.0000 2      1
  5  1  0  1.0000 0 2.0000 0  7.00000  . 1 -26.0216 2      1
  6  1  0  1.0000 0 2.0000 0  7.00000  . 2 -26.0216 2      1
  7  1  0  2.0000 0 3.0000 0  7.00000  . 0  -0.0000 3      1
  8  1  0  2.0000 0 3.0000 0  7.00000  . 1 -26.0216 3      1
  9  1  0  2.0000 0 3.0000 0  7.00000  . 2 -26.0216 3      1
 10  1  0  3.0000 0 4.0000 0  7.00000  . 0  -0.0000 4      1
 11  1  0  3.0000 0 4.0000 0  7.00000  . 1 -26.0216 4      1
 12  1  0  3.0000 0 4.0000 0  7.00000  . 2 -26.0216 4      1
 13  1  0  4.0000 0 5.0000 0  7.00000  . 0  -0.1054 5      1
 14  1  0  4.0000 0 5.0000 0  7.00000  . 1  -2.3026 5      1
 15  1  0  4.0000 0 5.0000 0  7.00000  . 2 -25.3284 5      1
```

```
 16  1  0  5.0000 0 6.0000 0  7.00000  . 0  -0.3567 6      1
 17  1  0  5.0000 0 6.0000 0  7.00000  . 1  -1.2040 6      1
 18  1  0  5.0000 0 6.0000 0  7.00000  . 2 -25.3284 6      1
 19  1  0  6.0000 0 7.0000 0  7.00000  . 0  -0.6931 7      1
 20  1  0  6.0000 0 7.0000 0  7.00000  . 1  -0.6931 7      1
 21  1  0  6.0000 0 7.0000 0  7.00000  . 2 -25.3284 7      1
 22  1  0  7.0000 0 8.0000 1  7.00000  . 0  -1.2040 8      1
 23  1  0  7.0000 0 8.0000 1  7.00000  . 1  -0.3567 8      1
 24  1  0  7.0000 0 8.0000 1  7.00000  . 2 -25.3284 8      1
 25  1  0  8.0000 0 9.0000 1  7.00000  . 0  -1.6094 9      1
 26  1  0  8.0000 0 9.0000 1  7.00000  . 1  -0.5108 9      1
 27  1  0  8.0000 0 9.0000 1  7.00000  . 2  -1.6094 9      1
 28  1  0  9.0000 010.0000 1  7.00000  . 0 -25.3284 10     1
 29  1  0  9.0000 010.0000 1  7.00000  . 1  -0.3567 10     1
 30  1  0  9.0000 010.0000 1  7.00000  . 2  -1.2040 10     1
 31  1  0 10.0000 011.0000 1  7.00000  . 0 -25.3284 11     1
 32  1  0 10.0000 011.0000 1  7.00000  . 1  -0.5108 11     1
 33  1  0 10.0000 011.0000 1  7.00000  . 2  -0.9163 11     1
 34  1  0 11.0000 012.0000 1  7.00000  . 0 -25.3284 12     1
 35  1  0 11.0000 012.0000 1  7.00000  . 1  -0.6931 12     1
 36  1  0 11.0000 012.0000 1  7.00000  . 2  -0.6931 12     1
 37  2  0  0.4381 0 1.0000 0  7.00000  . 0  -0.0000 1      1
 38  2  0  0.4381 0 1.0000 0  7.00000  . 1 -26.0216 1      1
...
289  9  1  0.4383 0 1.0000 1  0.43830  1 0  -0.0000 1      4
290  9  1  0.4383 0 1.0000 1  0.43830  1 1 -26.0216 1      4
291  9  1  0.4383 0 1.0000 1  0.43830  1 2 -26.0216 1      4
292  9  1  1.0000 0 2.0000 1  0.43830  1 0  -0.0000 2      4
293  9  1  1.0000 0 2.0000 1  0.43830  1 1 -26.0216 2      4
294  9  1  1.0000 0 2.0000 1  0.43830  1 2 -26.0216 2      4
295  9  1  2.0000 0 3.0000 1  0.43830  1 0  -0.0000 3      4
296  9  1  2.0000 0 3.0000 1  0.43830  1 1 -26.0216 3      4
297  9  1  2.0000 0 3.0000 1  0.43830  1 2 -26.0216 3      4
298  9  1  3.0000 0 4.0000 1  0.43830  1 0  -0.0000 4      4
299  9  1  3.0000 0 4.0000 1  0.43830  1 1 -26.0216 4      4
300  9  1  3.0000 0 4.0000 1  0.43830  1 2 -26.0216 4      4
301  9  1  4.0000 0 5.0000 1  0.43830  1 0  -0.1054 5      4
302  9  1  4.0000 0 5.0000 1  0.43830  1 1  -2.3026 5      4
303  9  1  4.0000 0 5.0000 1  0.43830  1 2 -25.3284 5      4
304  9  1  5.0000 0 6.0000 1  0.43830  1 0  -0.3567 6      4
305  9  1  5.0000 0 6.0000 1  0.43830  1 1  -1.2040 6      4
306  9  1  5.0000 0 6.0000 1  0.43830  1 2 -25.3284 6      4
307  9  1  6.0000 0 7.0000 1  0.43830  1 0  -0.6931 7      4
308  9  1  6.0000 0 7.0000 1  0.43830  1 1  -0.6931 7      4
309  9  1  6.0000 0 7.0000 1  0.43830  1 2 -25.3284 7      4
310  9  1  7.0000 0 8.0000 1  0.43830  1 0  -1.2040 8      4
311  9  1  7.0000 0 8.0000 1  0.43830  1 1  -0.3567 8      4
312  9  1  7.0000 0 8.0000 1  0.43830  1 2 -25.3284 8      4
313  9  1  8.0000 0 8.8064 1  0.43830  1 0  -1.6094 9      4
314  9  1  8.0000 1 8.8064 1  0.43830  1 1  -0.5108 9      4
315  9  1  8.0000 0 8.8064 1  0.43830  1 2  -1.6094 9      4
```

...

1.3.3 | SAS Code for SASA Model

```
PROC PHREG DATA=lessbig;
     MODEL (start, stop)*iev( 0 )= vac0 vactime0 vac1 vactime1 vac2 vactime2/OFFSET=off;
     STRATA siteid;
     vactime0=vac0*(stop-timevact0);
     vactime1=vac1*(stop-timevact1);
     vactime2=vac2*(stop-timevact2);
     IF vac0=0 THEN vactime0=0;
     IF vac1=0 THEN vactime1=0;
     IF vac2=0 THEN vactime2=0;
RUN;
```

1.4 | Additional Simulations

In this section we report results of simulations with the same structure as the simulations reported in Table 3 except the attack rate is much lower, with a pre-crossover placebo attack rate of about 130 and a post-crossover counterfactual placebo attack of about 100. This scenario is meant to approximate the Novavax trial. Results are qualitatively similar to Table 3 but with larger Monte Carlo standard deviations.

TABLE 2 Monte Carlo estimates and (standard deviations) of vaccine efficacy for 100 simulated deferred vaccination trials. Estimates are provided both for strain specific and mark parameterized vaccine efficacy models. Two scenarios are evaluated with VE_0, VE_1, $VE_2 = (0.90, 0.90, 0.90)$ for the top half and with VE_0, VE_1, $VE_2 = (0.92,0.78,0.39)$ for the bottom half. VE is constant over time. The left half fits models with a time constant VE, while the right half fits models with a log-linear decline in VE. The unstarred rows denote correct specification of $p(k, s)$ while * (**) denote misspecifications.

	Constant VE			Time-Varying VE		
	VE_0	VE_1	VE_2	β_{10}	β_{11}	β_{21}
TRUTH	0.90	0.90	0.90	0.00	0.00	0.00
SSSA	0.897	0.885	-	-0.014	0.001	-0.072
	(0.0364)	(0.0900)		(0.1483)	(0.1029)	(0.5695)
SASA	0.897	0.890	0.877	-0.016	-0.001	0.018
	(0.0356)	(0.0628)	(0.124)	(0.1480)	(0.0916)	(0.2600)
SASA-MARK	0.896	0.896	0.873			
	(0.0349)	(0.0535)	(0.1270)			
SASA*	0.900	0.865	0.849	-0.034	-0.001	0.044
	(0.0347)	(0.0797)	(0.1527)	(0.1495)	(0.0905)	(0.2628)
SASA-MARK*	0.898	0.885	0.844			
	(0.0341)	(0.0596)	(0.1585)			
SASA**	0.900	0.875	0.909	-0.024	-0.010	0.037
	(0.0356)	(0.0580)	(0.0777)	(0.1373)	(0.0958)	(0.2632)
SASA-MARK**	0.895	0.904	0.901			
	(0.0353)	(0.0435)	(0.0821)			
TRUTH	0.92	0.78	0.39	0.00	0.00	0.00
SSSA	0.916	0.754	-	-0.014	-0.003	0.002
	(0.0317)	(0.1489)		(0.1815)	(0.0592)	(0.0496)
SASA	0.916	0.767	0.326	-0.022	-0.001	0.001
	(0.0311)	(0.1132)	(0.3995)	(0.1708)	(0.0567)	(0.0483)
SASA-MARK	0.916	0.769	0.320			
	(0.0284)	(0.0853)	(0.3963)			
SASA*	0.918	0.719	0.191	-0.036	-0.016	0.013
	(0.0351)	(0.1442)	(0.4930)	(0.1756)	(0.0568)	(0.0482)
SASA-MARK*	0.914	0.750	0.217			
	(0.0287)	(0.0951)	(0.4798)			
SASA**	0.921	0.766	0.5565	-0.036	-0.016	0.011
	(0.0306)	(0.0961)	(0.2206)	(0.1542)	(0.0583)	(0.0481)
SASA-MARK**	0.911	0.815	0.590			
	(0.0295)	(0.0671)	(0.2234)			