

## Supplementary Data

### SARS-CoV-2 enzyme-linked immunosorbent assays as proxies for plaque reduction neutralisation tests

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### Supplementary Data 1 – R-Script Ordinal Outcomes Model

```
rm(list=ls())
library(MASS)
cv <- read.csv("PRNT_ELISA paper 06.07.21.csv")
cv$SAMPLE.DAYS.POST.SYMP <- as.numeric(cv$SAMPLE.DAYS.POST.SYMP)
#cv$PRNT80[cv$PRNT80==1290] <- 1280
cv$ll <- cv$PRNT80
cv$ul <- NA
cv$ul[cv$ll>0 & cv$ll < 2560] <- cv$PRNT80[cv$ll>0 & cv$ll < 2560]*2
cv$ul[cv$ll==0] <- 20
cv$ul[cv$ll==2560] <- Inf

mle <- function(formula,return.se=TRUE,cv) {
  D <- model.matrix(formula,cv)
  p <- ncol(D)
  ll <- cv$ll
  ul <- cv$ul
  llik <- function(par) {
    beta <- par[1:p]
    mu <- exp(as.numeric(D%*%beta))
    sigma2 <- exp(par[p+1])
    mean.ln <- log(mu/sqrt(1+sigma2/(mu^2)))
    sd.ln <- sqrt(log(1+sigma2/(mu^2)))
    out <- sum(log(plnorm(ul,meanlog = mean.ln,sdlog = sd.ln)-
      plnorm(ll,meanlog = mean.ln,sdlog = sd.ln)))
  }
}
```

```

start <- c(rep(0,p),1)
estim <- nlm(b, start, function(x) -l(x))
estim$reg.coef <- estim$par[1:p]
estim$sigma2 <- exp(estim$par[p+1])
estim$sigma <- sqrt(exp(estim$par[p+1]))
names(estim$reg.coef) <- colnames(D)
if(return.se) {
  library(numDeriv)
  H <- hessian(l, estim$par)
  S <- solve(-H)
  se <- sqrt(diag(S))
  estim$covariance <- S
  estim$reg.coef.ci <- cbind(
    estim$reg.coef - qnorm(0.975)*se[1:p],
    estim$reg.coef + qnorm(0.975)*se[1:p])
  estim$sigma2.ci <- exp(cbind(estim$par[p+1] - qnorm(0.975)*se[p+1],
    estim$par[p+1] + qnorm(0.975)*se[p+1]))
  estim$sigma.ci <- sqrt(estim$sigma2.ci)
}
return(estim)
}

```

```
str(cv)
```

```
# IgG__S1
```

```
fit_igg_s1_dps <- mle(~ 1 + IgG_S1 + SAMPLE.DAYS.POST.SYMP, cv=cv)
```

```
fit_igg_s1 <- mle(~ 1 + IgG_S1, cv=cv)
```

```
1-pchisq(2*(fit_igg_s1$objective - fit_igg_s1_dps$objective), df=2)
```

```
# IgM__S1
```

```
fit_igm_s1_dps <- mle(~ 1 + IgM_S1 + SAMPLE.DAYS.POST.SYMP, cv=cv)
```

```
fit_igm_s1 <- mle(~ 1 + IgM_S1, cv=cv)
```

```
1-pchisq(2*(fit_igm_s1$objective - fit_igm_s1_dps$objective), df=2)
```

```
# IgG__S2NP
```

```
fit_igg_s2_dps <- mle(~ 1 + IgG_S2NP + SAMPLE.DAYS.POST.SYMP, cv=cv)
```

```
fit_igg_s2 <- mle(~ 1 + IgG_S2NP, cv=cv)
```

```
1-pchisq(2*(fit_igg_s2$objective - fit_igg_s2_dps$objective), df=2)
```

```
# IgM__S2NP
```

```
fit_igm_s2_dps <- mle(~ 1 + IgM_S2NP + SAMPLE.DAYS.POST.SYMP, cv=cv)
```

```
fit_igm_s2 <- mle(~ 1 + IgM_S2NP, cv=cv)
```

```
1-pchisq(2*(fit_igm_s2$objective - fit_igm_s2_dps$objective), df=2)
```

```
which.min(c(fit_igg_s1$objective,
```

```
  fit_igm_s1$objective,
```

```
  fit_igg_s2$objective,
```

```

fit_igm_s2$objective))

lgM.val <- quantile(cv$IgM_S1,c(0.25,0.5,0.975))
lgG.val <- quantile(cv$IgG_S1,c(0.25,0.5,0.975))

Sigma.par.sroot <- t(chol(fit_igm_s1$covariance))
n.sim <- 10000
par.sim.igm <- sapply(1:n.sim, function(i) fit_igm_s1$par+
  Sigma.par.sroot%*%rnorm(length(fit_igm_s1$par)))
par.sim.igg <- sapply(1:n.sim, function(i) fit_igg_s1$par+
  Sigma.par.sroot%*%rnorm(length(fit_igm_s1$par)))

ll.set <- sort(unique(cv$ll))
ul.set <- sort(unique(cv$ul))
compute.probs <- function(beta,sigma2,x) {
  #lgG <- lgG.val[2]
  #beta <- fit2$reg.coef
  #sigma2 <- fit2$sigma2
  p <- length(beta)
  mu <- exp(sum(as.numeric(c(1,x)*beta)))
  mean.ln <- log(mu/sqrt(1+sigma2/(mu^2)))
  sd.ln <- sqrt(log(1+sigma2/(mu^2)))
  probs <- plnorm(ul.set,meanlog = mean.ln,sdlog = sd.ln)-
    plnorm(ll.set,meanlog = mean.ln,sdlog = sd.ln)
  return(probs)
}

n.titre <- length(unique(cv$PRNT80))
probs.samples.igm <- array(NA,dim=c(length(lgM.val),n.titre,n.sim))
for(i in 1:n.sim) {
  for(j in 1:length(lgM.val)) {
    p <- length(fit_igm_s1$par)-1
    beta.i <- par.sim.igm[1:p,i]
    sigma2.i <- exp(par.sim.igm[p+1,i])
    probs.samples.igm[j,,i] <- compute.probs(beta.i,sigma2.i,lgM.val[j])
  }
}

n.titre <- length(unique(cv$PRNT80))
probs.samples.igg <- array(NA,dim=c(length(lgG.val),n.titre,n.sim))
for(i in 1:n.sim) {
  for(j in 1:length(lgG.val)) {
    p <- length(fit_igg_s1$par)-1
    beta.i <- par.sim.igg[1:p,i]
    sigma2.i <- exp(par.sim.igg[p+1,i])
    probs.samples.igg[j,,i] <- compute.probs(beta.i,sigma2.i,lgG.val[j])
  }
}

```

```
}
```

```
prob.hat.igm <- apply(probs.samples.igm,c(1,2),mean)  
prob.q025.igm <- apply(probs.samples.igm,c(1,2),function(x) quantile(x,0.025))  
prob.q975.igm <- apply(probs.samples.igm,c(1,2),function(x) quantile(x,0.975))
```

```
prob.hat.igg <- apply(probs.samples.igg,c(1,2),mean)  
prob.q025.igg <- apply(probs.samples.igg,c(1,2),function(x) quantile(x,0.025))  
prob.q975.igg <- apply(probs.samples.igg,c(1,2),function(x) quantile(x,0.975))
```

```
pdf("First quartile IgM & IgG.pdf",width = 8,height = 8)  
xlab <- c("<1:20",paste("1:",sort(unique(cv$PRNT80)[-1]),sep=""))  
matplot(cbind(prob.hat.igg[1,],prob.q025.igg[1,],prob.q975.igg[1,],  
             prob.hat.igm[1,],prob.q025.igm[1,],prob.q975.igm[1,]),  
        type=c("b","l","l"),pch=20,col=c(1,1,1,2,2,2),  
        lty=c("solid","dashed","dashed","solid","dashed","dashed"),  
        axes=FALSE,ylab = "Probability",xlab="PRNT80",  
        main="1st Quartile IgM & IgG")  
axis(1,1:length(xlab),xlab)  
axis(2,seq(0,1,0.05),seq(0,1,0.05))  
legend(2,0.45,c("IgG S1","IgM S1"),col=c("black","red"),lty=1)  
dev.off()
```

```
pdf("Median IgM & IgG.pdf",width = 8,height = 8)  
xlab <- c("<1:20",paste("1:",sort(unique(cv$PRNT80)[-1]),sep=""))  
matplot(cbind(prob.hat.igg[2,],prob.q025.igg[2,],prob.q975.igg[2,],  
             prob.hat.igm[2,],prob.q025.igm[2,],prob.q975.igm[2,]),  
        type=c("b","l","l"),pch=20,col=c(1,1,1,2,2,2),  
        lty=c("solid","dashed","dashed"),  
        axes=FALSE,ylab = "Probability",xlab="PRNT80",  
        main="Median IgM & IgG")  
axis(1,1:length(xlab),xlab)  
axis(2,seq(0,1,0.05),seq(0,1,0.05))  
legend(2,0.3,c("IgG S1","IgM S1"),col=c("black","red"),lty=1)  
dev.off()
```

```
pdf("Third Quartile IgM & IgG.pdf",width = 8,height = 8)  
xlab <- c("<1:20",paste("1:",sort(unique(cv$PRNT80)[-1]),sep=""))  
matplot(cbind(prob.hat.igg[3,],prob.q025.igg[3,],prob.q975.igg[3,],  
             prob.hat.igm[3,],prob.q025.igm[3,],prob.q975.igm[3,]),  
        type=c("b","l","l"),pch=20,col=c(1,1,1,2,2,2),  
        lty=c("solid","dashed","dashed"),  
        axes=FALSE,ylab = "Probability",xlab="PRNT80",  
        main="3rd Quartile IgM & IgG")  
axis(1,1:length(xlab),xlab)  
axis(2,seq(0,1,0.05),seq(0,1,0.05))
```

```

legend(2,0.5,c("IgG S1", "IgM S1"),col=c("black","red"),lty=1)
dev.off()

lgM.set <- seq(-0.352,2.337,length=1000)
lgG.set <- seq(-0.352,2.337,length=1000)

mean.samples.igm <- matrix(NA,nrow=length(lgM.set),ncol=n.sim)
for(i in 1:n.sim) {
  p <- length(fit_igm_s1$par)-1
  beta.i <- par.sim.igm[1:p,i]
  mean.samples.igm[,i] <- exp(beta.i[1]+beta.i[2]*lgM.set)
}

mean.samples.igg <- matrix(NA,nrow=length(lgG.set),ncol=n.sim)
for(i in 1:n.sim) {
  p <- length(fit_igg_s1$par)-1
  beta.i <- par.sim.igg[1:p,i]
  mean.samples.igg[,i] <- exp(beta.i[1]+beta.i[2]*lgM.set)
}

mean.hat.igm <- apply(mean.samples.igm,1,mean)
mean.q025.igm <- apply(mean.samples.igm,1,function(x) quantile(x,0.025))
mean.q975.igm <- apply(mean.samples.igm,1,function(x) quantile(x,0.975))

mean.hat.igg <- apply(mean.samples.igg,1,mean)
mean.q025.igg <- apply(mean.samples.igg,1,function(x) quantile(x,0.025))
mean.q975.igg <- apply(mean.samples.igg,1,function(x) quantile(x,0.975))

pdf("Predicted_nAB_vs_IgM_IgG.pdf",width = 8,height = 8)
xlab <- c("<1:20",paste("1:",sort(unique(cv$PRNT80)[-1]),sep=""))
matplot(lgM.set,cbind(mean.hat.igg,mean.q025.igg,mean.q975.igg,
  mean.hat.igm,mean.q025.igm,mean.q975.igm),
  type=c("l", "l", "l"),pch=20,col=c(1,1,1,2,2,2),
  lty=c("solid", "dashed", "dashed"),
  ylab = "nAB",xlab="lgM")
legend(0,1500,c("IgG S1", "IgM S1"),col=c("black","red"),lty=1)
dev.off()

round(rbind(cbind(fit_igm_s1$reg.coef,fit_igm_s1$reg.coef.ci),
  sqrt(c(fit_igm_s1$sigma2,fit_igm_s1$sigma2.ci))),3)

```