eAppendix1

Within a specified time period of Δt in a stable population, the number of subjects transferring from H to P is equal to that of those from P to D, that is,

$$\begin{aligned}
&\text{Number of subjects transferring from H to P in } \Delta t \\
&= (\text{Transition rate from H to P}) \times (\text{Total H person-time}) \\
&= I_1 \times (\text{Number of H subjects} \times \Delta t) \\
&= \text{Number of subjects transferring from P to D in } \Delta t \\
&= (\text{Transition rate from P to D}) \times (\text{Total P person-time}) \\
&= I_2 \times (\text{Number of P subjects} \times \Delta t).
\end{aligned}$$

Therefore, we have $\dfrac{\text{Number of H subjects}}{\text{Number of P subjects}} = \dfrac{I_2}{I_1}$.

eAppendix2

```
par(mfrow=c(3,4),cex=0.385)
for(k in c(1,1/2,0)){
for(j in c(1,2,5,10)){
for(z in c(5,1/5)){
for(m in c(1,2,3)){
TT=365*24
FF=365/73
CT=24*73
N=10*TT
Na=2000
Nb=2000
RRhbs=z
RRbss=1
p=j
tDhs=25
tDbss=m
tIChs=1/tDhs
IChbs=(Na+Nb)*tIChs/(Na*RRhbs+Nb)
Dhbs=1/IChbs
IChbsE=RRhbs*IChbs
DhbsE=1/IChbsE
tICbss=1/tDbss
ICbss=(Na+Nb)*tICbss/(Na*RRbss+Nb)
Dbss=1/ICbss
ICbssE=RRbss*ICbss
DbssE=1/ICbssE
HE=vector(mode="numeric",length=N+1)
BsE=vector(mode="numeric",length=N+1)
SE=vector(mode="numeric",length=N+1)
ICES=vector(mode="numeric",length=N)
ICE=vector(mode="numeric",length=N/CT+1)
Tw=vector(mode="numeric",length=N/CT+1)
HE[1]=Na*ICbssE/(IChbsE+ICbssE)
```

```
bse=(IChbsE*k)/(IChbsE+ICbssE)
BsE[1]=Na*bse
#HE[1]=1
#BsE[1]=0
SE[1]=0
for(i in 1:N){
 a1=HE[i]*(1/TT)*IChbsE*p
 HE[i+1]=HE[i]-a1
 b1=BsE[i]*(1/TT)*ICbssE*p
 BsE[i+1]=BsE[i]+a1-b1
 SE[i+1]=SE[i]+b1
 ICES[i]=(b1)/((HE[i]+BsE[i])*(1/TT))
}
Tnct=N/CT
Tnct2=Tnct+1
for(i in 1:Tnct){
 ICE[i]=ICES[(i-1)*CT+1]
}
ICE[Tnct2]=ICES[N]
for(i in 1:Tnct){
 Tw[i]=(i-1)/(FF)
}
Tw[Tnct2]=Tnct/FF
TY=Tw
H=vector(mode="numeric",length=N+1)
Bs=vector(mode="numeric",length=N+1)
S=vector(mode="numeric",length=N+1)
ICS=vector(mode="numeric",length=N)
IC=vector(mode="numeric",length=N/CT+1)
H[1]=Nb*ICbss/(IChbs+ICbss)
Bs[1]=Nb*(IChbs*k)/(IChbs+ICbss)
#H[1]=1
#Bs[1]=0
S[1]=0
for(i in 1:N){
```

```
  a2=H[i]*(1/TT)*IChbs*p
  H[i+1]=H[i]-a2
  b2=Bs[i]*(1/TT)*ICbss*p
  Bs[i+1]=Bs[i]+a2-b2
  S[i+1]=S[i]+b2
  ICS[i]=(b2)/((H[i]+Bs[i])*(1/TT))
}
for(i in 1:Tnct2){
  IC[i]=ICS[(i-1)*CT+1]
}
IC[Tnct2]=ICS[N]
IRR=ICE/IC
Rbias=100*(IRR-RRhbs)/RRhbs
y0=-20
y1=-15
y2=-10
y3=-5
y4=0
y5=5
y6=10
y7=15
y8=20
xx1=0.35
xx2=0.33
l1=0.8
l2=0.6
l3=0.4
m1=1
m2=2
j2=2
j3=5
lgx=1
lgy=14
lgw=2
line1=3
```

```
line2=4
line3=1
w1=1.5
w2=1.5
if(k==1){
if(j==1){
if(m==m1){
if(z==5){
ccol=gray(0.5)
par(mai=c(xx1,xx2,0,0),lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="Relative Bias
 (%)",col=ccol,type="l",lty=line1,axes=F,cex.lab=w1)
lines(c(0,10),c(0,0))
text(lgx,lgy,c("A"),cex=lgw)
axis(side=1,at=c(-1,0,2,4,6,8,10),tick=T,cex.axis=w2)
axis(side=2,at=c(y0,y1,y2,y3,y4,y5,y6,y7,y8),tick=T,cex.axis=w2)
}else{
ccol=1
par(mai=c(xx1,xx2,0,0),new=TRUE,lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
}
}else if(m==m2){
par(mai=c(xx1,xx2,0,0),new=TRUE,lwd=l2)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line2,axes=F,cex.l
 ab=w1)
}else{
par(mai=c(xx1,xx2,0,0),new=TRUE,lwd=l3)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line3,axes=F,cex.l
 ab=w1)
}
}else if(j==j2){
if(m==m1){
if(z==5){
ccol=gray(0.5)
```

```
par(mai=c(xx1,xx2*2/3,0,xx2/3),lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
lines(c(0,10),c(0,0))
text(lgx,lgy,c("D"),cex=lgw)
axis(side=1,at=c(-1,0,2,4,6,8,10),tick=T,cex.axis=w2)
axis(side=2,at=c(y0,y1,y2,y3,y4,y5,y6,y7,y8),tick=T,cex.axis=w2)
}else{
ccol=1
par(mai=c(xx1,xx2*2/3,0,xx2/3),new=TRUE,lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
}
}else if(m==m2){
par(mai=c(xx1,xx2*2/3,0,xx2/3),new=TRUE,lwd=l2)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line2,axes=F,cex.l
 ab=w1)
}else{
par(mai=c(xx1,xx2*2/3,0,xx2/3),new=TRUE,lwd=l3)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line3,axes=F,cex.l
 ab=w1)
}
}else if(j==j3){
if(m==m1){
if(z==5){
ccol=gray(0.5)
par(mai=c(xx1,xx2/3,0,xx2*2/3),lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
lines(c(0,10),c(0,0))
text(lgx,lgy,c("G"),cex=lgw)
axis(side=1,at=c(-1,0,2,4,6,8,10),tick=T,cex.axis=w2)
axis(side=2,at=c(y0,y1,y2,y3,y4,y5,y6,y7,y8),tick=T,cex.axis=w2)
}else{
ccol=1
```

```
par(mai=c(xx1,xx2/3,0,xx2*2/3),new=TRUE,lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
}
}else if(m==m2){
par(mai=c(xx1,xx2/3,0,xx2*2/3),new=TRUE,lwd=l2)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line2,axes=F,cex.l
 ab=w1)
}else{
par(mai=c(xx1,xx2/3,0,xx2*2/3),new=TRUE,lwd=l3)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line3,axes=F,cex.l
 ab=w1)
}
}else{
if(m==m1){
if(z==5){
ccol=gray(0.5)
par(mai=c(xx1,0,0,xx2),lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
lines(c(0,10),c(0,0))
text(lgx,lgy,c("J"),cex=lgw)
axis(side=1,at=c(-1,0,2,4,6,8,10),tick=T,cex.axis=w2)
axis(side=2,at=c(y0,y1,y2,y3,y4,y5,y6,y7,y8),tick=T,cex.axis=w2)
}else{
ccol=1
par(mai=c(xx1,0,0,xx2),new=TRUE,lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
}
}else if(m==m2){
par(mai=c(xx1,0,0,xx2),new=TRUE,lwd=l2)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line2,axes=F,cex.l
 ab=w1)
}else{
```

```
par(mai=c(xx1,0,0,xx2),new=TRUE,lwd=l3)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line3,axes=F,cex.l
 ab=w1)
}
}
}else if(k==0.5){
if(j==1){
if(m==m1){
if(z==5){
ccol=gray(0.5)
par(mai=c(xx1,xx2,0,0),lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="Relative Bias
 (%)",col=ccol,type="l",lty=line1,axes=F,cex.lab=w1)
lines(c(0,10),c(0,0))
text(lgx,lgy,c("B"),cex=lgw)
axis(side=1,at=c(-1,0,2,4,6,8,10),tick=T,cex.axis=w2)
axis(side=2,at=c(y0,y1,y2,y3,y4,y5,y6,y7,y8),tick=T,cex.axis=w2)
}else{
ccol=1
par(mai=c(xx1,xx2,0,0),new=TRUE,lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
}
}else if(m==m2){
par(mai=c(xx1,xx2,0,0),new=TRUE,lwd=l2)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line2,axes=F,cex.l
 ab=w1)
}else{
par(mai=c(xx1,xx2,0,0),new=TRUE,lwd=l3)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line3,axes=F,cex.l
 ab=w1)
}
}else if(j==j2){
if(m==m1){
if(z==5){
```

```
ccol=gray(0.5)
par(mai=c(xx1,xx2*2/3,0,xx2/3),lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
lines(c(0,10),c(0,0))
text(lgx,lgy,c("E"),cex=lgw)
axis(side=1,at=c(-1,0,2,4,6,8,10),tick=T,cex.axis=w2)
axis(side=2,at=c(y0,y1,y2,y3,y4,y5,y6,y7,y8),tick=T,cex.axis=w2)
}else{
ccol=1
par(mai=c(xx1,xx2*2/3,0,xx2/3),new=TRUE,lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
}
}else if(m==m2){
par(mai=c(xx1,xx2*2/3,0,xx2/3),new=TRUE,lwd=l2)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line2,axes=F,cex.l
 ab=w1)
}else{
par(mai=c(xx1,xx2*2/3,0,xx2/3),new=TRUE,lwd=l3)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line3,axes=F,cex.l
 ab=w1)
}
}else if(j==j3){
if(m==m1){
if(z==5){
ccol=gray(0.5)
par(mai=c(xx1,xx2/3,0,xx2*2/3),lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
lines(c(0,10),c(0,0))
text(lgx,lgy,c("H"),cex=lgw)
axis(side=1,at=c(-1,0,2,4,6,8,10),tick=T,cex.axis=w2)
axis(side=2,at=c(y0,y1,y2,y3,y4,y5,y6,y7,y8),tick=T,cex.axis=w2)
}else{
```

```
ccol=1
par(mai=c(xx1,xx2/3,0,xx2*2/3),new=TRUE,lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
}
}else if(m==m2){
par(mai=c(xx1,xx2/3,0,xx2*2/3),new=TRUE,lwd=l2)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line2,axes=F,cex.l
 ab=w1)
}else{
par(mai=c(xx1,xx2/3,0,xx2*2/3),new=TRUE,lwd=l3)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line3,axes=F,cex.l
 ab=w1)
}
}else{
if(m==m1){
if(z==5){
ccol=gray(0.5)
par(mai=c(xx1,0,0,xx2),lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
lines(c(0,10),c(0,0))
text(lgx,lgy,c("K"),cex=lgw)
axis(side=1,at=c(-1,0,2,4,6,8,10),tick=T,cex.axis=w2)
axis(side=2,at=c(y0,y1,y2,y3,y4,y5,y6,y7,y8),tick=T,cex.axis=w2)
}else{
ccol=1
par(mai=c(xx1,0,0,xx2),new=TRUE,lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
}
}else if(m==m2){
par(mai=c(xx1,0,0,xx2),new=TRUE,lwd=l2)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line2,axes=F,cex.l
 ab=w1)
```

```
}else{
par(mai=c(xx1,0,0,xx2),new=TRUE,lwd=l3)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line3,axes=F,cex.l
 ab=w1)
}
}
}else{
if(j==1){
if(m==m1){
if(z==5){
ccol=gray(0.5)
par(mai=c(xx1,xx2,0,0),lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="Follow-up Time (Years)",ylab="Relative Bias
 (%)",col=ccol,type="l",lty=line1,axes=F,cex.lab=w1)
lines(c(0,10),c(0,0))
text(lgx,lgy,c("C"),cex=lgw)
axis(side=1,at=c(-1,0,2,4,6,8,10),tick=T,cex.axis=w2)
axis(side=2,at=c(y0,y1,y2,y3,y4,y5,y6,y7,y8),tick=T,cex.axis=w2)
}else{
ccol=1
par(mai=c(xx1,xx2,0,0),new=TRUE,lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
}
}else if(m==m2){
par(mai=c(xx1,xx2,0,0),new=TRUE,lwd=l2)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line2,axes=F,cex.l
 ab=w1)
}else{
par(mai=c(xx1,xx2,0,0),new=TRUE,lwd=l3)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line3,axes=F,cex.l
 ab=w1)
}
}else if(j==j2){
if(m==m1){
```

```
if(z==5){
ccol=gray(0.5)
par(mai=c(xx1,xx2*2/3,0,xx2/3),lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="Follow-up Time
 (Years)",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.lab=w1)
text(lgx,lgy,c("F"),cex=lgw)
lines(c(0,10),c(0,0))
axis(side=1,at=c(-1,0,2,4,6,8,10),tick=T,cex.axis=w2)
axis(side=2,at=c(y0,y1,y2,y3,y4,y5,y6,y7,y8),tick=T,cex.axis=w2)
}else{
ccol=1
par(mai=c(xx1,xx2*2/3,0,xx2/3),new=TRUE,lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
}
}else if(m==m2){
par(mai=c(xx1,xx2*2/3,0,xx2/3),new=TRUE,lwd=l2)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line2,axes=F,cex.l
 ab=w1)
}else{
par(mai=c(xx1,xx2*2/3,0,xx2/3),new=TRUE,lwd=l3)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line3,axes=F,cex.l
 ab=w1)
}
}else if(j==j3){
if(m==m1){
if(z==5){
ccol=gray(0.5)
par(mai=c(xx1,xx2/3,0,xx2*2/3),lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="Follow-up Time
 (Years)",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.lab=w1)
lines(c(0,10),c(0,0))
text(lgx,lgy,c("I"),cex=lgw)
axis(side=1,at=c(-1,0,2,4,6,8,10),tick=T,cex.axis=w2)
axis(side=2,at=c(y0,y1,y2,y3,y4,y5,y6,y7,y8),tick=T,cex.axis=w2)
```

```
}else{
ccol=1
par(mai=c(xx1,xx2/3,0,xx2*2/3),new=TRUE,lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
}
}else if(m==m2){
par(mai=c(xx1,xx2/3,0,xx2*2/3),new=TRUE,lwd=l2)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line2,axes=F,cex.l
 ab=w1)
}else{
par(mai=c(xx1,xx2/3,0,xx2*2/3),new=TRUE,lwd=l3)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line3,axes=F,cex.l
 ab=w1)
}
}else{
if(m==m1){
if(z==5){
ccol=gray(0.5)
par(mai=c(xx1,0,0,xx2),lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="Follow-up Time
 (Years)",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.lab=w1)
text(lgx,lgy,c("L"),cex=lgw)
lines(c(0,10),c(0,0))
axis(side=1,at=c(-1,0,2,4,6,8,10),tick=T,cex.axis=w2)
axis(side=2,at=c(y0,y1,y2,y3,y4,y5,y6,y7,y8),tick=T,cex.axis=w2)
}else{
ccol=1
par(mai=c(xx1,0,0,xx2),new=TRUE,lwd=l1)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line1,axes=F,cex.l
 ab=w1)
}
}else if(m==m2){
par(mai=c(xx1,0,0,xx2),new=TRUE,lwd=l2)
```

```
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line2,axes=F,cex.l
 ab=w1)
}else{
par(mai=c(xx1,0,0,xx2),new=TRUE,lwd=l3)
plot(TY,Rbias,xlim=c(0,N/(FF*CT)),ylim=c(y1,y7),xlab="",ylab="",col=ccol,type="l",lty=line3,axes=F,cex.l
 ab=w1)
}
}
}
}
}
}
}
```

eAppendix3

For the exposed, the observed disease incidence at $t=0$ is

$$I_{\text{obs}}^{\text{E}}(0)=\frac{\text{P}^{\text{E}}(0)\times I_2^{\text{E}}}{\text{H}^{\text{E}}(0)+\text{P}^{\text{E}}(0)}=\frac{N^{\text{E}}\times\frac{I_1^{\text{E}}}{I_1^{\text{E}}+I_2^{\text{E}}}\times I_2^{\text{E}}}{N^{\text{E}}\times\frac{I_2^{\text{E}}}{I_1^{\text{E}}+I_2^{\text{E}}}+N^{\text{E}}\times\frac{I_1^{\text{E}}}{I_1^{\text{E}}+I_2^{\text{E}}}}=\frac{I_1^{\text{E}}\times I_2^{\text{E}}}{I_1^{\text{E}}+I_2^{\text{E}}}.$$

For the unexposed, the value is $I_{\text{obs}}^{\bar{\text{E}}}(0)=\frac{I_1^{\bar{\text{E}}}\times I_2^{\bar{\text{E}}}}{I_1^{\bar{\text{E}}}+I_2^{\bar{\text{E}}}}$. Therefore,

$$\begin{aligned}\text{RR}_{\text{obs}}(0)&=\frac{I_{\text{obs}}^{\text{E}}(0)}{I_{\text{obs}}^{\bar{\text{E}}}(0)}\\&=\frac{I_1^{\text{E}}}{I_1^{\bar{\text{E}}}}\times\frac{I_2^{\text{E}}}{I_2^{\bar{\text{E}}}}\times\left(\frac{I_1^{\bar{\text{E}}}+I_2^{\bar{\text{E}}}}{I_1^{\text{E}}+I_2^{\text{E}}}\right)\\&=w\times\frac{I_1^{\text{E}}}{I_1^{\bar{\text{E}}}}+(1-w)\times\frac{I_2^{\text{E}}}{I_2^{\bar{\text{E}}}}\\&=w\times\text{RR}_{\text{true}}+(1-w)\times\frac{I_2^{\text{E}}}{I_2^{\bar{\text{E}}}},\end{aligned}$$

where $w=\frac{I_2^{\text{E}}}{I_1^{\text{E}}+I_2^{\text{E}}}$. This implies that the observed incidence rate ratio at $t=0$ is a weighted average of RR_{true} and $\frac{I_2^{\text{E}}}{I_2^{\bar{\text{E}}}}$. In general, exposure status would not affect the diagnosis of disease ($\frac{I_2^{\text{E}}}{I_2^{\bar{\text{E}}}}=1$). Therefore, RR_{obs} at $t=0$ is between RR_{true} and 1, namely, the initial selection bias is toward the null.

eAppendix4

Accumulated from time 0 to t, the total person-time is $\int_0^t \left[\mathrm{H}^{\mathrm{E}}(x) + \mathrm{P}^{\mathrm{E}}(x) \right] dx$ for E, and $\int_0^t \left[\mathrm{H}^{\bar{\mathrm{E}}}(x) + \mathrm{P}^{\bar{\mathrm{E}}}(x) \right] dx$ for $\bar{\mathrm{E}}$, respectively, and the total observed new events, $\int_0^t \mathrm{P}^{\mathrm{E}}(x) I_2 dx$ for E, and $\int_0^t \mathrm{P}^{\bar{\mathrm{E}}}(x) I_2 dx$ for $\bar{\mathrm{E}}$, respectively. The average incidence rates between time 0 and t are $\overline{I_{\mathrm{obs}}^{\mathrm{E}}(t)} = \dfrac{\int_0^t \mathrm{P}^{\mathrm{E}}(x) I_2 dx}{\int_0^t \left[\mathrm{H}^{\mathrm{E}}(x) + \mathrm{P}^{\mathrm{E}}(x) \right] dx}$ for E, and $\overline{I_{\mathrm{obs}}^{\bar{\mathrm{E}}}(t)} = \dfrac{\int_0^t \mathrm{P}^{\bar{\mathrm{E}}}(x) I_2 dx}{\int_0^t \left[\mathrm{H}^{\bar{\mathrm{E}}}(x) + \mathrm{P}^{\bar{\mathrm{E}}}(x) \right] dx}$ for $\bar{\mathrm{E}}$, respectively. The ratio of the average incidence rates between time 0 and t is therefore:

$$
\begin{aligned}
\overline{\mathrm{RR}_{\mathrm{obs}}(t)} &= \frac{\overline{I_{\mathrm{obs}}^{\mathrm{E}}(t)}}{\overline{I_{\mathrm{obs}}^{\bar{\mathrm{E}}}(t)}} \\
&= \frac{\int_0^t \mathrm{P}^{\mathrm{E}}(x) I_2 dx}{\int_0^t \left[\mathrm{H}^{\mathrm{E}}(x) + \mathrm{P}^{\mathrm{E}}(x) \right] dx} \Bigg/ \frac{\int_0^t \mathrm{P}^{\bar{\mathrm{E}}}(x) I_2 dx}{\int_0^t \left[\mathrm{H}^{\bar{\mathrm{E}}}(x) + \mathrm{P}^{\bar{\mathrm{E}}}(x) \right] dx} \\
&= \int_0^t \left(\begin{array}{l} \dfrac{\mathrm{P}^{\bar{\mathrm{E}}}(x) I_2}{\int_0^t \mathrm{P}^{\bar{\mathrm{E}}}(y) I_2 dy} \\ \quad \times \dfrac{\mathrm{H}^{\mathrm{E}}(x) + \mathrm{P}^{\mathrm{E}}(x)}{\int_0^t \left[\mathrm{H}^{\mathrm{E}}(y) + \mathrm{P}^{\mathrm{E}}(y) \right] dy} \Bigg/ \dfrac{\mathrm{H}^{\bar{\mathrm{E}}}(x) + \mathrm{P}^{\bar{\mathrm{E}}}(x)}{\int_0^t \left[\mathrm{H}^{\bar{\mathrm{E}}}(y) + \mathrm{P}^{\bar{\mathrm{E}}}(y) \right] dy} \\ \quad \times \dfrac{\mathrm{P}^{\mathrm{E}}(x) I_2}{\mathrm{H}^{\mathrm{E}}(x) + \mathrm{P}^{\mathrm{E}}(x)} \Bigg/ \dfrac{\mathrm{P}^{\bar{\mathrm{E}}}(x) I_2}{\mathrm{H}^{\bar{\mathrm{E}}}(x) + \mathrm{P}^{\bar{\mathrm{E}}}(x)} \end{array} \right) dx \\
&= \int_0^t \omega(x) \kappa(x) \mathrm{RR}_{\mathrm{obs}}(x) dx \\
&\approx \int_0^t \omega(x) \mathrm{RR}_{\mathrm{obs}}(x) dx,
\end{aligned}
$$

where $\omega(x) = \dfrac{\mathrm{P}^{\bar{\mathrm{E}}}(x) I_2}{\int_0^t \mathrm{P}^{\bar{\mathrm{E}}}(y) I_2 dy} \geq 0$ and $\int_0^t \omega(x) dx = 1$, and

$\kappa(x) = \dfrac{\mathrm{H}^{\mathrm{E}}(x) + \mathrm{P}^{\mathrm{E}}(x)}{\int_0^t \left[\mathrm{H}^{\mathrm{E}}(y) + \mathrm{P}^{\mathrm{E}}(y)\right] dy} \Bigg/ \dfrac{\mathrm{H}^{\bar{\mathrm{E}}}(x) + \mathrm{P}^{\bar{\mathrm{E}}}(x)}{\int_0^t \left[\mathrm{H}^{\bar{\mathrm{E}}}(y) + \mathrm{P}^{\bar{\mathrm{E}}}(y)\right] dy} \approx 1$ if $\mathrm{RR}_{\mathrm{true}} \approx 1$. Because

$\overline{\mathrm{RR}_{\mathrm{obs}}(t)}$ is approximately a time-weighted average of $\mathrm{RR}_{\mathrm{obs}}(t)$ between 0 and t,

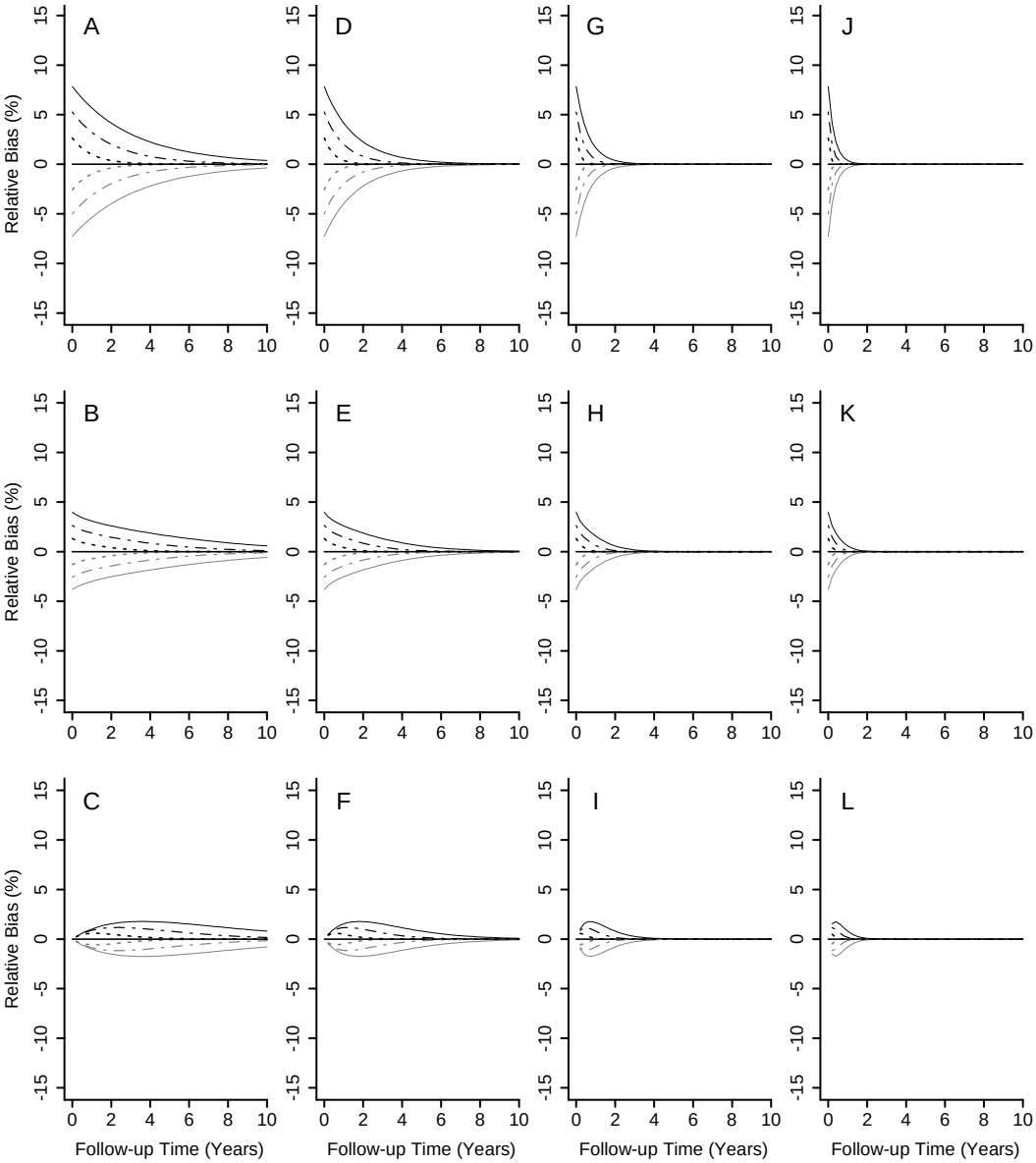
the time course of the bias can be even more protracted if for $t' < t$,

$\mathrm{RR}_{\mathrm{obs}}(t') > \mathrm{RR}_{\mathrm{obs}}(t) > \mathrm{RR}_{\mathrm{true}}$ or $\mathrm{RR}_{\mathrm{obs}}(t') < \mathrm{RR}_{\mathrm{obs}}(t) < \mathrm{RR}_{\mathrm{true}}$.

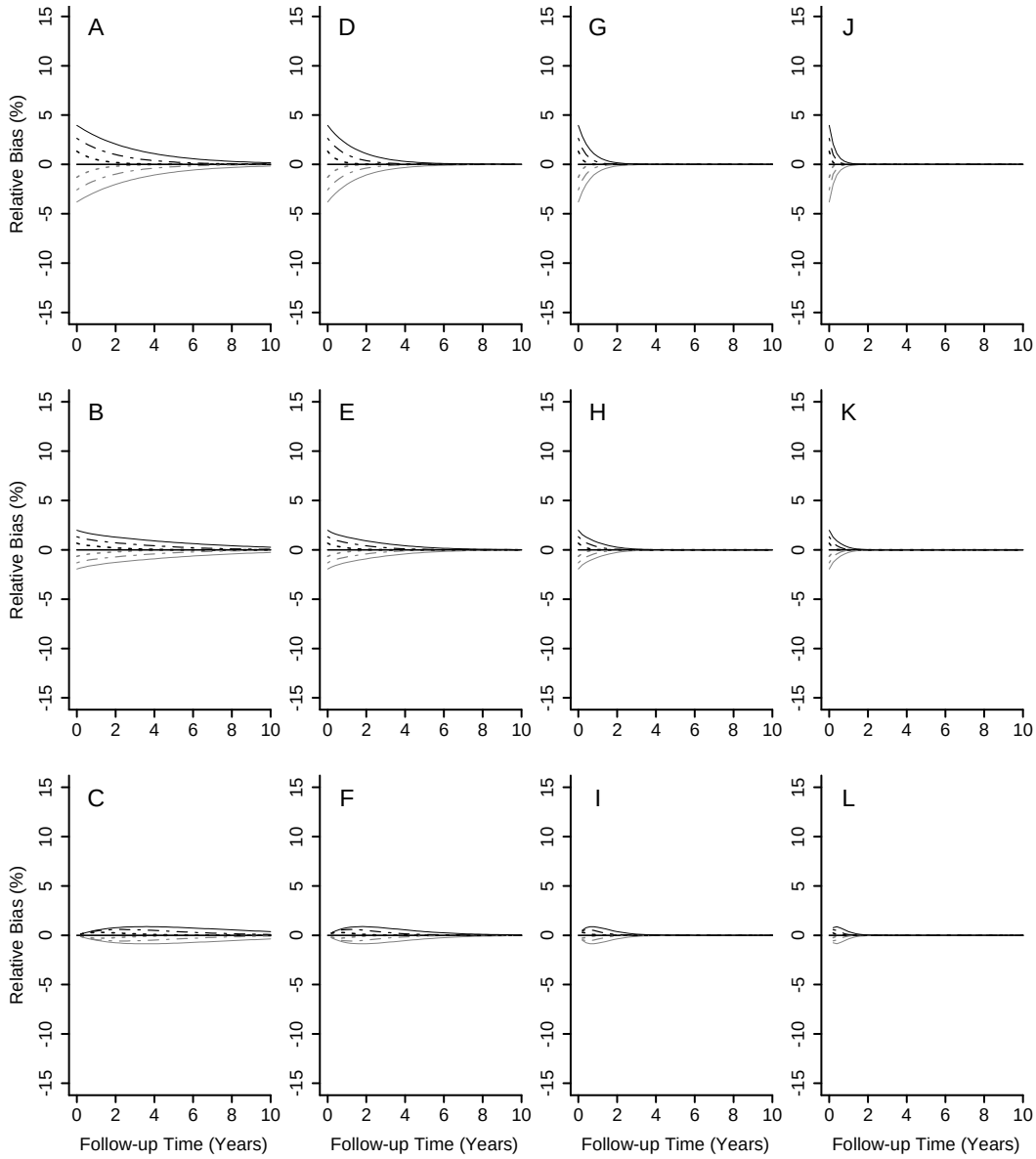
eFigures

eFigure 1. Selection bias when $\overline{I_1} = 1/50$ (black lines: $RR_{true} = 5$; grey lines: $RR_{true} = 1/5$; solid lines: $I_2 = 1/3$; dash lines: $I_2 = 1/2$; dotted lines: $I_2 = 1$; A: $k = 0, r = 1$; B: $k = 0.5, r = 1$; C: $k = 1, r = 1$; D: $k = 0, r = 2$; E: $k = 0.5, r = 2$; F: $k = 1, r = 2$; G: $k = 0, r = 5$; H: $k = 0.5, r = 5$; I: $k = 1, r = 5$; J: $k = 0, r = 10$; K: $k = 0.5, r = 10$; L: $k = 1, r = 10$).

eFigure 2. Selection bias when $\overline{I_1} = 1/100$ (black lines: $RR_{true} = 5$; grey lines: $RR_{true} = 1/5$; solid lines: $I_2 = 1/3$; dash lines: $I_2 = 1/2$; dotted lines: $I_2 = 1$; A: $k = 0, r = 1$; B: $k = 0.5, r = 1$; C: $k = 1, r = 1$; D: $k = 0, r = 2$; E: $k = 0.5, r = 2$; F: $k = 1, r = 2$; G: $k = 0, r = 5$; H: $k = 0.5, r = 5$; I: $k = 1, r = 5$; J: $k = 0, r = 10$; K: $k = 0.5, r = 10$; L: $k = 1, r = 10$).


A
B
C
D
E
F
G
H
I
J
K
L
Relative Bias (%)
Follow-up Time (Years)
-15
-10
-5
0
5
10
15
0
2
4
6
8
10

eFigure 1.


A
D
G
J
B
E
H
K
C
F
I
L
Relative Bias (%)
Follow-up Time (Years)
-15
-10
-5
0
5
10
15
0
2
4
6
8
10

eFigure 2.