

eAppendix for:

Sibling comparison designs: Bias from non-shared confounders and measurement error

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This supplement includes:

eAppendix 1 R code for simulations.

eAppendix 2 Parameter values used to generate the Table.

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eAppendix 1 R code for simulations.

Simulations were done in R 2.13.0 (64-bit)

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# Required libraries
library(mvtnorm)

# n of pairs in simulations
n <- 1000000

# Parameters:

corC <- 0.455 # Tetrachoric correlation in C
corX <- .942 # Correlation for "residuals" in X

b0 <- -4.75 # intercept for Y
byx <- 2    # effect of X on Y
byc <- 3    # effect of C on Y

bxc <- -0.93 # effect of C on X

sens <- 0.8 # Sensitivity
spec <- 1.0 # Specificity

# We generate C, X from the bivariate normal distribution
# and then dichotomize them

c <- rmvnorm(n=n, mean=c(0,0), sigma=matrix(c(1, corC, corC, 1), nrow=2))
cb <- matrix(0, nrow=n, ncol=2)
cb[c>0] <- 1 # Prevalence of C = 0.5

x <- bxc*cb+rmvnorm(n=n, mean=c(0,0), sigma=matrix(c(1, corX, corX, 1), nrow=2))
xb <- matrix(0, nrow=n, ncol=2)
xb[x>qnorm(0.80, mean=mean(x), sd=sd(x)[1])] <- 1 # Prevalence of X = 0.2

# Probability for Y follow a logit model
p <- exp(b0+byx*xb+byc*cb)/(1+exp(b0+byx*xb+byc*cb))
# Generate Y from Bernoulli distribution
yb <- apply(p, c(1,2),rbinom, n=1, size=1)

ally <- c(yb)
allx <- c(xb)
allc <- c(cb)

# The average X in each pair
mx <- (xb[,1]+xb[,2])/2
mx <- c(mx, mx)
mx <- factor(mx)

glm(ally~allx, family='binomial') # The crude estimate
glm(ally~allx+mx, family='binomial') # The within pair estimate

# The observed X may be subject to random misclassification

random <- runif(n=length(xb), 0, 1)

ox <- xb
```

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ox[xb==1][random[xb==1]>spec] <-0
ox[xb==0][random[xb==0]>sens] <-1

allox <- c(ox)
mox <- (ox[,1]+ox[,2])/2
mox <- c(mox, mox)
mox <- factor(mox)

glm(ally~allox, family='binomial')$coef # Attenuated crude effect
glm(ally~allox+mox, family='binomial')$coef # Attenuated within pair estimate
```

eAppendix 2 Parameter values used to generate the Table

Confounding		bxc	CorC	CorX	b0	byx	byc
Cor(X1, X2)	Cor(C1, C2)						
0.6	1	0,625	1	0,82	-5,12	1,763	3
0.6	0.6	0,625	0,81	0,858	-5,12	1,763	3
0.6	0.3	0,625	0,455	0,89	-5,12	1,763	3
0.6	0	0,625	0	0,925	-5,12	1,763	3
0.3	1	0,625	1	0,46	-5,12	1,763	3
0.3	0.6	0,625	0,81	0,5	-5,12	1,763	3
0.3	0.3	0,625	0,455	0,525	-5,12	1,763	3
0.3	0	0,625	0	0,56	-5,12	1,763	3
Inverse confounding							
Cor(X1, X2)	Cor(C1, C2)						
0.6	1	-0,93	1	0,8	-4,75	2	3
0.6	0.6	-0,93	0,81	0,875	-4,75	2	3
0.6	0.3	-0,93	0,455	0,942	-4,75	2	3
0.6	0	-0,93	0	0,995	-4,75	2	3
0.3	1	-0,93	1	0,4	-4,75	2	3
0.3	0.6	-0,93	0,81	0,48	-4,75	2	3
0.3	0.3	-0,93	0,455	0,55	-4,75	2	3
0.3	0	-0,93	0	0,62	-4,75	2	3
Measurement error in exposure		0	0.5	0.51	-9.9	1.97	8