

Proximal/Distal Analysis

Gustafson et. al.

```
### global reproducibility of this output
set.seed(12345)

plot.custom <- F ### leave as False for regular pdf report
if (plot.custom) {
  setwd("C:/Users/Paul Gustafson/ownCloud/RES_Dilution")
  source("C:/Users/Paul Gustafson/ownCloud/OPUS2/Rcode/AuxFunctions.R")
}
```

Set hyperparameters

```
rng.CFR <- c(0.02, 0.30)

rng.Sn.LC.Carman <- c(0.22, 0.26)

rng.Sn.LC.Potter <- c(0.19, 0.3)

rng.Sn.ILI.Potter <- rng.Sn.ILI.Lemaitre <- c(0.54, 0.78)

rng.Sn.ILI.Hayward <- rng.Sn.ILI.Potter + 0.2

rng.Sp.LC <- c(1,1)

rng.Sp.ILI.Potter <- rng.Sp.ILI.Lemaitre <- c(0.50, 0.71)

rng.Sp.ILI.Hayward <- c(.3,.71)

rho.ILI <- (-0.95)

rng.a <- c(.07,.3)

rng.k.Carman <- c(1.1, 1.4*1.5)
rng.k.Potter <- c(1.1, 1.6*1.5)
rng.k.Hayward <- c(1.1, 1.2*1.5)
rng.k.Lemaitre <- c(1.1, 1.3*1.5)

### if the study period were 1 year
rng.b.YR <- c(0.11,.17)

rng.b.Carman <- round((4.5/12)*rng.b.YR, 3)
rng.b.Potter <- round((5/12)*rng.b.YR, 3)
rng.b.Hayward <- rng.b.Lemaitre <- round((2.5/12)*rng.b.YR,3)
```

Confirm settings in table format

##	Parameter	Instance	Lower	Upper
----	-----------	----------	-------	-------

## 1	Case Fatality Rate		0.020	0.300
## 2	Sensitivity	(Lab-confirmed, Carman)	0.220	0.260
## 3		(Lab-confirmed, Potter)	0.190	0.300
## 4		(ILI Potter, Lemaitre)	0.540	0.780
## 5		(ILI Hayward)	0.740	0.980
## 6	Specificity	(Lab-confirmed)	1.000	1.000
## 7		(ILI Potter, Lemaitre)	0.500	0.710
## 8		(ILI Hayward)	0.300	0.710
## 9	a		0.070	0.300
## 10	k	(Carman)	1.100	2.100
## 11		(Potter)	1.100	2.400
## 12		(Lemaitre)	1.100	1.950
## 13		(Hayward)	1.100	1.800
## 14	b	(Carman)	0.041	0.064
## 15		(Potter)	0.046	0.071
## 16		(Lemaitre)	0.023	0.035
## 17		(Hayward)	0.023	0.035

Specify study characteristics

```

specs.carman <- list(
  n.sites=20,
  n.persite=72,
  n.fstr=27,
  y.cn=c(154,688),
  y.tr=c(102,749),
  fstr.cn=c(18,269),
  fstr.tr=c(14,258))

specs.potter.lc <- list(
  n.sites=12,
  n.persite=90,
  n.fstr=20,
  y.cn=c(98,569),
  y.tr=c(50,490),
  fstr.cn=c(6,107),
  fstr.tr=c(5,118))

specs.potter.ili <- specs.potter.lc
specs.potter.ili$n.fstr=90
specs.potter.ili$fstr.cn=c(42,569)
specs.potter.ili$fstr.tr=c(22,490)

specs.lemaitre <- list(
  n.sites=40,
  n.persite=85,
  n.fstr=85,
  y.cn=c(100,1678),
  y.tr=c(89,1722),
  fstr.cn=c(163,1678),
  fstr.tr=c(116,1722))

```

```
specs.hayward <- list(
  n.sites=44,
  n.persite=59,
  n.fstr=59,
  y.cn=c(203,1371),
  y.tr=c(140,1233),
  fstr.cn=c(300,1371),
  fstr.tr=c(142,1233))
```

Confirm characteristics in table format

```
## [1] "control columns to left, treatment columns to right"

##           Study # fac. # res. # infl. # deaths # res. # infl. # deaths
## 1      Carman    20   688      154    749      102
## 2                269      18    258      14
## 3 Potter (ILI)   12   569      98    490      22    50
## 4      (LTI)     107      6    118      5
## 5   Lemaitre    40  1678     163   100   1722     116    89
## 6    Hayward   44  1371     300   203   1233     142   140
```

Function to generate the Step 1 plot

Input is an ensemble of CFR values

```
FirstPlot <- function(cfr, dat.obs, xyl=c(-.05,.15)) {

  dy.hat <- dat.obs$y.cn[1]/dat.obs$y.cn[2] -
    dat.obs$y.tr[1]/dat.obs$y.tr[2]

  dfstr.hat <- dat.obs$fstr.cn[1]/dat.obs$fstr.cn[2] -
    dat.obs$fstr.tr[1]/dat.obs$fstr.tr[2]

  plot(-2,-2, xlim=xyl, ylim=xyl,
        xlab=expression(Delta(F)),
        ylab=expression(Delta(Y)),
        main="(1)")
  polygon(c(0,1,1), c(0,0,1), col=gray(0.75),border=NA)
  abline(v=0); abline(h=0)
  points(dfstr.hat,dy.hat, pch=22)

  for (slp in quantile(cfr, (1:15)/16)) {
    abline(c(0, slp))
  }
}
```

Function to generate the Step 2 plot

Additional inputs are ensembles of sensitivity and specificity values

```
SecondPlot <- function(cfr, sn, sp, dat.obs, xyl=c(-.05,.15)) {
  dy.hat <- dat.obs$y.cn[1]/dat.obs$y.cn[2] -
```

```

        dat.obs$y.tr[1]/dat.obs$y.tr[2]
dfstr.hat <- dat.obs$fstr.cn[1]/dat.obs$fstr.cn[2] -
        dat.obs$fstr.tr[1]/dat.obs$fstr.tr[2]
plot(-2,-2, xlim=xyl, ylim=xyl,
     xlab=expression(Delta(F["*"])),
     ylab=expression(Delta(Y)),
     main="(2)")
polygon(c(0,1,1),c(0,0,1), col=gray(.75),border=NA)
abline(v=0); abline(h=0)
points(dfstr.hat,dy.hat, pch=22)

for (slp in quantile(cfr/(sn+sp-1), (1:15)/16)) {
  abline(c(0, slp))
}
}

```

Function to generate the Step 3 plot

Additional inputs are ensembles of a and k values (giving rise to Δ_F values).

```

ThirdPlot <- function(cfr, sn, sp, deltf,
                     dat.obs, xyl=c(-.05,.15)) {

  dy.hat <- dat.obs$y.cn[1]/dat.obs$y.cn[2] -
    dat.obs$y.tr[1]/dat.obs$y.tr[2]
  dfstr.hat <- dat.obs$fstr.cn[1]/dat.obs$fstr.cn[2] -
    dat.obs$fstr.tr[1]/dat.obs$fstr.tr[2]
  plot(-2,-2, xlim=xyl, ylim=xyl,
       xlab=expression(Delta(F["*"])),
       ylab=expression(Delta(Y)),
       main="(3)")
  polygon(c(0,1,1),c(0,0,1), col=gray(.75),border=NA)
  abline(v=0)
  abline(h=0)
  points(dfstr.hat,dy.hat, pch=22)

  for (i in 1:length(cfr)) {
    points((sn[i]+sp[i]-1)*deltf[i], cfr[i]*deltf[i], cex=.25, pch=20)
  }
}

```

Function to generate the Step 4 plot

Additional input is an ensemble of b values

```

FourthPlot <- function(cfr, sn, sp, a, k, b, specs,
                      xyl=c(-0.05,.15)) {

  dy.hat <- specs$y.cn[1]/specs$y.cn[2] -
    specs$y.tr[1]/specs$y.tr[2]
  dfstr.hat <- specs$fstr.cn[1]/specs$fstr.cn[2] -
    specs$fstr.tr[1]/specs$fstr.tr[2]

```

```

plot(-2,-2, xlim=xyl, ylim=xyl,
     xlab=expression(paste("Est. ", Delta(F["*"]))),
     ylab=expression(paste("Est. ", Delta(Y))),
     main="(4)")
polygon(c(0,1,1),c(0,0,1), col=gray(.75),border=NA)
abline(v=0); abline(h=0)
points(dfstr.hat,dy.hat, pch=22)

for (i in 1:length(cfr)) {

  smry.fstr <- smry.f <- smry.y <- rep(0,4)

  ### control facilities
  for (j in 1:(specs$n.sites/2)) {
    f <- rbinom(specs$n.persite, size=1, prob=rbeta(1, 1, 1/a[i]-1))
    fstr <- rbinom(specs$n.persite, size=1, prob=(1-f)*(1-sp[i])+f*sn[i])
    y <- rbinom(specs$n.persite, size=1, prob=runif(1, 0, b[i])+f*cfr[i])
    smry.f <- smry.f + c(0,0,specs$n.fstr,sum(f[1:specs$n.fstr]))
    smry.fstr <- smry.fstr + c(0,0,specs$n.fstr,sum(fstr[1:specs$n.fstr]))
    smry.y <- smry.y + c(0,0,specs$n.persite,sum(y))
  }

  ### case facilities
  for (j in 1:(specs$n.sites/2)) {
    f <- rbinom(specs$n.persite, size=1, prob=rbeta(1, 1, k[i]/a[i]-1))
    fstr <- rbinom(specs$n.persite, size=1, prob=(1-f)*(1-sp[i])+f*sn[i])
    y <- rbinom(specs$n.persite, size=1, prob=runif(1, 0, b[i])+f*cfr[i])
    smry.f <- smry.f + c(specs$n.fstr,sum(f[1:specs$n.fstr]),0,0)
    smry.fstr <- smry.fstr + c(specs$n.fstr,sum(fstr[1:specs$n.fstr]),0,0)
    smry.y <- smry.y + c(specs$n.persite,sum(y),0,0)
  }

  points(smry.fstr[4]/smry.fstr[3] - smry.fstr[2]/smry.fstr[1],
        smry.y[4]/smry.y[3] - smry.y[2]/smry.y[1],cex=.25, pch=20)
}
}

```

Carry out the Carman assessment

```

### number of Monte Carlo draws
n.rep <- 1500

### axis range for these plots
xyl <- c(-0.1,0.14)

### risk difference in mortality (flu minus no-flu)
cfr <- rtri(n.rep, rng.CFR[1], rng.CFR[2])

### now can do first plot

### sens/spec for flu surrogate

```

```

sn <- rtri(n.rep, rng.Sn.LC.Carman[1], rng.Sn.LC.Carman[2])
sp <- rtri(n.rep, rng.Sp.LC[1], rng.Sp.LC[2])

### now can do second plot

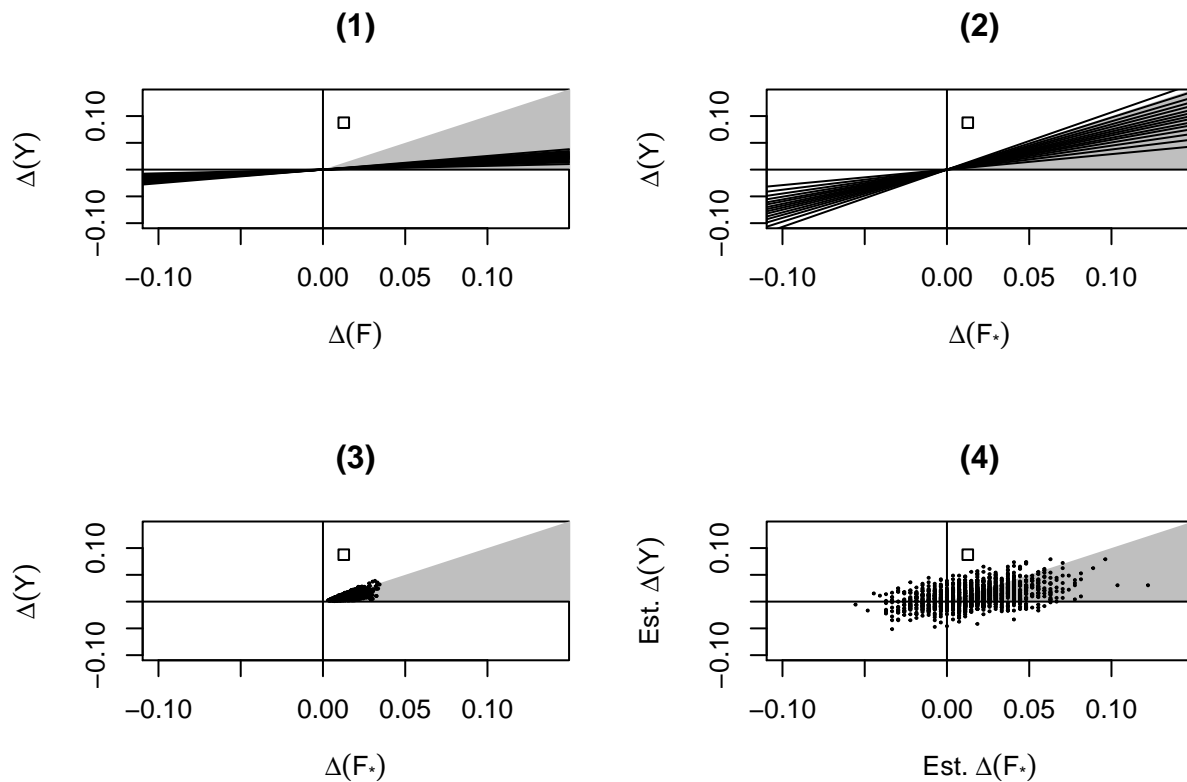
### a and k values
a <- rtri(n.rep, rng.a[1],rng.a[2])
k <- rtri(n.rep, rng.k.Carman[1],rng.k.Carman[2])

### now can do third plot

### b values
b <- rtri(n.rep, rng.b.Carman[1], rng.b.Carman[2])

### now can do fourth plot

```



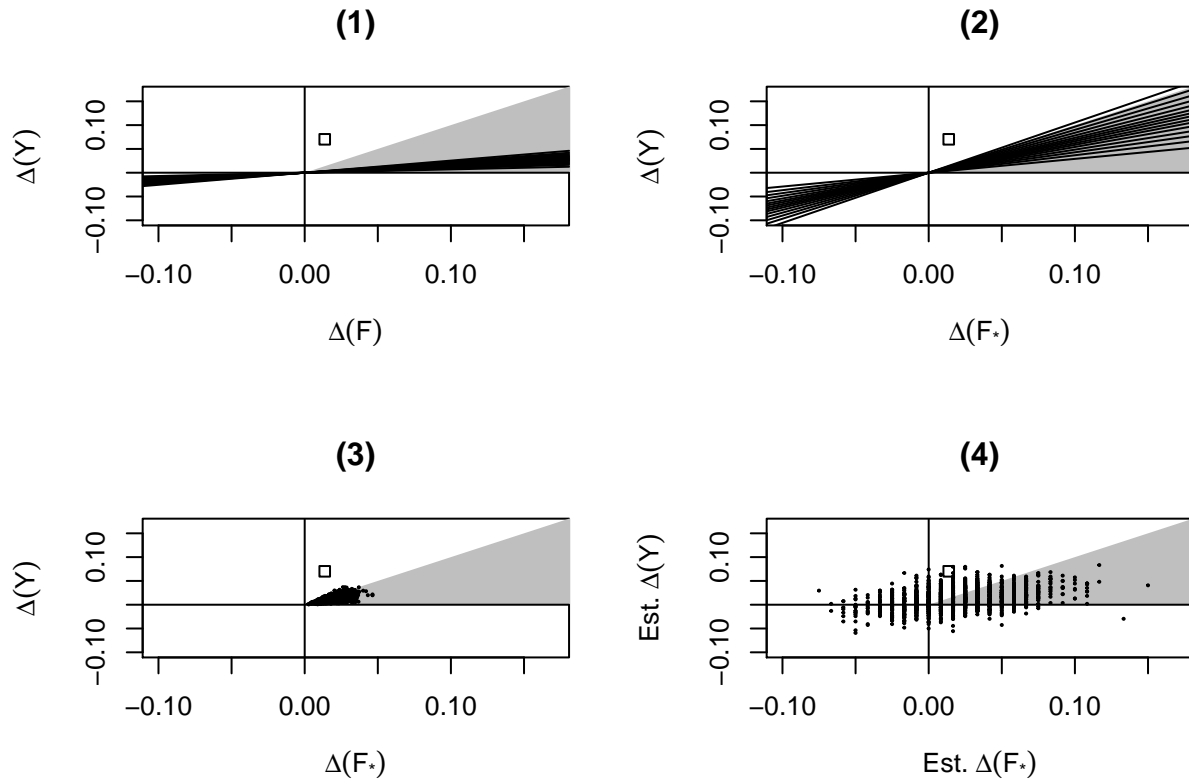
Potter, lab-confirmed influenza

Same sequence of four plots as previously, but with the following settings changed.

```

sn <- rtri(n.rep, rng.Sn.LC.Potter[1], rng.Sn.LC.Potter[2])
k <- rtri(n.rep, rng.k.Potter[1], rng.k.Potter[2])
b <- rtri(n.rep, rng.b.Potter[1], rng.b.Potter[2])
xyl <- c(-0.10,0.17) ### plotting range

```

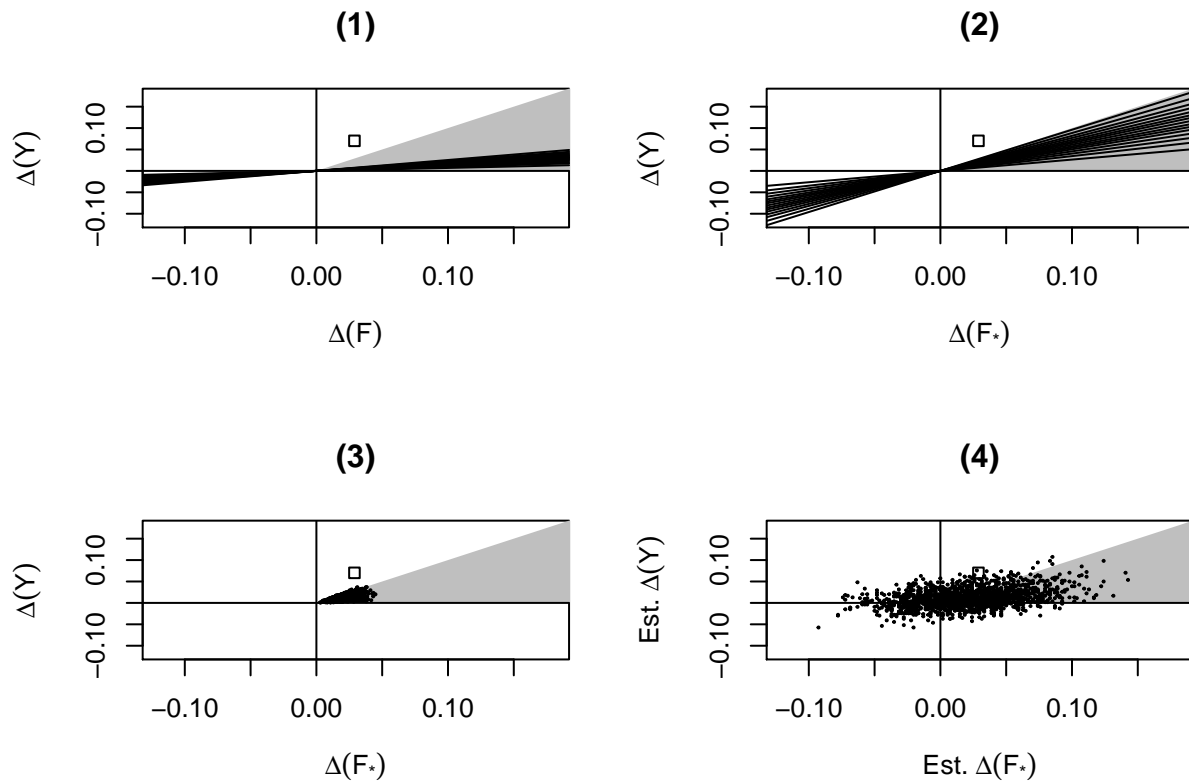


Potter, ILI

All the settings are as above, except for

```
nrm1 <- rnorm(n.rep); nrm2 <- rho.ILI*nrm1 + sqrt(1-rho.ILI^2)*rnorm(n.rep)
sn <- qtri(pnorm(nrm1), rng.Sn.ILI.Potter[1], rng.Sn.ILI.Potter[2])
sp <- qtri(pnorm(nrm2), rng.Sp.ILI.Potter[1], rng.Sp.ILI.Potter[2])

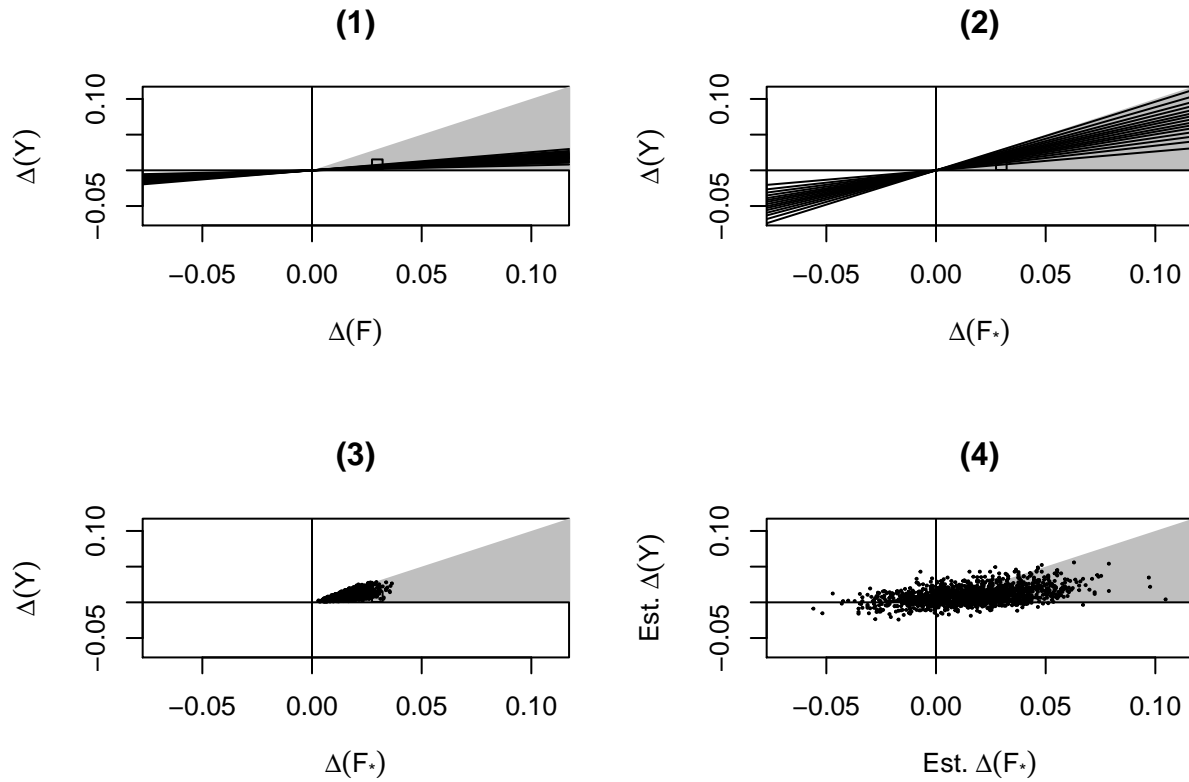
xyl <- c(-0.12,0.18) ### axis range
```



Lemaitre, ILI

All the settings are as above, except for

```
k <- rtri(n.rep, rng.k.Lemaitre[1], rng.k.Lemaitre[2])
b <- rtri(n.rep, rng.b.Lemaitre[1], rng.b.Lemaitre[2])
xyl <- c(-0.07, 0.11) ### axis range
```

Hayward, ILI

All the settings are as above, except for

```
nrm1 <- rnorm(n.rep); nrm2 <- rho.ILI*nrm1 + sqrt(1-rho.ILI^2)*rnorm(n.rep)
sn <- qtri(pnorm(nrm1), rng.Sn.ILI.Hayward[1], rng.Sn.ILI.Hayward[2])
sp <- qtri(pnorm(nrm2), rng.Sp.ILI.Hayward[1], rng.Sp.ILI.Hayward[2])

k <- rtri(n.rep, rng.k.Hayward[1],rng.k.Hayward[2])
b <- rtri(n.rep, rng.b.Hayward[1], rng.b.Hayward[2])
xyl <- c(-0.09,0.15) ### axis range
```

