Dilution Analysis REVISED

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

```
SENS <- F  ### set to TRUE to replace triangular with beta (or scaled-beta) dists
```

```
plot.custom <- F
### set to TRUE for production-level plots (option for author)
### set to FASLE to embed plots in regular output report
if (plot.custom) {
  setwd("C:/Users/Paul Gustafson/ownCloud/RES_Dilution")
  source("C:/Users/Paul Gustafson/ownCloud/OPUS2/Rcode/AuxFunctions.R")
}
```

Set hyperparameters

```
### case fatality rate
rng.CFR <- c(0.01, 0.2)

### sensitivity of surrogate for F
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 <- c(.76, .84)

### specificity of surrogate for F
rng.Sp.LC <- c(1,1)

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

rng.Sp.ILI.Hayward <- c(.42, .55)

### for ILI, neg dependence between Sn, Sp, due to case def
rho.ILI <- (-0.95)

### attack rate
rng.a <- c(.07,.3)

### intervention effect
rng.k.Carman <- c(1, 1.37*1.35)
rng.k.Potter <- c(1, 1.56*1.35)
rng.k.Hayward <- c(1, 1.25*1.35)
rng.k.Lemaitre <- c(1, 1.30*1.35)
```

```
### mortality without influenza
### if the study period were 1 year
rng.b.YR <- c(.11, .26)

### so for less than 1 year ...
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                           0.010 0.2000
## 2         Sensitivity (Lab-confirmed, Carman) 0.220 0.2600
## 3                     (Lab-confirmed, Potter) 0.190 0.3000
## 4                      (ILI Potter, Lemaitre) 0.540 0.7800
## 5                               (ILI Hayward) 0.760 0.8400
## 6         Specificity         (Lab-confirmed) 1.000 1.0000
## 7                      (ILI Potter, Lemaitre) 0.500 0.7100
## 8                               (ILI Hayward) 0.420 0.5500
## 9                   a                          0.070 0.3000
## 10                  k                (Carman) 1.000 1.8495
## 11                                   (Potter) 1.000 2.1060
## 12                                 (Lemaitre) 1.000 1.7550
## 13                                  (Hayward) 1.000 1.6875
## 14                  b                (Carman) 0.041 0.0980
## 15                                   (Potter) 0.046 0.1080
## 16                                 (Lemaitre) 0.023 0.0540
## 17                                  (Hayward) 0.023 0.0540
```

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      42       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=.005, pch=20)
```

```
  }
}
```

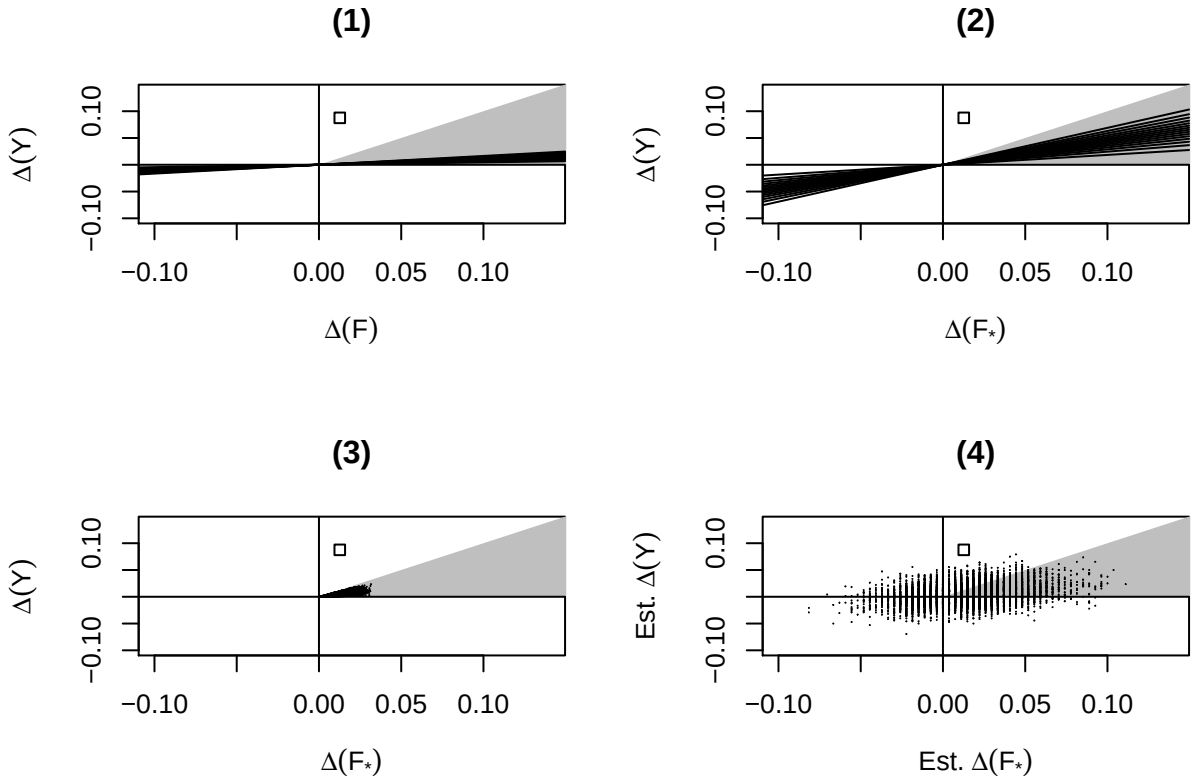
Function to generate the Step 4 plot

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=.005,
           pch=20)
  }
}
```

Carry out the Carman assessment

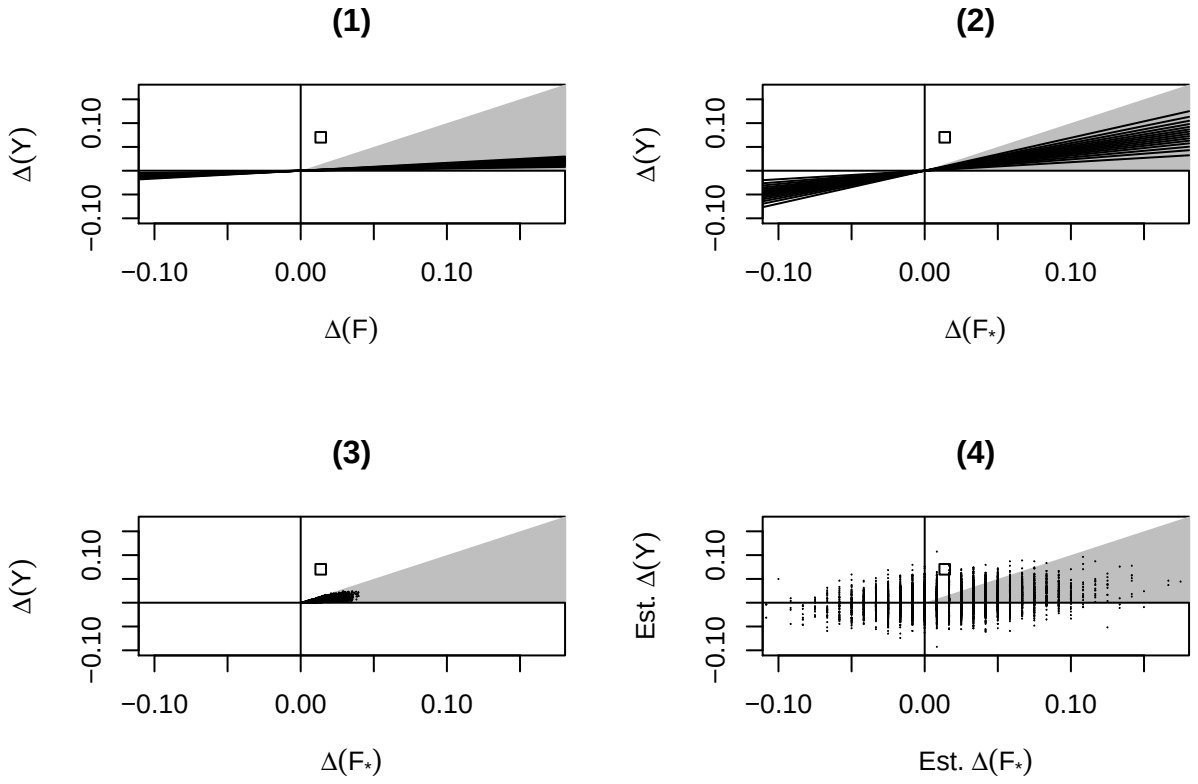
```
### number of Monte Carlo draws
n.rep <- 10000

### 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.

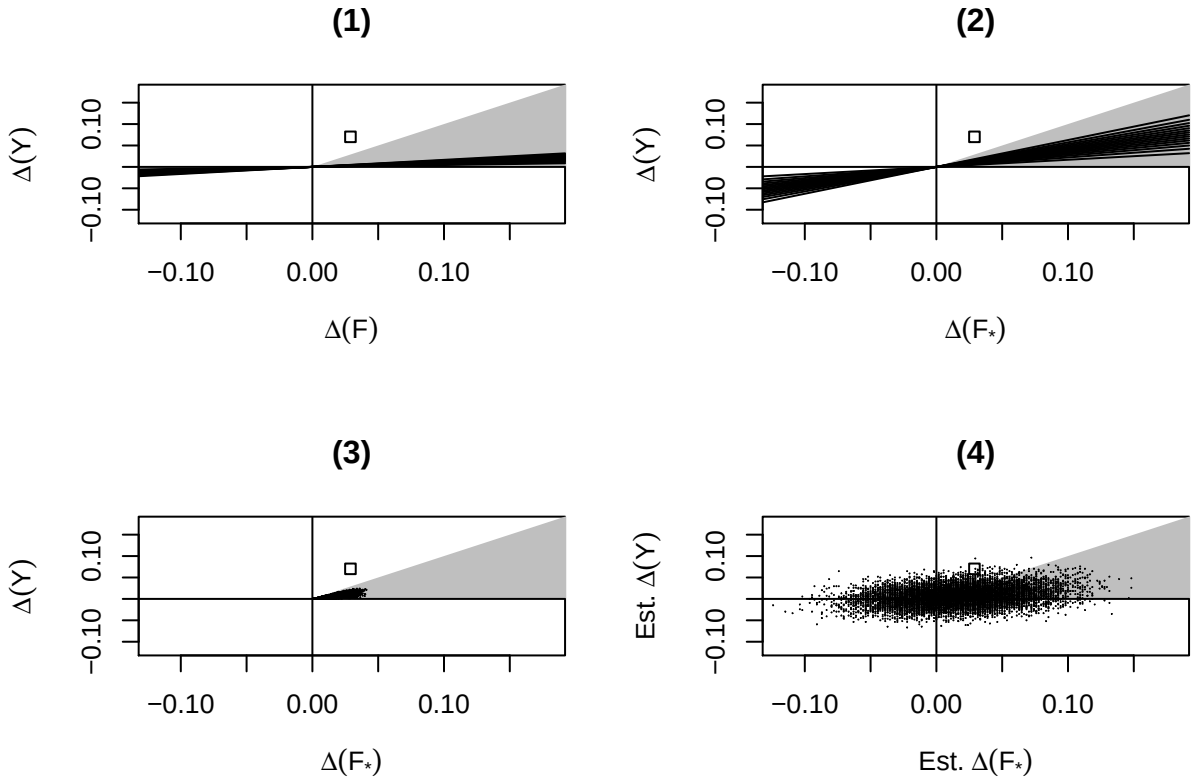
```
sn <- rtri(n.rep, rng.Sn.LC.Potter[1], rng.Sn.LC.Potter[2])
k <- rtri(n.rep, rng.k.Potter[1], rng.k.Potter[2])
b <- rtri(n.rep, rng.b.Potter[1], rng.b.Potter[2])
xyl <- c(-0.10,0.17) ### plotting range
```



Potter, ILI

All the settings are as above, except for

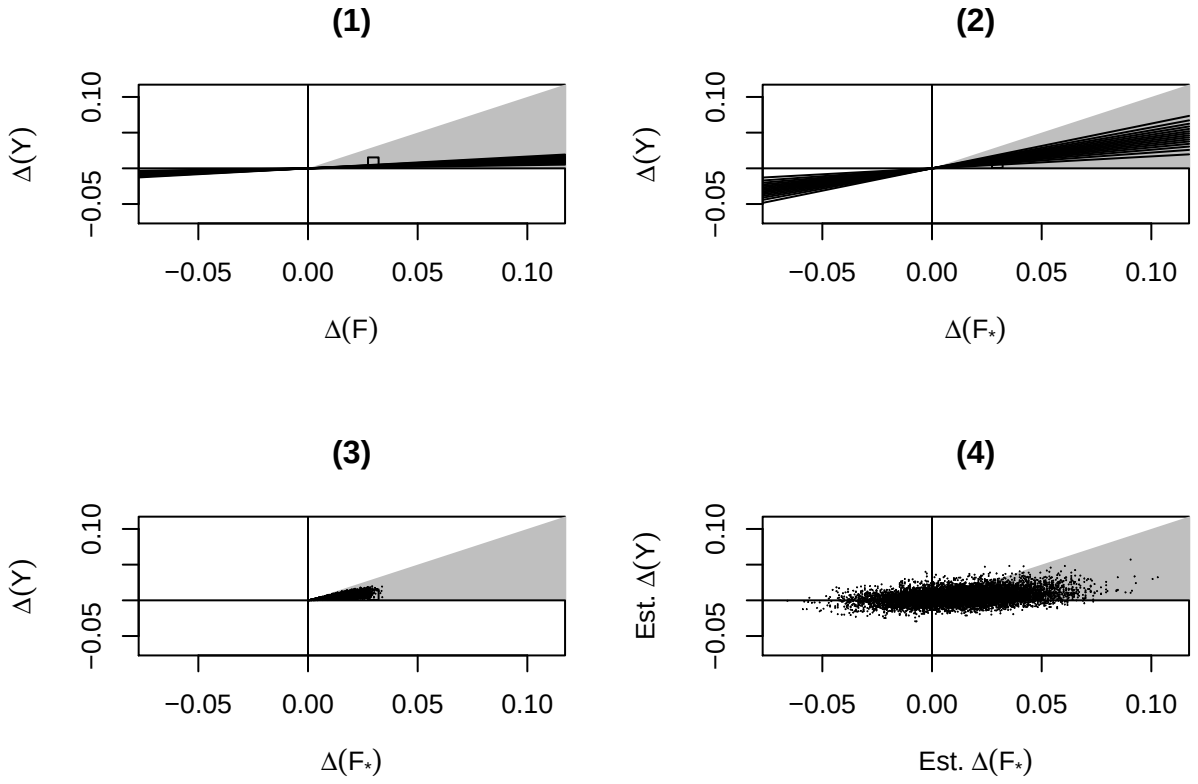
```
nrm1 <- rnorm(n.rep); nrm2 <- rho.ILI*nrm1 + sqrt(1-rho.ILI^2)*rnorm(n.rep)
sn <- qtri(pnorm(nrm1), rng.Sn.ILI.Potter[1], rng.Sn.ILI.Potter[2])
sp <- qtri(pnorm(nrm2), rng.Sp.ILI.Potter[1], rng.Sp.ILI.Potter[2])

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



Lemaitre, ILI

All the settings are as above, except for

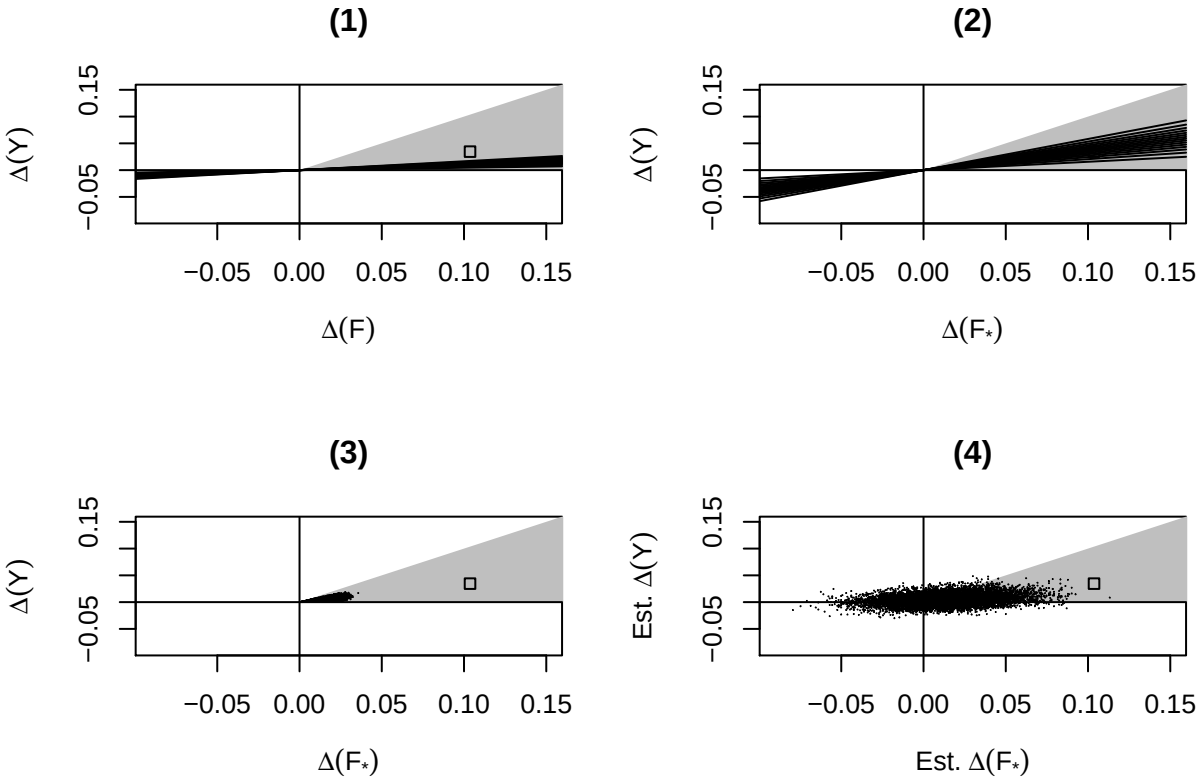
```
k <- rtri(n.rep, rng.k.Lemaitre[1], rng.k.Lemaitre[2])
b <- rtri(n.rep, rng.b.Lemaitre[1], rng.b.Lemaitre[2])
xyl <- c(-0.07,0.11) ### axis range
```



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
```


(1)
(2)
(3)
(4)
Δ(Y)
Δ(F)
Δ(F*)
Est. Δ(Y)
Est. Δ(F*)
−0.05
0.00
0.05
0.10
0.15