# Phaco meta analysis

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## Load data

We load data from a CSV exported from Stata. The `Mo` variables refer to what happens after 6 months. The `W`, `X`, `Y`, `Z`, `AA` variables refer to what happens after 12 months. That's a bug in how Stata exports names of variables which start with a number - the columns were named `6mo...` and `12mo...`.

```
library(tidyverse)
```

```
## Loading tidyverse: ggplot2
## Loading tidyverse: tibble
## Loading tidyverse: tidyr
## Loading tidyverse: readr
## Loading tidyverse: purrr
## Loading tidyverse: dplyr

## Conflicts with tidy packages ----------------------------------------------

## filter(): dplyr, stats
## lag():    dplyr, stats
```

```
library(meta)
```

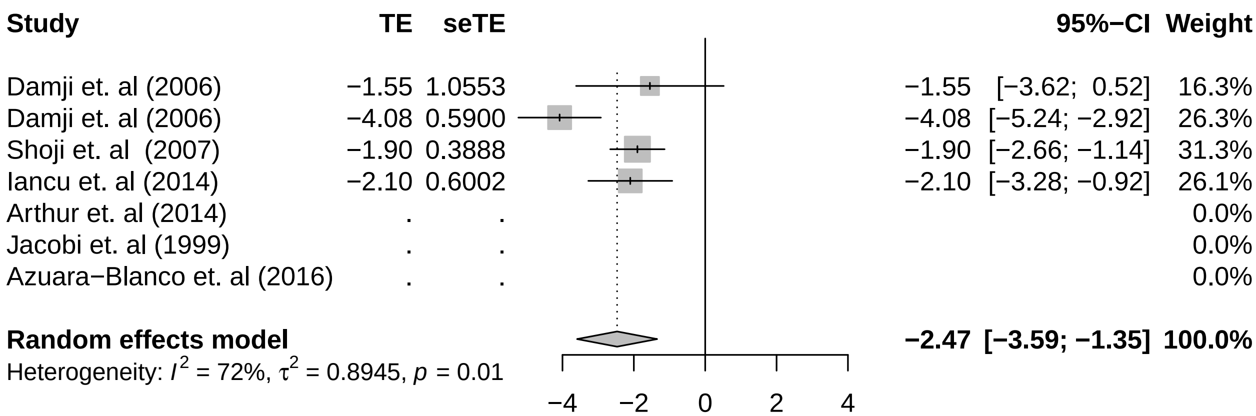
```
## Loading 'meta' package (version 4.7-0).
## Type 'help("meta-package")' for a brief overview.
```

```
library(ggrepel)

setwd("~/Documents/phaco")
df <- read.csv("phaco.csv", na.strings='-')
df <- df %>% rename(SixMoEyes = MoEyes,
              SixMoIOPMean = MoIOPMean,
              SixMoIOPStdDev = MoIOPStdDev,
              SixMoAbsIOPChangeMean = MoAbsIOPChangeMean,
              SixMoAbsIOPChangeStdDev = MoAbsIOPChangeStdDev,
              OneYEyes = W,
              OneYIOPMean = X,
              OneYIOPStdDev = Y,
              OneYAbsIOPChangeMean = Z,
              OneYAbsIOPChangeStdDev = AA,
              LastPeriodAbsIOPChangeStdDev = LastPeriodAbsIOPChangeStd,
              LastPeriodEyes = LastPeriodofEyes
              )

df <- df %>% mutate(subtype = as.factor(ifelse(is.na(OAG), 'OAG',
                        ifelse(OAG > 50, 'OAG',
                               ifelse(ACG > 50, 'ACG',
                                      ifelse(PXG > 50, 'PXG', NA))))))

df <- df %>% mutate(study.name = paste0(Author, ' (', Year, ')'))
```

# Analysis without imputation

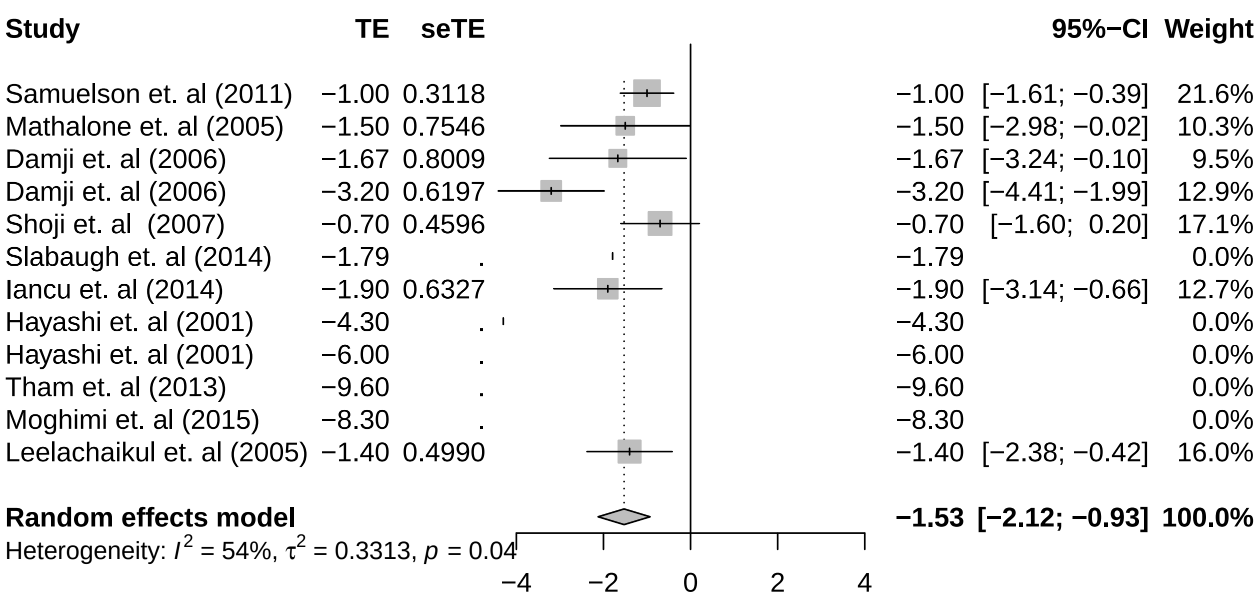
## 6 month follow-up

```r
m <- metagen(SixMoAbsIOPChangeMean,
             SixMoAbsIOPChangeStdDev / sqrt(SixMoEyes),
             study.name,
             data=df,
             subset=!is.na(df$SixMoEyes))
forest(m, comb.fixed=FALSE)
```



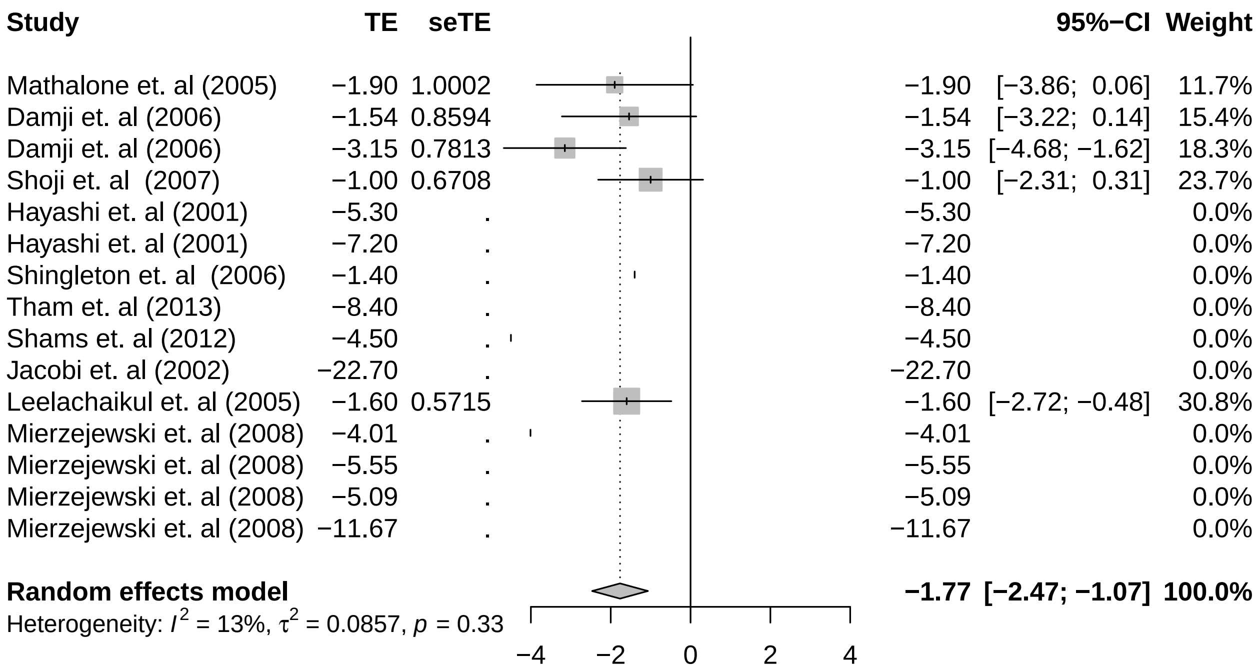

## 12-month follow up

```r
m <- metagen(OneYAbsIOPChangeMean,
             OneYAbsIOPChangeStdDev / sqrt(OneYEyes),
             study.name,
             data=df,
             subset=!is.na(df$OneYAbsIOPChangeMean))
forest(m, comb.fixed = FALSE)
```



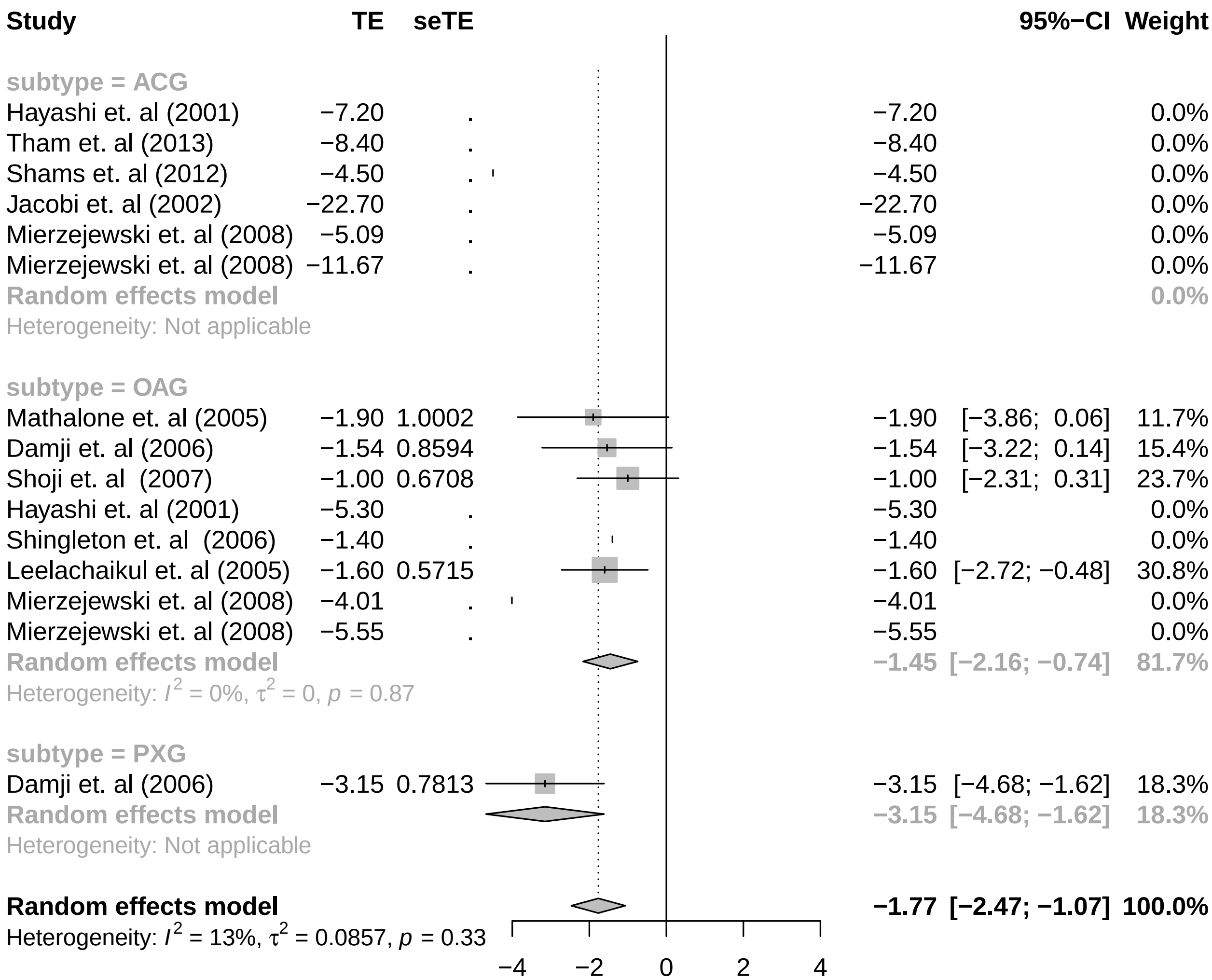
## Last period

```r
m <- metagen(LastPeriodAbsIOPChangeMean,
             LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
             study.name,
             data=df,
             subset=!is.na(df$LastPeriodAbsIOPChangeMean))
forest(m, comb.fixed = FALSE)
```




### Subgroup analysis

```r
m <- metagen(LastPeriodAbsIOPChangeMean,
             LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
             study.name,
             data=df,
             subset=!is.na(df$LastPeriodAbsIOPChangeMean),
             byvar=subtype)
forest(m, comb.fixed = FALSE)
```




## Analyses with imputation

I'm going to start by imputing on the basis of a low loss in follow up, high correlation between pre and post measures, and no change in relative IOP for those patients that were lost in follow up.

```
# Consider two range of loss of follow up.
losses <- list(lo=c(.94, .91, .87),
               hi=c(.82, .72, .51))

# Assume a range of correlations between PreOp and PostOp periods.
corrs <- list(lo=c(.25, .25, .25),
              hi=c(.45, .45, .45))

# And a range of outcomes for the missing eyes.
deltas <- list(lo=c(0, 0, 0),   # Same outcome in the unseen arm.
               hi=c(5, 5, 5))   # Worse outcome in the unseen arm.

infer.mean.sem <- function(N.b, m.b, s.b, N.a, m.a, s.a, m.d, s.d, rho, m.delta) {
  # Infer the mean and SEM of the deviation in the metric measured before and after the intervention.
  # N.b, m.b, s.b: N, mean, S.D. of metric before the intervention
```

```r
  # N.a, m.a, s.a: N, mean, S.D. of metric after the intervention
  # m.d, s.d: mean, S.D. of metric after intervention minus the metric before the intervention for
  #   the group of survivors (N.a). Can be NA.
  # rho: Assumed correlation between before and after scores. Will be used to infer s.d. if s.d is NA
  # m.delta: the assumed mean delta between the m.b for the non-survivors minus the survivors.
  # Use equations in Section 6.1 of Schwarzer, Carpenter & Rucker (2014), Meta-Analysis with R
  m.d <- ifelse(is.na(m.d), m.a - m.b, m.d)
  s.d <- ifelse(is.na(s.d), sqrt(s.a ** 2 + s.b ** 2 - 2 * rho * s.a * s.b), s.d)

  # Now generalize the mean difference from the observed subset to the full dataset.
  # pi := unobserved portion
  pi = (N.b - N.a) / N.b
  m.d.full <- m.d + pi * m.delta
  # Let's assume that delta ~ N(m.delta, s.d)
  sem.d.full <- sqrt(1 + pi ** 2) * s.d / sqrt(N.a)
  return(data.frame(m=m.d.full, sem=sem.d.full))
}

library(testthat)
```

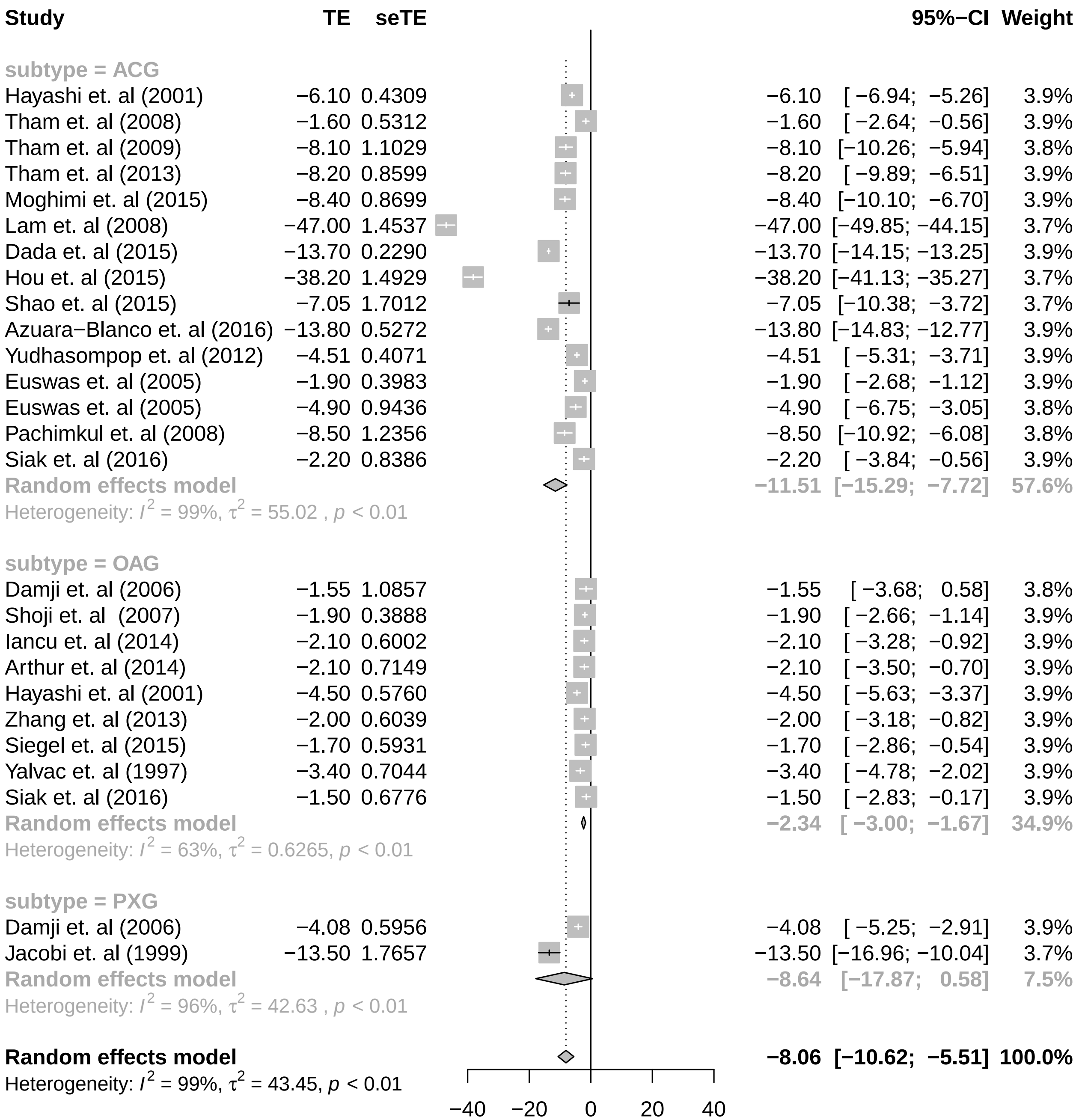
```
##
## Attaching package: 'testthat'

## The following object is masked from 'package:dplyr':
##
##     matches

## The following object is masked from 'package:purrr':
##
##     is_null
```

```r
expect_equal(infer.mean.sem(25, 0, 1, 25, 0, 1, NA, NA, 0, 0)$sem, sqrt(2)/sqrt(25))
expect_equal(infer.mean.sem(25, 0, 1, 25, 0, 1, NA, NA, 0.5, 0)$sem, 1/sqrt(25))
expect_equal(infer.mean.sem(25, 0, 1, 25, 0, 1, NA, NA, 0, 0)$m, 0)
expect_equal(infer.mean.sem(25, 0, 1, 16, 0, 1, NA, NA, 0, 0)$sem, sqrt(1 + (9 / 25) ** 2) * sqrt(2)/sq
expect_equal(infer.mean.sem(25, -1, 1, 16, 2, 1, NA, NA, 0, 0)$m, 3)
expect_equal(infer.mean.sem(25, -1, 1, 16, 2, 1, NA, NA, 0, 0)$m, 3)
expect_equal(infer.mean.sem(20, 5, 1, 20, -5, 1, NA, NA, 0, 10)$m, -10)
expect_equal(infer.mean.sem(20, 5, 1, 10, -5, 1, NA, NA, 0, 20)$m, 0)

impute.df <- function(df, loss, corr, delta) {
  # Impute missing data using the bone-headed method of just assuming the mean effect of
  # - loss of follow-up
  # - correlation between Pre and Post IOP metrics
  # - delta between IOP of eyes that were lost in follow up and eyes that were ok.
  df <- df %>% mutate(imp.SixMoEyes = ifelse(is.na(SixMoEyes), round(loss[1] * PreOpEyes), SixMoEyes),
                      imp.OneYEyes = ifelse(is.na(OneYEyes), round(loss[2] * PreOpEyes), OneYEyes),
                      imp.LastPeriodEyes = ifelse(is.na(LastPeriodEyes), round(loss[3] * PreOpEyes), La

  df_ <- with(df, infer.mean.sem(PreOpEyes, PreOpIOPMean, PreOpIOPStdDev,
                                 imp.SixMoEyes, SixMoIOPMean, SixMoIOPStdDev,
                                 SixMoAbsIOPChangeMean, SixMoAbsIOPChangeStdDev, corr[1], delta[1]))

  df$imp.SixMoIOPChangeMean <- df_$m
  df$imp.SixMoIOPChangeSEM <- df_$sem
```

```
  df_ <- with(df, infer.mean.sem(PreOpEyes, PreOpIOPMean, PreOpIOPStdDev,
                                 imp.OneYEyes, OneYIOPMean, OneYIOPStdDev,
                                 OneYAbsIOPChangeMean, OneYAbsIOPChangeStdDev, corr[2], delta[2]))
  df$imp.OneYIOPChangeMean <- df_$m
  df$imp.OneYIOPChangeSEM <- df_$sem

  df_ <- with(df, infer.mean.sem(PreOpEyes, PreOpIOPMean, PreOpIOPStdDev,
                                 imp.LastPeriodEyes, LastPeriodIOPMean, LastPeriodIOPStdDev,
                                 LastPeriodAbsIOPChangeMean, LastPeriodAbsIOPChangeStdDev, corr[3], del
  df$imp.LastPeriodIOPChangeMean <- df_$m
  df$imp.LastPeriodIOPChangeSEM <- df_$sem

  # Patch up NAs for std dev of medications.
  df$imp.RxPreOpStdDev <- ifelse(is.na(df$RxPreOpStdDev),
                                 .5* df$RxPreOpMean + .2,
                                 pmax(df$RxPreOpStdDev, .2))

  df$imp.RxPostOpStdDev <- ifelse(is.na(df$RxPostOpStdDev),
                                 .5* df$RxPostOpMean + .2,
                                 pmax(df$RxPostOpStdDev, .2))


  return(df)
}

# Q: are we dealing properly with loss of follow-up means?
# Verify where available if the before, after measurements, and changes match up.

df <- impute.df(df, losses[['lo']], corrs[['hi']], deltas[['lo']])
```

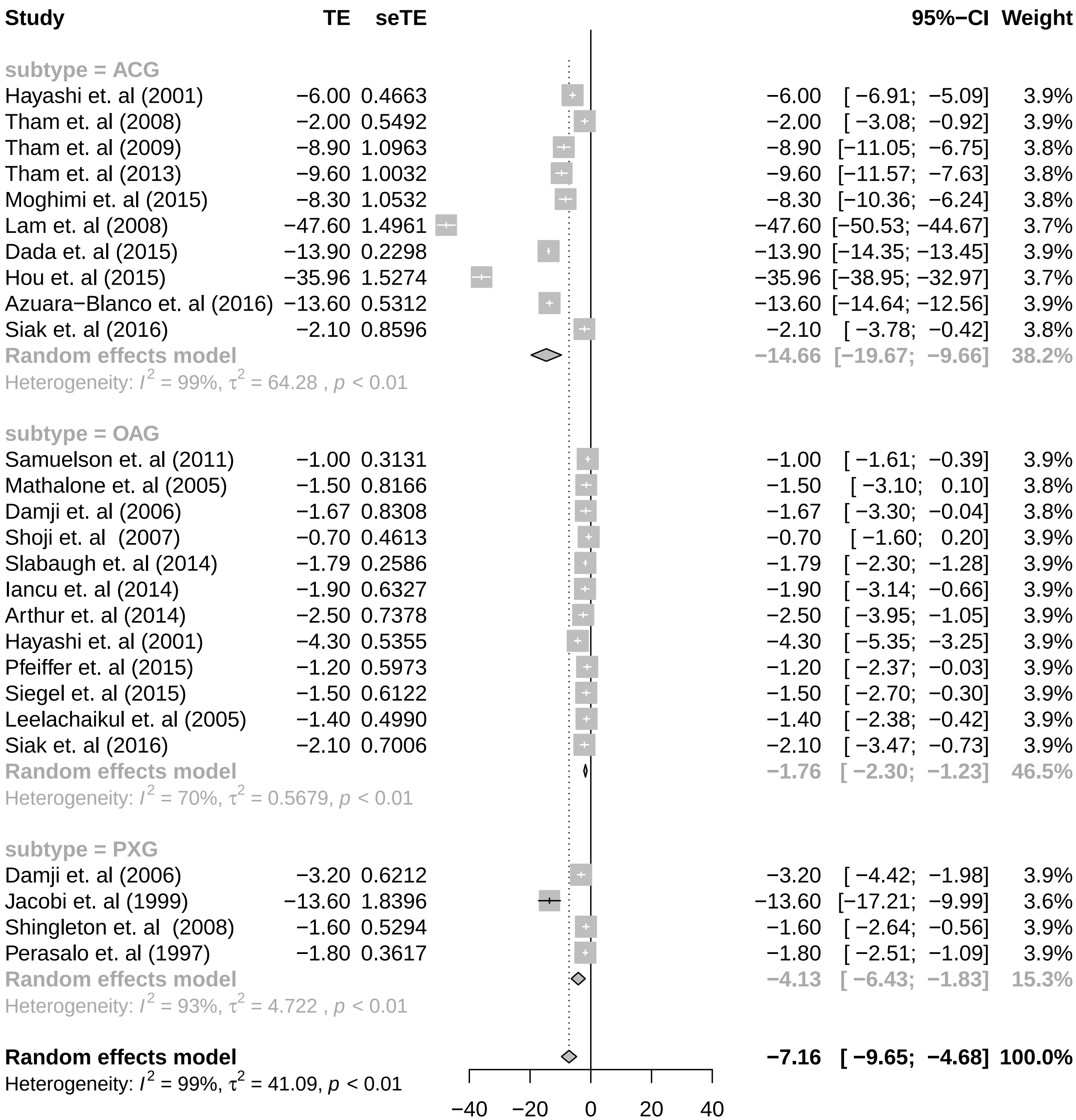
### 6 month follow-up

```
m <- metagen(imp.SixMoIOPChangeMean,
             imp.SixMoIOPChangeSEM,
             study.name,
             data=df,
             subset=!is.na(imp.SixMoIOPChangeSEM),
             byvar=subtype)
forest(m, comb.fixed=FALSE)
```



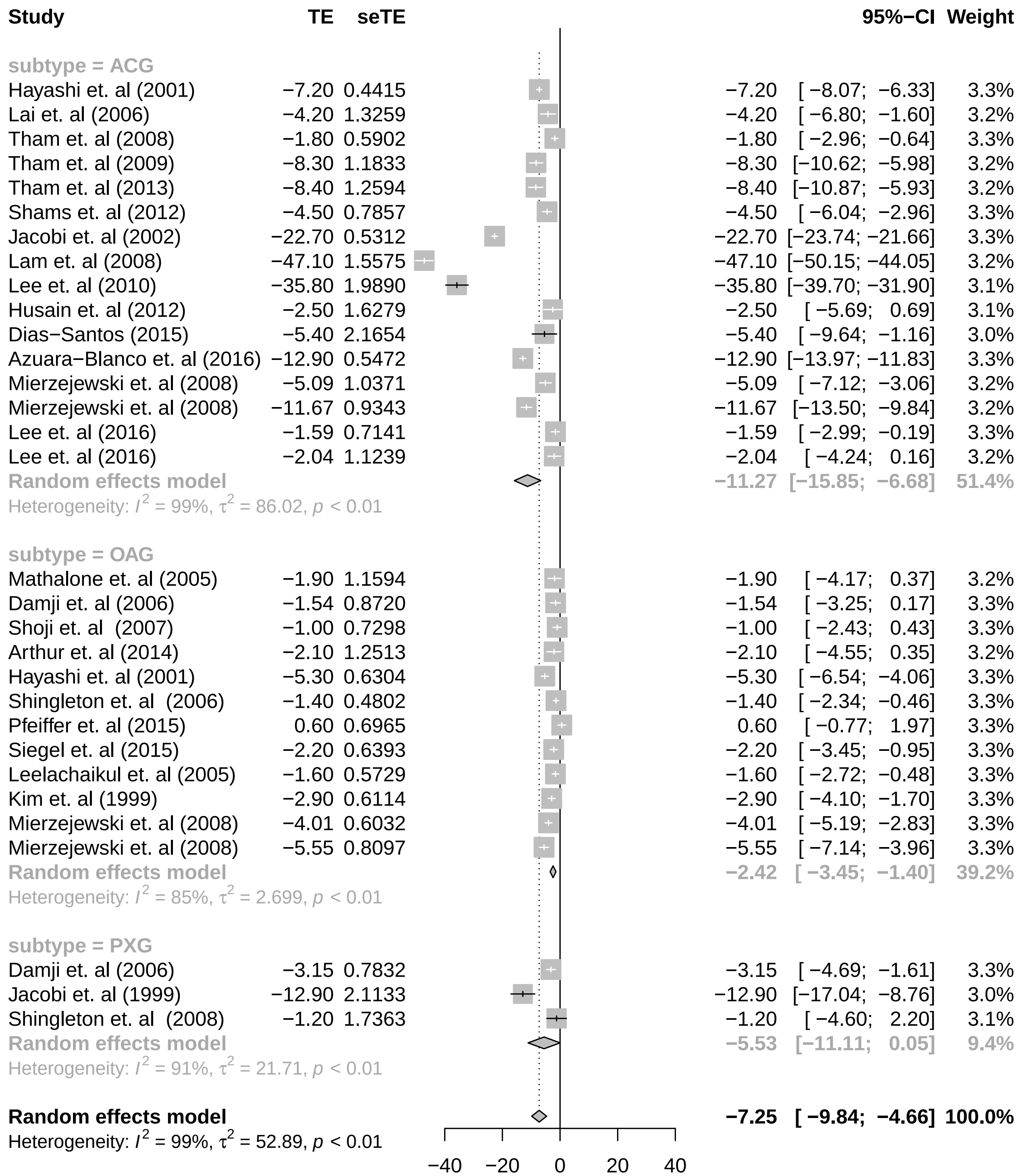

## 12-month follow up

```
m <- metagen(imp.OneYIOPChangeMean,
             imp.OneYIOPChangeSEM,
             study.name,
             data=df,
             subset=!is.na(imp.OneYIOPChangeSEM),
             byvar=subtype)
forest(m, comb.fixed=FALSE)
```




## Last period

```
m <- metagen(imp.LastPeriodIOPChangeMean,
             imp.LastPeriodIOPChangeSEM,
             study.name,
             data=df,
             subset=!is.na(imp.LastPeriodIOPChangeSEM) & MIGsYorN == 'N',
             byvar=subtype)
forest(m, comb.fixed=FALSE)
```

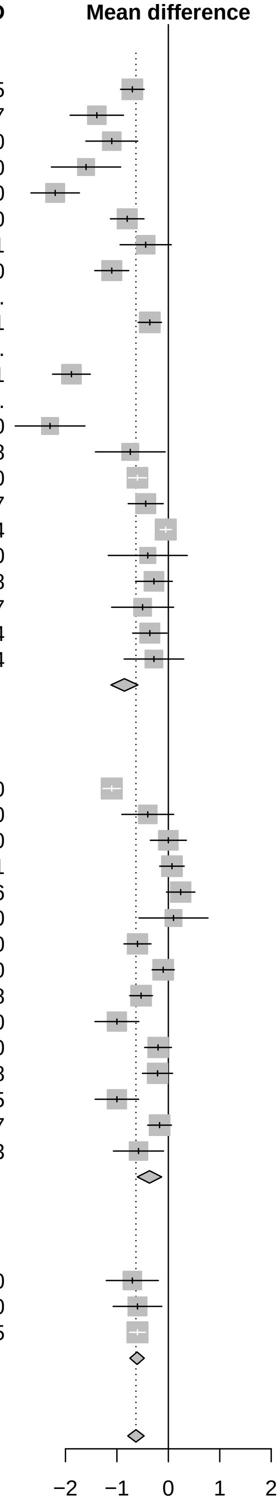



## Meds

```
m <- metacont(imp.LastPeriodEyes,
              RxPostOpMean,
              imp.RxPostOpStdDev,
              PreOpEyes,
```

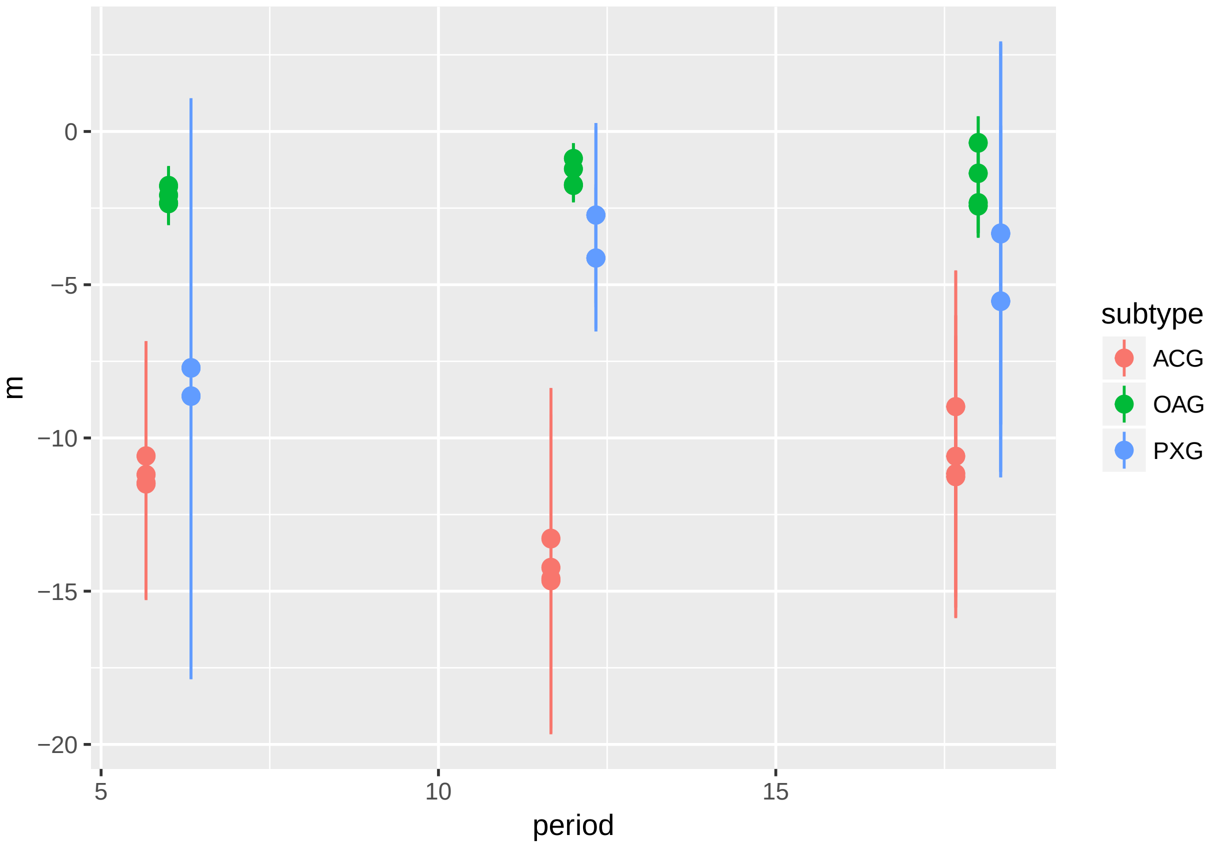
```r
               RxPreOpMean,
               imp.RxPreOpStdDev,
               study.name,
               data=df,
               subset=!is.na(imp.RxPostOpStdDev) & !is.na(imp.RxPostOpStdDev) & MIGsYorN == 'N',
               byvar=subtype)
forest(m, comb.fixed=FALSE)
```

| Study | Experimental Total | Experimental Mean | Experimental SD | Control Total | Control Mean | Control SD | MD | 95%−CI | Weight |
|---|---|---|---|---|---|---|---|---|---|
| **subtype = ACG** | | | | | | | | | |
| Hayashi et. al (2001) | 64 | 0.600 | 0.500 | 74 | 1.30 | 0.85 | −0.70 | [−0.93; −0.47] | 3.0% |
| Lai et. al (2006) | 18 | 0.520 | 0.870 | 21 | 1.91 | 0.77 | −1.39 | [−1.91; −0.87] | 2.4% |
| Tham et. al (2008) | 30 | 1.100 | 1.200 | 35 | 2.20 | 0.80 | −1.10 | [−1.60; −0.60] | 2.4% |
| Tham et. al (2009) | 23 | 1.700 | 1.300 | 27 | 3.30 | 1.10 | −1.60 | [−2.27; −0.93] | 2.0% |
| Tham et. al (2013) | 23 | 1.500 | 0.950 | 26 | 3.70 | 0.70 | −2.20 | [−2.67; −1.73] | 2.5% |
| Liu et. al (2011) | 49 | 1.000 | 0.700 | 56 | 1.80 | 1.00 | −0.80 | [−1.13; −0.47] | 2.8% |
| Shams et. al (2012) | 48 | 0.960 | 1.170 | 55 | 1.40 | 1.41 | −0.44 | [−0.94; 0.06] | 2.4% |
| Moghimi et. al (2015) | 40 | 0.100 | 0.300 | 46 | 1.20 | 1.10 | −1.10 | [−1.43; −0.77] | 2.8% |
| Jacobi et. al (2002) | 37 | 0.180 | 0.450 | 43 | . | . | | | 0.0% |
| Lam et. al (2008) | 27 | 0.030 | 0.200 | 31 | 0.39 | 0.61 | −0.36 | [−0.59; −0.13] | 3.0% |
| Lee et. al (2010) | 23 | 0.100 | 0.250 | 26 | . | . | | | 0.0% |
| Dada et. al (2015) | 38 | 0.136 | 0.268 | 44 | 2.02 | 1.21 | −1.88 | [−2.25; −1.52] | 2.7% |
| Hou et. al (2015) | 22 | 0.480 | 0.440 | 25 | . | . | | | 0.0% |
| Shao et. al (2015) | 17 | 0.650 | 1.090 | 20 | 2.95 | 1.00 | −2.30 | [−2.98; −1.62] | 2.0% |
| Dias−Santos (2015) | 13 | 0.930 | 0.590 | 15 | 1.67 | 1.18 | −0.74 | [−1.42; −0.06] | 2.0% |
| Azuara−Blanco et. al (2016) | 182 | 0.400 | 0.800 | 208 | 1.00 | 1.00 | −0.60 | [−0.78; −0.42] | 3.0% |
| Yudhasompop et. al (2012) | 52 | 1.430 | 1.030 | 60 | 1.87 | 0.77 | −0.44 | [−0.78; −0.10] | 2.8% |
| Euswas et. al (2005) | 30 | 0.030 | 0.215 | 34 | 0.08 | 0.24 | −0.05 | [−0.16; 0.06] | 3.1% |
| Euswas et. al (2005) | 12 | 1.400 | 0.900 | 14 | 1.80 | 1.10 | −0.40 | [−1.17; 0.37] | 1.8% |
| Mierzejewski et. al (2008) | 22 | 1.240 | 0.660 | 25 | 1.52 | 0.58 | −0.28 | [−0.64; 0.08] | 2.7% |
| Mierzejewski et. al (2008) | 3 | 1.000 | 0.200 | 4 | 1.50 | 0.57 | −0.50 | [−1.10; 0.10] | 2.2% |
| Lee et. al (2016) | 37 | 0.690 | 0.680 | 42 | 1.05 | 0.84 | −0.36 | [−0.70; −0.02] | 2.8% |
| Lee et. al (2016) | 12 | 1.430 | 0.540 | 14 | 1.71 | 0.94 | −0.28 | [−0.86; 0.30] | 2.2% |
| **Random effects model** | **822** | | | **945** | | | **−0.85** | **[−1.12; −0.59]** | **50.7%** |
| Heterogeneity: $I^2 = 92\%$, $\tau^2 = 0.3045$, $p < 0.01$ | | | | | | | | | |
| **subtype = OAG** | | | | | | | | | |
| Samuelson et. al (2011) | 107 | 0.400 | 0.700 | 123 | 1.50 | 0.60 | −1.10 | [−1.27; −0.93] | 3.1% |
| Mathalone et. al (2005) | 24 | 1.100 | 1.120 | 58 | 1.50 | 0.90 | −0.40 | [−0.90; 0.10] | 2.4% |
| Shoji et. al (2007) | 20 | 0.800 | 0.600 | 35 | 0.80 | 0.70 | 0.00 | [−0.35; 0.35] | 2.7% |
| Slabaugh et. al (2014) | 137 | 1.920 | 1.070 | 157 | 1.85 | 1.01 | 0.07 | [−0.17; 0.31] | 3.0% |
| Iancu et. al (2014) | 33 | 2.900 | 0.530 | 38 | 2.66 | 0.66 | 0.24 | [−0.04; 0.52] | 2.9% |
| Arthur et. al (2014) | 17 | 1.500 | 1.200 | 37 | 1.40 | 1.10 | 0.10 | [−0.57; 0.77] | 2.0% |
| Hayashi et. al (2001) | 59 | 0.800 | 0.600 | 68 | 1.40 | 0.90 | −0.60 | [−0.86; −0.34] | 2.9% |
| Shingleton et. al (2006) | 48 | 1.000 | 0.600 | 55 | 1.10 | 0.50 | −0.10 | [−0.32; 0.12] | 3.0% |
| Zhang et. al (2013) | 37 | 0.230 | 0.430 | 43 | 0.76 | 0.58 | −0.53 | [−0.75; −0.31] | 3.0% |
| Pfeiffer et. al (2015) | 43 | 1.000 | 1.000 | 50 | 2.00 | 1.10 | −1.00 | [−1.43; −0.57] | 2.6% |
| Siegel et. al (2015) | 45 | 1.300 | 0.610 | 52 | 1.50 | 0.70 | −0.20 | [−0.46; 0.06] | 2.9% |
| Leelachaikul et. al (2005) | 54 | 0.990 | 0.950 | 58 | 1.20 | 0.58 | −0.21 | [−0.50; 0.08] | 2.9% |
| Kim et. al (1999) | 27 | 0.700 | 0.550 | 31 | 1.70 | 1.05 | −1.00 | [−1.42; −0.58] | 2.6% |
| Mierzejewski et. al (2008) | 45 | 1.360 | 0.590 | 52 | 1.53 | 0.57 | −0.17 | [−0.40; 0.06] | 3.0% |
| Mierzejewski et. al (2008) | 17 | 1.160 | 0.760 | 19 | 1.74 | 0.73 | −0.58 | [−1.07; −0.09] | 2.4% |
| **Random effects model** | **713** | | | **876** | | | **−0.37** | **[−0.60; −0.13]** | **41.4%** |
| Heterogeneity: $I^2 = 90\%$, $\tau^2 = 0.1881$, $p < 0.01$ | | | | | | | | | |
| **subtype = PXG** | | | | | | | | | |
| Jacobi et. al (1999) | 13 | 1.500 | 0.700 | 22 | 2.20 | 0.80 | −0.70 | [−1.21; −0.19] | 2.4% |
| Shingleton et. al (2008) | 22 | 1.000 | 1.100 | 240 | 1.60 | 0.90 | −0.60 | [−1.07; −0.13] | 2.5% |
| Perasalo et. al (1997) | 197 | 0.900 | 0.650 | 226 | 1.50 | 0.95 | −0.60 | [−0.75; −0.45] | 3.1% |
| **Random effects model** | **232** | | | **488** | | | **−0.61** | **[−0.75; −0.47]** | **8.0%** |
| Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.93$ | | | | | | | | | |
| **Random effects model** | **1767** | | | **2309** | | | **−0.63** | **[−0.79; −0.47]** | **100.0%** |
| Heterogeneity: $I^2 = 91\%$, $\tau^2 = 0.2086$, $p < 0.01$ | | | | | | | | | |



## Impute under every scenario

```
results <- list()
for(loss in c('lo', 'hi')) {
  for(corr in c('lo', 'hi')) {
    for(delta in c('lo', 'hi')) {
      df <- impute.df(df, losses[[loss]], corrs[[corr]], deltas[[delta]])
      s <- (metagen(imp.SixMoIOPChangeMean,
                    imp.SixMoIOPChangeSEM,
                    study.name,
                    data=df,
                    subset=!is.na(imp.SixMoIOPChangeSEM) & MIGsYorN == 'N',
                    byvar=subtype))
      row <- data.frame(loss=loss, corr=corr, delta=delta, m=s$TE.random.w, ci.lo=s$upper.random.w, ci.h
      results[[length(results) + 1]] <- row

      s <- (metagen(imp.OneYIOPChangeMean,
                    imp.OneYIOPChangeSEM,
                    study.name,
                    data=df,
                    subset=!is.na(imp.OneYIOPChangeSEM) & MIGsYorN == 'N',
                    byvar=subtype))
      row <- data.frame(loss=loss, corr=corr, delta=delta, m=s$TE.random.w, ci.lo=s$upper.random.w, ci.h
      results[[length(results) + 1]] <- row

      s <- (metagen(imp.LastPeriodIOPChangeMean,
                    imp.LastPeriodIOPChangeSEM,
                    study.name,
                    data=df,
                    subset=!is.na(imp.LastPeriodIOPChangeSEM) & MIGsYorN == 'N',
                    byvar=subtype))
      row <- data.frame(loss=loss, corr=corr, delta=delta, m=s$TE.random.w, ci.lo=s$upper.random.w, ci.h
      results[[length(results) + 1]] <- row
    }
  }
}

all.df <- do.call(rbind, results)

p <- position_dodge(width=1)
ggplot(all.df, aes(x=period, y = m, ymin=ci.lo, ymax=ci.hi, color=subtype)) + geom_pointrange(position=p
```




```
summary(metagen(imp.LastPeriodIOPChangeMean,
             imp.LastPeriodIOPChangeSEM,
             study.name,
             data=df,
             subset=!is.na(imp.LastPeriodIOPChangeSEM) & MIGsYorN == 'N',
             byvar=subtype))
```

```
## Number of studies combined: k = 31
##
##                                          95%-CI      z  p-value
## Fixed effect model   -3.6871 [-4.0248; -3.3495] -21.40 < 0.0001
## Random effects model -4.9922 [-7.4405; -2.5439]  -4.00 < 0.0001
##
## Quantifying heterogeneity:
##  tau^2 = 46.3999; H = 7.10 [6.55; 7.70]; I^2 = 98.0% [97.7%; 98.3%];
##  Rb = 95.9% [93.5%; 98.4%]
##
## Test of heterogeneity:
##        Q d.f.  p-value
##  1512.21   30 < 0.0001
##
## Results for subgroups (fixed effect model):
##                   k                      95%-CI      Q   tau^2   I^2    Rb
## subtype = ACG    16 -8.1521 [-8.6777; -7.6265] 967.26   78.74 98.4% 96.6%
## subtype = OAG    12 -0.2848 [-0.7518;  0.1823]  34.76   1.5   68.4% 65.9%
## subtype = PXG     3 -2.6970 [-4.0226; -1.3713]  27.02   27.9  92.6% 91.4%
##
```

```
## Test for subgroup differences (fixed effect model):
##                      Q d.f.  p-value
## Between groups  483.17    2 < 0.0001
## Within groups  1029.04   28 < 0.0001
##
## Results for subgroups (random effects model):
##                  k                      95%-CI      Q   tau^2   I^2    Rb
## subtype = ACG   16 -8.9804 [-13.4047; -4.5562] 967.26   78.74 98.4% 96.6%
## subtype = OAG   12 -0.3569 [ -1.2107;  0.4969]  34.76   1.5   68.4% 65.9%
## subtype = PXG    3 -3.3124 [ -9.5628;  2.9381]  27.02   27.9  92.6% 91.4%
##
## Test for subgroup differences (random effects model):
##                      Q d.f.  p-value
## Between groups   14.75    2   0.0006
##
## Details on meta-analytical method:
## - Inverse variance method
## - DerSimonian-Laird estimator for tau^2
```

```
summary(metagen(imp.LastPeriodIOPChangeMean,
             imp.LastPeriodIOPChangeSEM,
             study.name,
             data=df,
             subset=!is.na(imp.LastPeriodIOPChangeSEM) & MIGsYorN == 'N',
             byvar=subtype))
```

```
## Number of studies combined: k = 31
##
##                                          95%-CI      z  p-value
## Fixed effect model   -3.6871 [-4.0248; -3.3495] -21.40 < 0.0001
## Random effects model -4.9922 [-7.4405; -2.5439]  -4.00 < 0.0001
##
## Quantifying heterogeneity:
##  tau^2 = 46.3999; H = 7.10 [6.55; 7.70]; I^2 = 98.0% [97.7%; 98.3%];
##  Rb = 95.9% [93.5%; 98.4%]
##
## Test of heterogeneity:
##        Q d.f.  p-value
##  1512.21   30 < 0.0001
##
## Results for subgroups (fixed effect model):
##                  k                    95%-CI      Q   tau^2   I^2    Rb
## subtype = ACG   16 -8.1521 [-8.6777; -7.6265] 967.26   78.74 98.4% 96.6%
## subtype = OAG   12 -0.2848 [-0.7518;  0.1823]  34.76   1.5   68.4% 65.9%
## subtype = PXG    3 -2.6970 [-4.0226; -1.3713]  27.02   27.9  92.6% 91.4%
##
## Test for subgroup differences (fixed effect model):
##                      Q d.f.  p-value
## Between groups  483.17    2 < 0.0001
## Within groups  1029.04   28 < 0.0001
##
## Results for subgroups (random effects model):
##                  k                      95%-CI      Q   tau^2   I^2    Rb
## subtype = ACG   16 -8.9804 [-13.4047; -4.5562] 967.26   78.74 98.4% 96.6%
## subtype = OAG   12 -0.3569 [ -1.2107;  0.4969]  34.76   1.5   68.4% 65.9%
```

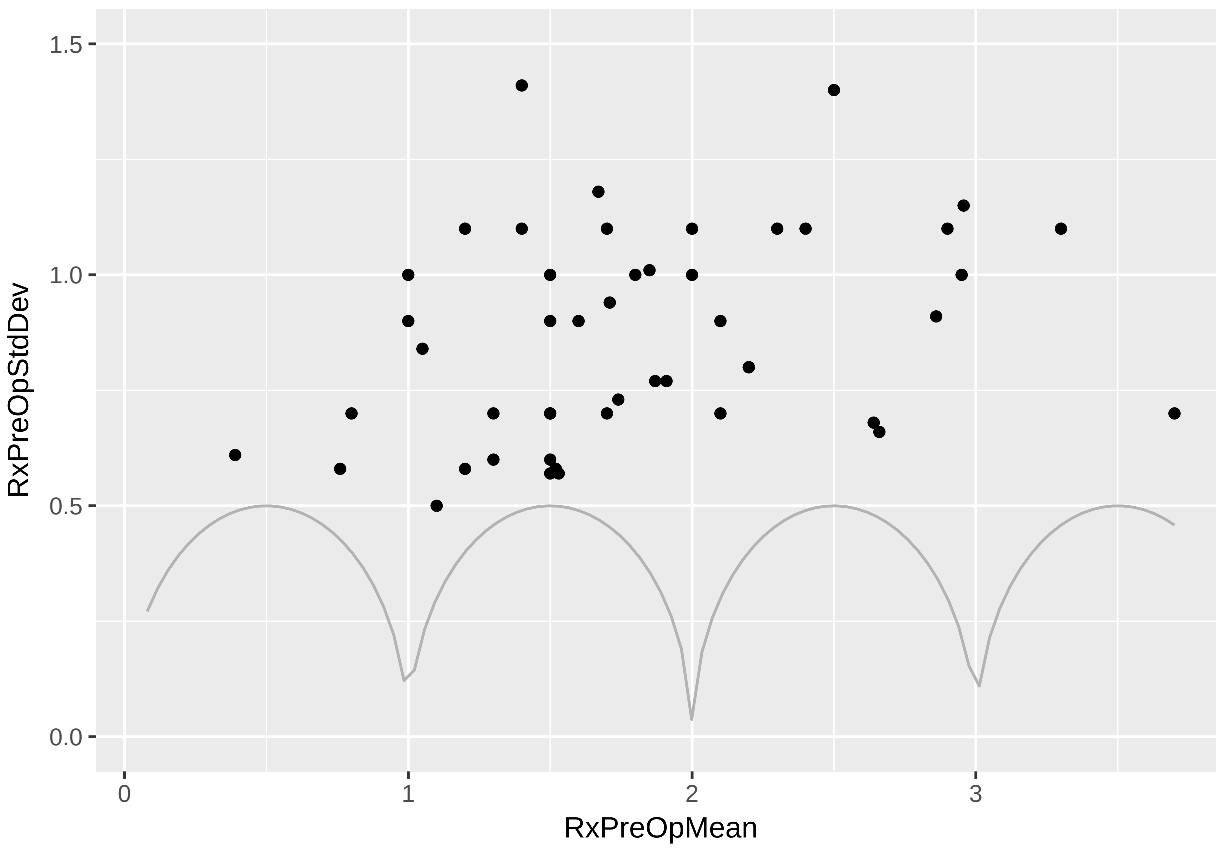
```
## subtype = PXG   3 -3.3124 [ -9.5628;  2.9381]  27.02   27.9  92.6% 91.4%
##
## Test for subgroup differences (random effects model):
##                      Q d.f.  p-value
## Between groups   14.75    2   0.0006
##
## Details on meta-analytical method:
## - Inverse variance method
## - DerSimonian-Laird estimator for tau^2
```

## Sanity check data graphically

Check the relationship between RxPreOpMean and s.d.

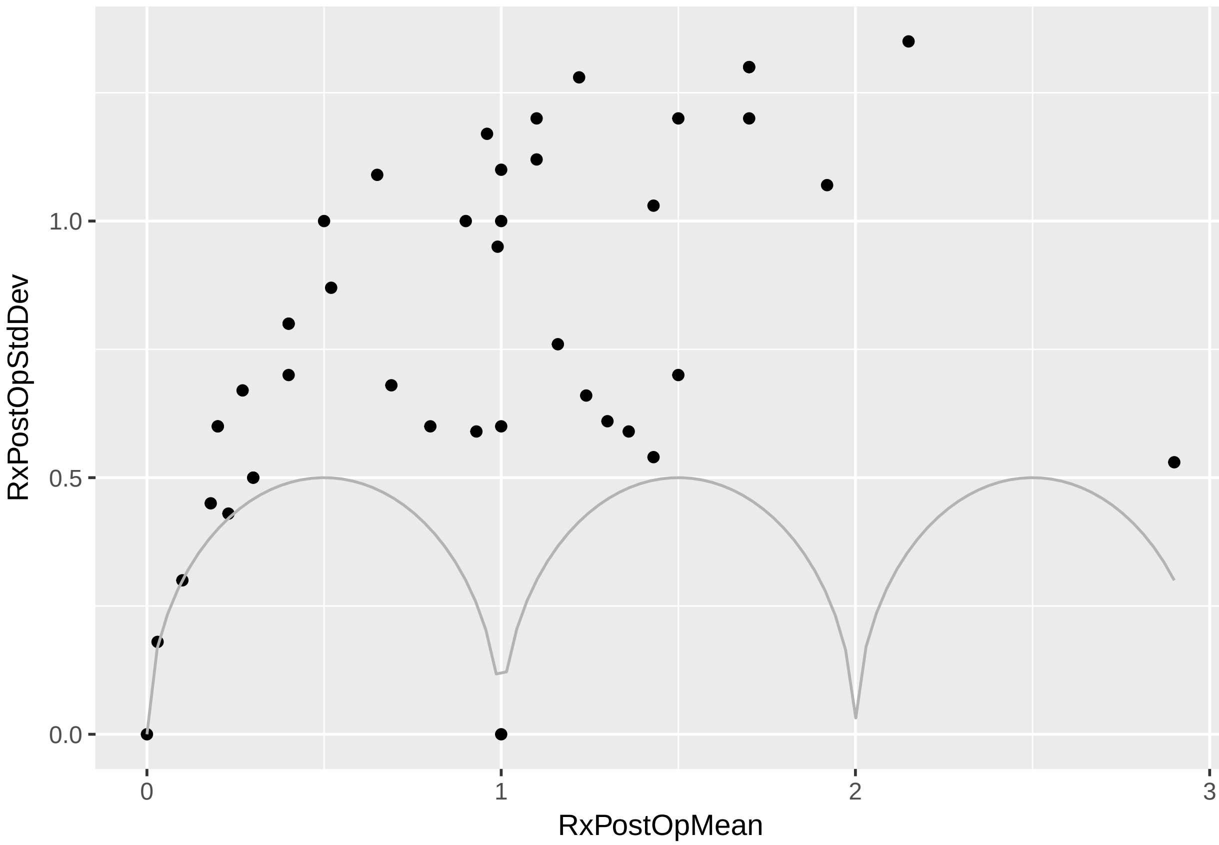
```
ggplot(df, aes(x = RxPreOpMean, y = RxPreOpStdDev)) +
  geom_point() +
  coord_cartesian(y=c(0, 1.5)) +
  stat_function(fun = function(x) sqrt((x - floor(x)) * (1 - (x - floor(x)))), color="gray70")
```

```
## Warning: Removed 19 rows containing missing values (geom_point).
```




```
ggplot(df, aes(x = RxPostOpMean, y = RxPostOpStdDev)) + geom_point() +
  stat_function(fun = function(x) sqrt((x - floor(x)) * (1 - (x - floor(x)))), color="gray70")
```

```
## Warning: Removed 24 rows containing missing values (geom_point).
```

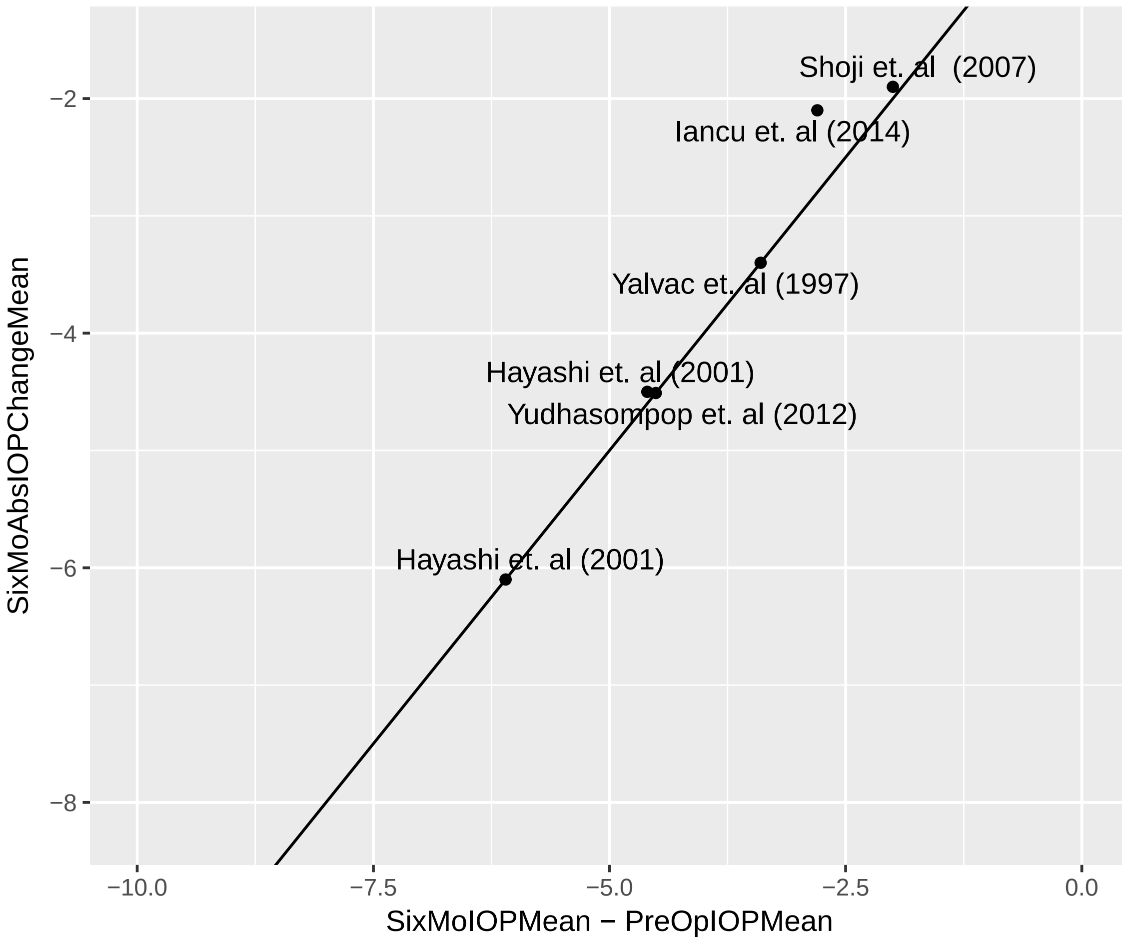



Check that changes add up.

```
ggplot(df, aes(x = SixMoIOPMean - PreOpIOPMean, y = SixMoAbsIOPChangeMean, label = study.name)) +
  geom_point() +
  coord_cartesian(xlim=c(-10, 0)) +
  geom_abline() +
  geom_text_repel()
```

```
## Warning: Removed 61 rows containing missing values (geom_point).
```

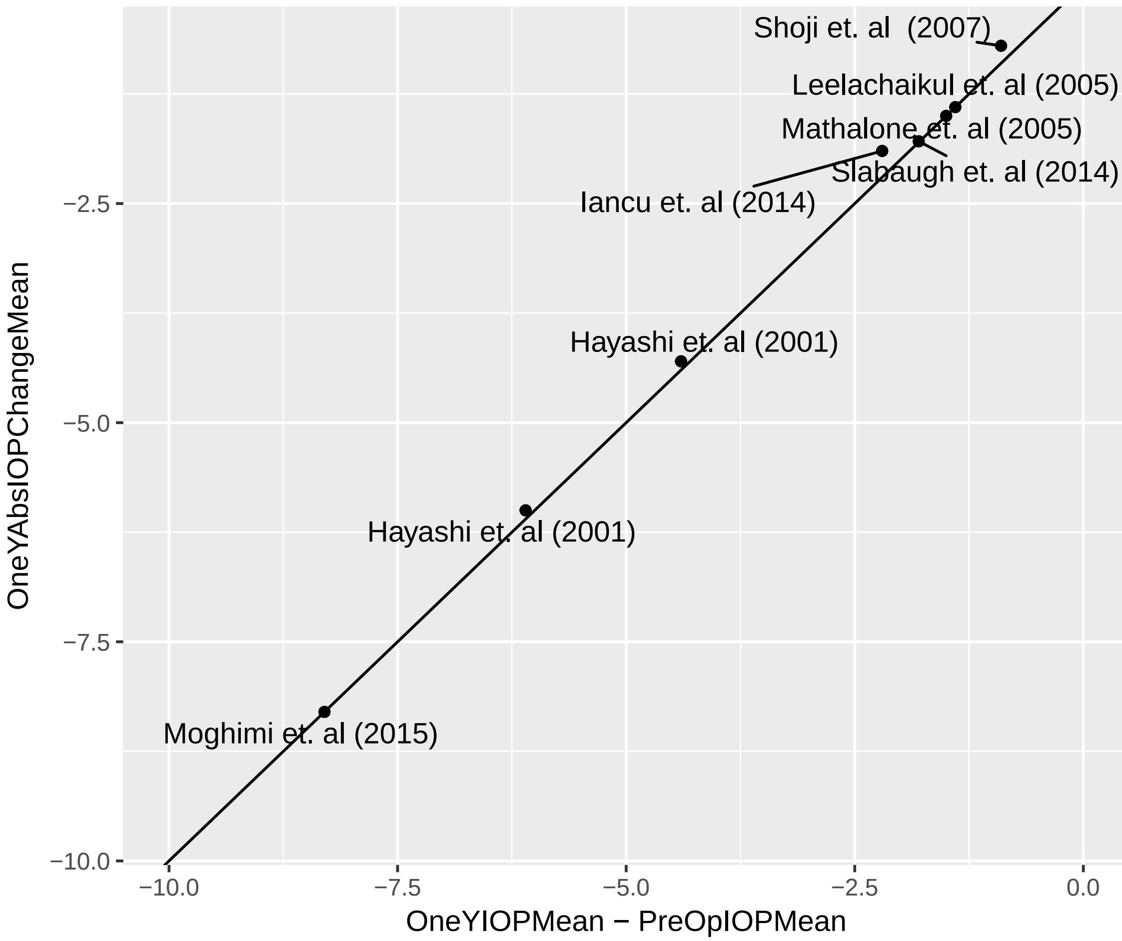
```
## Warning: Removed 61 rows containing missing values (geom_text_repel).
```




```r
ggplot(df, aes(x = OneYIOPMean - PreOpIOPMean, y = OneYAbsIOPChangeMean, label = study.name)) +
  geom_point() +
  coord_cartesian(xlim=c(-10, 0)) +
  geom_abline() +
  geom_text_repel()
```

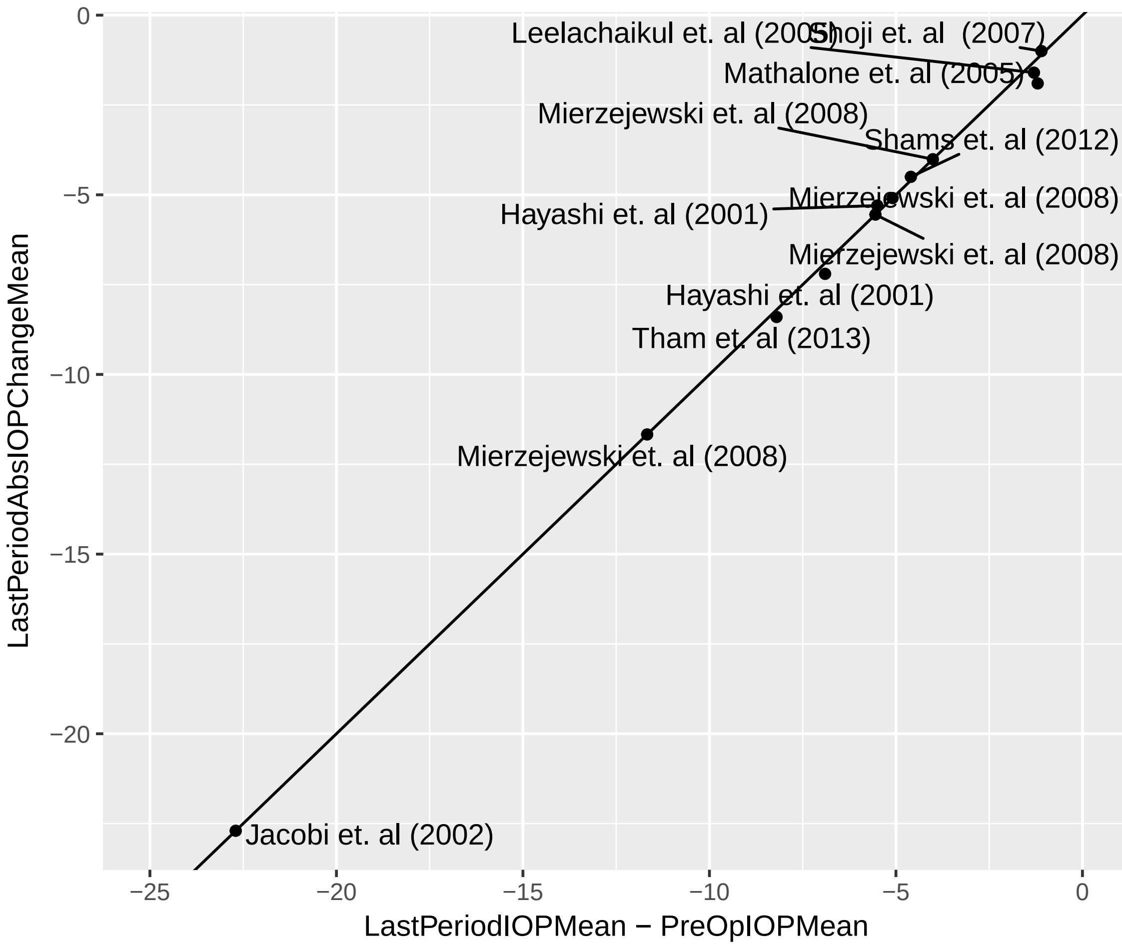
```
## Warning: Removed 59 rows containing missing values (geom_point).
```

```
## Warning: Removed 59 rows containing missing values (geom_text_repel).
```




```
ggplot(df, aes(x = LastPeriodIOPMean - PreOpIOPMean, y = LastPeriodAbsIOPChangeMean, label = study.name
  geom_point() +
  coord_cartesian(xlim=c(-25, 0)) +
  geom_abline() +
  geom_text_repel()
```

```
## Warning: Removed 55 rows containing missing values (geom_point).
## Warning: Removed 55 rows containing missing values (geom_text_repel).
```

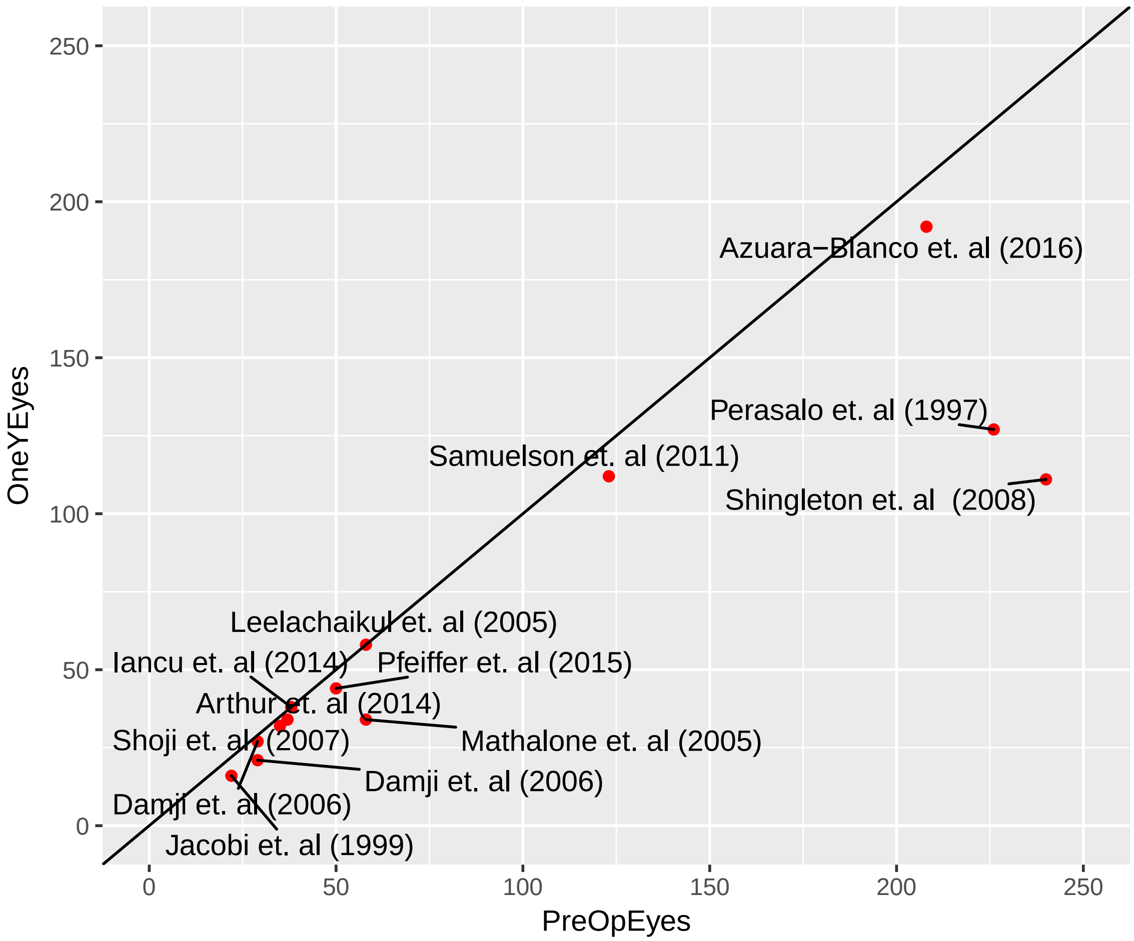



Examine loss at one year.

```
ggplot(df, aes(x=PreOpEyes, y=OneYEyes, label=study.name)) +
  geom_point(color="red") +
  geom_abline() +
  geom_text_repel() + coord_cartesian(xlim=c(0, 250), ylim=c(0, 250))
```

```
## Warning: Removed 54 rows containing missing values (geom_point).
```

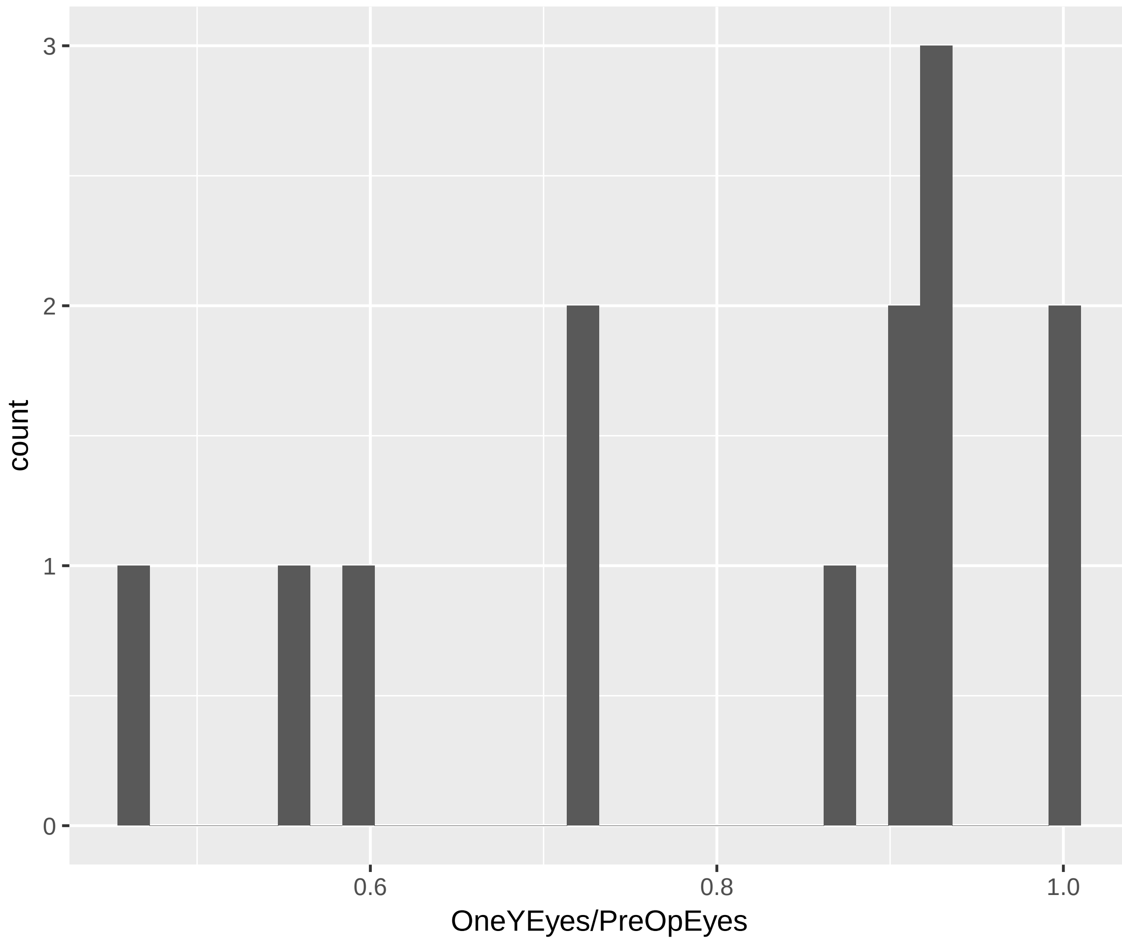
```
## Warning: Removed 54 rows containing missing values (geom_text_repel).
```




```r
ggplot(df, aes(x=OneYEyes / PreOpEyes, label=study.name)) +
  geom_histogram() +
  coord_cartesian()
```

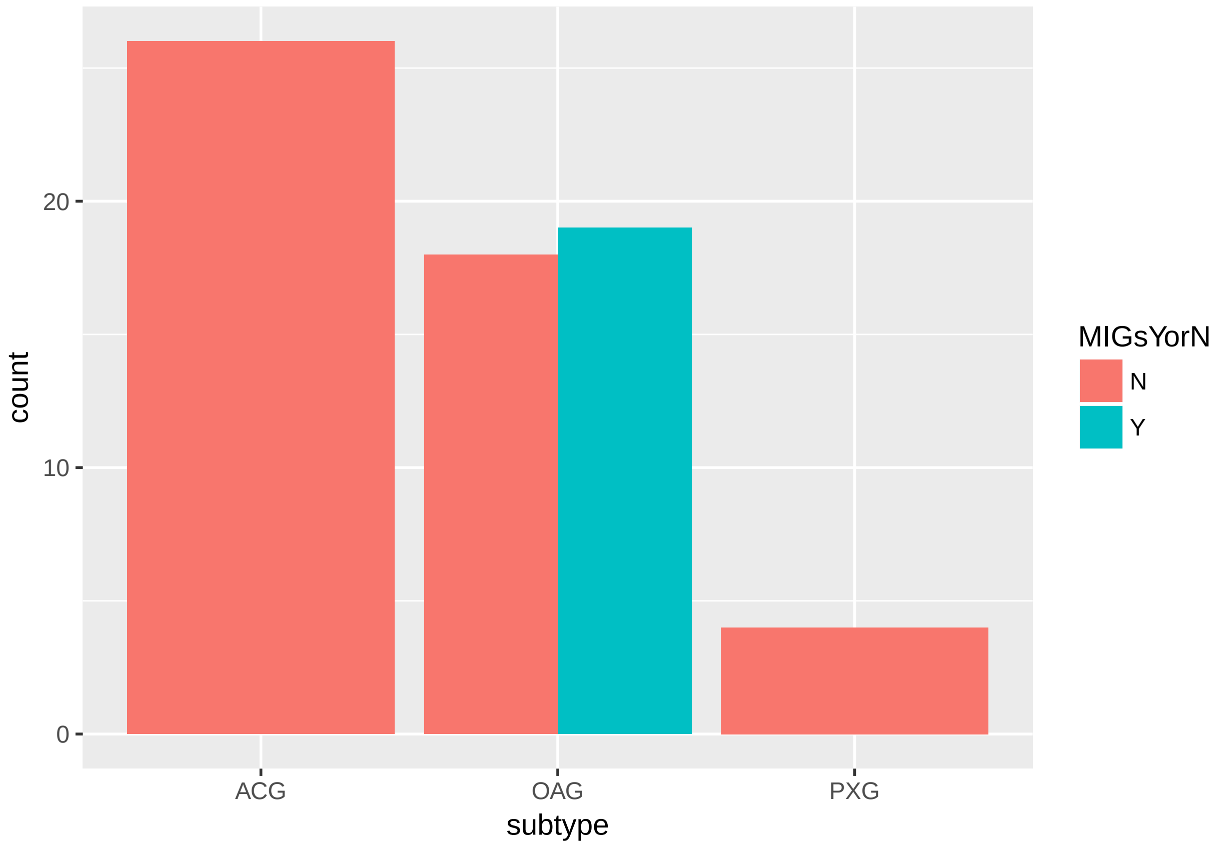
```
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```

```
## Warning: Removed 54 rows containing non-finite values (stat_bin).
```



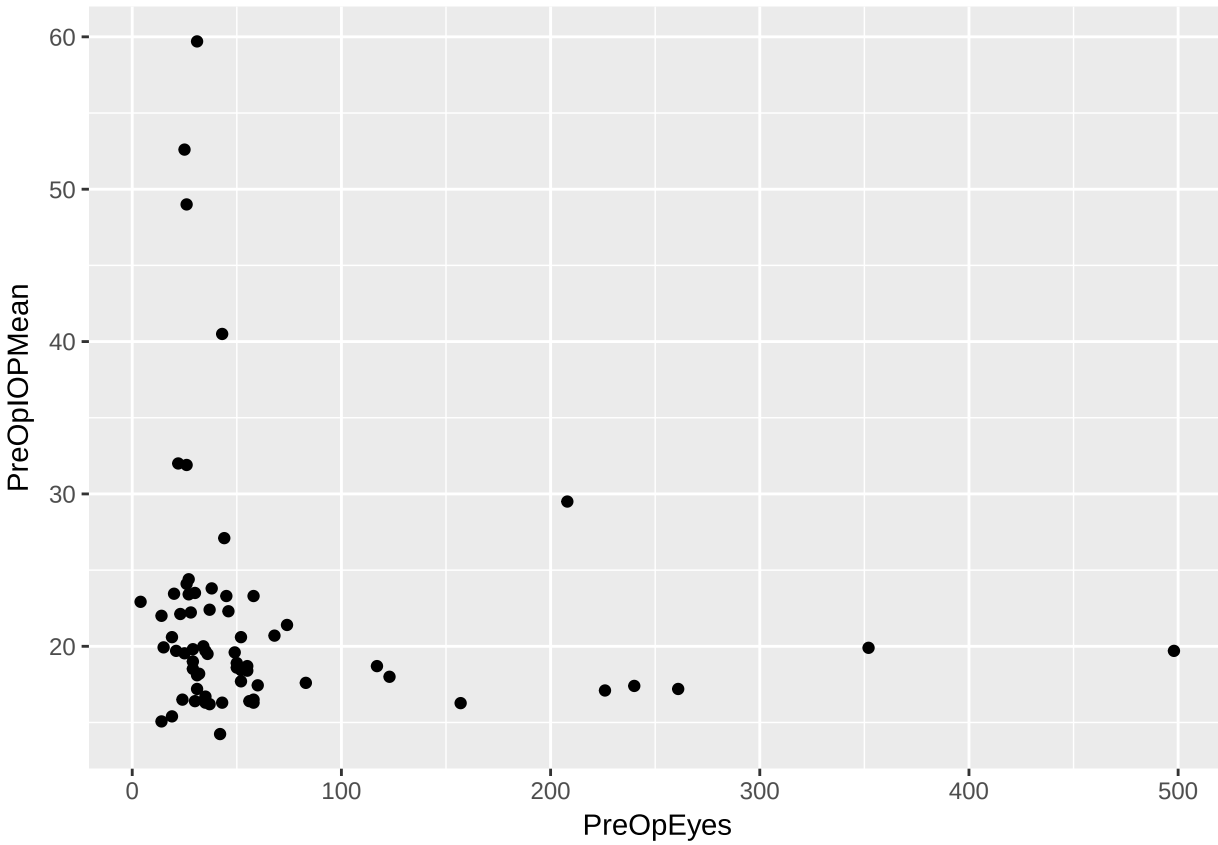

```
ggplot(df, aes(x=subtype, fill=MIGsYorN)) + geom_histogram(stat="count", position = 'dodge')
```

```
## Warning: Ignoring unknown parameters: binwidth, bins, pad
```



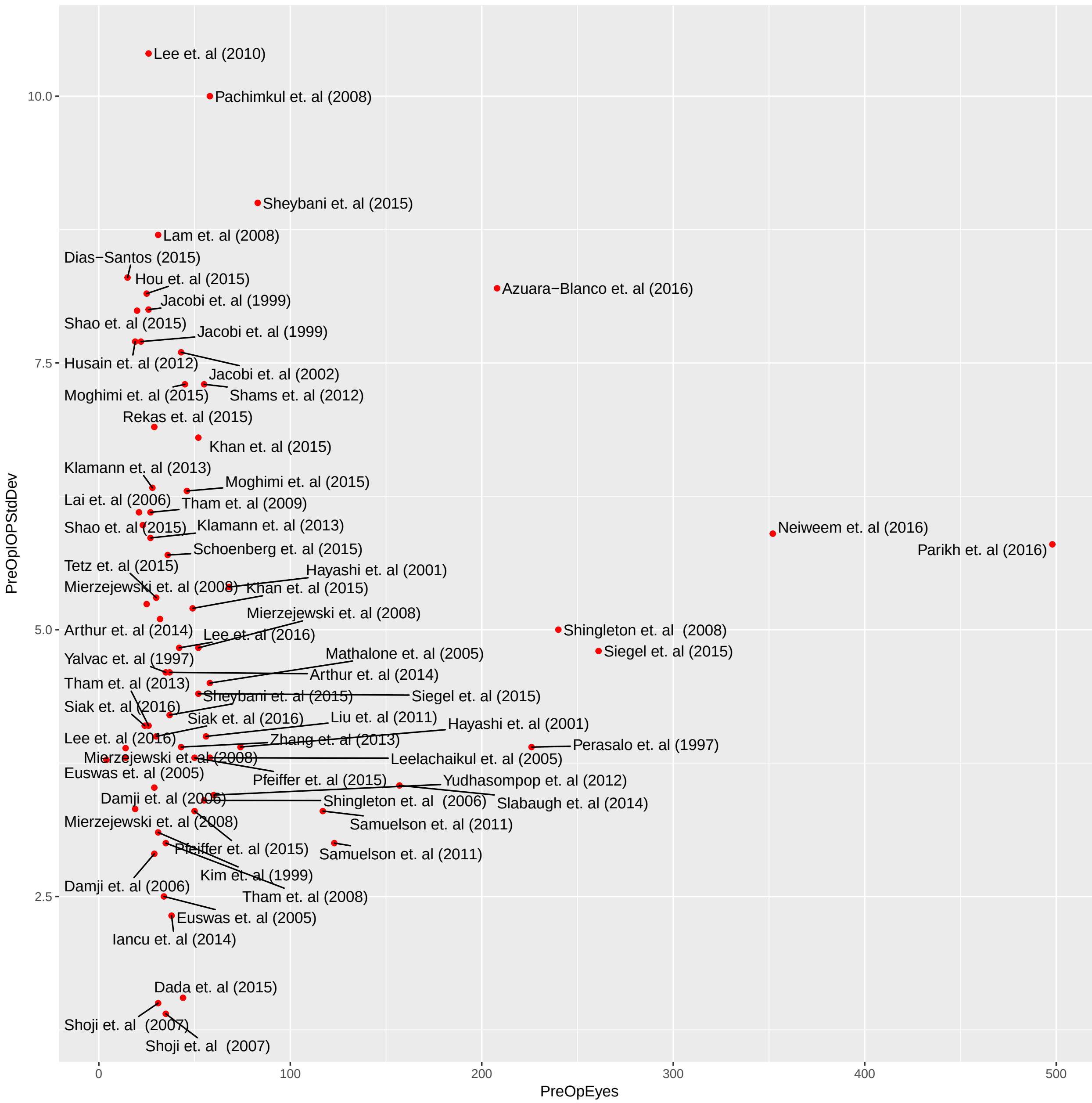

Look at the distribution of eyes and IOP means.

```
ggplot(df, aes(x=PreOpEyes, y=PreOpIOPMean)) + geom_point()
```




Look at number of eyes and standard deviation.

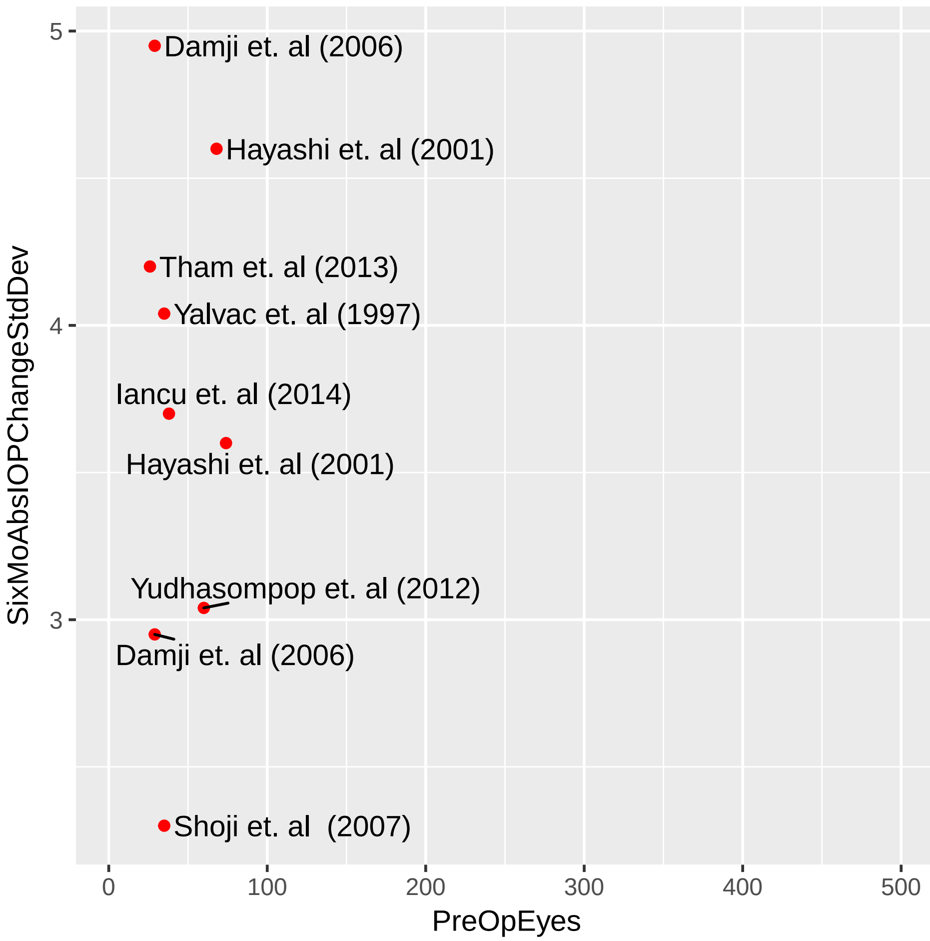
```
ggplot(df, aes(x=PreOpEyes, y=PreOpIOPStdDev, label=study.name)) + geom_point(color="red") + geom_text_
```




```
ggplot(df, aes(x=PreOpEyes, y=SixMoAbsIOPChangeStdDev, label=study.name)) + geom_point(color="red") + g
```

```
## Warning: Removed 58 rows containing missing values (geom_point).
```

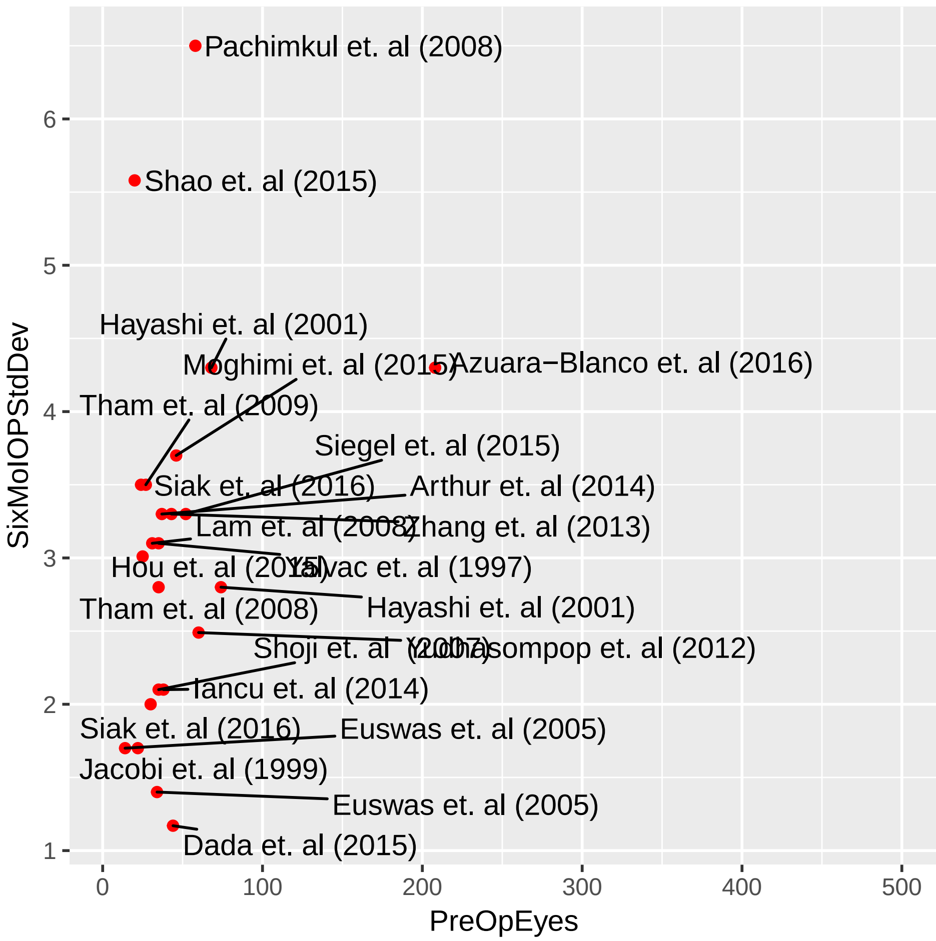
```
## Warning: Removed 58 rows containing missing values (geom_text_repel).
```




```
ggplot(df, aes(x=PreOpEyes, y=SixMoIOPStdDev, label=study.name)) + geom_point(color="red") + geom_text_r
```

```
## Warning: Removed 44 rows containing missing values (geom_point).
```

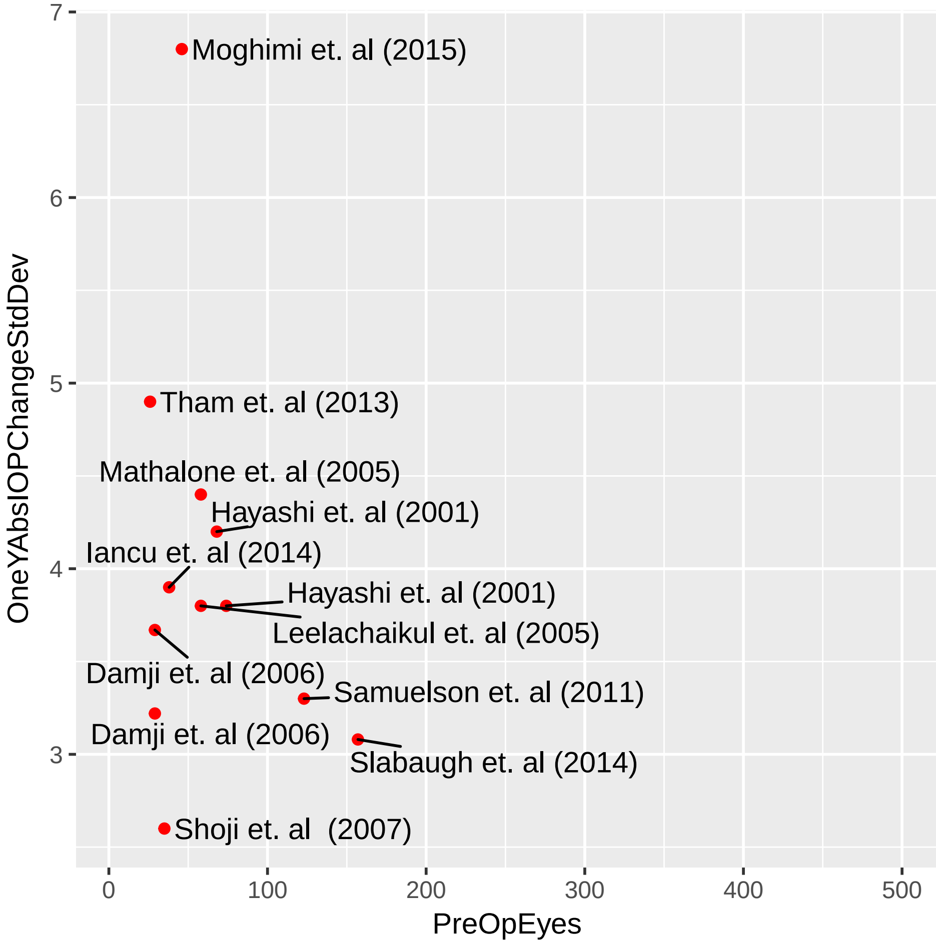
```
## Warning: Removed 44 rows containing missing values (geom_text_repel).
```




```
ggplot(df, aes(x=PreOpEyes, y=OneYAbsIOPChangeStdDev, label=study.name)) + geom_point(color="red") + ge
```

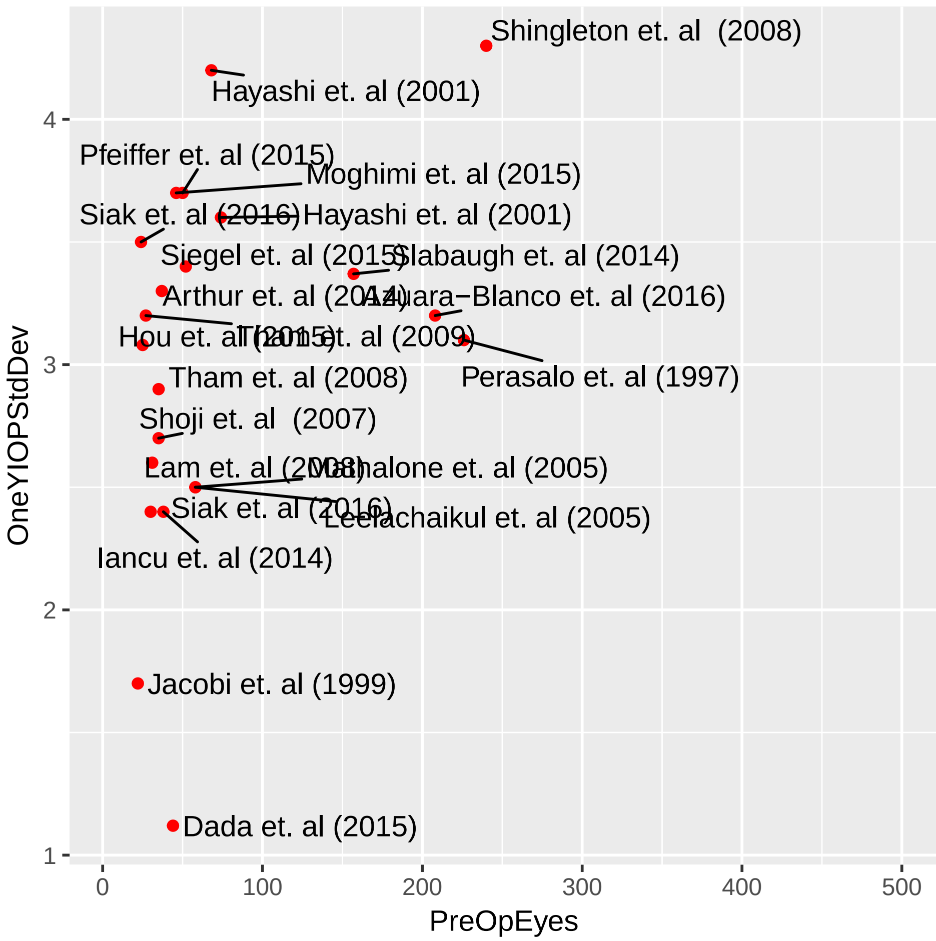
```
## Warning: Removed 55 rows containing missing values (geom_point).
```

```
## Warning: Removed 55 rows containing missing values (geom_text_repel).
```




```
ggplot(df, aes(x=PreOpEyes, y=OneYIOPStdDev, label=study.name)) + geom_point(color="red") + geom_text_r
```

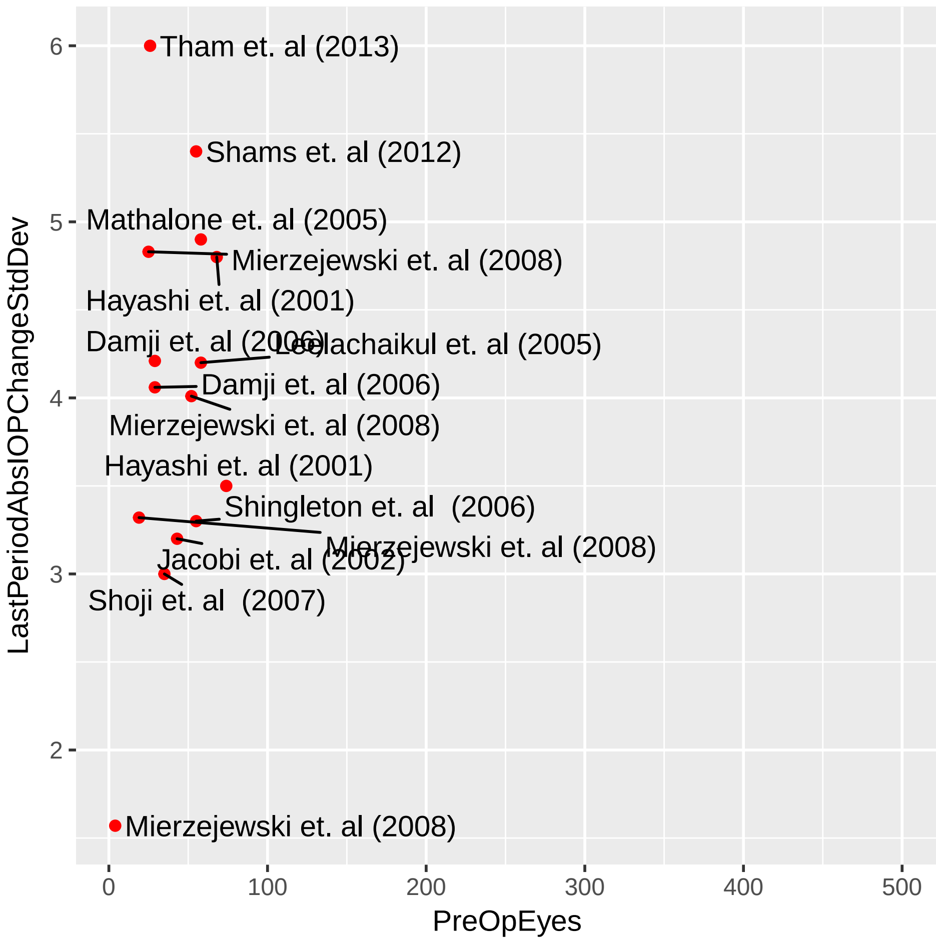
```
## Warning: Removed 45 rows containing missing values (geom_point).

## Warning: Removed 45 rows containing missing values (geom_text_repel).
```




```
ggplot(df, aes(x=PreOpEyes, y=LastPeriodAbsIOPChangeStdDev, label=study.name)) + geom_point(color="red")
```

```
## Warning: Removed 52 rows containing missing values (geom_point).
```

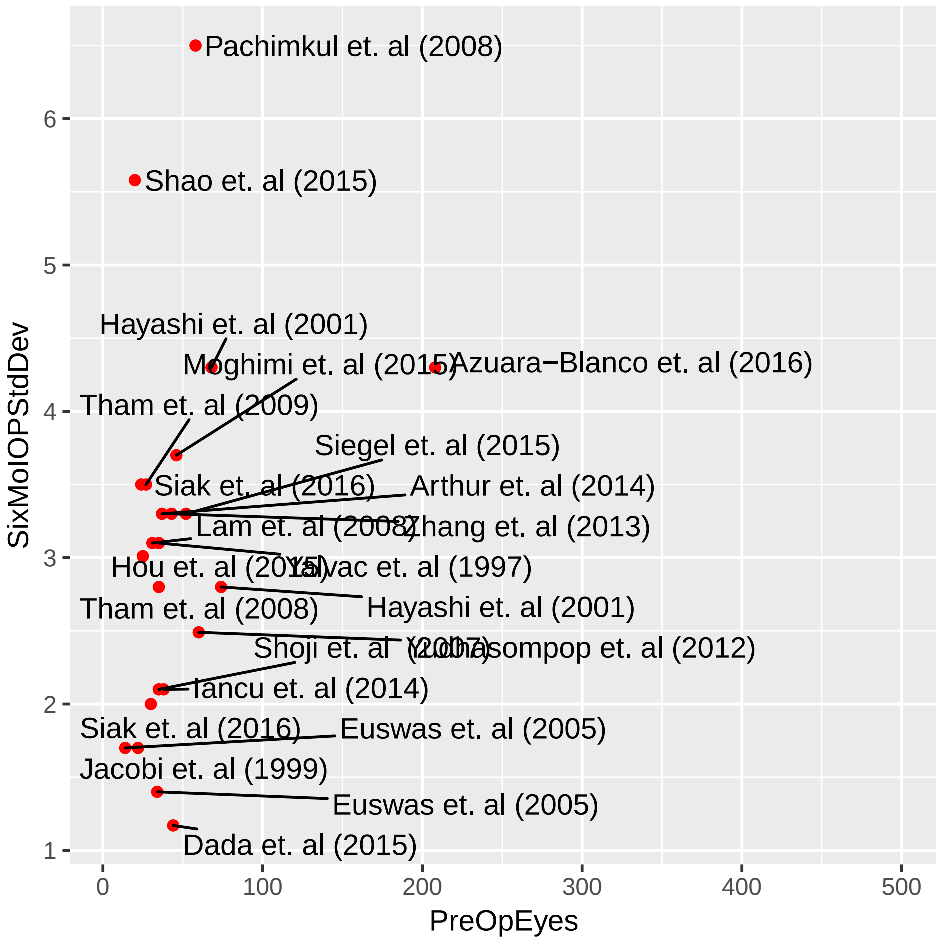
```
## Warning: Removed 52 rows containing missing values (geom_text_repel).
```




```
ggplot(df, aes(x=PreOpEyes, y=SixMoIOPStdDev, label=study.name)) + geom_point(color="red") + geom_text_
```

```
## Warning: Removed 44 rows containing missing values (geom_point).
```

```
## Warning: Removed 44 rows containing missing values (geom_text_repel).
```




## Some notes on the analysis and the studies

- None of the studies are randomized, except the EAGLE one – (2016) Azuara-Bianco et al., Lancet
- There's no control arm in any of the studies
- Main outcome is IOP drop
  - The older studies are phaco + glaucoma surgery
  - The new ones are phaco + MIGS - minimally invasive glaucoma surgery

### Slicings to look at

- MIGS
  - Don't look at MIGS
- Type of glaucoma:
  - OAG -> open angle glaucoma ** ~2-3mm **
  - NTG -> normal tension glaucoma ?
  - ACG -> angle closure glaucoma ** known to be effective **
  - PXG: pseudo-exfoliation ?

## Dimensions to look at - meta-regression

- Initial severity (IOP before)
- Size of study (number of eyes)
- Year

## Different outcomes

- Primary is IOP drop
  - time points 6 mo, 12 mo, (last time point)

  - most important is 12 months
- Number of meds
  - Huge confound, because it's controlled by the doctor
  - Meds themselves decrease the IOP
  - A handful of studies use washout pre and post (measuring the IOP without meds) to undo the confounding
    * EAGLE, Samuelson studies have washout
    * Lack of washout will have a tendency to decrease the apparent effectiveness of the studies
  - One med ~= 20% decrease in IOP
  - One med := decrease in quality of life
  - RxPostOpMean is at the same time as LastPeriod
- (visual acuity but it's kind of obvious)

## Additional analyses to perform

- Funnel plot for small / medium large studies
- Deal appropriately with multiple arms of same study, e.g. Damji et al., Merz…
- Deal with three forms of lossiness:
  - Absolutes reported, relatives needed
  - Can patch up using estimate of rho – sqrt(s_1 ** 2 + s_2 ** 2 - 2 * rho * s_1 * s_2)
  - Try rho = 0, rho = 0.5
  - Loss of follow-up
  - Can deal with by assuming that follow up is either MCAR or worse than MCAR
  - Try mean_delta = 0, mean_delta = -3, mean_delta = -5
  - Not all metrics reported for every study
  - Use mvmeta