

Phaco meta analysis

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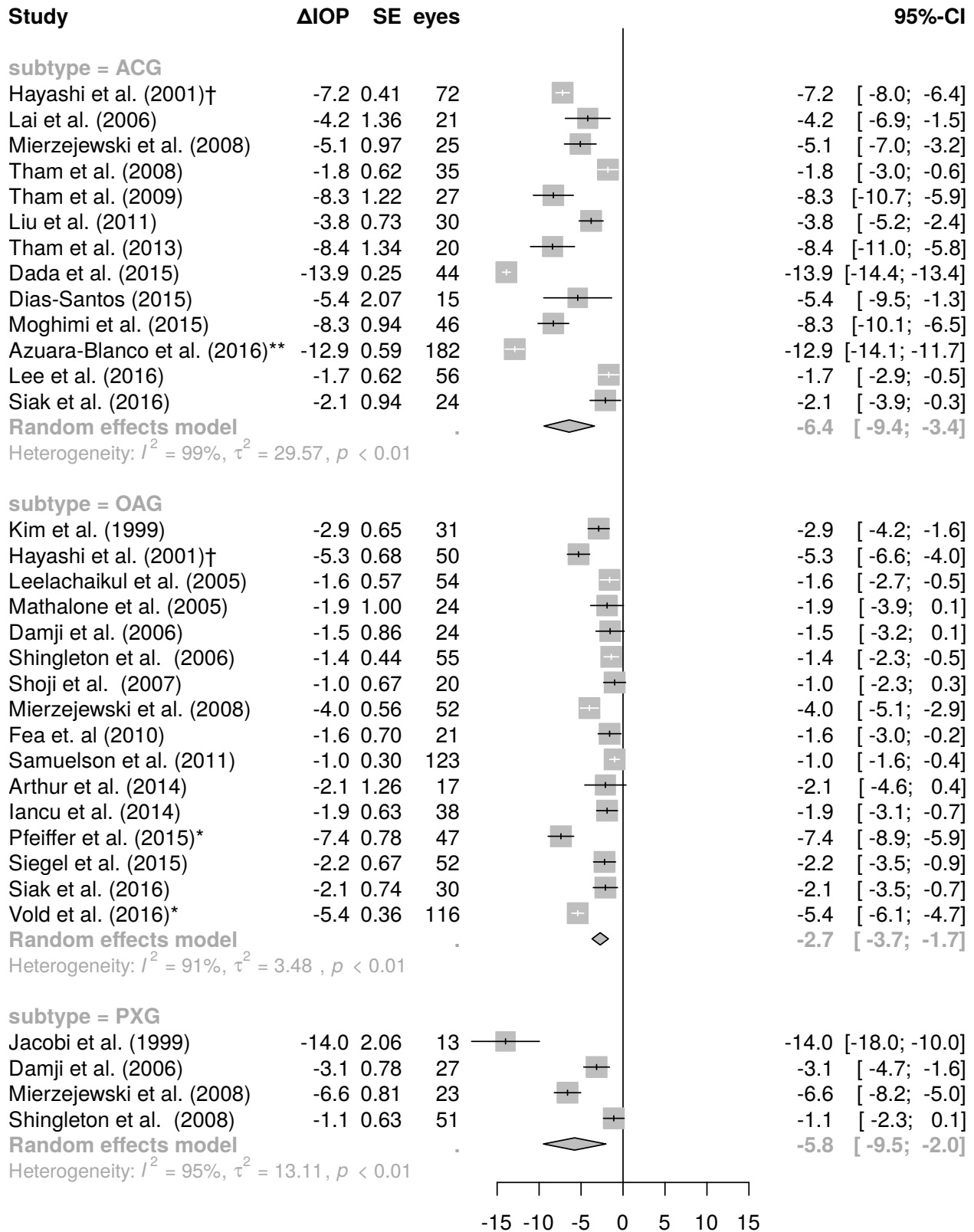
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Analysis of full dataset

Main analysis: 12-month+ follow up

```
df_ <- df %>%
  filter(!is.na(LastPeriodAbsIOPChangeMean), subtype != "AACG", MIGsYorN == 'N') %>%
  mutate(subtype=factor(subtype))
m <- metagen(LastPeriodAbsIOPChangeMean,
             LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
             study.name,
             data=df_,
             byvar=subtype,
             n.e=LastPeriodEyes)
forest(m,
       comb.fixed=FALSE,
       digits=1,
       digits.se = 2,
       overall=FALSE,
       leftcols=c("studlab", "TE", "seTE", "n.e"),
       leftlabs=c("Study", " $\Delta$ IOP", "SE", "eyes"))
```



AACG

```
df_ <- df %>%
  filter(!is.na(LastPeriodAbsIOPChangeMean), subtype == "AACG", MIGsYorN == 'N') %>%
  mutate(subtype=factor(subtype)) %>% dplyr::arrange(Year)
m <- metagen(LastPeriodAbsIOPChangeMean,
             LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
             study.name,
             data=df_,
             n.e=LastPeriodEyes, comb.fixed = FALSE)
print(m)

df_ <- df %>%
  filter(!is.na(LastPeriodAbsIOPChangeMean), subtype == "AACG", MIGsYorN == 'N') %>%
  mutate(subtype=factor(subtype)) %>% dplyr::arrange(Year)
m <- metagen(RxChangeMean,
             RxChangeStdDev / sqrt(LastPeriodEyes),
             study.name,
             data=df_,
             n.e=LastPeriodEyes, comb.fixed = FALSE)
print(m)

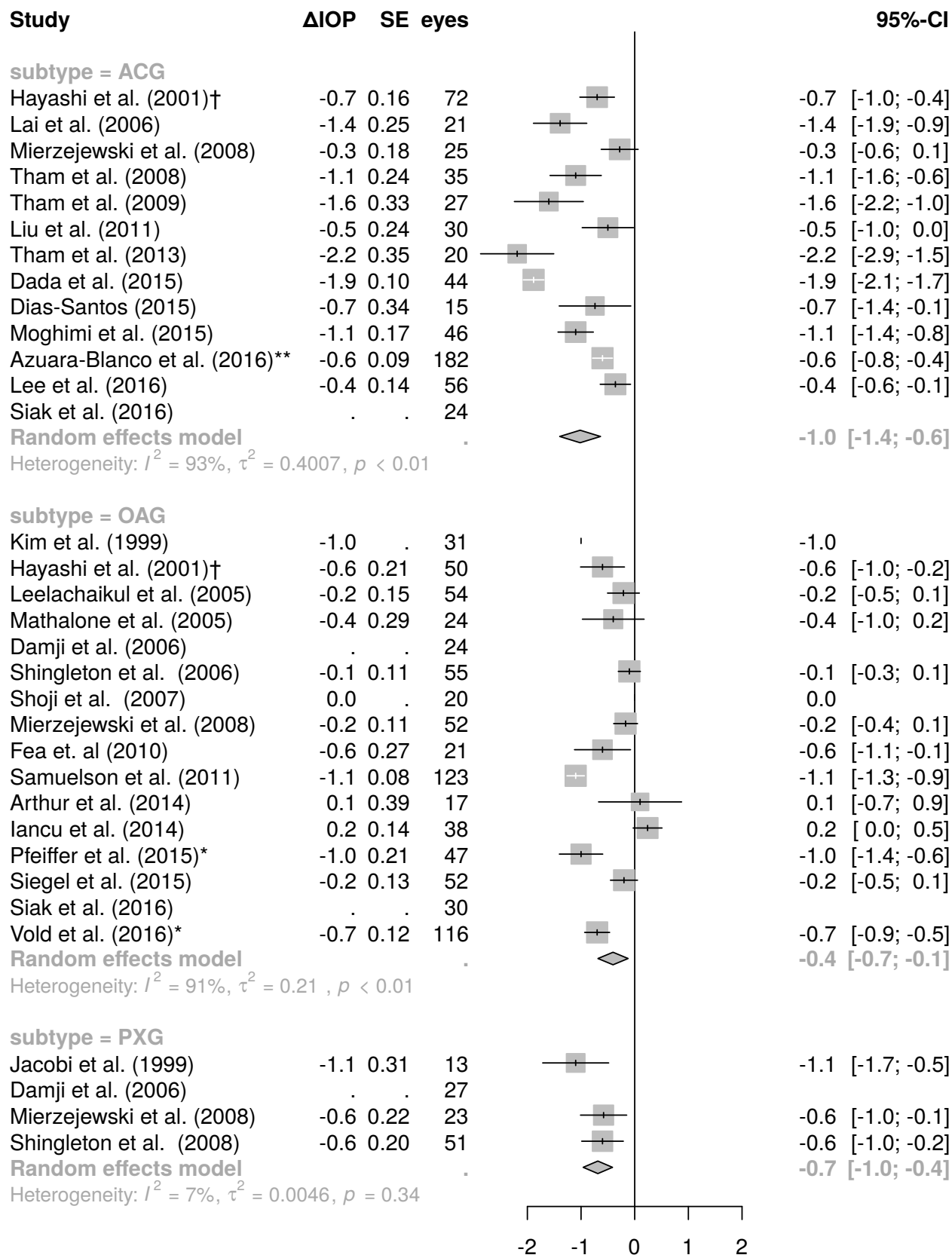
df_ %>% dplyr::select(RxPreOpMean, RxPostOpMean)
```

```
##                               95%-CI %W(random)
## Lam et al. (2008)      -47.1000 [-50.0948; -44.1052]      26.8
## Lee et al. (2010)      -35.8000 [-39.6379; -31.9621]      25.9
## Husain et al. (2012) -44.5000 [-52.0026; -36.9974]      20.6
## Hou et al. (2015)      -35.9600 [-39.0429; -32.8771]      26.7
##
## Number of studies combined: k = 4
##
##                               95%-CI      z  p-value
## Random effects model -40.665 [-47.1528; -34.1772] -12.28 < 0.0001
##
## Quantifying heterogeneity:
## tau^2 = 38.5307; H = 3.36 [2.26; 4.99]; I^2 = 91.1% [80.4%; 96.0%];
## Rb = 87.9% [68.9%; 100.0%]
##
## Test of heterogeneity:
##      Q d.f.  p-value
## 33.84    3 < 0.0001
##
## Details on meta-analytical method:
## - Inverse variance method
## - DerSimonian-Laird estimator for tau^2
##                               95%-CI %W(random)
## Lam et al. (2008)      -0.3600 [-0.5876; -0.1324]      100.0
## Lee et al. (2010)              NA                      0.0
## Husain et al. (2012)              NA                      0.0
## Hou et al. (2015)              NA                      0.0
##
## Number of studies combined: k = 1
```

```
##
##                               95%-CI      z  p-value
## Random effects model -0.36 [-0.5876; -0.1324] -3.10  0.0019
##
## Quantifying heterogeneity:
## tau^2 = 0; H = NA; I^2 = NA;
## Rb = NA
##
## Details on meta-analytical method:
## - Inverse variance method
## - DerSimonian-Laird estimator for tau^2
## RxPreOpMean RxPostOpMean
## 1          0.39          0.03
## 2           NA          0.10
## 3           NA           NA
## 4           NA          0.48
```

Meds

```
df_ <- df %>%
  filter(!is.na(LastPeriodAbsIOPChangeMean),
         df$subtype != "AACG", MIGsYorN == 'N') %>%
  mutate(subtype=factor(subtype))
m <- metagen(RxChangeMean,
             RxChangeStdDev / sqrt(LastPeriodEyes),
             study.name,
             data=df_,
             byvar=subtype,
             n.e=LastPeriodEyes)
forest(m,
       comb.fixed=FALSE,
       digits=1,
       digits.se = 2,
       overall=FALSE,
       leftcols=c("studlab", "TE", "seTE", "n.e"),
       leftlabs=c("Study", "ΔIOP", "SE", "eyes"))
```



Correlation between meds and drop in IOP

How is IOP drop related to change in meds? Two hypotheses:

- Those studies that see the largest IOP drops also have drop in meds, as doctors see that can use the newfound *slack* to decrease the number of meds people take
- The studies that see the largest IOP drops are those that don't change meds, because dropping meds would also increase IOP

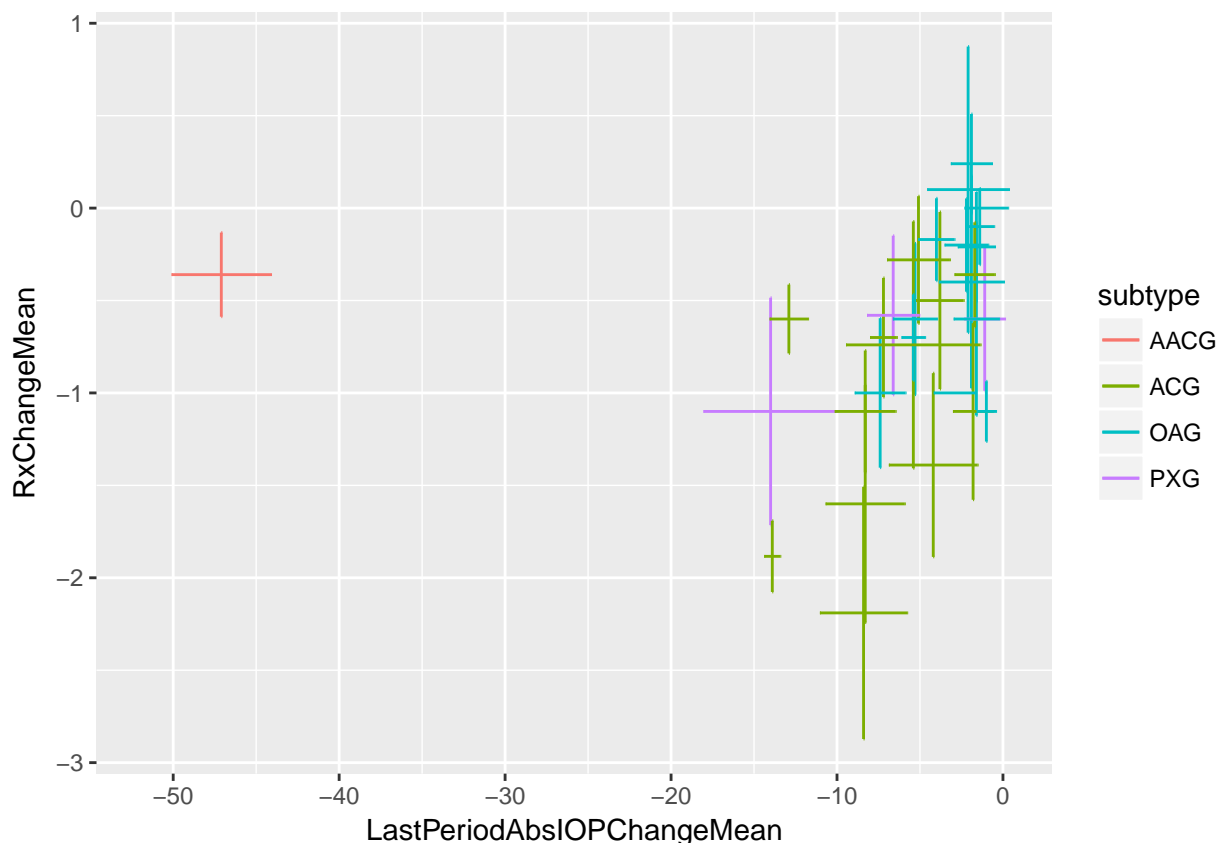
So which is it?

```
df_ <- df %>% mutate(RxChangeSEM = RxChangeStdDev / sqrt>LastPeriodEyes),
                    LastPeriodAbsIOPChangeSEM = LastPeriodAbsIOPChangeStdDev / sqrt>LastPeriodEyes))

ggplot(df_, aes(x =LastPeriodAbsIOPChangeMean,
                xmin=LastPeriodAbsIOPChangeMean - 1.96*LastPeriodAbsIOPChangeSEM,
                xmax=LastPeriodAbsIOPChangeMean + 1.96*LastPeriodAbsIOPChangeSEM,
                y =RxChangeMean,
                ymin=RxChangeMean - 1.96*RxChangeSEM,
                ymax=RxChangeMean + 1.96*RxChangeSEM,
                color=subtype
            )) + geom_errorbar() + geom_errorbarh()
```

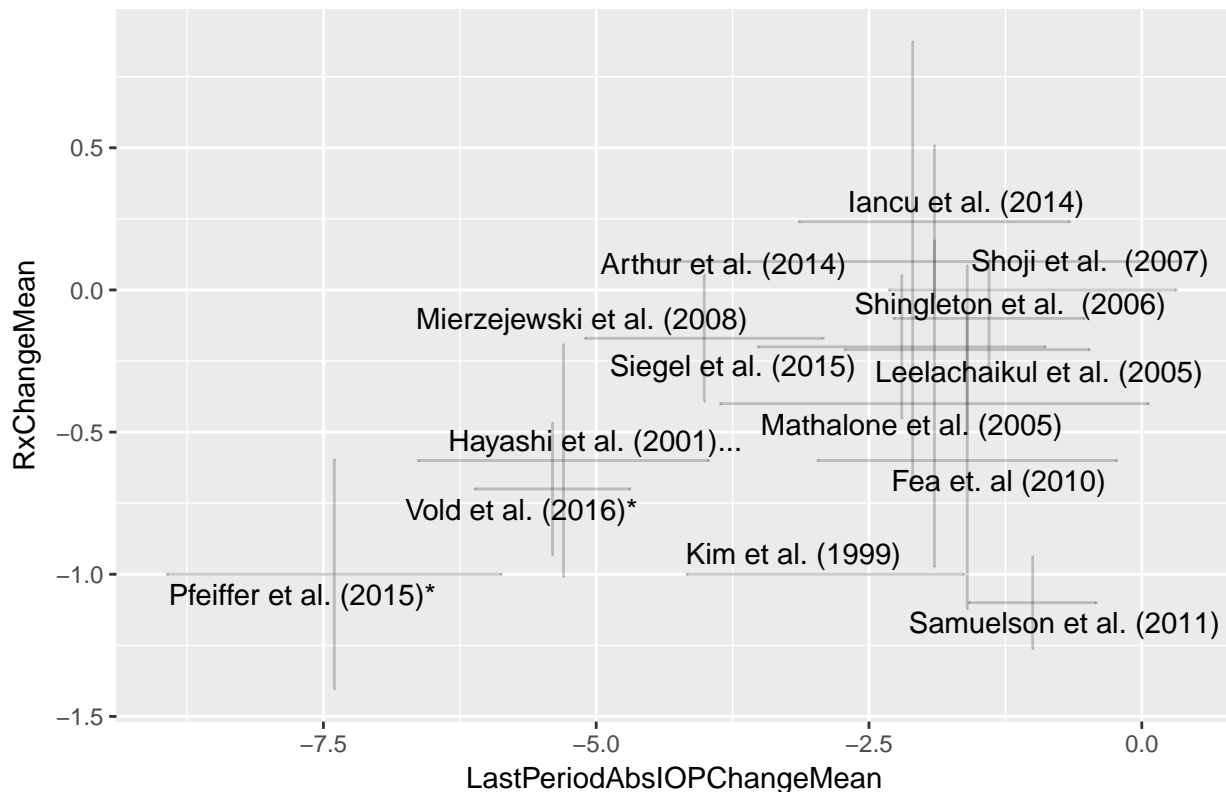
```
## Warning: Removed 17 rows containing missing values (geom_errorbar).
```

```
## Warning: Removed 15 rows containing missing values (geom_errorbarh).
```



```
ggplot(df_ %>% filter(subtype=='OAG' & MIGsYorN == 'N'),
  aes(x =LastPeriodAbsIOPChangeMean,
    xmin=LastPeriodAbsIOPChangeMean - 1.96*LastPeriodAbsIOPChangeSEM,
    xmax=LastPeriodAbsIOPChangeMean + 1.96*LastPeriodAbsIOPChangeSEM,
    y =RxChangeMean,
    ymin=RxChangeMean - 1.96*RxChangeSEM,
    ymax=RxChangeMean + 1.96*RxChangeSEM,
    label=study.name
  )) + geom_errorbar(alpha=.2) + geom_errorbarh(alpha=.2) + ggtitle('OAG only') + geom_text_repel
```

OAG only



There is an apparent positive correlation between the two effect sizes: studies with larger drops in IOP also tend to see larger drops in Rx.

```
draw.corr <- function(x.mean, x.sem, y.mean, y.sem) {
  d_ <- data.frame(x = rnorm(n = length(x.mean), mean=x.mean, sd = x.sem),
    y = rnorm(n = length(x.mean), mean=y.mean, sd = y.sem))
  with(d_ %>% filter(!is.na(x) & !is.na(y)), cor(x, y))
}

cat("Mean +- SE correlation, all studies\n")
```

```
## Mean +- SE correlation, all studies
```

```
df_ <- df %>% filter(subtype=='OAG', MIGsYorN == 'N')
drawn.corr <- with(df_, replicate(n = 100,
  draw.corr(LastPeriodAbsIOPChangeMean,
```



```

LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
RxChangeMean,
RxChangeStdDev / sqrt(LastPeriodEyes)))
mean(drawn.corrs)

## [1] 0.3812048

sd(drawn.corrs)

## [1] 0.1348602

cat("Mean +- SE correlation, no washout\n")

## Mean +- SE correlation, no washout

df_ <- filter.data(df, 'nowashout') %>% filter(subtype=='OAG', MIGsYorN == 'N')
drawn.corrs <- with(df_, replicate(n = 100,
                                draw.corr(LastPeriodAbsIOPChangeMean,
                                           LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
                                           RxChangeMean,
                                           RxChangeStdDev / sqrt(LastPeriodEyes))))
mean(drawn.corrs)

## [1] -0.02253974

sd(drawn.corrs)

## [1] 0.1941081

```

However, this effect goes away when we focus on the studies which don't have washout.

Separate meta-analysis for each time period

```
df <- read.data(fill.last = FALSE)
```

6 month follow-up

```

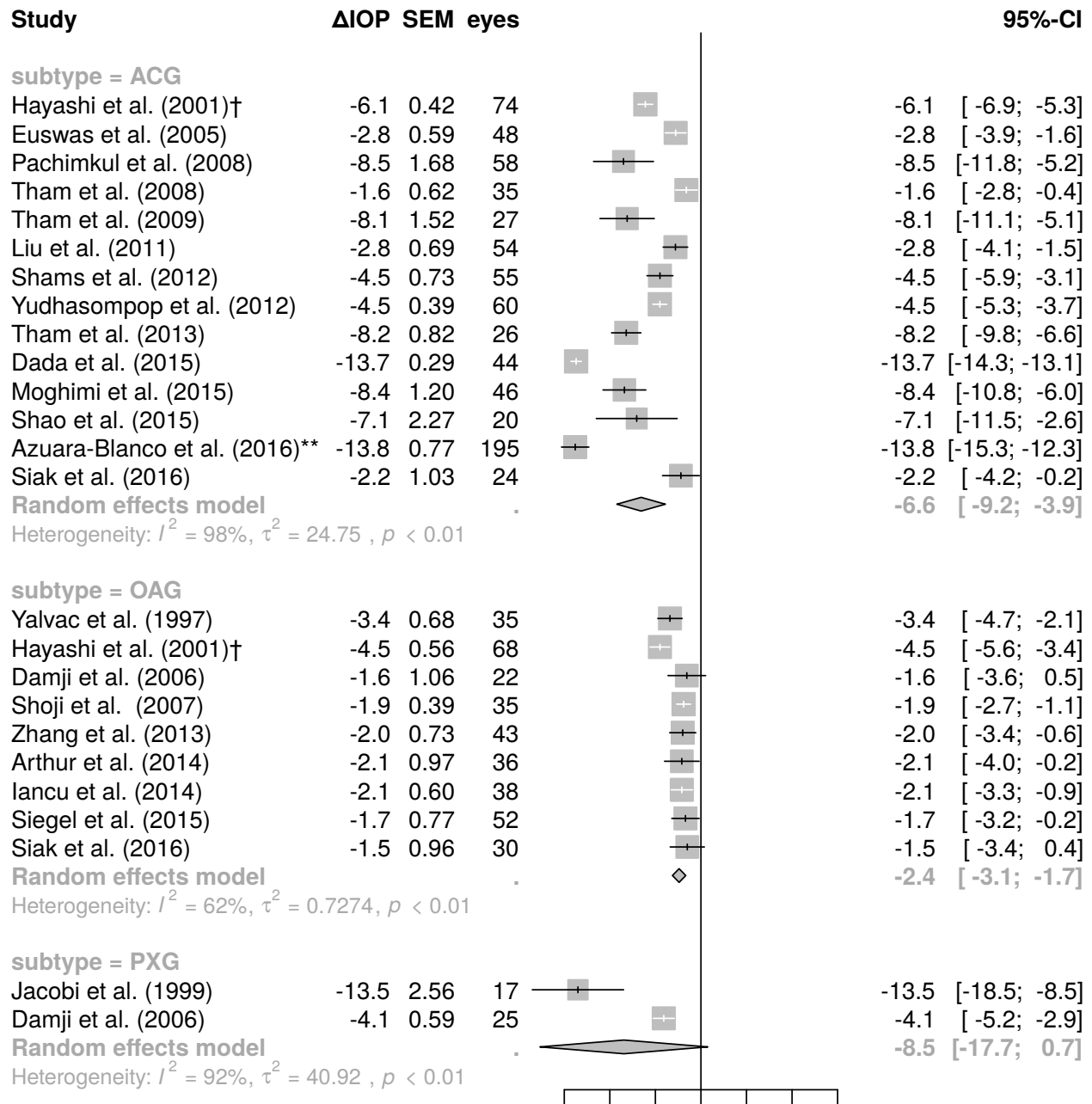
df_ <- df %>%
  filter(!is.na(SixMoAbsIOPChangeMean), subtype != "AACG") %>%
  mutate(subtype=factor(subtype))
m <- metagen(SixMoAbsIOPChangeMean,
             SixMoAbsIOPChangeStdDev / sqrt(SixMoEyes),
             study.name,
             data=df_,
             byvar=subtype,

```

```

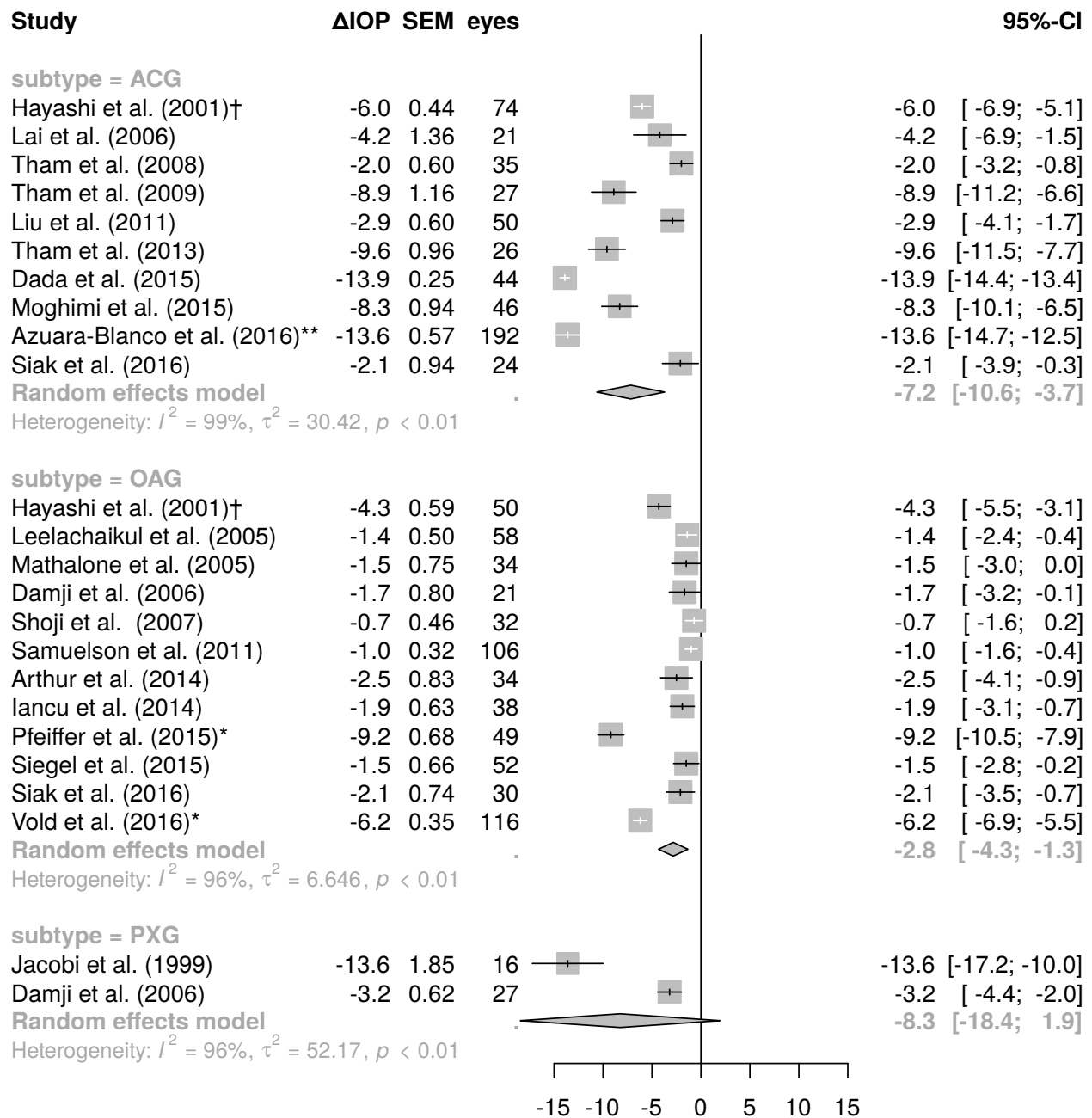
n.e=SixMoEyes)
forest(m,
  comb.fixed=FALSE,
  digits=1,
  digits.se = 2,
  overall=FALSE,
  leftcols=c("studlab", "TE", "seTE", "n.e"),
  leftlabs=c("Study", "ΔIOP", "SEM", "eyes"))

```



12-month follow up

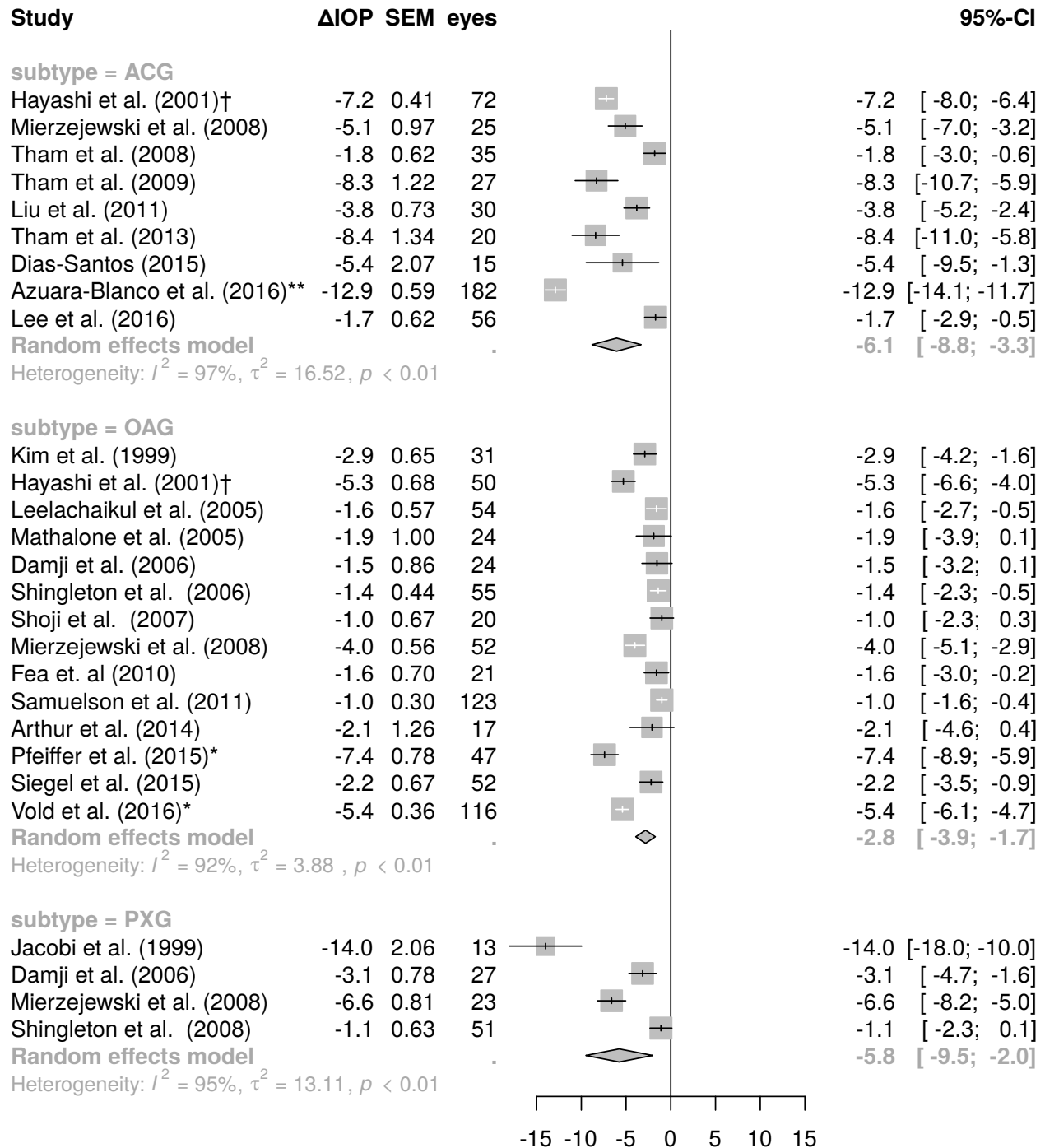
```
df_ <- df %>%
  filter(!is.na(OneYAbsIOPChangeMean), subtype != "AACG", MIGsYorN == 'N') %>%
  mutate(subtype=factor(subtype))
m <- metagen(OneYAbsIOPChangeMean,
             OneYAbsIOPChangeStdDev / sqrt(OneYEyes),
             study.name,
             data=df_,
             byvar=subtype,
             n.e=OneYEyes)
forest(m,
       comb.fixed=FALSE,
       digits=1,
       digits.se = 2,
       overall=FALSE,
       leftcols=c("studlab", "TE", "seTE", "n.e"),
       leftlabs=c("Study", " $\Delta$ IOP", "SEM", "eyes"))
```



Last period

```
df_ <- df %>%
  filter(!is.na>LastPeriodAbsIOPChangeMean), subtype != "AACG", MIGsYorN == 'N') %>%
  mutate(subtype=factor(subtype))
m <- metagen>LastPeriodAbsIOPChangeMean,
  LastPeriodAbsIOPChangeStdDev / sqrt>LastPeriodEyes),
  study.name,
  data=df_,
  byvar=subtype,
  n.e>LastPeriodEyes)
```

```
forest(m,
  comb.fixed=FALSE,
  digits=1,
  digits.se = 2,
  overall=FALSE,
  leftcols=c("studlab", "TE", "seTE", "n.e"),
  leftlabs=c("Study", "ΔIOP", "SEM", "eyes"))
```



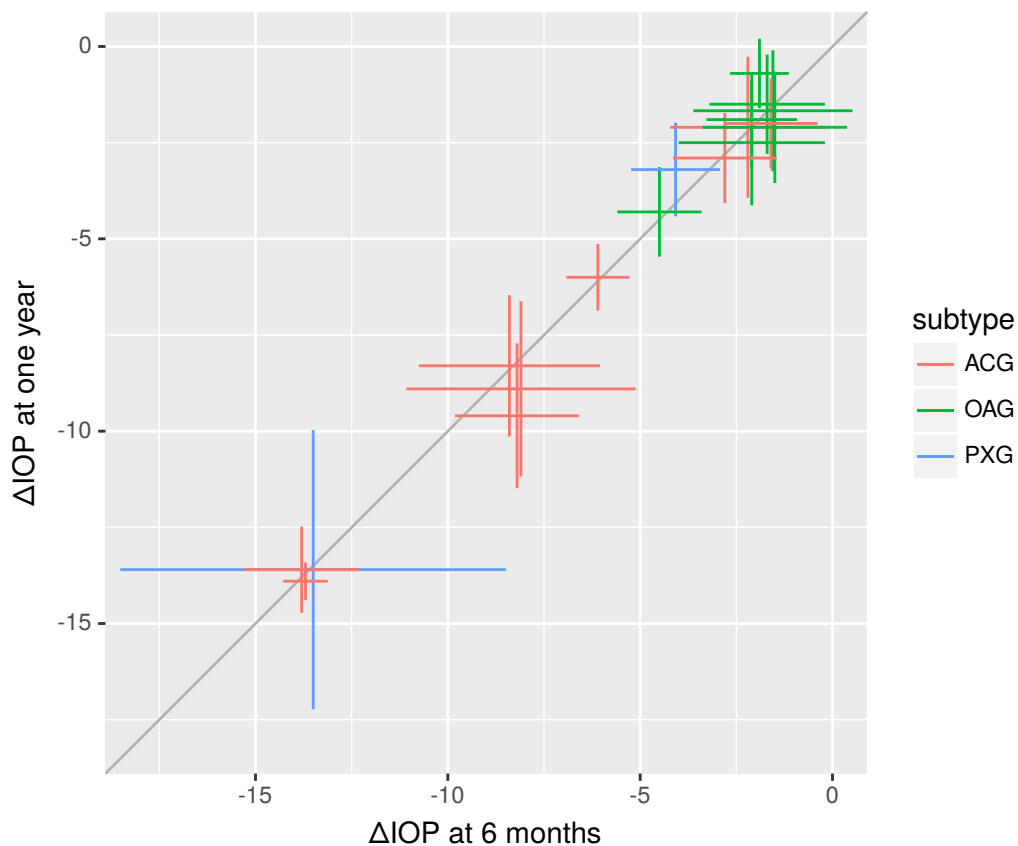
Correlation among time points

Measure the correlation between different outcomes (IOP at 6 months vs. 12 months).

```
ggplot(df %>% filter(subtype != 'AACG') %>% mutate(subtype = factor(subtype))),
  aes(x = SixMoAbsIOPChangeMean,
      xmin=SixMoAbsIOPChangeMean - 1.96*SixMoAbsIOPChangeStdDev / sqrt(SixMoEyes),
      xmax=SixMoAbsIOPChangeMean + 1.96*SixMoAbsIOPChangeStdDev / sqrt(SixMoEyes),
      y = OneYAbsIOPChangeMean,
      ymin= OneYAbsIOPChangeMean - 1.96*OneYAbsIOPChangeStdDev / sqrt(OneYEyes),
      ymax= OneYAbsIOPChangeMean + 1.96*OneYAbsIOPChangeStdDev / sqrt(OneYEyes),
      label=study.name,
      color=subtype
  )) +
  geom_abline(slope = 1, color="gray70") +
  geom_errorbar() +
  geom_errorbarh() +
  xlab('ΔIOP at 6 months') +
  ylab('ΔIOP at one year') +
  coord_fixed(xlim=c(-18, 0), ylim=c(-18,0))
```

```
## Warning: Removed 22 rows containing missing values (geom_errorbar).
```

```
## Warning: Removed 22 rows containing missing values (geom_errorbarh).
```



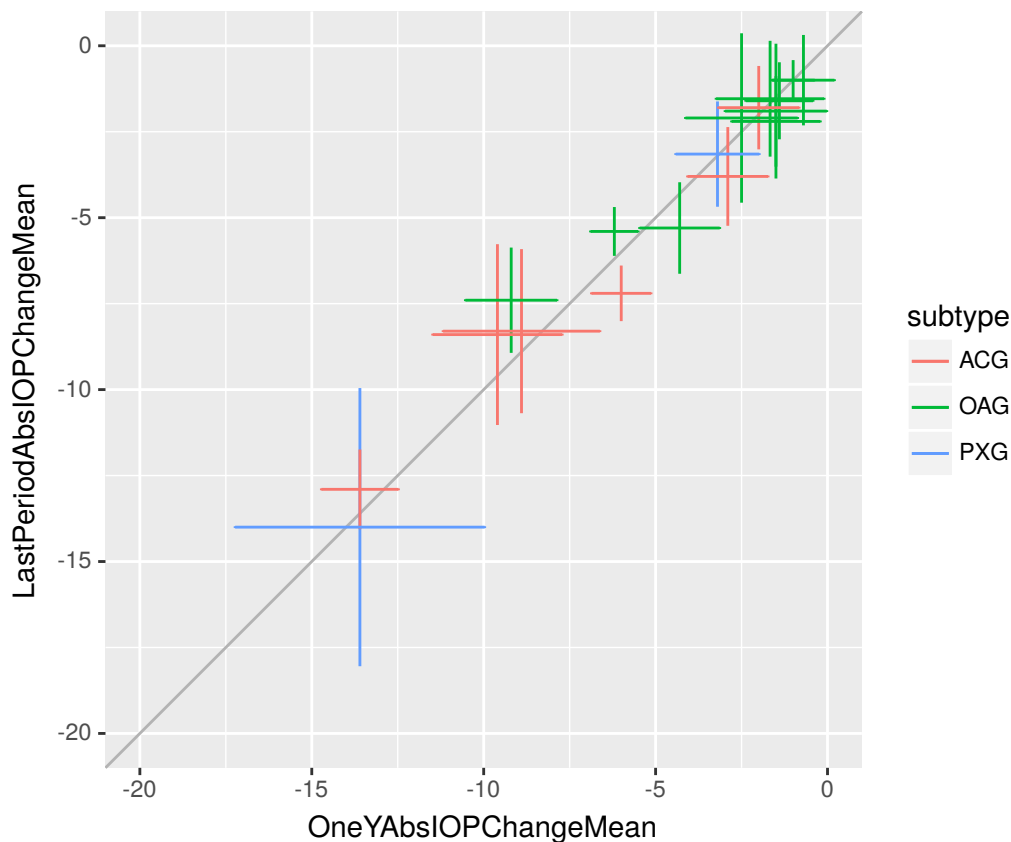
It's very clear that six months and 12 months IOP are highly correlated.

Similarly for one-year vs. last period:

```
ggplot(df %>% filter(subtype != 'AACG') %>% mutate(subtype = factor(subtype)),
  aes(y = LastPeriodAbsIOPChangeMean,
      ymin=LastPeriodAbsIOPChangeMean - 1.96*LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
      ymax=LastPeriodAbsIOPChangeMean + 1.96*LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
      x = OneYAbsIOPChangeMean,
      xmin= OneYAbsIOPChangeMean - 1.96*OneYAbsIOPChangeStdDev / sqrt(OneYEyes),
      xmax= OneYAbsIOPChangeMean + 1.96*OneYAbsIOPChangeStdDev / sqrt(OneYEyes),
      label=study.name,
      color=subtype
  )) +
  geom_abline(slope = 1, color="gray70") +
  geom_errorbar() + geom_errorbarh() +
  coord_fixed(xlim=c(-20, 0), ylim=c(-20,0))
```

```
## Warning: Removed 22 rows containing missing values (geom_errorbar).
```

```
## Warning: Removed 22 rows containing missing values (geom_errorbarh).
```



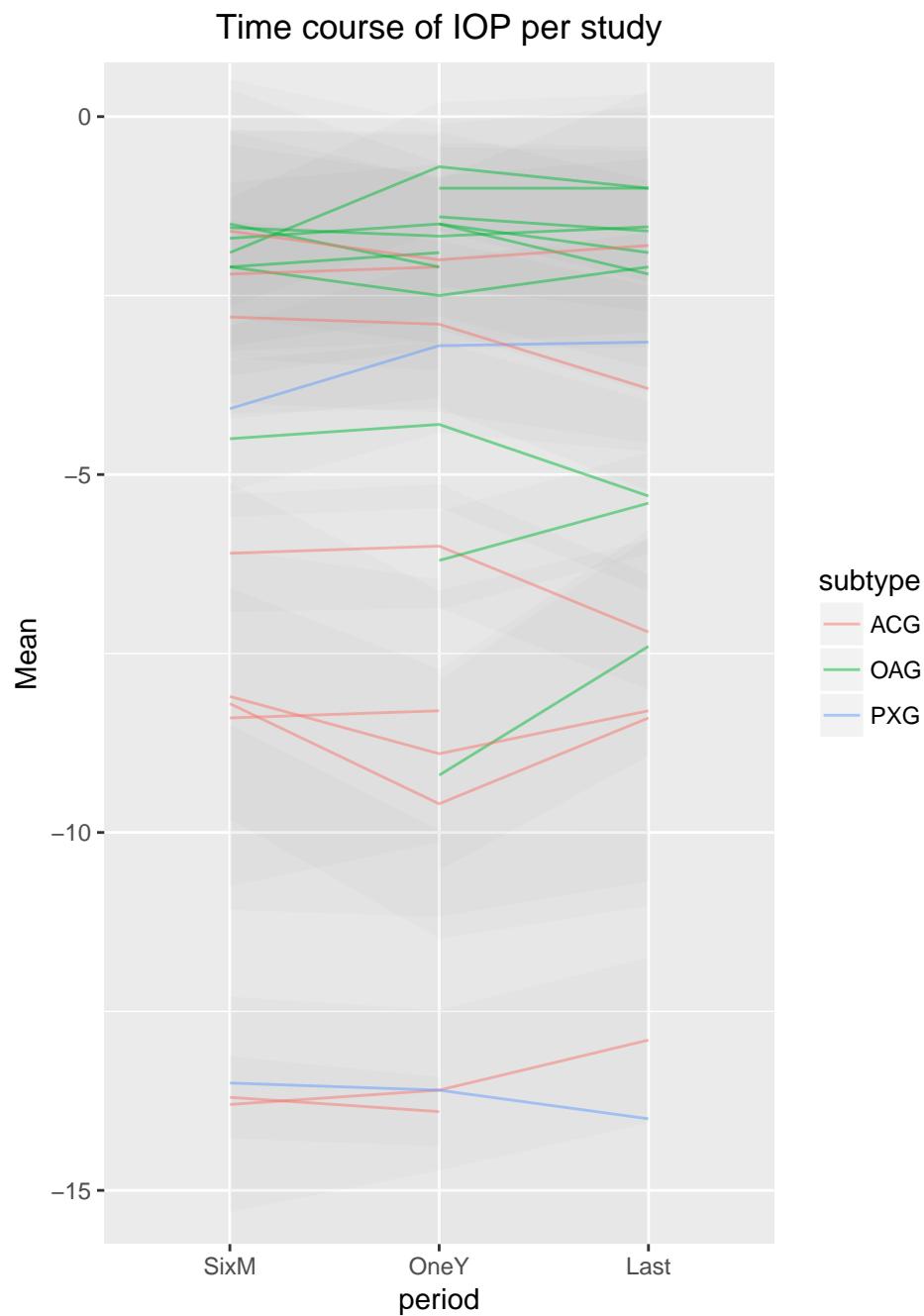
Again, correlations are very high. Present this in another way.

```
library(reshape2)
```

```
##
## Attaching package: 'reshape2'
```

```
## The following object is masked from 'package:tidyr':
##
## smiths
```

```
nd <- melt(df %>%
  filter(MIGsYorN == 'N',
    subtype != 'AACG',
    1*is.na(SixMoAbsIOPChangeMean) +
    1*is.na(OneYAbsIOPChangeMean) +
    1*is.na>LastPeriodAbsIOPChangeMean) < 2) %>%
  mutate(SixMoChangeSEM = SixMoAbsIOPChangeStdDev / sqrt(SixMoEyes),
    OneYChangeSEM = OneYAbsIOPChangeStdDev / sqrt(OneYEyes),
    LastPeriodChangeSEM = LastPeriodAbsIOPChangeStdDev / sqrt>LastPeriodEyes)) %>%
  select(study.name, subtype,
    SixMoAbsIOPChangeMean,
    OneYAbsIOPChangeMean,
    LastPeriodAbsIOPChangeMean,
    SixMoChangeSEM,
    OneYChangeSEM,
    LastPeriodChangeSEM), id.vars=c("study.name", "subtype"))
nd$metric <- substr(nd$variable, nchar(as.character(nd$variable)) - 3, nchar(as.character(nd$variable)))
nd$period <- substr(nd$variable, 0, 4)
df_ <- dcast(nd, formula = study.name + subtype + period ~ metric)
df_ <- df_ %>% mutate(period = factor(period, c('SixM', 'OneY', 'Last')),
  g = paste(study.name, as.character(subtype))) %>% filter(!is.na(Mean))
ggplot(df_, aes(y =Mean,
  ymin=Mean - 1.96*eSEM,
  ymax=Mean + 1.96*eSEM,
  x = period,
  label=study.name,
  group=g)) +
  geom_ribbon(alpha=.02) +
  geom_line(alpha=.5, aes(color=subtype)) +
  coord_cartesian(y=c(-15, 0)) + ggtitle('Time course of IOP per study') + theme(plot.title = element_t
```

It's remarkable how consistent measurements are between time periods. At most, we find a change of ± 2.5 mm Hg between the first and last period.

```
df_ <- df %>% filter(subtype=='OAG')
drawn.corr <- with(df_, replicate(n = 100,
  draw.corr(SixMoAbsIOPChangeMean,
    SixMoAbsIOPChangeStdDev / sqrt(SixMoEyes),
    OneYAbsIOPChangeMean,
    OneYAbsIOPChangeStdDev / sqrt(OneYEyes))))
cat("Mean +- SE correlation, OAG only\n")
```

```
## Mean +- SE correlation, OAG only
```

```
print(mean(drawn.corrs))
```

```
## [1] 0.6287425
```

```
print(sd(drawn.corrs))
```

```
## [1] 0.1808015
```

```
df_ <- df
drawn.corrs <- with(df_, replicate(n = 100,
                                   draw.corr(SixMoAbsIOPChangeMean,
                                              SixMoAbsIOPChangeStdDev / sqrt(SixMoEyes),
                                              OneYAbsIOPChangeMean,
                                              OneYAbsIOPChangeStdDev / sqrt(OneYEyes))))
cat("Mean +- SE correlation, All subtypes\n")
```

```
## Mean +- SE correlation, All subtypes
```

```
print(mean(drawn.corrs))
```

```
## [1] 0.9912487
```

```
print(sd(drawn.corrs))
```

```
## [1] 0.003900496
```

```
cat("Regression of one year against 6 months")
```

```
## Regression of one year against 6 months
```

```
print(summary(lm(OneYAbsIOPChangeMean ~ SixMoAbsIOPChangeMean,
                 df,
                 weights = OneYAbsIOPChangeStdDev / sqrt(OneYEyes))))
```

```
##
```

```
## Call:
```

```
## lm(formula = OneYAbsIOPChangeMean ~ SixMoAbsIOPChangeMean, data = df,
```

```
##     weights = OneYAbsIOPChangeStdDev/sqrt(OneYEyes))
```

```
##
```

```
## Weighted Residuals:
```

```
##      Min      1Q   Median      3Q      Max
```

```
## -1.54354 -0.22175  0.06606  0.24424  2.17907
```

```
##
```

```
## Coefficients:
```

```
##              Estimate Std. Error t value Pr(>|t|)
```

```
## (Intercept)    -0.18172    0.25885  -0.702    0.492
```

```
## SixMoAbsIOPChangeMean  0.98209    0.01326  74.083 <2e-16 ***
```

```
## ---
```

```
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.8044 on 18 degrees of freedom
## (25 observations deleted due to missingness)
## Multiple R-squared:  0.9967, Adjusted R-squared:  0.9965
## F-statistic: 5488 on 1 and 18 DF,  p-value: < 2.2e-16
```

This is also reflected in the correlations - even accounting for noise, the correlations are $> .9$ between month 6 and month 12.

Multivariate inference

Let's use `mvmeta` to infer the effect size for all periods together.

```
library(mvmeta)
```

```
## This is mvmeta 0.4.7. For an overview type: help('mvmeta-package').
```

```
fill.na <- function(x, y, z) {
  return(ifelse(!is.na(x),
                x,
                ifelse(is.na(y),
                      z,
                      ifelse(is.na(z),
                            y,
                            sqrt((y**2 + z**2) / 2 )))))
}

get.correlation.matrices.tri <- function(x, y, z, assumed.rho) {
  S <- list()
  for(i in 1:length(x)) {
    xx <- fill.na(x[i], y[i], z[i])
    yy <- fill.na(y[i], x[i], z[i])
    zz <- fill.na(z[i], x[i], y[i])
    S[[i]] <- matrix(c(xx ** 2, xx * yy * assumed.rho, xx * zz * assumed.rho ** 2,
                      xx * yy * assumed.rho, yy ** 2, zz * yy * assumed.rho,
                      xx * zz * assumed.rho ** 2, zz * yy * assumed.rho, zz * zz), ncol=3)
  }
  S
}

df_ <- df %>% filter(!is.na>LastPeriodAbsIOPChangeStdDev) |
  !is.na(SixMoAbsIOPChangeStdDev) |
  !is.na(OneYAbsIOPChangeStdDev), subtype %in% c('OAG', 'ACG'), MIGsYorN == 'N')

thefit <- mvmeta(cbind(SixMoAbsIOPChangeMean, OneYAbsIOPChangeMean, LastPeriodAbsIOPChangeMean) ~ subtype,
  S=get.correlation.matrices.tri(df_$SixMoAbsIOPChangeStdDev / sqrt(df_$SixMoEyes),
                                df_$OneYAbsIOPChangeStdDev / sqrt(df_$OneYEyes),
                                df_$LastPeriodAbsIOPChangeStdDev / sqrt(df_$LastPeriodEyes), .7),
  data=df_,
  method="reml")
```

```
summary(thefit)
```

```
## Call: mvmeta(formula = cbind(SixMoAbsIOPChangeMean, OneYAbsIOPChangeMean,
##   LastPeriodAbsIOPChangeMean) ~ subtype, S = get.correlation.matrices.tri(df_$SixMoAbsIOPChangeStdDev/
##   df_$OneYAbsIOPChangeStdDev/sqrt(df_$OneYEyes), df_$LastPeriodAbsIOPChangeStdDev/sqrt(df_$LastPeriod
##   0.7), data = df_, method = "reml")
##
## Multivariate random-effects meta-regression
## Dimension: 3
## Estimation method: REML
##
## Fixed-effects coefficients
## SixMoAbsIOPChangeMean :
##           Estimate Std. Error      z Pr(>|z|) 95%ci.lb 95%ci.ub
## (Intercept)  -5.9092    0.7536 -7.8415  0.0000  -7.3862  -4.4322
## subtypeOAG    2.9191    1.0558  2.7648  0.0057   0.8497   4.9884
##
## (Intercept) ***
## subtypeOAG    **
## OneYAbsIOPChangeMean :
##           Estimate Std. Error      z Pr(>|z|) 95%ci.lb 95%ci.ub
## (Intercept)  -6.0973    0.7637 -7.9839  0.0000  -7.5941  -4.6004
## subtypeOAG    3.3817    1.0607  3.1882  0.0014   1.3028   5.4606
##
## (Intercept) ***
## subtypeOAG    **
## LastPeriodAbsIOPChangeMean :
##           Estimate Std. Error      z Pr(>|z|) 95%ci.lb 95%ci.ub
## (Intercept)  -6.2665    0.6835 -9.1681  0.0000  -7.6061  -4.9268
## subtypeOAG    3.5782    0.9378  3.8157  0.0001   1.7402   5.4162
##
## (Intercept) ***
## subtypeOAG    ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Between-study random-effects (co)variance components
## Structure: General positive-definite
##
##           Std. Dev      Corr
## SixMoAbsIOPChangeMean  2.9873 SixMoAbsIOPChangeMean
## OneYAbsIOPChangeMean   3.0257      0.9969
## LastPeriodAbsIOPChangeMean 2.6062      0.9901
##
## SixMoAbsIOPChangeMean      OneYAbsIOPChangeMean
## OneYAbsIOPChangeMean
## LastPeriodAbsIOPChangeMean      0.9823
##
## Multivariate Cochran Q-test for residual heterogeneity:
## Q = 1520.2986 (df = 62), p-value = 0.0000
## I-square statistic = 95.9%
##
## 36 studies, 68 observations, 6 fixed and 6 random-effects parameters
##      logLik      AIC      BIC
```

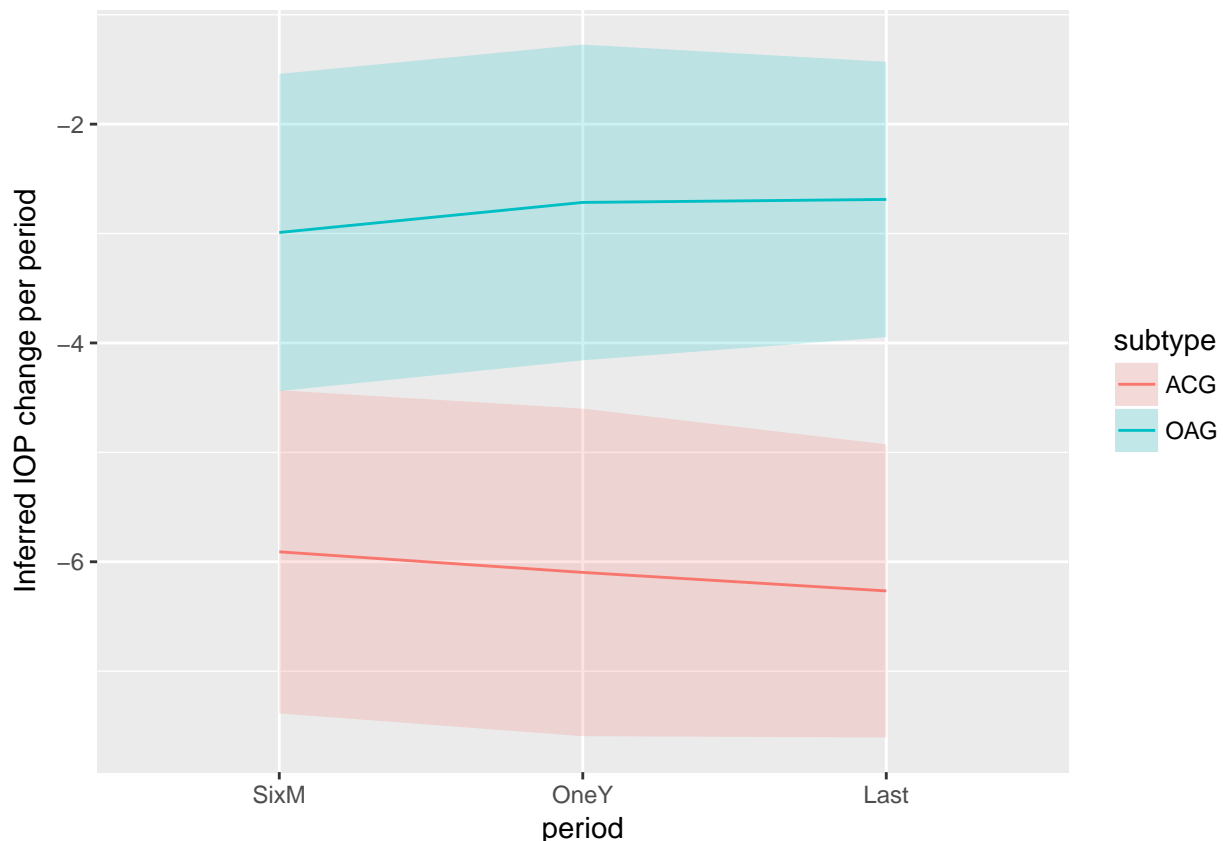
```
## -118.9294    261.8587    287.3844
```

```
newdata <- data.frame(subtype=c('OAG', 'ACG'))
pred <- predict(theft, newdata, se=TRUE)
newdata$SixMoAbsIOPChangeMean <- pred$fit[,1]
newdata$OneYAbsIOPChangeMean <- pred$fit[,2]
newdata$LastPeriodAbsIOPChangeMean <- pred$fit[,3]
newdata$SixMoAbsIOPChangeSEM <- pred$se[,1]
newdata$OneYAbsIOPChangeSEM <- pred$se[,2]
newdata$LastPeriodAbsIOPChangeSEM <- pred$se[,3]
```

```
library(reshape2)
nd <- melt(newdata)
```

```
## Using subtype as id variables
```

```
nd$period <- substr(nd$variable, 0, 4)
nd$metric <- substr(nd$variable, nchar(as.character(nd$variable)) - 3, nchar(as.character(nd$variable)))
df_ <- dcast(nd, formula = subtype + period ~ metric)
df_$period <- factor(df_$period, c('SixM', 'OneY', 'Last'))
ggplot(df_, aes(x=period,
  y=Mean,
  ymin=Mean - 1.96*eSEM,
  ymax=Mean + 1.96*eSEM,
  group=subtype,
  fill=subtype)) + geom_ribbon(alpha=.2) + geom_line(aes(color=subtype)) + ylab("Inferred
```



Meta-regression

Consider relationships between different covariates and outcomes. Focus on the IOP drop at one year and its correlation with different factors.

```
df <- read.data()

## These retrospective studies are losing eyes per period - not impossible, but unusual:

## Mathalone et al. (2005)
## Leelachaikul et al. (2005)
## Shoji et al. (2007)
## Liu et al. (2011)
## Arthur et al. (2014)
## Tetz et al. (2015)

## These retrospective studies are gaining eyes as the study goes

## Samuelson et al. (2011)

df_ <- df %>% filter(!is.na>LastPeriodAbsIOPChangeMean),
               subtype != "AACG",
               MIGsYorN == 'N') %>%
  mutate(coarseWashoutType=factor(washout.type, c("None", "Partial", "Pre", "Both")),
         subtype=relevel(factor(subtype), ref="OAG"))
levels(df_$coarseWashoutType) <- c("None", "None", "Pre", "Both")

m <- metagen>LastPeriodAbsIOPChangeMean,
      LastPeriodAbsIOPChangeStdDev / sqrt>LastPeriodEyes),
      study.name,
      data=df_,
      byvar=subtype,
      n.e=OneYEyes)

# Leveled against OAG
print(metareg(~ LastPeriodEyes, x=m))

##
## Mixed-Effects Model (k = 33; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):      25.5650 (SE = 9.4030)
## tau (square root of estimated tau^2 value):             5.0562
## I^2 (residual heterogeneity / unaccounted variability): 98.53%
## H^2 (unaccounted variability / sampling variability):    67.85
## R^2 (amount of heterogeneity accounted for):             0.00%
##
## Test for Residual Heterogeneity:
## QE(df = 31) = 2103.4367, p-val < .0001
##
## Test of Moderators (coefficient(s) 2):
## QM(df = 1) = 0.8172, p-val = 0.3660
##
```

```
## Model Results:
##
##           estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt          -3.5035  1.4564  -2.4055  0.0161  -6.3580  -0.6489 *
## LastPeriodEyes   -0.0231  0.0256  -0.9040  0.3660  -0.0733   0.0270
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
print(metareg(~ Year, x=m))
```

```
##
## Mixed-Effects Model (k = 33; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):      21.8899 (SE = 8.0755)
## tau (square root of estimated tau^2 value):             4.6787
## I^2 (residual heterogeneity / unaccounted variability): 98.30%
## H^2 (unaccounted variability / sampling variability):    58.68
## R^2 (amount of heterogeneity accounted for):             7.84%
##
## Test for Residual Heterogeneity:
## QE(df = 31) = 1818.9826, p-val < .0001
##
## Test of Moderators (coefficient(s) 2):
## QM(df = 1) = 0.0863, p-val = 0.7690
##
## Model Results:
##
##           estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt    90.1158  322.2445   0.2797  0.7797  -541.4717  721.7034
## Year       -0.0471   0.1603  -0.2937  0.7690   -0.3614   0.2672
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
print(metareg(~ PreOpIOPMean * subtype + coarseWashoutType + AgeMean + Male, x=m))
```

```
## Warning in metafor::rma.uni(yi = TE, sei = seTE, data = dataset, mods =
## formula, : Studies with NAs omitted from model fitting.
```

```
##
## Mixed-Effects Model (k = 28; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):      0.7168 (SE = 0.4429)
## tau (square root of estimated tau^2 value):             0.8466
## I^2 (residual heterogeneity / unaccounted variability): 60.81%
## H^2 (unaccounted variability / sampling variability):    2.55
## R^2 (amount of heterogeneity accounted for):             97.28%
##
## Test for Residual Heterogeneity:
## QE(df = 18) = 45.9263, p-val = 0.0003
##
```

```
## Test of Moderators (coefficient(s) 2,3,4,5,6,7,8,9,10):
## QM(df = 9) = 316.5158, p-val < .0001
##
## Model Results:
##
##               estimate      se      zval      pval      ci.lb
## intrcpt          -4.5154  6.4041  -0.7051  0.4808 -17.0672
## PreOpIOPMean      -0.1719  0.1532  -1.1223  0.2617  -0.4721
## subtypeACG         9.9779  3.3923   2.9414  0.0033   3.3292
## subtypePXG        12.4617  4.6754   2.6654  0.0077   3.2980
## coarseWashoutTypePre  1.3583  1.4319   0.9486  0.3428  -1.4481
## coarseWashoutTypeBoth -1.8649  1.3670  -1.3642  0.1725  -4.5442
## AgeMean           0.0891  0.0683   1.3042  0.1922  -0.0448
## Male              -0.0232  0.0238  -0.9748  0.3297  -0.0698
## PreOpIOPMean:subtypeACG -0.6667  0.1807  -3.6904  0.0002  -1.0208
## PreOpIOPMean:subtypePXG -0.6791  0.2347  -2.8933  0.0038  -1.1391
##               ci.ub
## intrcpt          8.0364
## PreOpIOPMean      0.1283
## subtypeACG        16.6266 **
## subtypePXG        21.6253 **
## coarseWashoutTypePre  4.1647
## coarseWashoutTypeBoth  0.8144
## AgeMean           0.2229
## Male              0.0234
## PreOpIOPMean:subtypeACG -0.3126 ***
## PreOpIOPMean:subtypePXG -0.2191 **
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
# Leveled against ACG
df_ <- df_ %>% mutate(subtype=relevel(factor(subtype), ref="ACG"))

m <- metagen(LastPeriodAbsIOPChangeMean,
             LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
             study.name,
             data=df_,
             byvar=subtype,
             n.e=OneYEyes)

print(metareg(~ LastPeriodEyes, x=m))
```

```
##
## Mixed-Effects Model (k = 33; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):      25.5650 (SE = 9.4030)
## tau (square root of estimated tau^2 value):             5.0562
## I^2 (residual heterogeneity / unaccounted variability): 98.53%
## H^2 (unaccounted variability / sampling variability):    67.85
## R^2 (amount of heterogeneity accounted for):             0.00%
##
## Test for Residual Heterogeneity:
## QE(df = 31) = 2103.4367, p-val < .0001
```



```
##
## Test of Moderators (coefficient(s) 2):
## QM(df = 1) = 0.8172, p-val = 0.3660
##
## Model Results:
##
##           estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt      -3.5035  1.4564  -2.4055  0.0161  -6.3580  -0.6489  *
## LastPeriodEyes -0.0231  0.0256  -0.9040  0.3660  -0.0733   0.0270
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
print(metareg(~ Year, x=m))
```

```
##
## Mixed-Effects Model (k = 33; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):      21.8899 (SE = 8.0755)
## tau (square root of estimated tau^2 value):             4.6787
## I^2 (residual heterogeneity / unaccounted variability): 98.30%
## H^2 (unaccounted variability / sampling variability):    58.68
## R^2 (amount of heterogeneity accounted for):             7.84%
##
## Test for Residual Heterogeneity:
## QE(df = 31) = 1818.9826, p-val < .0001
##
## Test of Moderators (coefficient(s) 2):
## QM(df = 1) = 0.0863, p-val = 0.7690
##
## Model Results:
##
##           estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt    90.1158  322.2445   0.2797  0.7797  -541.4717  721.7034
## Year       -0.0471   0.1603  -0.2937  0.7690   -0.3614   0.2672
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
print(metareg(~ PreOpIOPMean * subtype + coarseWashoutType + AgeMean + Male, x=m))
```

```
## Warning in metafor::rma.uni(yi = TE, sei = seTE, data = dataset, mods =
## formula, : Studies with NAs omitted from model fitting.
```

```
##
## Mixed-Effects Model (k = 28; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):      0.7168 (SE = 0.4429)
## tau (square root of estimated tau^2 value):             0.8466
## I^2 (residual heterogeneity / unaccounted variability): 60.81%
## H^2 (unaccounted variability / sampling variability):    2.55
## R^2 (amount of heterogeneity accounted for):             97.28%
```

```
##
## Test for Residual Heterogeneity:
## QE(df = 18) = 45.9263, p-val = 0.0003
##
## Test of Moderators (coefficient(s) 2,3,4,5,6,7,8,9,10):
## QM(df = 9) = 316.5158, p-val < .0001
##
## Model Results:
##
##               estimate      se      zval      pval      ci.lb
## intrcpt          5.4625  6.4172   0.8512  0.3946   -7.1149
## PreOpIOPMean     -0.8386  0.1066  -7.8633 <.0001   -1.0476
## subtypeOAG       -9.9779  3.3923  -2.9414  0.0033  -16.6266
## subtypePXG        2.4838  4.0456   0.6139  0.5393   -5.4455
## coarseWashoutTypePre  1.3583  1.4319   0.9486  0.3428   -1.4481
## coarseWashoutTypeBoth -1.8649  1.3670  -1.3642  0.1725   -4.5442
## AgeMean           0.0891  0.0683   1.3042  0.1922   -0.0448
## Male             -0.0232  0.0238  -0.9748  0.3297   -0.0698
## PreOpIOPMean:subtypeOAG  0.6667  0.1807   3.6904  0.0002    0.3126
## PreOpIOPMean:subtypePXG -0.0124  0.1985  -0.0625  0.9501   -0.4014
##               ci.ub
## intrcpt          18.0399
## PreOpIOPMean     -0.6296 ***
## subtypeOAG       -3.3292 **
## subtypePXG       10.4130
## coarseWashoutTypePre  4.1647
## coarseWashoutTypeBoth  0.8144
## AgeMean           0.2229
## Male              0.0234
## PreOpIOPMean:subtypeOAG  1.0208 ***
## PreOpIOPMean:subtypePXG  0.3765
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
# Leveled against PXG
df_ <- df_ %>% mutate(subtype=relevel(factor(subtype), ref="PXG"))

m <- metagen(LastPeriodAbsIOPChangeMean,
             LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
             study.name,
             data=df_,
             byvar=subtype,
             n.e=OneYEyes)

print(metareg(~ LastPeriodEyes, x=m))
```

```
##
## Mixed-Effects Model (k = 33; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):      25.5650 (SE = 9.4030)
## tau (square root of estimated tau^2 value):             5.0562
## I^2 (residual heterogeneity / unaccounted variability): 98.53%
## H^2 (unaccounted variability / sampling variability):    67.85
```

```
## R^2 (amount of heterogeneity accounted for):          0.00%
##
## Test for Residual Heterogeneity:
## QE(df = 31) = 2103.4367, p-val < .0001
##
## Test of Moderators (coefficient(s) 2):
## QM(df = 1) = 0.8172, p-val = 0.3660
##
## Model Results:
##
##           estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt      -3.5035  1.4564  -2.4055  0.0161  -6.3580  -0.6489  *
## LastPeriodEyes -0.0231  0.0256  -0.9040  0.3660  -0.0733   0.0270
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
print(metareg(~ Year, x=m))
```

```
##
## Mixed-Effects Model (k = 33; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):      21.8899 (SE = 8.0755)
## tau (square root of estimated tau^2 value):             4.6787
## I^2 (residual heterogeneity / unaccounted variability): 98.30%
## H^2 (unaccounted variability / sampling variability):    58.68
## R^2 (amount of heterogeneity accounted for):            7.84%
##
## Test for Residual Heterogeneity:
## QE(df = 31) = 1818.9826, p-val < .0001
##
## Test of Moderators (coefficient(s) 2):
## QM(df = 1) = 0.0863, p-val = 0.7690
##
## Model Results:
##
##           estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt    90.1158  322.2445   0.2797  0.7797  -541.4717  721.7034
## Year       -0.0471   0.1603  -0.2937  0.7690   -0.3614   0.2672
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
print(metareg(~ PreOpIOPMean * subtype + coarseWashoutType + AgeMean + Male, x=m))
```

```
## Warning in metafor::rma.uni(yi = TE, sei = seTE, data = dataset, mods =
## formula, : Studies with NAs omitted from model fitting.
```

```
##
## Mixed-Effects Model (k = 28; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):      0.7168 (SE = 0.4429)
```

```

## tau (square root of estimated tau^2 value):          0.8466
## I^2 (residual heterogeneity / unaccounted variability): 60.81%
## H^2 (unaccounted variability / sampling variability): 2.55
## R^2 (amount of heterogeneity accounted for):          97.28%
##
## Test for Residual Heterogeneity:
## QE(df = 18) = 45.9263, p-val = 0.0003
##
## Test of Moderators (coefficient(s) 2,3,4,5,6,7,8,9,10):
## QM(df = 9) = 316.5158, p-val < .0001
##
## Model Results:
##
##               estimate      se      zval      pval      ci.lb
## intrcpt          7.9463  6.8357   1.1625  0.2450   -5.4515
## PreOpIOPMean     -0.8510  0.1792  -4.7490 <.0001   -1.2022
## subtypeACG       -2.4838  4.0456  -0.6139  0.5393  -10.4130
## subtypeOAG      -12.4617  4.6754  -2.6654  0.0077  -21.6253
## coarseWashoutTypePre  1.3583  1.4319   0.9486  0.3428   -1.4481
## coarseWashoutTypeBoth -1.8649  1.3670  -1.3642  0.1725   -4.5442
## AgeMean           0.0891  0.0683   1.3042  0.1922   -0.0448
## Male             -0.0232  0.0238  -0.9748  0.3297   -0.0698
## PreOpIOPMean:subtypeACG  0.0124  0.1985   0.0625  0.9501   -0.3765
## PreOpIOPMean:subtypeOAG  0.6791  0.2347   2.8933  0.0038    0.2191
##               ci.ub
## intrcpt          21.3441
## PreOpIOPMean     -0.4998 ***
## subtypeACG         5.4455
## subtypeOAG        -3.2980 **
## coarseWashoutTypePre  4.1647
## coarseWashoutTypeBoth  0.8144
## AgeMean           0.2229
## Male              0.0234
## PreOpIOPMean:subtypeACG  0.4014
## PreOpIOPMean:subtypeOAG  1.1391 **
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

```
# Restricted to OAG only
```

```

df %>%
  filter(subtype == 'OAG', washout.type != 'Both', !is.na>LastPeriodAbsIOPChangeStdDev)) %>%
  summarize(min = min(PreOpIOPMean),
            max = max(PreOpIOPMean),
            sd = sd(PreOpIOPMean),
            mean = mean(PreOpIOPMean))

```

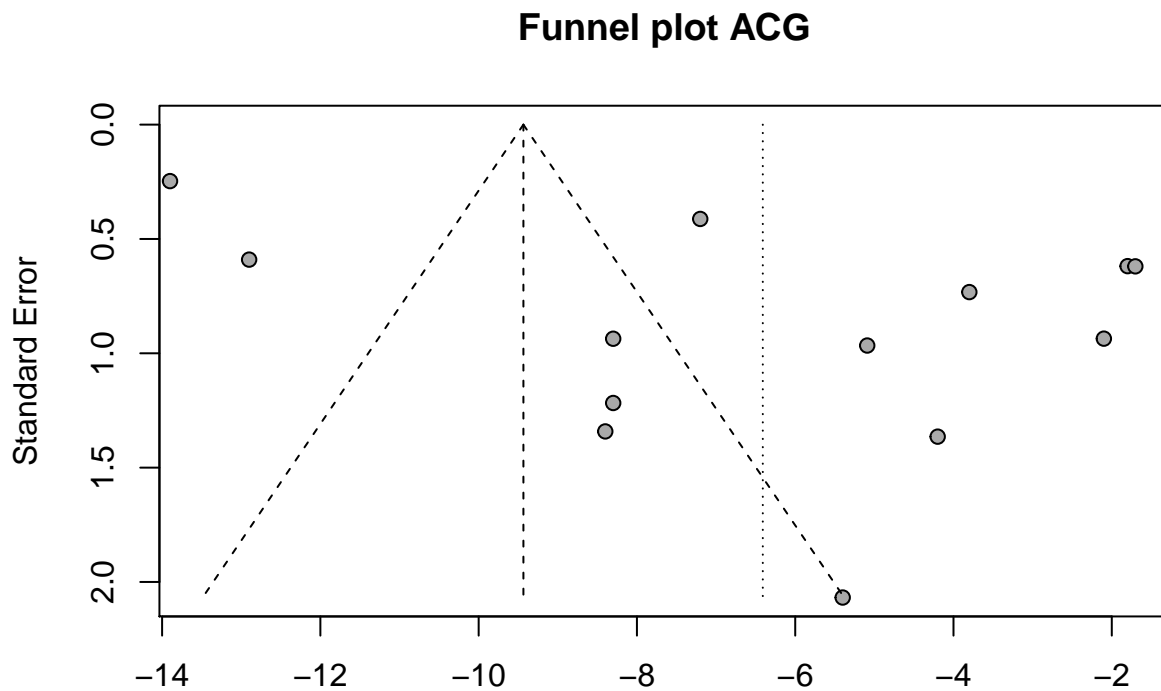
```

##      min  max      sd      mean
## 1 16.2 23.8 2.012705 18.12571

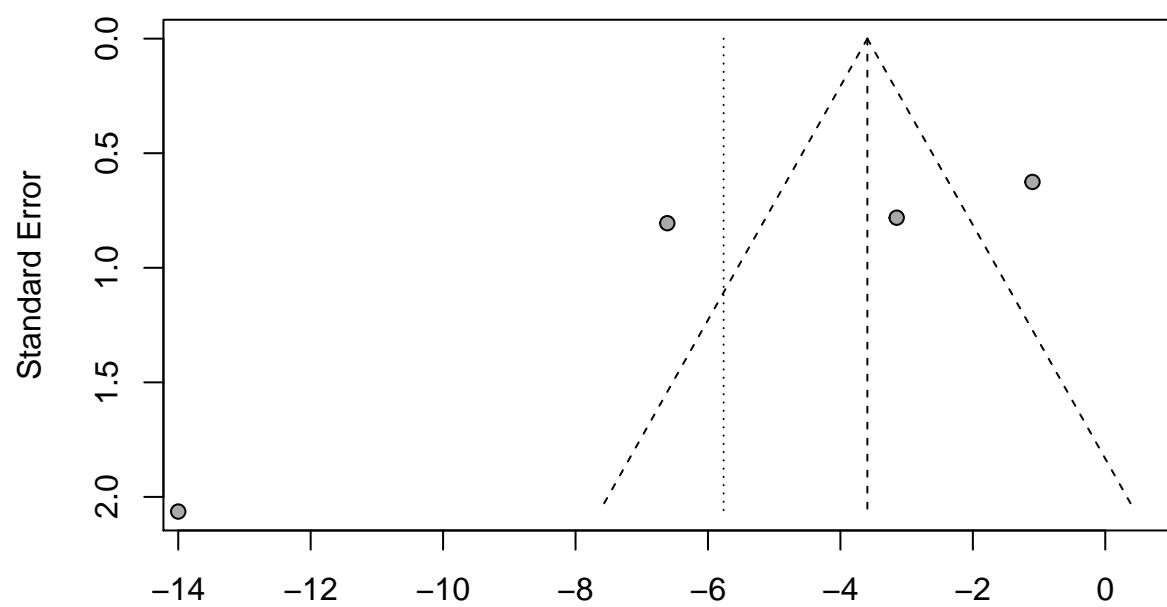
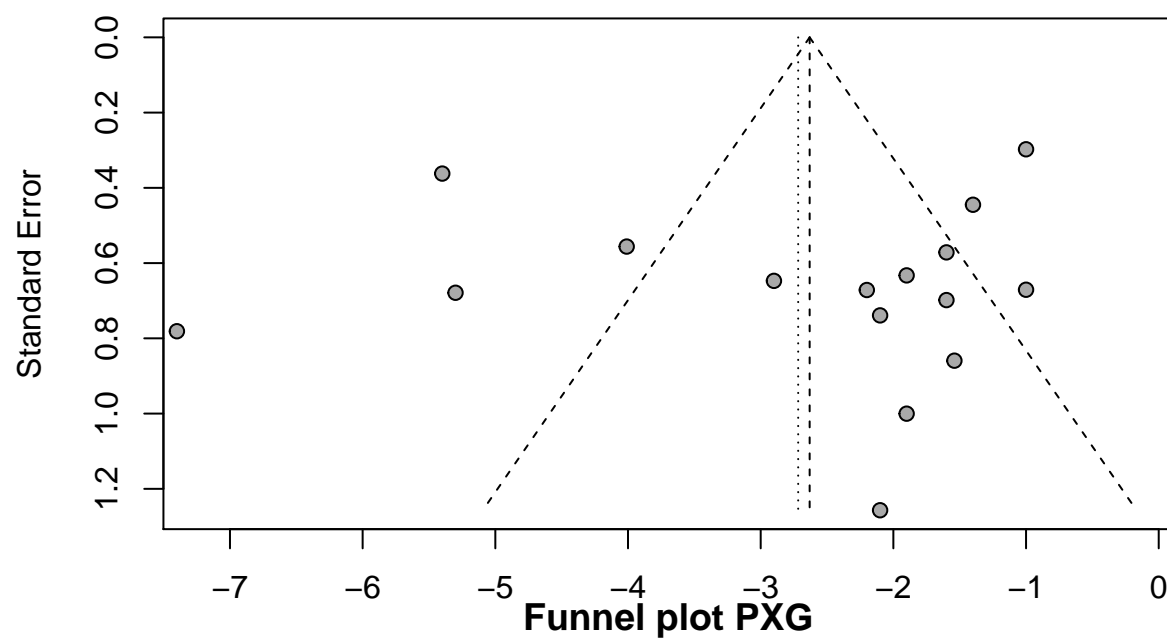
```

Small study bias

```
df_ <- df %>% filter(!is.na(df$LastPeriodAbsIOPChangeMean),
                      df$subtype != "AACG",
                      MIGsYorN == 'N') %>% mutate(subtype=factor(subtype))
for(l in levels(df_$subtype)) {
  m <- metagen(LastPeriodAbsIOPChangeMean,
               LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
               study.name,
               data=df_ %>% filter(subtype == l),
               n.e=LastPeriodEyes)
  funnel(m)
  title(paste('Funnel plot', l))
}
```

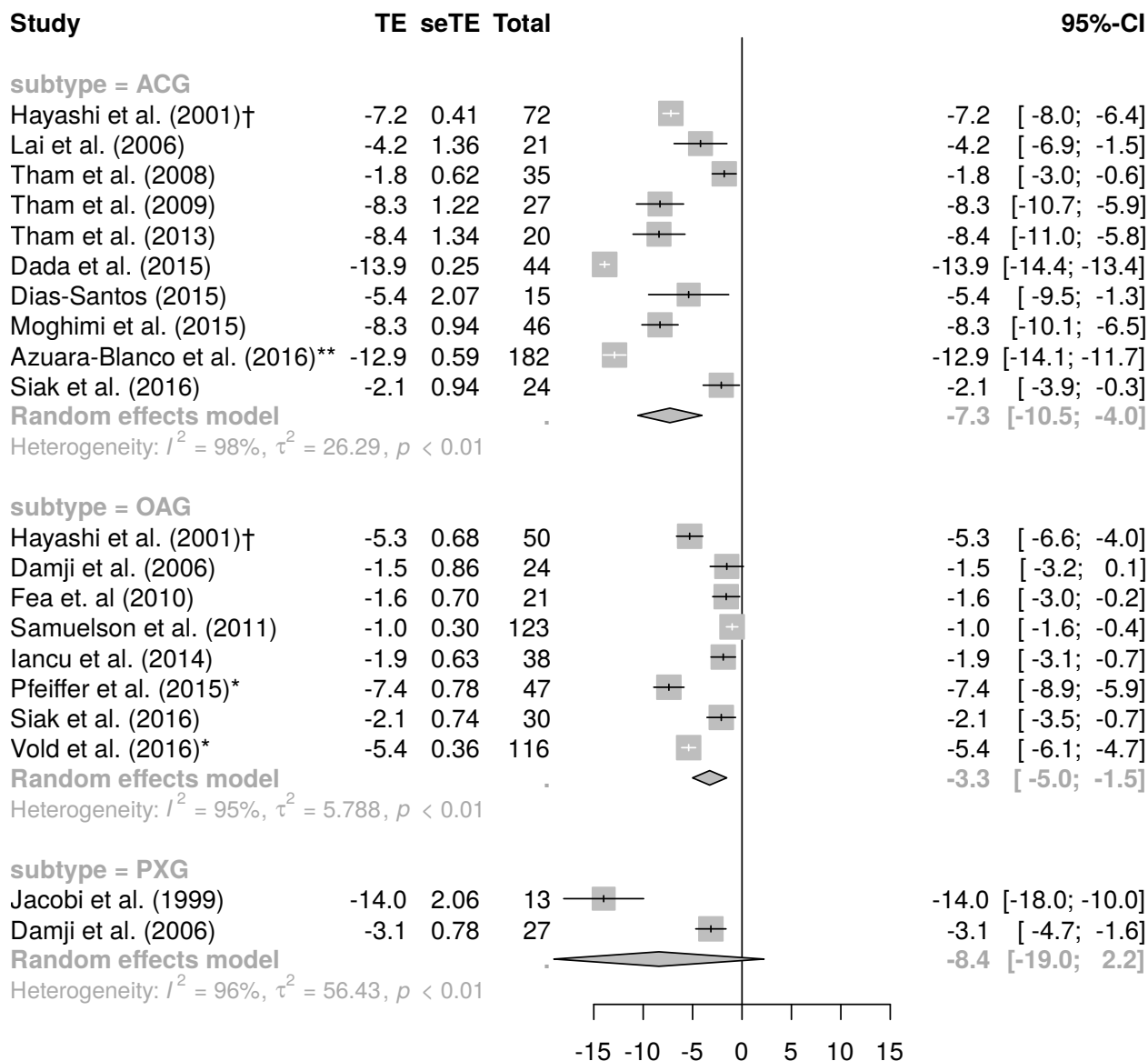


Funnel plot OAG



Alternative filterings of the data

Prospective studies only



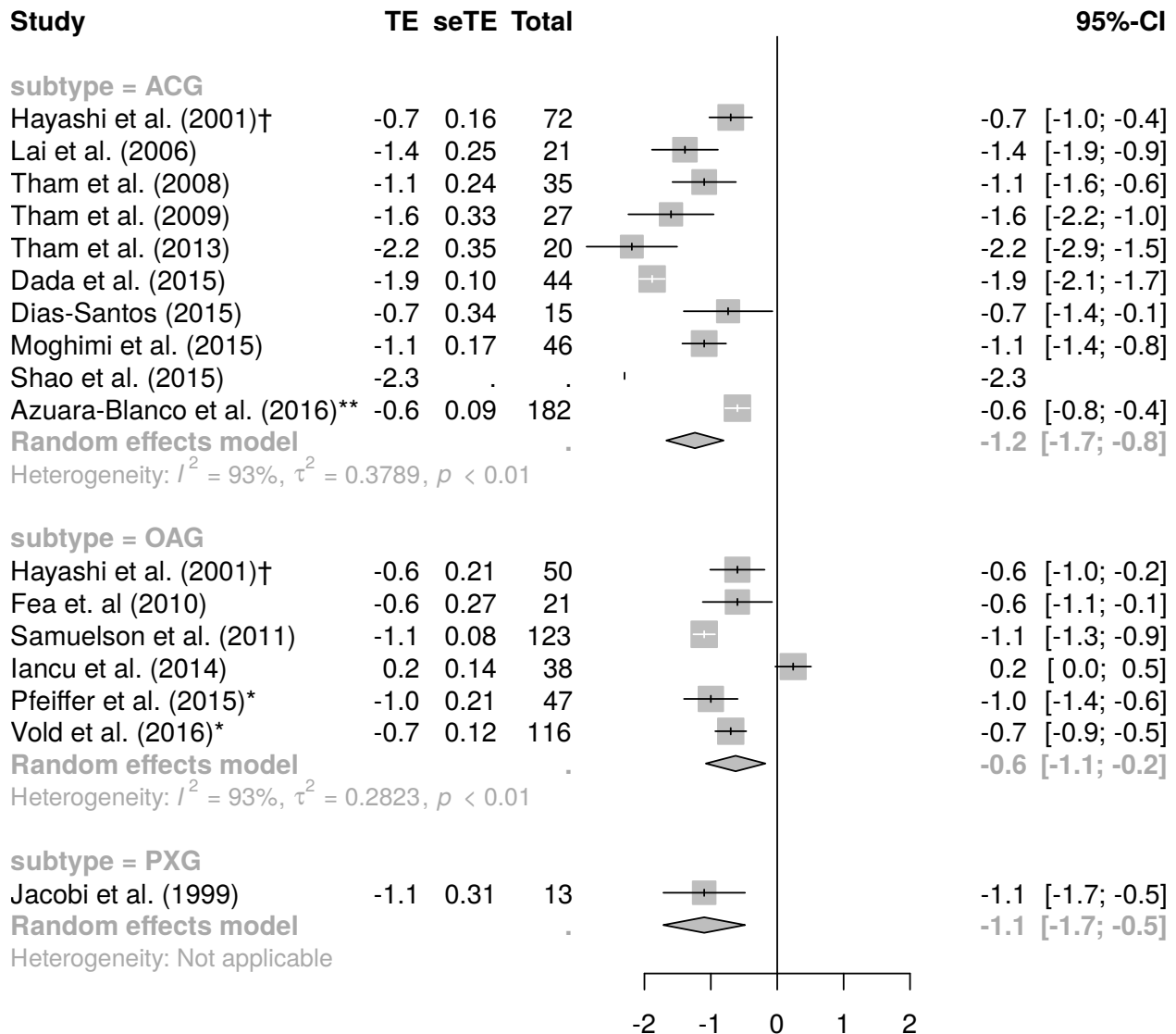
Meds

```
df_ <- df %>%
  filter(!is.na(RxChangeMean), !is.na(RxChangeStdDev),
         df$subtype != "AACG", MIGsYorN == 'N') %>%
  mutate(subtype=factor(subtype))
m <- metagen(RxChangeMean,
             sqrt(RxPostOpStdDev** 2 + RxPreOpStdDev ** 2) / sqrt>LastPeriodEyes),
             study.name,
```

```

data=df_,
byvar=subtype,
n.e=LastPeriodEyes)
forest(m,
  comb.fixed=FALSE,
  digits=1,
  digits.se = 2,
  overall=FALSE,
  leftcols=c("studlab", "TE", "seTE", "n.e"))

```



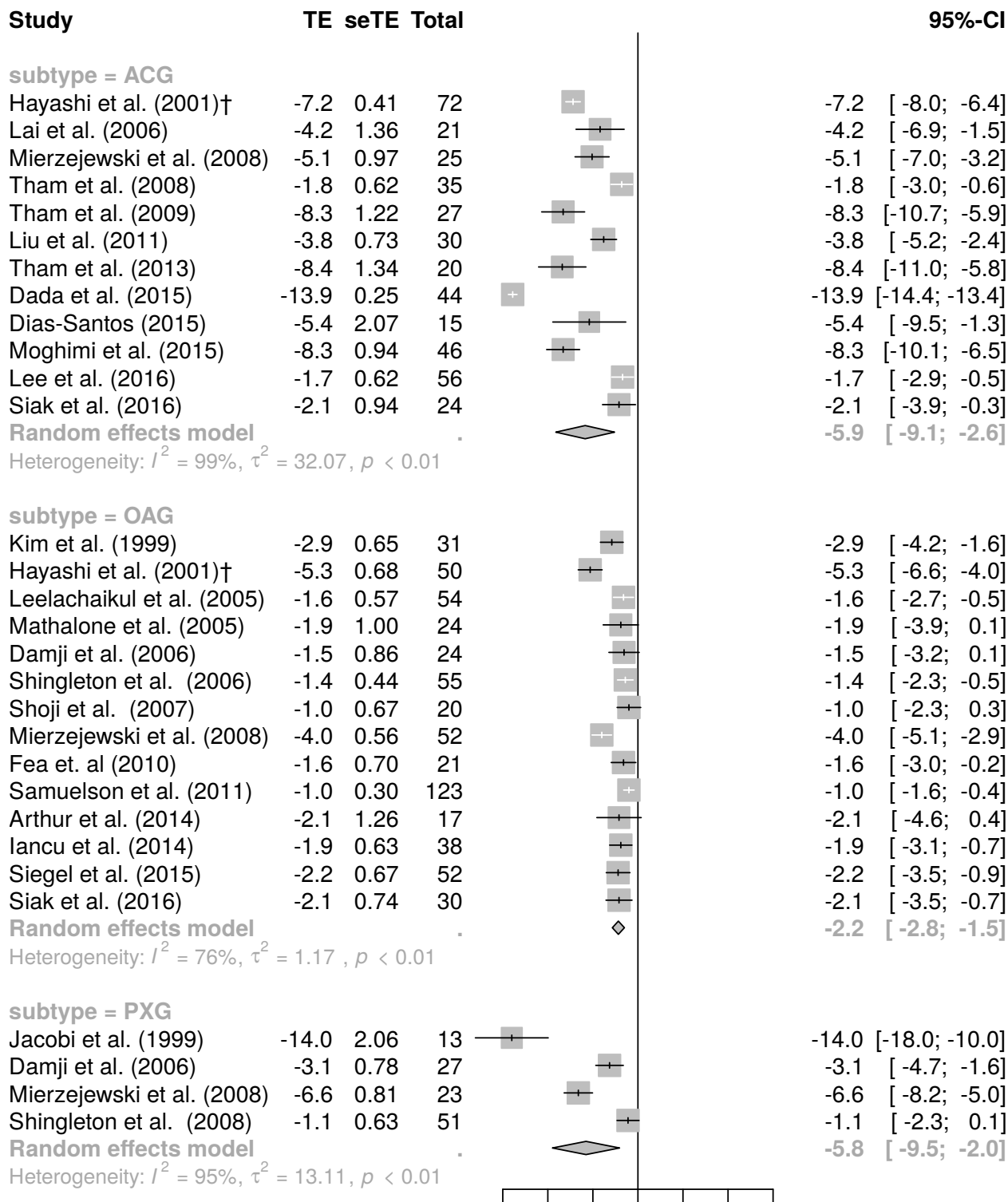
Excluding washout studies

Last period


```

df_ <- df %>%
  filter(!is.na(LastPeriodAbsIOPChangeMean), subtype != "AACG", MIGsYorN == 'N') %>%
  mutate(subtype=factor(subtype))
m <- metagen(LastPeriodAbsIOPChangeMean,
             LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
             study.name,
             data=df_,
             byvar=subtype,
             n.e=LastPeriodEyes)
forest(m,
       comb.fixed=FALSE,
       digits=1,
       digits.se = 2,
       overall=FALSE,
       leftcols=c("studlab", "TE", "seTE", "n.e"))

```



Meds

```
df_ <- df %>%
  filter(!is.na(RxChangeMean), !is.na(RxChangeStdDev),
```

```

      df$subtype != "AACG", MIGsYorN == 'N') %>%
  mutate(subtype=factor(subtype))
m <- metagen(RxChangeMean,
             sqrt(RxPostOpStdDev** 2 + RxPreOpStdDev ** 2) / sqrt>LastPeriodEyes),
             study.name,
             data=df_,
             byvar=subtype,
             n.e>LastPeriodEyes)
forest(m,
       comb.fixed=FALSE,
       digits=1,
       digits.se = 2,
       overall=FALSE,
       leftcols=c("studlab", "TE", "seTE", "n.e"))

```

```

## Warning in grid.Call(L_textBounds, as.graphicsAnnot(x$label), x$x, x
## $y, : conversion failure on 'Hayashi et al. (2001)†' in 'mbcsToSbcs': dot
## substituted for <e2>

```

```

## Warning in grid.Call(L_textBounds, as.graphicsAnnot(x$label), x$x, x
## $y, : conversion failure on 'Hayashi et al. (2001)†' in 'mbcsToSbcs': dot
## substituted for <80>

```

```

## Warning in grid.Call(L_textBounds, as.graphicsAnnot(x$label), x$x, x
## $y, : conversion failure on 'Hayashi et al. (2001)†' in 'mbcsToSbcs': dot
## substituted for <a0>

```

```

## Warning in grid.Call(L_textBounds, as.graphicsAnnot(x$label), x$x, x
## $y, : conversion failure on 'Hayashi et al. (2001)†' in 'mbcsToSbcs': dot
## substituted for <e2>

```

```

## Warning in grid.Call(L_textBounds, as.graphicsAnnot(x$label), x$x, x
## $y, : conversion failure on 'Hayashi et al. (2001)†' in 'mbcsToSbcs': dot
## substituted for <80>

```

```

## Warning in grid.Call(L_textBounds, as.graphicsAnnot(x$label), x$x, x
## $y, : conversion failure on 'Hayashi et al. (2001)†' in 'mbcsToSbcs': dot
## substituted for <a0>

```

```

## Warning in grid.Call.graphics(L_text, as.graphicsAnnot(x$label), x$x, x
## $y, : conversion failure on 'Hayashi et al. (2001)†' in 'mbcsToSbcs': dot
## substituted for <e2>

```

```

## Warning in grid.Call.graphics(L_text, as.graphicsAnnot(x$label), x$x, x
## $y, : conversion failure on 'Hayashi et al. (2001)†' in 'mbcsToSbcs': dot
## substituted for <80>

```

```

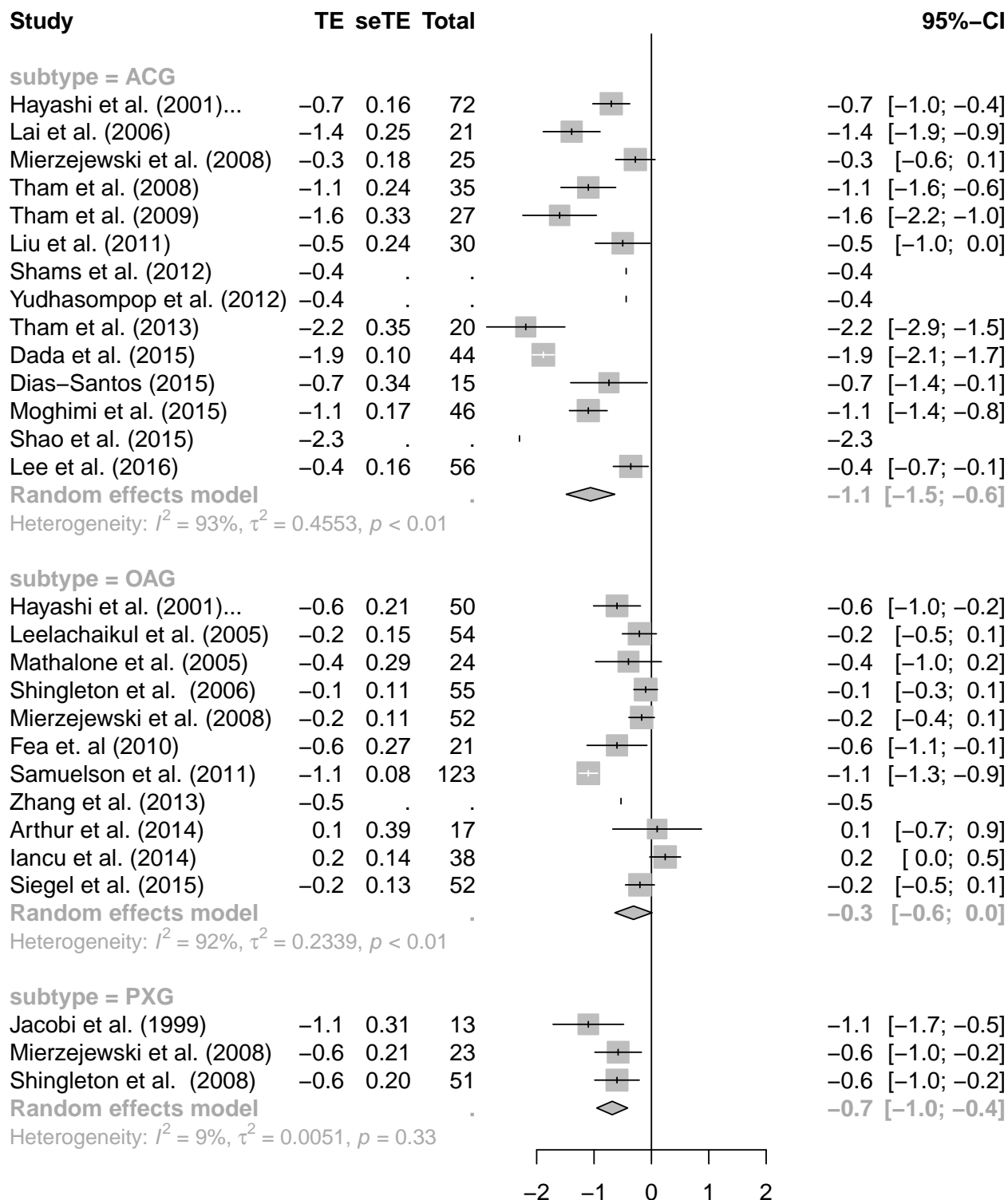
## Warning in grid.Call.graphics(L_text, as.graphicsAnnot(x$label), x$x, x
## $y, : conversion failure on 'Hayashi et al. (2001)†' in 'mbcsToSbcs': dot
## substituted for <a0>

```

```
## Warning in grid.Call.graphics(L_text, as.graphicsAnnot(x$label), x$x, x
## $y, : conversion failure on 'Hayashi et al. (2001)†' in 'mbcsToSbcs': dot
## substituted for <e2>
```

```
## Warning in grid.Call.graphics(L_text, as.graphicsAnnot(x$label), x$x, x
## $y, : conversion failure on 'Hayashi et al. (2001)†' in 'mbcsToSbcs': dot
## substituted for <80>
```

```
## Warning in grid.Call.graphics(L_text, as.graphicsAnnot(x$label), x$x, x
## $y, : conversion failure on 'Hayashi et al. (2001)†' in 'mbcsToSbcs': dot
## substituted for <a0>
```



Sensitivity to missingness

Simulate what the results would look like if there was no effect in the eyes lost to follow up ($\Delta IOP = 0$).

```

meta.analysis.with.sensitivity <- function(missingness='zero') {
  df <- read.data()
  df <- filter.data(df, 'prospective')

  df_ <- df %>%
    filter(!is.na>LastPeriodAbsIOPChangeMean), subtype != "AACG") %>%
    mutate(subtype=factor(subtype))

  # Simulate a 0 effect in the unobserved fraction.
  df.missing <- df_
  if(missingness == 'zero') {
    # Zero out.
    df.missing <- df.missing %>% mutate>LastPeriodEyes = PreOpEyes - LastPeriodEyes,
      LastPeriodAbsIOPChangeMean = 0)
  } else {
    # Add 5 mm Hg to each missing eye.
    df.missing <- df.missing %>% mutate>LastPeriodEyes = PreOpEyes - LastPeriodEyes,
      LastPeriodAbsIOPChangeMean = LastPeriodAbsIOPChangeMean + 5)
  }

  df_ <- rbind(df_, df.missing)
  # Aggregate two by two
  for(i in seq(nrow(df.missing), 1)) {
    idx <- rep(FALSE, nrow(df_))
    idx[i] <- TRUE
    idx[i*2] <- TRUE
    df_ <- agg.arms(df_, idx)
  }

  df_ <- df_ %>% dplyr::arrange(Year, study.name)

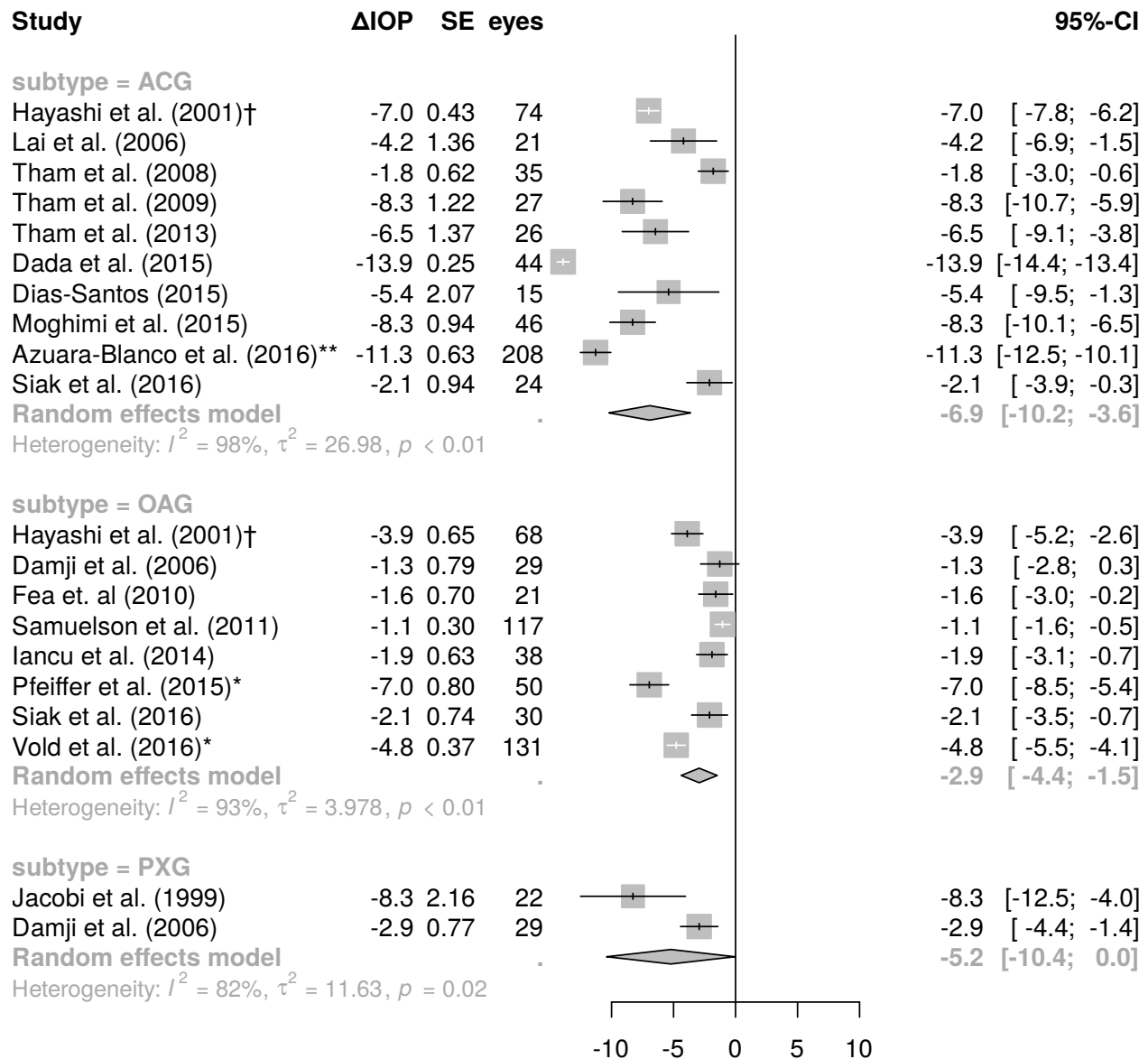
  m <- metagen>LastPeriodAbsIOPChangeMean,
    LastPeriodAbsIOPChangeStdDev / sqrt>LastPeriodEyes),
    study.name,
    data=df_,
    byvar=subtype,
    n.e=LastPeriodEyes)

  forest(m,
    comb.fixed=FALSE,
    digits=1,
    digits.se = 2,
    overall=FALSE,
    leftcols=c("studlab", "TE", "seTE", "n.e"),
    leftlabs=c("Study", " $\Delta$ IOP", "SE", "eyes"))
}

meta.analysis.with.sensitivity()
grid.text(paste0("Simulated net change IOP when  $\Delta$ IOP = 0 in eyes lost to follow up"), .5, .97, gp=gpar(

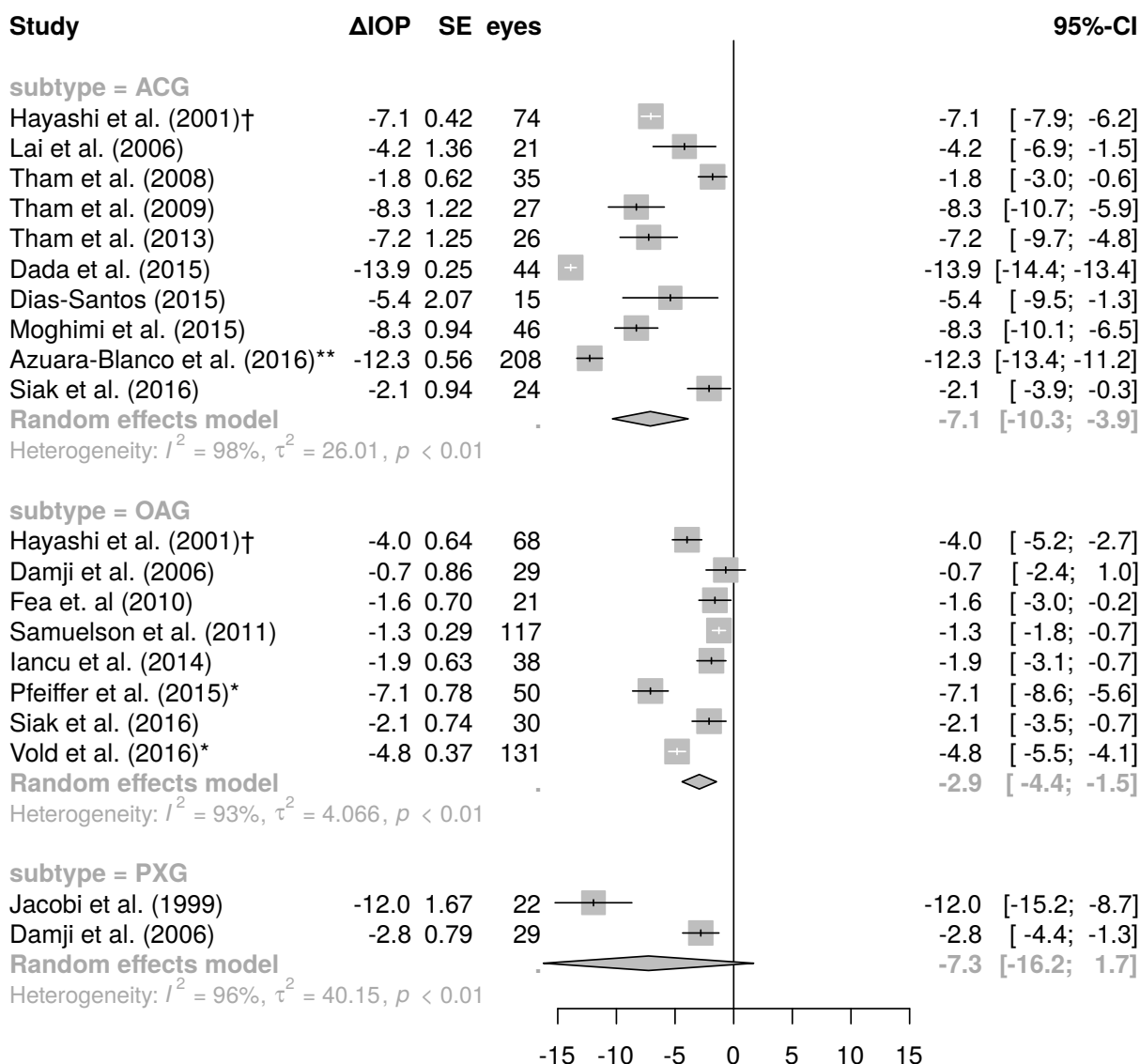
```

Simulated net change IOP when $\Delta IOP = 0$ in eyes lost to follow up



```
meta.analysis.with.sensitivity('five')
grid.text(paste0("Simulated net change IOP when  $\Delta IOP = 5$  mm Hg higher in eyes lost to follow up"), .5,
```

Simulated net change IOP when $\Delta\text{IOP} = 5$ mm Hg higher in eyes lost to follow up



MIGS

We don't report these results because it's a bit misleading – the studies aren't very similar to each other, and we don't use the information in their control arms. We can do a much better job through, for example, network meta-analysis, which we plan to do in a future paper.

```
df <- read.data(drop.migs = FALSE)
```

```
## These retrospective studies are losing eyes per period - not impossible, but unusual:
```

```
## Mathalone et al. (2005)
## Leelachaikul et al. (2005)
```



```
## Shoji et al. (2007)
## Liu et al. (2011)
## Arthur et al. (2014)
## Tetz et al. (2015)
```

```
## These retrospective studies are gaining eyes as the study goes
```

```
## Samuelson et al. (2011)
```

```
df_ <- df %>%
  filter(!is.na>LastPeriodAbsIOPChangeMean), subtype != "AACG", MIGsYorN == 'Y') %>%
  mutate(subtype=factor(subtype)) %>% dplyr::arrange(TypesofMIGSifany, Year)
m <- metagen>LastPeriodAbsIOPChangeMean,
  LastPeriodAbsIOPChangeStdDev / sqrt>LastPeriodEyes),
  study.name,
  data=df_,
  n.e>LastPeriodEyes)
forest(m,
  comb.fixed=FALSE,
  digits=1,
  digits.se = 2,
  overall=TRUE,
  leftcols=c("studlab", "TE", "seTE", "n.e", "TypesofMIGSifany"),
  leftlabs=c("Study", "TE", "seTE", "Total", "Type"))
```

