Phaco meta analysis

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Contents

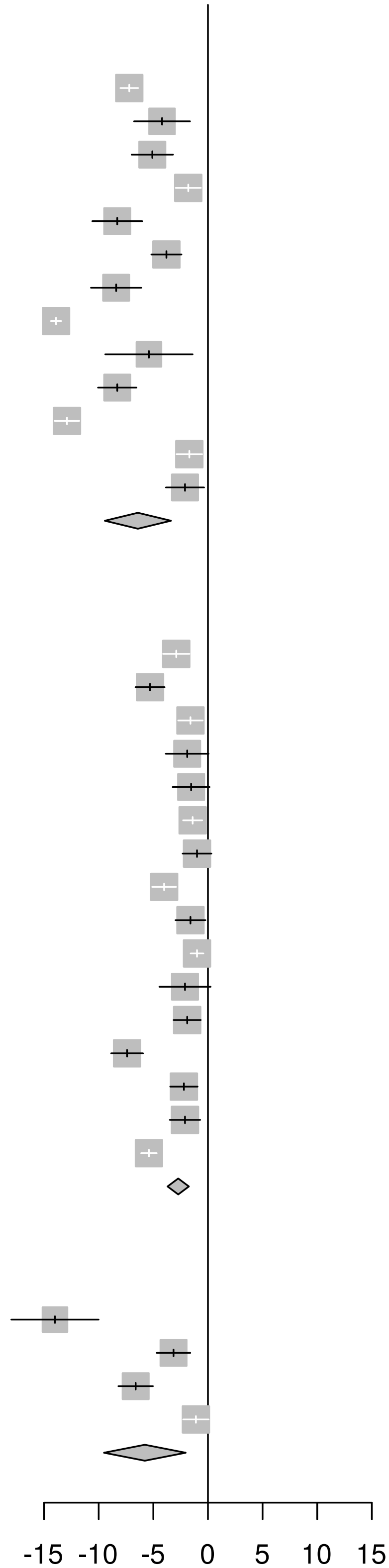
Analysis of full dataset

Main analysis: ≥ 12 month follow up

```
df_ <- df %>%
  filter(!is.na(LastPeriodAbsIOPChangeMean), subtype != "acute", 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", "SE", "eyes"))
```

Study	ΔIOP	SE	eyes	95%-CI
subtype = ACG				
Hayashi et al. (2001)	-7.2	0.41	72	-7.2 [-8.0; -6.4]
Lai et al. (2006)	-4.2	1.31	21	-4.2 [-6.8; -1.6]
Mierzejewski et al. (2008)	-5.1	0.97	25	-5.1 [-7.0; -3.2]
Tham et al. (2008)	-1.8	0.59	35	-1.8 [-3.0; -0.6]
Tham et al. (2009)	-8.3	1.16	27	-8.3 [-10.6; -6.0]
Liu et al. (2011)	-3.8	0.70	30	-3.8 [-5.2; -2.4]
Tham et al. (2013)	-8.4	1.18	26	-8.4 [-10.7; -6.1]
Dada et al. (2015)	-13.9	0.24	44	-13.9 [-14.4; -13.4]
Dias-Santos (2015)	-5.4	2.04	15	-5.4 [-9.4; -1.4]
Moghimi et al. (2015)	-8.3	0.90	46	-8.3 [-10.1; -6.5]
Azuara-Blanco et al. (2016)**	-12.9	0.57	182	-12.9 [-14.0; -11.8]
Lee et al. (2016)	-1.7	0.60	56	-1.7 [-2.9; -0.5]
Siak et al. (2016)	-2.1	0.89	24	-2.1 [-3.8; -0.4]
Random effects model			.	-6.4 [-9.4; -3.4]
Heterogeneity: $I^2 = 99\%$, $\tau^2 = 30.04$, $p < 0.01$				
subtype = OAG				
Kim et al. (1999)	-2.9	0.62	31	-2.9 [-4.1; -1.7]
Hayashi et al. (2001)	-5.3	0.68	50	-5.3 [-6.6; -4.0]
Leelachaikul et al. (2005)	-1.6	0.57	54	-1.6 [-2.7; -0.5]
Mathalone et al. (2005)	-1.9	1.00	24	-1.9 [-3.9; 0.1]
Damji et al. (2006)	-1.5	0.86	24	-1.5 [-3.2; 0.1]
Shingleton et al. (2006)	-1.4	0.44	55	-1.4 [-2.3; -0.5]
Shoji et al. (2007)	-1.0	0.67	20	-1.0 [-2.3; 0.3]
Mierzejewski et al. (2008)	-4.0	0.56	52	-4.0 [-5.1; -2.9]
Fea et. al (2010)	-1.6	0.70	21	-1.6 [-3.0; -0.2]
Samuelson et al. (2011)	-1.0	0.30	123	-1.0 [-1.6; -0.4]
Arthur et al. (2014)	-2.1	1.20	17	-2.1 [-4.4; 0.2]
Iancu et al. (2014)	-1.9	0.63	38	-1.9 [-3.1; -0.7]
Pfeiffer et al. (2015)*	-7.4	0.74	47	-7.4 [-8.9; -5.9]
Siegel et al. (2015)	-2.2	0.64	52	-2.2 [-3.5; -0.9]
Siak et al. (2016)	-2.1	0.71	30	-2.1 [-3.5; -0.7]
Vold et al. (2016)*	-5.4	0.36	116	-5.4 [-6.1; -4.7]
Random effects model			.	-2.7 [-3.7; -1.7]
Heterogeneity: $I^2 = 91\%$, $\tau^2 = 3.5$, $p < 0.01$				
subtype = PXG				
Jacobi et al. (1999)	-14.0	2.04	13	-14.0 [-18.0; -10.0]
Damji et al. (2006)	-3.1	0.78	27	-3.1 [-4.7; -1.6]
Mierzejewski et al. (2008)	-6.6	0.81	23	-6.6 [-8.2; -5.0]
Shingleton et al. (2008)	-1.1	0.59	51	-1.1 [-2.3; 0.1]
Random effects model			.	-5.8 [-9.5; -2.0]
Heterogeneity: $I^2 = 95\%$, $\tau^2 = 13.25$, $p < 0.01$				



Acute

```
df_ <- df %>%
  filter(!is.na(LastPeriodAbsIOPChangeMean), subtype == "acute", 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)
```

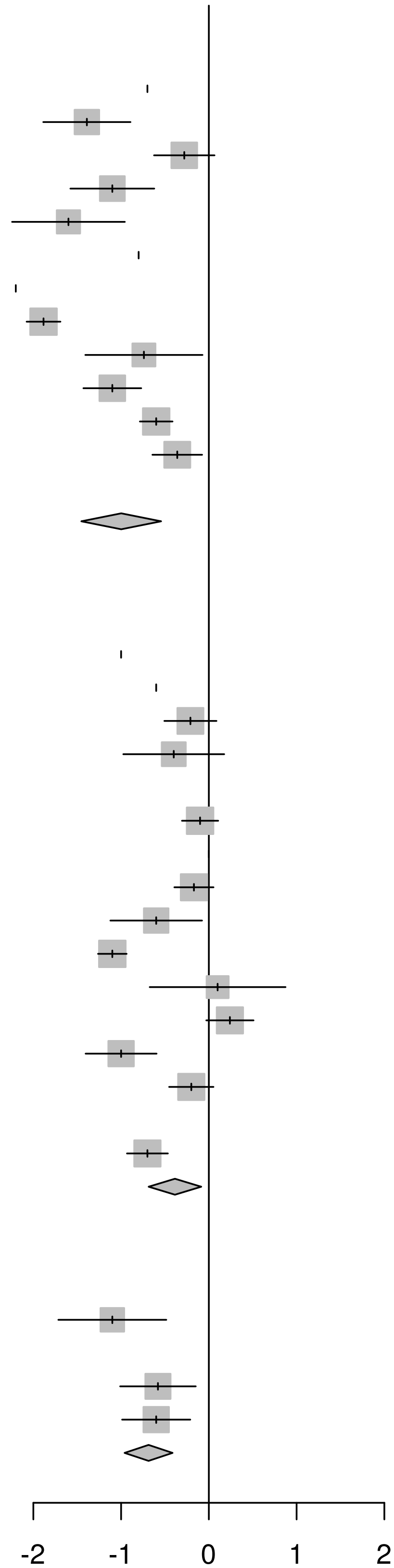
```
##                                                95%-CI %W(random)
## Jacobi et al. (2002) -22.7000 [-23.6565; -21.7435]       20.5
## Lam et al. (2008)    -47.1000 [-50.0449; -44.1551]       20.3
## Lee et al. (2010)    -35.8000 [-39.5586; -32.0414]       20.1
## Husain et al. (2012) -44.5000 [-51.8668; -37.1332]       18.9
## Hou et al. (2015)    -35.9600 [-38.9540; -32.9660]       20.3
##
## Number of studies combined: k = 5
##
##                                              95%-CI     z  p-value
## Random effects model -37.076 [-48.2779; -25.8742] -6.49 < 0.0001
##
## Quantifying heterogeneity:
##  tau^2 = 158.9410; H = 9.13 [7.57; 11.00]; I^2 = 98.8% [98.3%; 99.2%];
##  Rb = 97.3% [92.7%; 100.0%]
##
## Test of heterogeneity:
##       Q d.f.  p-value
##  333.21    4 < 0.0001
##
## Details on meta-analytical method:
## - Inverse variance method
## - DerSimonian-Laird estimator for tau^2
```

Meds

```
df_ <- df %>%
  filter(!is.na(LastPeriodAbsIOPChangeMean),
         df$subtype != "acute", 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"))
```

Study	ΔIOP	SE	eyes	95%-CI
subtype = ACG				
Hayashi et al. (2001)	-0.7	.	72	-0.7
Lai et al. (2006)	-1.4	0.25	21	-1.4 [-1.9; -0.9]
Mierzejewski et al. (2008)	-0.3	0.18	25	-0.3 [-0.6; 0.1]
Tham et al. (2008)	-1.1	0.24	35	-1.1 [-1.6; -0.6]
Tham et al. (2009)	-1.6	0.33	27	-1.6 [-2.2; -1.0]
Liu et al. (2011)	-0.8	.	30	-0.8
Tham et al. (2013)	-2.2	.	26	-2.2
Dada et al. (2015)	-1.9	0.10	44	-1.9 [-2.1; -1.7]
Dias-Santos (2015)	-0.7	0.34	15	-0.7 [-1.4; -0.1]
Moghimi et al. (2015)	-1.1	0.17	46	-1.1 [-1.4; -0.8]
Azuara-Blanco et al. (2016)**	-0.6	0.09	182	-0.6 [-0.8; -0.4]
Lee et al. (2016)	-0.4	0.14	56	-0.4 [-0.6; -0.1]
Siak et al. (2016)	.	.	24	
Random effects model			.	**-1.0 [-1.5; -0.5]**
Heterogeneity: $I^2 = 94\%$, $\tau^2 = 0.4369$, $p < 0.01$				
subtype = OAG				
Kim et al. (1999)	-1.0	.	31	-1.0
Hayashi et al. (2001)	-0.6	.	50	-0.6
Leelachaikul et al. (2005)	-0.2	0.15	54	-0.2 [-0.5; 0.1]
Mathalone et al. (2005)	-0.4	0.29	24	-0.4 [-1.0; 0.2]
Damji et al. (2006)	.	.	24	
Shingleton et al. (2006)	-0.1	0.11	55	-0.1 [-0.3; 0.1]
Shoji et al. (2007)	0.0	.	20	0.0
Mierzejewski et al. (2008)	-0.2	0.11	52	-0.2 [-0.4; 0.1]
Fea et. al (2010)	-0.6	0.27	21	-0.6 [-1.1; -0.1]
Samuelson et al. (2011)	-1.1	0.08	123	-1.1 [-1.3; -0.9]
Arthur et al. (2014)	0.1	0.39	17	0.1 [-0.7; 0.9]
Iancu et al. (2014)	0.2	0.14	38	0.2 [0.0; 0.5]
Pfeiffer et al. (2015)*	-1.0	0.21	47	-1.0 [-1.4; -0.6]
Siegel et al. (2015)	-0.2	0.13	52	-0.2 [-0.5; 0.1]
Siak et al. (2016)	.	.	30	
Vold et al. (2016)*	-0.7	0.12	116	-0.7 [-0.9; -0.5]
Random effects model			.	**-0.4 [-0.7; -0.1]**
Heterogeneity: $I^2 = 92\%$, $\tau^2 = 0.2214$, $p < 0.01$				
subtype = PXG				
Jacobi et al. (1999)	-1.1	0.31	13	-1.1 [-1.7; -0.5]
Damji et al. (2006)	.	.	27	
Mierzejewski et al. (2008)	-0.6	0.22	23	-0.6 [-1.0; -0.1]
Shingleton et al. (2008)	-0.6	0.20	51	-0.6 [-1.0; -0.2]
Random effects model			.	**-0.7 [-1.0; -0.4]**
Heterogeneity: $I^2 = 7\%$, $\tau^2 = 0.0046$, $p = 0.34$				



Correlation between meds and drop in IOP

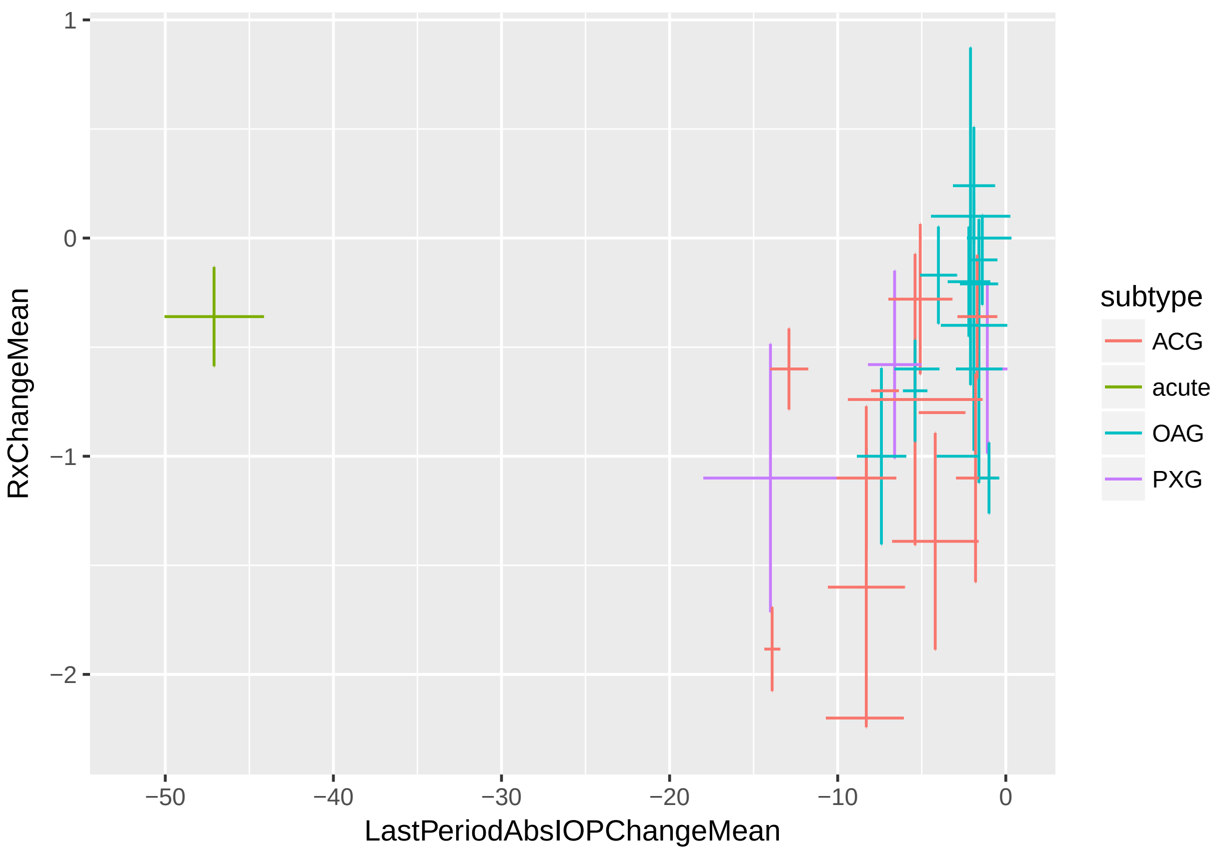
How is IOP drop related to change in meds? Two hypotheses:

- 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?

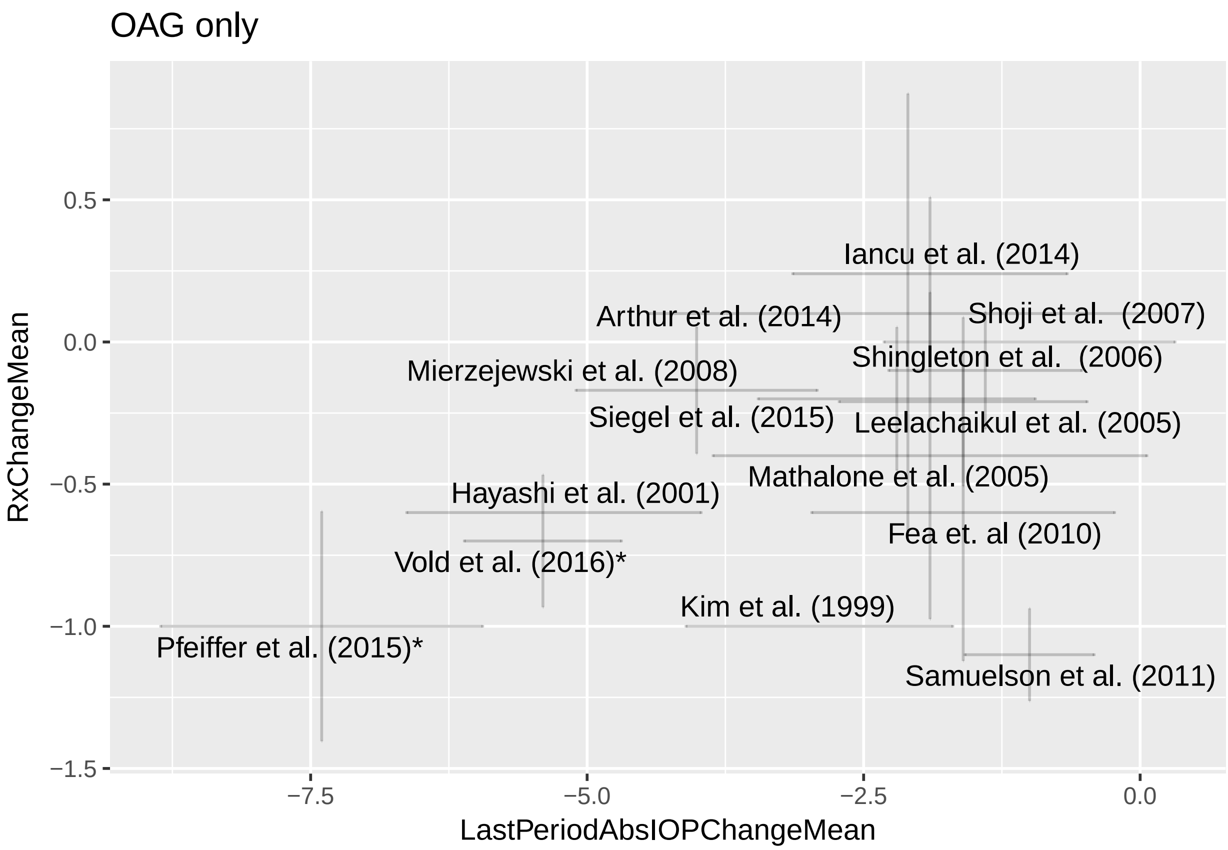
```
df_ <- df %>% mutate(RxChangeSEM  = RxChangeStdDev / sqrt(LastPeriodEyes),
                     LastPeriodAbsIOPChangeSEM = LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes))

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 21 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_re
```



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.corrs <- with(df_, replicate(n = 100,
                                   draw.corr(LastPeriodAbsIOPChangeMean,
                                             LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
                                             RxChangeMean,
                                             RxChangeStdDev / sqrt(LastPeriodEyes))))
mean(drawn.corrs)
```

```
## [1] 0.3715412
```

```r
sd(drawn.corrs)
```

```
## [1] 0.1244077
```

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

```
## Mean +- SE correlation, no washout
```

```r
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] -0.2513868
```

```r
sd(drawn.corrs)
```

```
## [1] 0.2229067
```

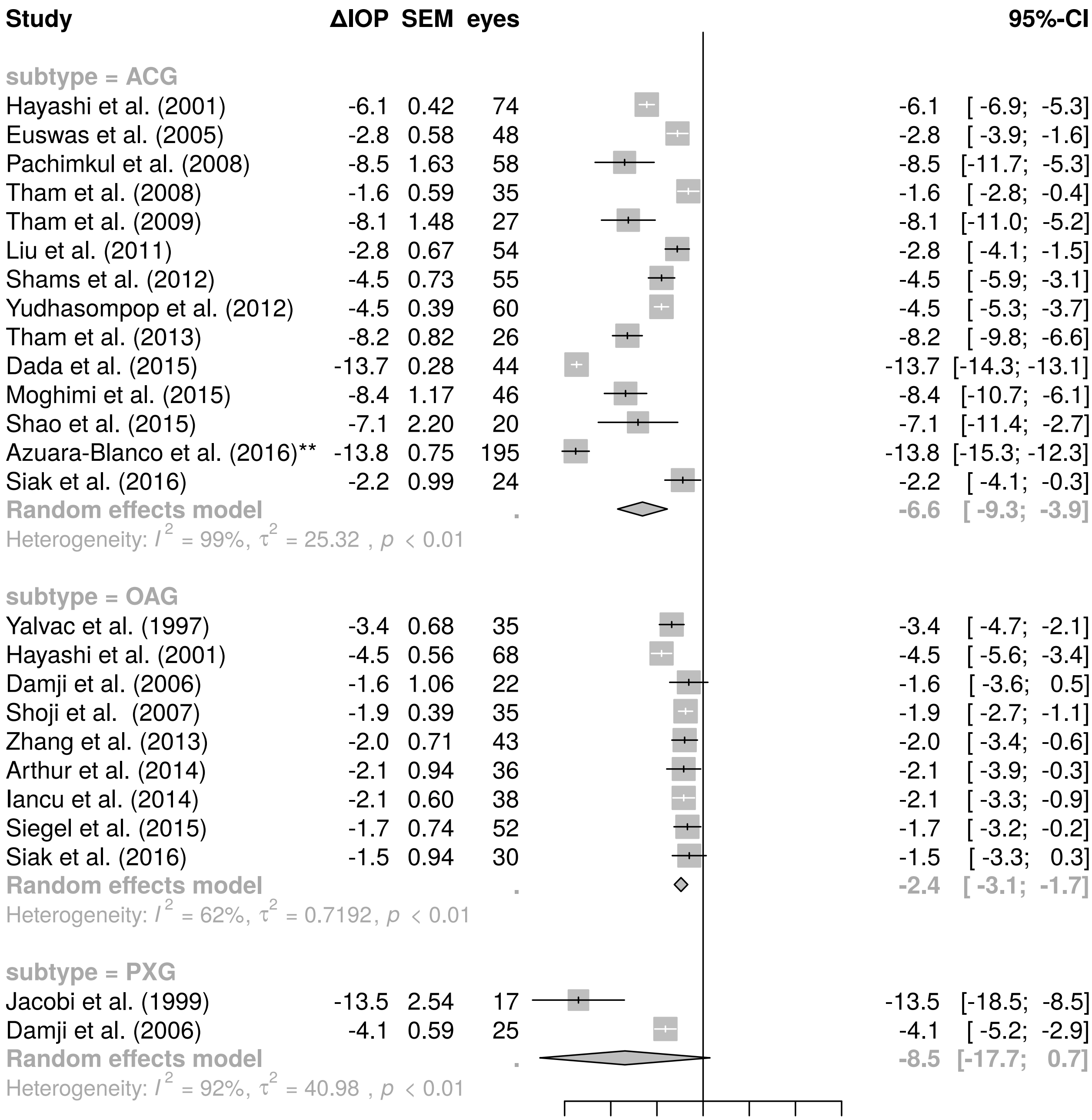
However, this effect goes away when we focus on the studies which don't have washout.

Separate meta-analysis for each time period

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

6 month follow-up

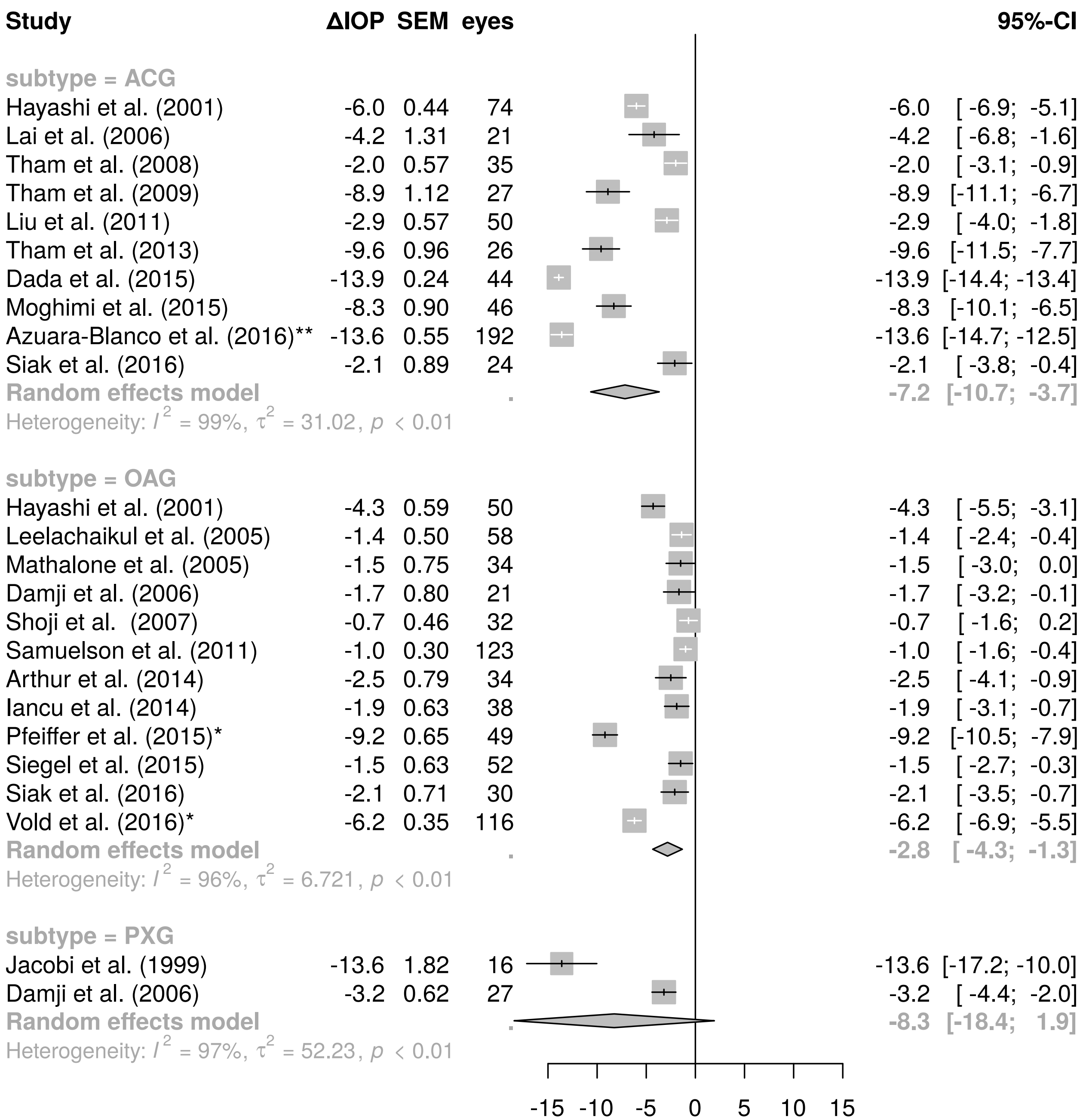
```r
df_ <- df %>%
  filter(!is.na(SixMoAbsIOPChangeMean), subtype != "acute") %>%
  mutate(subtype=factor(subtype))
m <- metagen(SixMoAbsIOPChangeMean,
             SixMoAbsIOPChangeStdDev / sqrt(SixMoEyes),
             study.name,
             data=df_,
             byvar=subtype,
             n.e=SixMoEyes)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

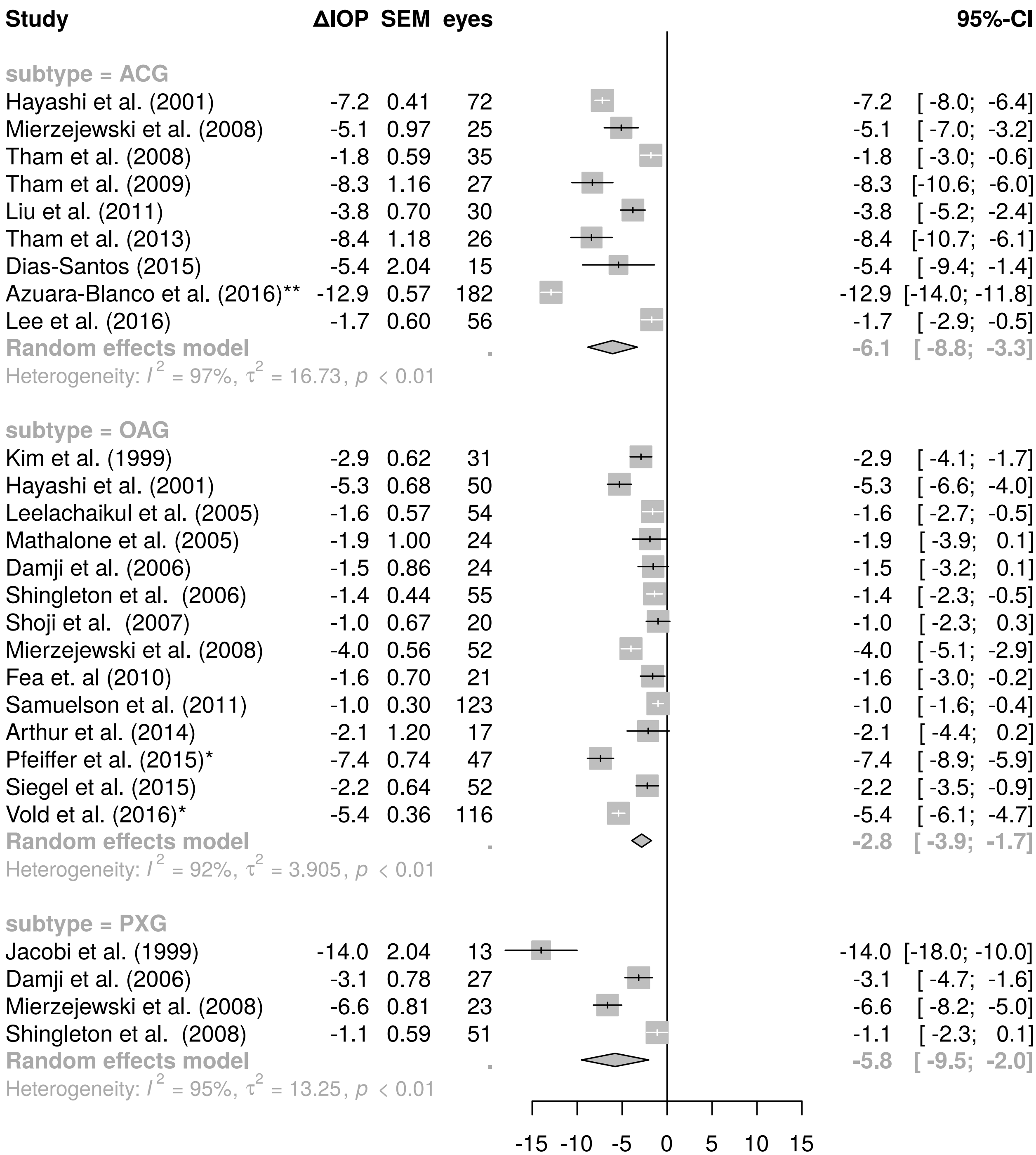
```
df_ <- df %>%
  filter(!is.na(OneYAbsIOPChangeMean), subtype != "acute", MIGsYorN == 'N') %>%
  mutate(subtype=factor(subtype))
m <- metagen(OneYAbsIOPChangeMean,
             OneYAbsIOPChangeStdDev / sqrt(OneYEyes),
             study.name,
             data=df_,
             byvar=subtype,
   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

```r
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"))
```



Last period

```
df_ <- df %>%
  filter(!is.na(LastPeriodAbsIOPChangeMean), subtype != "acute", 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"))
```



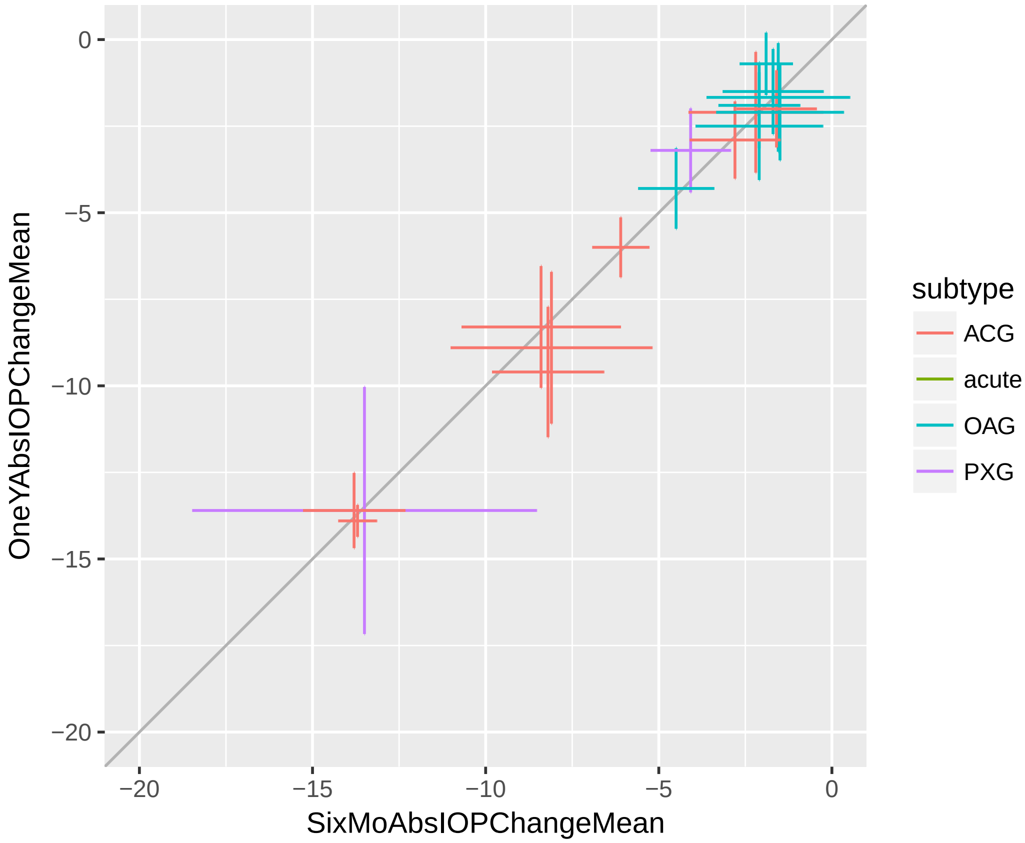
Correlation among time points

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

```
ggplot(df, 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() +
  coord_fixed(xlim=c(-20, 0), ylim=c(-20,0))
```

```
## Warning: Removed 25 rows containing missing values (geom_errorbar).

## Warning: Removed 25 rows containing missing values (geom_errorbarh).
```

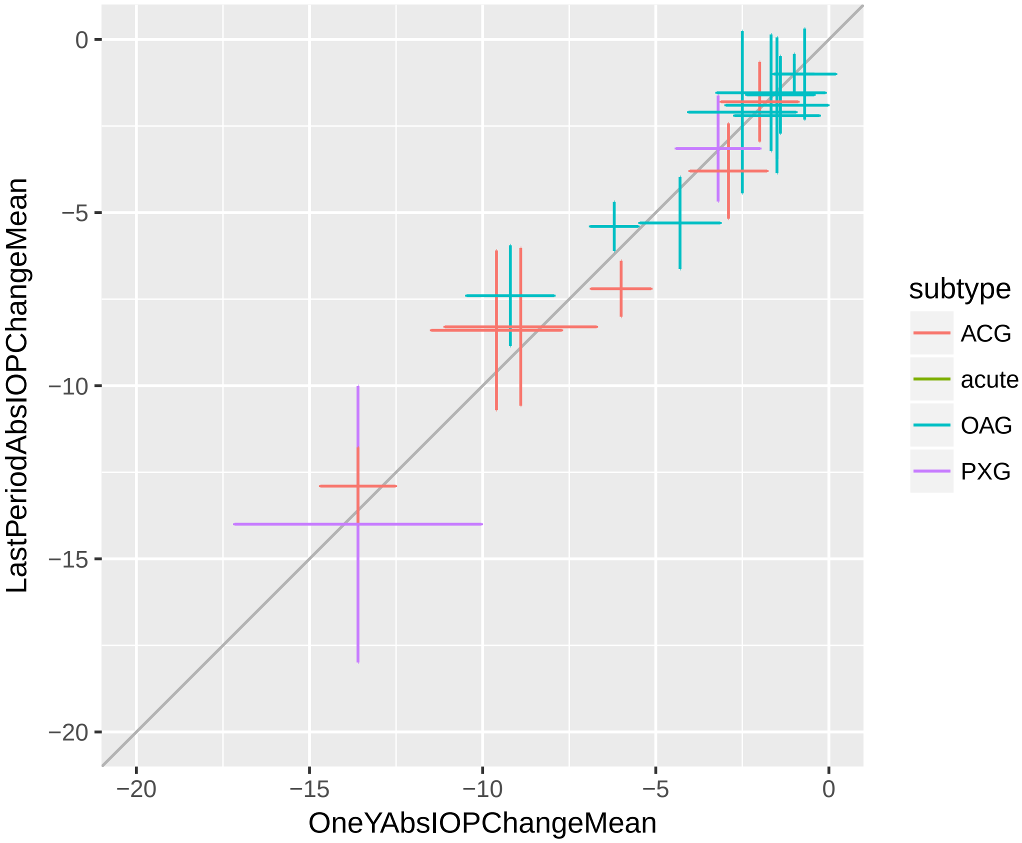


It's very clear that six months and 12 months IOP are highly correlated.

Similarly for one-year vs. last period:

```
ggplot(df, aes(y   =LastPeriodAbsIOPChangeMean,
               ymin=LastPeriodAbsIOPChangeMean - 1.96*LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEye
               ymax=LastPeriodAbsIOPChangeMean + 1.96*LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEye
               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 26 rows containing missing values (geom_errorbar).
## Warning: Removed 26 rows containing missing values (geom_errorbarh).
```



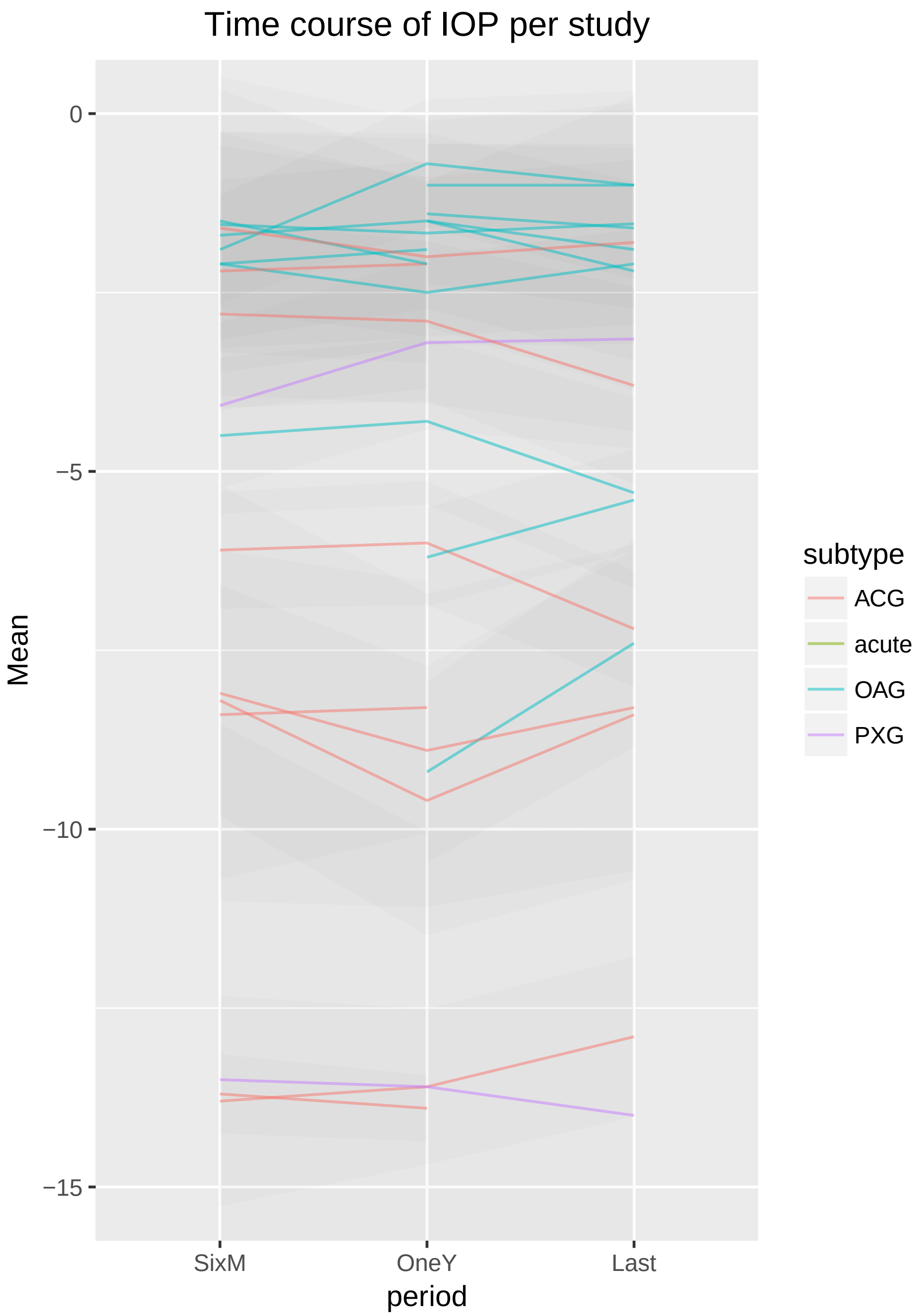
Again, correlations are very high. Present this in another way.

```r
library(reshape2)
```

```
##
## Attaching package: 'reshape2'
## The following object is masked from 'package:tidyr':
##
##     smiths
```

```r
nd <- melt(df %>%
             filter(MIGsYorN == 'N',
                    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_te
```



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.corrs <- 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
```

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

```
## [1] 0.6202973
```

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

```
## [1] 0.2077722
```

```r
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
```

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

```
## [1] 0.9925379
```

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

```
## [1] 0.003406047
```

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.

```r
library(mvmeta)
```

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

```r
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)
  }
```

```r
  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) ~ subtyp
       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)
```

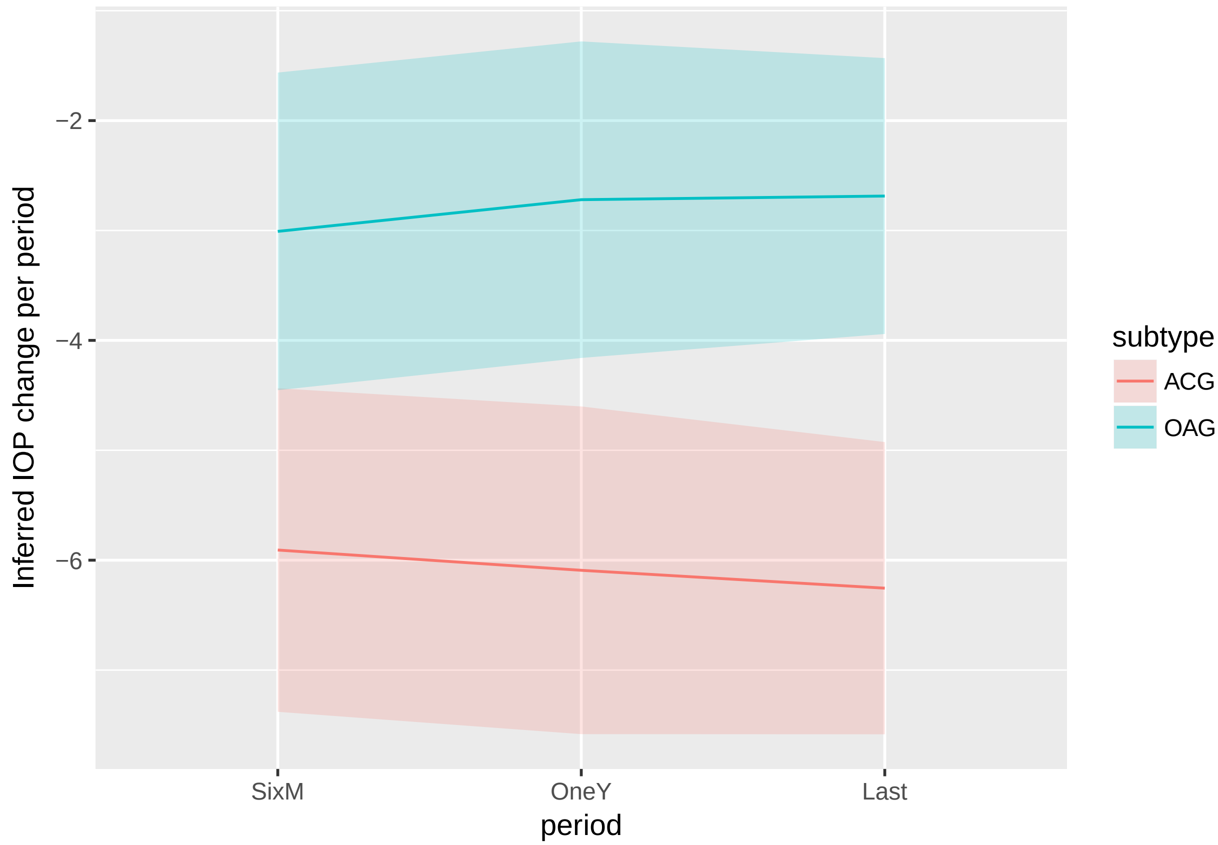
```
## Call:  mvmeta(formula = cbind(SixMoAbsIOPChangeMean, OneYAbsIOPChangeMean,
##    LastPeriodAbsIOPChangeMean) ~ subtype, S = get.correlation.matrices.tri(df_$SixMoAbsIOPChangeStdDev/
##    df_$OneYAbsIOPChangeStdDev/sqrt(df_$OneYEyes), df_$LastPeriodAbsIOPChangeStdDev/sqrt(df_$LastPerio
##      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)   -5.9077      0.7511  -7.8657    0.0000   -7.3797   -4.4356
## subtypeOAG     2.8997      1.0525   2.7551    0.0059    0.8368    4.9625
##
## (Intercept)  ***
## subtypeOAG    **
## OneYAbsIOPChangeMean :
##              Estimate  Std. Error        z  Pr(>|z|)  95%ci.lb  95%ci.ub
## (Intercept)   -6.0920      0.7607  -8.0089    0.0000   -7.5828   -4.6011
## subtypeOAG     3.3725      1.0576   3.1888    0.0014    1.2996    5.4454
##
## (Intercept)  ***
## subtypeOAG    **
## LastPeriodAbsIOPChangeMean :
##              Estimate  Std. Error        z  Pr(>|z|)  95%ci.lb  95%ci.ub
## (Intercept)   -6.2546      0.6784  -9.2199    0.0000   -7.5842   -4.9250
## subtypeOAG     3.5680      0.9329   3.8246    0.0001    1.7396    5.3965
##
## (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           2.9877  SixMoAbsIOPChangeMean
```

```
## OneYAbsIOPChangeMean          3.0236                 0.9981
## LastPeriodAbsIOPChangeMean    2.6030                 0.9919
##
## SixMoAbsIOPChangeMean       OneYAbsIOPChangeMean
## OneYAbsIOPChangeMean
## LastPeriodAbsIOPChangeMean                0.9821
##
## Multivariate Cochran Q-test for residual heterogeneity:
## Q = 1625.2906 (df = 62), p-value = 0.0000
## I-square statistic = 96.2%
##
## 36 studies, 68 observations, 6 fixed and 6 random-effects parameters
##    logLik        AIC        BIC
## -118.5856   261.1712   286.6968
```

```
newdata <- data.frame(subtype=c('OAG', 'ACG'))
pred <- predict(thefit, 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 != "acute", MIGsYorN == 'N') %>%
  mutate(subtype=relevel(factor(subtype), ref="OAG"))
m <- metagen(LastPeriodAbsIOPChangeMean,
             LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
             study.name,
             data=df_,
             byvar=subtype,
             n.e=OneYEyes)
```

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

```
##
## Mixed-Effects Model (k = 33; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):     26.2513 (SE = 9.6875)
## tau (square root of estimated tau^2 value):             5.1236
## I^2 (residual heterogeneity / unaccounted variability): 98.62%
## H^2 (unaccounted variability / sampling variability):   72.73
## R^2 (amount of heterogeneity accounted for):            0.00%
##
## Test for Residual Heterogeneity:
## QE(df = 31) = 2254.5144, p-val < .0001
##
## Test of Moderators (coefficient(s) 2):
## QM(df = 1) = 0.8360, p-val = 0.3605
##
## Model Results:
##
##                 estimate      se     zval    pval    ci.lb    ci.ub
## intrcpt          -3.4752  1.4802  -2.3478  0.0189  -6.3764  -0.5740  *
## LastPeriodEyes   -0.0238  0.0260  -0.9144  0.3605  -0.0747   0.0272
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
print(metareg(~ LastPeriodEyes * subtype, x=m))
```

```
##
## Mixed-Effects Model (k = 33; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):     15.5304 (SE = 5.8744)
## tau (square root of estimated tau^2 value):             3.9409
## I^2 (residual heterogeneity / unaccounted variability): 97.52%
## H^2 (unaccounted variability / sampling variability):   40.31
## R^2 (amount of heterogeneity accounted for):            36.43%
##
## Test for Residual Heterogeneity:
## QE(df = 27) = 1088.3177, p-val < .0001
##
## Test of Moderators (coefficient(s) 2,3,4,5,6):
## QM(df = 5) = 13.5909, p-val = 0.0184
##
## Model Results:
##
##                            estimate      se     zval    pval     ci.lb
## intrcpt                     -2.0693  1.8525  -1.1171  0.2640   -5.7002
## LastPeriodEyes              -0.0135  0.0328  -0.4125  0.6800   -0.0778
## subtypeACG                  -2.1400  2.5047  -0.8544  0.3929   -7.0492
## subtypePXG                 -12.1575  5.1350  -2.3676  0.0179  -22.2219
## LastPeriodEyes:subtypeACG   -0.0332  0.0422  -0.7882  0.4306   -0.1159
## LastPeriodEyes:subtypePXG    0.2999  0.1512   1.9839  0.0473    0.0036
##                              ci.ub
## intrcpt                     1.5615
```

```
## LastPeriodEyes              0.0508
## subtypeACG                  2.7691
## subtypePXG                 -2.0932  *
## LastPeriodEyes:subtypeACG   0.0494
## LastPeriodEyes:subtypePXG   0.5962  *
##
## ---
## 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):     22.3228 (SE = 8.2207)
## tau (square root of estimated tau^2 value):             4.7247
## I^2 (residual heterogeneity / unaccounted variability): 98.40%
## H^2 (unaccounted variability / sampling variability):   62.34
## R^2 (amount of heterogeneity accounted for):            8.63%
##
## Test for Residual Heterogeneity:
## QE(df = 31) = 1932.3895, p-val < .0001
##
## Test of Moderators (coefficient(s) 2):
## QM(df = 1) = 0.0830, p-val = 0.7732
##
## Model Results:
##
##          estimate        se     zval    pval      ci.lb     ci.ub
## intrcpt   89.0966  324.9770   0.2742  0.7840  -547.8466  726.0397
## Year      -0.0466    0.1617  -0.2881  0.7732    -0.3635    0.2703
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

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

```
##
## Mixed-Effects Model (k = 33; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):     13.5115 (SE = 4.9389)
## tau (square root of estimated tau^2 value):             3.6758
## I^2 (residual heterogeneity / unaccounted variability): 97.20%
## H^2 (unaccounted variability / sampling variability):   35.67
## R^2 (amount of heterogeneity accounted for):            44.70%
##
## Test for Residual Heterogeneity:
## QE(df = 27) = 963.1148, p-val < .0001
##
## Test of Moderators (coefficient(s) 2,3,4,5,6):
## QM(df = 5) = 12.4364, p-val = 0.0293
##
## Model Results:
##
##                     estimate         se     zval    pval       ci.lb
```

```
## intrcpt            101.1568   356.9373   0.2834  0.7769   -598.4274
## Year                -0.0517     0.1776  -0.2910  0.7710     -0.3999
## subtypeACG         215.3198   581.9158   0.3700  0.7114   -925.2142
## subtypePXG       -2425.5387  1160.3658  -2.0903  0.0366  -4699.8138
## Year:subtypeACG     -0.1088     0.2894  -0.3761  0.7069     -0.6761
## Year:subtypePXG      1.2078     0.5785   2.0879  0.0368      0.0740
##                      ci.ub
## intrcpt           800.7410
## Year                0.2965
## subtypeACG       1355.8538
## subtypePXG       -151.2635  *
## Year:subtypeACG     0.4584
## Year:subtypePXG     2.3415  *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
print(metareg(~ PreOpIOPMean, x=m))
```

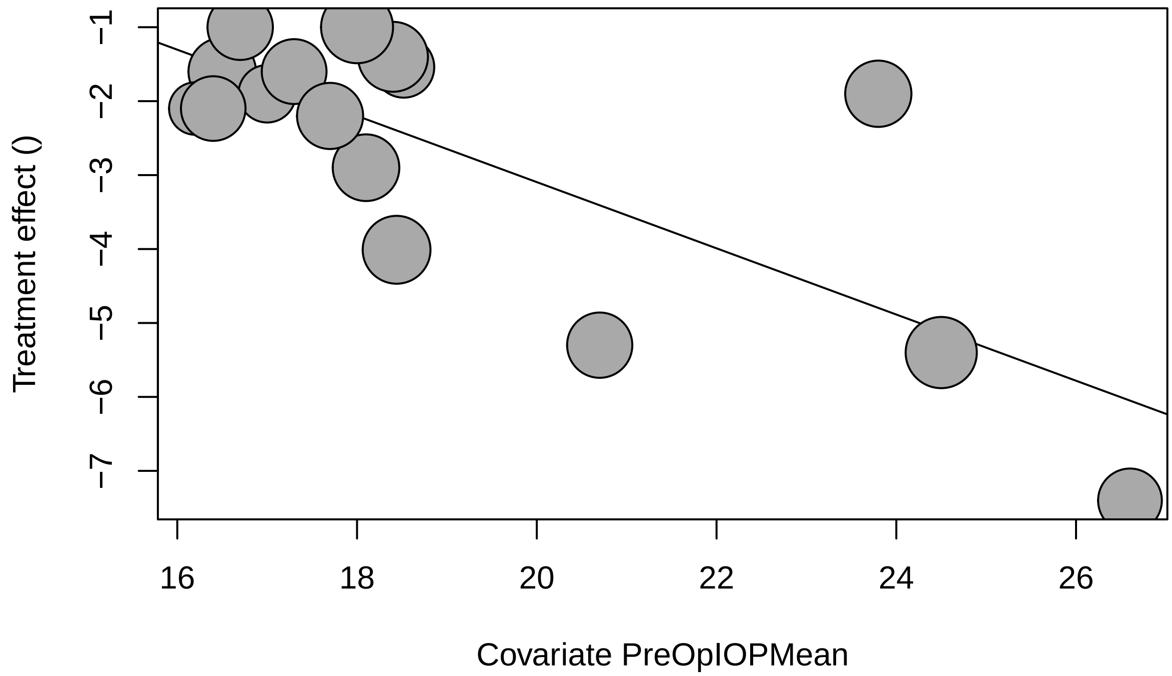
```
##
## Mixed-Effects Model (k = 33; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):     5.0095 (SE = 1.8023)
## tau (square root of estimated tau^2 value):             2.2382
## I^2 (residual heterogeneity / unaccounted variability): 92.99%
## H^2 (unaccounted variability / sampling variability):   14.27
## R^2 (amount of heterogeneity accounted for):            79.50%
##
## Test for Residual Heterogeneity:
## QE(df = 31) = 442.4039, p-val < .0001
##
## Test of Moderators (coefficient(s) 2):
## QM(df = 1) = 57.5862, p-val < .0001
##
## Model Results:
##
##               estimate      se     zval    pval    ci.lb    ci.ub
## intrcpt        11.3336  2.1216   5.3421  <.0001   7.1754  15.4918  ***
## PreOpIOPMean   -0.7859  0.1036  -7.5886  <.0001  -0.9888  -0.5829  ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
print(metareg(~ PreOpIOPMean * subtype, x=m))
```

```
##
## Mixed-Effects Model (k = 33; tau^2 estimator: DL)
##
## tau^2 (estimated amount of residual heterogeneity):     1.3374 (SE = 0.5549)
## tau (square root of estimated tau^2 value):             1.1564
## I^2 (residual heterogeneity / unaccounted variability): 77.18%
## H^2 (unaccounted variability / sampling variability):   4.38
## R^2 (amount of heterogeneity accounted for):            94.53%
##
## Test for Residual Heterogeneity:
```

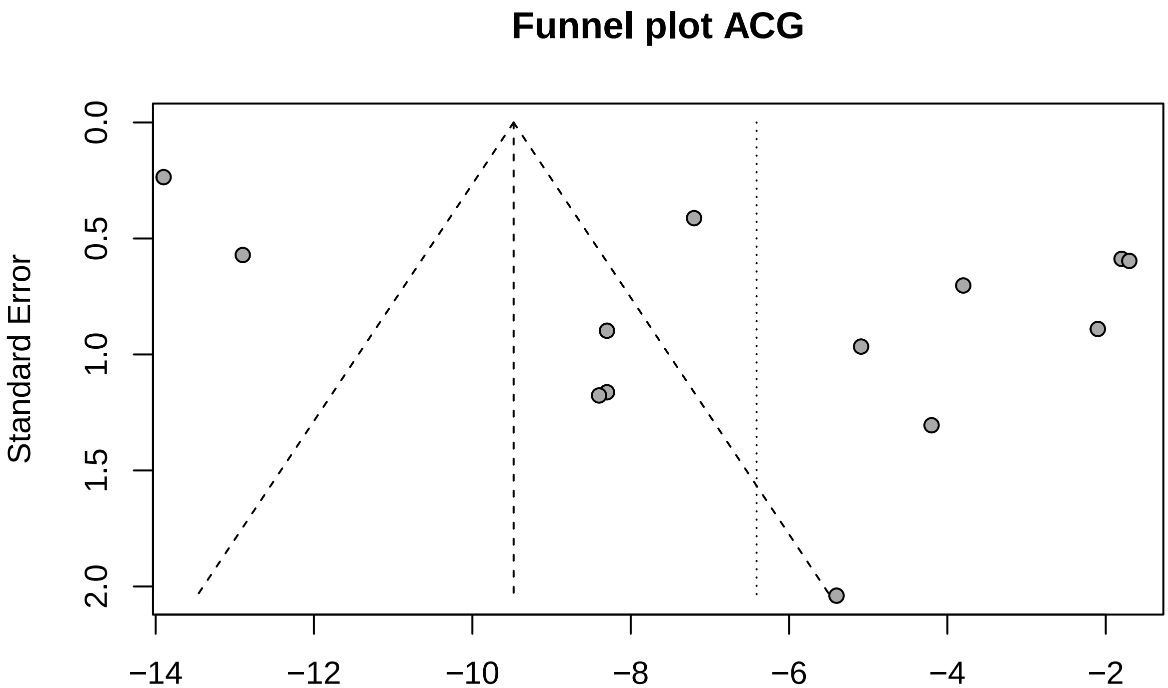
```
## QE(df = 27) = 118.3200, p-val < .0001
##
## Test of Moderators (coefficient(s) 2,3,4,5,6):
## QM(df = 5) = 202.7962, p-val < .0001
##
## Model Results:
##
##                          estimate      se     zval    pval    ci.lb
## intrcpt                    5.8521  2.1063   2.7784  0.0055   1.7238
## PreOpIOPMean              -0.4475  0.1085  -4.1251  <.0001  -0.6601
## subtypeACG                 5.5905  2.7842   2.0079  0.0447   0.1336
## subtypePXG                 8.8300  4.5191   1.9539  0.0507  -0.0272
## PreOpIOPMean:subtypeACG   -0.4137  0.1375  -3.0091  0.0026  -0.6832
## PreOpIOPMean:subtypePXG   -0.4777  0.2179  -2.1928  0.0283  -0.9047
##                            ci.ub
## intrcpt                   9.9803   **
## PreOpIOPMean             -0.2349  ***
## subtypeACG               11.0475    *
## subtypePXG               17.6873    .
## PreOpIOPMean:subtypeACG  -0.1443   **
## PreOpIOPMean:subtypePXG  -0.0507    *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

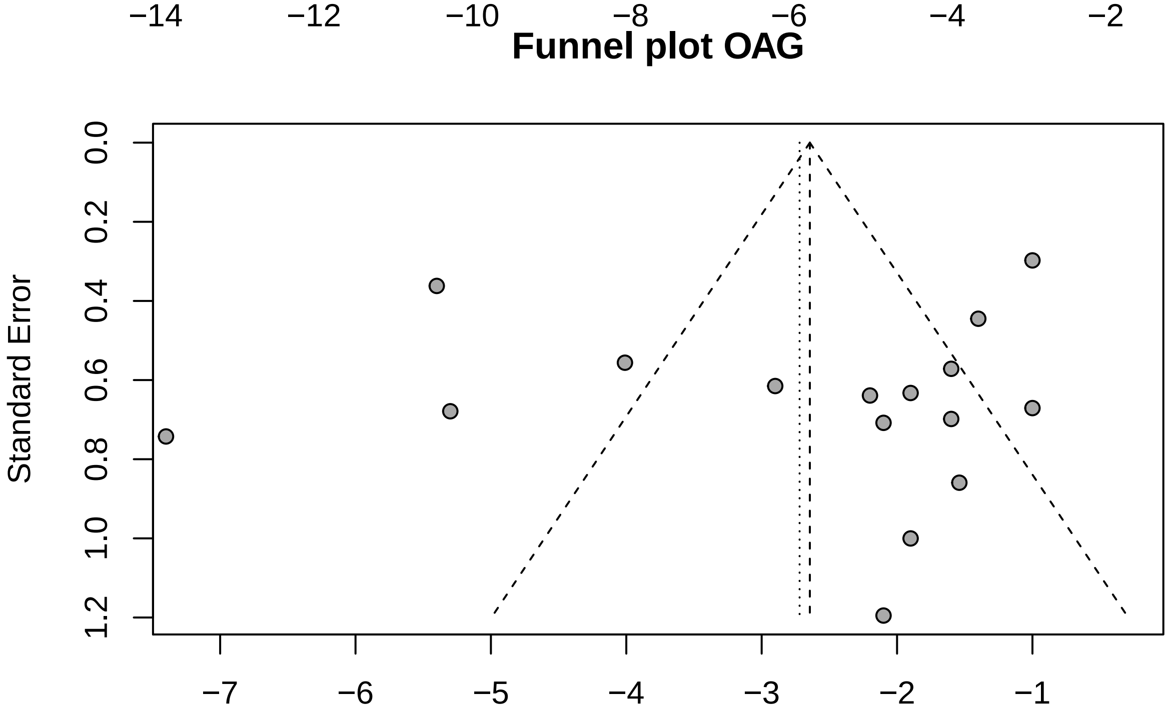
```r
# Same, restricted to OAG only
df_ <- df %>% filter(!is.na(LastPeriodAbsIOPChangeMean), subtype == "OAG", MIGsYorN == 'N') %>%
  mutate(subtype=relevel(factor(subtype), ref="OAG"))
m <- metagen(LastPeriodAbsIOPChangeMean,
             LastPeriodAbsIOPChangeStdDev / sqrt(LastPeriodEyes),
             study.name,
             data=df_,
             byvar=subtype,
             n.e=LastPeriodEyes)

bubble(metareg(~ PreOpIOPMean, x=m))
```

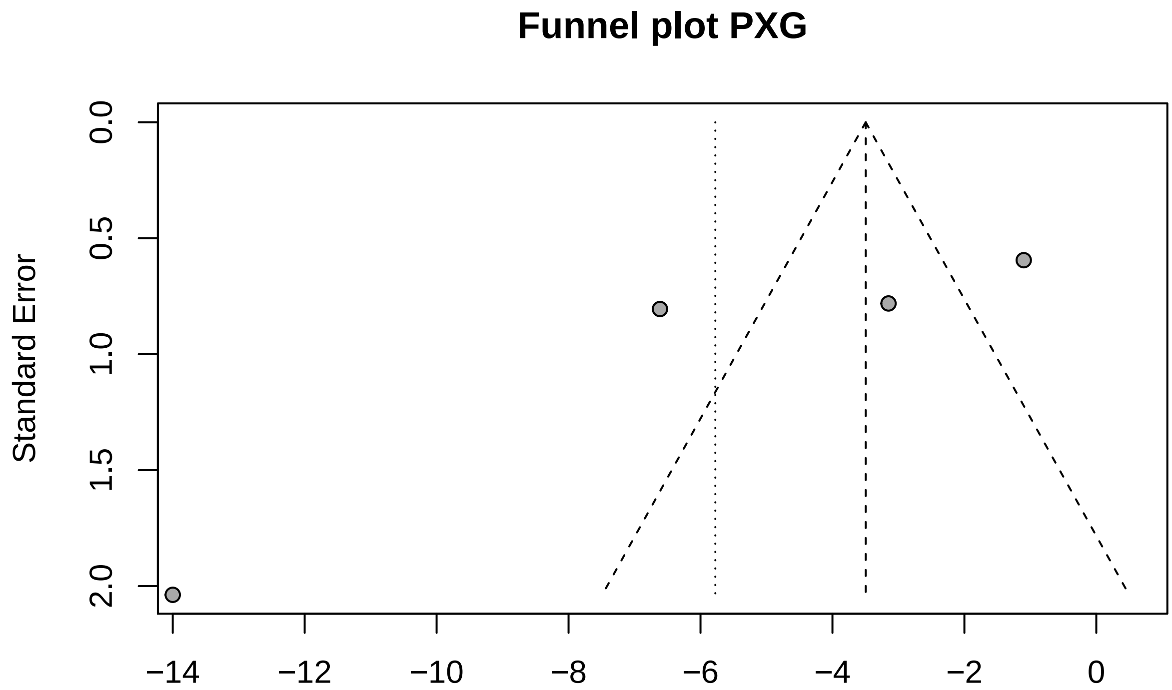


Small study bias

```
df_ <- df %>% filter(!is.na(df$LastPeriodAbsIOPChangeMean),
                     df$subtype != "acute",
                     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))
}
```

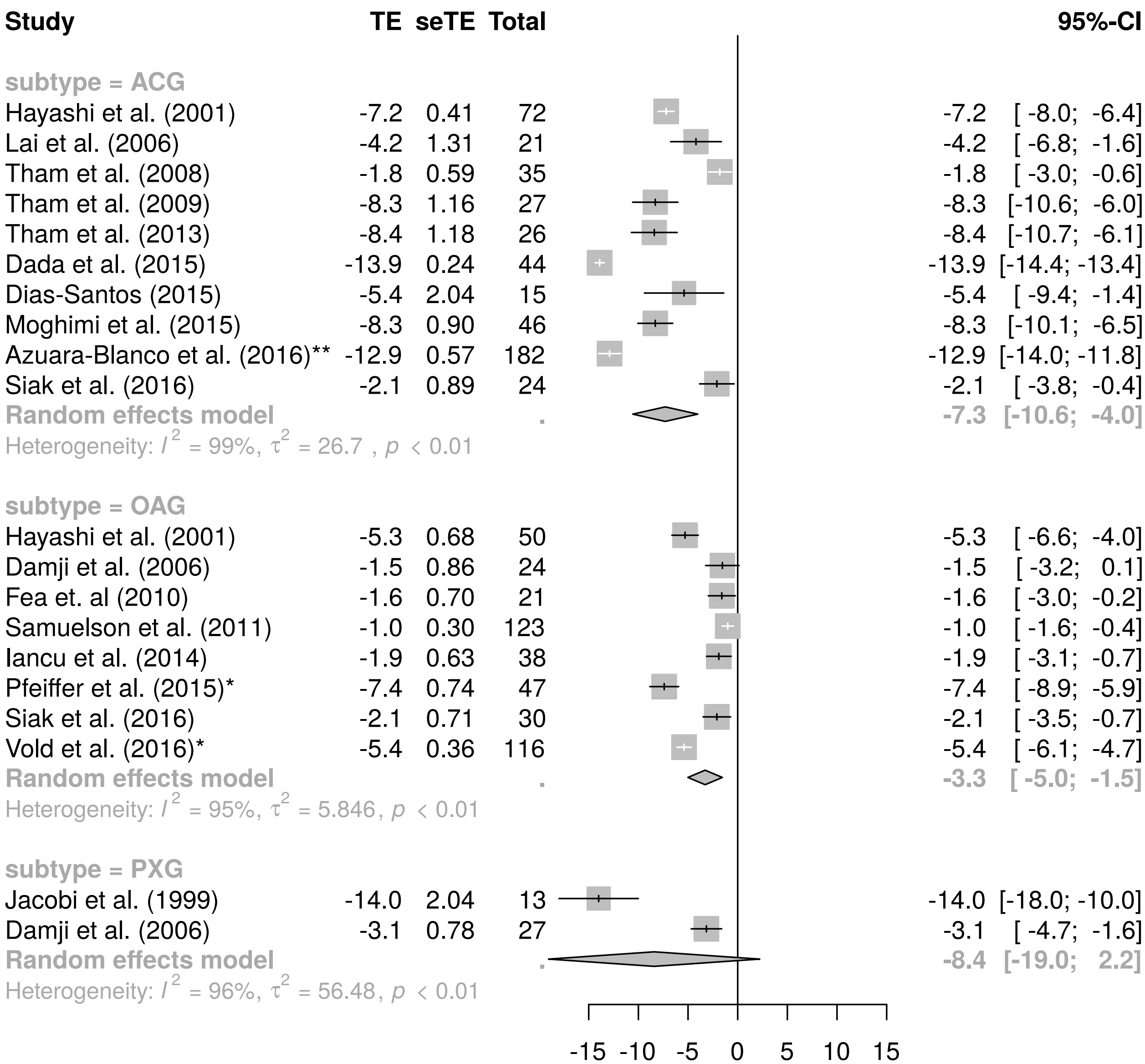

Funnel plot ACG
Standard Error
0.0
0.5
1.0
1.5
2.0
−14
−12
−10
−8
−6
−4
−2


Funnel plot OAG
Standard Error
0.0
0.2
0.4
0.6
0.8
1.0
1.2
−7
−6
−5
−4
−3
−2
−1


Funnel plot PXG
Standard Error
0.0
0.5
1.0
1.5
2.0
−14
−12
−10
−8
−6
−4
−2
0

Alternative filterings of the data

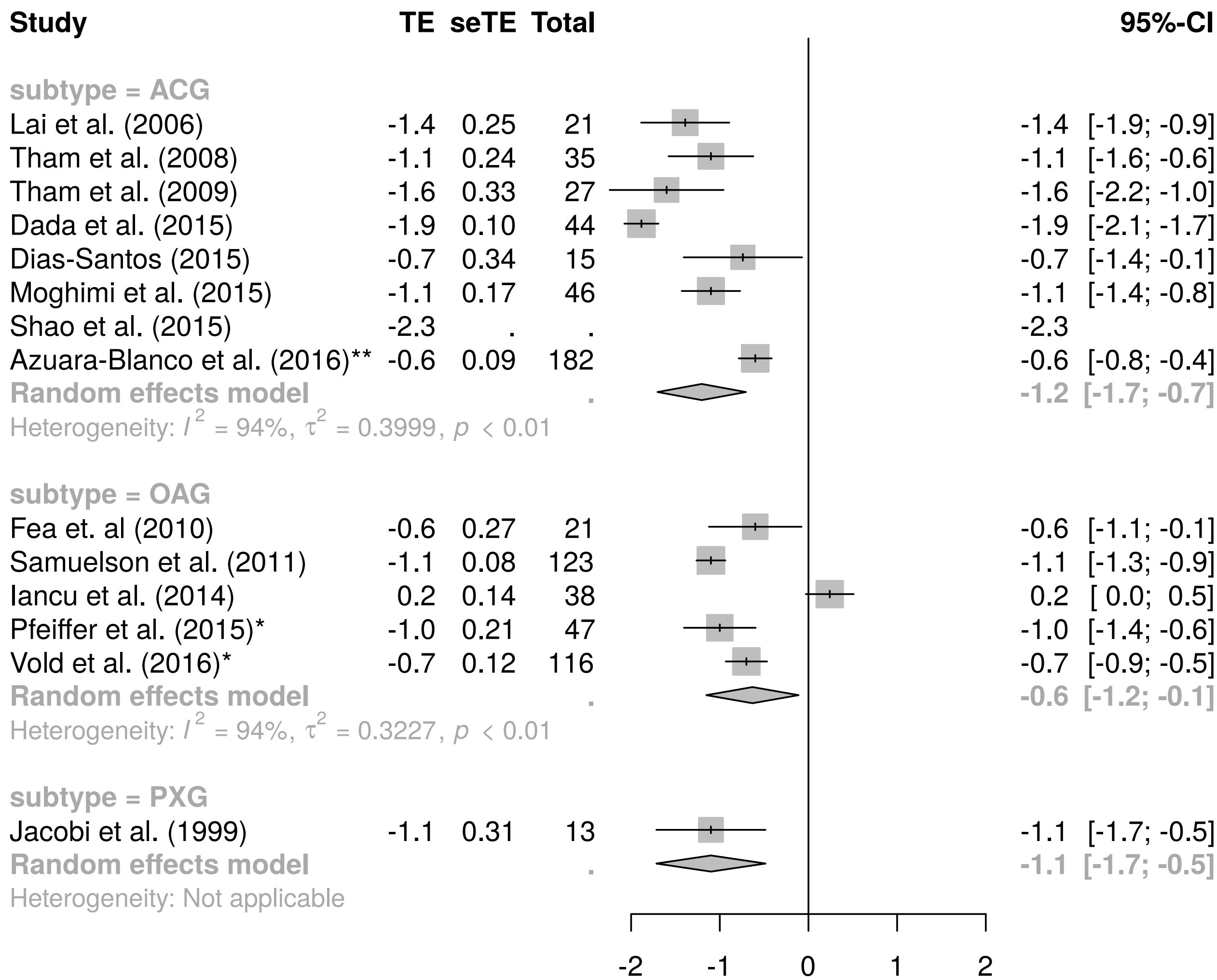
Prospective studies only



Meds

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

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



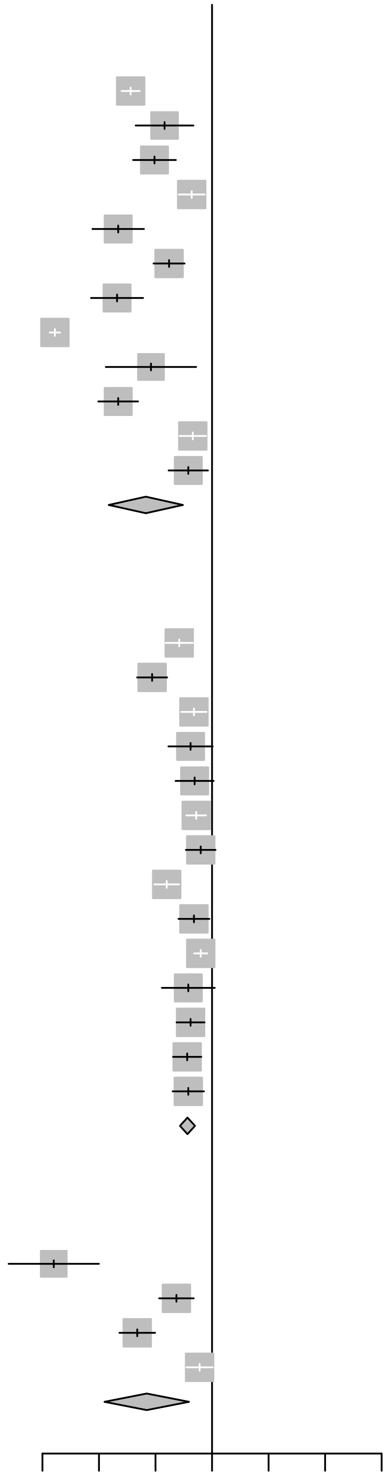
Excluding washout studies

Last period

```r
df_ <- df %>%
  filter(!is.na(LastPeriodAbsIOPChangeMean), subtype != "acute", 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"))
```

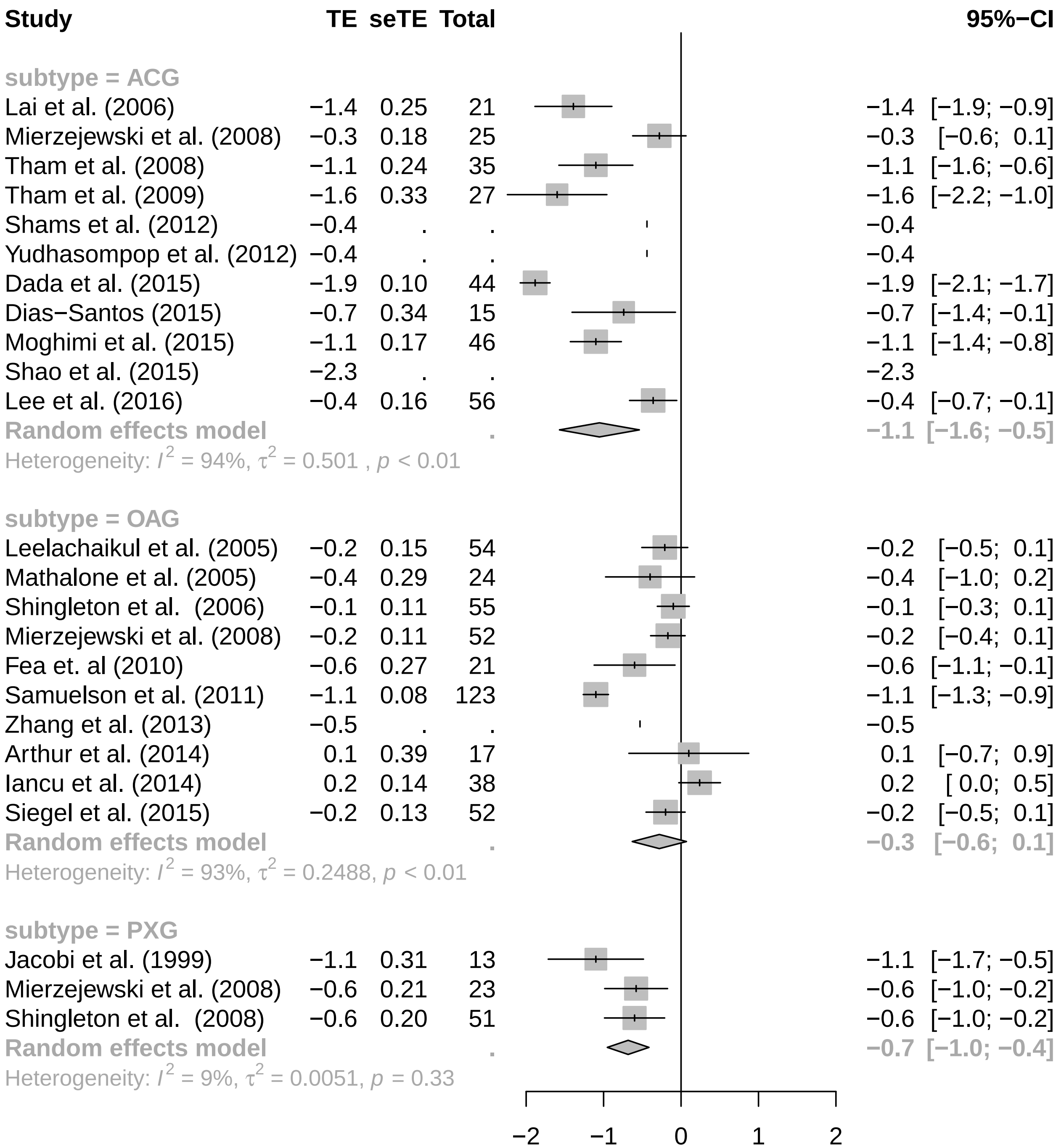
Study	TE	seTE	Total		95%-CI
subtype = ACG					
Hayashi et al. (2001)	-7.2	0.41	72	-7.2	[-8.0; -6.4]
Lai et al. (2006)	-4.2	1.31	21	-4.2	[-6.8; -1.6]
Mierzejewski et al. (2008)	-5.1	0.97	25	-5.1	[-7.0; -3.2]
Tham et al. (2008)	-1.8	0.59	35	-1.8	[-3.0; -0.6]
Tham et al. (2009)	-8.3	1.16	27	-8.3	[-10.6; -6.0]
Liu et al. (2011)	-3.8	0.70	30	-3.8	[-5.2; -2.4]
Tham et al. (2013)	-8.4	1.18	26	-8.4	[-10.7; -6.1]
Dada et al. (2015)	-13.9	0.24	44	-13.9	[-14.4; -13.4]
Dias-Santos (2015)	-5.4	2.04	15	-5.4	[-9.4; -1.4]
Moghimi et al. (2015)	-8.3	0.90	46	-8.3	[-10.1; -6.5]
Lee et al. (2016)	-1.7	0.60	56	-1.7	[-2.9; -0.5]
Siak et al. (2016)	-2.1	0.89	24	-2.1	[-3.8; -0.4]
Random effects model			.	**-5.9**	**[-9.1; -2.6]**
Heterogeneity: $I^2 = 99\%$, $\tau^2 = 32.63$, $p < 0.01$					
subtype = OAG					
Kim et al. (1999)	-2.9	0.62	31	-2.9	[-4.1; -1.7]
Hayashi et al. (2001)	-5.3	0.68	50	-5.3	[-6.6; -4.0]
Leelachaikul et al. (2005)	-1.6	0.57	54	-1.6	[-2.7; -0.5]
Mathalone et al. (2005)	-1.9	1.00	24	-1.9	[-3.9; 0.1]
Damji et al. (2006)	-1.5	0.86	24	-1.5	[-3.2; 0.1]
Shingleton et al. (2006)	-1.4	0.44	55	-1.4	[-2.3; -0.5]
Shoji et al. (2007)	-1.0	0.67	20	-1.0	[-2.3; 0.3]
Mierzejewski et al. (2008)	-4.0	0.56	52	-4.0	[-5.1; -2.9]
Fea et. al (2010)	-1.6	0.70	21	-1.6	[-3.0; -0.2]
Samuelson et al. (2011)	-1.0	0.30	123	-1.0	[-1.6; -0.4]
Arthur et al. (2014)	-2.1	1.20	17	-2.1	[-4.4; 0.2]
Iancu et al. (2014)	-1.9	0.63	38	-1.9	[-3.1; -0.7]
Siegel et al. (2015)	-2.2	0.64	52	-2.2	[-3.5; -0.9]
Siak et al. (2016)	-2.1	0.71	30	-2.1	[-3.5; -0.7]
Random effects model			.	**-2.2**	**[-2.8; -1.5]**
Heterogeneity: $I^2 = 76\%$, $\tau^2 = 1.154$, $p < 0.01$					
subtype = PXG					
Jacobi et al. (1999)	-14.0	2.04	13	-14.0	[-18.0; -10.0]
Damji et al. (2006)	-3.1	0.78	27	-3.1	[-4.7; -1.6]
Mierzejewski et al. (2008)	-6.6	0.81	23	-6.6	[-8.2; -5.0]
Shingleton et al. (2008)	-1.1	0.59	51	-1.1	[-2.3; 0.1]
Random effects model			.	**-5.8**	**[-9.5; -2.0]**
Heterogeneity: $I^2 = 95\%$, $\tau^2 = 13.25$, $p < 0.01$					



Meds

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

```
         df$subtype != "acute", 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"))
```

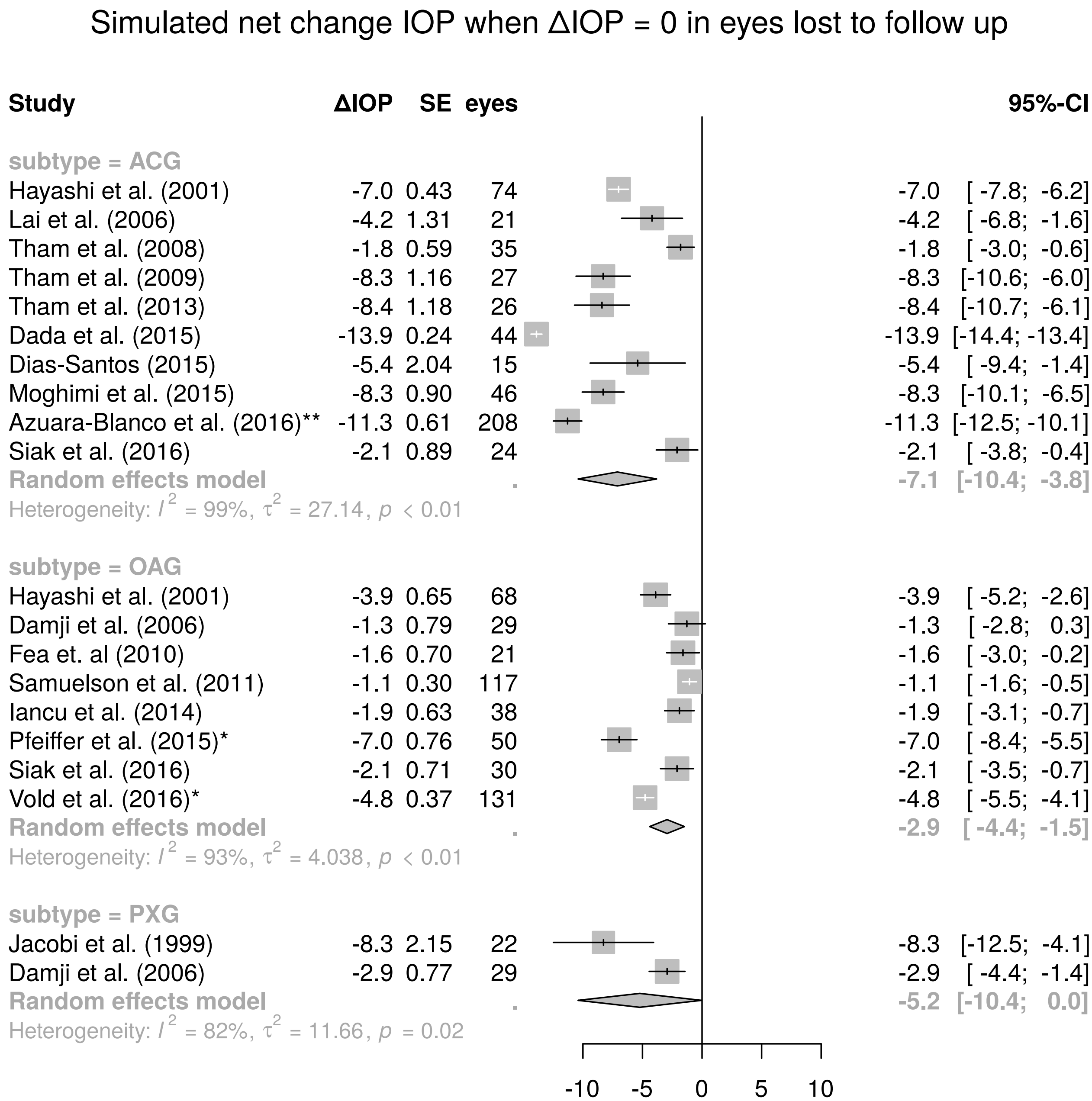


Sensitivity to missingness

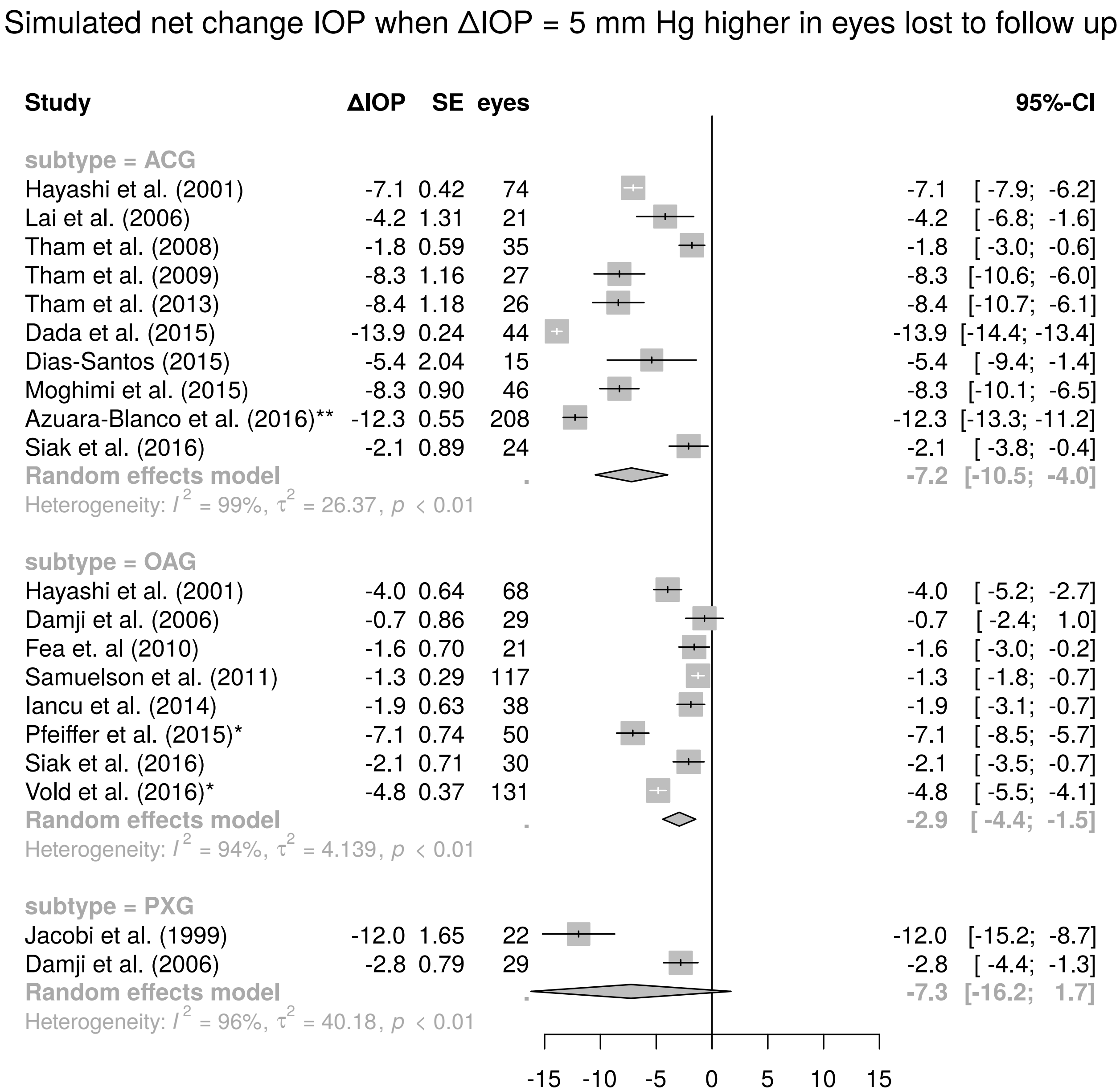
Simulate what the results would look like if there was no effect in the eyes lost to follow up ($\Delta IOP = 0$).

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

  df_ <- df %>%
```

```r
    filter(!is.na(LastPeriodAbsIOPChangeMean), subtype != "acute") %>%
    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", "ΔIOP", "SE", "eyes"))
}

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




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



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.

```r
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)
```

```r
df_ <- df %>%
  filter(!is.na(LastPeriodAbsIOPChangeMean), subtype != "acute", 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"))
```

Study	TE	seTE	Total	Type	95%-CI	Weight
Khan et al. (2015)	-5.3	0.72	49	2 site iStent	-5.3 [-6.7; -3.9]	5.0%
Klamann et al. (2013)	-9.3	1.06	27	Ab interno trabeculectomy	-9.3 [-11.4; -7.2]	4.5%
Neiweem et al. (2016)	-4.5	0.31	352	Ab Interno Trabeculectomy	-4.5 [-5.1; -3.9]	5.3%
Khan et al. (2015)	-3.3	1.05	52	Ab interno Trabeculotomy	-3.3 [-5.4; -1.2]	4.6%
Shoji et al. (2007)	-3.1	0.45	16	Canaloplasty	-3.1 [-4.0; -2.2]	5.2%
Arthur et al. (2014)	-5.3	1.56	11	Canaloplasty	-5.3 [-8.4; -2.2]	3.8%
Schoenberg et al. (2015)	-5.1	0.98	36	Canaloplasty	-5.1 [-7.0; -3.2]	4.7%
Tetz et al. (2015)	-9.9	1.01	27	Canaloplasty	-9.9 [-11.9; -7.9]	4.6%
Rekas et al. (2015)	-6.4	1.20	29	Canoloplasty	-6.4 [-8.8; -4.0]	4.4%
Vold et al. (2016)*	-7.4	0.24	332	Cypass	-7.4 [-7.9; -6.9]	5.3%
Sheybani et al. (2015)	-3.2	0.93	83	Endocyclophotocoagulation	-3.2 [-5.0; -1.4]	4.7%
Siegel et al. (2015)	-2.5	0.29	261	Endocyclophotocoagulation	-2.5 [-3.1; -1.9]	5.3%
Sheybani et al. (2015)	-7.0	0.72	34	Gelatin stent	-7.0 [-8.4; -5.6]	4.9%
Shao et al. (2015)	-8.5	1.17	23	Goniosynechialysis	-8.5 [-10.8; -6.2]	4.4%
Pfeiffer et al. (2015)*	-9.4	0.68	43	Hydrus Microstent	-9.4 [-10.7; -8.1]	5.0%
Fea et. al (2010)	-3.2	0.87	12	iStent	-3.2 [-4.9; -1.5]	4.8%
Samuelson et al. (2011)	-1.5	0.28	117	iStent	-1.5 [-2.0; -1.0]	5.3%
Parikh et al. (2016)	-4.2	0.25	498	Trabectome	-4.2 [-4.7; -3.7]	5.3%
Jacobi et al. (1999)	-13.1	1.47	26	Trabecular Aspiration	-13.1 [-16.0; -10.2]	4.0%
Klamann et al. (2013)	-5.1	1.17	28	Trabecular Aspiration	-5.1 [-7.4; -2.8]	4.4%
Moghimi et al. (2015)	-8.8	1.02	45	Viscogonioplasty	-8.8 [-10.8; -6.8]	4.6%
Random effects model			**2101**		**-5.9 [-7.0; -4.7]**	**100.0%**

Heterogeneity: $I^2 = 96\%$, $\tau^2 = 6.191$, $p < 0.01$