

Simulations for ‘Characterising the use of internal meta-analyses and assessing their impact’

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Dependencies

```
library(tidyverse)
library(metafor)
library(colorspace)
```

Session info

```
sessionInfo()
```

```
## R version 3.6.0 (2019-04-26)
## Platform: x86_64-apple-darwin15.6.0 (64-bit)
## Running under: macOS 10.15.3
##
## Matrix products: default
## BLAS: /Library/Frameworks/R.framework/Versions/3.6/Resources/lib/libRblas.0.dylib
## LAPACK: /Library/Frameworks/R.framework/Versions/3.6/Resources/lib/libRlapack.dylib
##
## locale:
## [1] en_GB.UTF-8/en_GB.UTF-8/en_GB.UTF-8/C/en_GB.UTF-8/en_GB.UTF-8
##
## attached base packages:
## [1] stats      graphics  grDevices  utils      datasets  methods   base
##
## other attached packages:
## [1] colorspace_1.4-1 metafor_2.2-8      Matrix_1.2-17      forcats_0.5.0
## [5] stringr_1.4.0     dplyr_0.8.4        purrr_0.3.3        readr_1.3.1
## [9] tidyr_1.0.2       tibble_2.1.3       ggplot2_3.2.1      tidyverse_1.3.0
##
## loaded via a namespace (and not attached):
## [1] tidyselect_1.0.0 xfun_0.12          haven_2.2.0        lattice_0.20-38
## [5] vctrs_0.2.3      generics_0.0.2     htmltools_0.4.0    yaml_2.2.1
## [9] rlang_0.4.4      pillar_1.4.3       withr_2.1.2        glue_1.3.1
## [13] DBI_1.1.0         dbplyr_1.4.2       modelr_0.1.6       readxl_1.3.1
## [17] lifecycle_0.1.0  munsell_0.5.0      gtable_0.3.0       cellranger_1.1.0
## [21] rvest_0.3.5      evaluate_0.14      knitr_1.28         fansi_0.4.1
## [25] broom_0.5.5      Rcpp_1.0.3         scales_1.1.0       backports_1.1.5
## [29] jsonlite_1.6.1   fs_1.3.1           hms_0.5.3          digest_0.6.25
## [33] stringi_1.4.6    grid_3.6.0         cli_2.0.2          tools_3.6.0
## [37] magrittr_1.5     lazyeval_0.2.2     crayon_1.3.4       pkgconfig_2.0.3
## [41] xml2_1.2.2       reprex_0.3.0       lubridate_1.7.4    assertthat_0.2.1
## [45] rmarkdown_2.1    httr_1.4.1         rstudioapi_0.11    R6_2.4.1
## [49] nlme_3.1-139     compiler_3.6.0
```

Define functions

sim_func()

A function for simulating an independent samples t-test with sample size n and population effect size d . Observed scores are drawn from a normal distribution. The function lists resulting effect size (Cohen's d) and p-value.

```
sim_func <- function(n, d = 0) {  
  dat <- tibble(  
    grp = rep(LETTERS[1:2], each = n),  
    score = c(rnorm(n, d, 1), rnorm(n, 0, 1))  
  )  
  #t-test on simulated data  
  myt <- t.test(score ~ grp, dat)  
  #get p-value  
  p <- myt$p.value  
  #get effect size  
  es <- cohens_d(myt$statistic[[1]], n, n)  
  list("p" = p, "es" = es)  
}
```

cohens_d()

A function for calculating Cohen's d for an independent samples t-test using a formula from Lakens (2013). The function requires a t-statistic and two sample sizes.

```
cohens_d <- function(t, n1, n2 = n1){  
  t*sqrt(1/n1 + 1/n2)  
}
```

var_d()

A function for calculating variance needed to calculate internal meta-analysis. The formula was obtained from Vosgerau, Simonsohn, Nelson, & Simmons (2019). Requires an effect size and a sample size.

```
var_d <- function(d,n){  
  df <- (2*n-2)  
  (2/n+(d^2)/(2*df)) * ((2*n)/(df))  
}
```

mini_meta()

A function that runs an internal meta-analysis for a user-specified number of studies, with a population effect size d and sample size n (per group). Can use methods available in `rma()`, here “FE” (fixed effect) and “HE” (random effects).

```
mini_meta <- function(n.studies, # no. of studies
                     d, # effect size
                     n, # sample size (per group)
                     method = "HE"){ # method for rma()

  study.ps <- vector() # vector for p-values
  study.effects <- vector() # vector for effect sizes
  study.var <- vector() # vector for variances

  for (i in 1:n.studies) { # loop until specified number of studies is reached
    study <- sim_func(n, d) # simulate study with n sample and d effect size
    study.ps[i] <- study$p # p-values in vector
    study.effects[i] <- study$es # effect sizes in vector
    study.var[i] <- var_d(study.effects[i], n) # variances in vector
  }
  # run internal meta-analysis
  minimeta <- rma(yi = study.effects, vi = study.var, method = method)

  data.frame( # add results to a data.frame
    study = 1:length(study.ps),
    p = study.ps,
    es = study.effects
  ) %>%
  add_row(
    study = 0, # internal meta-analysis results
    p = minimeta$pval, # meta-analysed p-value
    es = minimeta$beta[[1]] # meta-analysed effect size
  )
}
```

p_bound_meta()

A function that runs a user-specified number of studies all with a group sample size of n and true effect size of d . If specified conditions are met (e.g. first p -value < 0.05 and last p -value < 0.1), then results are mini meta-analysed. Can run fixed-effect or random-effects models (specified using “method”).

```
p_bound_meta <- function(n.studies, # no. of studies
                        d, # effect size
                        n, # sample size
                        method = "HE", # method for rma()
                        pmax.first = .05, # threshold for first p
                        pmax.last = .05){ # threshold for last p

  study.ps <- vector() # vector for p-values
  study.effects <- vector() # vector for effect sizes
  study.var <- vector() # vector for variances

  study <- sim_func(n, d) # simulate first study
  study.ps[1] <- study$p
  study.effects[1] <- study$es
  study.var[1] <- var_d(study.effects[1], n)

  if (study.ps[1] >= pmax.first) { # if first study p > pmax.first
    tbl <- data.frame( # create table of results
      study = 1,
      p = study.ps,
      es = study.effects
    )
    return(tbl)
  }
  # else, keep running studies until n.studies
  for (i in 2:n.studies) {
    study <- sim_func(n, d)
    study.ps[i] <- study$p
    study.effects[i] <- study$es
    study.var[i] <- var_d(study.effects[i], n)

    # unless p < pmax.last, then stop running more studies
    if (study$p < pmax.last) break
  }
  # run internal meta-analysis
  minimeta <- rma(yi = study.effects, vi = study.var, method = method)

  data.frame( # add results to a dataframe
    study = 1:length(study.ps),
    p = study.ps,
    es = study.effects
  ) %>%
  add_row(
    study = 0, # meta-analysis results
    p = minimeta$pval, # meta-analysed p-value
    es = minimeta$beta[[1]] # meta-analyseds effect size
  )
}
```

meta_hack()

A function that runs an internal meta-analysis after every new study is added. It allows user to specify both a first p-value threshold (pmax.first) as well as a 'minitarget', i.e. a threshold for the meta-analysed p-value that stops the running of more studies (unless max number of studies is reached before).

```
meta_hack <- function(n.studies, # no. of studies
                     d, # effect size
                     n, # sample size
                     method = "HE", # method for rma()
                     pmax.first = .05, # first p threshold
                     minitarget = .05){ # meta-analysed p threshold

  # setting up results vectors
  study.ps <- vector()
  study.effects <- vector()
  study.var <- vector()

  # results of first study
  study <- sim_func(n, d)
  study.ps[1] <- study$p
  study.effects[1] <- study$es
  study.var[1] <- var_d(study.effects[1], n)

  if (study.ps[1] >= pmax.first) { # if first study p > pmax.first
    tbl <- data.frame( # create table of results
      study = 1,
      p = study.ps,
      es = study.effects)
    return(tbl)
  }

  # else, keep running studies until n.studies or
  for (i in 2:n.studies) {
    study <- sim_func(n, d)
    study.ps[i] <- study$p
    study.effects[i] <- study$es
    study.var[i] <- var_d(study.effects[i], n)
    # meta p < minitarget
    minimeta <- rma(yi = study.effects, vi = study.var, method = method)
    if (minimeta$pval < minitarget) break
  }
  data.frame( # add results to data frame
    study = 1:length(study.ps),
    p = study.ps,
    es = study.effects
  ) %>%
  add_row(
    study = 0, # meta-analysis results
    p = minimeta$pval, # meta p
    es = minimeta$beta[[1]] # meta es
  )
}
```

Analysis

Power

Simulation 1

Simulation 1 is a power analysis for fixed and random effects internal meta-analyses, with varied number of studies, effect sizes and sample sizes. The simulation was split by number of studies (2, 3, 4, and 5) to reduce the duration of a single simulation. Iterations were also kept at 1000 to save time.

Parameters

- Iterations: 1000
- Number of studies: 2, 3, 4 and 5
- Effect size: 0.1-1
- Sample sizes: 50-500
- Method: random (HE) and fixed (FE) effects

```
set.seed(1337) # reproducible seed

# 2 studies combined in internal meta-analysis

params <- crossing( # all simulation parameters are fully crossed
  n.studies = 2,
  n = seq(50, 500, 50),
  d = seq(0.1, 1, 0.1),
  iter = 1:1000,
  method = c("HE", "FE")
)

tmp2 <- purrr::pmap_dfr(params, function(...) {
  dots <- list(...)
  mini_meta(n.studies = dots$n.studies,
            d = dots$d,
            n = dots$n,
            method = dots$method) %>%
    mutate(!!!dots)
})

save(tmp2, file = "power2_tmp.RData")

# 3 studies combined in internal meta-analysis

params <- crossing( # all simulation parameters are fully crossed
  n.studies = 3,
  n = seq(50, 500, 50),
  d = seq(0.1, 1, 0.1),
  iter = 1:1000,
  method = c("HE", "FE")
)

tmp3 <- purrr::pmap_dfr(params, function(...) {
  dots <- list(...)
```

```

    mini_meta(n.studies = dots$n.studies,
              d = dots$d,
              n = dots$n,
              method = dots$method) %>%
    mutate(!!!dots)
  })

save(tmp3, file = "power3_tmp.RData")

# 4 studies combined in internal meta-analysis

params <- crossing( # all simulation parameters are fully crossed
  n.studies = 4,
  n = seq(50, 500, 50),
  d = seq(0.1, 1, 0.1),
  iter = 1:1000,
  method = c("HE", "FE")
)

tmp4 <- purrr::pmap_dfr(params, function(...) {
  dots <- list(...)
  mini_meta(n.studies = dots$n.studies,
            d = dots$d,
            n = dots$n,
            method = dots$method) %>%
    mutate(!!!dots)
})

save(tmp4, file = "power4_tmp.RData")

# 5 studies combined in internal meta-analysis

params <- crossing( # all simulation parameters are fully crossed
  n.studies = 5,
  n = seq(50, 500, 50),
  d = seq(0.1, 1, 0.1),
  iter = 1:1000,
  method = c("HE", "FE")
)

tmp5 <- purrr::pmap_dfr(params, function(...) {
  dots <- list(...)
  mini_meta(n.studies = dots$n.studies,
            d = dots$d,
            n = dots$n,
            method = dots$method) %>%
    mutate(!!!dots)
})

save(tmp5, file = "power5_tmp.RData")

```


Visualisation 1

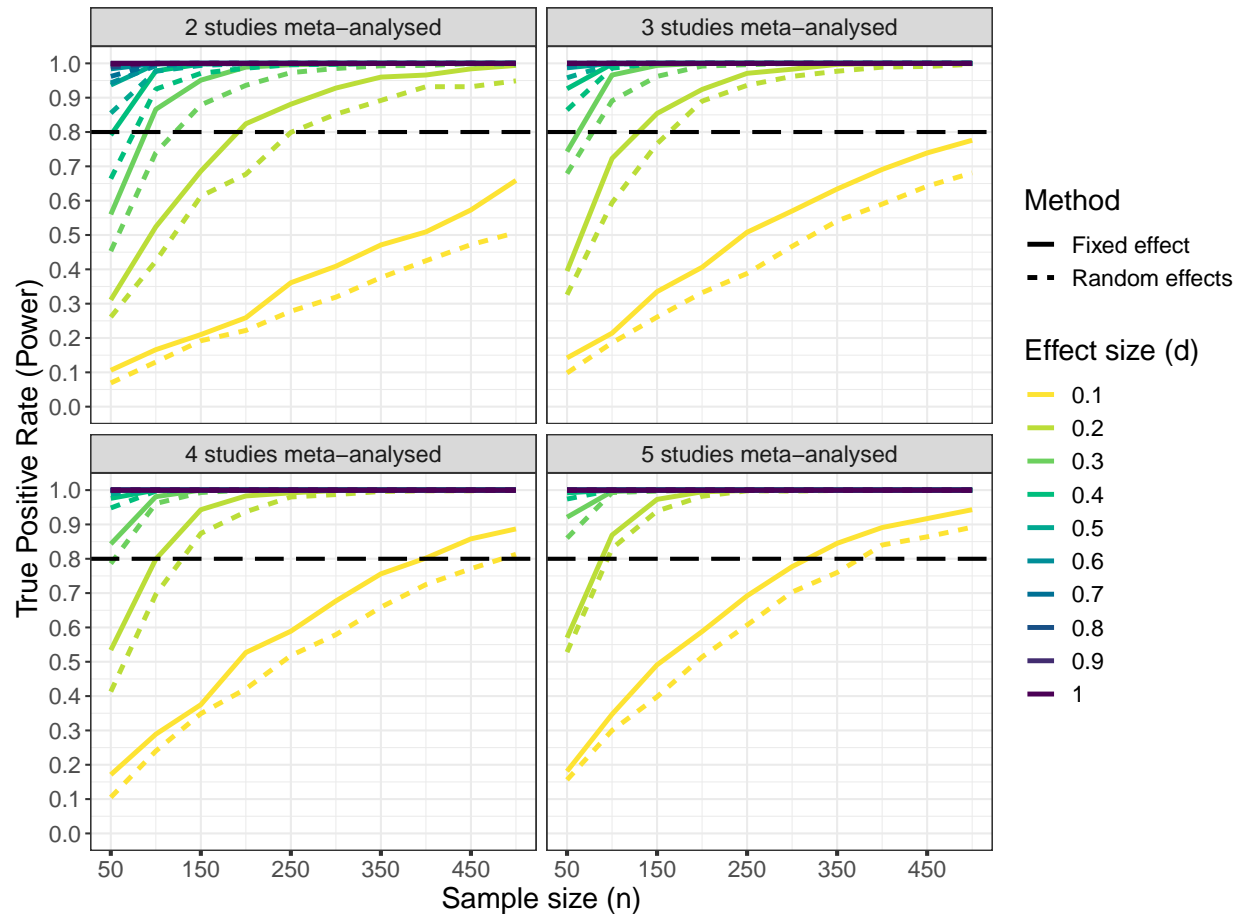
```
# load saved simulation results from chunk above
load("power2_tmp.RData")
load("power3_tmp.RData")
load("power4_tmp.RData")
load("power5_tmp.RData")

# facet labels
supp.labs <- c('2' = "2 studies meta-analysed",
              '3' = "3 studies meta-analysed",
              '4' = "4 studies meta-analysed",
              '5' = "5 studies meta-analysed")

# create dataframe of all study sizes
power_dat <- bind_rows(tmp2, tmp3, tmp4, tmp5) %>%
  filter(study == 0) %>%
  group_by(n, method, d, n.studies) %>%
  summarise(power = mean(p < .05)) %>% # calculate power
  ungroup()

# plot
ggplot(power_dat, aes(n, power)) +
  geom_line(aes(color = factor(d),
                 linetype = factor(method)), size=1.2) +
  facet_wrap(~n.studies,
            labeller = as_labeller(supp.labs)) +
  scale_y_continuous(limits = c(0, 1),
                    breaks = seq(0, 1, 0.1)) +
  scale_x_continuous(limits = c(50, 500),
                    breaks = seq(50, 500, 100)) +
  theme_bw() +
  scale_color_discrete_sequential("Viridis", name = "Effect size (d)") +
  scale_linetype(name = "Method",
                labels = c("Fixed effect", "Random effects")) +
  theme(axis.title = element_text(size = 15),
        title = element_text(size = 15),
        axis.text = element_text(size = 10),
        axis.ticks.x = element_line(size = 1),
        axis.text.x = element_text(size=12),
        axis.text.y = element_text(size=12),
        legend.text = element_text(size = 12),
        strip.text.x = element_text(size = 12)) +
  labs(x = "Sample size (n)",
       y = "True Positive Rate (Power)",
       title = "Statistical power of internal meta-analysis") +
  geom_hline(yintercept = 0.8, linetype = "longdash", size = 1)
```

Statistical power of internal meta-analysis



```
# ggsave("minimeta_power_plot.png", width = 10, height = 7)
```

No hacking FPR

Simulation 2

Simulation 2 simulates fixed and random effects internal meta-analyses, with varied number of studies, effect sizes and sample sizes. Iterations were kept at 1000 to be time efficient. The number of studies was set at 4 as that was the average number of studies in the coded literature.

Parameters

- Iterations: 1000
- Number of studies: 4
- Effect size: 0
- Sample sizes: 20-500
- Method: random (HE) and fixed (FE) effects

```
params <- crossing( # all simulation parameters are fully crossed
  n.studies = 4,
  n = seq(20, 500, 20),
  d = 0,
  iter = 1:1000,
  method = c("HE", "FE")
)

nohack_tmp <- purrr::pmap_dfr(params, function(...) {
  dots <- list(...)
  mini_meta(n.studies = dots$n.studies,
            d = dots$d,
            n = dots$n,
            method = dots$method) %>%
    mutate(!!!dots)
})

save(nohack_tmp, file = "nohack_tmp.RData")
```

Visualisation 2

```
# load saved simulation results from chunk above
load("nohack_tmp.RData")

# create dataframe of all study sizes
nohack_dat <- nohack_tmp %>%
  filter(study == 0) %>%
  group_by(n, method, d, n.studies) %>%
  summarise(power = mean(p < .05)) %>% # calculate power
  ungroup()

# colourblind-friendly palette
cbPalette <- c("#E69F00", "#56B4E9", "#009E73",
               "#F0E442", "#0072B2", "#D55E00", "#CC79A7")

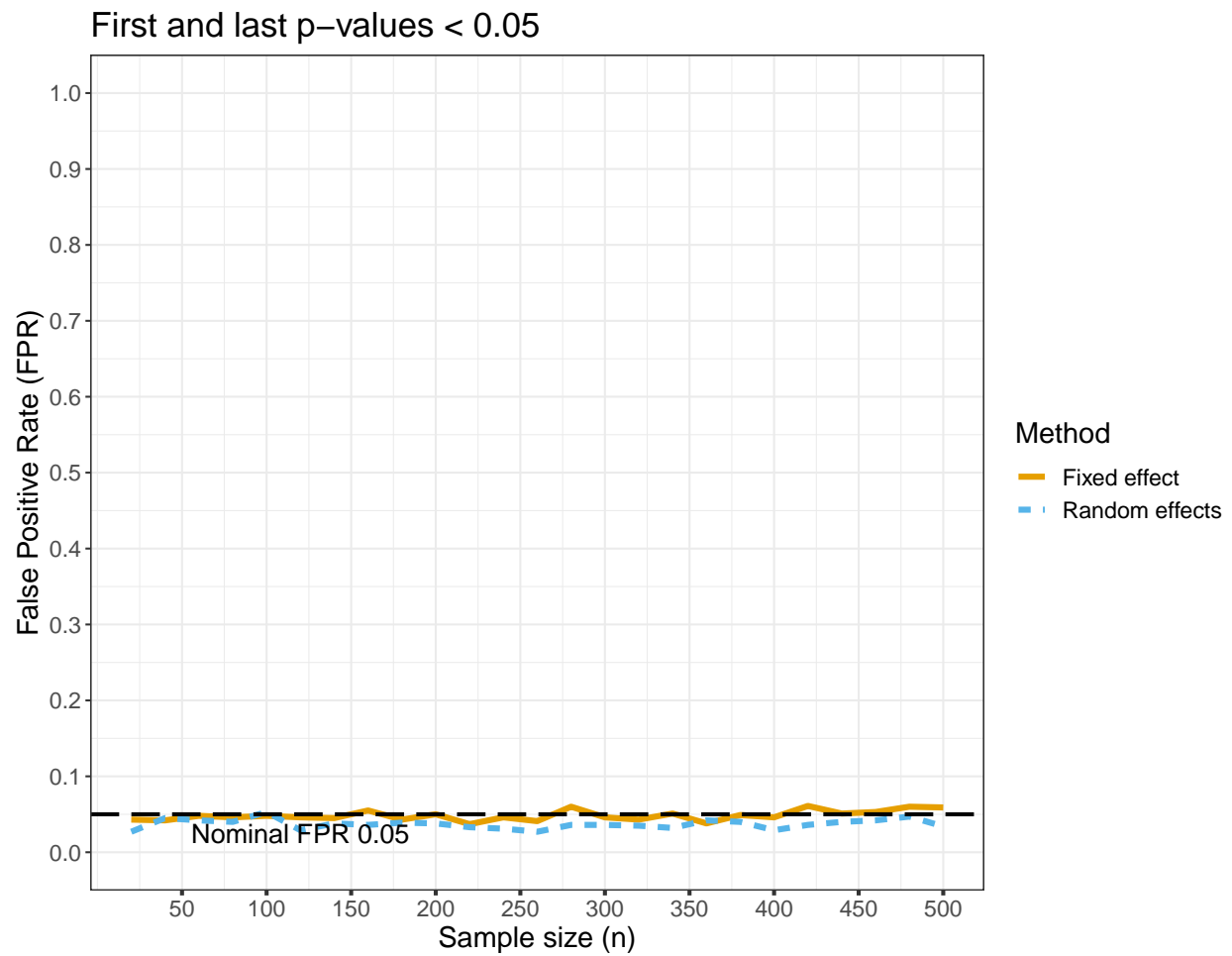
# renaming figure legend
```

```

nohack_dat <- nohack_dat %>%
  rename(Method = method) %>%
  mutate(Method = recode(Method,
    "HE" = "Random effects",
    "FE" = "Fixed effect"))

# plot
ggplot(nohack_dat, aes(n, power)) +
  geom_line(aes(linetype = Method,
    color = Method), size=1.5) +
  scale_y_continuous(limits = c(0, 1),
    breaks = seq(0, 1, 0.1)) +
  scale_x_continuous(limits = c(20, 500),
    breaks = seq(50, 500, 50)) +
  geom_hline(yintercept = 0.05, size = 1,
    linetype = "longdash") +
  scale_color_manual(values=cbPalette) +
  theme_bw() +
  theme(axis.title = element_text(size = 15),
    title = element_text(size = 15),
    axis.text = element_text(size = 10),
    axis.ticks.x = element_line(size = 1),
    axis.text.x = element_text(size=12),
    axis.text.y = element_text(size=12),
    legend.text = element_text(size = 12)) +
  labs(x = "Sample size (n)",
    y = "False Positive Rate (FPR)",
    title = "First and last p-values < 0.05") +
  annotate("text", x = 120, y = 0.025,
    label = "Nominal FPR 0.05", size = 5)

```



```
# ggsave("nohack_fpr_plot.png", width = 10, height = 7)
```

p-threshold

Simulation 3

Simulation 3 estimates the false positive rate of internal meta-analyses with p-value thresholds for the first study and a p-value threshold stopping rule. Sample sizes and methods (fixed or random effects) were varied, whereas p thresholds and the max number of studies were constant.

Parameters

- Iterations: 10000
- Max number of studies: 12
- Effect size: 0
- Sample sizes: 20-500
- First p max: 0.05
- Last p max: 0.05
- Method: random (HE) and fixed (FE) effects

```
set.seed(1337) # reproducible seed

# simulation parameters
params <- crossing(
  i = 1:10000, # iterations
  n.studies = 12, # maximum no. of studies (based on lit coding)
  n = seq(20, 500, 20), # vector of sample sizes (based on lit coding)
  pmax.first = 0.05, # vector of first p-values (based on lit coding)
  pmax.last = 0.05, # vector of last p-values (based on lit coding)
  method = c("HE", "FE")
)

# using p_bound_meta()

tmp <- purrr::pmap_dfr(params, function(...) {
  dots <- list(...)
  p_bound_meta(n.studies = dots$n.studies,
    d = dots$d,
    n = dots$n,
    method = dots$method,
    pmax.first = dots$pmax.first,
    pmax.last = dots$pmax.last) %>%
  mutate(!!!dots)
})

# save all results
save(tmp, file = "p_bound_tmp.RData")

# calculate how many meta-analysed p-values
outof <- tmp %>%
  filter(study == 0) %>%
  group_by(pmax.first, pmax.last, n, method, d) %>%
  count() %>%
  rename(metatotal = nn)
```

```

# calculate how many significant meta-analysed p-values
dat <- tmp %>%
  filter(study == 0, p < .05) %>% # all significant meta results
  group_by(pmax.first, pmax.last, n, method, d) %>%
  count() %>%
  ungroup() %>%
  mutate(power = nn/outof$metatotal) # calculate false positive rate

# save false positive rates for each combination
save(dat, outof, file = "p_bound_dat.RData")

```

Visualisation 3

The colourblind-friendly palette used in the plot was obtained from Okaboe & Ito (2002).

```

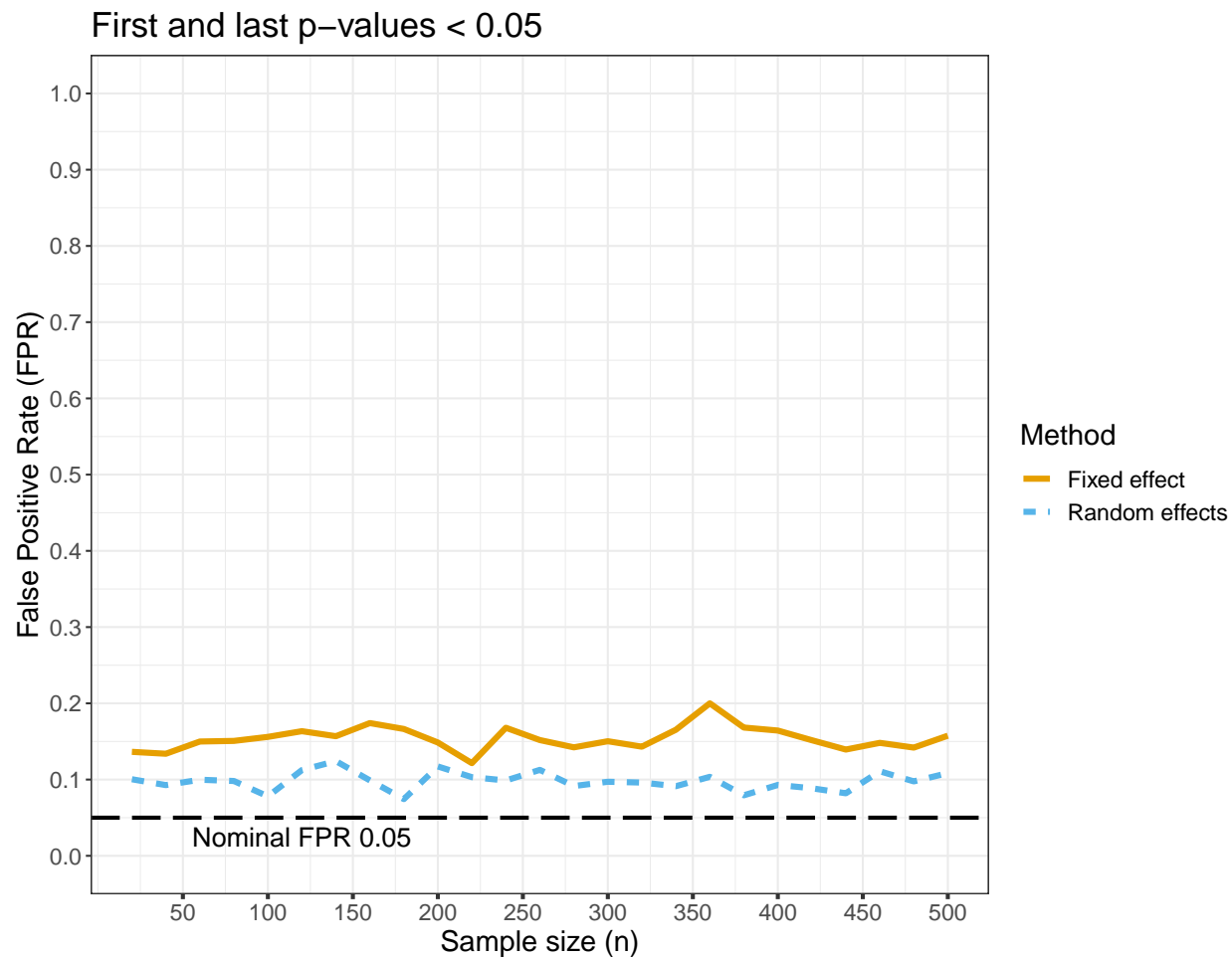
#load("p_bound_tmp.RData")
load("p_bound_dat.RData") # load saved results for plot

# colourblind-friendly palette
cbPalette <- c("#E69F00", "#56B4E9", "#009E73",
               "#F0E442", "#0072B2", "#D55E00", "#CC79A7")

dat <- dat %>%
  rename(Method = method) %>%
  mutate(Method = recode(Method, "HE" = "Random effects", "FE" = "Fixed effect"))

ggplot(dat, aes(n, power)) +
  geom_line(aes(linetype = Method,
               color = Method), size=1.5) +
  scale_y_continuous(limits = c(0, 1),
                    breaks = seq(0, 1, 0.1)) +
  scale_x_continuous(limits = c(20, 500),
                    breaks = seq(50, 500, 50)) +
  geom_hline(yintercept = 0.05, size = 1,
            linetype = "longdash") +
  scale_color_manual(values=cbPalette) +
  theme_bw() +
  theme(axis.title = element_text(size = 15),
        title = element_text(size = 15),
        axis.text = element_text(size = 10),
        axis.ticks.x = element_line(size = 1),
        axis.text.x = element_text(size=12),
        axis.text.y = element_text(size=12),
        legend.text = element_text(size = 12)) +
  labs(x = "Sample size (n)",
       y = "False Positive Rate (FPR)",
       title = "First and last p-values < 0.05") +
  annotate("text", x = 120, y = 0.025,
         label = "Nominal FPR 0.05", size = 5)

```



```
# ggsave("minimeta_pbound_plot.png", width = 10, height = 7)
```


Meta-hacking

Simulation 4

Simulation 4 estimates the false positive rate of internal meta-analyses with p-value thresholds for the first study and a meta-analysed p threshold stopping rule. Sample sizes and methods (fixed or random effects) were varied, whereas p thresholds and the max number of studies were constant.

Parameters

- Iterations: 10000
- Max number of studies: 12
- Effect size: 0
- Sample sizes: 20-500
- First p max: 0.05
- Minitarget: 0.05
- Method: random (HE) and fixed (FE) effects

```
set.seed(1337) # reproducible seed

# simulation parameters
params <- crossing(
  i = 1:10000, # iterations
  n.studies = 12, # max no. of studies
  d = 0, # true effect size
  n = seq(20, 500, 20), # vector of sample sizes
  pmax.first = 0.05, # first p-value threshold
  minitarget = 0.05, # minimeta threshold
  method = c("HE", "FE") # random (HE) and fixed effect (FE)
)

# simulation
tmp <- purrr::pmap_dfr(params, function(...) {
  dots <- list(...)
  meta_hack(n.studies = dots$n.studies,
            d = dots$d,
            n = dots$n,
            method = dots$method,
            pmax.first = dots$pmax.first,
            minitarget = dots$minitarget) %>%
    mutate(!!!dots)
})

# save all results
save(tmp, file = "metahack_tmp.RData")

# all meta-analysed p-values
outof <- tmp %>%
  filter(study == 0) %>%
  group_by(pmax.first, minitarget, n, method, d) %>%
  count() %>%
  rename(metatotal = nn) %>%
  ungroup()
```

```

# all significant meta-analysed p-values
dat <- tmp %>%
  filter(study == 0, p < .05) %>% # all significant meta results
  group_by(pmax.first, minitarget, n, method, d) %>%
  count() %>%
  ungroup()

power.dat <- left_join(dat, outof, by = c("n", "method")) %>%
  ungroup() %>%
  select(n, method, nn, metatotal) %>%
  mutate(power = nn/metatotal) # calculate false positive rate

# save false positive rate results
save(dat, outof, power.dat, file = "metahack_dat.RData")

```

Visualisation 4

The colourblind-friendly palette used in the plot was obtained from Okaboe & Ito (2002).

```

#load("metahack_tmp.RData")
load("metahack_dat.RData") # load saved results for plot

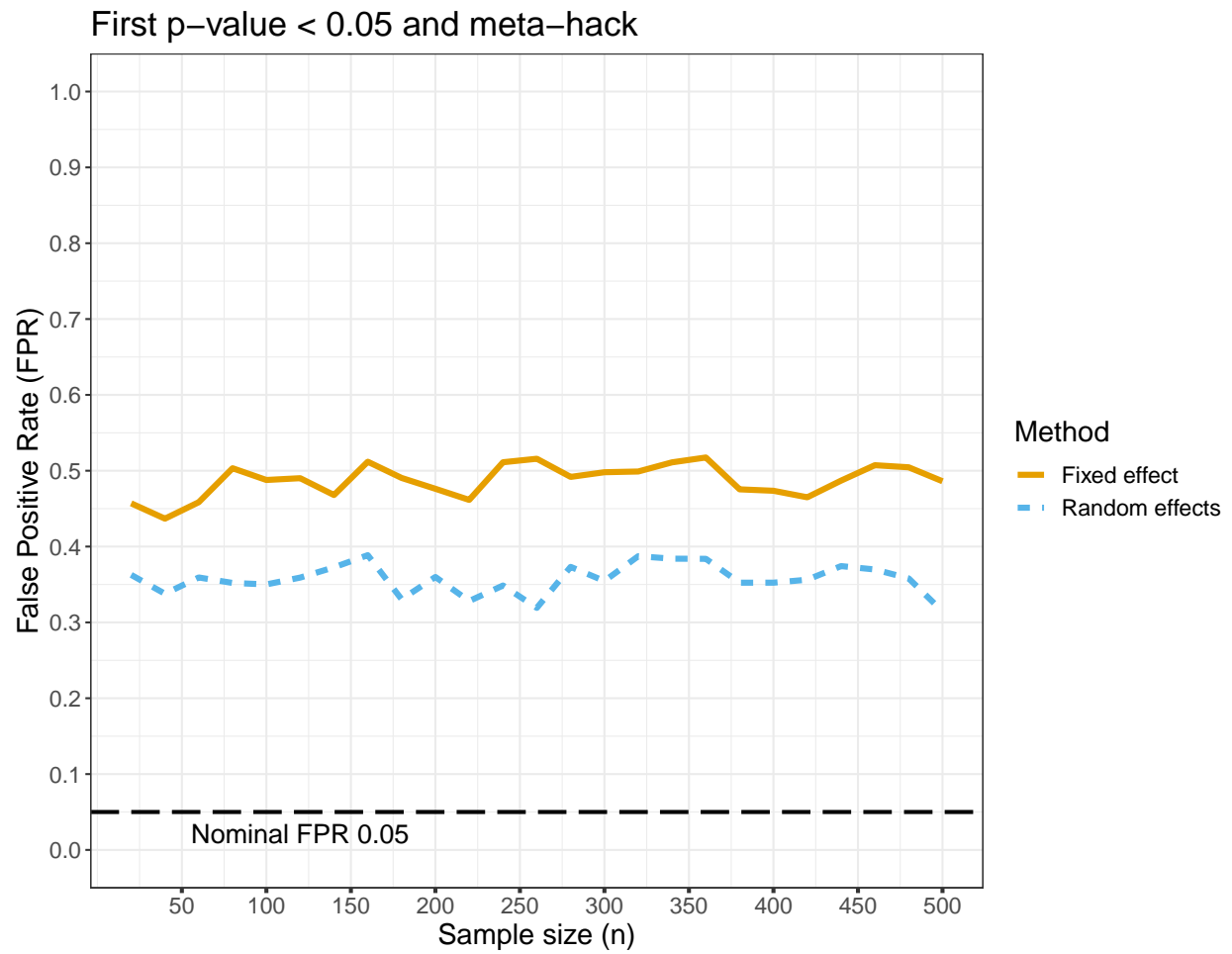
# changing column and row names for plot
power.dat <- power.dat %>%
  rename(Method = method) %>%
  mutate(Method = recode(Method, "HE" = "Random effects", "FE" = "Fixed effect"))

# colourblind-friendly palette
cbPalette <- c("#E69F00", "#56B4E9", "#009E73",
               "#F0E442", "#0072B2", "#D55E00", "#CC79A7")

ggplot(power.dat, aes(n, power)) +
  geom_line(aes(linetype = Method,
                color = Method), size=1.5) +
  scale_y_continuous(limits = c(0, 1),
                     breaks = seq(0, 1, 0.1)) +
  scale_x_continuous(limits = c(20, 500),
                     breaks = seq(50, 500, 50)) +
  geom_hline(yintercept = 0.05, size = 1, linetype = "longdash") +
  scale_color_manual(values=cbPalette) +
  theme_bw() +
  theme(axis.title = element_text(size = 15),
        title = element_text(size = 15),
        axis.text = element_text(size = 10),
        axis.ticks.x = element_line(size = 1),
        axis.text.x = element_text(size=12),
        axis.text.y = element_text(size=12),
        legend.text = element_text(size = 12)) +
  labs(x = "Sample size (n)",
       y = "False Positive Rate (FPR)",
       title = "First p-value < 0.05 and meta-hack") +
  annotate("text", x = 120, y = 0.022,

```

```
label = "Nominal FPR 0.05", size = 5)
```



```
# ggsave("minimeta_metahack_plot.png", width = 10, height = 7)
```

References

- Lakens, D. (2013). Calculating and reporting effect sizes to facilitate cumulative science : A practical primer for t-tests and anovas. *Frontiers in Psychology*, 4, 1–12.
- Okaboe, M., & Ito, K. (2002). Color universal design (cud) how to make figures and presentations that are friendly to colorblind people. Retrieved from <https://jfly.uni-koeln.de/color/>
- Vosgerau, J., Simonsohn, U., Nelson, L., & Simmons, J. (2019). 99. *Journal of Experimental Psychology: General*, 148(9), 1628–1639.