

```

N <- 300
Nsims <- 20 * 1000

maxFollow <- 84
cens.type <- "weibull"
##### Forest search criteria
hr.threshold <- 1.25 # Initial candidates
hr.consistency <- 1 # Candidates for many splits

pconsistency.threshold <- 0.9
stop.threshold <- 0.95

maxk <- 2
nmin.fs <- 60
pstop_futile <- 0.7

# Limit timing for forestsearch
max.minutes <- 3
ml.threshold <- Inf # Turning this off (Default)
# pconsistency.threshold<-0.70 # Minimum threshold (will choose max among
# subgroups satisfying)
fs.splits <- 400 # How many times to split for consistency
# vi is % factor is selected in cross-validation --> higher more important
vi.grf.min <- (-1) * 0.2 # This is default (to NOT exclude via VI)
# Null, turns off grf screening
d.min <- 10 # Min number of events for both arms (d0.min=d1.min=d.min)
# default=5

##### Virtual twins analysis Counter-factual difference
##### (C-E) >= vt.threshold Large values in favor of C
##### (control)
vt.threshold <- 0.225 # For VT delta
treat.threshold <- 0

maxdepth <- 2
n.min <- 60
ntree <- 1000

# GRF criteria
dmin.grf <- 12 # For GRF delta
# Note: For CRT this represents dmin.grf/2 RMS for control (-dmin.grf/2 for
# treatment)
frac.tau <- 0.6

# For forestsearch algorithm use same as GRF
frac.tau_fs <- 0.6
dmin.grf_fs <- 12
maxdepth_fs <- 2

label.analyses <- c("FS1", "GRF", "VT(24)", "VT#(24)", "VT(36)", "VT#(36)", "GRF.60")
# Classification table names
est_names <- c("$FS_{g}$", "$FS_{lg}$", "$GRF$", "$GRF_{60}$", "$VT(24)$", "${VT}^{\#\#}(24)$",
"$VT(36)$", "${VT}^{\#\#}(36)$")

outcome.name <- c("y.sim")

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event.name <- c("event.sim")
id.name <- c("id")
treat.name <- c("treat")

cox.formula.sim <- as.formula(paste("Surv(y.sim,event.sim)~treat"))
cox.formula.adj.sim <- as.formula(paste("Surv(y.sim,event.sim)~treat+v1+v2+v3+v4+v5"))

get.FS <- TRUE
get.VT <- TRUE
get.GRF <- TRUE

fl_prefix <- paste0("oc_sims=", Nsims, "_")

out.loc <- paste0("results/", fl_prefix)

# m1 -censoring adjustment
muC.adj <- log(1.5)

# 0, 3, or 5
n_add_noise <- 5

mindex <- "m4c"
file.index <- "v0-4cuts"

z1_frac <- 0.25

if (mindex == "m4a") {
  k.z3 <- 1
  k.treat <- 0.9
  pH_super <- 0.125 # non-NULL re-defines z1_frac
}

if (mindex == "m4aB") {
  k.z3 <- 1
  k.treat <- 0.9
  pH_super <- 0.2 # non-NULL re-defines z1_frac
}

if (mindex == "m4b") {
  k.z3 <- 1
  k.treat <- 1.25
  pH_super <- 0.3 # non-NULL re-defines z1_frac
}

if (mindex == "m4c") {
  k.z3 <- 1
  k.treat <- 1.5
  pH_super <- 0.3 # non-NULL re-defines z1_frac
}

model.index <- paste0(mindex, "-Noise=", "")
model.index <- paste0(model.index, n_add_noise, "")

if (is.null(pH_super)) {
  # pH_check<-with(gbbsg,mean(pgr<=quantile(pgr,c(z3_frac),1,0) &

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    # er<=quantile(er,z1_frac))
    pH_check <- with(gbsg, mean(meno == 0 & er <= quantile(er, z1_frac)))
    cat("Underlying pH_super", c(pH_check), "\n")
}
# pH_super specified If pH_super then override z1_frac and find z1_frac to
# yield pH_super

if (!is.null(pH_super)) {
  # Approximate Z1 quantile to yield pH proportion
  z1_q <- uniroot(propH.obj4, c(0, 1), tol = 1e-04, pH.target = pH_super)$root
  # pH_check<-with(gbsg,mean(pgr<=quantile(pgr,c(z3_frac),1,0) &
  # er<=quantile(er,z1_q)))
  pH_check <- with(gbsg, mean(meno == 0 & er <= quantile(er, z1_q)))
  cat("pH", c(pH_check), "\n")
  rel_error <- (pH_super - pH_check)/pH_super
  if (abs(rel_error) >= 0.1)
    stop("pH_super approximation relative error exceeds 10%")
  z1_frac <- z1_q
  cat("Underlying pH_super", c(pH_check), "\n")
}

## pH 0.3002915
## Underlying pH_super 0.3002915

# Bootstrap on log(hr) scale converted to HR (est.loghr=TRUE & est.scale='hr')
est.loghr <- TRUE
est.scale <- "hr"
t.start.all <- proc.time()[3]

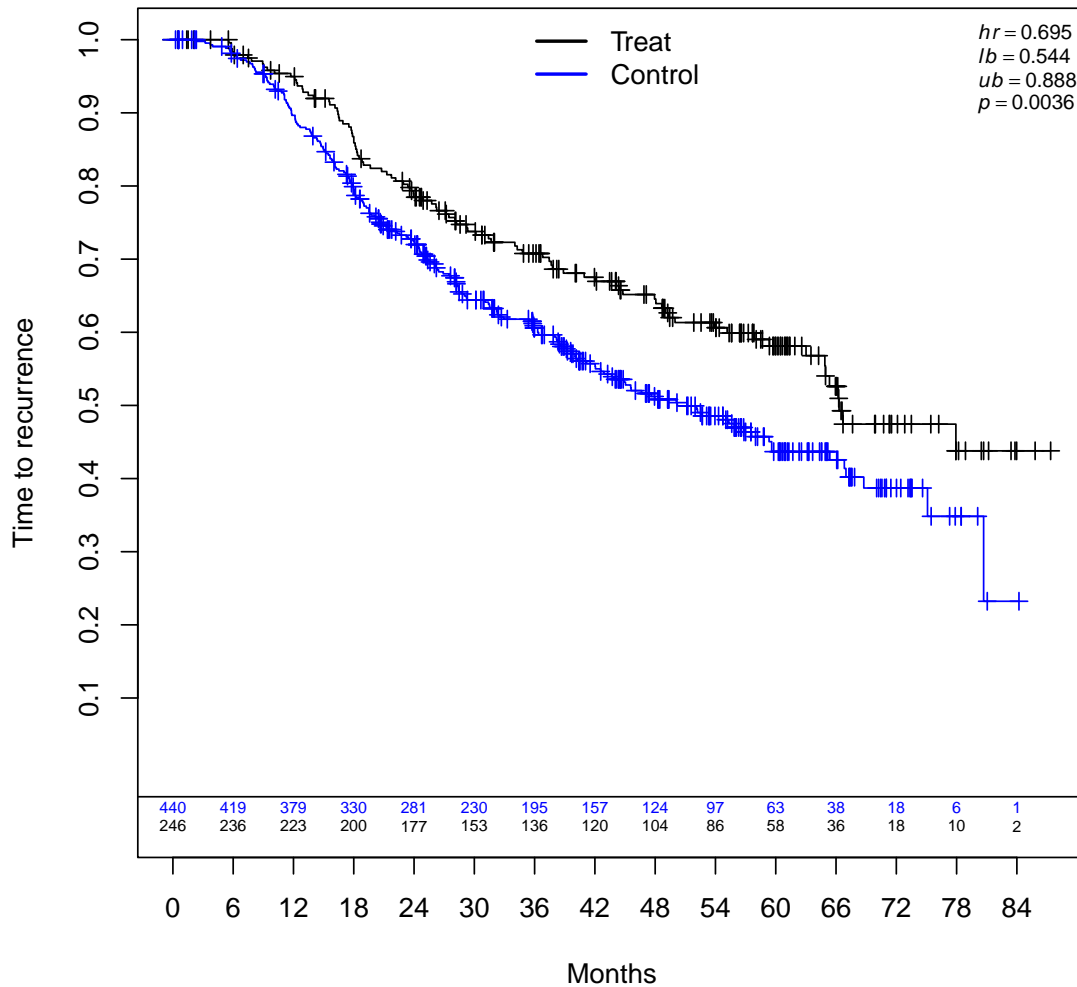
# Classification table names Note: within tab_tests (summary.VTFS) we rename so
# that denominator in ppv(hatH) is # hatH Manuscript section 3.2 will be
# updated accordingly

stat_names <- c("any(H)", "${sens}(\hat{H})$", "${sens}(\hat{H}^C)$", "${ppv}(\hat{H})$",
  "${ppv}(\hat{H}^C)$", "${avg}\|vert \hat{H} \|vert$", "${min}\|vert \hat{H} \|vert$",
  "${max}\|vert \hat{H} \|vert$", "${avg}\|vert \hat{H}^C \|vert$", "${min}\|vert \hat{H}^C \|vert$",
  "${max}\|vert \hat{H}^C \|vert$")

if (!get.FS) est_names <- est_names[-c(1:3)]

mod.harm <- "null"
this.dgm <- get.dgm4.OG(mod.harm = mod.harm, N = N, k.treat = k.treat, model.index = model.index,
  sol_tol = 10^-8, hrH.target = hrH.target, cens.type = cens.type, out.loc = out.loc,
  file.index = file.index, details = TRUE, parms_torand = FALSE)

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```
## Super-population empirical harm and non-harm hazard ratios= NA 0.5517234
## Causal HR (empirical ITT)= 0.5517234

dgm <- this.dgm$dgm
output.file <- this.dgm$out.file

if (!is.null(output.file) & !grepl(mod.harm, output.file)) stop("Wrong file name for mod.harm")

# Show first simulation ans1 <- oc_analyses_m4_FS4(1)

t.start <- proc.time()[3]
res <- foreach(sim = seq_len(Nsims), .options.future = list(seed = TRUE), .combine = "rbind",
  .errorhandling = "pass") %dofuture% {
  ans <- oc_analyses_m4FourCuts_FS4(sim)
  return(ans)
}

## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 45.33113 2
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## leaf.node control.mean control.size control.se depth
## 1 2 -6.60 256.00 1.60 1
## 2 4 -8.24 200.00 1.81 2
## leaf.node control.mean control.size control.se depth
## 1 2 -6.6 256.0 1.6 1
## GRF subgroup NOT found
## NO GRF cuts meeting delta(RMST): dmin.grf= 12
## # of continuous/categorical characteristics 6 6
## Continuous characteristics: size noise1 noise2 noise3 noise4 noise5
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## Default cuts included (1st 20)
## Categorical: z1 z2 z3 z4 z5 grade3
## # of candidate subgroup factors= 25
## [1] "size <= 29.6" "size <= 25" "size <= 21" "size <= 35"
## [5] "noise1 <= 0" "noise1 <= -0.6" "noise1 <= 0.7" "noise2 <= 0"
## [9] "noise2 <= -0.7" "noise2 <= 0.7" "noise3 <= 0" "noise3 <= -0.7"
## [13] "noise3 <= 0.8" "noise4 <= 0" "noise4 <= -0.8" "noise4 <= 0.7"
## [17] "noise5 <= -0.1" "noise5 <= -0.8" "noise5 <= 0.5" "z1"
## [21] "z2" "z3" "z4" "z5"
## [25] "grade3"
## Number of factors evaluated= 25
## Confounders per grf screening q4 q23 q16 q19 q3 q20 q5 q24 q2 q17 q22 q8 q14 q11 q21 q10 q1 q12 q7 q
## Factors Labels VI(grf)
## 4 size <= 35 q4 0.0947
## 23 z4 q23 0.0735
## 16 noise4 <= 0.7 q16 0.0710
## 19 noise5 <= 0.5 q19 0.0693
## 3 size <= 21 q3 0.0624
## 20 z1 q20 0.0518
## 5 noise1 <= 0 q5 0.0417
## 24 z5 q24 0.0413
## 2 size <= 25 q2 0.0411
## 17 noise5 <= -0.1 q17 0.0411
## 22 z3 q22 0.0400
## 8 noise2 <= 0 q8 0.0379
## 14 noise4 <= 0 q14 0.0352
## 11 noise3 <= 0 q11 0.0336
## 21 z2 q21 0.0299
## 10 noise2 <= 0.7 q10 0.0297
## 1 size <= 29.6 q1 0.0280
## 12 noise3 <= -0.7 q12 0.0271
## 7 noise1 <= 0.7 q7 0.0263
## 13 noise3 <= 0.8 q13 0.0237
## 9 noise2 <= -0.7 q9 0.0236
## 18 noise5 <= -0.8 q18 0.0209
## 6 noise1 <= -0.6 q6 0.0208
## 25 grade3 q25 0.0177
## 15 noise4 <= -0.8 q15 0.0176
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 1275
## Approximately 5% of max_count met: minutes 0.00205
## Approximately 10% of max_count met: minutes 0.00315
## Approximately 20% of max_count met: minutes 0.006033333
## Approximately 33% of max_count met: minutes 0.008883333
## Approximately 50% of max_count met: minutes 0.01401667
## Approximately 75% of max_count met: minutes 0.02173333

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## Approximately 90% of max_count met: minutes 0.02563333
## # of subgroups evaluated based on (up to) maxk-factor combinations 1275
## % of all-possible combinations (<= maxk) 100
## k.max= 2
## Events criteria for control,exp= 10 10
## # of subgroups with events less than criteria: control, experimental 179 333
## # of subgroups with sample size less than criteria 543
## # of subgroups meeting all criteria = 705
## # of subgroups fitted (Cox model estimable) = 705
## *Subgroup Searching Minutes=* 0.02736667
## Number of subgroups meeting HR threshold 0
## NO subgroup candidate found (FS)
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 45.33113 2
## leaf.node control.mean control.size control.se depth
## 1 2 -6.60 256.00 1.60 1
## 2 4 -8.24 200.00 1.81 2
## leaf.node control.mean control.size control.se depth
## 1 2 -6.6 256.0 1.6 1
## GRF subgroup NOT found
## NO GRF cuts meeting delta(RMST): dmin.grf= 12
## # of continuous/categorical characteristics 6 6
## Continuous characteristics: size noise1 noise2 noise3 noise4 noise5
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## CV lambda = 0.04773978
## 12 x 1 sparse Matrix of class "dgCMatrix"
## s0
## z1 .
## z2 .
## z3 .
## z4 0.43629892
## z5 -0.52002399
## size .
## grade3 .
## noise1 .
## noise2 -0.03740061
## noise3 .
## noise4 .
## noise5 .
## Cox-LASSO selected: z4 z5 noise2
## Cox-LASSO not selected: z1 z2 z3 size grade3 noise1 noise3 noise4 noise5
## Default cuts included from Lasso:
## Categorical after Lasso: z4 z5
## # of candidate subgroup factors= 21
## [1] "size <= 29.6" "size <= 25" "size <= 21" "size <= 35"
## [5] "noise1 <= 0" "noise1 <= -0.6" "noise1 <= 0.7" "noise2 <= 0"
## [9] "noise2 <= -0.7" "noise2 <= 0.7" "noise3 <= 0" "noise3 <= -0.7"
## [13] "noise3 <= 0.8" "noise4 <= 0" "noise4 <= -0.8" "noise4 <= 0.7"
## [17] "noise5 <= -0.1" "noise5 <= -0.8" "noise5 <= 0.5" "z4"
## [21] "z5"
## Number of factors evaluated= 21
## Confounders per grf screening q4 q20 q16 q19 q3 q17 q8 q5 q21 q2 q14 q11 q10 q7 q12 q1 q18 q6 q9 q15
## Factors Labels VI(grf)
## 4 size <= 35 q4 0.1035
## 20 z4 q20 0.0892

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## 16 noise4 <= 0.7      q16 0.0833
## 19 noise5 <= 0.5      q19 0.0786
## 3      size <= 21      q3 0.0651
## 17 noise5 <= -0.1     q17 0.0495
## 8      noise2 <= 0      q8 0.0494
## 5      noise1 <= 0      q5 0.0474
## 21      z5      q21 0.0472
## 2      size <= 25      q2 0.0465
## 14      noise4 <= 0      q14 0.0398
## 11      noise3 <= 0      q11 0.0393
## 10      noise2 <= 0.7     q10 0.0371
## 7      noise1 <= 0.7     q7 0.0346
## 12 noise3 <= -0.7     q12 0.0324
## 1      size <= 29.6      q1 0.0302
## 18 noise5 <= -0.8     q18 0.0270
## 6      noise1 <= -0.6     q6 0.0262
## 9      noise2 <= -0.7     q9 0.0258
## 15 noise4 <= -0.8     q15 0.0247
## 13 noise3 <= 0.8      q13 0.0232
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 903
## Approximately 5% of max_count met: minutes 0.001816667
## Approximately 10% of max_count met: minutes 0.002066667
## Approximately 20% of max_count met: minutes 0.006366667
## Approximately 33% of max_count met: minutes 0.008283333
## Approximately 50% of max_count met: minutes 0.0115
## Approximately 75% of max_count met: minutes 0.0166
## Approximately 90% of max_count met: minutes 0.0188333
## # of subgroups evaluated based on (up to) maxk-factor combinations 903
## % of all-possible combinations (<= maxk) 100
## k.max= 2
## Events criteria for control,exp= 10 10
## # of subgroups with events less than criteria: control, experimental 140 232
## # of subgroups with sample size less than criteria 393
## # of subgroups meeting all criteria = 486
## # of subgroups fitted (Cox model estimable) = 486
## *Subgroup Searching Minutes=* 0.02021667
## Number of subgroups meeting HR threshold 0
## NO subgroup candidate found (FS)
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 45.32879 2
## leaf.node control.mean control.size control.se depth
## 1      2      -4.25      284.00      1.46      1
## 11      4      -6.05      111.00      2.27      2
## 4      7      -7.56      122.00      2.36      2
## leaf.node control.mean control.size control.se depth
## 1      2      -4.25      284.00      1.46      1
## GRF subgroup NOT found
## NO GRF cuts meeting delta(RMST): dmin.grf= 12
## # of continuous/categorical characteristics 6 6
## Continuous characteristics: size noise1 noise2 noise3 noise4 noise5
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## Default cuts included (1st 20)
## Categorical: z1 z2 z3 z4 z5 grade3
## # of candidate subgroup factors= 26
## [1] "size <= 27.9" "size <= 25" "size <= 20" "size <= 34"

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## [5] "noise1 <= 0.1" "noise1 <= -0.7" "noise1 <= 0.7" "noise2 <= 0"
## [9] "noise2 <= -0.1" "noise2 <= -0.6" "noise2 <= 0.7" "noise3 <= 0"
## [13] "noise3 <= -0.7" "noise3 <= 0.7" "noise4 <= 0" "noise4 <= -0.8"
## [17] "noise4 <= 0.7" "noise5 <= 0.1" "noise5 <= -0.5" "noise5 <= 0.8"
## [21] "z1" "z2" "z3" "z4"
## [25] "z5" "grade3"
## Number of factors evaluated= 26
## Confounders per grf screening q24 q1 q2 q16 q22 q25 q15 q18 q5 q20 q12 q3 q21 q8 q26 q9 q23 q7 q10 q
## Factors Labels VI(grf)
## 24 z4 q24 0.0994
## 1 size <= 27.9 q1 0.0618
## 2 size <= 25 q2 0.0614
## 16 noise4 <= -0.8 q16 0.0614
## 22 z2 q22 0.0599
## 25 z5 q25 0.0580
## 15 noise4 <= 0 q15 0.0546
## 18 noise5 <= 0.1 q18 0.0431
## 5 noise1 <= 0.1 q5 0.0425
## 20 noise5 <= 0.8 q20 0.0385
## 12 noise3 <= 0 q12 0.0382
## 3 size <= 20 q3 0.0346
## 21 z1 q21 0.0338
## 8 noise2 <= 0 q8 0.0308
## 26 grade3 q26 0.0295
## 9 noise2 <= -0.1 q9 0.0288
## 23 z3 q23 0.0273
## 7 noise1 <= 0.7 q7 0.0260
## 10 noise2 <= -0.6 q10 0.0234
## 19 noise5 <= -0.5 q19 0.0234
## 6 noise1 <= -0.7 q6 0.0233
## 4 size <= 34 q4 0.0229
## 11 noise2 <= 0.7 q11 0.0224
## 13 noise3 <= -0.7 q13 0.0206
## 14 noise3 <= 0.7 q14 0.0188
## 17 noise4 <= 0.7 q17 0.0157
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 1378
## Approximately 5% of max_count met: minutes 0.002916667
## Approximately 10% of max_count met: minutes 0.0053
## Approximately 20% of max_count met: minutes 0.0095
## Approximately 33% of max_count met: minutes 0.01625
## Approximately 50% of max_count met: minutes 0.02488333
## Approximately 75% of max_count met: minutes 0.03638333
## Approximately 90% of max_count met: minutes 0.04121667
## # of subgroups evaluated based on (up to) maxk-factor combinations 1378
## % of all-possible combinations (<= maxk) 100
## k.max= 2
## Events criteria for control,exp= 10 10
## # of subgroups with events less than criteria: control, experimental 203 440
## # of subgroups with sample size less than criteria 575
## # of subgroups meeting all criteria = 752
## # of subgroups fitted (Cox model estimable) = 752
## *Subgroup Searching Minutes=* 0.04413333
## Number of subgroups meeting HR threshold 0
## NO subgroup candidate found (FS)
## FS:GRF stage for cut selection with dmin,tau= 12 0.6

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## tau, maxdepth= 45.32879 2
##      leaf.node control.mean control.size control.se depth
## 1         2         -4.25         284.00         1.46     1
## 11        4         -6.05         111.00         2.27     2
## 4         7         -7.56         122.00         2.36     2
##      leaf.node control.mean control.size control.se depth
## 1         2         -4.25         284.00         1.46     1
## GRF subgroup NOT found
## NO GRF cuts meeting delta(RMST): dmin.grf= 12
## # of continuous/categorical characteristics 6 6
## Continuous characteristics: size noise1 noise2 noise3 noise4 noise5
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## CV lambda = 0.04396711
## 12 x 1 sparse Matrix of class "dgCMatrix"
##              s0
## z1          .
## z2          .
## z3          .
## z4      0.7509354
## z5     -0.9007276
## size        .
## grade3       .
## noise1       .
## noise2       .
## noise3       .
## noise4       .
## noise5       .
## Cox-LASSO selected: z4 z5
## Cox-LASSO not selected: z1 z2 z3 size grade3 noise1 noise2 noise3 noise4 noise5
## Default cuts included from Lasso:
## Categorical after Lasso: z4 z5
## # of candidate subgroup factors= 22
## [1] "size <= 27.9" "size <= 25" "size <= 20" "size <= 34"
## [5] "noise1 <= 0.1" "noise1 <= -0.7" "noise1 <= 0.7" "noise2 <= 0"
## [9] "noise2 <= -0.1" "noise2 <= -0.6" "noise2 <= 0.7" "noise3 <= 0"
## [13] "noise3 <= -0.7" "noise3 <= 0.7" "noise4 <= 0" "noise4 <= -0.8"
## [17] "noise4 <= 0.7" "noise5 <= 0.1" "noise5 <= -0.5" "noise5 <= 0.8"
## [21] "z4" "z5"
## Number of factors evaluated= 22
## Confounders per grf screening q21 q1 q2 q16 q22 q15 q18 q5 q20 q12 q3 q8 q6 q7 q9 q4 q14 q19 q11 q13
##      Factors Labels VI(grf)
## 21          z4      q21 0.1197
## 1      size <= 27.9      q1 0.0803
## 2      size <= 25      q2 0.0719
## 16 noise4 <= -0.8      q16 0.0685
## 22          z5      q22 0.0659
## 15      noise4 <= 0      q15 0.0602
## 18      noise5 <= 0.1      q18 0.0529
## 5      noise1 <= 0.1      q5 0.0505
## 20      noise5 <= 0.8      q20 0.0493
## 12      noise3 <= 0      q12 0.0427
## 3      size <= 20      q3 0.0387
## 8      noise2 <= 0      q8 0.0346
## 6      noise1 <= -0.7      q6 0.0313
## 7      noise1 <= 0.7      q7 0.0302

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## 9  noise2 <= -0.1      q9  0.0287
## 4      size <= 34      q4  0.0278
## 14 noise3 <= 0.7      q14 0.0273
## 19 noise5 <= -0.5     q19 0.0273
## 11 noise2 <= 0.7      q11 0.0248
## 13 noise3 <= -0.7     q13 0.0246
## 10 noise2 <= -0.6     q10 0.0232
## 17 noise4 <= 0.7      q17 0.0196
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 990
## Approximately 5% of max_count met: minutes 0.002233333
## Approximately 10% of max_count met: minutes 0.0036
## Approximately 20% of max_count met: minutes 0.007033333
## Approximately 33% of max_count met: minutes 0.01148333
## Approximately 50% of max_count met: minutes 0.01623333
## Approximately 75% of max_count met: minutes 0.02393333
## Approximately 90% of max_count met: minutes 0.02735
## # of subgroups evaluated based on (up to) maxk-factor combinations 990
## % of all-possible combinations (<= maxk) 100
## k.max= 2
## Events criteria for control,exp= 10 10
## # of subgroups with events less than criteria: control, experimental 160 313
## # of subgroups with sample size less than criteria 417
## # of subgroups meeting all criteria = 537
## # of subgroups fitted (Cox model estimable) = 537
## *Subgroup Searching Minutes=* 0.02943333
## Number of subgroups meeting HR threshold 0
## NO subgroup candidate found (FS)
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 45.42348 2
##   leaf.node control.mean control.size control.se depth
## 2           3          -6.97         291.00         1.49    1
## 21          5         -14.58          77.00         2.86    2
## 3           6           6.45          63.00         2.91    2
## 4           7          -9.23         144.00         2.02    2
##   leaf.node control.mean control.size control.se depth
## 3           6           6.45          63.00         2.91    2
## GRF subgroup found
## All splits
## [1] "noise5 <= -0.51" "noise3 <= -0.7" "noise5 <= 0.01"
## Terminating node at max.diff (sg.harm.id)
## [1] "noise5 <= 0.00807090609630402"
## # of continuous/categorical characteristics 6 6
## Continuous characteristics: size noise1 noise2 noise3 noise4 noise5
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## Default cuts included (1st 20)
## Categorical: z1 z2 z3 z4 z5 grade3
## Factors per GRF: noise5 <= -0.51 noise3 <= -0.7 noise5 <= 0.01
## Initial GRF cuts included noise5 <= -0.51 noise3 <= -0.7 noise5 <= 0.01
## # of candidate subgroup factors= 30
## [1] "noise5 <= -0.51" "noise3 <= -0.7" "noise5 <= 0.01" "size <= 29.7"
## [5] "size <= 27"      "size <= 21"      "size <= 35"      "noise1 <= -0.1"
## [9] "noise1 <= -0.8"  "noise1 <= 0.7"   "noise2 <= -0.1"  "noise2 <= -0.8"
## [13] "noise2 <= 0.5"   "noise3 <= 0.1"   "noise3 <= 0"     "noise3 <= -0.6"
## [17] "noise3 <= 0.8"   "noise4 <= 0.1"   "noise4 <= 0"     "noise4 <= -0.6"
## [21] "noise4 <= 0.8"   "noise5 <= 0"     "noise5 <= -0.7"  "noise5 <= 0.7"

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## [25] "z1"          "z2"          "z3"          "z4"
## [29] "z5"          "grade3"
## Number of factors evaluated= 30
## Confounders per grf screening q28 q3 q25 q30 q22 q1 q19 q29 q26 q11 q12 q8 q5 q23 q2 q16 q6 q18 q27
## Factors Labels VI(grf)
## 28          z4      q28  0.1662
## 3  noise5 <= 0.01    q3  0.0948
## 25          z1      q25  0.0595
## 30          grade3  q30  0.0417
## 22  noise5 <= 0      q22  0.0416
## 1  noise5 <= -0.51    q1  0.0410
## 19  noise4 <= 0      q19  0.0396
## 29          z5      q29  0.0379
## 26          z2      q26  0.0366
## 11  noise2 <= -0.1    q11  0.0331
## 12  noise2 <= -0.8    q12  0.0325
## 8   noise1 <= -0.1    q8   0.0296
## 5   size <= 27        q5   0.0271
## 23  noise5 <= -0.7    q23  0.0247
## 2   noise3 <= -0.7    q2   0.0243
## 16  noise3 <= -0.6    q16  0.0242
## 6   size <= 21        q6   0.0230
## 18  noise4 <= 0.1     q18  0.0217
## 27          z3      q27  0.0212
## 4   size <= 29.7      q4   0.0205
## 14  noise3 <= 0.1     q14  0.0204
## 17  noise3 <= 0.8     q17  0.0196
## 24  noise5 <= 0.7     q24  0.0183
## 13  noise2 <= 0.5     q13  0.0173
## 9   noise1 <= -0.8    q9   0.0172
## 15  noise3 <= 0       q15  0.0172
## 20  noise4 <= -0.6    q20  0.0160
## 21  noise4 <= 0.8     q21  0.0147
## 10  noise1 <= 0.7     q10  0.0108
## 7   size <= 35       q7   0.0079
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 1830
## Approximately 5% of max_count met: minutes 0.005316667
## Approximately 10% of max_count met: minutes 0.008333333
## Approximately 20% of max_count met: minutes 0.017566667
## Approximately 33% of max_count met: minutes 0.024966667
## Approximately 50% of max_count met: minutes 0.034433333
## Approximately 75% of max_count met: minutes 0.04885
## Approximately 90% of max_count met: minutes 0.0554
## # of subgroups evaluated based on (up to) maxk-factor combinations 1830
## % of all-possible combinations (<= maxk) 100
## k.max= 2
## Events criteria for control,exp= 10 10
## # of subgroups with events less than criteria: control, experimental 321 496
## # of subgroups with sample size less than criteria 754
## # of subgroups meeting all criteria = 1004
## # of subgroups fitted (Cox model estimable) = 1004
## *Subgroup Searching Minutes=* 0.05971667
## Number of subgroups meeting HR threshold 6
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) = 6

```

```

## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##      n  E d1   HR L(HR) q28.0 q28.1 q3.0 q3.1 q25.0 q25.1
## 1 64 29 17 1.63 0.77      0      0      0      1      0      0
## 2 62 28 17 1.60 0.75      0      0      0      0      0      0
## 3 81 38 21 1.30 0.68      0      0      0      1      0      0
## 4 75 36 20 1.28 0.66      0      0      0      1      0      0
## 5 79 37 21 1.27 0.66      0      0      0      0      0      0
## 6 65 35 18 1.26 0.65      0      0      0      0      0      0
## Consistency 0.83
## Consistency 0.77
## Consistency 0.5425
## Subgroup Consistency Minutes= 0.09938333
## NO subgroup found (FS)
## Minutes forestsearch overall= 0.1663833
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 45.42348 2
##      leaf.node control.mean control.size control.se depth
## 2              3          -6.97          291.00          1.49      1
## 21             5          -14.58          77.00          2.86      2
## 3              6           6.45          63.00          2.91      2
## 4              7          -9.23          144.00          2.02      2
##      leaf.node control.mean control.size control.se depth
## 3              6           6.45          63.00          2.91      2
## GRF subgroup found
## All splits
## [1] "noise5 <= -0.51" "noise3 <= -0.7" "noise5 <= 0.01"
## Terminating node at max.diff (sg.harm.id)
## [1] "noise5 <= 0.00807090609630402"
## # of continuous/categorical characteristics 6 6
## Continuous characteristics: size noise1 noise2 noise3 noise4 noise5
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## CV lambda = 0.04541205
## 12 x 1 sparse Matrix of class "dgCMatrix"
##              s0
## z1            .
## z2            .
## z3            .
## z4      0.7803413
## z5     -0.6626916
## size          .
## grade3         .
## noise1 0.0240149
## noise2         .
## noise3         .
## noise4         .
## noise5         .
## Cox-LASSO selected: z4 z5 noise1
## Cox-LASSO not selected: z1 z2 z3 size grade3 noise2 noise3 noise4 noise5
## Default cuts included from Lasso:
## Categorical after Lasso: z4 z5
## Factors per GRF: noise5 <= -0.51 noise3 <= -0.7 noise5 <= 0.01
## Initial GRF cuts included noise5 <= -0.51 noise3 <= -0.7 noise5 <= 0.01
## Factors included per GRF (not in lasso) noise5 <= -0.51 noise3 <= -0.7 noise5 <= 0.01
## # of candidate subgroup factors= 26
## [1] "noise5 <= -0.51" "noise3 <= -0.7" "noise5 <= 0.01" "size <= 29.7"

```

```

## [5] "size <= 27"      "size <= 21"      "size <= 35"      "noise1 <= -0.1"
## [9] "noise1 <= -0.8"  "noise1 <= 0.7"   "noise2 <= -0.1"  "noise2 <= -0.8"
## [13] "noise2 <= 0.5"   "noise3 <= 0.1"   "noise3 <= 0"     "noise3 <= -0.6"
## [17] "noise3 <= 0.8"   "noise4 <= 0.1"   "noise4 <= 0"     "noise4 <= -0.6"
## [21] "noise4 <= 0.8"   "noise5 <= 0"     "noise5 <= -0.7"  "noise5 <= 0.7"
## [25] "z4"              "z5"
## Number of factors evaluated= 26
## Confounders per grf screening q25 q3 q19 q22 q26 q1 q11 q8 q16 q12 q5 q2 q23 q17 q18 q6 q14 q15 q4 q
## Factors Labels VI(grf)
## 25      z4      q25  0.2192
## 3      noise5 <= 0.01      q3  0.1034
## 19      noise4 <= 0      q19  0.0524
## 22      noise5 <= 0      q22  0.0482
## 26      z5      q26  0.0445
## 1      noise5 <= -0.51      q1  0.0443
## 11      noise2 <= -0.1      q11  0.0424
## 8       noise1 <= -0.1      q8   0.0375
## 16      noise3 <= -0.6      q16  0.0330
## 12      noise2 <= -0.8      q12  0.0328
## 5       size <= 27      q5   0.0311
## 2       noise3 <= -0.7      q2   0.0279
## 23      noise5 <= -0.7      q23  0.0263
## 17      noise3 <= 0.8      q17  0.0256
## 18      noise4 <= 0.1      q18  0.0255
## 6       size <= 21      q6   0.0246
## 14      noise3 <= 0.1      q14  0.0226
## 15      noise3 <= 0      q15  0.0220
## 4       size <= 29.7      q4   0.0213
## 24      noise5 <= 0.7      q24  0.0209
## 13      noise2 <= 0.5      q13  0.0204
## 9       noise1 <= -0.8      q9   0.0195
## 20      noise4 <= -0.6      q20  0.0161
## 21      noise4 <= 0.8      q21  0.0147
## 10      noise1 <= 0.7      q10  0.0140
## 7       size <= 35      q7   0.0099
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 1378
## Approximately 5% of max_count met: minutes 0.00415
## Approximately 10% of max_count met: minutes 0.0074
## Approximately 20% of max_count met: minutes 0.01336667
## Approximately 33% of max_count met: minutes 0.02003333
## Approximately 50% of max_count met: minutes 0.02795
## Approximately 75% of max_count met: minutes 0.03698333
## Approximately 90% of max_count met: minutes 0.04458333
## # of subgroups evaluated based on (up to) maxk-factor combinations 1378
## % of all-possible combinations (<= maxk) 100
## k.max= 2
## Events criteria for control,exp= 10 10
## # of subgroups with events less than criteria: control, experimental 262 384
## # of subgroups with sample size less than criteria 574
## # of subgroups meeting all criteria = 741
## # of subgroups fitted (Cox model estimable) = 741
## *Subgroup Searching Minutes=* 0.04928333
## Number of subgroups meeting HR threshold 6
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) = 6

```

```

## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##      n  E d1   HR L(HR) q25.0 q25.1 q3.0 q3.1 q19.0 q19.1
## 1 64 29 17 1.63 0.77      0      0      0      1      0      0
## 2 62 28 17 1.60 0.75      0      0      0      0      0      0
## 3 81 38 21 1.30 0.68      0      0      0      1      0      0
## 4 75 36 20 1.28 0.66      0      0      0      1      0      0
## 5 79 37 21 1.27 0.66      0      0      0      0      0      0
## 6 65 35 18 1.26 0.65      0      0      0      0      0      0
## Consistency 0.83
## Consistency 0.77
## Consistency 0.5425
## Subgroup Consistency Minutes= 0.1055
## NO subgroup found (FS)
## Minutes forestsearch overall= 0.1648667

t.now <- proc.time()[3]
t.min <- (t.now - t.start)/60

print(table(res$analysis))

##
##      FS1      FS1g      GRF  GRF.60  VT(24)  VT(36)  VT#(24)  VT#(36)
## 20000 20000 20000 20000 20000 20000 20000 20000

check <- c(c(table(res$analysis)) - Nsims)
if (all(check != 0)) stop("All analyses not complete")

dgm_alt <- dgm
outres <- out.results(res = res, dgm = dgm, output.file = output.file, t.min = t.min,
  out_analysis = "FS1")

## [1] "results/oc_sims=20000_m4c-Noise=5_N=300_null_ktreat=1.5_v0-4cuts.Rdata"
##      sim sizeH_true propH_true sizeHc_true propHc_true any.H size.H size.Hc
##      <int>      <num>      <num>      <int>      <num> <num> <num> <int>
## 1:      1          0          0          300          1      0      0      300
## 2:      1          0          0          300          1      0      0      300
## 3:      1          0          0          300          1      0      0      300
## 4:      1          0          0          300          1      0      0      300
## 5:      1          0          0          300          1      0      0      300
## 6:      1          0          0          300          1      0      0      300
##      ppv      npv specificity sensitivity found.1 found.2 found.both found.al3
##      <lgcl> <num>      <num>      <num> <int> <int>      <num> <num>
## 1:      NA      1          1          NA      0      0          0      0
## 2:      NA      1          1          NA      0      0          0      0
## 3:      NA      1          1          NA      NA      NA          NA      NA
## 4:      NA      1          1          NA      NA      NA          NA      NA
## 5:      NA      1          1          NA      0      0          0      0
## 6:      NA      1          1          NA      0      0          0      0
##      hr.H.true hr.Hc.true hr.H.hat hr.Hc.hat  b1.H  b2.H b1.Hc  b2.Hc
##      <lgcl>      <num>      <num>      <num> <lgcl> <lgcl> <num> <num>
## 1:      NA 0.6000708      NA 0.6000708      NA      NA      0 0.04834743
## 2:      NA 0.6000708      NA 0.6000708      NA      NA      0 0.04834743
## 3:      NA 0.6000708      NA 0.6000708      NA      NA      0 0.04834743
## 4:      NA 0.6000708      NA 0.6000708      NA      NA      0 0.04834743
## 5:      NA 0.6000708      NA 0.6000708      NA      NA      0 0.04834743
## 6:      NA 0.6000708      NA 0.6000708      NA      NA      0 0.04834743

```

```

##      p.cens analysis      taumax      hr.itt      l.itt      u.itt hr.adj.itt l.adj.itt
##      <num>   <char>      <num>      <num>      <num>      <num>      <num>      <num>
## 1:    0.45      FSl 75.55189 0.6000708 0.4404799 0.8174834 0.5166355 0.37681
## 2:    0.45      FSlg 45.33113 0.6000708 0.4404799 0.8174834 0.5166355 0.37681
## 3:    0.45      GRF 75.55189 0.6000708 0.4404799 0.8174834 0.5166355 0.37681
## 4:    0.45      GRF.60 45.33113 0.6000708 0.4404799 0.8174834 0.5166355 0.37681
## 5:    0.45      VT(24) 75.55189 0.6000708 0.4404799 0.8174834 0.5166355 0.37681
## 6:    0.45      VT#(24) 75.55189 0.6000708 0.4404799 0.8174834 0.5166355 0.37681
##      u.adj.itt l.H.true u.H.true l.Hc.true u.Hc.true l.H.hat u.H.hat l.Hc.hat
##      <num>   <lgcl>   <lgcl>   <num>   <num>   <num>   <num>   <num>
## 1: 0.708347      NA      NA 0.4404799 0.8174834      NA      NA 0.4404799
## 2: 0.708347      NA      NA 0.4404799 0.8174834      NA      NA 0.4404799
## 3: 0.708347      NA      NA 0.4404799 0.8174834      NA      NA 0.4404799
## 4: 0.708347      NA      NA 0.4404799 0.8174834      NA      NA 0.4404799
## 5: 0.708347      NA      NA 0.4404799 0.8174834      NA      NA 0.4404799
## 6: 0.708347      NA      NA 0.4404799 0.8174834      NA      NA 0.4404799
##      u.Hc.hat
##      <num>
## 1: 0.8174834
## 2: 0.8174834
## 3: 0.8174834
## 4: 0.8174834
## 5: 0.8174834
## 6: 0.8174834
## Subgroup HRs: H, H^c, Causal= NA 0.5517234 0.5517234
## Simulations= 20000
## Avg censoring= 0.501857
## Min,Max,Avg tau.max= 59.38268 83.94994 78.95074
## P(H) approximation at causal(Hrc), n=60, approx= 0.5517234 0.008107176
## P(H) approximation at plim(Hrc), n=60, approx= 0.5427458 0.007193425
## Minutes,hours 93.4978 1.558297
##      FSl      FSlg      GRF      GRF.60      VT(24)      VT#(24)      VT(36)      VT#(36)
## any.H      0.040      0.040      0.130      0.070      0.010      0.000      0.020      0.010
## sensH      NaN      NaN      NaN      NaN      NaN      NaN      NaN      NaN
## sensHc      0.990      0.990      0.970      0.980      1.000      1.000      0.990      1.000
## ppH      0.000      0.000      0.000      0.000      0.000      0.000      0.000      0.000
## ppHc      1.000      1.000      1.000      1.000      1.000      1.000      1.000      1.000
## Avg(#H)      73.000      73.000      74.000      71.000      71.000      69.000      74.000      70.000
## minH      61.000      61.000      60.000      60.000      60.000      60.000      60.000      60.000
## maxH      150.000      150.000      160.000      136.000      125.000      102.000      138.000      125.000
## Avg(#Hc)      297.000      297.000      291.000      295.000      299.000      300.000      298.000      300.000
## minHc      150.000      150.000      140.000      164.000      175.000      198.000      162.000      175.000
## maxHc      300.000      300.000      300.000      300.000      300.000      300.000      300.000      300.000
## hat(H*)      NaN      NaN      NaN      NaN      NaN      NaN      NaN      NaN
## hat(hat[H])      1.991      1.992      1.726      1.515      1.095      1.283      1.130      1.496
## hat(Hc*)      0.693      0.697      0.636      0.622      0.607      0.632      0.614      0.638
## hat(hat[Hc])      0.499      0.502      0.460      0.474      0.513      0.513      0.511      0.497
## hat(H*)all      NaN      NaN      NaN      NaN      NaN      NaN      NaN      NaN
## hat(Hc*)all      0.543      0.543      0.543      0.543      0.543      0.543      0.543      0.543
## hat(ITT)all      0.543      0.543      0.543      0.543      0.543      0.543      0.543      0.543
## hat(ITTadj)all      0.488      0.488      0.488      0.488      0.488      0.488      0.488      0.488

missC <- tab_tests(res = res)

pA <- as.character(round(outres$pAnyH.approx2, 4))

```

```
tabsim_missC <- get_tabsim(missC = missC, pA = pA, est_names = est_names, stat_names = stat_names,
  mod.harm = mod.harm, Nsims = Nsims)
```

Table 1: Average classification rates: $avg|\hat{H}|$, $min|\hat{H}|$, and $max|\hat{H}|$, denote the average, minimum, and maximum of the number of subjects in the estimated subgroup \hat{H} (analogously for \hat{H}^c). Note that under the null $sens(\hat{H})$ is undefined and $ppv(\hat{H}) = 0$.

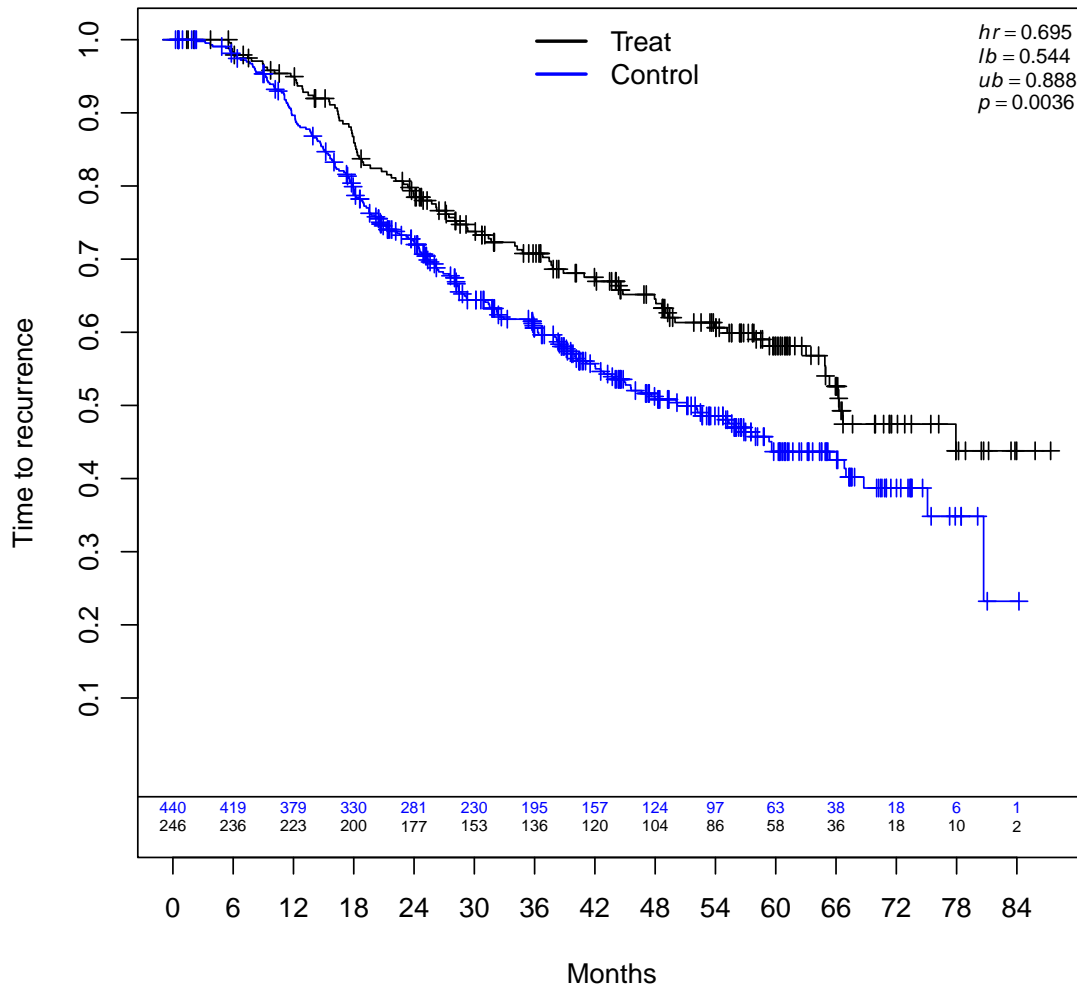
	FS_g	FS_{lg}	GRF	GRF_{60}	$VT(24)$	$VT^\#(24)$	$VT(36)$	$VT^\#(36)$
Finding H								
any(H)	0.04	0.04	0.13	0.07	0.01	0	0.02	0.01
$sens(\hat{H})$
$sens(\hat{H}^c)$	0.99	0.99	0.97	0.98	1	1	0.99	1
$ppv(\hat{H})$	0	0	0	0	0	0	0	0
$ppv(\hat{H}^c)$	1	1	1	1	1	1	1	1
Size of H and H-complement								
$avg \hat{H} $	73	73	74	71	71	69	74	70
$min \hat{H} $	61	61	60	60	60	60	60	60
$max \hat{H} $	150	150	160	136	125	102	138	125
$avg \hat{H}^c $	297	297	291	295	299	300	298	300
$min \hat{H}^c $	150	150	140	164	175	198	162	175
$max \hat{H}^c $	300	300	300	300	300	300	300	300

Note: Number of simulations= 20000 .

Note: Probability approximation= 0.0072 .

```
mod.harm <- "alt"
hrH.target <- 2

this.dgm <- get_dgm4.OC(mod.harm = mod.harm, N = N, k.treat = k.treat, model.index = model.index,
  sol_tol = 10^-8, hrH.target = hrH.target, cens.type = cens.type, out.loc = out.loc,
  file.index = file.index, details = TRUE, parms_torand = FALSE)
```

```
## Super-population empirical harm and non-harm hazard ratios= 1.999999 0.557631
## Causal HR (empirical ITT)= 0.7363833

dgm <- this.dgm$dgm
output.file <- this.dgm$out.file

if (!is.null(output.file) & !grepl(mod.harm, output.file)) stop("Wrong file name for mod.harm")

# Show first simulation ans1 <- oc_analyses_m4_FS4(2)

t.start <- proc.time()[3]
res <- foreach(sim = seq_len(Nsims), .options.future = list(seed = TRUE), .combine = "rbind",
  .errorhandling = "pass") %dofuture% {
  ans <- oc_analyses_m4FourCuts_FS4(sim)
  return(ans)
}

## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 49.06126 2
```

```

##   leaf.node control.mean control.size control.se depth
## 1         2        -2.85        256.00        1.95    1
## 2         5         7.97         82.00         3.50    2
## 3         6        -7.10        146.00         2.45    2
##   leaf.node control.mean control.size control.se depth
## 2         5         7.97         82.00         3.50    2
## GRF subgroup found
## All splits
## [1] "noise5 <= -0.4" "noise2 <= -0.77" "noise5 <= 1.07"
## Terminating node at max.diff (sg.harm.id)
## [1] "noise2 <= -0.768600960339892"
## # of continuous/categorical characteristics 6 6
## Continuous characteristics: size noise1 noise2 noise3 noise4 noise5
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## Default cuts included (1st 20)
## Categorical: z1 z2 z3 z4 z5 grade3
## Factors per GRF: noise5 <= -0.4 noise2 <= -0.77 noise5 <= 1.07
## Initial GRF cuts included noise5 <= -0.4 noise2 <= -0.77 noise5 <= 1.07
## # of candidate subgroup factors= 28
## [1] "noise5 <= -0.4" "noise2 <= -0.77" "noise5 <= 1.07" "size <= 29.6"
## [5] "size <= 25"      "size <= 21"      "size <= 35"      "noise1 <= 0"
## [9] "noise1 <= -0.6"  "noise1 <= 0.7"   "noise2 <= 0"     "noise2 <= -0.7"
## [13] "noise2 <= 0.7"   "noise3 <= 0"     "noise3 <= -0.7"  "noise3 <= 0.8"
## [17] "noise4 <= 0"     "noise4 <= -0.8"  "noise4 <= 0.7"   "noise5 <= -0.1"
## [21] "noise5 <= -0.8"  "noise5 <= 0.5"   "z1"              "z2"
## [25] "z3"              "z4"              "z5"              "grade3"
## Number of factors evaluated= 28
## Confounders per grf screening q6 q25 q7 q3 q24 q23 q22 q19 q1 q27 q4 q14 q26 q5 q11 q8 q17 q20 q21 q
##           Factors Labels VI(grf)
## 6         size <= 21      q6  0.1003
## 25         z3            q25 0.0794
## 7         size <= 35      q7  0.0733
## 3  noise5 <= 1.07      q3  0.0687
## 24         z2            q24 0.0653
## 23         z1            q23 0.0463
## 22  noise5 <= 0.5      q22 0.0453
## 19  noise4 <= 0.7      q19 0.0404
## 1  noise5 <= -0.4      q1  0.0389
## 27         z5            q27 0.0365
## 4         size <= 29.6    q4  0.0359
## 14  noise3 <= 0        q14 0.0345
## 26         z4            q26 0.0334
## 5         size <= 25      q5  0.0311
## 11  noise2 <= 0        q11 0.0304
## 8         noise1 <= 0     q8  0.0298
## 17  noise4 <= 0        q17 0.0295
## 20  noise5 <= -0.1      q20 0.0288
## 21  noise5 <= -0.8      q21 0.0227
## 15  noise3 <= -0.7      q15 0.0193
## 10  noise1 <= 0.7      q10 0.0189
## 13  noise2 <= 0.7      q13 0.0166
## 12  noise2 <= -0.7      q12 0.0161
## 9   noise1 <= -0.6      q9  0.0158
## 16  noise3 <= 0.8      q16 0.0143
## 28         grade3       q28 0.0106

```

```

## 18 noise4 <= -0.8      q18 0.0103
## 2  noise2 <= -0.77     q2 0.0076
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 1596
## Approximately 5% of max_count met: minutes 0.0028
## Approximately 10% of max_count met: minutes 0.004083333
## Approximately 20% of max_count met: minutes 0.006516667
## Approximately 33% of max_count met: minutes 0.01075
## Approximately 50% of max_count met: minutes 0.0155
## Approximately 75% of max_count met: minutes 0.02465
## Approximately 90% of max_count met: minutes 0.02916667
## # of subgroups evaluated based on (up to) maxk-factor combinations 1596
## % of all-possible combinations (<= maxk) 100
## k.max= 2
## Events criteria for control,exp= 10 10
## # of subgroups with events less than criteria: control, experimental 252 309
## # of subgroups with sample size less than criteria 713
## # of subgroups meeting all criteria = 855
## # of subgroups fitted (Cox model estimable) = 855
## *Subgroup Searching Minutes=* 0.03105
## Number of subgroups meeting HR threshold 49
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) = 49
## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##      n E d1  HR L(HR) q6.0 q6.1 q25.0 q25.1 q7.0 q7.1 q3.0 q3.1 q24.0 q24.1
## 1  67 42 22 1.89 1.03  0  0  0  0  0  1  0  0  0  0
## 2  67 42 22 1.89 1.03  1  0  0  0  0  1  0  0  0  0
## 3  63 42 20 1.80 0.98  0  0  0  0  0  0  0  0  0  0
## 4  72 45 25 1.71 0.95  0  0  0  0  0  0  0  0  0  1
## 5  70 43 28 1.69 0.90  0  0  0  0  0  0  0  0  0  0
## 6  69 41 23 1.56 0.84  0  0  0  0  0  0  0  0  0  0
## 7  80 60 31 1.56 0.94  0  0  0  1  0  0  0  0  0  0
## 8  74 58 29 1.52 0.90  0  0  0  0  0  0  0  0  0  1
## 9  78 57 31 1.48 0.88  0  0  0  0  0  0  0  0  0  0
## 10 61 37 19 1.48 0.77  0  0  0  0  0  0  0  0  0  0
## Consistency 0.95
## # of splits= 400
## Model, % Consistency Met= ![size <= 35] 0.95
## SG focus= hr
## Subgroup Consistency Minutes= 0.02448333
## Subgroup found (FS)
## Minutes forestsearch overall= 0.06066667
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 49.06126 2
##   leaf.node control.mean control.size control.se depth
## 1         2        -2.85        256.00        1.95    1
## 2         5         7.97         82.00         3.50    2
## 3         6        -7.10        146.00         2.45    2
##   leaf.node control.mean control.size control.se depth
## 2         5         7.97         82.00         3.50    2
## GRF subgroup found
## All splits
## [1] "noise5 <= -0.4" "noise2 <= -0.77" "noise5 <= 1.07"
## Terminating node at max.diff (sg.harm.id)
## [1] "noise2 <= -0.768600960339892"
## # of continuous/categorical characteristics 6 6

```

```

## Continuous characteristics: size noise1 noise2 noise3 noise4 noise5
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## CV lambda = 0.03751062
## 12 x 1 sparse Matrix of class "dgCMatrix"
##           s0
## z1      0.06313344
## z2      .
## z3      0.28641313
## z4      0.57548664
## z5     -0.61782376
## size    .
## grade3  .
## noise1  .
## noise2 -0.06786117
## noise3  .
## noise4  .
## noise5  .
## Cox-LASSO selected: z1 z3 z4 z5 noise2
## Cox-LASSO not selected: z2 size grade3 noise1 noise3 noise4 noise5
## Default cuts included from Lasso:
## Categorical after Lasso: z1 z3 z4 z5
## Factors per GRF: noise5 <= -0.4 noise2 <= -0.77 noise5 <= 1.07
## Initial GRF cuts included noise5 <= -0.4 noise2 <= -0.77 noise5 <= 1.07
## Factors included per GRF (not in lasso) noise5 <= -0.4 noise2 <= -0.77 noise5 <= 1.07
## # of candidate subgroup factors= 26
## [1] "noise5 <= -0.4" "noise2 <= -0.77" "noise5 <= 1.07" "size <= 29.6"
## [5] "size <= 25" "size <= 21" "size <= 35" "noise1 <= 0"
## [9] "noise1 <= -0.6" "noise1 <= 0.7" "noise2 <= 0" "noise2 <= -0.7"
## [13] "noise2 <= 0.7" "noise3 <= 0" "noise3 <= -0.7" "noise3 <= 0.8"
## [17] "noise4 <= 0" "noise4 <= -0.8" "noise4 <= 0.7" "noise5 <= -0.1"
## [21] "noise5 <= -0.8" "noise5 <= 0.5" "z1" "z3"
## [25] "z4" "z5"
## Number of factors evaluated= 26
## Confounders per grf screening q24 q6 q7 q3 q23 q22 q1 q19 q4 q25 q8 q26 q14 q11 q17 q5 q20 q15 q9 q2
##           Factors Labels VI(grf)
## 24           z3      q24 0.1086
## 6      size <= 21      q6 0.1004
## 7      size <= 35      q7 0.0713
## 3  noise5 <= 1.07      q3 0.0712
## 23          z1      q23 0.0556
## 22  noise5 <= 0.5      q22 0.0444
## 1  noise5 <= -0.4      q1 0.0416
## 19  noise4 <= 0.7      q19 0.0415
## 4      size <= 29.6      q4 0.0398
## 25          z4      q25 0.0366
## 8      noise1 <= 0      q8 0.0352
## 26          z5      q26 0.0352
## 14      noise3 <= 0      q14 0.0340
## 11      noise2 <= 0      q11 0.0335
## 17      noise4 <= 0      q17 0.0326
## 5      size <= 25      q5 0.0301
## 20  noise5 <= -0.1      q20 0.0285
## 15  noise3 <= -0.7      q15 0.0279
## 9      noise1 <= -0.6      q9 0.0205
## 21  noise5 <= -0.8      q21 0.0205

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## 10  noise1 <= 0.7    q10  0.0199
## 13  noise2 <= 0.7    q13  0.0182
## 12  noise2 <= -0.7   q12  0.0143
## 16  noise3 <= 0.8    q16  0.0143
## 18  noise4 <= -0.8   q18  0.0135
## 2   noise2 <= -0.77  q2   0.0106
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 1378
## Approximately 5% of max_count met: minutes 0.00235
## Approximately 10% of max_count met: minutes 0.0039
## Approximately 20% of max_count met: minutes 0.0061
## Approximately 33% of max_count met: minutes 0.00945
## Approximately 50% of max_count met: minutes 0.01385
## Approximately 75% of max_count met: minutes 0.0222
## Approximately 90% of max_count met: minutes 0.02636667
## # of subgroups evaluated based on (up to) maxk-factor combinations 1378
## % of all-possible combinations (<= maxk) 100
## k.max= 2
## Events criteria for control,exp= 10 10
## # of subgroups with events less than criteria: control, experimental 223 257
## # of subgroups with sample size less than criteria 612
## # of subgroups meeting all criteria = 739
## # of subgroups fitted (Cox model estimable) = 739
## *Subgroup Searching Minutes=* 0.02791667
## Number of subgroups meeting HR threshold 41
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) = 41
## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##      n  E d1  HR L(HR) q24.0 q24.1 q6.0 q6.1 q7.0 q7.1 q3.0 q3.1 q23.0 q23.1
## 1  67 42 22 1.89 1.03    0    0    0    0    1    0    0    0    0    0
## 2  67 42 22 1.89 1.03    0    0    1    0    1    0    0    0    0    0
## 3  63 42 20 1.80 0.98    0    0    0    0    0    0    0    0    0    1
## 4  70 43 28 1.69 0.90    0    0    0    0    0    0    0    0    0    0
## 5  69 41 23 1.56 0.84    0    0    0    0    0    0    0    0    0    0
## 6  80 60 31 1.56 0.94    0    1    0    0    0    0    0    0    0    1
## 7  78 57 31 1.48 0.88    0    0    0    0    0    0    0    0    0    0
## 8  61 37 19 1.48 0.77    0    0    0    0    0    0    0    0    0    0
## 9  74 42 24 1.47 0.79    0    0    0    0    0    0    0    0    0    0
## 10 61 40 20 1.43 0.76    0    1    0    0    0    0    0    0    0    0
## Consistency 0.95
## # of splits= 400
## Model, % Consistency Met= ![size <= 35] 0.95
## SG focus= hr
## Subgroup Consistency Minutes= 0.0232
## Subgroup found (FS)
## Minutes forestsearch overall= 0.05636667
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 47.98043 2
##      leaf.node control.mean control.size control.se depth
## 1          2        -3.81        170.00        2.10    1
## 2          3         4.92        130.00        2.58    1
## 11         4        -8.26         80.00        2.96    2
## 4          7         7.43        114.00        2.72    2
##      leaf.node control.mean control.size control.se depth
## 4          7         7.43        114.00        2.72    2
## GRF subgroup found

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## All splits
## [1] "z2 <= 0"          "noise4 <= 0.29" "z1 <= 0"
## Terminating node at max.diff (sg.harm.id)
## [1] "z1 <= 0"
## # of continuous/categorical characteristics 6 6
## Continuous characteristics: size noise1 noise2 noise3 noise4 noise5
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## Default cuts included (1st 20)
## Categorical: z1 z2 z3 z4 z5 grade3
## Factors per GRF: z2 <= 0 noise4 <= 0.29 z1 <= 0
## Initial GRF cuts included z2 <= 0 noise4 <= 0.29 z1 <= 0
## # of candidate subgroup factors= 27
## [1] "noise4 <= 0.29" "size <= 27.9" "size <= 25" "size <= 20"
## [5] "size <= 34" "noise1 <= 0.1" "noise1 <= -0.7" "noise1 <= 0.7"
## [9] "noise2 <= 0" "noise2 <= -0.1" "noise2 <= -0.6" "noise2 <= 0.7"
## [13] "noise3 <= 0" "noise3 <= -0.7" "noise3 <= 0.7" "noise4 <= 0"
## [17] "noise4 <= -0.8" "noise4 <= 0.7" "noise5 <= 0.1" "noise5 <= -0.5"
## [21] "noise5 <= 0.8" "z1" "z2" "z3"
## [25] "z4" "z5" "grade3"
## Number of factors evaluated= 27
## Confounders per grf screening q24 q17 q22 q3 q2 q1 q15 q6 q14 q26 q25 q4 q21 q23 q16 q13 q19 q5 q12
## Factors Labels VI(grf)
## 24 z3 q24 0.0991
## 17 noise4 <= -0.8 q17 0.0654
## 22 z1 q22 0.0605
## 3 size <= 25 q3 0.0567
## 2 size <= 27.9 q2 0.0535
## 1 noise4 <= 0.29 q1 0.0471
## 15 noise3 <= 0.7 q15 0.0468
## 6 noise1 <= 0.1 q6 0.0444
## 14 noise3 <= -0.7 q14 0.0400
## 26 z5 q26 0.0397
## 25 z4 q25 0.0369
## 4 size <= 20 q4 0.0348
## 21 noise5 <= 0.8 q21 0.0338
## 23 z2 q23 0.0318
## 16 noise4 <= 0 q16 0.0305
## 13 noise3 <= 0 q13 0.0304
## 19 noise5 <= 0.1 q19 0.0303
## 5 size <= 34 q5 0.0290
## 12 noise2 <= 0.7 q12 0.0275
## 10 noise2 <= -0.1 q10 0.0262
## 9 noise2 <= 0 q9 0.0237
## 27 grade3 q27 0.0237
## 20 noise5 <= -0.5 q20 0.0228
## 8 noise1 <= 0.7 q8 0.0217
## 7 noise1 <= -0.7 q7 0.0154
## 11 noise2 <= -0.6 q11 0.0145
## 18 noise4 <= 0.7 q18 0.0135
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 1485
## Approximately 5% of max_count met: minutes 0.0031
## Approximately 10% of max_count met: minutes 0.005966667
## Approximately 20% of max_count met: minutes 0.009433333
## Approximately 33% of max_count met: minutes 0.01551667
## Approximately 50% of max_count met: minutes 0.02283333

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## Approximately 75% of max_count met: minutes 0.03336667
## Approximately 90% of max_count met: minutes 0.0404
## # of subgroups evaluated based on (up to) maxk-factor combinations 1485
## % of all-possible combinations (<= maxk) 100
## k.max= 2
## Events criteria for control,exp= 10 10
## # of subgroups with events less than criteria: control, experimental 216 339
## # of subgroups with sample size less than criteria 621
## # of subgroups meeting all criteria = 828
## # of subgroups fitted (Cox model estimable) = 828
## *Subgroup Searching Minutes=* 0.04376667
## Number of subgroups meeting HR threshold 56
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) = 56
## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##      n  E d1   HR L(HR) q24.0 q24.1 q17.0 q17.1 q22.0 q22.1 q3.0 q3.1 q2.0 q2.1
## 1    96 61 29 1.95  1.17    0    1    0    0    0    1    0    0    0    0
## 2    73 36 20 1.89  0.98    0    0    0    0    0    0    0    0    0    0
## 3    79 41 23 1.75  0.94    0    0    0    0    0    0    0    0    0    0
## 4    95 57 29 1.73  1.03    0    0    0    0    0    1    0    0    0    0
## 5    61 38 20 1.71  0.90    0    1    0    0    0    0    0    0    0    0
## 6    68 53 27 1.70  0.98    0    1    0    0    0    0    0    0    0    0
## 7    64 34 19 1.68  0.85    0    1    0    0    0    0    0    1    0    0
## 8    72 45 22 1.67  0.93    0    1    0    0    0    0    0    0    0    0
## 9   106 63 33 1.66  1.01    0    1    0    0    0    0    0    0    0    0
## 10   71 44 24 1.65  0.91    0    1    0    0    0    0    0    0    0    0
## Consistency 0.995
## # of splits= 400
## Model, % Consistency Met= {z3} {z1} 0.995
## SG focus= hr
## Subgroup Consistency Minutes= 0.03203333
## Subgroup found (FS)
## Minutes forestsearch overall= 0.08255
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 47.98043 2
##      leaf.node control.mean control.size control.se depth
## 1           2          -3.81         170.00         2.10    1
## 2           3           4.92         130.00         2.58    1
## 11          4          -8.26          80.00         2.96    2
## 4           7           7.43         114.00         2.72    2
##      leaf.node control.mean control.size control.se depth
## 4           7           7.43         114.00         2.72    2
## GRF subgroup found
## All splits
## [1] "z2 <= 0"          "noise4 <= 0.29" "z1 <= 0"
## Terminating node at max.diff (sg.harm.id)
## [1] "z1 <= 0"
## # of continuous/categorical characteristics 6 6
## Continuous characteristics: size noise1 noise2 noise3 noise4 noise5
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## CV lambda = 0.03590407
## 12 x 1 sparse Matrix of class "dgCMatrix"
##           s0
## z1          .
## z2          .

```

```

## z3      0.3594938
## z4      0.9719108
## z5     -0.9809366
## size    .
## grade3  .
## noise1  .
## noise2  .
## noise3  .
## noise4  .
## noise5  .
## Cox-LASSO selected: z3 z4 z5
## Cox-LASSO not selected: z1 z2 size grade3 noise1 noise2 noise3 noise4 noise5
## Default cuts included from Lasso:
## Categorical after Lasso: z3 z4 z5
## Factors per GRF: z2 <= 0 noise4 <= 0.29 z1 <= 0
## Initial GRF cuts included z2 <= 0 noise4 <= 0.29 z1 <= 0
## Factors included per GRF (not in lasso) z2 <= 0 noise4 <= 0.29 z1 <= 0
## # of candidate subgroup factors= 26
## [1] "noise4 <= 0.29" "size <= 27.9" "size <= 25" "size <= 20"
## [5] "size <= 34" "noise1 <= 0.1" "noise1 <= -0.7" "noise1 <= 0.7"
## [9] "noise2 <= 0" "noise2 <= -0.1" "noise2 <= -0.6" "noise2 <= 0.7"
## [13] "noise3 <= 0" "noise3 <= -0.7" "noise3 <= 0.7" "noise4 <= 0"
## [17] "noise4 <= -0.8" "noise4 <= 0.7" "noise5 <= 0.1" "noise5 <= -0.5"
## [21] "noise5 <= 0.8" "z3" "z4" "z5"
## [25] "z2 <= 0" "z1 <= 0"
## Number of factors evaluated= 26
## Confounders per grf screening q22 q17 q3 q26 q2 q15 q6 q1 q4 q14 q24 q23 q19 q5 q13 q16 q10 q21 q25
## Factors Labels VI(grf)
## 22 z3 q22 0.1122
## 17 noise4 <= -0.8 q17 0.0648
## 3 size <= 25 q3 0.0634
## 26 z1 <= 0 q26 0.0614
## 2 size <= 27.9 q2 0.0504
## 15 noise3 <= 0.7 q15 0.0454
## 6 noise1 <= 0.1 q6 0.0448
## 1 noise4 <= 0.29 q1 0.0442
## 4 size <= 20 q4 0.0399
## 14 noise3 <= -0.7 q14 0.0385
## 24 z5 q24 0.0385
## 23 z4 q23 0.0354
## 19 noise5 <= 0.1 q19 0.0325
## 5 size <= 34 q5 0.0319
## 13 noise3 <= 0 q13 0.0312
## 16 noise4 <= 0 q16 0.0305
## 10 noise2 <= -0.1 q10 0.0299
## 21 noise5 <= 0.8 q21 0.0295
## 25 z2 <= 0 q25 0.0291
## 12 noise2 <= 0.7 q12 0.0282
## 20 noise5 <= -0.5 q20 0.0263
## 8 noise1 <= 0.7 q8 0.0245
## 9 noise2 <= 0 q9 0.0231
## 11 noise2 <= -0.6 q11 0.0167
## 7 noise1 <= -0.7 q7 0.0156
## 18 noise4 <= 0.7 q18 0.0124
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 1378

```



```

## Approximately 5% of max_count met: minutes 0.0032
## Approximately 10% of max_count met: minutes 0.006133333
## Approximately 20% of max_count met: minutes 0.009383333
## Approximately 33% of max_count met: minutes 0.01485
## Approximately 50% of max_count met: minutes 0.0213
## Approximately 75% of max_count met: minutes 0.031
## Approximately 90% of max_count met: minutes 0.03693333
## # of subgroups evaluated based on (up to) maxk-factor combinations 1378
## % of all-possible combinations (<= maxk) 100
## k.max= 2
## Events criteria for control,exp= 10 10
## # of subgroups with events less than criteria: control, experimental 199 310
## # of subgroups with sample size less than criteria 559
## # of subgroups meeting all criteria = 783
## # of subgroups fitted (Cox model estimable) = 783
## *Subgroup Searching Minutes=* 0.04003333
## Number of subgroups meeting HR threshold 56
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) = 56
## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##      n  E d1  HR L(HR) q22.0 q22.1 q17.0 q17.1 q3.0 q3.1 q26.0 q26.1 q2.0 q2.1
## 1    96 61 29 1.95 1.17    0    1    0    0    0    0    1    0    0    0
## 2    73 36 20 1.89 0.98    0    0    0    0    0    0    0    0    0    0
## 3    79 41 23 1.75 0.94    0    0    0    0    0    0    0    0    0    0
## 4    95 57 29 1.73 1.03    0    0    0    0    0    0    1    0    0    0
## 5    61 38 20 1.71 0.90    0    1    0    0    0    0    0    0    0    0
## 6    68 53 27 1.70 0.98    0    1    0    0    0    0    0    0    0    0
## 7    64 34 19 1.68 0.85    0    1    0    0    0    1    0    0    0    0
## 8    72 45 22 1.67 0.93    0    1    0    0    0    0    0    0    0    0
## 9   106 63 33 1.66 1.01    0    1    0    0    0    0    0    0    0    0
## 10   71 44 24 1.65 0.91    0    1    0    0    0    0    0    0    0    0
## Consistency 0.995
## # of splits= 400
## Model, % Consistency Met= {z3} !{z1 <= 0} 0.995
## SG focus= hr
## Subgroup Consistency Minutes= 0.03001667
## Subgroup found (FS)
## Minutes forestsearch overall= 0.07901667
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 45.36853 2
##      leaf.node control.mean control.size control.se depth
## 1          2        -5.62        176.00         2.00    1
## 2          3         5.14        124.00         2.53    1
## 3          4         8.89         78.00         3.09    2
## 4          5        -7.27         80.00         2.89    2
## 5          6         4.88         63.00         3.53    2
## 6          7        -9.76         79.00         2.88    2
##      leaf.node control.mean control.size control.se depth
## 3          4         8.89         78.00         3.09    2
## GRF subgroup found
## All splits
## [1] "noise1 <= -0.07" "noise5 <= 0.01" "noise4 <= -0.06"
## Terminating node at max.diff (sg.harm.id)
## [1] "noise5 <= 0.00807090609630402"
## # of continuous/categorical characteristics 6 6

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```

## Continuous characteristics: size noise1 noise2 noise3 noise4 noise5
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## Default cuts included (1st 20)
## Categorical: z1 z2 z3 z4 z5 grade3
## Factors per GRF: noise1 <= -0.07 noise5 <= 0.01 noise4 <= -0.06
## Initial GRF cuts included noise1 <= -0.07 noise5 <= 0.01 noise4 <= -0.06
## # of candidate subgroup factors= 30
## [1] "noise1 <= -0.07" "noise5 <= 0.01" "noise4 <= -0.06" "size <= 29.7"
## [5] "size <= 27" "size <= 21" "size <= 35" "noise1 <= -0.1"
## [9] "noise1 <= -0.8" "noise1 <= 0.7" "noise2 <= -0.1" "noise2 <= -0.8"
## [13] "noise2 <= 0.5" "noise3 <= 0.1" "noise3 <= 0" "noise3 <= -0.6"
## [17] "noise3 <= 0.8" "noise4 <= 0.1" "noise4 <= 0" "noise4 <= -0.6"
## [21] "noise4 <= 0.8" "noise5 <= 0" "noise5 <= -0.7" "noise5 <= 0.7"
## [25] "z1" "z2" "z3" "z4"
## [29] "z5" "grade3"
## Number of factors evaluated= 30
## Confounders per grf screening q26 q27 q2 q28 q22 q3 q25 q1 q29 q11 q5 q8 q15 q23 q14 q24 q18 q17 q4
## Factors Labels VI(grf)
## 26 z2 q26 0.1636
## 27 z3 q27 0.1613
## 2 noise5 <= 0.01 q2 0.1153
## 28 z4 q28 0.0785
## 22 noise5 <= 0 q22 0.0542
## 3 noise4 <= -0.06 q3 0.0409
## 25 z1 q25 0.0309
## 1 noise1 <= -0.07 q1 0.0291
## 29 z5 q29 0.0266
## 11 noise2 <= -0.1 q11 0.0252
## 5 size <= 27 q5 0.0211
## 8 noise1 <= -0.1 q8 0.0208
## 15 noise3 <= 0 q15 0.0208
## 23 noise5 <= -0.7 q23 0.0177
## 14 noise3 <= 0.1 q14 0.0175
## 24 noise5 <= 0.7 q24 0.0168
## 18 noise4 <= 0.1 q18 0.0158
## 17 noise3 <= 0.8 q17 0.0153
## 4 size <= 29.7 q4 0.0145
## 19 noise4 <= 0 q19 0.0141
## 16 noise3 <= -0.6 q16 0.0130
## 13 noise2 <= 0.5 q13 0.0121
## 12 noise2 <= -0.8 q12 0.0119
## 9 noise1 <= -0.8 q9 0.0115
## 30 grade3 q30 0.0104
## 6 size <= 21 q6 0.0101
## 21 noise4 <= 0.8 q21 0.0100
## 20 noise4 <= -0.6 q20 0.0089
## 7 size <= 35 q7 0.0072
## 10 noise1 <= 0.7 q10 0.0048
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 1830
## Approximately 5% of max_count met: minutes 0.004066667
## Approximately 10% of max_count met: minutes 0.008333333
## Approximately 20% of max_count met: minutes 0.01538333
## Approximately 33% of max_count met: minutes 0.025
## Approximately 50% of max_count met: minutes 0.03513333
## Approximately 75% of max_count met: minutes 0.04775

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```

## Approximately 90% of max_count met: minutes 0.05418333
## # of subgroups evaluated based on (up to) maxk-factor combinations 1830
## % of all-possible combinations (<= maxk) 100
## k.max= 2
## Events criteria for control,exp= 10 10
## # of subgroups with events less than criteria: control, experimental 293 321
## # of subgroups with sample size less than criteria 701
## # of subgroups meeting all criteria = 1078
## # of subgroups fitted (Cox model estimable) = 1078
## *Subgroup Searching Minutes=* 0.05716667
## Number of subgroups meeting HR threshold 183
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) = 183
## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##      n  E d1  HR L(HR) q26.0 q26.1 q27.0 q27.1 q2.0 q2.1 q28.0 q28.1 q22.0
## 1  70 45 23 3.04 1.62    0    0    0    1    0    0    0    0    0
## 2  70 45 23 3.04 1.62    0    0    0    1    0    0    0    0    0
## 3  64 44 24 2.85 1.53    0    0    0    1    0    0    0    0    0
## 4  85 51 28 2.80 1.57    0    1    0    0    0    0    0    0    0
## 5  85 51 28 2.80 1.57    0    1    0    0    0    0    0    0    0
## 6  66 44 23 2.44 1.33    0    0    0    1    0    0    0    0    0
## 7  94 63 32 2.40 1.44    0    0    0    1    0    0    0    0    0
## 8  72 43 27 2.36 1.26    0    1    0    0    0    0    0    0    0
## 9  90 61 35 2.32 1.39    0    0    0    1    0    0    0    0    0
## 10 93 63 34 2.28 1.36    0    0    0    1    0    0    0    0    0
##      q22.1
## 1      0
## 2      0
## 3      0
## 4      0
## 5      0
## 6      0
## 7      0
## 8      0
## 9      0
## 10     0
## Consistency 1
## # of splits= 400
## Model, % Consistency Met= {z3} {noise1 <= -0.07} 1
## SG focus= hr
## Subgroup Consistency Minutes= 0.02946667
## Subgroup found (FS)
## Minutes forestsearch overall= 0.0931
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 45.36853 2
##      leaf.node control.mean control.size control.se depth
## 1          2         -5.62         176.00         2.00    1
## 2          3          5.14         124.00         2.53    1
## 3          4          8.89          78.00         3.09    2
## 4          5         -7.27          80.00         2.89    2
## 5          6          4.88          63.00         3.53    2
## 6          7         -9.76          79.00         2.88    2
##      leaf.node control.mean control.size control.se depth
## 3          4          8.89          78.00         3.09    2
## GRF subgroup found

```

```

## All splits
## [1] "noise1 <= -0.07" "noise5 <= 0.01" "noise4 <= -0.06"
## Terminating node at max.diff (sg.harm.id)
## [1] "noise5 <= 0.00807090609630402"
## # of continuous/categorical characteristics 6 6
## Continuous characteristics: size noise1 noise2 noise3 noise4 noise5
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## CV lambda = 0.03128063
## 12 x 1 sparse Matrix of class "dgCMatrix"
##              s0
## z1      0.114944573
## z2      .
## z3      0.553874965
## z4      0.974097466
## z5     -0.737588173
## size    .
## grade3   .
## noise1  0.082835678
## noise2  0.017275498
## noise3   .
## noise4   .
## noise5 -0.001910096
## Cox-LASSO selected: z1 z3 z4 z5 noise1 noise2 noise5
## Cox-LASSO not selected: z2 size grade3 noise3 noise4
## Default cuts included from Lasso:
## Categorical after Lasso: z1 z3 z4 z5
## Factors per GRF: noise1 <= -0.07 noise5 <= 0.01 noise4 <= -0.06
## Initial GRF cuts included noise1 <= -0.07 noise5 <= 0.01 noise4 <= -0.06
## Factors included per GRF (not in lasso) noise1 <= -0.07 noise5 <= 0.01 noise4 <= -0.06
## # of candidate subgroup factors= 28
## [1] "noise1 <= -0.07" "noise5 <= 0.01" "noise4 <= -0.06" "size <= 29.7"
## [5] "size <= 27"      "size <= 21"      "size <= 35"      "noise1 <= -0.1"
## [9] "noise1 <= -0.8"  "noise1 <= 0.7"   "noise2 <= -0.1"  "noise2 <= -0.8"
## [13] "noise2 <= 0.5"   "noise3 <= 0.1"   "noise3 <= 0"     "noise3 <= -0.6"
## [17] "noise3 <= 0.8"   "noise4 <= 0.1"   "noise4 <= 0"     "noise4 <= -0.6"
## [21] "noise4 <= 0.8"   "noise5 <= 0"     "noise5 <= -0.7"  "noise5 <= 0.7"
## [25] "z1"              "z3"              "z4"              "z5"
## Number of factors evaluated= 28
## Confounders per grf screening q26 q2 q27 q22 q3 q25 q28 q1 q11 q24 q23 q18 q8 q15 q14 q4 q5 q13 q19
##          Factors Labels VI(grf)
## 26          z3      q26 0.2530
## 2  noise5 <= 0.01      q2 0.1186
## 27          z4      q27 0.0926
## 22  noise5 <= 0      q22 0.0578
## 3  noise4 <= -0.06    q3 0.0413
## 25          z1      q25 0.0369
## 28          z5      q28 0.0337
## 1  noise1 <= -0.07    q1 0.0288
## 11 noise2 <= -0.1     q11 0.0241
## 24  noise5 <= 0.7     q24 0.0232
## 23 noise5 <= -0.7     q23 0.0222
## 18  noise4 <= 0.1     q18 0.0220
## 8   noise1 <= -0.1     q8 0.0219
## 15  noise3 <= 0       q15 0.0212
## 14  noise3 <= 0.1     q14 0.0203

```

```

## 4      size <= 29.7      q4  0.0201
## 5      size <= 27      q5  0.0188
## 13     noise2 <= 0.5    q13 0.0181
## 19     noise4 <= 0      q19 0.0172
## 17     noise3 <= 0.8    q17 0.0161
## 12     noise2 <= -0.8   q12 0.0155
## 16     noise3 <= -0.6   q16 0.0154
## 9      noise1 <= -0.8   q9  0.0137
## 21     noise4 <= 0.8    q21 0.0114
## 6      size <= 21      q6  0.0112
## 20     noise4 <= -0.6   q20 0.0099
## 10     noise1 <= 0.7    q10 0.0078
## 7      size <= 35      q7  0.0072
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 1596
## Approximately 5% of max_count met: minutes 0.003533333
## Approximately 10% of max_count met: minutes 0.006683333
## Approximately 20% of max_count met: minutes 0.01345
## Approximately 33% of max_count met: minutes 0.02121667
## Approximately 50% of max_count met: minutes 0.02983333
## Approximately 75% of max_count met: minutes 0.0407
## Approximately 90% of max_count met: minutes 0.04628333
## # of subgroups evaluated based on (up to) maxk-factor combinations 1596
## % of all-possible combinations (<= maxk) 100
## k.max= 2
## Events criteria for control,exp= 10 10
## # of subgroups with events less than criteria: control, experimental 261 285
## # of subgroups with sample size less than criteria 603
## # of subgroups meeting all criteria = 945
## # of subgroups fitted (Cox model estimable) = 945
## *Subgroup Searching Minutes=* 0.04951667
## Number of subgroups meeting HR threshold 140
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) = 140
## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##      n  E d1  HR L(HR) q26.0 q26.1 q2.0 q2.1 q27.0 q27.1 q22.0 q22.1 q3.0 q3.1
## 1  70 45 23 3.04 1.62    0    1    0    0    0    0    0    0    0    0
## 2  70 45 23 3.04 1.62    0    1    0    0    0    0    0    0    0    0
## 3  64 44 24 2.85 1.53    0    1    0    0    0    0    0    0    0    0
## 4  66 44 23 2.44 1.33    0    1    0    0    0    0    0    0    0    0
## 5  94 63 32 2.40 1.44    0    1    0    0    0    0    0    0    0    0
## 6  90 61 35 2.32 1.39    0    1    0    0    0    0    0    0    0    0
## 7  93 63 34 2.28 1.36    0    1    0    0    0    0    0    0    0    0
## 8  69 50 31 2.20 1.23    0    1    0    1    0    0    0    0    0    0
## 9  68 49 31 2.18 1.20    0    1    0    0    0    0    0    1    0    0
## 10 89 72 41 2.15 1.32    0    1    0    0    0    0    0    0    0    0
## Consistency 1
## # of splits= 400
## Model, % Consistency Met= {z3} {noise1 <= -0.07} 1
## SG focus= hr
## Subgroup Consistency Minutes= 0.03228333
## Subgroup found (FS)
## Minutes forestsearch overall= 0.08936667

t.now <- proc.time()[3]
t.min <- (t.now - t.start)/60

```

```

print(table(res$analysis))

##
##      FS1      FS1g      GRF  GRF.60  VT(24)  VT(36)  VT#(24)  VT#(36)
##  20000  20000  20000  20000  20000  20000  20000  20000

check <- c(c(table(res$analysis)) - Nsims)
if (all(check != 0)) stop("All analyses not complete")

dgm_alt <- dgm

outres <- out.results(res = res, dgm = dgm, output.file = output.file, t.min = t.min,
  out_analysis = "FS1")

## [1] "results/oc_sims=20000_m4c-Noise=5_N=300_alt_ktreat=1.5_hrH=2_v0-4cuts.Rdata"
##      sim sizeH_true propH_true sizeHc_true propHc_true any.H size.H size.Hc
##      <int>      <num>      <num>      <int>      <num> <num> <num> <int>
## 1:      1          80  0.2666667          220  0.7333333      1     67    233
## 2:      1          80  0.2666667          220  0.7333333      1     67    233
## 3:      1          80  0.2666667          220  0.7333333      1    101    199
## 4:      1          80  0.2666667          220  0.7333333      1     82    218
## 5:      1          80  0.2666667          220  0.7333333      1     80    220
## 6:      1          80  0.2666667          220  0.7333333      1     80    220
##      ppv      npv specificity sensitivity found.1 found.2 found.both found.al3
##      <num>      <num>      <num>      <num>      <num> <num>      <num>      <num>
## 1:  0.20  0.7681818  0.7253219  0.2388060      0      0      0      0
## 2:  0.20  0.7681818  0.7253219  0.2388060      0      0      0      0
## 3:  0.40  0.6863636  0.7587940  0.3168317      NA     NA     NA     NA
## 4:  0.35  0.7545455  0.7614679  0.3414634      NA     NA     NA     NA
## 5:  1.00  1.0000000  1.0000000  1.0000000      0      0      0      0
## 6:  1.00  1.0000000  1.0000000  1.0000000      0      0      0      0
##      hr.H.true hr.Hc.true hr.H.hat hr.Hc.hat      b1.H      b2.H      b1.Hc
##      <num>      <num>      <num>      <num>      <num>      <num>      <num>
## 1:  1.559409  0.6836811  1.891602  0.6831815  0.33219378 -0.1083970 -0.0004996335
## 2:  1.559409  0.6836811  1.891602  0.6831815  0.33219378 -0.1083970 -0.0004996335
## 3:  1.559409  0.6836811  1.599971  0.6172136  0.04056242 -0.4000284 -0.0664675443
## 4:  1.559409  0.6836811  1.405952  0.7059411 -0.15345651 -0.5940473  0.0222599774
## 5:  1.559409  0.6836811  1.559409  0.6836811  0.00000000 -0.4405908  0.0000000000
## 6:  1.559409  0.6836811  1.559409  0.6836811  0.00000000 -0.4405908  0.0000000000
##      b2.Hc      p.cens analysis      taumax      hr.itt      l.itt      u.itt
##      <num>      <num>      <char>      <num>      <num>      <num>      <num>
## 1:  0.12555050  0.4033333      FS1  81.76877  0.8477298  0.6315583  1.137893
## 2:  0.12555050  0.4033333      FS1g 49.06126  0.8477298  0.6315583  1.137893
## 3:  0.05958259  0.4033333      GRF  81.76877  0.8477298  0.6315583  1.137893
## 4:  0.14831011  0.4033333      GRF.60 49.06126  0.8477298  0.6315583  1.137893
## 5:  0.12605013  0.4033333      VT(24) 81.76877  0.8477298  0.6315583  1.137893
## 6:  0.12605013  0.4033333      VT#(24) 81.76877  0.8477298  0.6315583  1.137893
##      hr.adj.itt l.adj.itt u.adj.itt l.H.true u.H.true l.Hc.true u.Hc.true
##      <num>      <num>      <num>      <num>      <num>      <num>      <num>
## 1:  0.8490589  0.6265376  1.150611  0.9351283  2.600451  0.4758943  0.9821926
## 2:  0.8490589  0.6265376  1.150611  0.9351283  2.600451  0.4758943  0.9821926
## 3:  0.8490589  0.6265376  1.150611  0.9351283  2.600451  0.4758943  0.9821926
## 4:  0.8490589  0.6265376  1.150611  0.9351283  2.600451  0.4758943  0.9821926
## 5:  0.8490589  0.6265376  1.150611  0.9351283  2.600451  0.4758943  0.9821926

```

```

## 6: 0.8490589 0.6265376 1.150611 0.9351283 2.600451 0.4758943 0.9821926
##      l.H.hat u.H.hat l.Hc.hat u.Hc.hat
##      <num>   <num>   <num>   <num>
## 1: 1.0260505 3.487313 0.4870878 0.9582194
## 2: 1.0260505 3.487313 0.4870878 0.9582194
## 3: 0.9467982 2.703751 0.4287005 0.8886217
## 4: 0.7789088 2.537782 0.5015604 0.9936048
## 5: 0.9351283 2.600451 0.4758943 0.9821926
## 6: 0.9351283 2.600451 0.4758943 0.9821926
## Subgroup HRs: H, H^c, Causal= 1.999999 0.557631 0.7363833
## Simulations= 20000
## Avg censoring= 0.4375567
## Min,Max,Avg tau.max= 58.28239 83.94548 78.62153
## P(H) approximation at causal(H), n(sg)=60, approx= 1.999999 60 0.8326675
## P(H) approximation at causal(H), Avg(n(sg)), approx= 1.999999 90 0.9052625
## P(H) approximation at plim(H), Avg(n(sg)), approx= 2.246475 90 0.9522671
## Minutes,hours 123.6496 2.060826
##
##      FSl      FSlg      GRF      GRF.60      VT(24) VT#(24)      VT(36) VT#(36)
## any.H      0.970      0.960      0.960      0.870      0.510      0.560      0.530      0.650
## sensH      0.680      0.660      0.730      0.620      0.350      0.420      0.380      0.520
## sensHc     0.930      0.930      0.880      0.870      0.950      0.960      0.950      0.960
## ppH        0.780      0.750      0.700      0.590      0.390      0.450      0.400      0.550
## ppHc       0.880      0.870      0.890      0.860      0.790      0.810      0.800      0.840
## Avg(#H)    78.000      77.000      95.000      96.000      83.000      83.000      85.000      85.000
## minH       61.000      61.000      60.000      60.000      60.000      60.000      60.000      60.000
## maxH      143.000     143.000     229.000     230.000     172.000     176.000     180.000     191.000
## Avg(#Hc)   225.000     226.000     209.000     216.000     258.000     254.000     255.000     245.000
## minHc     157.000     157.000      71.000      70.000     128.000     124.000     120.000     109.000
## maxHc     300.000     300.000     300.000     300.000     300.000     300.000     300.000     300.000
## hat(H*)    2.278      2.285      2.277      2.319      2.451      2.450      2.468      2.439
## hat(hat[H]) 2.588      2.571      2.213      2.071      2.191      2.286      2.261      2.386
## hat(Hc*)   0.555      0.555      0.555      0.555      0.559      0.555      0.558      0.555
## hat(hat[Hc]) 0.592      0.597      0.550      0.574      0.637      0.618      0.622      0.595
## hat(H*)all 2.246      2.246      2.246      2.246      2.246      2.246      2.246      2.246
## hat(Hc*)all 0.553      0.553      0.553      0.553      0.553      0.553      0.553      0.553
## hat(ITT)all 0.849      0.849      0.849      0.849      0.849      0.849      0.849      0.849
## hat(ITTadj)all 0.896      0.896      0.896      0.896      0.896      0.896      0.896      0.896

missC <- tab_tests(res = res)

pA <- as.character(round(outres$pAnyH.approx2, 4))

tabsim_missC <- get_tabsim(missC = missC, pA = pA, est_names = est_names, stat_names = stat_names,
  mod.harm = mod.harm, Nsims = Nsims)

t.done <- proc.time()[3]
t.min <- (t.done - t.start.all)/60
cat("Minutes and hours to finish", c(t.min, t.min/60), "\n")

## Minutes and hours to finish 217.5104 3.625174

cat("Minutes and hours per 10,000 to finish", (10000/Nsims) * c(t.min, t.min/60),
  "\n")

## Minutes and hours per 10,000 to finish 108.7552 1.812587

```

Table 2: Average classification rates: $avg|\hat{H}|$, $min|\hat{H}|$, and $max|\hat{H}|$, denote the average, minimum, and maximum of the number of subjects in the estimated subgroup \hat{H} (analogously for \hat{H}^c). Note that under the null $sens(\hat{H})$ is undefined and $ppv(\hat{H}) = 0$.

	FS_g	FS_{lg}	GRF	GRF_{60}	$VT(24)$	$VT^\#(24)$	$VT(36)$	$VT^\#(36)$
Finding H								
any(H)	0.97	0.96	0.96	0.87	0.51	0.56	0.53	0.65
$sens(\hat{H})$	0.68	0.66	0.73	0.62	0.35	0.42	0.38	0.52
$sens(\hat{H}^c)$	0.93	0.93	0.88	0.87	0.95	0.96	0.95	0.96
$ppv(\hat{H})$	0.78	0.75	0.7	0.59	0.39	0.45	0.4	0.55
$ppv(\hat{H}^c)$	0.88	0.87	0.89	0.86	0.79	0.81	0.8	0.84
Size of H and H-complement								
$avg \hat{H} $	78	77	95	96	83	83	85	85
$min \hat{H} $	61	61	60	60	60	60	60	60
$max \hat{H} $	143	143	229	230	172	176	180	191
$avg \hat{H}^c $	225	226	209	216	258	254	255	245
$min \hat{H}^c $	157	157	71	70	128	124	120	109
$max \hat{H}^c $	300	300	300	300	300	300	300	300

Note: Number of simulations= 20000 .

Note: Probability approximation= 0.9053 .

```
# cat('Machine=',c(Sys.info()[[4]]),'\n') cat('Number of
# cores=',c(detectCores(logical = FALSE)),'\n')
require(benchmarkme)
my_system <- get_cpu()
my_ram <- get_ram()
cat("Running on system:", c(my_system$model_name), "\n")

## Running on system: AMD Ryzen Threadripper PRO 5995WX 64-Cores

cat("with number of cores and cpu/GB=", c(my_system$no_of_cores, round(c(my_ram)/10^9,
0)), "\n")

## with number of cores and cpu/GB= 128 270
```