```r
N <- 700
Nsims <- 20*1000

maxFollow<-84
cens.type<-"weibull"
########################
# Forest search criteria
########################
hr.threshold<-1.25    # Initital candidates
hr.consistency<-1.0   # 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<-3.0
m1.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<-0.0

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

# GRF criteria
dmin.grf<-12.0 # For GRF delta
# Note: For CRT this represents dmin.grf/2 RMS for control (-dmin.grf/2 for treatment)
frac.tau <- 0.60

# For forestsearch algorithm use same as GRF
frac.tau_fs <- 0.60
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}
```

```r
outcome.name<-c("y.sim")
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 <- 0.0

mindex <- "m4a"
file.index<-"v0-4cuts"

z1_frac <- 0.25

if(mindex=="m4a"){
k.z3 <- 1.0
k.treat <- 0.9
pH_super <- 0.125 # non-NULL re-defines z1_frac
}

if(mindex=="m4aB"){
k.z3 <- 1.0
k.treat <- 0.9
pH_super <- 0.20 # non-NULL re-defines z1_frac
}

if(mindex=="m4b"){
k.z3 <- 1.0
k.treat <- 1.25
pH_super <- 0.30 # non-NULL re-defines z1_frac
}

if(mindex=="m4c"){
k.z3 <- 1.0
k.treat <- 1.5
pH_super <- 0.30 # non-NULL re-defines z1_frac
}

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

if(is.null(pH_super)){
```

```r
#pH_check<-with(gbsg,mean(pgr<=quantile(pgr,c(z3_frac),1,0) & 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=0.0001,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 0.122449
## Underlying pH_super 0.122449

# 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.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_tora
```
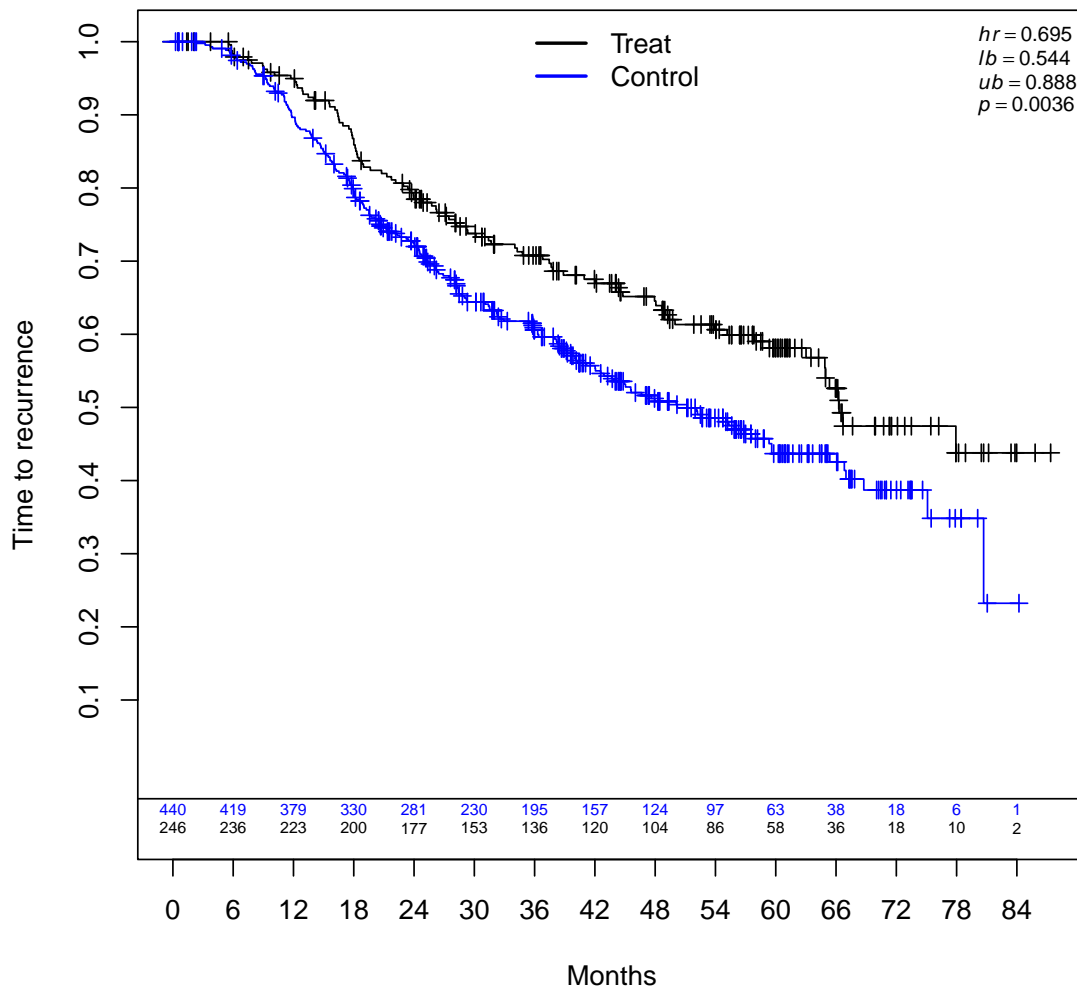
```
## Super-population empirical harm and non-harm hazard ratios= NA 0.701027
## Causal HR (empirical ITT)= 0.701027

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= 49.01796 2
##    leaf.node control.mean control.size control.se depth
## 1          2         1.58        77.00       2.99     1
## 2          3        -4.47       623.00       1.15     1
## 11         4        -5.22       179.00       2.04     2
## 21         5         1.69       171.00       1.89     2
## 4          7        -6.87       324.00       1.69     2
##    leaf.node control.mean control.size control.se depth
## 21         5         1.69       171.00       1.89     2
## GRF subgroup NOT found
## NO GRF cuts meeting delta(RMST): dmin.grf= 12
## # of continuous/categorical characteristics 1 6
## Continuous characteristics: size
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## Default cuts included (1st 20)
## Categorical: z1 z2 z3 z4 z5 grade3
## # of candidate subgroup factors= 10
##  [1] "size <= 29.4" "size <= 25"   "size <= 20"   "size <= 35"   "z1"
##  [6] "z2"           "z3"           "z4"           "z5"           "grade3"
## Number of factors evaluated= 10
## Confounders per grf screening q6 q8 q4 q9 q7 q10 q5 q3 q1 q2
##         Factors Labels VI(grf)
## 6            z2     q6  0.1982
## 8            z4     q8  0.1410
## 4     size <= 35    q4  0.1131
## 9            z5     q9  0.0978
## 7            z3     q7  0.0954
## 10       grade3    q10  0.0824
## 5            z1     q5  0.0805
## 3     size <= 20    q3  0.0759
## 1   size <= 29.4    q1  0.0582
## 2     size <= 25    q2  0.0577
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 210
## Approximately 5% of max_count met: minutes 0.0003166667
## Approximately 10% of max_count met: minutes 5e-04
## Approximately 20% of max_count met: minutes 0.0008166667
## Approximately 33% of max_count met: minutes 0.0014
## Approximately 50% of max_count met: minutes 0.001883333
## Approximately 75% of max_count met: minutes 0.002933333
## Approximately 90% of max_count met: minutes 0.003483333
## # of subgroups evaluated based on (up to) maxk-factor combinations 210
## % 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 21 20
## # of subgroups with sample size less than criteria 26
## # of subgroups meeting all criteria = 177
## # of subgroups fitted (Cox model estimable) = 177
## *Subgroup Searching Minutes=* 0.003733333
## 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= 49.01796 2
##    leaf.node control.mean control.size control.se depth
## 1           2         1.58        77.00       2.99     1
## 2           3        -4.47       623.00       1.15     1
## 11          4        -5.22       179.00       2.04     2
## 21          5         1.69       171.00       1.89     2
## 4           7        -6.87       324.00       1.69     2
##    leaf.node control.mean control.size control.se depth
## 21          5         1.69       171.00       1.89     2
## GRF subgroup NOT found
## NO GRF cuts meeting delta(RMST): dmin.grf= 12
## # of continuous/categorical characteristics 1 6
## Continuous characteristics: size
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## CV lambda = 0.02832378
## 7 x 1 sparse Matrix of class "dgCMatrix"
##                 s0
## z1      0.06829145
## z2       .
## z3       .
## z4      0.48686291
## z5     -0.73974508
## size     .
## grade3   .
## Cox-LASSO selected: z1 z4 z5
## Cox-LASSO not selected: z2 z3 size grade3
## Default cuts included from Lasso:
## Categorical after Lasso: z1 z4 z5
## # of candidate subgroup factors= 7
## [1] "size <= 29.4" "size <= 25"   "size <= 20"   "size <= 35"   "z1"
## [6] "z4"           "z5"
## Number of factors evaluated= 7
## Confounders per grf screening q6 q4 q7 q5 q3 q1 q2
##        Factors Labels VI(grf)
## 6           z4     q6  0.2141
## 4   size <= 35     q4  0.1769
## 7           z5     q7  0.1596
## 5           z1     q5  0.1365
## 3   size <= 20     q3  0.1181
## 1 size <= 29.4     q1  0.0991
## 2   size <= 25     q2  0.0956
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 105
## Approximately 5% of max_count met: minutes 1e-04
## Approximately 10% of max_count met: minutes 2e-04
## Approximately 20% of max_count met: minutes 0.0005166667
## Approximately 33% of max_count met: minutes 0.0007666667
## Approximately 50% of max_count met: minutes 0.001233333
## Approximately 75% of max_count met: minutes 0.002116667
## Approximately 90% of max_count met: minutes 0.002416667
## # of subgroups evaluated based on (up to) maxk-factor combinations 105
## % 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 15 15
```

```
## # of subgroups with sample size less than criteria 18
## # of subgroups meeting all criteria = 81
## # of subgroups fitted (Cox model estimable) = 81
## *Subgroup Searching Minutes=* 0.002483333
## 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= 48.41962 2
##     leaf.node control.mean control.size control.se depth
## 1           2        -5.05       689.00       1.07     1
## 11          4        -5.11       573.00       1.17     2
## 3           6        -8.44        83.00       3.56     2
##   leaf.node control.mean control.size control.se depth
## 1         2        -5.05       689.00       1.07     1
## GRF subgroup NOT found
## NO GRF cuts meeting delta(RMST): dmin.grf= 12
## # of continuous/categorical characteristics 1 6
## Continuous characteristics: size
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## Default cuts included (1st 20)
## Categorical: z1 z2 z3 z4 z5 grade3
## # of candidate subgroup factors= 10
##  [1] "size <= 28.5" "size <= 25"   "size <= 20"   "size <= 35"   "z1"
##  [6] "z2"           "z3"           "z4"           "z5"           "grade3"
## Number of factors evaluated= 10
## Confounders per grf screening q9 q5 q7 q8 q3 q2 q6 q10 q1 q4
##          Factors Labels VI(grf)
## 9             z5     q9  0.2292
## 5             z1     q5  0.1849
## 7             z3     q7  0.0904
## 8             z4     q8  0.0818
## 3     size <= 20     q3  0.0766
## 2     size <= 25     q2  0.0749
## 6             z2     q6  0.0710
## 10        grade3    q10  0.0693
## 1   size <= 28.5     q1  0.0619
## 4     size <= 35     q4  0.0599
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 210
## Approximately 5% of max_count met: minutes 0.0003166667
## Approximately 10% of max_count met: minutes 0.00065
## Approximately 20% of max_count met: minutes 0.001116667
## Approximately 33% of max_count met: minutes 0.002216667
## Approximately 50% of max_count met: minutes 0.003133333
## Approximately 75% of max_count met: minutes 0.004866667
## Approximately 90% of max_count met: minutes 0.006083333
## # of subgroups evaluated based on (up to) maxk-factor combinations 210
## % 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 18 21
## # of subgroups with sample size less than criteria 26
## # of subgroups meeting all criteria = 177
## # of subgroups fitted (Cox model estimable) = 177
## *Subgroup Searching Minutes=* 0.00645
## Number of subgroups meeting HR threshold 1
```

```
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) =  1
## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##     n  E d1  HR L(HR) q9.0
## 1 159 62 35 1.4  0.84    0
## Consistency 0.805
## Subgroup Consistency Minutes= 0.02055
## NO subgroup found (FS)
## Minutes forestsearch overall= 0.05845
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 48.41962 2
##    leaf.node control.mean control.size control.se depth
## 1          2        -5.05       689.00       1.07     1
## 11         4        -5.11       573.00       1.17     2
## 3          6        -8.44        83.00       3.56     2
##   leaf.node control.mean control.size control.se depth
## 1         2        -5.05       689.00       1.07     1
## GRF subgroup NOT found
## NO GRF cuts meeting delta(RMST): dmin.grf= 12
## # of continuous/categorical characteristics 1 6
## Continuous characteristics: size
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## CV lambda = 0.0294912
## 7 x 1 sparse Matrix of class "dgCMatrix"
##                 s0
## z1      0.07600026
## z2       .
## z3       .
## z4      0.38336979
## z5     -0.84959529
## size    .
## grade3  .
## Cox-LASSO selected: z1 z4 z5
## Cox-LASSO not selected: z2 z3 size grade3
## Default cuts included from Lasso:
## Categorical after Lasso: z1 z4 z5
## # of candidate subgroup factors= 7
## [1] "size <= 28.5" "size <= 25"   "size <= 20"   "size <= 35"   "z1"
## [6] "z4"           "z5"
## Number of factors evaluated= 7
## Confounders per grf screening q7 q5 q6 q2 q3 q4 q1
##        Factors Labels VI(grf)
## 7            z5     q7  0.2751
## 5            z1     q5  0.2106
## 6            z4     q6  0.1208
## 2    size <= 25     q2  0.1118
## 3    size <= 20     q3  0.1075
## 4    size <= 35     q4  0.0914
## 1 size <= 28.5     q1  0.0828
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 105
## Approximately 5% of max_count met: minutes 0.0001166667
## Approximately 10% of max_count met: minutes 0.0002666667
## Approximately 20% of max_count met: minutes 0.0005166667
## Approximately 33% of max_count met: minutes 0.0009833333
## Approximately 50% of max_count met: minutes 0.00135
```

```
## Approximately 75% of max_count met: minutes 0.00185
## Approximately 90% of max_count met: minutes 0.002216667
## # of subgroups evaluated based on (up to) maxk-factor combinations 105
## % 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 14 16
## # of subgroups with sample size less than criteria 18
## # of subgroups meeting all criteria = 81
## # of subgroups fitted (Cox model estimable) = 81
## *Subgroup Searching Minutes=* 0.002316667
## 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= 48.09494 2
##   leaf.node control.mean control.size control.se depth
## 1         2        -3.20        690.00       1.05    1
## 2         4        -2.84        296.00       1.54    2
## 3         5         2.22         78.00       3.36    2
## 4         6        -4.87        316.00       1.58    2
##   leaf.node control.mean control.size control.se depth
## 3         5         2.22         78.00       3.36    2
## GRF subgroup NOT found
## NO GRF cuts meeting delta(RMST): dmin.grf= 12
## # of continuous/categorical characteristics 1 6
## Continuous characteristics: size
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## Default cuts included (1st 20)
## Categorical: z1 z2 z3 z4 z5 grade3
## # of candidate subgroup factors= 10
##  [1] "size <= 29.8" "size <= 26.5" "size <= 21"   "size <= 35"   "z1"
##  [6] "z2"           "z3"           "z4"           "z5"           "grade3"
## Number of factors evaluated= 10
## Confounders per grf screening q8 q9 q7 q4 q1 q10 q6 q3 q5 q2
##        Factors Labels VI(grf)
## 8           z4     q8  0.1267
## 9           z5     q9  0.1181
## 7           z3     q7  0.1042
## 4    size <= 35     q4  0.0993
## 1  size <= 29.8     q1  0.0981
## 10      grade3    q10  0.0965
## 6           z2     q6  0.0963
## 3    size <= 21     q3  0.0962
## 5           z1     q5  0.0917
## 2  size <= 26.5     q2  0.0729
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 210
## Approximately 5% of max_count met: minutes 2e-04
## Approximately 10% of max_count met: minutes 0.0004333333
## Approximately 20% of max_count met: minutes 0.0009166667
## Approximately 33% of max_count met: minutes 0.00155
## Approximately 50% of max_count met: minutes 0.002533333
## Approximately 75% of max_count met: minutes 0.00365
## Approximately 90% of max_count met: minutes 0.0046
## # of subgroups evaluated based on (up to) maxk-factor combinations 210
## % 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 18 24
## # of subgroups with sample size less than criteria 25
## # of subgroups meeting all criteria = 176
## # of subgroups fitted (Cox model estimable) = 176
## *Subgroup Searching Minutes=* 0.005233333
## 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= 48.09494 2
##   leaf.node control.mean control.size control.se depth
## 1         2        -3.20       690.00       1.05     1
## 2         4        -2.84       296.00       1.54     2
## 3         5         2.22        78.00       3.36     2
## 4         6        -4.87       316.00       1.58     2
##   leaf.node control.mean control.size control.se depth
## 3         5         2.22        78.00       3.36     2
## GRF subgroup NOT found
## NO GRF cuts meeting delta(RMST): dmin.grf= 12
## # of continuous/categorical characteristics 1 6
## Continuous characteristics: size
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## CV lambda = 0.00234943
## 7 x 1 sparse Matrix of class "dgCMatrix"
##                  s0
## z1       0.22103202
## z2      -0.56112951
## z3       0.41478275
## z4       0.71312294
## z5      -0.93657843
## size    -0.00321610
## grade3 -0.06430816
## Cox-LASSO selected: z1 z2 z3 z4 z5 size grade3
## Cox-LASSO not selected:
## Default cuts included from Lasso:
## Categorical after Lasso: z1 z2 z3 z4 z5 grade3
## # of candidate subgroup factors= 10
##  [1] "size <= 29.8" "size <= 26.5" "size <= 21"   "size <= 35"   "z1"
##  [6] "z2"           "z3"           "z4"           "z5"           "grade3"
## Number of factors evaluated= 10
## Confounders per grf screening q8 q9 q7 q4 q1 q10 q6 q3 q5 q2
##          Factors Labels VI(grf)
## 8             z4     q8  0.1267
## 9             z5     q9  0.1181
## 7             z3     q7  0.1042
## 4     size <= 35     q4  0.0993
## 1   size <= 29.8     q1  0.0981
## 10        grade3    q10  0.0965
## 6             z2     q6  0.0963
## 3     size <= 21     q3  0.0962
## 5             z1     q5  0.0917
## 2   size <= 26.5     q2  0.0729
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 210
## Approximately 5% of max_count met: minutes 0.0002333333
```

```
## Approximately 10% of max_count met: minutes 0.0004666667
## Approximately 20% of max_count met: minutes 0.00085
## Approximately 33% of max_count met: minutes 0.001766667
## Approximately 50% of max_count met: minutes 0.002783333
## Approximately 75% of max_count met: minutes 0.0036
## Approximately 90% of max_count met: minutes 0.004216667
## # of subgroups evaluated based on (up to) maxk-factor combinations 210
## % 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 18 24
## # of subgroups with sample size less than criteria 25
## # of subgroups meeting all criteria = 176
## # of subgroups fitted (Cox model estimable) = 176
## *Subgroup Searching Minutes=* 0.004666667
## Number of subgroups meeting HR threshold 0
## NO subgroup candidate found (FS)
```

```r
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
```

```r
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_m4a-Noise=0_N=700_null_ktreat=0.9_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         700            1     0      0     700
## ## 2:    1          0          0         700            1     0      0     700
## ## 3:    1          0          0         700            1     0      0     700
## ## 4:    1          0          0         700            1     0      0     700
## ## 5:    1          0          0         700            1     0      0     700
## ## 6:    1          0          0         700            1     0      0     700
##       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  0.6155054       NA 0.6155054     NA     NA     0 -0.08552157
## ## 2:      NA  0.6155054       NA 0.6155054     NA     NA     0 -0.08552157
## ## 3:      NA  0.6155054       NA 0.6155054     NA     NA     0 -0.08552157
## ## 4:      NA  0.6155054       NA 0.6155054     NA     NA     0 -0.08552157
```

```
## 5:        NA  0.6155054        NA 0.6155054      NA      NA     0 -0.08552157
## 6:        NA  0.6155054        NA 0.6155054      NA      NA     0 -0.08552157
##       p.cens analysis    taumax    hr.itt      l.itt    u.itt hr.adj.itt
##        <num>   <char>     <num>     <num>      <num>    <num>      <num>
## 1: 0.4642857      FSl 81.69660 0.6155054 0.5014207 0.755547  0.5906047
## 2: 0.4642857     FSlg 49.01796 0.6155054 0.5014207 0.755547  0.5906047
## 3: 0.4642857      GRF 81.69660 0.6155054 0.5014207 0.755547  0.5906047
## 4: 0.4642857   GRF.60 49.01796 0.6155054 0.5014207 0.755547  0.5906047
## 5: 0.4642857   VT(24) 81.69660 0.6155054 0.5014207 0.755547  0.5906047
## 6: 0.4642857  VT#(24) 81.69660 0.6155054 0.5014207 0.755547  0.5906047
##    l.adj.itt u.adj.itt l.H.true u.H.true l.Hc.true u.Hc.true l.H.hat u.H.hat
##        <num>     <num>   <lgcl>   <lgcl>     <num>     <num>   <num>   <num>
## 1:  0.480604 0.7257825       NA       NA 0.5014207  0.755547      NA      NA
## 2:  0.480604 0.7257825       NA       NA 0.5014207  0.755547      NA      NA
## 3:  0.480604 0.7257825       NA       NA 0.5014207  0.755547      NA      NA
## 4:  0.480604 0.7257825       NA       NA 0.5014207  0.755547      NA      NA
## 5:  0.480604 0.7257825       NA       NA 0.5014207  0.755547      NA      NA
## 6:  0.480604 0.7257825       NA       NA 0.5014207  0.755547      NA      NA
##     l.Hc.hat u.Hc.hat
##        <num>    <num>
## 1: 0.5014207 0.755547
## 2: 0.5014207 0.755547
## 3: 0.5014207 0.755547
## 4: 0.5014207 0.755547
## 5: 0.5014207 0.755547
## 6: 0.5014207 0.755547
## Subgroup HRs: H, H^c, Causal= NA 0.701027 0.701027
## Simulations= 20000
## Avg censoring= 0.4617969
## Min,Max,Avg tau.max= 71.81152 83.99787 81.70761
## P(H) approximation at causal(Hrc), n=60, approx= 0.701027 0.03396618
## P(H) approximation at plim(Hrc), n=60, approx= 0.7066595 0.03564707
## Minutes,hours 445.905 7.431749
##                  FSl    FSlg     GRF  GRF.60  VT(24) VT#(24)  VT(36) VT#(36)
## any.H          0.070   0.050   0.250   0.050   0.030   0.020   0.030   0.020
## sensH            NaN     NaN     NaN     NaN     NaN     NaN     NaN     NaN
## sensHc         0.990   0.990   0.970   0.990   1.000   1.000   1.000   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)       98.000  99.000  88.000  77.000  78.000  77.000  79.000  76.000
## minH          61.000  61.000  60.000  60.000  60.000  60.000  60.000  60.000
## maxH         287.000 287.000 328.000 199.000 168.000 160.000 199.000 124.000
## Avg(#Hc)     694.000 695.000 678.000 696.000 698.000 699.000 697.000 699.000
## minHc        413.000 413.000 372.000 501.000 532.000 540.000 501.000 576.000
## maxHc        700.000 700.000 700.000 700.000 700.000 700.000 700.000 700.000
## hat(H*)          NaN     NaN     NaN     NaN     NaN     NaN     NaN     NaN
## hat(hat[H])    1.797   1.795   1.532   1.524   1.298   1.408   1.309   1.579
## hat(Hc*)       0.780   0.781   0.739   0.736   0.738   0.744   0.732   0.745
## hat(hat[Hc])   0.691   0.690   0.670   0.676   0.693   0.691   0.686   0.686
## hat(H*)all       NaN     NaN     NaN     NaN     NaN     NaN     NaN     NaN
## hat(Hc*)all    0.707   0.707   0.707   0.707   0.707   0.707   0.707   0.707
## hat(ITT)all    0.707   0.707   0.707   0.707   0.707   0.707   0.707   0.707
## hat(ITTadj)all 0.664   0.664   0.664   0.664   0.664   0.664   0.664   0.664


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,
```

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 $ppv(\hat{H}) = 0$.
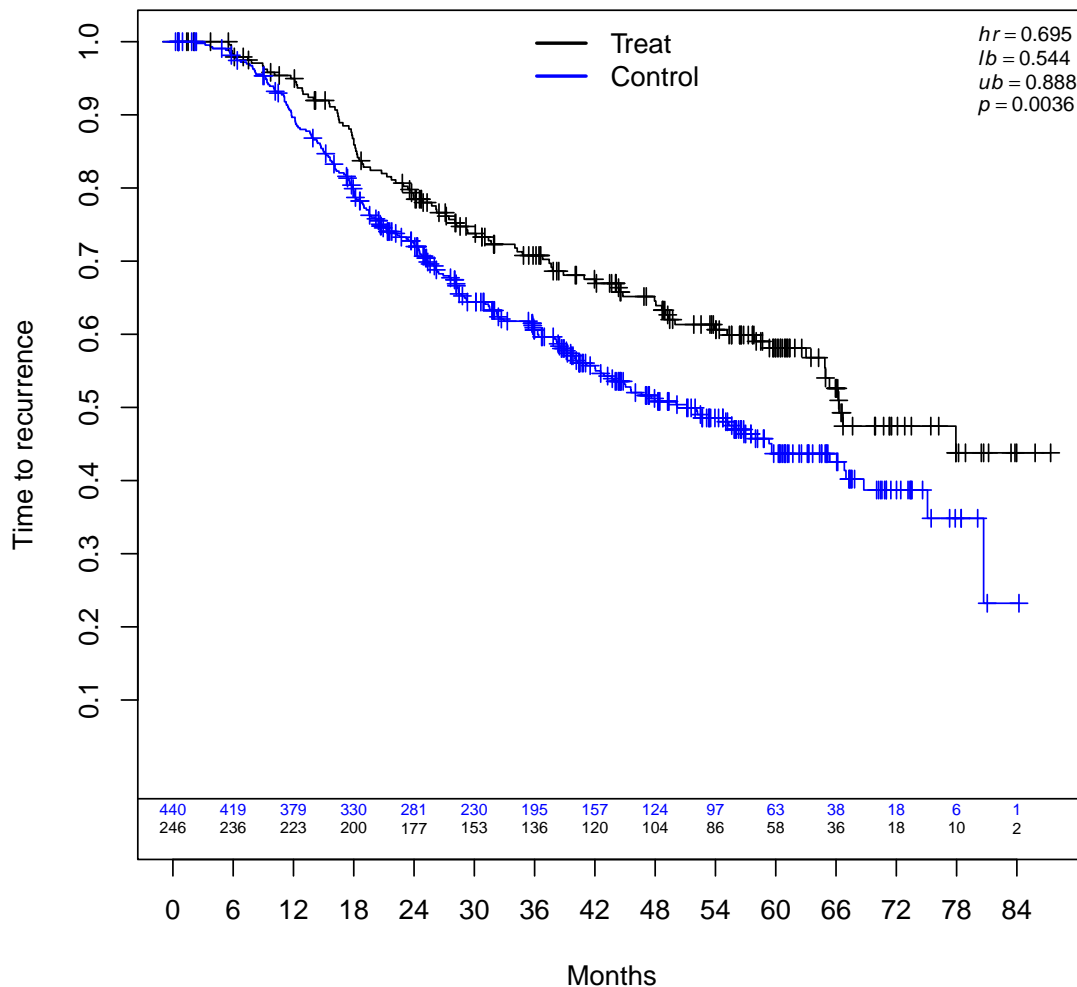
	FS_g	FS_{lg}	GRF	GRF_{60}	$VT(24)$	$VT^{\#}(24)$	$VT(36)$	$VT^{\#}(36)$
Finding H								
any(H)	0.07	0.05	0.25	0.05	0.03	0.02	0.03	0.02
$sens(\hat{H})$	.	.	.	.	.	.	.	.
$sens(\hat{H}^C)$	0.99	0.99	0.97	0.99	1	1	1	1
$ppv(\hat{H})$	0	0	0	0	0	0	0	0
$ppv(\hat{H}^C)$	1	1	1	1	1	1	1	1
Size of H and H-complement								
$avg|\hat{H}|$	98	99	88	77	78	77	79	76
$min|\hat{H}|$	61	61	60	60	60	60	60	60
$max|\hat{H}|$	287	287	328	199	168	160	199	124
$avg|\hat{H}^C|$	694	695	678	696	698	699	697	699
$min|\hat{H}^C|$	413	413	372	501	532	540	501	576
$max|\hat{H}^C|$	700	700	700	700	700	700	700	700

Note: Number of simulations= 20000 .

Note: Probability approximation= 0.0356 .

```
mod.harm <- "alt"
hrH.target <- 2.0

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_toran
```

```
## Super-population empirical harm and non-harm hazard ratios= 2.000007 0.6466405
## Causal HR (empirical ITT)= 0.7057463

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= 48.86072 2
##   leaf.node control.mean control.size control.se depth
## 1         2        -4.39       509.00       1.22     1
## 2         3         2.61       191.00       2.23     1
## 3         4        -3.89       213.00       1.97     2
## 4         5         4.31        62.00       2.96     2
## 5         6        -5.79       313.00       1.61     2
## 6         7         5.68       112.00       2.82     2
##   leaf.node control.mean control.size control.se depth
## 6         7         5.68       112.00       2.82     2
## GRF subgroup NOT found
## NO GRF cuts meeting delta(RMST): dmin.grf= 12
## # of continuous/categorical characteristics 1 6
## Continuous characteristics: size
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## Default cuts included (1st 20)
## Categorical: z1 z2 z3 z4 z5 grade3
## # of candidate subgroup factors= 10
##  [1] "size <= 29.4" "size <= 25"   "size <= 20"   "size <= 35"   "z1"
##  [6] "z2"           "z3"           "z4"           "z5"           "grade3"
## Number of factors evaluated= 10
## Confounders per grf screening q6 q7 q5 q9 q8 q4 q10 q3 q1 q2
##          Factors Labels VI(grf)
## 6             z2     q6  0.2600
## 7             z3     q7  0.2139
## 5             z1     q5  0.1753
## 9             z5     q9  0.0652
## 8             z4     q8  0.0596
## 4     size <= 35     q4  0.0561
## 10        grade3    q10  0.0485
## 3     size <= 20     q3  0.0456
## 1   size <= 29.4     q1  0.0400
## 2     size <= 25     q2  0.0358
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 210
## Approximately 5% of max_count met: minutes 0.0002166667
## Approximately 10% of max_count met: minutes 0.0004166667
## Approximately 20% of max_count met: minutes 0.0008333333
## Approximately 33% of max_count met: minutes 0.001416667
## Approximately 50% of max_count met: minutes 0.002566667
## Approximately 75% of max_count met: minutes 0.003783333
## Approximately 90% of max_count met: minutes 0.004333333
## # of subgroups evaluated based on (up to) maxk-factor combinations 210
## % 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 21 20
## # of subgroups with sample size less than criteria 26
## # of subgroups meeting all criteria = 177
## # of subgroups fitted (Cox model estimable) = 177
## *Subgroup Searching Minutes=* 0.004583333
## 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) q6.0 q6.1 q7.0 q7.1 q5.0 q5.1
## 1  95 78 44 1.74  1.11   0    0    0    1    0    1
## 2 122 95 52 1.48  0.98   0    1    0    0    0    1
## 3 100 80 41 1.47  0.94   0    0    0    0    0    1
## 4  77 55 30 1.41  0.83   0    0    0    0    0    1
## 5  90 64 32 1.31  0.80   0    0    0    0    0    1
## 6  67 39 21 1.30  0.69   0    0    0    1    0    0
## Consistency 0.9675
## # of splits= 400
## Model, % Consistency Met= {z3} {z1} 0.9675
## SG focus= hr
## Subgroup Consistency Minutes= 0.01863333
## Subgroup found (FS)
## Minutes forestsearch overall= 0.03615
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 48.86072 2
##   leaf.node control.mean control.size control.se depth
## 1         2        -4.39       509.00       1.22     1
## 2         3         2.61       191.00       2.23     1
## 3         4        -3.89       213.00       1.97     2
## 4         5         4.31        62.00       2.96     2
## 5         6        -5.79       313.00       1.61     2
## 6         7         5.68       112.00       2.82     2
##   leaf.node control.mean control.size control.se depth
## 6         7         5.68       112.00       2.82     2
## GRF subgroup NOT found
## NO GRF cuts meeting delta(RMST): dmin.grf= 12
## # of continuous/categorical characteristics 1 6
## Continuous characteristics: size
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## CV lambda = 0.01355153
## 7 x 1 sparse Matrix of class "dgCMatrix"
##              s0
## z1      0.32115232
## z2       .
## z3      0.09066173
## z4      0.48299291
## z5     -0.78083587
## size    .
## grade3  .
## Cox-LASSO selected: z1 z3 z4 z5
## Cox-LASSO not selected: z2 size grade3
## Default cuts included from Lasso:
## Categorical after Lasso: z1 z3 z4 z5
## # of candidate subgroup factors= 8
## [1] "size <= 29.4" "size <= 25"   "size <= 20"    "size <= 35"    "z1"
## [6] "z3"           "z4"            "z5"
## Number of factors evaluated= 8
## Confounders per grf screening q6 q5 q7 q8 q4 q3 q2 q1
##         Factors Labels VI(grf)
## 6            z3     q6  0.3739
## 5            z1     q5  0.2273
```

```
## 7            z4     q7  0.0830
## 8            z5     q8  0.0790
## 4   size <= 35      q4  0.0683
## 3   size <= 20      q3  0.0623
## 2   size <= 25      q2  0.0534
## 1 size <= 29.4      q1  0.0528
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 136
## Approximately 5% of max_count met: minutes 2e-04
## Approximately 10% of max_count met: minutes 0.0003833333
## Approximately 20% of max_count met: minutes 0.0006833333
## Approximately 33% of max_count met: minutes 0.0012
## Approximately 50% of max_count met: minutes 0.00215
## Approximately 75% of max_count met: minutes 0.002966667
## Approximately 90% of max_count met: minutes 0.0039
## # of subgroups evaluated based on (up to) maxk-factor combinations 136
## % 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 16 16
## # of subgroups with sample size less than criteria 19
## # of subgroups meeting all criteria = 111
## # of subgroups fitted (Cox model estimable) = 111
## *Subgroup Searching Minutes=* 0.004033333
## Number of subgroups meeting HR threshold 5
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) =  5
## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##     n  E d1   HR L(HR) q6.0 q6.1 q5.0 q5.1 q7.0
## 1   95 78 44 1.74  1.11    0    1    0    1    0
## 2 100 80 41 1.47  0.94    0    0    0    1    0
## 3  77 55 30 1.41  0.83    0    0    0    1    0
## 4  90 64 32 1.31  0.80    0    0    0    1    0
## 5  67 39 21 1.30  0.69    0    1    0    0    0
## Consistency 0.9675
## # of splits= 400
## Model, % Consistency Met= {z3} {z1} 0.9675
## SG focus= hr
## Subgroup Consistency Minutes= 0.02013333
## Subgroup found (FS)
## Minutes forestsearch overall= 0.04918333
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 49.18697 2
##   leaf.node control.mean control.size control.se depth
## 1         2        -3.68       689.00       1.11     1
## 2         2        -4.54       506.00       1.25     2
## 3         4       -10.91        90.00       3.15     2
## 4         5         7.23       104.00       3.15     2
##   leaf.node control.mean control.size control.se depth
## 4         5         7.23       104.00       3.15     2
## GRF subgroup found
## All splits
## [1] "z1 <= 0" "z3 <= 0"
## Terminating node at max.diff (sg.harm.id)
## [1] "z3 <= 0"
## # of continuous/categorical characteristics 1 6
```

```
## Continuous characteristics: size
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## Default cuts included (1st 20)
## Categorical: z1 z2 z3 z4 z5 grade3
## Factors per GRF: z1 <= 0 z3 <= 0
## Initial GRF cuts included z1 <= 0 z3 <= 0
## # of candidate subgroup factors= 10
##   [1] "size <= 28.5" "size <= 25"   "size <= 20"   "size <= 35"   "z1"
##   [6] "z2"           "z3"           "z4"           "z5"           "grade3"
## Number of factors evaluated= 10
## Confounders per grf screening q7 q9 q8 q5 q6 q10 q3 q2 q4 q1
##          Factors Labels VI(grf)
## 7              z3     q7  0.2509
## 9              z5     q9  0.1665
## 8              z4     q8  0.1259
## 5              z1     q5  0.1021
## 6              z2     q6  0.0986
## 10         grade3    q10  0.0570
## 3     size <= 20     q3  0.0546
## 2     size <= 25     q2  0.0503
## 4     size <= 35     q4  0.0501
## 1  size <= 28.5     q1  0.0441
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 210
## Approximately 5% of max_count met: minutes 3e-04
## Approximately 10% of max_count met: minutes 0.0005833333
## Approximately 20% of max_count met: minutes 0.0015
## Approximately 33% of max_count met: minutes 0.002866667
## Approximately 50% of max_count met: minutes 0.004233333
## Approximately 75% of max_count met: minutes 0.005766667
## Approximately 90% of max_count met: minutes 0.006783333
## # of subgroups evaluated based on (up to) maxk-factor combinations 210
## % 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 18 21
## # of subgroups with sample size less than criteria 26
## # of subgroups meeting all criteria = 177
## # of subgroups fitted (Cox model estimable) = 177
## *Subgroup Searching Minutes=* 0.00725
## Number of subgroups meeting HR threshold 8
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) =  8
## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##      n   E d1   HR L(HR) q7.0 q7.1 q9.0 q9.1 q8.0 q8.1 q5.0 q5.1
## 1 159  66 40 1.75  1.07    0    1    0    1    0    0    0    0
## 2 104  83 47 1.65  1.06    0    1    0    0    0    0    0    1
## 3 139  80 50 1.45  0.92    0    1    0    0    0    0    0    0
## 4  76  42 26 1.41  0.75    0    1    0    0    0    0    0    0
## 5 231 132 78 1.38  0.97    0    1    0    0    0    0    0    0
## 6 166  97 59 1.35  0.90    0    1    0    0    0    0    0    0
## 7 141 101 60 1.29  0.87    0    1    0    0    0    1    0    0
## 8 195  80 44 1.28  0.82    0    0    0    1    0    0    0    0
## Consistency 0.98
## # of splits= 400
## Model, % Consistency Met= {z3} {z5} 0.98
```

```
## SG focus= hr
## Subgroup Consistency Minutes= 0.01793333
## Subgroup found (FS)
## Minutes forestsearch overall= 0.05941667
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 49.18697 2
##   leaf.node control.mean control.size control.se depth
## 1          2        -3.68       689.00       1.11    1
## 2          2        -4.54       506.00       1.25    2
## 3          4       -10.91        90.00       3.15    2
## 4          5         7.23       104.00       3.15    2
##   leaf.node control.mean control.size control.se depth
## 4          5         7.23       104.00       3.15    2
## GRF subgroup found
## All splits
## [1] "z1 <= 0" "z3 <= 0"
## Terminating node at max.diff (sg.harm.id)
## [1] "z3 <= 0"
## # of continuous/categorical characteristics 1 6
## Continuous characteristics: size
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## CV lambda = 0.03027528
## 7 x 1 sparse Matrix of class "dgCMatrix"
##                 s0
## z1      0.3191255
## z2          .
## z3          .
## z4      0.3696701
## z5     -0.8302139
## size        .
## grade3      .
## Cox-LASSO selected: z1 z4 z5
## Cox-LASSO not selected: z2 z3 size grade3
## Default cuts included from Lasso:
## Categorical after Lasso: z1 z4 z5
## Factors per GRF: z1 <= 0 z3 <= 0
## Initial GRF cuts included z1 <= 0 z3 <= 0
## Factors included per GRF (not in lasso) z3 <= 0
## # of candidate subgroup factors= 8
## [1] "size <= 28.5" "size <= 25"   "size <= 20"   "size <= 35"   "z1"
## [6] "z4"           "z5"           "z3 <= 0"
## Number of factors evaluated= 8
## Confounders per grf screening q8 q7 q6 q5 q3 q4 q2 q1
##        Factors Labels VI(grf)
## 8      z3 <= 0     q8  0.3130
## 7           z5     q7  0.1799
## 6           z4     q6  0.1495
## 5           z1     q5  0.1057
## 3    size <= 20     q3  0.0690
## 4    size <= 35     q4  0.0681
## 2    size <= 25     q2  0.0622
## 1 size <= 28.5      q1  0.0526
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 136
## Approximately 5% of max_count met: minutes 0.0001833333
## Approximately 10% of max_count met: minutes 0.0004333333
```

```
## Approximately 20% of max_count met: minutes 0.001033333
## Approximately 33% of max_count met: minutes 0.001433333
## Approximately 50% of max_count met: minutes 0.002
## Approximately 75% of max_count met: minutes 0.002966667
## Approximately 90% of max_count met: minutes 0.003466667
## # of subgroups evaluated based on (up to) maxk-factor combinations 136
## % 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 15 17
## # of subgroups with sample size less than criteria 19
## # of subgroups meeting all criteria = 111
## # of subgroups fitted (Cox model estimable) = 111
## *Subgroup Searching Minutes=* 0.003716667
## Number of subgroups meeting HR threshold 7
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) =  7
## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##      n    E  d1    HR L(HR) q8.0 q8.1 q7.0 q7.1 q6.0 q6.1 q5.0
## 1 159   66 40 1.75  1.07    1    0    0    1    0    0    0
## 2 104   83 47 1.65  1.06    1    0    0    0    0    0    0
## 3 139   80 50 1.45  0.92    1    0    0    0    0    0    0
## 4  76   42 26 1.41  0.75    1    0    0    0    0    0    0
## 5 231 132 78 1.38  0.97    1    0    0    0    0    0    0
## 6 166   97 59 1.35  0.90    1    0    0    0    0    0    0
## 7 141 101 60 1.29  0.87    1    0    0    0    0    1    0
## Consistency 0.98
## # of splits= 400
## Model, % Consistency Met= !{z3 <= 0} {z5} 0.98
## SG focus= hr
## Subgroup Consistency Minutes= 0.01971667
## Subgroup found (FS)
## Minutes forestsearch overall= 0.05111667
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 49.86585 2
##    leaf.node control.mean control.size control.se depth
## 1          2        -3.60       523.00       1.22     1
## 2          3         2.64       177.00       2.43     1
## 11         4        -4.36       332.00       1.44     2
## 3          6        -4.18       214.00       2.14     2
## 4          7         6.25       137.00       2.66     2
##   leaf.node control.mean control.size control.se depth
## 4         7         6.25       137.00       2.66     2
## GRF subgroup found
## All splits
## [1] "z4 <= 0" "z1 <= 0" "z3 <= 0"
## Terminating node at max.diff (sg.harm.id)
## [1] "z3 <= 0"
## # of continuous/categorical characteristics 1 6
## Continuous characteristics: size
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## Default cuts included (1st 20)
## Categorical: z1 z2 z3 z4 z5 grade3
## Factors per GRF: z4 <= 0 z1 <= 0 z3 <= 0
## Initial GRF cuts included z4 <= 0 z1 <= 0 z3 <= 0
```

```
## # of candidate subgroup factors= 10
##  [1] "size <= 29.8" "size <= 26.5" "size <= 21"   "size <= 35"   "z1"
##  [6] "z2"           "z3"           "z4"           "z5"           "grade3"
## Number of factors evaluated= 10
## Confounders per grf screening q5 q8 q7 q10 q9 q3 q1 q6 q4 q2
##          Factors Labels VI(grf)
## 5             z1     q5  0.2088
## 8             z4     q8  0.1477
## 7             z3     q7  0.1190
## 10        grade3    q10  0.1090
## 9             z5     q9  0.0889
## 3     size <= 21     q3  0.0737
## 1   size <= 29.8     q1  0.0736
## 6             z2     q6  0.0656
## 4     size <= 35     q4  0.0617
## 2   size <= 26.5     q2  0.0520
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 210
## Approximately 5% of max_count met: minutes 0.00025
## Approximately 10% of max_count met: minutes 0.0006166667
## Approximately 20% of max_count met: minutes 0.0012
## Approximately 33% of max_count met: minutes 0.001933333
## Approximately 50% of max_count met: minutes 0.003333333
## Approximately 75% of max_count met: minutes 0.004783333
## Approximately 90% of max_count met: minutes 0.0054
## # of subgroups evaluated based on (up to) maxk-factor combinations 210
## % 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 18 22
## # of subgroups with sample size less than criteria 25
## # of subgroups meeting all criteria = 176
## # of subgroups fitted (Cox model estimable) = 176
## *Subgroup Searching Minutes=* 0.005933333
## Number of subgroups meeting HR threshold 8
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) =  8
## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##      n    E d1   HR L(HR) q5.0 q5.1 q8.0 q8.1 q7.0 q7.1 q10.0 q10.1
## 1   86   70 37 1.70  1.06    0    1    0    0    0    1     0     0
## 2   75   49 23 1.59  0.90    0    1    0    0    0    0     0     0
## 3   69   44 23 1.50  0.82    0    0    0    0    0    0     0     1
## 4   86   55 27 1.38  0.81    0    0    0    0    0    0     0     1
## 5  137  102 53 1.35  0.92    0    0    0    1    0    1     0     0
## 6   90   60 30 1.35  0.81    0    1    0    0    0    0     0     0
## 7   82   56 27 1.26  0.75    0    1    0    0    0    0     0     1
## 8  130   88 45 1.25  0.82    0    0    0    1    0    0     0     1
## Consistency 0.9725
## # of splits= 400
## Model, % Consistency Met= {z1} {z3} 0.9725
## SG focus= hr
## Subgroup Consistency Minutes= 0.01833333
## Subgroup found (FS)
## Minutes forestsearch overall= 0.05841667
## FS: GRF stage for cut selection with dmin,tau= 12 0.6
## tau, maxdepth= 49.86585 2
```

```
##    leaf.node control.mean control.size control.se depth
## 1          2        -3.60       523.00       1.22     1
## 2          3         2.64       177.00       2.43     1
## 11         4        -4.36       332.00       1.44     2
## 3          6        -4.18       214.00       2.14     2
## 4          7         6.25       137.00       2.66     2
##   leaf.node control.mean control.size control.se depth
## 4         7         6.25       137.00       2.66     2
## GRF subgroup found
## All splits
## [1] "z4 <= 0" "z1 <= 0" "z3 <= 0"
## Terminating node at max.diff (sg.harm.id)
## [1] "z3 <= 0"
## # of continuous/categorical characteristics 1 6
## Continuous characteristics: size
## Categorical characteristics: z1 z2 z3 z4 z5 grade3
## CV lambda = 0.003052534
## 7 x 1 sparse Matrix of class "dgCMatrix"
##                  s0
## z1       0.456793411
## z2      -0.559915450
## z3       0.572323151
## z4       0.706710215
## z5      -0.902306015
## size    -0.004450463
## grade3 -0.019602502
## Cox-LASSO selected: z1 z2 z3 z4 z5 size grade3
## Cox-LASSO not selected:
## Default cuts included from Lasso:
## Categorical after Lasso: z1 z2 z3 z4 z5 grade3
## Factors per GRF: z4 <= 0 z1 <= 0 z3 <= 0
## Initial GRF cuts included z4 <= 0 z1 <= 0 z3 <= 0
## Factors included per GRF (not in lasso)
## # of candidate subgroup factors= 10
##  [1] "size <= 29.8" "size <= 26.5" "size <= 21"   "size <= 35"   "z1"
##  [6] "z2"           "z3"           "z4"           "z5"           "grade3"
## Number of factors evaluated= 10
## Confounders per grf screening q5 q8 q7 q10 q9 q3 q1 q6 q4 q2
##          Factors Labels VI(grf)
## 5             z1     q5  0.2088
## 8             z4     q8  0.1477
## 7             z3     q7  0.1190
## 10        grade3    q10  0.1090
## 9             z5     q9  0.0889
## 3      size <= 21     q3  0.0737
## 1    size <= 29.8     q1  0.0736
## 6             z2     q6  0.0656
## 4      size <= 35     q4  0.0617
## 2    size <= 26.5     q2  0.0520
## Number of possible configurations (<= maxk): maxk, # <= maxk 2 210
## Approximately 5% of max_count met: minutes 0.0002833333
## Approximately 10% of max_count met: minutes 6e-04
## Approximately 20% of max_count met: minutes 0.001133333
## Approximately 33% of max_count met: minutes 0.001766667
## Approximately 50% of max_count met: minutes 0.003
```

```
## Approximately 75% of max_count met: minutes 0.004533333
## Approximately 90% of max_count met: minutes 0.005683333
## # of subgroups evaluated based on (up to) maxk-factor combinations 210
## % 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 18 22
## # of subgroups with sample size less than criteria 25
## # of subgroups meeting all criteria = 176
## # of subgroups fitted (Cox model estimable) = 176
## *Subgroup Searching Minutes=* 0.005983333
## Number of subgroups meeting HR threshold 8
## Subgroup candidate(s) found (FS)
## # of candidate subgroups (meeting HR criteria) =  8
## SGs (1st 10) meeting screening thresholds sorted by sg_focus= hr
##      n   E d1   HR L(HR) q5.0 q5.1 q8.0 q8.1 q7.0 q7.1 q10.0 q10.1
## 1   86  70 37 1.70  1.06    0    1    0    0    0    1     0     0
## 2   75  49 23 1.59  0.90    0    1    0    0    0    0     0     0
## 3   69  44 23 1.50  0.82    0    0    0    0    0    0     0     1
## 4   86  55 27 1.38  0.81    0    0    0    0    0    0     0     1
## 5  137 102 53 1.35  0.92    0    0    0    1    0    1     0     0
## 6   90  60 30 1.35  0.81    0    1    0    0    0    0     0     0
## 7   82  56 27 1.26  0.75    0    1    0    0    0    0     0     1
## 8  130  88 45 1.25  0.82    0    0    0    1    0    0     0     1
## Consistency 0.9725
## # of splits= 400
## Model, % Consistency Met= {z1} {z3} 0.9725
## SG focus= hr
## Subgroup Consistency Minutes= 0.01728333
## Subgroup found (FS)
## Minutes forestsearch overall= 0.06036667
```

```r
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
```

```r
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_m4a-Noise=0_N=700_alt_ktreat=0.9_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        95 0.1357143         605   0.8642857     1     95     605
## 2:      1        95 0.1357143         605   0.8642857     1     95     605
## 3:      1        95 0.1357143         605   0.8642857     1     95     605
## 4:      1        95 0.1357143         605   0.8642857     0      0     700
```

```
## 5:       1            95  0.1357143            605   0.8642857      0       0      700
## 6:       1            95  0.1357143            605   0.8642857      0       0      700
##       ppv   npv specificity sensitivity found.1 found.2 found.both found.al3
##     <num> <num>       <num>       <num>   <num>   <num>      <num>      <num>
## 1:      1     1   1.0000000           1       0       0          0          0
## 2:      1     1   1.0000000           1       0       0          0          0
## 3:      1     1   1.0000000           1      NA      NA         NA         NA
## 4:      0     1   0.8642857           0      NA      NA         NA          0
## 5:      0     1   0.8642857           0       0       0          0          0
## 6:      0     1   0.8642857           0       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:    1.74466  0.5577464  1.74466 0.5577464      0 -0.2553474 0.0000000
## 2:    1.74466  0.5577464  1.74466 0.5577464      0 -0.2553474 0.0000000
## 3:    1.74466  0.5577464  1.74466 0.5577464      0 -0.2553474 0.0000000
## 4:    1.74466  0.5577464       NA 0.6688550     NA         NA 0.1111086
## 5:    1.74466  0.5577464       NA 0.6688550     NA         NA 0.1111086
## 6:    1.74466  0.5577464       NA 0.6688550     NA         NA 0.1111086
##          b2.Hc    p.cens analysis    taumax    hr.itt     l.itt     u.itt
##          <num>     <num>   <char>     <num>     <num>     <num>     <num>
## 1: -0.08889407 0.4514286      FSl 81.43453 0.668855 0.5464683 0.8186513
## 2: -0.08889407 0.4514286     FSlg 48.86072 0.668855 0.5464683 0.8186513
## 3: -0.08889407 0.4514286      GRF 81.43453 0.668855 0.5464683 0.8186513
## 4:  0.02221450 0.4514286   GRF.60 48.86072 0.668855 0.5464683 0.8186513
## 5:  0.02221450 0.4514286   VT(24) 81.43453 0.668855 0.5464683 0.8186513
## 6:  0.02221450 0.4514286  VT#(24) 81.43453 0.668855 0.5464683 0.8186513
##    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:  0.6827343 0.5565269 0.8375626 1.105971 2.752186 0.4437854 0.7009717
## 2:  0.6827343 0.5565269 0.8375626 1.105971 2.752186 0.4437854 0.7009717
## 3:  0.6827343 0.5565269 0.8375626 1.105971 2.752186 0.4437854 0.7009717
## 4:  0.6827343 0.5565269 0.8375626 1.105971 2.752186 0.4437854 0.7009717
## 5:  0.6827343 0.5565269 0.8375626 1.105971 2.752186 0.4437854 0.7009717
## 6:  0.6827343 0.5565269 0.8375626 1.105971 2.752186 0.4437854 0.7009717
##      l.H.hat  u.H.hat  l.Hc.hat  u.Hc.hat
##        <num>    <num>     <num>     <num>
## 1: 1.105971 2.752186 0.4437854 0.7009717
## 2: 1.105971 2.752186 0.4437854 0.7009717
## 3: 1.105971 2.752186 0.4437854 0.7009717
## 4:       NA       NA 0.5464683 0.8186513
## 5:       NA       NA 0.5464683 0.8186513
## 6:       NA       NA 0.5464683 0.8186513
## Subgroup HRs: H, H^c, Causal= 2.000007 0.6466405 0.7057463
## Simulations= 20000
## Avg censoring= 0.4502911
## Min,Max,Avg tau.max= 69.89395 83.99237 81.61975
## P(H) approximation at causal(H), n(sg)=60, approx= 2.000007 60 0.8281929
## P(H) approximation at causal(H), Avg(n(sg)), approx= 2.000007 89 0.8997886
## P(H) approximation at plim(H), Avg(n(sg)), approx= 2.114003 89 0.9262042
## Minutes,hours 491.4375 8.190625
##                    FSl    FSlg     GRF   GRF.60   VT(24)  VT#(24)   VT(36)  VT#(36)
## any.H            0.910   0.860   0.940    0.720    0.490    0.540    0.470    0.610
## sensH            0.850   0.800   0.850    0.650    0.450    0.520    0.420    0.590
## sensHc           0.990   0.990   0.970    0.980    0.990    0.990    0.990    0.990
## ppH              0.840   0.790   0.780    0.610    0.440    0.510    0.410    0.570
```

```
## ppHc              0.980   0.970   0.980   0.960   0.930   0.940   0.930   0.950
## Avg(#H)          89.000  91.000 102.000  99.000  92.000  92.000  92.000  92.000
## minH             61.000  61.000  60.000  60.000  60.000  60.000  60.000  60.000
## maxH            290.000 272.000 397.000 293.000 204.000 198.000 249.000 189.000
## Avg(#Hc)        619.000 621.000 605.000 629.000 655.000 650.000 657.000 644.000
## minHc           410.000 428.000 303.000 407.000 496.000 502.000 451.000 511.000
## maxHc           700.000 700.000 700.000 700.000 700.000 700.000 700.000 700.000
## hat(H*)           2.194   2.213   2.154   2.252   2.390   2.378   2.416   2.355
## hat(hat[H])       2.228   2.204   2.018   2.066   2.284   2.308   2.290   2.304
## hat(Hc*)          0.653   0.653   0.651   0.647   0.653   0.652   0.652   0.652
## hat(hat[Hc])      0.653   0.652   0.645   0.646   0.655   0.653   0.656   0.651
## hat(H*)all        2.114   2.114   2.114   2.114   2.114   2.114   2.114   2.114
## hat(Hc*)all       0.652   0.652   0.652   0.652   0.652   0.652   0.652   0.652
## hat(ITT)all       0.755   0.755   0.755   0.755   0.755   0.755   0.755   0.755
## hat(ITTadj)all    0.742   0.742   0.742   0.742   0.742   0.742   0.742   0.742

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,
```

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)	0.91	0.86	0.94	0.72	0.49	0.54	0.47	0.61
$sens(\hat{H})$	0.85	0.8	0.85	0.65	0.45	0.52	0.42	0.59
$sens(\hat{H}^C)$	0.99	0.99	0.97	0.98	0.99	0.99	0.99	0.99
$ppv(\hat{H})$	0.84	0.79	0.78	0.61	0.44	0.51	0.41	0.57
$ppv(\hat{H}^C)$	0.98	0.97	0.98	0.96	0.93	0.94	0.93	0.95
Size of H and H-complement								
$avg|\hat{H}|$	89	91	102	99	92	92	92	92
$min|\hat{H}|$	61	61	60	60	60	60	60	60
$max|\hat{H}|$	290	272	397	293	204	198	249	189
$avg|\hat{H}^C|$	619	621	605	629	655	650	657	644
$min|\hat{H}^C|$	410	428	303	407	496	502	451	511
$max|\hat{H}^C|$	700	700	700	700	700	700	700	700

Note: Number of simulations= 20000 .
Note: Probability approximation= 0.8998 .

```
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 937.5919 15.62653

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 468.796 7.813266
```

```r
#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: Apple M1 Max

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= 10 34
```