Using PwrGSD to compute Operating Characteristics of a candidate monitoring scheme at a specified hypothetical trial scenario (Version 2.3.1)

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1 Introduction

The function **PwrGSD** computes several operating characteristics, such as power, expected duration and relative risks at the stopping boundaries, given a specification of the interim monitoring scheme and choice of test statistic under a specified hypothetical progression of the trial. The capabilities of **PwrGSD** allow for

1 **Non-proportional hazards alternatives** via the specification of trial arm specific piecewise constant hazard rates, piecewise exponential survival functions, or the stipulation of one of these in arm 0 together with a piecewise constant hazard ratio for the main endpoint.

2 **Flexible specification of the censoring distribution** The trial arm specific censoring distributions may be specified via piecewise constant hazard or piecewise exponential survival functions.

3 **Two modes of non-compliance per each of the two trial arms** Each form of non-compliance is stipulated via a waiting time distribution, specified via piecewise constant hazards or piecewise exponential survival, together with a post-noncompliance main endpoint distribution, also specified via hazards or survival functions.

4 **Choice of test statistic** Currently, the asymptotic method of calculation supports several members of the weighted log-rank family of statistics: Fleming-Harrington wieghts of given exponents $FH(g, \rho)$, a variant $SFH(g, \rho, x)$ which is equal to the $FH(g, \rho)$ function but stopped at the value attained at x, or the $Ramp(x)$ function, which has linear rise from zero to its maximum value, attained at x and then constant weight thereafter. The simulation method of calculation supports all of these plus the integrated survival difference statistic.

5 **Choice of boundary construction method:** Currently either Lan-Demets with a variety of possible spending functions

   i O'Brien-Fleming

   ii Pocock

   iii Wang-Tsiatis Power Family

   The Haybittle method is also supported in the case of efficacy bounds only

6 **Efficacy bounds only or simultaneous calculation of efficacy and futility bounds**

The goal of this vignette is to understand the features and capabilities of **PwrGSD** by trying several examples.

In the first example, we compute power at a specific alternative, `rhaz`, under an interim analysis plan with roughly one analysis per year, some crossover between intervention and control arms, with Efficacy and futility boundaries constructed via the Lan-Demets procedure with O'Brien-Fleming spending. We investigate the behavior of three weighted log-rank statistics: (i) the Fleming-Harrington(0,1) statistic, (ii) a stopped version of the F-H(0,1) statistic capped off at 10 years, and (iii) the deterministic weighting function with linear increase between time 0 and time 10 with constant weight thereafter.

```
>   tlook <- c(7.14, 8.14, 9.14, 10.14, 10.64, 11.15, 12.14, 13.14,
+              14.14, 15.14, 16.14, 17.14, 18.14, 19.14, 20.14)
>   t0 <- 0:19
>   h0 <- c(rep(3.73e-04, 2), rep(7.45e-04, 3), rep(1.49e-03, 15))
>   rhaz <-c(1, 0.9125, 0.8688, 0.7814, 0.6941, 0.6943, 0.6072, 0.5202,
+            0.4332, 0.652, 0.6524, 0.6527, 0.653, 0.6534, 0.6537,
+            0.6541, 0.6544, 0.6547, 0.6551, 0.6554)
>   hc <- c(rep(1.05e-02, 2), rep(2.09e-02, 3), rep(4.19e-02, 15))
>   hd1B <- c(0.1109, 0.1381, 0.1485, 0.1637, 0.2446, 0.2497, 0)

>   library(PwrGSD)
>   example.1 <-
+     PwrGSD(EfficacyBoundary=LanDemets(alpha=0.05, spending= ObrienFleming),
+            FutilityBoundary=LanDemets(alpha=0.1, spending=ObrienFleming),
+            RR.Futility = 0.82, sided="1<",method="A",accru =7.73, accrat=9818.65,
+            tlook =tlook, tcut0 =t0, h0=h0, tcut1=t0, rhaz=rhaz,
+            tcutc0=t0, hc0=hc, tcutc1=t0, hc1=hc,
+            tcutd0B =c(0, 13), hd0B =c(0.04777, 0),
+            tcutd1B =0:6, hd1B =hd1B,
+            noncompliance =crossover, gradual =TRUE,
+            WtFun =c("FH", "SFH", "Ramp"),
+            ppar =c(0, 1, 0, 1, 10, 10))
```

In the next example, we construct the efficacy boundary using the stochastic curtailment procedure.

```
>   example.2 <- update(example.1, EfficacyBoundary=LanDemets(alpha=0.05, spending=Pow(1)))
```