# Using PwrGSD to compute Operating Characteristics of a candidate monitoring scheme at a specified hypothetical trial scenario (Version 1.15)

Grant Izmirlian

July 11, 2008

## 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(0.000373, 2), rep(0.000745, 3), rep(0.00149,
+     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(0.0105, 2), rep(0.0209, 3), rep(0.0419, 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 <- example.1
> example.2$call$EfficacyBoundary <- as.call(expression(SC,
+     alpha = 0.05, crit = 0.9))
> example.2 <- update(example.2)
```