

Group sequential clinical trials

Design a Pocock group sequential clinical trial with
five equal groups, distance 2.9 between the null and
alternative parameters, standard deviation 4.8,
significance level 0.05, and power 0.9.

```
> library(clinfun)
> gsdesign.normal( ifrac=(1:5)/5, delta=2.9, sd=4.8,
+                 sig.level=0.05, power=0.9, delta.eb=0)
```

Group sequential design for comparing normal data with delta = 2.9 , sd = 4.8
 power family of boundary; 0 (Pocock) to 0.5 (O'Brien-Fleming)

```
sample size (per arm) = 69.52065
information fraction = 0.2 0.4 0.6 0.8 1.0
  efficacy boundary = 2.414 2.414 2.414 2.414 2.414 (power = 0)
    sig.level = 0.05
      power = 0.9
alternative = two.sided
```

Here ifrac = information fraction (0.2, 0.4, ..., 1.0),
delta.eb = boundary for efficacy, it = 0 means Pocock boundaries
(delta.fb = boundary for futility, = 0.5 means O'Brien-Fleming)
As a result, we sample ceiling(69.6/5) = 14 patients for each group.
The trial will stop and reject H_0 as soon as $|Z(k)| > 2.417$.

Design an O'Brien-Fleming test for the same problem.

```
> gsdesign.normal( ifrac=(1:5)/5, delta=2.9, sd=4.8,
+                 sig.level=0.05, power=0.9, delta.eb=0.5)
```

Group sequential design for comparing normal data with delta = 2.9 , sd = 4.8
 power family of boundary; 0 (Pocock) to 0.5 (O'Brien-Fleming)

```
sample size (per arm) = 59.13287
information fraction = 0.2 0.4 0.6 0.8 1.0
  efficacy boundary = 4.564 3.227 2.635 2.282 2.041 (power = 0.5)
    sig.level = 0.05
      power = 0.9
alternative = two.sided
```

> # For the O'Brien-Fleming test, we sample ceiling(59.1/5) = 12 patients
> # for each group. The trial will stop
> # - after the 1st group if $|Z(1)| > 4.56$, otherwise,
> # - after the 2nd group if $|Z(2)| > 3.224$, otherwise,
> # - after the 3rd group if $|Z(3)| > 2.633$, otherwise,
> # - after the 4th group if $|Z(4)| > 2.28$, otherwise,
> # - after the 5th group if $|Z(5)| > 2.039$.