Crossover Trial Power Using Simulation

Eamonn O'Brien

24 July, 2019

Contents

Contents

List of Figures

List of Tables

Function to simulate crossover trial using lme4

```
# n - number of patients in each order group sdW - within
# patient standard deviation sdB - between patient standard
# deviation beta - coefficient vector c(Intercept, Treatment,
# Order, Treatment:Order)

require("lme4")

simulatec <- function(n = 10, sdW = 4, sdB = 1, beta = c(8, 1,
    0, 0), alpha = 0.05) {

    # generate data
    Patient <- as.factor(rep(1:(2 * n), rep(2, 2 * n)))
    Treatment <- c(rep(c("Treatment1", "Treatment2"), n), rep(c("Treatment2",
        "Treatment1"), n))
    Order <- rep(c("First", "Second"), 2 * n)
    Data <- data.frame(Patient, Treatment, Order)
    FMat <- model.matrix(~Treatment * Order, data = Data)
    RMat <- model.matrix(~0 + Patient, data = Data)
    Response <- FMat %*% beta + RMat %*% rnorm(2 * n, 0, sdB) +
        rnorm(4 * n, 0, sdW)
    Data$Response <- Response

    # analyse
    Fit <- lmer(Response ~ (1 | Patient) + Treatment * Order,
        data = Data)
    Est <- fixef(Fit)[2]
    Ste <- sqrt(vcov(Fit)[2, 2])
    prod(Est + c(-1, 1) * qnorm(1 - alpha/2) * Ste) > 0
}

# power for n=20 and treatment effect 4
mean(replicate(1000, simulatec(n = 20, beta = c(8, 4, 0, 0))))
```

```
[1] 0.868
```

```
# (many warning messages: boundary (singular) fit: see
# ?isSingular)
```

Function to simulate crossover trial using nlme

```r
# no warning messages for equivalent analyses compared to
# lme4 A random effect very near zero seems to be the reason
# for the warning message using lme4

require(nlme)

simulaten <- function(n = 10, sdW = 4, sdB = 1, beta = c(8, 1,
    0, 0), alpha = 0.05) {

    # generate data
    Patient <- as.factor(rep(1:(2 * n), rep(2, 2 * n)))
    Treatment <- c(rep(c("Treatment1", "Treatment2"), n), rep(c("Treatment2",
        "Treatment1"), n))
    Order <- rep(c("First", "Second"), 2 * n)
    Data <- data.frame(Patient, Treatment, Order)
    FMat <- model.matrix(~Treatment * Order, data = Data)
    RMat <- model.matrix(~0 + Patient, data = Data)
    Response <- FMat %*% beta + RMat %*% rnorm(2 * n, 0, sdB) +
        rnorm(4 * n, 0, sdW)
    Data$Response <- Response

    # analyse
    Fit <- lme(Response ~ Treatment * Order, random = ~1 | Patient,
        data = Data, na.action = "na.omit")
    Est <- fixed.effects(Fit)[2]
    Ste <- sqrt(vcov(Fit)[2, 2])
    prod(Est + c(-1, 1) * qnorm(1 - alpha/2) * Ste) > 0
}

# power for n=20 and treatment effect 4
mean(replicate(1000, simulaten(n = 20, beta = c(8, 4, 0, 0))))
```

```
[1] 0.855
```

Computing Environment

```
sessionInfo()
```

```
R version 3.6.1 (2019-07-05)
Platform: x86_64-w64-mingw32/x64 (64-bit)
Running under: Windows 10 x64 (build 17134)

Matrix products: default

locale:
[1] LC_COLLATE=English_United Kingdom.1252
[2] LC_CTYPE=English_United Kingdom.1252
[3] LC_MONETARY=English_United Kingdom.1252
[4] LC_NUMERIC=C
[5] LC_TIME=English_United Kingdom.1252

attached base packages:
[1] stats     graphics  grDevices utils     datasets
[6] methods   base

other attached packages:
[1] nlme_3.1-140  lme4_1.1-21   Matrix_1.2-17 knitr_1.23

loaded via a namespace (and not attached):
 [1] Rcpp_1.0.1      lattice_0.20-38 digest_0.6.20
 [4] MASS_7.3-51.4   grid_3.6.1      formatR_1.7
 [7] magrittr_1.5    evaluate_0.14   stringi_1.4.3
[10] minqa_1.2.4     nloptr_1.2.1    boot_1.3-22
[13] rmarkdown_1.14  splines_3.6.1   tools_3.6.1
[16] stringr_1.4.0   xfun_0.8        yaml_2.2.0
[19] compiler_3.6.1  htmltools_0.3.6
```

This took 66.31 seconds to execute.