GenTwoArmsTrialSize: An R Statistical Software Package to estimate Generalized Two Arms Clinical Trial Sample Size

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Outline

Background

- **Why Sample Size Calculations in Clinical Trials ?:**
  - Economic considerations
  - Ethical considerations
  - Scientific considerations.

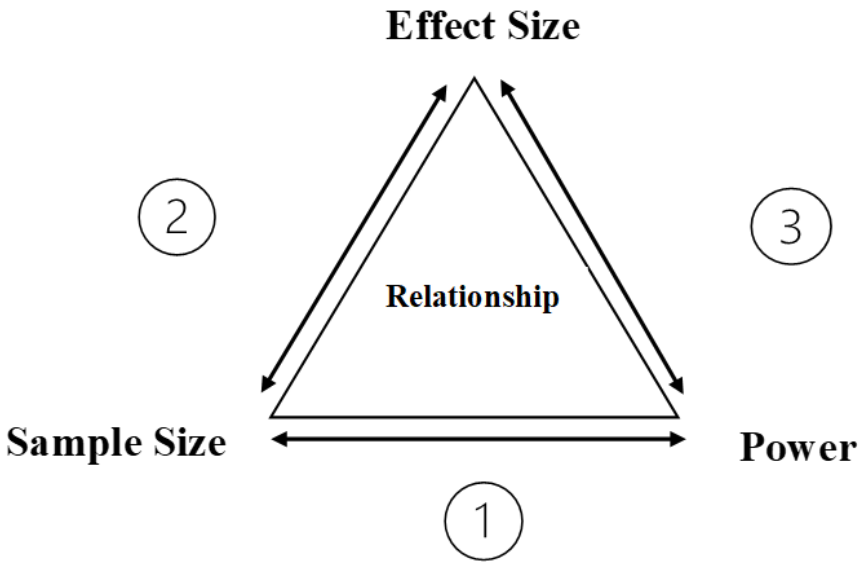

Figure 1: Three way relationships between the key elements of sample size calculation.

- **Relationships:**

Motivation

- No developed Statistical software yet has considered noncompliance and loss of follow-up in calculations:
  - nQuery
  - PASS
  - R
  - SAS
- No R package yet estimates sample size for two-arms ordinal endpoints.
- Need to use various R packages and different functions for sample size calculations:
  - Trial Size: 15 functions !
  - Hmisc: one function (incomplete) !

Introduction

- Generalizes R Package "Trialsize" in terms:
  - noncompliance
  - loss of follow-up
- Adds three more scenarios to R package "Hmisc"
- Uniforms functions in the generalization process
- Covers 20 scenarios by:
  - Endpoint (Continuous/Binary/TTE/Ordinal)
  - Design(Parallel/Crossover)
  - Hypothesis Test(Equality/Noninferiority/Superiority/Equivalence)
- Depends on only two R packages(Trialsize/Hmisc)

Description

- Installation & Loading:

```
line #1: > install.packages("GenTwoArmsTrialSize",
dependencies=TRUE)
line #2: > library(GenTwoArmsTrialSize)
```

- Functions:
  - First(10 parameters):
    getSizeMean(design,test,alpha, beta, sigma, k, delta, TTE, rho,r)
  - Second(11 parameters):
    getSizeProp(design,test,alpha,beta,varsigma,k,seqnumber,delta,TTE,rho,r)
  - Third(12 parameters):
    getSizeTTE(design,test,alpha,beta,varlambda,k,ttotal,taccrual,gamma,delta,rho,r)
  - Fourth(10 parameters):
    getSizeOrd(design,test,alpha,beta,varcatprob,k,theta,delta,rho,r)

Trial Description

- Sponsor: Endologix Inc, USA
- Trial: Looking at EVAR Outcomes by Primary Analysis of Randomized Data (LEOPARD)
- Design: Two Arm parallel randomized clinical trial
- Goal: Assess safety and efficacy of AFX Endovascular system vs. EVAR system
- Endpoint: Binary Response Status(Positive/Negative)
- Patients: Aged 64-80 years with infrarenal Abdominal Aortic Aneurysms in 80 American Centers
- Sample Size Estimation Info:
  - Hypothesis Test: Superiority of AFX vs. EVAR
  - Ratio: 1:1
  - Power: 80%
  - Responses: AFX(86%); EVAR (79%)

Sample Size Variation by Noncompliance and Loss of Follow-up

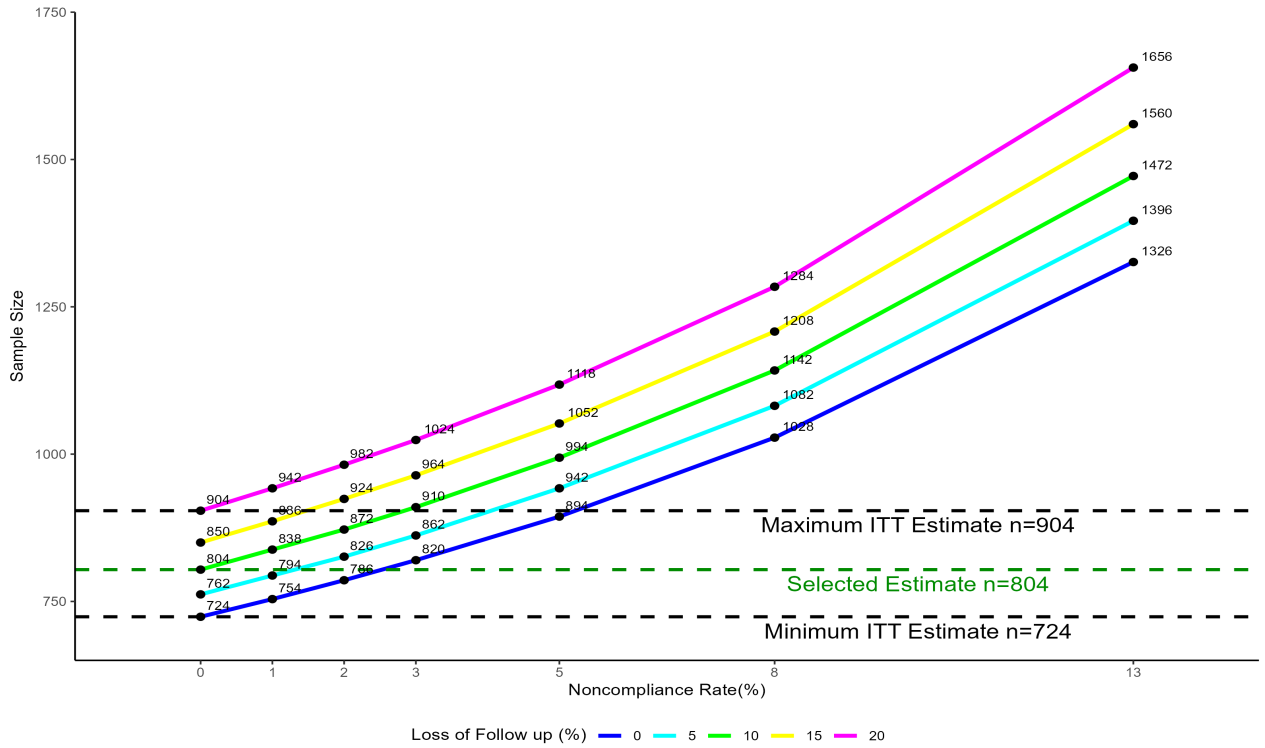

Figure 2: Estimates of total sample size for binary end point scenario in Endologix Inc LEOPARD trial in terms of equal arms noncompliance rates and loss of follow up.

Statistical Software Role in Estimations

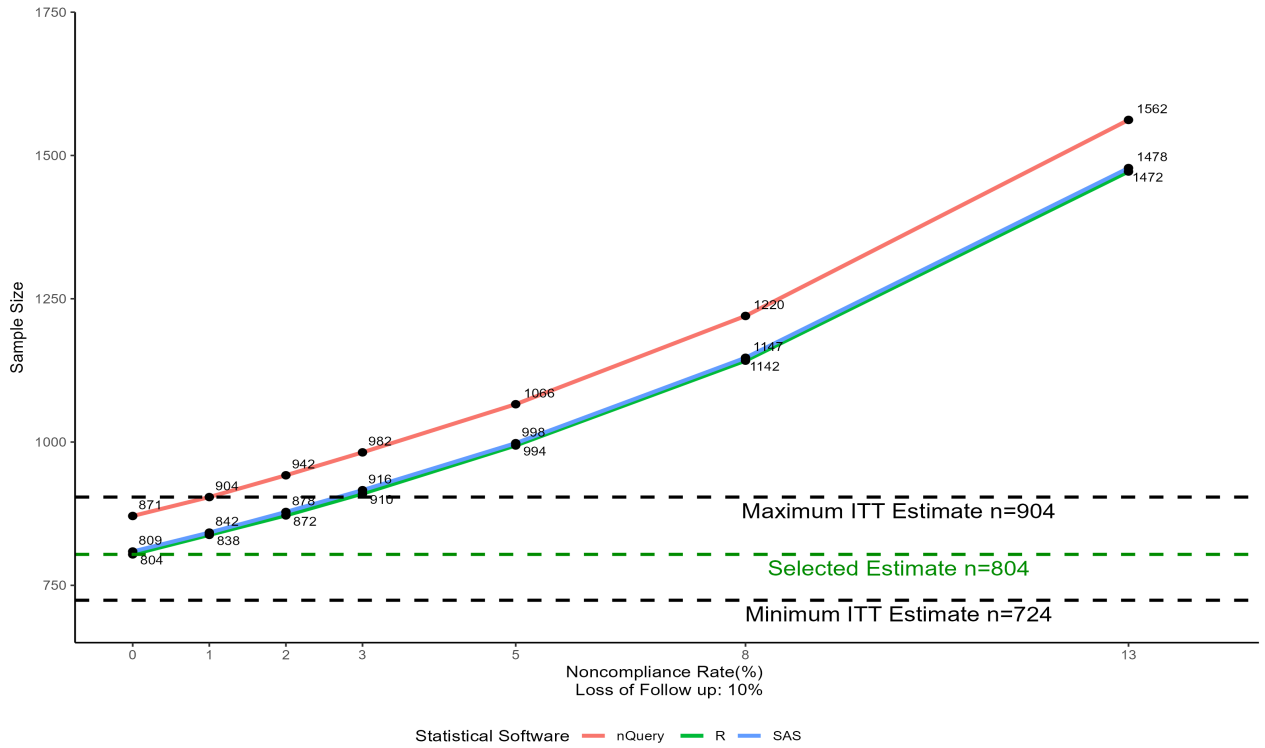

Figure 3: Estimates of total sample size for binary end point scenario in Endologix Inc LEOPARD trial in terms of noncompliance rates and statistical software

Package Generalization Directions

- Multiple Endpoint Trials (Unordered)
- Bioequivalence Trials (difference/ratio)
- Multiple Arm Trials
- Standard Effect Size vs. Non standard effect size
- Adaptive design vs. Fixed design
- Power Calculation in terms of:
  - Sample Size
  - Effect Size

Tutorial & Source Code

[1] Soltanifar, M.; Lee, C.H.; Shirazi, A; Behnke, M; Raymond-Loher, I; & Dagne, G.A. (2024). GenTwoArmsTrialSize: An R Statistical Software Package to estimate Generalized Two Arms Randomized Clinical Trial Sample Size. Mathematics (In press).

[2] Soltanifar, M; & Lee C. GenTwoArmsTrialSize: Generalized Two Arms Clinical Trial Sample Size Calculation. R package version 0.0.5, Published on 16 March 2024, accessed on (16 March 2024). Access URL on Comprehensive R Archive Network(CRAN): `https://CRAN.R-project.org/package=GenTwoArmsTrialSize`


THANK YOU
Any Questions?