**Supplemental Online Content**

**Power and sample sizes estimation in clinical trials with treatment switching in intention-to-treat analysis: a simulation study**

Lejun Deng1#, Chih-Yuan Hsu2,3#, Yu Shyr2,3\*

1Montgomery Bell Academy, Nashville, TN, 37205, USA

2Department of Biostatistics, Vanderbilt University Medical Center, Nashville, TN 37232, USA

3Center for Quantitative Sciences, Vanderbilt University Medical Center, Nashville, TN 37232, USA

\*corresponding authors: Yu Shyr (yu.shyr@vanderbilt.edu)

# These authors contributed equally.

* **Details for censoring distribution**
* **Parameters determination in beta, gamma, uniform, and independent exponential distributions via *pt* and *rho***
* **Figure s1:** Weibull survival functions with different shapes and = 1 and = 1.5.
* **Table s1:** Simulation results for powers and sample sizes under and administrative censoring only (*censor.rate* = “AC.only”).
* **Table s2:** Simulation results for powers and sample sizes under and administrative censoring only (*censor.rate* = “AC.only”).

**Details for censoring distribution**

The censoring consists of both dropout censoring and administrative censoring. The distribution of the censoring can be expressed as follows:

where is the entry time which follows a uniform distribution , and and are the density function and survival function of dropout censoring, respectively. is the indicator function. For simplicity, we assume a uniform distribution for the dropout censoring, i.e., . is determined by the formula of with a given censoring rate of the control group assuming no treatment switching, where is a function of and can be explicitly expressed as follows:

WhereFor ,

where and .

For ,

 .

For ,

**Parameters determination in beta, gamma, uniform, and independent exponential distributions via *pt* and *rho***

We consider using and *rho* to determine the parameters in the assumed distributions for the switching time, where denotes the ratio of the average switching time to the average survival time of the control group, and *rho* denotes the correlation between and . When and are given, the parameters in the assumed distributions can be obtained through solving the two equations: and

where

When and , and . When and , and . When follows an exponential distribution and is independent of , the mean parameter can be determined by When and follows a uniform distribution , i.e., follows a uniform distribution , then equals 0.5 and is a constant (= 0.775 if follows an exponential distribution).

****

**Figure s1.** Weibull survival functions with different shapes and = 1 and = 1.5.

**Table s1.** Simulation results for powers and sample sizes under and administrative censoring only (*censor.rate* = “AC.only”). *power* = 0.8, *alpha* = 0.05, = 1, = 3, = 5.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  | (no switch) | (switch) | Ratio of | Power based on  |
| 1 | 0.2 | 1.25 | 369 | 501 | 1.358 | 0.668 |
|  |  | 1.50 | 115 | 160 | 1.391 | 0.665 |
|  |  | 1.75 | 63 | 87 | 1.396 | 0.652 |
|  |  | 2.00 | 42 | 59 | 1.404 | 0.647 |
| 1 | 0.4 | 1.25 | 369 | 715 | 1.938 | 0.525 |
|  |  | 1.50 | 115 | 234 | 2.035 | 0.516 |
|  |  | 1.75 | 63 | 129 | 2.048 | 0.505 |
|  |  | 2.00 | 42 | 87 | 2.071 | 0.504 |
| 1 | 0.6 | 1.25 | 369 | 1064 | 2.883 | 0.365 |
|  |  | 1.50 | 115 | 364 | 3.165 | 0.355 |
|  |  | 1.75 | 63 | 199 | 3.159 | 0.353 |
|  |  | 2.00 | 42 | 139 | 3.310 | 0.350 |
| 1 | 0.8 | 1.25 | 369 | 1849 | 5.011 | 0.246 |
|  |  | 1.50 | 115 | 616 | 5.617 | 0.223 |
|  |  | 1.75 | 63 | 343 | 5.444 | 0.227 |
|  |  | 2.00 | 42 | 233 | 5.548 | 0.235 |
| 1 | 1.0 | 1.25 | 369 | 3728 | 10.103 | 0.142 |
|  |  | 1.50 | 115 | 1230 | 10.696 | 0.141 |
|  |  | 1.75 | 63 | 691 | 10.968 | 0.138 |
|  |  | 2.00 | 42 | 487 | 11.595 | 0.134 |
| 2 | 0.2 | 1.25 | 271 | 371 | 1.369 | 0.675 |
|  |  | 1.50 | 82 | 117 | 1.427 | 0.652 |
|  |  | 1.75 | 45 | 66 | 1.467 | 0.663 |
|  |  | 2.00 | 31 | 46 | 1.484 | 0.665 |
| 2 | 0.4 | 1.25 | 271 | 535 | 1.974 | 0.526 |
|  |  | 1.50 | 82 | 170 | 2.073 | 0.507 |
|  |  | 1.75 | 45 | 94 | 2.089 | 0.515 |
|  |  | 2.00 | 31 | 63 | 2.032 | 0.501 |
| 2 | 0.6 | 1.25 | 271 | 810 | 2.980 | 0.375 |
|  |  | 1.50 | 82 | 262 | 3.195 | 0.362 |
|  |  | 1.75 | 45 | 148 | 3.289 | 0.361 |
|  |  | 2.00 | 31 | 102 | 3.290 | 0.366 |
| 2 | 0.8 | 1.25 | 271 | 1395 | 5.148 | 0.239 |
|  |  | 1.50 | 82 | 457 | 5.573 | 0.233 |
|  |  | 1.75 | 45 | 252 | 5.600 | 0.232 |
|  |  | 2.00 | 31 | 178 | 5.742 | 0.238 |
| 2 | 1.0 | 1.25 | 271 | 2796 | 10.314 | 0.147 |
|  |  | 1.50 | 82 | 937 | 11.427 | 0.139 |
|  |  | 1.75 | 45 | 513 | 11.400 | 0.148 |
|  |  | 2.00 | 31 | 361 | 11.645 | 0.161 |

 and denote the required sample size with and without treatment switching, respectively.

**Table s2.** Simulation results for powers and sample sizes under and administrative censoring only (*censor.rate* = “AC.only”). *power* = 0.8, *alpha* = 0.05, = 1, = 3, = 5.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  | (no switch) | (switch) | Ratio of | Power based on  |
| 1 | 0.2 | 1.25 | 369 | 446 | 1.209 | 0.716 |
|  |  | 1.50 | 115 | 143 | 1.243 | 0.700 |
|  |  | 1.75 | 63 | 81 | 1.286 | 0.693 |
|  |  | 2.00 | 42 | 56 | 1.310 | 0.689 |
| 1 | 0.4 | 1.25 | 369 | 560 | 1.518 | 0.610 |
|  |  | 1.50 | 115 | 179 | 1.557 | 0.620 |
|  |  | 1.75 | 63 | 98 | 1.556 | 0.595 |
|  |  | 2.00 | 42 | 68 | 1.619 | 0.600 |
| 1 | 0.6 | 1.25 | 369 | 706 | 1.913 | 0.507 |
|  |  | 1.50 | 115 | 231 | 2.009 | 0.504 |
|  |  | 1.75 | 63 | 128 | 2.032 | 0.513 |
|  |  | 2.00 | 42 | 86 | 2.048 | 0.514 |
| 1 | 0.8 | 1.25 | 369 | 916 | 2.482 | 0.423 |
|  |  | 1.50 | 115 | 299 | 2.600 | 0.409 |
|  |  | 1.75 | 63 | 168 | 2.667 | 0.418 |
|  |  | 2.00 | 42 | 119 | 2.833 | 0.407 |
| 1 | 1.0 | 1.25 | 369 | 1278 | 3.463 | 0.324 |
|  |  | 1.50 | 115 | 401 | 3.487 | 0.313 |
|  |  | 1.75 | 63 | 225 | 3.514 | 0.313 |
|  |  | 2.00 | 42 | 156 | 3.714 | 0.300 |
| 2 | 0.2 | 1.25 | 271 | 329 | 1.214 | 0.723 |
|  |  | 1.50 | 82 | 103 | 1.256 | 0.716 |
|  |  | 1.75 | 45 | 57 | 1.267 | 0.711 |
|  |  | 2.00 | 31 | 41 | 1.323 | 0.708 |
| 2 | 0.4 | 1.25 | 271 | 409 | 1.509 | 0.634 |
|  |  | 1.50 | 82 | 131 | 1.598 | 0.628 |
|  |  | 1.75 | 45 | 72 | 1.600 | 0.621 |
|  |  | 2.00 | 31 | 48 | 1.548 | 0.613 |
| 2 | 0.6 | 1.25 | 271 | 516 | 1.904 | 0.528 |
|  |  | 1.50 | 82 | 168 | 2.049 | 0.521 |
|  |  | 1.75 | 45 | 92 | 2.044 | 0.495 |
|  |  | 2.00 | 31 | 64 | 2.065 | 0.503 |
| 2 | 0.8 | 1.25 | 271 | 684 | 2.524 | 0.434 |
|  |  | 1.50 | 82 | 223 | 2.720 | 0.418 |
|  |  | 1.75 | 45 | 124 | 2.756 | 0.421 |
|  |  | 2.00 | 31 | 83 | 2.677 | 0.429 |
| 2 | 1.0 | 1.25 | 271 | 918 | 3.387 | 0.329 |
|  |  | 1.50 | 82 | 306 | 3.732 | 0.312 |
|  |  | 1.75 | 45 | 168 | 3.733 | 0.340 |
|  |  | 2.00 | 31 | 116 | 3.742 | 0.329 |

 and denote the required sample size with and without treatment switching, respectively.