A simulation study of the behaviour of the logrank test under different levels of stratification and sample sizes

by

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Declaration

I Jubane Ido, hereby declare that the work contained in this mini dissertation is entirely my own and I acknowledge that all references are accurately recorded.

Dated at University of Fort Hare, on this 25th February 2013

Ido Jubane Date

Statement by Supervisor
Submission of Msc.(Biostatistics)

I hereby submit, as supervisor, Mr Ido Jubane' s dissertation

entitled: **An investigation of the behaviour of the logrank test under different levels of stratification and sample sizes**

I deem it appropriate for the degree of Msc.(Biostatistics)

Prof Joanne Tyler Date

Abstract

In clinical trials, patients are enrolled into two treatment arms. A researcher may be interested in studying the effectiveness of a new drug or the comparison of two drugs for the treatment of a disease. This survival data is later analysed using the logrank test or the Cox regression model to detect differences in survivor functions. However, the power function of the logrank test depends solely on the number of patients enrolled into the study.

Because statisticians will always minimise type I and type II errors, a researcher carrying out a clinical trial must define beforehand, the number of patients to be enrolled into the clinical study. Without proper sample size and power estimation a clinical trial may fail to detect a false hypothesis of the equality of survivor functions.

This study presents through simulation, a way of power and sample size estimation for clinical trials that use the logrank test for their data analysis and suggests an easy method to estimate power and sample size in such clinical studies. Findings on power analysis and sample size estimation on logrank test are applied to two real examples: one is the Veterans' Administration Lung Cancer study; and the other is the data from a placebo controlled trial of gamma interferon in chronic granulotomous disease.

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CHAPTER 1: RESEARCH INTRODUCTION

1.1. INTRODUCTION

In clinical trials, patients are enrolled into two arms. A researcher may be interested in studying the effectiveness of a new drug or the comparison of two drugs for a disease. The variable of interest in this case is the number of days or years that an individual survives. The researcher is interested in comparing survival times of these groups when one group is given a new drug and the other group is given a currently used drug or alternatively a placebo.

The appropriate test statistic is the logrank test, designed particularly to detect a difference between survival curves which results when the mortality rate in one group is consistently higher than the corresponding rate in a second group and the ratio of these two rates is constant over time [4]. In survival analysis, the unstratified logrank test (ULRT) is known to be the most efficient invariant test under contiguous alternatives in the proportional hazards model [17].

It is often necessary to apply stratified sampling to systematically over-sample to particular "rare events" of interest [8]. Stratification is incorporated into the logrank test by using a stratified logrank test (SLRT).

In this paper a data simulation technique is used to determine the sample size for use in clinical trials required to achieve the desired power of both the logrank test and stratified logrank test

1.2. RESEARCH PROBLEM

During the design and planning of a clinical study an adequate number of subjects should be enrolled so that the study is sufficiently powered. If the sample size is too low, the clinical study will lack the precision to provide reliable answers to the questions about survival functions.

If it is known that a particular group of patients possessing special characteristics will affect the result of the study, then the event of interest should be compared across that stratum [6]. The way that individuals are allocated across strata has an effect on the power of the test. Thus a problem of strata allocation and sample size have adverse effects on whether the log rank test will have enough power to reject a false null hypothesis. In this paper, sample size estimation and strata allocation are the two techniques to be investigated.

During statistical analysis of treatment results, it is highly desirable to have as equal groups as possible regarding both the patient characteristics and diagnosis of disease. Although methods of statistical analysis exist to compensate for unequal treatment groups, it is more convincing to present data from equivalent groups, and stratification is a method for equalizing treatment groups [18]. If we know the factors that may influence the outcome of a specific treatment, we will have to stratify for those factors.

Generally, sample size and strata allocation need to be laid down before a clinical trial begins. Since in most studies, the survivor function of the two groups will be compared, it is necessary to have a log rank test that detects a false null hypothesis. Strata allocation methods should increase the power of the stratified log rank test.

1.3. RESEARCH OBJECTIVES

The primary objective of this research is to set a standard technique of sample size estimation in clinical trials and ways of dealing with a two strata allocation problem. This will enable the simple and stratified log rank test to be powerful enough to reject a false null hypothesis of equal survival functions.

The overall objective maps into a series of sub-objectives the most important of which are:

- Generate times from a Weibull or Exponential distribution for a two treatments and two strata study.
- Have many simulations of the generated data and determine the power of the simple and stratified log rank test under the null hypothesis and alternative hypothesis.
- Compare the power of the tests for different sample sizes and stratum effect.

These results will enable biostatisticians to be advised on sample size estimation and power analysis in clinical trials.

1.4. RESEARCH CONTEXT AND SCOPE

This research will use a data simulation program to be run in *R* and power analysis will be computed using PASS 2011. The estimation methods in R can be used to simulate data many times with which power and sample size analysis would be made. Since PASS was developed mainly as a Power Analysis Statistical Software, it computes power more conveniently than R's `powerCT` function. R is an integrated suite of software facilities for data manipulation, simulation, calculation and graphical display. R handles and analyzes data very effectively and is effective in Monte Carlo studies. Therefore, future clinical studies can use these suggestions for determining a way of allocating patients into groups with sample size and power consideration.

CHAPTER 2: LITERATURE REVIEW

2.1 INTRODUCTION

This chapter explains why the log rank test and the stratified log rank test are the best tests in analysing survival data. Various sample sizes are considered at different levels of two way stratification and the power of the log rank test is computed. The concept of survival analysis and the techniques used to analyse survival data are derived in this chapter.

2.2 CHOICE OF A TEST OF HYPOTHESIS

There are generally five different available tests for analysing censored survival data of which most are nonparametric [12].

(i) Gehan's generalized Wilcoxon test,
(ii) the Cox-Mantel test,
(iii) the Cox's *F* test ,
(iv) the log-rank test, and
(v) Peto and Peto's generalized Wilcoxon test.

Most of these tests will only yield reliable results with fairly large samples sizes.

When the Ghehan’s test is compared to several alternatives, [15] showed that the Cox-Mantel test and the log-rank test are more powerful regardless of censoring when the samples are drawn from a population that follows an exponential or Weibull distribution; under those conditions there is little difference between the Cox-Mantel test and the log-rank test. The ordinary log rank test ignoring strata effect is conservative and is biased when there is treatment imbalance in each prognostic subgroup [16]. The stratified logrank test on the other hand is unbiased and retains high efficiency as long as the number of strata gets small. However when the number of strata gets large, the stratified logrank test can become very inefficient unless there is a large strata effect [11].

2.2.1 DEFINITION OF TERMS AND ACRONYMS

Covariate: a covariate is a variable that is possibly predictive of the outcome under study. A covariate may be of direct interest or it may be a confounding or interacting variable.

Propensity score matching (PSM**)**: is a methodology attempting to provide unbiased estimation of treatment-effects.

Statistical power is the probability of rejecting a false null hypothesis.
Beta is the probability of accepting a false null hypothesis.

Accrual Time is the time during which subjects are enlisted into the study. It is sometimes known as the enlistment period or recruitment period.

USLRT: - Unstratified Logrank Test
SLRT: - Stratified Logrank Test
PASS: - Power Analysis Statistical Software

2.3 HAZARD RATIOS

Let T be the elapsed time until the occurrence of a specified event. The event may be death, occurrence of a disease, disappearance of a disease, appearance of a tumour. The probability distribution of T may be specified using the survival function or the hazard rate.

1. The probability density function is denoted by $f(t)$, which is the probability that an event occurs at time t.
2. The cumulative distribution function $F(t)$, is the probability that an individual survives until time t.

$$F(t) = \int_0^t f(x)dx$$

3 The **survival function**, denoted by $S(T)$, gives us the probability that an individual survives beyond time t. This is usually the first quantity that is studied. It may be estimated using the nonparametric Kaplan-Meier curve or one of the parametric distribution functions.

$$\begin{aligned} S(T) &= \int_T^\infty f(T)dx \\ &= 1 - F(T) \end{aligned}$$

The **hazard rate**, denoted by $h(T)$, is the probability that an individual at time t experiences the event in the next instant. It is a fundamental quantity in survival analysis. The empirical hazard rate may be used to identify the appropriate probability distribution of a particular mechanism, since each distribution has a different hazard rate function. Some distributions have a hazard rate that decreases with time, others have a hazard rate that increases with time, some are constant, and some exhibit all three behaviours at different points in time [9].

$$h(T) = \frac{f(T)}{S(T)}$$

The relationship between the survival function and the hazard function can be seen from the equation:

$$\begin{aligned} S(T) &= \exp\left[-\int_0^T h(x)dx\right] \\ &= \exp\left[-H(x)\right] \end{aligned}$$

4 The cumulative hazard function is denoted by $H(t)$. This is integral of $h(t)$ from 0 to t.

$$\begin{aligned} H(T) &= \int_0^T h(t)dx \\ &= -\ln\left[S(T)\right] \end{aligned}$$

$h_i(t)$ is the hazard at time *t* of the i^{th} individual and $h_0(t)$ is called the baseline hazard at time *t*. **The baseline hazard function** is the hazard function in the absence of covariates.

It will be useful to compare the hazard rates of two groups. This is most often accomplished by creating the hazard ratio. The Cox-Mantel estimate of the hazard ratio for two groups A and B is given by

$$HR_{CM} = \frac{H_A}{H_B} = \frac{O_A / E_A}{O_B / E_B}$$

Where

O_A and O_B are the observed number of deaths in group A and B respectively. E_A and E_B are, respectively, are the expected number of deaths in groups A and B [9].

2.3.1 THE LOGRANK TEST STATISTIC

The logrank statistic L is defined as

$$L = \frac{\sum_{i=1}^{d}\left[X_i - \frac{n_{1i}}{n_{1i} + n_{2i}}\right]}{\sqrt{\sum_{i=1}^{d}\frac{n_{1i}n_{2i}}{(n_{1i} + n_{2i})^2}}}$$

where X_i is an indicator for the control group, n_{1i} is the number at risk in the experimental group just before the ith event (death), and n_{2i} is the number at risk in the control group just before the ith event $[9]$.

Following $[6]$ and $[14]$, the trial is partitioned into K equal intervals. The distribution of L is asymptotically normal with mean E and variance V given by

$$E = \frac{\sum_{k=1}^{K}\sum_{i=1}^{d_k}\left[\frac{\phi_{ki}\theta_{ki}}{1+\phi_{ki}\theta_{ki}} - \frac{\phi_{ki}}{1+\phi_{ki}}\right]}{\sqrt{\sum_{k=1}^{K}\sum_{i=1}^{d_k}\frac{\phi_{ki}}{(1+\phi_{ki})^2}}}$$

$$V = \frac{\sum_{k=1}^{K}\sum_{i=1}^{d_i}\frac{\phi_{ki}\theta_{ki}}{(1+\phi_{ki}\theta_{ki})^2}}{\sum_{k=1}^{K}\sum_{i=1}^{d_k}\frac{\phi_{ki}}{(1+\phi_{ki})^2}}$$

where $\phi_{ki} = \frac{n_{1ki}}{n_{2ki}}, \ \theta_{ki} = \frac{h_{1ki}}{h_{2ki}}$

and h_{1ki} and h_{2ki} are the hazards of dying in the treatment and control groups respectively, just before the ith death in the kth interval. d_k is the number of deaths in the kth interval $[10]$.

If we assume that the intervals are short enough so that the parameters are constant within an interval. That is, so that

$$\phi_{ki} = \phi_k, \ \theta_{ki} = \theta_k, \ h_{1ki} = h_{1k}, \ h_{2ki} = h_{2k}$$

The values of E and V then reduce to

$$E = \sqrt{d}\,\frac{\sum_{k=1}^{K}\left[\left(\frac{d_k}{d}\right)\left(\frac{\phi_k\theta_k}{1+\phi_k\theta_k}-\frac{\phi_k}{1+\phi_k}\right)\right]}{\sqrt{\sum_{k=1}^{K}\left[\left(\frac{d_k}{d}\right)\left(\frac{\phi_k}{(1+\phi_k)^2}\right)\right]}} = \sqrt{d}\,\frac{\sum_{k=1}^{K}\left[\rho_k\left(\frac{\phi_k\theta_k}{1+\phi_k\theta_k}-\frac{\phi_k}{1+\phi_k}\right)\right]}{\sqrt{\sum_{k=1}^{K}\left[\rho_k\left(\frac{\phi_k}{(1+\phi_k)^2}\right)\right]}}$$

and

$$V = \frac{\sum_{k=1}^{K}\left[\left(\frac{d_k}{d}\right)\frac{\phi_k\theta_k}{(1+\phi_k\theta_k)^2}\right]}{\sum_{k=1}^{K}\left[\left(\frac{d_k}{d}\right)\frac{d_k\theta_k}{(1+\phi_k)^2}\right]} = \frac{\sum_{k=1}^{K}\left[\rho_k\,\frac{\phi_k\theta_k}{(1+\phi_k\theta_k)^2}\right]}{\sum_{k=1}^{K}\left[\rho_k\,\frac{d_k\phi_k}{(1+\phi_k)^2}\right]}$$

where

$$d = \sum_{k=1}^{K} d_k$$

and ρ_k is the proportion of the events (deaths) that occur in interval k.
The intervals mentioned above are constructed to correspond to a non-stationary Markov process, one for each group $[10]$.

2.3.2 HYPOTHESIS TESTS

Once data has been collected and the times have been recorded in a spread sheet, then what is left to us is to test the hypothesis that the survival curves, and thus the hazard rates of two populations are equal against all alternatives, we consider the following specific set of hypotheses:

$$\begin{aligned} H_0 &: h_1(T) = h_2(T) \\ H_1 &: h_1(T) \neq h_2(T) \end{aligned}$$

or using the survivor function

$$\begin{aligned} H_0 &: S_1(T) = S_2(T) \\ H_1 &: S_1(T) \neq S_2(T) \end{aligned}$$

In other words, the null hypothesis is that the hazard rates of the two populations are equal at all times and is tested against the alternative hypothesis which states that the hazard rates of the two groups are different.

We observe the test statistic $L = \frac{E^2}{V}$

In large samples, L is approximately distributed as a chi-square random variable with 1 degree of freedom $[2]$. This test has optimum power when the hazard rates of the two populations are proportional to each other. The logrank test is also known as the **Mantel-Haenszel logrank** test statistic.

2.4 STRUCTURE OF SURVIVAL DATA

Survival data is somewhat more difficult to enter because of the presence of various types of censoring – a form of missing data problem common in survival analysis. A failed observation is one in which the time until the terminal event was measured exactly; for example, the mouse died of the disease being studied. Some patients may still be alive or in remission at the end of the study period but the exact survival times of these subjects may be unknown. These are called **censored observation** or **censored times** and can also occur when individuals are lost to follow-up after a period of study

2.4.1 RIGHT CENSORED DATA

A right censored observation provides a lower bound for the actual failure time. All that is known is that the failure occurred (or will occur) at some point after the given time value. Right censored observations occur when a study is terminated before all items have failed. They also occur when an item fails due to an event other than the one of interest. For example: 2.2; 3+; 8.4; 7.5+.

This means the second observation is larger than 3 but we do not know by how much. These often happen when subjects are still alive when we terminate the study. To handle the two types of observations, we use two indicators, one for the numbers and another one to indicate if the number is a right censored one.

Table 1: Format of survival data (right censored)

Time	Censor indicator	Treatment
8	1	1
8	1	1
10	1	1
12	1	1
12	1	1
13	0	1
9	1	2
12	1	2
15	1	2
20	1	2
30	0	2
30	0	2

Each patient has their own zero time, the time at which the patient entered the study. For each patient we record time to event of interest or **censoring time**, whichever is the smaller, and the status or censoring indicator, $\delta = 0$ if the event occurs and $\delta = 1$ if the patient is censored.

2.5 MODEL FORMULATIONS

Having highlighted that survival data cannot be modeled with a normal distribution, computations about survival times need to be approximated with other parametric distributions. The impact of the covariates on the hazard function can be estimated using parametric or semi-parametric techniques. The simplest models are parametric models that require restrictive assumptions regarding the functional form of the baseline hazard function such as

Exponential: $\lambda(\mathbf{t},\mathbf{x},\mathbf{b}) = \exp\left[\mathbf{x}'\mathbf{b}\right]$

Weibull: $\lambda(\mathbf{t},\mathbf{x},\mathbf{b},\mathbf{a}) = \alpha t^{\alpha-1}\exp\left[\mathbf{x}'\mathbf{b}\right]$

The exponential model assumes a constant baseline hazard for each patient while the baseline hazard for the Weibull model is strictly increasing or decreasing depending on the value of α, that is, the parameter α assumes only positive values. If $\alpha > 1$ then the hazard function increases monotonically, if $\alpha < 1$ then it decreases monotonically and if $\alpha = 1$ the model collapses to the exponential case.

The necessary duration of a trial depends on the functional form of the survival and censoring distributions as well as the various parameters involved. The literature on estimation of duration generally assumes that the lifetimes follow a Weibull distribution, and that three parameters remain to be specified: the rate of accrual, the duration of the accrual period, and the duration of the follow-up period. Various authors fix one or more of these parameters and solve for those remaining [7].

2.6 SIMULATION STUDIES

Simulation studies present an important statistical tool to investigate the performance, properties and adequacy of statistical models/tests in pre-specified situations. Data for this research will be simulated in R and power calculations for the stratified logrank test will be computed using PASS 2011.

In this paper, a simulation model is developed based on the Weibull distribution whereby two cohorts of size N each are generated with a censoring indicator variable (right censoring), treatment group and time to failure. The probability of occurrence of the event of interest is the same for subjects in both groups. Accrual rate and follow-up period determine censoring distribution for the two independent groups.

CHAPTER 3: RESEARCH METHODOLOGY

3.1 PREVIOUS RELATED RESEARCH

Much work has emerged in an effort to estimate sample sizes in clinical trials. One of interesting papers related to this work is by [20]. In his paper, [20] proposes a sample size calculation method for rank tests for paired two-sample survival data using a simulation method.

A paired exponential survival model is specified by the marginal hazard rates and the correlation coefficient. Input variables include type I and II error probabilities, marginal hazard rates under the alternative hypothesis, accrual rate and follow-up period. Using efficient algorithms, the simulation method provides required sample size within minutes. The method is easily extended to sample size calculation for K-sample tests under dependence and the data can be analysed using the marginal proportional hazards adjusting for stratification factors in randomization.

Akazawa K., evaluated through simulation, the loss of power of a stratified log-rank test due to the heterogeneity in clinical trials [1]. He argues that the power of the stratified log-rank test decreases due to two reasons: (i) the stratum size may be too small and (ii) the individuals in the same stratum are heterogeneous. The simulation shows that the loss of power is substantial when the stratum size is very small and “the total number of failures and the treatment effect are fixed”. From the stratified Cox regression model in survival analysis, [1] see that if the stratum size is small, its contribution to the overall test is small with censored data in the stratum. This may decrease the power of the stratified log-rank test.

Changyong Feng considered the case where there is a large number of strata, but each stratum has a relatively small sample size [3]. They assumed that patients are homogeneous within each treatment group. For this kind of data, they constructed both the stratified and unstratified logrank tests. They also derived a variance relation between the SLRT and ULRT and quantified the power loss due to unnecessary stratification by this relation. They illustrated their approach with data from a multi-centre clinical trial to test the treatment effect of an implantable defibrillator on survival of patients with reduced left ventricular function after myocardial infarction.

Moreover, [14] presents a method of estimating sample sizes for the comparison of survival curves by the log-rank statistic in the presence of unrestricted rates of noncompliance, lag time, and so forth. The method applies to stratified trials in which the above conditions may vary across the different strata, and does not assume proportional hazards. Power and duration, as well as sample sizes, can be estimated.

3.2 HYPOTHESIS TEST

In this paper, we assume a clinical trial is being designed to test a therapeutic drug to combat Tuberculosis. This new drug will be compared to an existing drug on patients who have just been diagnosed with TB. It is known however, that the HIV status of patients is likely to prolong recovery from TB; therefore patients enrolled to the study must confirm their HIV status. Thus on the analysis stage of the clinical trial, the unstratified logrank test will have the null hypothesis specified as:

H_0 : The survival time of patients allocated to the current drug is not different from the survival time of patients taking a new drug

and is tested against the alternative hypothesis :

H_1 : Survival time of patients differ with respect to the treatment administered.

The hypotheses of the stratified log rank statistics, is specified as:

H_0 : Survival distributions of patients receiving TB treatment and placebo are identical in every stratum of HIV status.

versus

H_1 : Survival distributions of patients receiving the TB treatment and placebo differ in every stratum of HIV status

3.3 RESEARCH DESIGN

The simulation of Weibull distributed censoring times and a lifetime vector will be done independently. Times generated using different parameters and options to the `SimSurv` function form an allocation scheme; to the new drug and the current drug. A strata variable is generated from a uniform distribution.

We suppose that subjects are uniformly accrued during the accrual period and followed up during follow-up period after the completion of accrual. Assuming that censoring occurs only by completion of study, that is, administrative censoring; common censoring variable C_i is a column of 0s and 1s when we observe if censoring time is greater than the survival time. Thus the survival time is the minimum between the observed times and the censoring times.

~~R, as a programming language, is easier to use when compared to SAS especially in data simulation. This makes R more efficient in simulating data when compared to SAS. However it is interesting to learn how SAS's `lifetest` procedure gives detailed output. To obtain the same, one must write many lines in R.~~

3.4 DATA SIMULATION

The programming code for generating survival data is the function `SimSurv` which inherits functions from the `prodlim` package of R.

We assume that the treatment group has a censoring baseline hazard of 0.7 and a survival baseline hazard of 3.3. For the control group, the censoring baseline hazard is set to 0.001 and the survival baseline hazard to 0.4. The following code creates a data frame of a time variable, censoring indicator (event), treatment indicator and a strata variable and then simulates that data frame 1000 times.

Table 2: R simulation code using the `simsurv` function.

```
Lbrary(prodlim)
n<-300;
LRT.hr1=c(NA)
LRT.hr2=c(NA)
SLRT.hr1=c(NA)
SLRT.hr2=c(NA)
LRT<-c(NA)
LRT.pvalues=c(NA)
SLRT.pvalues=c(NA)
SLRT<-c(NA)
mySim <- function(n){
s1 <- SimSurv(n/2,cens.baseline<-0.7,surv.baseline<-3.3)
s2<- SimSurv(n/2,cens.baseline<-0.001,surv.baseline<-0.4)
group <- c(rep(1,(n/2)),rep(2,n/2))
HIV <- as.numeric((runif(n))>.75)
time<-c(s1$time,s2$time)
event<-c(s1$status,s2$status)
result<-data.frame(time,event,group,HIV)
return(result)
}



for(i in 1:1000) {
rt <-mySim(n)
f1 <- survdiff(Surv(rt$time,rt$event)~rt$group)
f2 <- survdiff(Surv(rt$time,rt$event)~rt$group+strata(rt$HIV))
LRT[i] <- f1$chisq
SLRT[i]<- f2$chisq
LRT.pvalues[i]<-pchisq(f1$chisq,1,lower.tail=FALSE)
SLRT.pvalues[i]<- pchisq(f2$chisq,1,lower.tail=FALSE)
LRT.hr1[i]=f1$obs[1]/f1$exp[1]
LRT.hr2[i]=f1$obs[2]/f1$exp[2]
SLRT.hr1[i]=sum(f2$obs[1,])/sum(f2$exp[1,])
SLRT.hr2[i]=sum(f2$obs[2,])/sum(f2$exp[2,])
}
```

3.4.1 SAMPLE SIZE SPECIFICATION

In addition to “small” sample sizes of 30, 50, 80 and 100 we propose generating 5 different data frames of sample sizes of 200, 300, 400, 500, 600, 700, 800, 1000, 5000 and 10000.

TABLE 3: EXAMPLE OF THE GENERATED DATA WITH $n = 30$

time	event	group	HIV
2.50038	1	E	1
1.72980	0	E	0
2.26058	1	E	0
$\vdots$	$\vdots$	$\vdots$	$\vdots$
0.89682	1	C	1
9.45467	1	C	1
0.21690	1	C	1
6.63618	1	C	0
5.11955	0	C	0
5.32739	0	C	0
5.94159	1	C	0

This data will be simulated 1000 times for each sample size.

TABLE 4: CENSORING PATTERN OF THE SIMULATION PROGRAM

Sample Size	**Censoring pattern**
30	26.67%
50	46%
80	48.75%
100	37%
250	38.4%
500	42.8%
1 000	39.6%
5 000	41.88%
10 000	39.65%

3.4.2 ANALYSING THE GENERATED DATA USING SAS

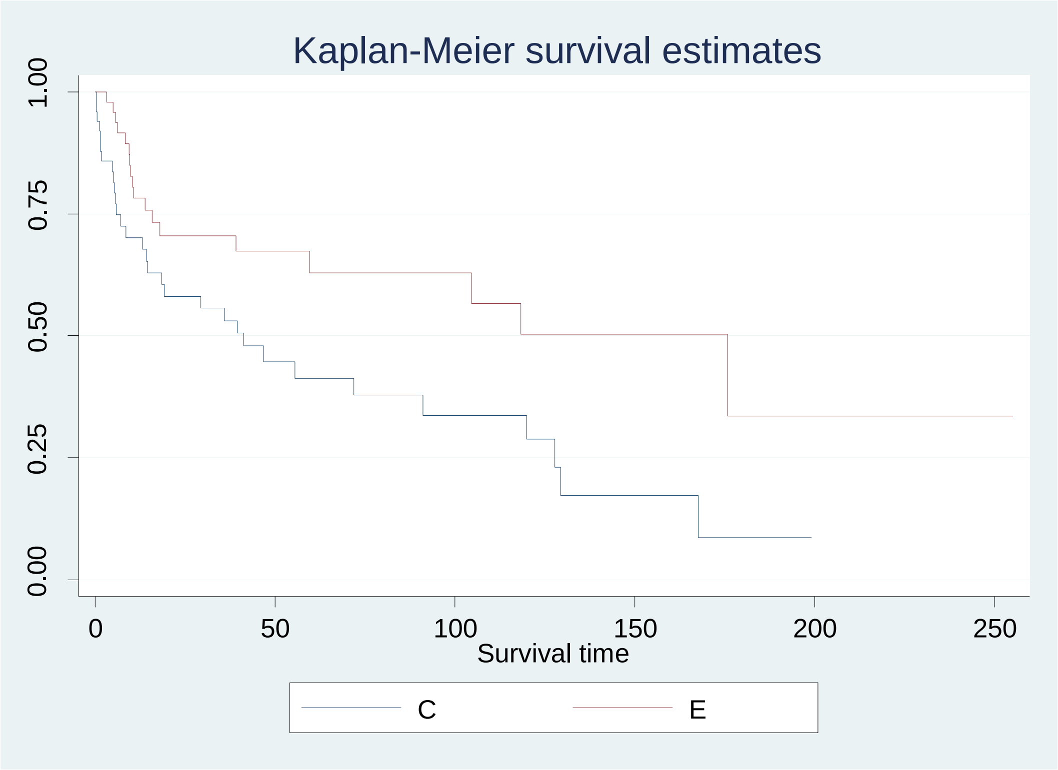
```
The SAS System      12:32 Thursday, January 23, 2012   1

                                      The LIFETEST Procedure
                                      Stratum 1: group = C

                                 Product-Limit Survival Estimates

                                                   Survival
                                                   Standard     Number      Number
                  time     Survival    Failure      Error       Failed       Left
                 0.000       1.0000           0           0        0          15
                 0.127       0.9333      0.0667      0.0644        1        14
                 0.575*           .           .           .        1          13
                 0.749       0.8615      0.1385      0.0911        2          12
                 1.064       0.7897      0.2103      0.1081        3          11
                 1.101*           .           .           .        3          10
                 2.104*           .           .           .        3           9
                 2.184       0.7020      0.2980      0.1268        4           8
                 3.174       0.6142      0.3858      0.1380        5           7
                 4.083*           .           .           .        5           6
                 4.861*           .           .           .        5           5
                 5.832       0.4914      0.5086      0.1558        6           4
                 6.798*           .           .           .        6           3
                 8.634*           .           .           .        6           2
                13.211*           .           .           .        6           1
                22.860            0      1.0000           0        7           0

           NOTE: The marked survival times are censored observations.

                            Summary Statistics for Time Variable time

                                        Quartile Estimates
                                        Point     95% Confidence Interval
                           Percent    Estimate      [Lower      Upper)

                                75      22.860       5.832      22.860
                                50       5.832       2.184      22.860
                                25       2.184       0.749      22.860

                                        Mean    Standard Error
                                      12.559             3.334
```

```
The SAS System      12:32 Thursday, January 23, 2012   2

                                      The LIFETEST Procedure
                                      Stratum 2: group = E
                                 Product-Limit Survival Estimates

                                                   Survival
                                                   Standard     Number      Number
                  time     Survival    Failure      Error       Failed       Left

                 0.000       1.0000           0           0        0          15
                 1.209*           .           .           .        0          14
                 2.552*           .           .           .        0          13
                 3.035       0.9231      0.0769      0.0739        1          12
                 4.371       0.8462      0.1538      0.1001        2          11
                 5.490*           .           .           .        2          10
                15.601*           .           .           .        2           9
                26.094*           .           .           .        2           8
                55.308       0.7404      0.2596      0.1321        3           7
                59.380       0.6346      0.3654      0.1497        4           6
                68.331       0.5288      0.4712      0.1578        5           5
               113.429       0.4231      0.5769      0.1577        6           4
               121.765       0.3173      0.6827      0.1496        7           3
               124.333*           .           .           .        7           2
               169.996*           .           .           .        7           1
               218.812            0      1.0000           0        8           0

                    NOTE: The marked survival times are censored observations.

                            Summary Statistics for Time Variable time
                                        Quartile Estimates

                                        Point     95% Confidence Interval
                           Percent    Estimate      [Lower      Upper)

                                75     218.812      68.331     218.812
                                50     113.429      55.308     218.812
                                25      55.308       4.371     113.429

                  The SAS System      12:32 Thursday, January 23, 2012   3
                                  Test of Equality over Strata
                                                               Pr >
                            Test      Chi-Square      DF    Chi-Square
                            Log-Rank      6.6896       1      0.0097
                            Wilcoxon      5.4645       1      0.0194
                            -2Log(LR)    17.2157       1      <.0001
```

The log rank tests for equality of survival distributions is significant at 5% level of significance (χ^2 =6.6896, $p = 0.0097$). Individuals enrolled into the treatment group (group=E) tend to live longer than those enrolled into the control group.

Kaplan-Meier curves provide insight into the shape of the survival function for each group and give an idea of whether or not the survival functions are approximately parallel.

FIGURE 1: KAPLAN-MEIER CURVES FOR COMPARING TWO TREATMENT GROUPS

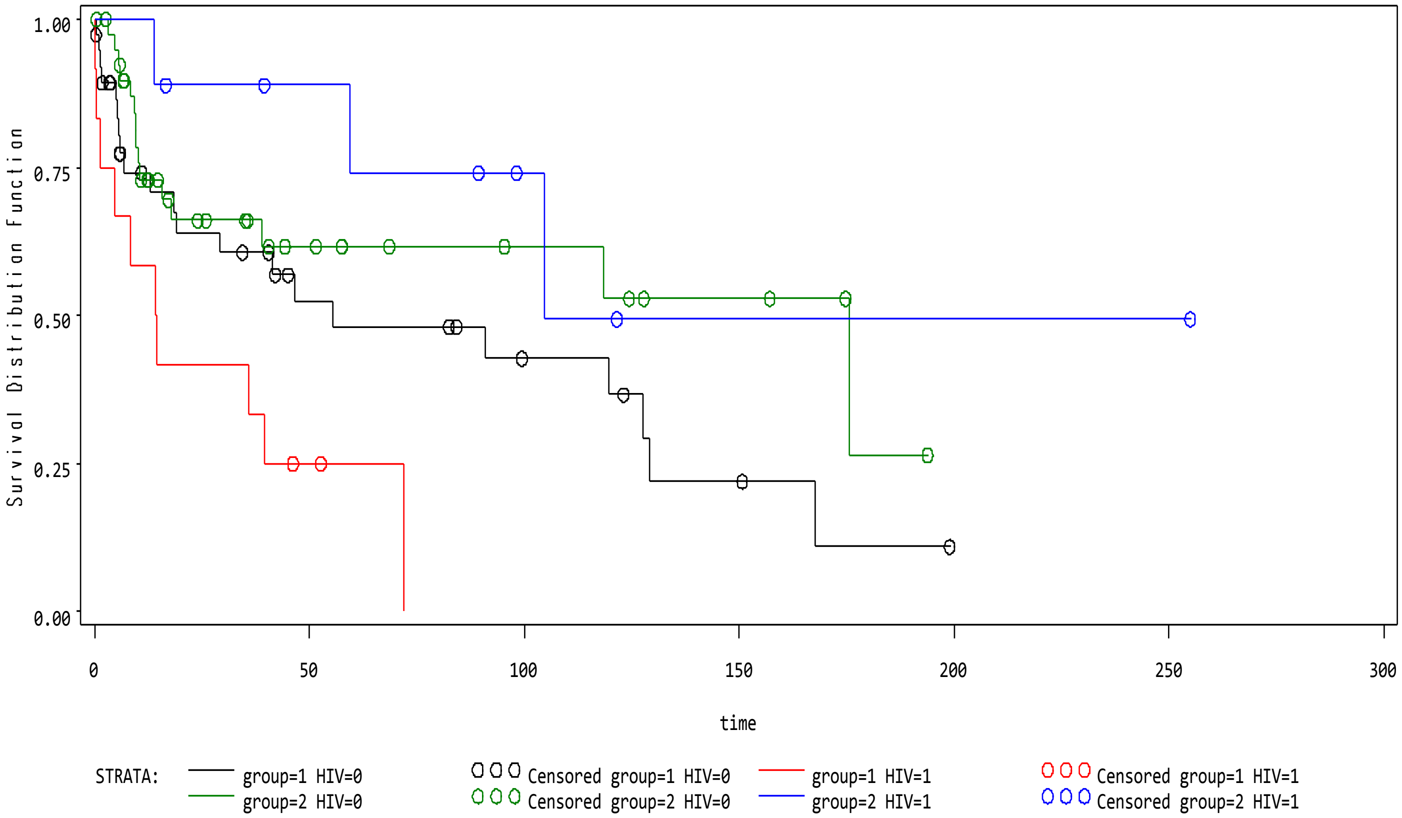


To increase power and protect against baseline imbalances, one could stratify by a variable with known prognostic value. Suppose that HIV status is thought to be related to survival time, and we want to study the treatment effect while adjusting for the HIV status of patients.

```
survdiff(Surv(result$time,result$event)~result$group+strata(result$HIV))
Call:
survdiff(formula = Surv(time, event) ~ group + strata(HIV), data = result)

         N Observed Expected (O-E)^2/E (O-E)^2/V
group=C 15        7      3.5      3.49      6.03
group=E 15        8     11.5      1.06      6.03

 Chisq= 6.03  on 1 degrees of freedom, p= 0.014
```

The strata effect is significant, chi-square = 6.03 with a *p*-value of 0.014. This means that HIV positive patients do not respond at the same rate to the TB treatment as HIV negative patients do.

FIGURE 2: KAPLAN-MEIER CURVES FOR COMPARING NEW DRUG AND A CURRENT DRUG STRATIFIED BY HIV STATUS



3.4.3 COMPUTING HAZARD RATES

Hazard rates can be read from R output and the hazard ratio be computed using the formulae given on **page 7**. Observed numbers are marked in bold and expected numbers are underlined.

```
Call:
survdiff(formula = Surv(result$time, result$event) ~ result$group)

                N Observed    Expected (O-E)^2/E (O-E)^2/V
result$group=1 50       31    22.2      3.44      6.35
result$group=2 50       18    26.8      2.86      6.35

 Chisq= 6.4  on 1 degrees of freedom, p= 0.0117
```

The hazard rate for group1 is $h_1 = 31/22.2 = 1.396396$ and the hazard rate for the second group is $h_2 = 18/26.8 = 0.6716418$

The hazard ratio is the hazard rate of the current drug divided by the hazard rate of the new drug. For our example, $HR = 2.079078$, thus anytime, twice as many patients in the treatment group are having an event proportionally to the comparator group.

CHAPTER 4: RESULTS

For the unstratified logrank test we use the `powerCT` function [19], from the package `powerSurvEpi` of R [21].

The following code simulates 1000 data frames for a specified sample size and then computes power for the USLRT and SLRT.

```
for(i in 1:1000) {
result <-mySim(n)
f1 <- survdiff(Surv(result$time,result$event)~result$group)
f2 <-
survdiff(Surv(result$time,result$event)~result$group+strata(result$HIV))
p200LRT[i] <- f1$chisq
p200SLRT[i]<- f2$chisq
p200LRT.pvalues[i]<-pchisq(f1$chisq,1,lower.tail=FALSE)
p200SLRT.pvalues[i]<- pchisq(f2$chisq,1,lower.tail=FALSE)
p200LRT.hr1[i]=f1$obs[1]/f1$exp[1]
p200LRT.hr2[i]=f1$obs[2]/f1$exp[2]
p200SLRT.hr1[i]=sum(f2$obs[1,])/sum(f2$exp[1,])
p200SLRT.hr2[i]=sum(f2$obs[2,])/sum(f2$exp[2,])
p200hr[i]=p200LRT.hr1[i]/p200LRT.hr2[i]
rr=p200LRT.hr1[i]/p200LRT.hr2[i]
p200LRT.power[i]=(powerCT(Surv(result$time, result$event) ~
result$group,dat=result,nE = n/2, nC = n/2, RR = rr))$power

}
p200=p200LRT.power
```

TABLE 5: UNSTRATIFIED LOGRANK TEST, NUMBER OF SIGNIFICANT TESTS

$\alpha = 0.05.$

N	30	50	80	100	200	300	400	500	600	700	800	1000	5000	10000
# of significant tests	761	923	992	999	ALL	ALL	ALL	ALL	ALL	ALL	ALL	ALL	ALL	ALL

As the sample size reaches 200 under these simulation settings, the logrank and the stratified logrank test became significant in all 1000 simulations.

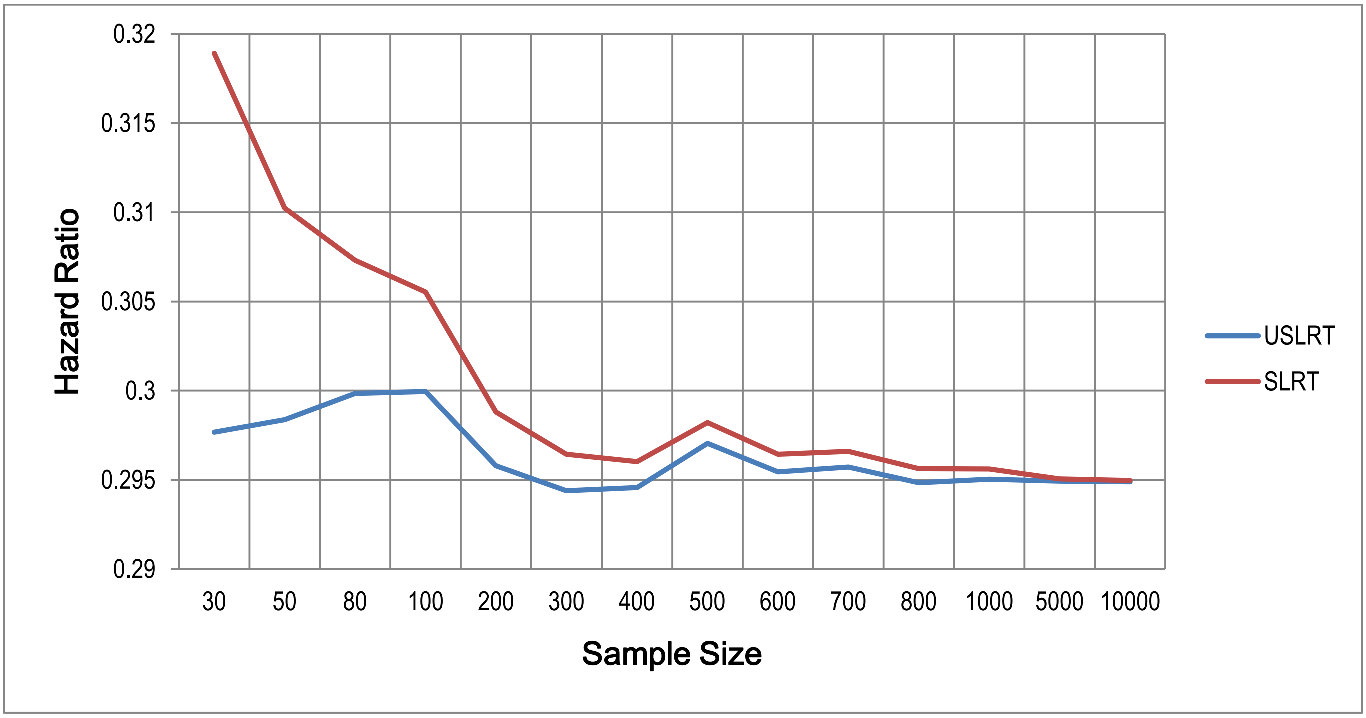
TABLE 6: STRATIFIED LOGRANK TEST, NUMBER OF SIGNIFICANT TESTS

$\alpha = 0.05.$

N	30	50	80	100	200	300	400	500	600	700	800	1000	5000	10000
# of significant tests	745	917	992	996	ALL	ALL	ALL	ALL	ALL	ALL	ALL	ALL	ALL	ALL

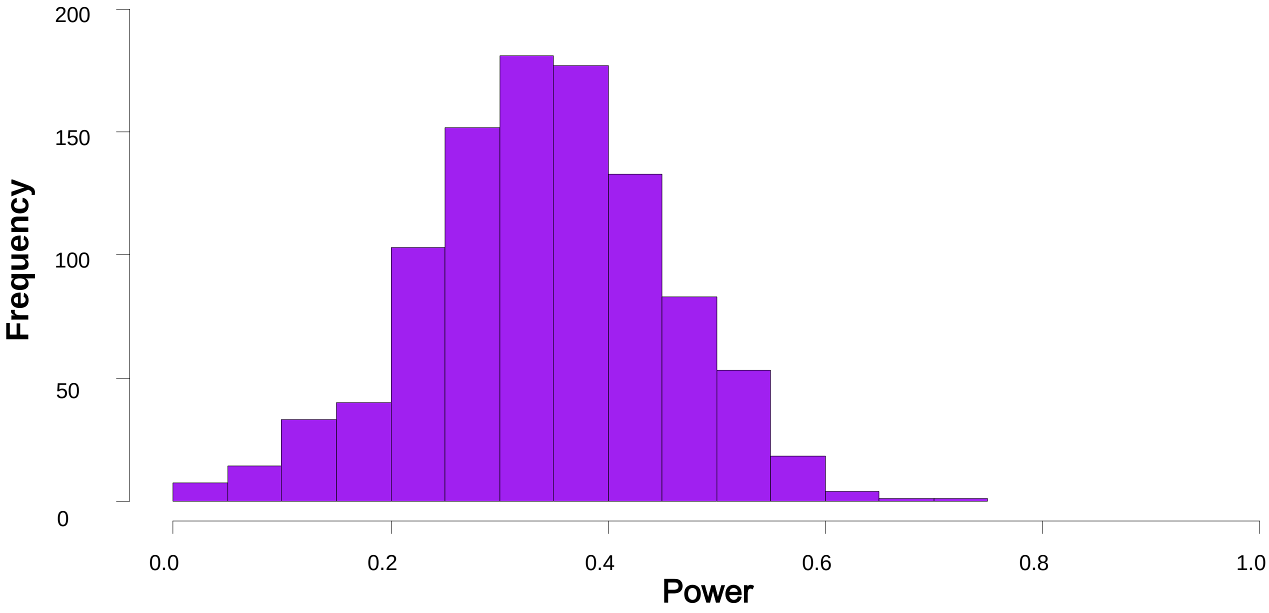
However, the logrank test has more significant tests in any sample size setting when compared to the stratified logrank test. That is, for a sample size of $n = 30$, 761 out of a thousand tests were significant for the simple logrank test while 745 out of 1000 tests were significant in the SLRT.

FIGURE 3: COMPARISON OF THE HAZARD RATIOS OF THE USLRT AND THE SLRT.



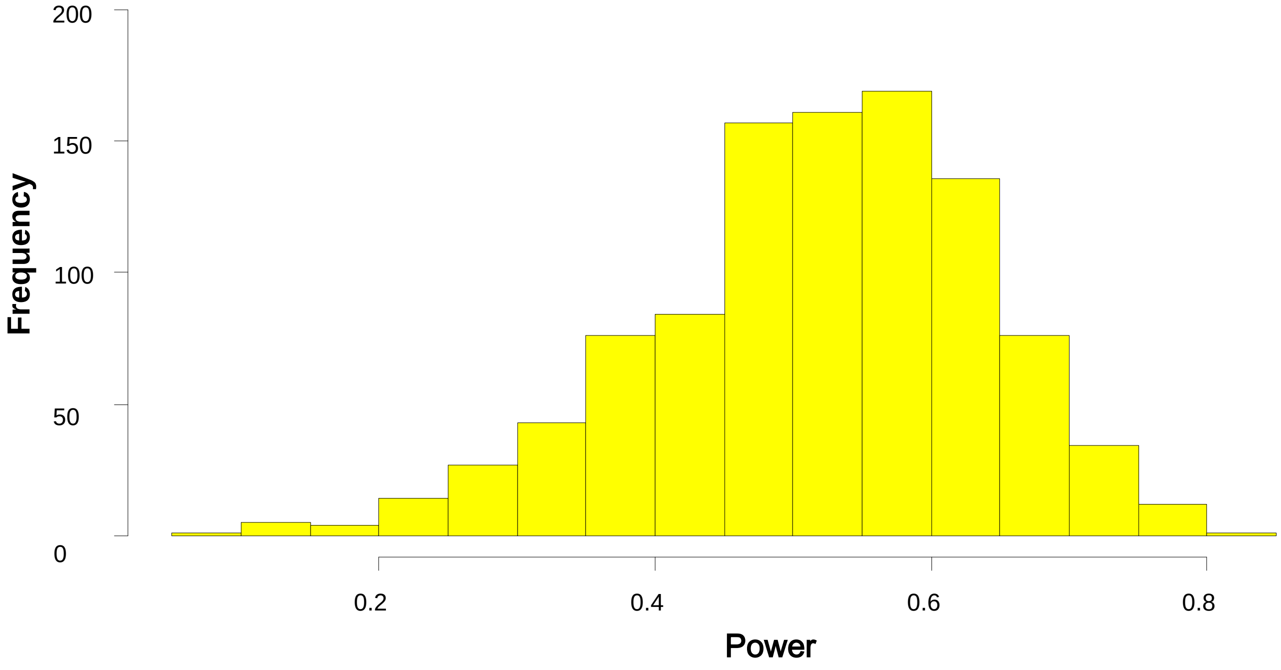
For a two strata study the power of the ULRT is significantly higher than that of SLRT. For a sample size of less than 300, the stratified logrank test yields consistently higher power compared to the unstratified logrank test. This means that for small sample sizes, one can achieve more power if he uses a stratified version of the logrank test than the unstratified logrank test. Stratification does not necessarily increase the power of the logrank test when the sample size is large.

FIGURE 4: POWER VALUES FOR A USLRT (N = 30) USING 1000 SIMULATIONS



When using a sample size of $n = 30$, the logrank test yields less power of roughly less than 60% in all 1000 simulations. When the sample size is increased to 50, the test gains power in such a way that the histogram is centred between 0.5 and 0.6. For $n = 50$, only one case has power greater that 80%.

FIGURE 5: POWER VALUES FOR A USLRT (N = 50) USING 1000 SIMULATIONS



For a sample size of $n = 80,$ 226 cases out of a 1000 had power greater than 80%

```
> table(p80> 0.8)

FALSE  TRUE
  774   226
```

TABLE 7: NUMBER OF INSTANCES WHEN USLRT ACHIEVED AT LEAST 80% POWER

N	30	50	80	100	200	300	400	500	600	700	800	1000	5000	10000
# of instances	0	1	226	637	ALL	ALL	ALL	ALL	ALL	ALL	ALL	ALL	ALL	ALL

A power of 0.8 or more is acceptable in power analysis. For sample sizes greater than 100, we note that good power is achieved in most tests. Therefore if one can use a sample size of $n = 200$, under these settings, one will be confident that the LR test will have enough power to detect a false null hypothesis.

FIGURE 6: POWER VALUES FOR A USLRT (N = 80) USING 1000 SIMULATIONS

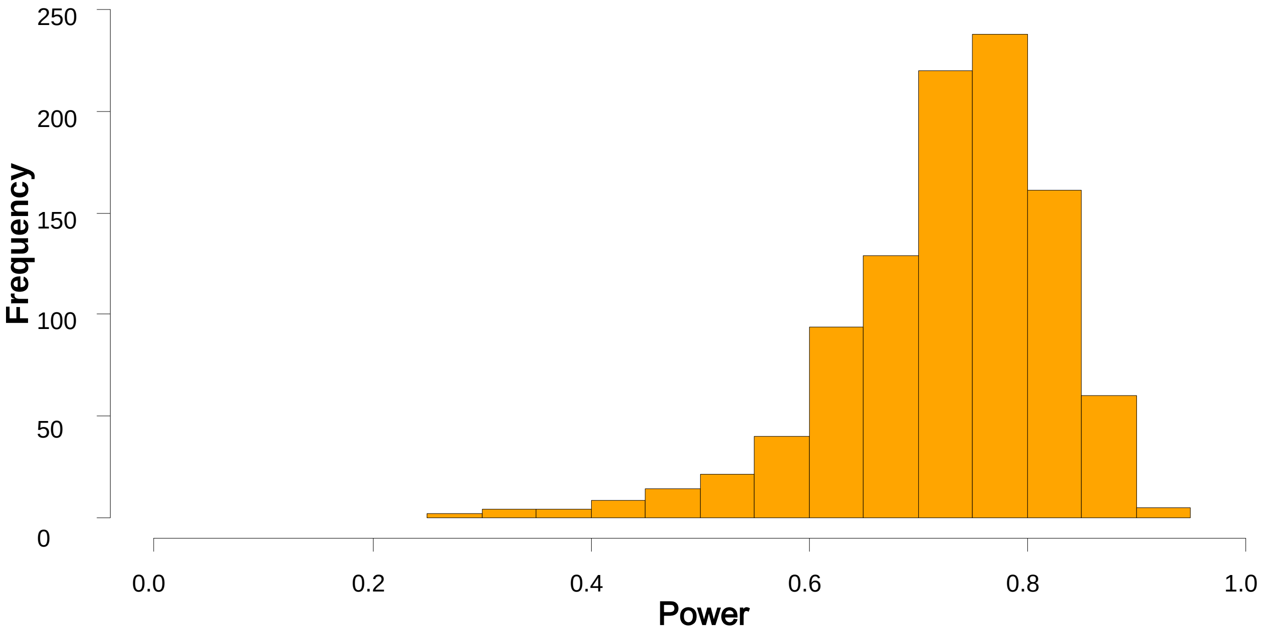


FIGURE 7: POWER VALUES FOR A USLRT (N = 100) USING 1000 SIMULATIONS

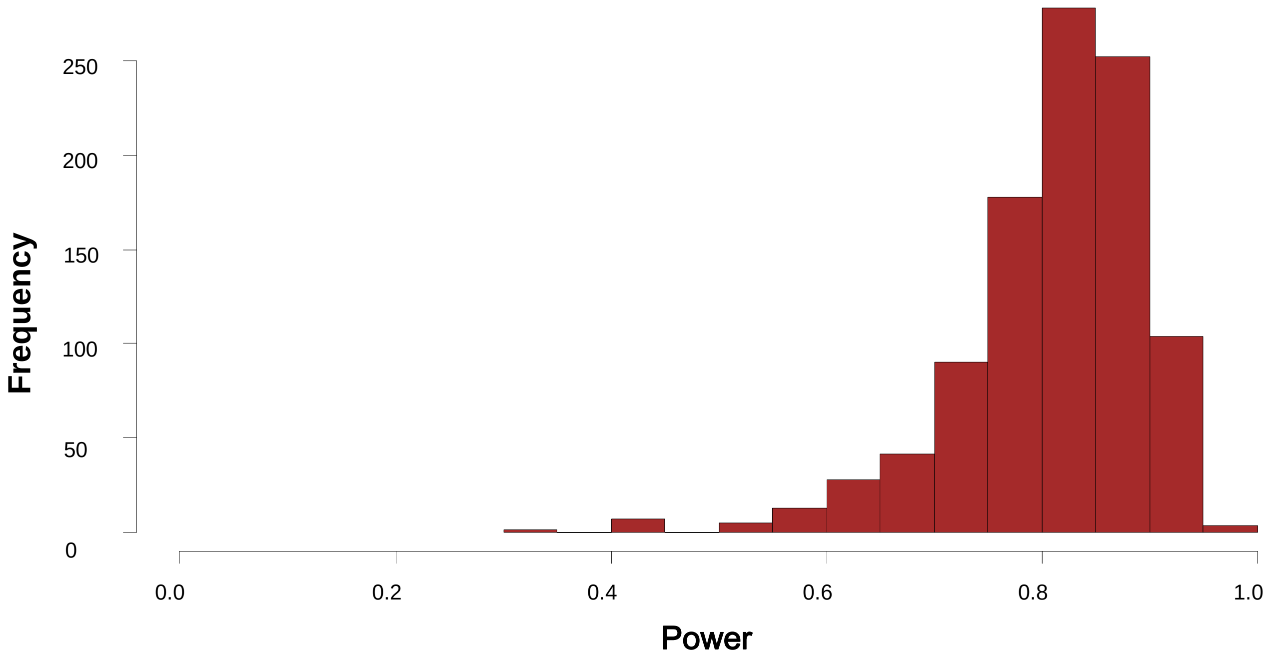


FIGURE 8: POWER VALUES FOR A USLRT (N = 300) USING 1000 SIMULATIONS

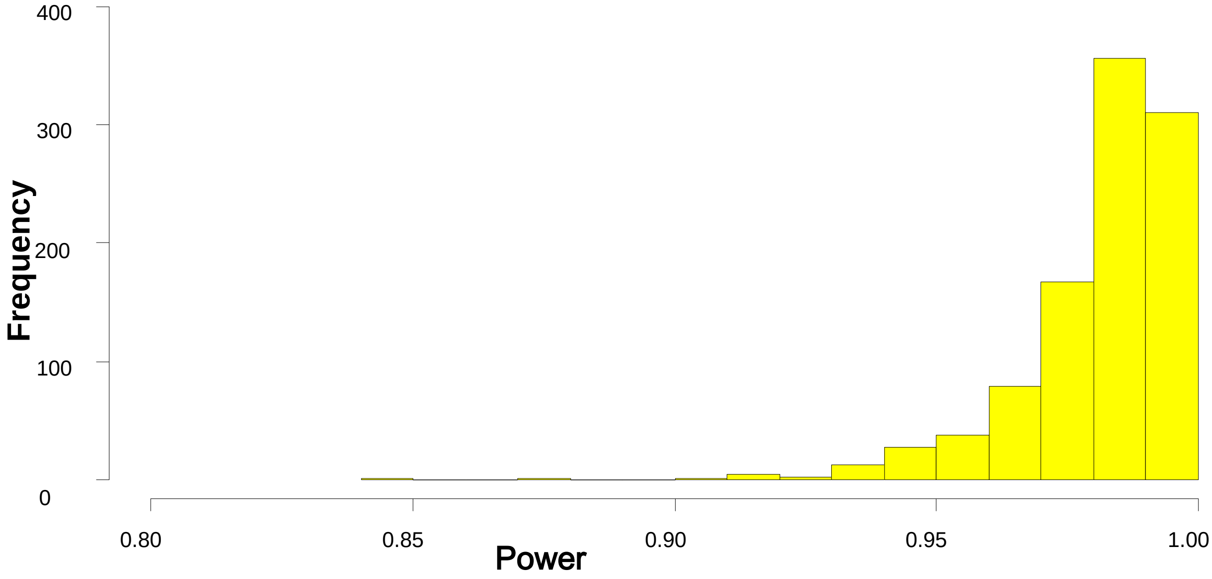


FIGURE 9: POWER VALUES FOR AN USLRT (N = 600) USING 1000 SIMULATIONS

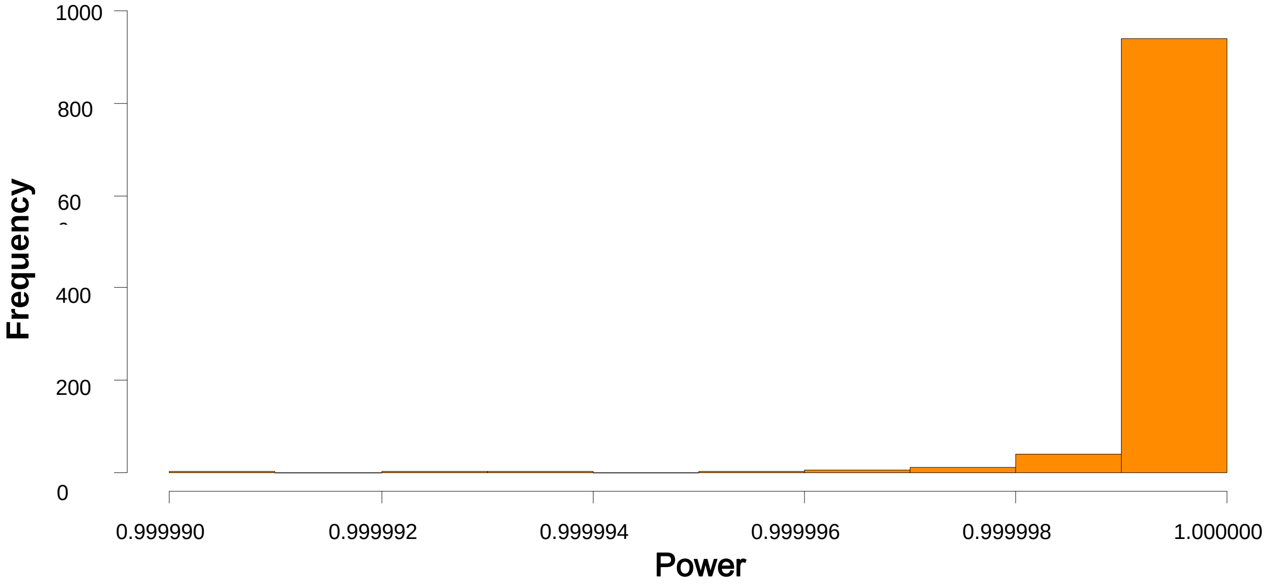
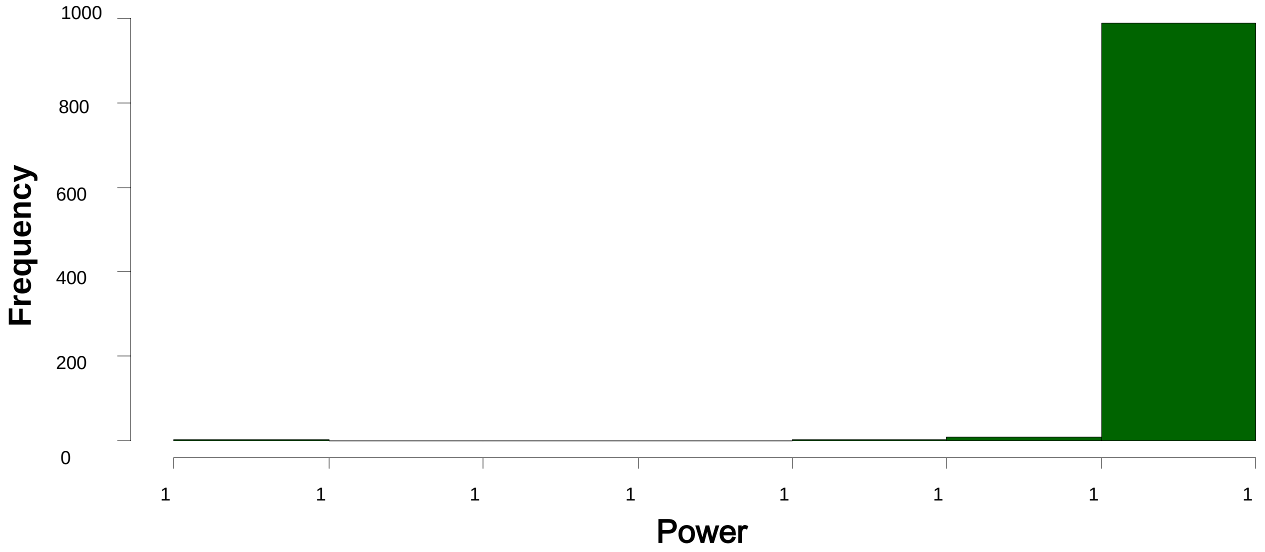


FIGURE 10: POWER VALUES FOR AN USLRT (N = 800) USING 1000 SIMULATIONS



As sample size increases, the logrank test gains more power. Histograms of sample sizes $N = 1000$, $N = 5000$ and $N = 10\,000$ are not different from

FIGURE 10 above. This suggests that, for a clinical trial having these settings, it would be a waste of resources to enrol 1000 or more patients when in fact the logrank test achieves same power by using $N = 500$ through $N = 800$.

4.1 DISCUSSION

Since a clinical trial desires that the treatment group should perform better than the control group, that is, we desire that the condition $h_2 > h_1$ be true, then increasing the sample size will increase the power of both SLRT and ULRT. We cannot come up with a rule of thumb to say how large the sample size must be to be considered “large” since the power depends on the hazard ratio, which in turn depends on the hazard rates. However, if we know the hazard ratio beforehand, sample size and power estimation becomes easy.

4.2 SOLVING FOR SAMPLE SIZE AND POWER

Calculating the power of the USLRT depends solely on the hazard rates of the two groups but generally the logrank test gains power as the sample size increase except when hazard rates are equal (then power will always be equal to the significance level). How will one know whether the logrank test when employed, will yield greatest power on a given sample size? We answer this question by using the PASS statistical package.

This PASS module uses the method of [14] because of its generality. The method is based on a Markov model that yields the asymptotic mean and variance of the logrank statistic under very general conditions.

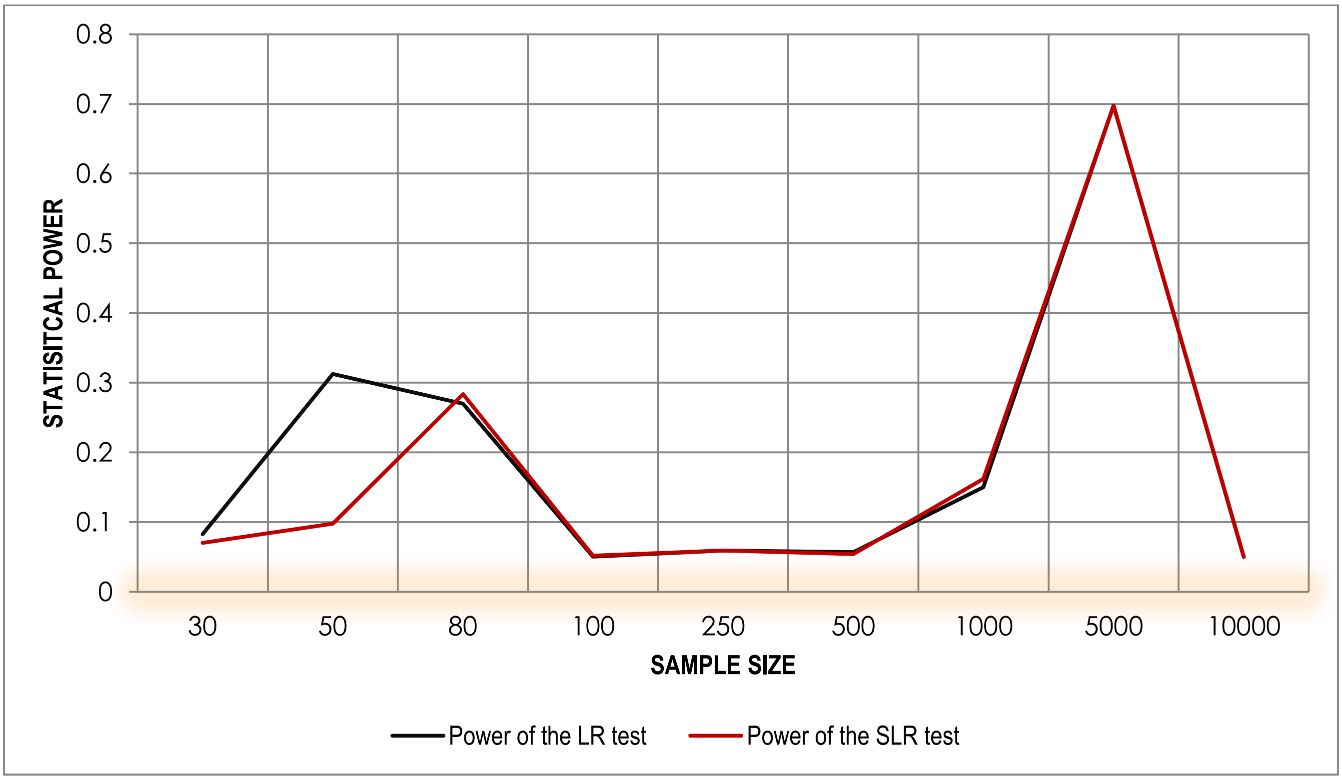
Accrual time, follow-up time, loss during follow up, noncompliance, and time-dependent hazard rates are parameters that can be set. This package enables one to solve for power, hazard ratio or sample size with little effort.

Setting control lost to 0, treatment lost to 0, accrual time to 2 years with an equal accrual pattern, control switch to treatments to zero as well as treatments switch to controls, this PASS module yielded the results tabulated in **Table 8** below.

TABLE 8: COMPUTED POWER OF THE USLRT AND SLRT

Sample size	**Hazard Rates**	**Power** of the **LR** test	**Power** of the **SLR** test
30	1.09 0.84	0.0826	0.07
50	1.165 0.898	0.3125	0.0975
80	1.25 0.89	0.2697	0.2835
100	0.997 1.003	0.0502	0.0516
250	1.02 0.98	0.0589	0.0589
500	1.01 0.985	0.0568	0.0543
1000	1.035 0.969	0.1498	0.1621
5000	1.04 0.96	0.6977	0.6977
10000	1 1	0.05	0.05

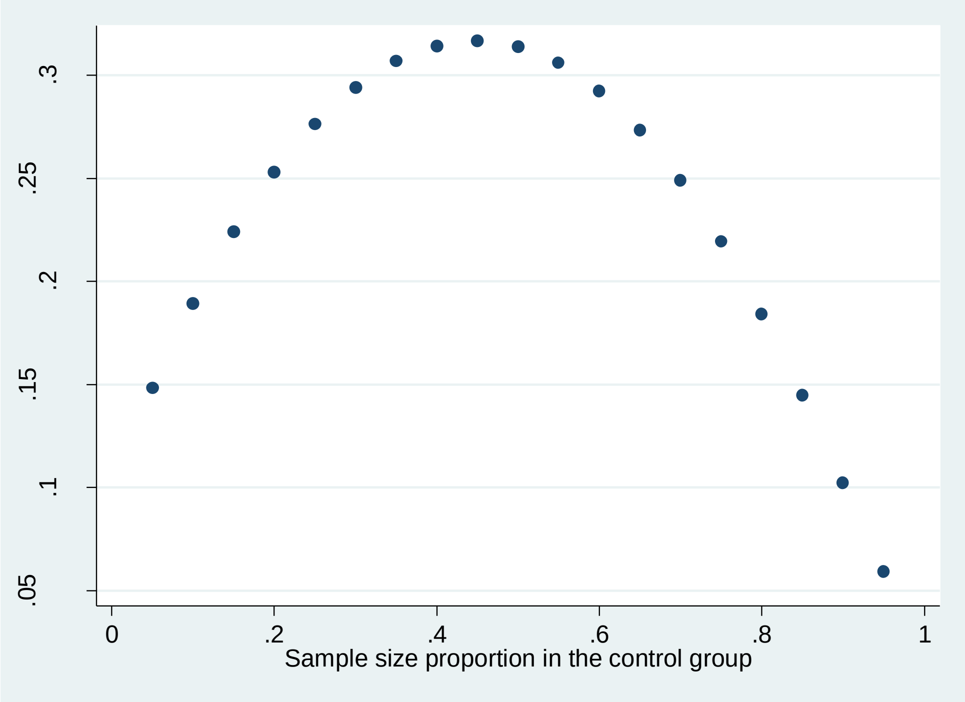
FIGURE 11: THE BEHAVIOUR OF THE USLRT/SLRT ON DIFFERENT SAMPLE SIZES



The results of this graph concord with the conclusion given in **Figure 3**, on page 24. Because in a two strata study, the power of the logrank test and that of the stratified logrank test behave the same for large sample sizes ($n \geq 80$), the generalisation is that when we derive conclusions based on the unstratified logrank test, such a conclusion also applies to the stratified logrank test.

We also consider whether unequal treatment allocations that we effected in the simulation program could have affected power results. To accomplish this, we compute the power of the logrank test for a sample of size 100 (hazard rates 0.997/1.003) and plot power against different proportions of sample sizes in the control/treatment group. The points on the scatter diagram below form a polynomial curve.

FIGURE 12: UNEQUAL TREATMENT ALLOCATION VERSUS EQUAL TREATMENT ALLOCATION

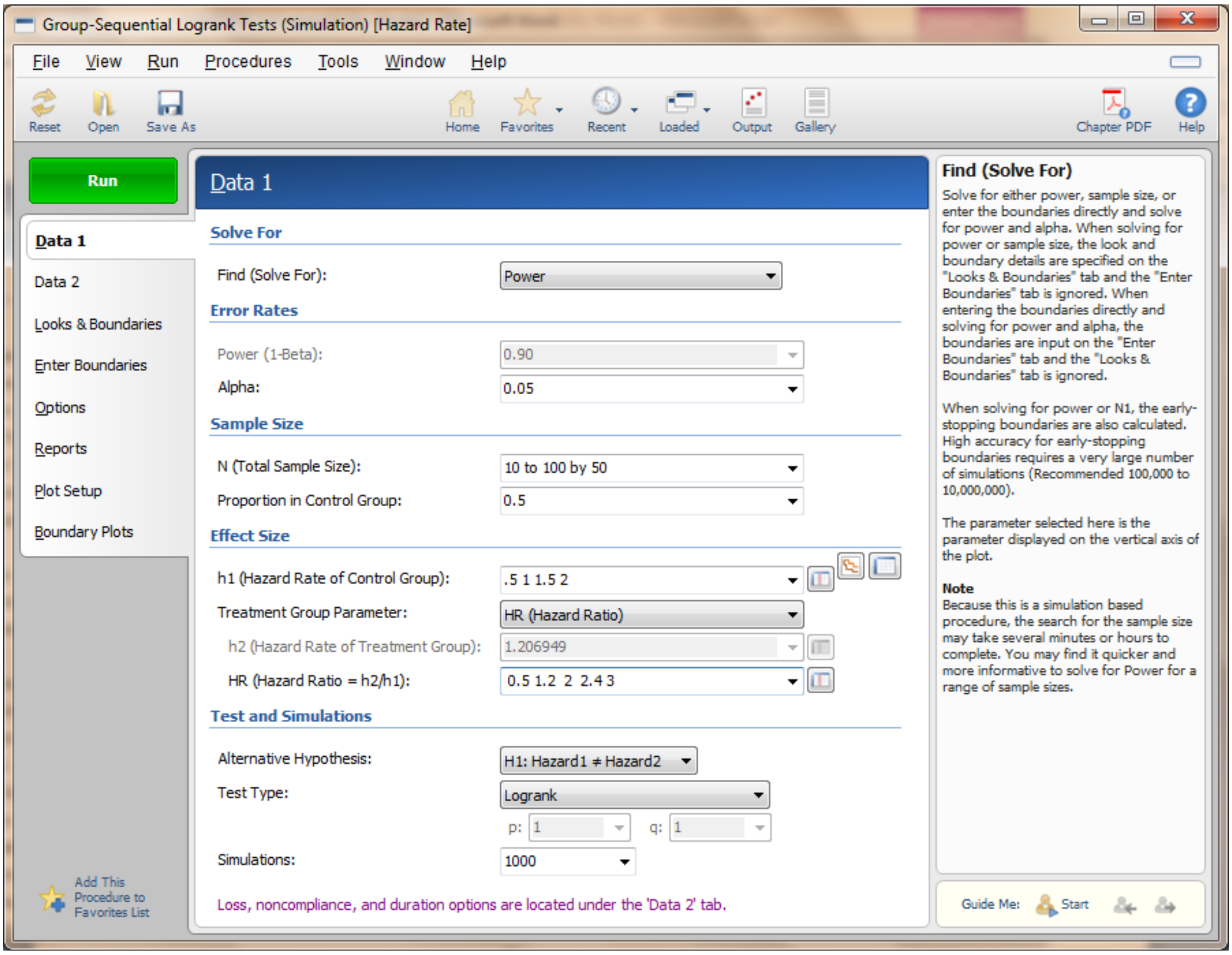


Fitting quadratic regression model for power as response gives the optimum power of 0.3167, attained when the proportion in control group is 0.448. Since treatment allocation for the simulation does not go against the immediate result, we have confidence that power calculations were not affected by weird treatment allocation.

4.3 FURTHER ANALYSIS

For a clinical trial, a researcher will favour a situation whereby the hazard rate of the treatment group is greater than that of the control group. If the researcher wants to investigate the sample sizes necessary to achieve good statistical power (greater than 0.8) and according to this postulation, we feed the PASS module with the necessary parameters and compute the power of the logrank test under the proportional exponential hazards.

FIGURE 13: PASS 2011 WINDOW FOR GROUP SEQUENTIAL LOGRANK TESTS (SIMULATION)



Data 1

Solve For

Find (Solve For): Power

Error Rates

Power (1-Beta): 0.90

Alpha: 0.05

Sample Size

N (Total Sample Size): 10 to 100 by 50

Proportion in Control Group: 0.5

Effect Size

h1 (Hazard Rate of Control Group): .5 1 1.5 2

Treatment Group Parameter: HR (Hazard Ratio)

h2 (Hazard Rate of Treatment Group): 1.206949

HR (Hazard Ratio = h2/h1): 0.5 1.2 2 2.4 3

Test and Simulations

Alternative Hypothesis: H1: Hazard1 ≠ Hazard2

Test Type: Logrank

p: 1 q: 1

Simulations: 1000

Loss, noncompliance, and duration options are located under the 'Data 2' tab.

Find (Solve For)

Solve for either power, sample size, or enter the boundaries directly and solve for power and alpha. When solving for power or sample size, the look and boundary details are specified on the "Looks & Boundaries" tab and the "Enter Boundaries" tab is ignored. When entering the boundaries directly and solving for power and alpha, the boundaries are input on the "Enter Boundaries" tab and the "Looks & Boundaries" tab is ignored.

When solving for power or N1, the early-stopping boundaries are also calculated. High accuracy for early-stopping boundaries requires a very large number of simulations (Recommended 100,000 to 10,000,000).

The parameter selected here is the parameter displayed on the vertical axis of the plot.

Note

Because this is a simulation based procedure, the search for the sample size may take several minutes or hours to complete. You may find it quicker and more informative to solve for Power for a range of sample sizes.

```
                  Group Sequential Survival Power Analysis using Simulation
Scenario 23 Numeric Results for Group Sequential Testing Hazard 1 = Hazard 2.
Hypotheses: H0: Hazard1=Hazard2; H1: Hazard1<>Hazard2
Test Statistic: Logrank Test
Alpha-Spending Function: O'Brien-Fleming Analog
Beta-Spending Function: None
Futility Boundary Type: None
Number of Looks: 5
Simulations: 1000
Numeric Summary for Scenario 23

----------------- Power ------------------    ------------------------- Alpha ---------------------------
Value         95% LCL    95% UCL       Target      Actual    95% LCL    95% UCL          Beta
0.183           0.159      0.207        0.050       0.059      0.044      0.074         0.817

                                                Accrual   Accrual     Total
N1            N2       HR        h1       h2       Time   Pattern      Time
55            55    1.200     1.000    1.200        2.0     Equal       5.0

                              ---------------- Noncompliance ----------------
Loss1        Loss2      Prop 1        h1     Prop 2          h2
0.000        0.000       0.000     1.000      0.000       1.000
```

```
Scenario 24 Numeric Results for Group Sequential Testing Hazard 1 = Hazard 2.
Numeric Summary for Scenario 24

----------------- Power ------------------    ------------------------- Alpha ---------------------------
Value         95% LCL    95% UCL       Target      Actual    95% LCL    95% UCL          Beta
0.223           0.197      0.249        0.050       0.046      0.033      0.059         0.777

                                                Accrual   Accrual     Total
N1            N2       HR        h1       h2       Time   Pattern      Time
80            80    1.200     1.000    1.200        2.0     Equal       5.0

                              ---------------- Noncompliance ----------------
Loss1        Loss2      Prop 1        h1     Prop 2          h2
0.000        0.000       0.000     1.000      0.000       1.000
```

The above computer output is an edited part of 162 pages of the PASS output on power analysis. The results are summarized below.

h_1 is the hazard rate for the control group (*set to vary*)

h_2 is the hazard rate for the treatment group (*set to vary*)

H is the hazard ratio, h_2/h_1

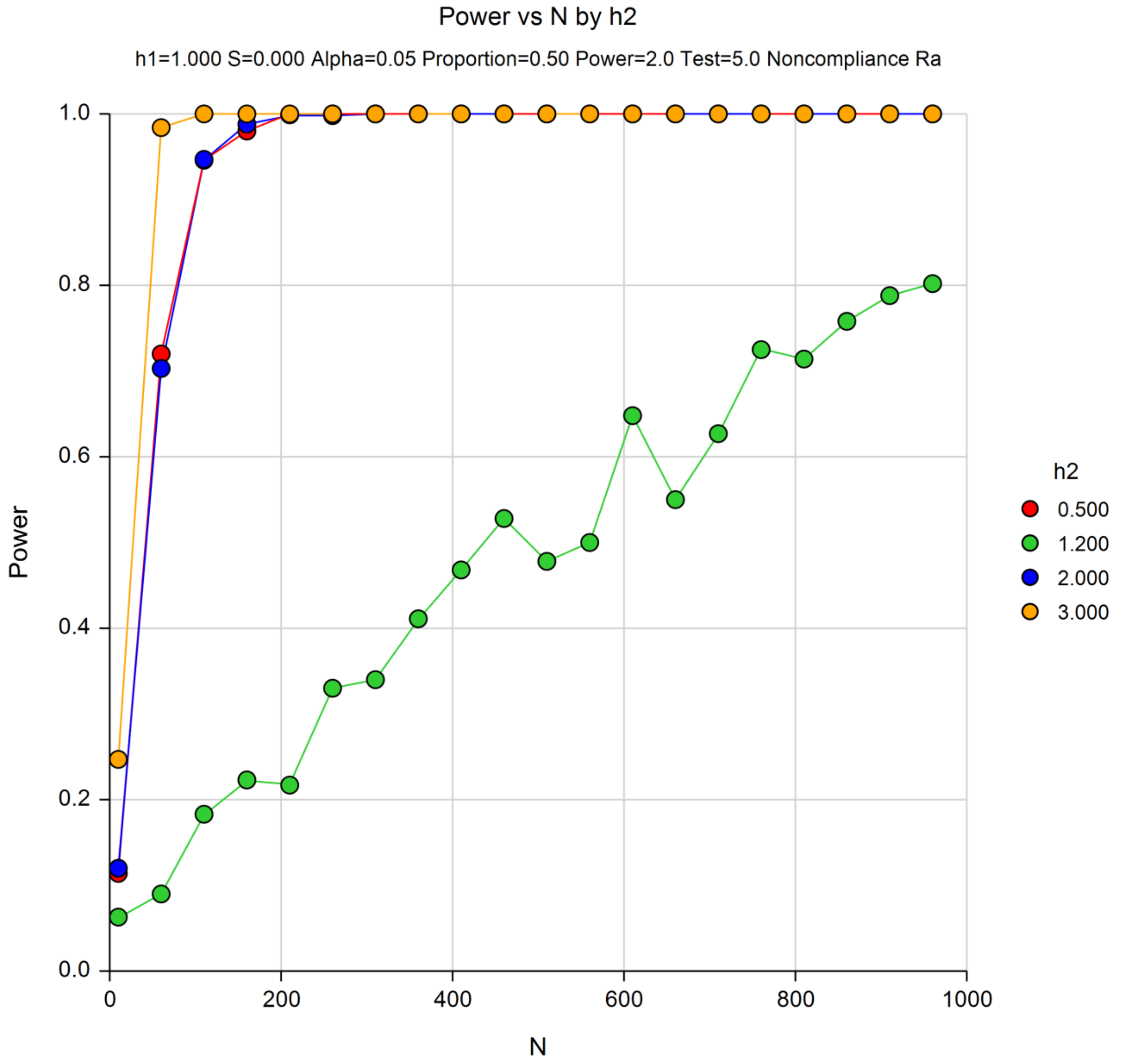
alpha is the significance level (*set to* 0.05)

S is the proportion of subjects lost in the treatment group (*set to zero*)

Proportion is the proportion of subjects in the control group (*set to* 0.5 that is, equal treatment allocation)

Noncompliance Ration is the proportion of noncompliant subjects in the control group

FIGURE 14: POWER VERSUS SAMPLE SIZE BY HAZARD RATE OF THE TREATMENT GROUP

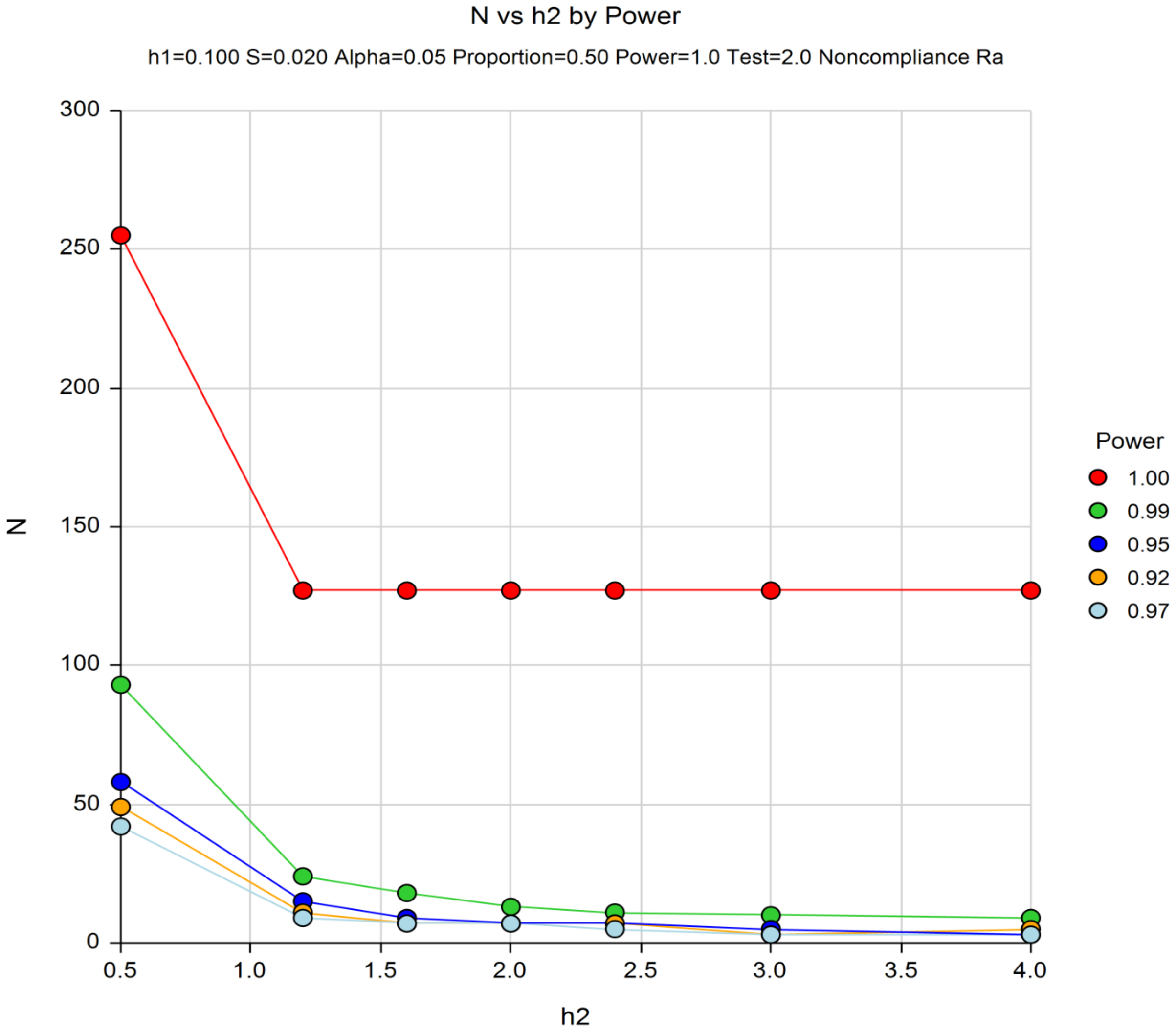


The green line $h_2 = 1.2$ (hence hazard ratio $= h_2/h_1 =$ 1.2), suggest that the power of the USLRT struggles to pass the 80% power border at a slow rate. For a clinical trial with these settings, it would need roughly 980 patients for the logrank test to achieve 80% power.

However if the postulated hazard ratio is 0.5, 3 or 2, the power of the logrank test increases steeply to 0.8 before a sample size of 100 after which the maximum power of 1 will be achieved for bigger sample sizes. A hazard rate of $h_2 = 0.5$ against $h_1 = 1, 2, \cdots$ means that the control group is doing better than the treatment group and thus the hazard ratios contribute to the highly increasing power.

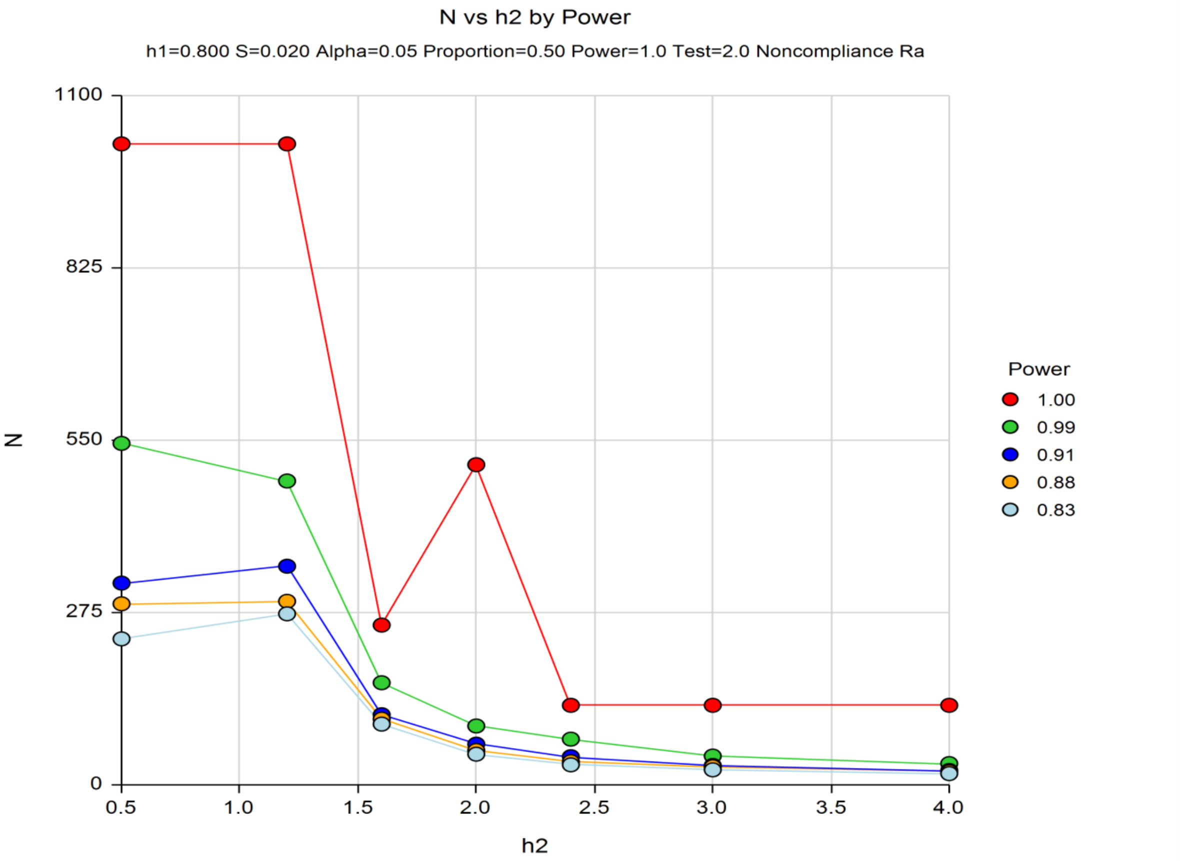
When solving for sample size, the charts appear as shown below:

FIGURE 15: SAMPLE SIZE VERSUS TREATMENT HAZARD RATE BY POWER



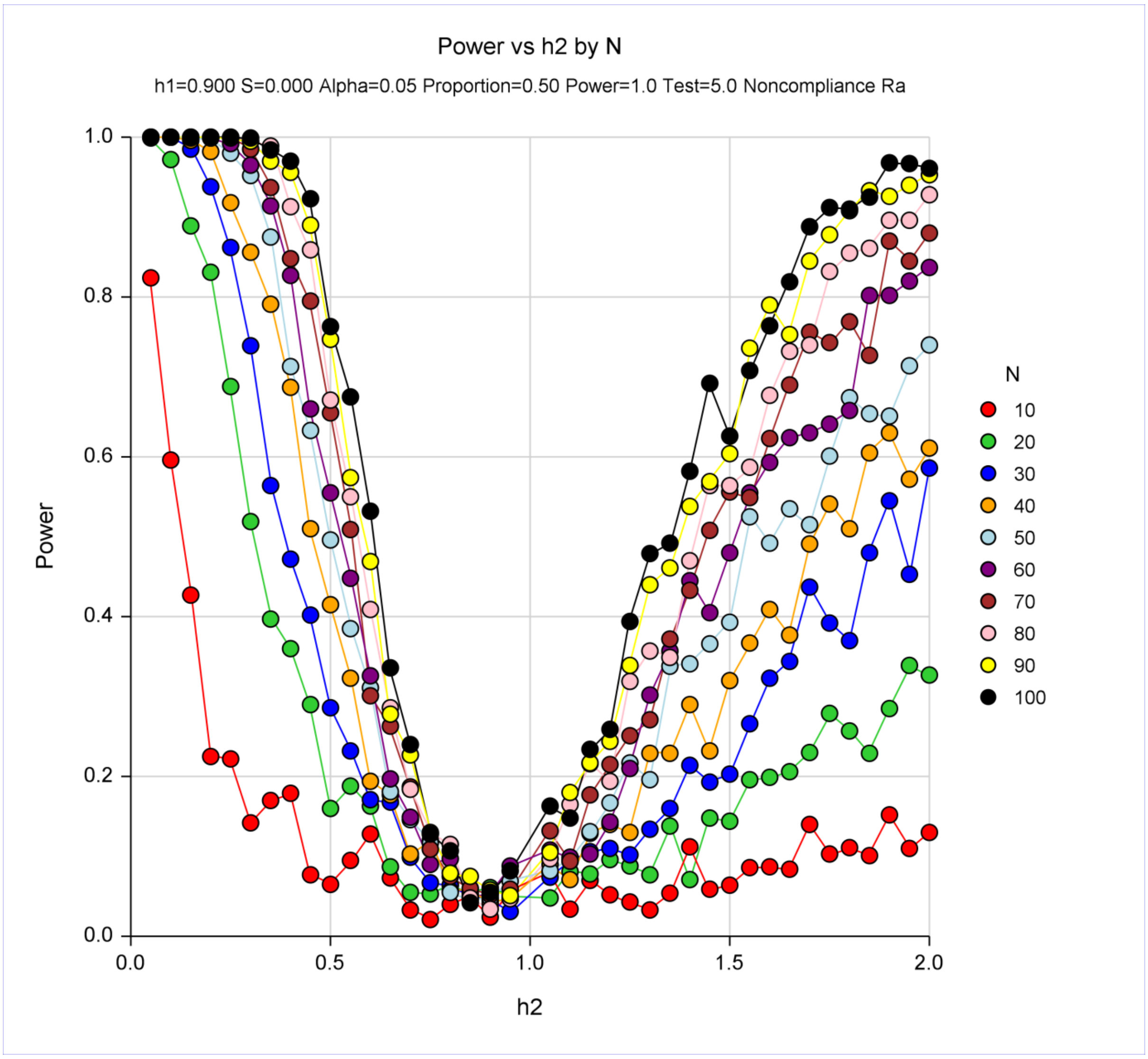
Given that the hazard rate of the control group is 0.1, a red line means that; one will achieve maximum power (power of 1) for all cases when $h_2 > 1.2$ by using a sample size of $N \simeq 125.$ For a treatment hazard rate of less than 1.2, one needs more subjects to achieve maximum power. For example, one will need 260 patients to achieve a power of approximately 1 when the hazard rate in the treatment group is 0.5 (this means that the hazard ratio is close to 1). A similar interpretation applies to the graph below where the hazard rate of the control group is 0.8

FIGURE 16: SAMPLE SIZE VERSUS THE TREATMENT HAZARD RATE BY POWER



For fixed h_1, one can achieve maximum power by using 1000 patients when the treatment hazard rate is 0.5. When the hazard ratio of two groups is greater than 1.875 (that is, $h_2 > 1.5$), the logrank test can achieve an acceptable power of 83% using a sample size of 100 patients while it is possible to achieve 99% power using a sample size of 140 patients under the same settings.

FIGURE 17: RELATIONSHIP OF SAMPLE SIZE AND POWER BY TREATMENT HAZARD RATE



Since $HR = h_2/h_1 = h_2/0.9 =$ 0.05, 0.1, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45… 1.85, 1.9, 1.95, 2. We see from the above graph that as long as h_2/h_1 or $(h_1/h_2)^{-1}$ wonders away from unity, the power of the logrank test increases. Given that there is a difference between the two drugs (as suggested by the hazard rates), using sample sizes of $N = 60$ or more, ensures that the logrank power will reach a comfortable boundary of 80% when the hazard ratio exceeds 1.75 (on average). Power values appearing when $h_2 \leq 0.9$ suggest that the current drug is doing better than the new drug which is an unfavourable condition.

4.4 APPLICATIONS

4.4.1 EXAMPLE1: POWER CALCULATION FOR VETERAN DATA

Veterans' Administration Lung Cancer study is a randomised trial of two treatment regimens for lung cancer (standard and test treatment) on 137 patients. Patients were followed up for 3 years and the outcome event is death [13]. This dataset (veteran) is found in the survival package of R.

Unstratified logrank test results

```
> survdiff(Surv(time,status)~trt,data=veteran)
Call:
survdiff(formula = Surv(time, status) ~ trt, data = veteran)

       N Observed Expected (O-E)^2/E (O-E)^2/V
trt=1 69       64     64.5   0.00388   0.00823
trt=2 68       64     63.5   0.00394   0.00823

 Chisq= 0.008  on 1 degrees of freedom, p= 0.928
```

Stratified logrank test results

```
> survdiff(Surv(time,status)~trt+strata(prior),data=veteran)
Call:
survdiff(formula = Surv(time, status) ~ trt + strata(prior), 
    data = veteran)

       N Observed Expected (O-E)^2/E (O-E)^2/V
trt=1 69       64     65.5    0.0365     0.079
trt=2 68       64     62.5    0.0383     0.079

 Chisq= 0.079  on 1 degrees of freedom, p= 0.779
```

In this example, the hazard ratios of both the USLR and SLRT are close to unity suggesting that there is no difference in treatment received neither does stratification by prior cause a difference. We use the logrank test to check if the survival curves are significantly different.

The unstratified logrank test is not significant at 5% level of significance ($\chi^2 = 0.00823$ and *p*-value$=$0.928), meaning that there is no difference in survival times of the two cancer treatments. The stratified logrank test is also insignificant

($\chi^2 = 0.079$ and p-value$=$0.779) though stratifying for prior increase the power of the logrank test.

FIGURE 18: KAPLAN MEIER CURVES FOR THE VETERAN DATA BY TREATMENT

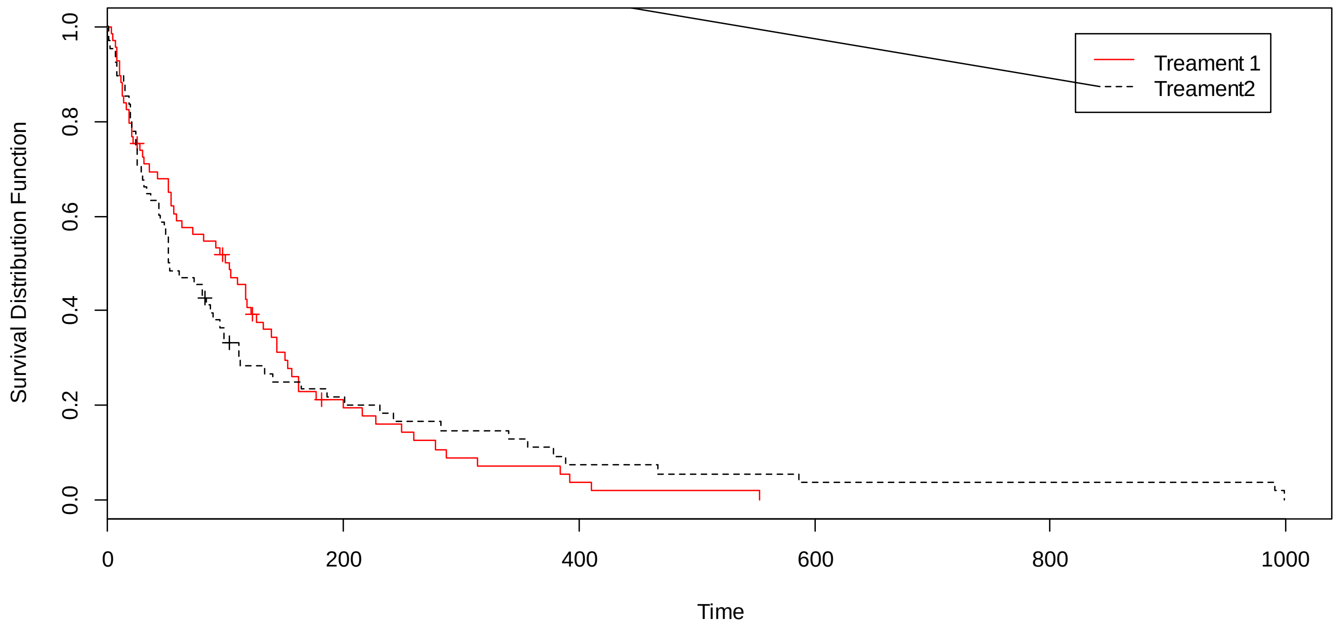
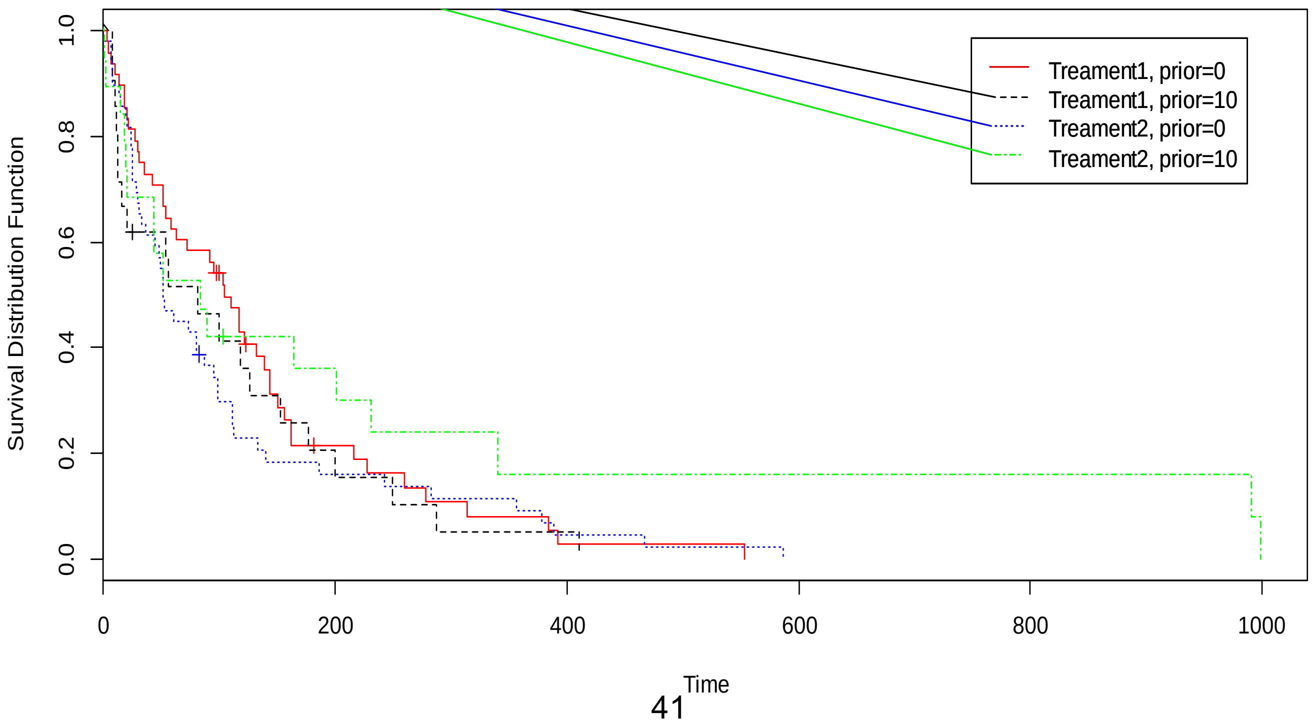


FIGURE 19: KAPLAN MEIER CURVES FOR THE VETERAN DATA BY TREATMENT AND PRIOR



Using the PASS module to compute power…

Logrank Test Power Analysis
Numeric Results in Terms of Sample Size when the Test is Two-Sided

Power	N1	N2	N	Haz Ratio (HR)	Ctrl Haz Rate (h1)	Trt Haz Rate (h2)	Accrual Pat'n	Accrual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl
0.0509	69	68	137	1.02	0.9922	1.01	Equal	1 / 3	0.0000	0.0000	0.0000	0.0000

A two-sided logrank test with an overall sample size of 137 subjects (69 in the control group and 68 in the treatment group) achieves low power of 5.1% using 5% significance level to detect a hazard ratio of 1.02 when the control group hazard rate is a hazard ratio of 0.9922. The study lasts for 3 time periods of which subject accrual occurs in the first time period.

Logrank Test Power Analysis
Numeric Results in Terms of Sample Size when the Test is Two-Sided

Power	N1	N2	N	Haz Ratio (HR)	Ctrl Haz Rate (h1)	Trt Haz Rate (h2)	Accrual Pat'n	Accrual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl
0.0579	69	68	137	1.05	0.9771	1.02	Equal	1 / 3	0.0000	0.0000	0.0000	0.0000

A two-sided logrank test with an overall sample size of 137 subjects (69 in the control group and 68 in the treatment group) achieves 5.8% power at a 5% significance level to detect a hazard ratio of 1.05 when the control group hazard rate is a hazard ratio of 0.9771. The study lasts for 3 time periods of which subject accrual occurs in the first time period.

The power of the USLRT is 0.0509 and the power of the SLRT is 0.0579. Stratifying in this case does not increase the power of the logrank test; actually the increase is very small. However for this hazard ratio, it would require group sample sizes of 59125 and 86861 for the USLRT and SLRT, respectively, to achieve 80% statistical power.

4.4.2 EXAMPLE 2: POWER CALCULATION FOR (cgd) DATA

Data are from a placebo controlled trial of gamma interferon in chronic granulotomous disease (CGD). Uses the complete data on time to first serious infection observed through end of study for each patient, which includes the initial serious infections observed through the 7/15/89 interim analysis data cut off, plus the residual data on occurrence of initial serious infections between the interim analysis cut off and the final blinded study visit for each patient. Only one patient was taken off on the day of his last infection [5].

```
> survdiff(Surv((tstop-tstart),status)~treat,data=cgd)
Call:
survdiff(formula = Surv((tstop - tstart), status) ~ treat, data = cgd)

                N Observed Expected (O-E)^2/E (O-E)^2/V
treat=placebo 120       56     37.8      8.81      18.1
treat=rIFN-g   83       20     38.2      8.70      18.1

 Chisq= 18.1  on 1 degrees of freedom, p= 2.12e-05
```

```
> survdiff(Surv((tstop-tstart),status)~treat+strata(sex),data=cgd)
Call:
survdiff(formula = Surv((tstop - tstart), status) ~ treat + strata(sex),
    data = cgd)

                N Observed Expected (O-E)^2/E (O-E)^2/V
treat=placebo 120       56       38      8.53      17.6
treat=rIFN-g   83       20       38      8.53      17.6

 Chisq= 17.6  on 1 degrees of freedom, p= 2.74e-05
```

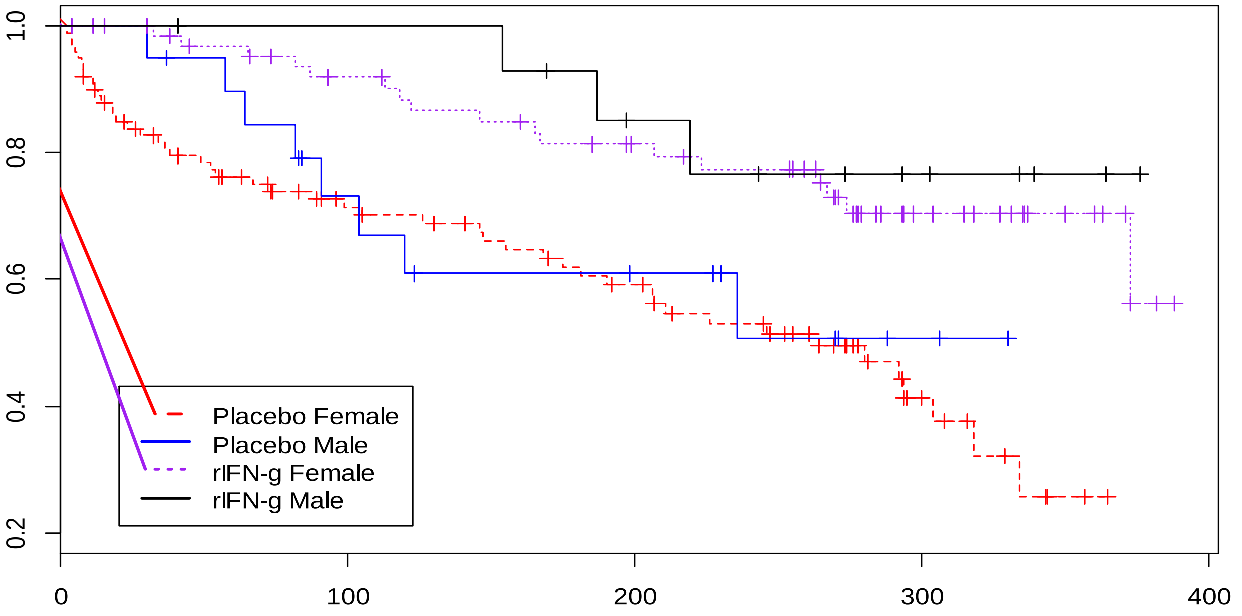
Patients taking the placebo have lower survival distribution when compared to those taking the gamma interferon ($\chi^2 = 18.1$ and *p*-value$=$2.12e-05). Of these patients, males have different survival distributions when compared to females ($\chi^2 = 17.6$ and *p*-value$=$2.74e-05)

Both the USLRT and SLRT achieve approximately 99.999% power.

$h_1 = 1.481481$ and $h_2 = 0.5235602$ for the USLRT, *HR*$=$0.3535

$h_1 = 1.473684$ and $h_2 = 0.5263158$ for the USLRT, *HR*$=$0.3571

FIGURE 20: KAPLAN-MEIER CURVES FOR COMPARING rIFN-g WITH A PLACEBO STRATIFIED BY GENDER OF PATIENT



The Kaplan Meier curve clearly indicates that there are differences in survival curves between males and females taking the rIFN-g and the placebo drug. There are no differences however between males and females taking the same drug. This is suggested by the crossing curves. Males appear to have a higher survival distribution than females in the treatment group and in the placebo group but the difference in survival distribution between females in the treatment group and males in the placebo group is statistically significant.

Under these settings, the clinical trial would have achieved the same power by using a sample size of $N = 248$, with $n_1 = 147$ and $n_2 = 101$. If the researcher had aimed for 90% power, that would require him to allocate 27 patients to the gamma interferon group and 20 patients to the placebo group. This example clearly suggests that required statistical power could be achieved in a clinical study by allocating more patients in the group with a higher hazard rate than using equal treatment allocation.

One of the objectives of this thesis was to provide means of power estimation for clinical trials intending to analyse data using the logrank test or stratified logrank test. It was shown in this paper that for a two strata study, the power of the unsratified logrank test and that of the stratified logrank test are close to each other for samples greater than 200. Samples less than 100 result in low power when the hazard ratio is close to a unity. In order to successfully estimate sample size for a clinical trial, one need to assume that the hazard rate of the treatment group is constantly higher than that of the control group, that is, the hazard ratio is greater than one. When the estimated hazard ratio is close to unity, a researcher will need a large sample size so that he/she will perceive an increase in power of the logrank test. If not, the results that will arise from such a trial may be statistically incorrect. Calculating power of the logrank test establishes whether we have confidence in our statistical findings.

When the number of patients in the treatment group is to differ from that in the control group, then the researcher must allocate more patients to the treatment group than in the control group as seen in **Table 9**. However randomisation techniques must be used to remove covariate imbalances.

Hazard rate combination required to achieve the targeted 80% power are shown in **Table 10**. If we consider the row of table 10 highlighted in yellow, we see that it will require a researcher to use a sample size of $N = 100$ using an equal sample size allocation scheme when the target population has a hazard ratio of 2.22 or alternatively when the hazard rates for the treatment group and control group are 0.225 and 0.1 respectively.

CHAPTER 5: SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

Power analysis is key in performing effective clinical studies. During the planning phase of the clinical trial, one must estimate time-dependent parameters, including length of study, hazard ratio based on a pilot data; the sample size needed for a successful sample size is easily computed thus helping the researcher not to waste resources by enrolling too many patients to compensate for uncertainty. These parameters can be estimated using experience from previous related clinical trials and sample size estimation can be done in PASS.

If we assume the hazard ratio to be equal to two, with equal treatment allocation, then no control hazard rate can achieve 80% power for sample sizes less than $N = 70.$ For the CGD clinical trial, **Table 10** guarantees that at least 99% power will be achieved. This makes sample size estimation and power analysis very easy. This paper has produced statistical tables that may guide researchers in sample size estimation.

There exists a minimum sample size that can produce a desired level of power for any particular clinical study. It should be emphasised that, enrolling more patients into an arm with the highest hazard rate produces desirable values of beta. However, when the hazard rates are approximately equal, the researcher will have to enrol many patients from hundreds to tens of thousands in order to compensate for uncertainty.

If a researcher wants to achieve 91% power, using a control group hazard rate of 0.1, the sample size will be doubled to 200 in comparison with a control hazard rate of 0.9. This means that, if a pilot study reveals that the hazard rates of the control group and treatment group are 0.2 and 0.74 respectively, then the researcher must enrol at least 100 patients to achieve at least the 80% power.

TABLE 9: POWER OF THE USLRT WHEN HR = 2 FOR VARIOUS HAZARD RATES AND SAMPLE SIZES

	HR = 2																	
N	h_1=0.1	h_1=0.2	h_1=0.3	h_1=0.4	h_1=0.5	h_1=0.6	h_1=0.7	h_1=0.8	h_1=1.0	h_1=1.1	h_1=1.2	h_1=1.3	h_1=1.4	h_1=1.5	h_1=1.6	h_1=1.7	h_1=1.8	h_1=1.9
20	0.18	0.26	0.30	0.31	0.32	0.32	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33
30	0.25	0.36	0.41	0.43	0.44	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45
40	0.32	0.45	0.51	0.54	0.55	0.56	0.56	0.56	0.56	0.56	0.56	0.56	0.56	0.56	0.56	0.56	0.56	0.56
50	0.38	0.54	0.61	0.63	0.64	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65
60	0.45	0.62	0.68	0.71	0.72	0.73	0.73	0.73	0.73	0.73	0.73	0.73	0.73	0.73	0.73	0.73	0.73	0.73
70	0.51	0.68	0.75	0.77	0.78	0.79	0.79	0.79	0.79	0.79	0.79	0.79	0.79	0.79	0.79	0.79	0.79	0.79
80	0.56	0.74	0.80	0.82	0.83	0.84	0.84	0.84	0.84	0.84	0.84	0.84	0.84	0.84	0.84	0.84	0.84	0.84
90	0.61	0.79	0.85	0.87	0.87	0.88	0.88	0.88	0.88	0.88	0.88	0.88	0.88	0.88	0.88	0.88	0.88	0.88
100	0.66	0.83	0.88	0.90	0.90	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	**0.91**
110	0.70	0.86	0.91	0.92	0.93	0.93	0.93	0.93	0.93	0.93	0.93	0.93	0.93	0.93	0.93	0.93	0.93	0.93
120	0.74	0.89	0.93	0.94	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.95
130	0.78	0.91	0.95	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96
140	0.81	0.93	0.96	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97
150	0.83	0.95	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98
160	0.86	0.96	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
170	0.88	0.97	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
180	0.89	0.97	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
190	0.91	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
200	**0.92**	0.98	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
210	0.93	0.99	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
220	0.94	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
230	0.95	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
240	0.96	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
250	0.97	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
260	0.97	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
270	0.98	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
280	0.98	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
290	0.98	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
300	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
310	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
320	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
330	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
340	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
350	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
360+	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

In the table above, highlighted power values guarantees a researcher of at least 80% power in the logrank test. Power values in white font guarantee no type II error.

TABLE 10: HAZARD RATIO AND TREATMENT HAZARD RATE FOR THE USLRT AT 90% POWER AND VARIOUS CONTROL HAZARD RATES AND SAMPLE SIZES

Power = 0.9												
	H_1=0.1		H_1=0.2		H_1=0.5		H_1=0.7		H_1=1		H_1=1.5	
N	**HR**	**H_2**	**HR**	**H_2**	**HR**	**H_2**	**HR**	**H_2**	**HR**	**H_2**	**HR**	**H_2**
20	6.33	0.63	5.79	1.16	5.75	2.87	5.75	4.02	5.75	5.75	5.70	8.55
30	4.59	0.46	4.01	0.80	3.87	1.94	3.87	2.71	3.87	3.87	3.88	5.81
90	2.58	0.26	2.24	0.45	2.07	1.03	2.06	1.44	2.06	2.06	2.06	3.08
100	2.47	0.25	2.15	0.43	1.99	0.99	1.98	1.38	1.97	1.97	1.97	2.96
110	2.38	0.24	2.08	0.42	1.92	0.96	1.91	1.34	1.91	1.91	1.91	2.86
120	2.31	0.23	2.02	0.40	1.87	0.93	1.86	1.30	1.85	1.85	1.85	2.78
180	2.01	0.20	1.79	0.36	1.66	0.83	1.65	1.15	1.64	1.64	1.64	2.47
190	1.98	0.20	1.76	0.35	1.64	0.82	1.63	1.14	1.62	1.62	1.62	2.43

The hazard ratio will not be always equal to two, thus the above table gives us hazard rates combinations needed to achieve 90% power. Since it is sometimes the case that the hazard rates are unknown but it may be anticipated that the treatment group will do better, **Table 10** is an extract from **Appendix I** and it locates exactly the hazard rates that will yield a desired 90% power against selected sample sizes.

This paper has provided statistical tables of the hazard ratio estimation at 80% power (**Appendix I**), at 90% power (**Appendix II**), at 95% power (**Appendix III**) and at 99% power (**Appendix IV**) versus samples of size 30, 80 100 and 200. The appendices assume that the study lasts for 5 time periods of which subject entry occurs in the first time period and that the null hypothesis will be rejected at 5% percent significance level.

Tables attached in the appendices can be used as a guide to sample size and power analysis. However it must be noted that the proportion of the control/treatment group that is lost during a single time period reduces the power of the logrank slightly. Increasing the length of the study period and stratifying for confounding factors increases the power of the logrank test.

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APPENDIX I

ESTIMATED SAMPLE SIZE AND *HR-h_2* COMBINATION NEEDED TO ACHIEVE 90% POWER.

Power = 0.9												
	H_1=0.1		H_1=0.2		H_1=0.5		H_1=0.7		H_1=1		H_1=1.5	
N	**HR**	**H_2**	**HR**	**H_2**	**HR**	**H_2**	**HR**	**H_2**	**HR**	**H_2**	**HR**	**H_2**
20	6.33	0.63	5.79	1.16	5.75	2.87	5.75	4.02	5.75	5.75	5.70	8.55
30	4.59	0.46	4.01	0.80	3.87	1.94	3.87	2.71	3.87	3.87	3.88	5.81
40	3.83	0.38	3.30	0.66	3.13	1.56	3.12	2.19	3.13	3.13	3.13	4.69
50	3.39	0.34	2.91	0.58	2.73	1.36	2.72	1.90	2.72	2.72	2.72	4.08
60	3.09	0.31	2.65	0.53	2.47	1.24	2.47	1.73	2.46	2.46	2.47	3.70
70	2.87	0.29	2.48	0.50	2.30	1.15	2.29	1.60	2.29	2.29	2.29	3.43
80	2.71	0.27	2.34	0.47	2.17	1.08	2.16	1.51	2.16	2.16	2.16	3.23
90	2.58	0.26	2.24	0.45	2.07	1.03	2.06	1.44	2.06	2.06	2.06	3.08
100	2.47	0.25	2.15	0.43	1.99	0.99	1.98	1.38	1.97	1.97	1.97	2.96
110	2.38	0.24	2.08	0.42	1.92	0.96	1.91	1.34	1.91	1.91	1.91	2.86
120	2.31	0.23	2.02	0.40	1.87	0.93	1.86	1.30	1.85	1.85	1.85	2.78
130	2.24	0.22	1.97	0.39	1.82	0.91	1.81	1.27	1.81	1.81	1.81	2.71
140	2.19	0.22	1.92	0.38	1.78	0.89	1.77	1.24	1.76	1.76	1.76	2.65
150	2.14	0.21	1.88	0.38	1.74	0.87	1.73	1.21	1.73	1.73	1.73	2.59
160	2.09	0.21	1.85	0.37	1.71	0.86	1.70	1.19	1.70	1.70	1.70	2.55
170	2.05	0.21	1.82	0.36	1.68	0.84	1.67	1.17	1.67	1.67	1.67	2.50
180	2.01	0.20	1.79	0.36	1.66	0.83	1.65	1.15	1.64	1.64	1.64	2.47
190	1.98	0.20	1.76	0.35	1.64	0.82	1.63	1.14	1.62	1.62	1.62	2.43
200	1.95	0.20	1.74	0.35	1.62	0.81	1.60	1.12	1.60	1.60	1.60	2.40
210	1.92	0.19	1.72	0.34	1.60	0.80	1.59	1.11	1.58	1.58	1.58	2.37
220	1.90	0.19	1.70	0.34	1.58	0.79	1.57	1.10	1.56	1.56	1.56	2.35
230	1.87	0.19	1.68	0.34	1.56	0.78	1.55	1.09	1.55	1.55	1.55	2.32
240	1.85	0.19	1.66	0.33	1.55	0.77	1.54	1.08	1.53	1.53	1.53	2.30
250	1.83	0.18	1.64	0.33	1.54	0.77	1.52	1.07	1.52	1.52	1.52	2.28
260	1.81	0.18	1.63	0.33	1.52	0.76	1.51	1.06	1.51	1.51	1.51	2.26
270	1.79	0.18	1.61	0.32	1.51	0.76	1.50	1.05	1.50	1.50	1.50	2.24
280	1.78	0.18	1.60	0.32	1.50	0.75	1.49	1.04	1.48	1.48	1.48	2.23
290	1.76	0.18	1.59	0.32	1.49	0.74	1.48	1.03	1.47	1.47	1.47	2.21
300	1.75	0.17	1.58	0.32	1.48	0.74	1.47	1.03	1.46	1.46	1.46	2.20
310	1.73	0.17	1.57	0.31	1.47	0.73	1.46	1.02	1.46	1.46	1.45	2.18
320	1.72	0.17	1.56	0.31	1.46	0.73	1.45	1.01	1.45	1.45	1.45	2.17
330	1.71	0.17	1.55	0.31	1.45	0.73	1.44	1.01	1.44	1.44	1.44	2.16
340	1.69	0.17	1.54	0.31	1.44	0.72	1.43	1.00	1.43	1.43	1.43	2.14
350	1.68	0.17	1.53	0.31	1.44	0.72	1.43	1.00	1.42	1.42	1.42	2.13
360	1.67	0.17	1.52	0.30	1.43	0.71	1.42	0.99	1.42	1.42	1.41	2.12
370	1.66	0.17	1.51	0.30	1.42	0.71	1.41	0.99	1.41	1.41	1.41	2.11
380	1.65	0.17	1.50	0.30	1.42	0.71	1.41	0.98	1.40	1.40	1.40	2.10
390	1.64	0.16	1.50	0.30	1.41	0.70	1.40	0.98	1.40	1.40	1.40	2.09
400	1.63	0.16	1.49	0.30	1.40	0.70	1.39	0.98	1.39	1.39	1.39	2.08

APPENDIX II $a)$

ESTIMATED *HR*-h_2 AND TREATMENT HAZARD RATE COMBINATION NEEDED TO ACHIEVE 80% POWER FOR N = 30.

80% Power, N= 30

N_1 = 15, N_2 = 15, $\beta = 0.2$

HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
12.09	0.01	0.121	3.11	0.43	1.34	3.1	0.85	2.63	3.1	1.27	3.93	3.1	1.69	5.24
7.87	0.02	0.157	3.1	0.44	1.37	3.1	0.86	2.66	3.1	1.28	3.97	3.1	1.7	5.27
6.31	0.03	0.189	3.1	0.45	1.4	3.1	0.87	2.69	3.1	1.29	4	3.1	1.71	5.3
5.48	0.04	0.219	3.1	0.46	1.43	3.1	0.88	2.73	3.1	1.3	4.03	3.1	1.72	5.33
4.96	0.05	0.248	3.1	0.47	1.46	3.1	0.89	2.76	3.1	1.31	4.06	3.1	1.73	5.36
4.6	0.06	0.276	3.1	0.48	1.49	3.1	0.9	2.79	3.1	1.32	4.09	3.1	1.74	5.39
4.33	0.07	0.303	3.1	0.49	1.52	3.1	0.91	2.82	3.1	1.33	4.12	3.1	1.75	5.42
4.13	0.08	0.331	3.1	0.5	1.55	3.1	0.92	2.85	3.1	1.34	4.15	3.1	1.76	5.45
3.97	0.09	0.358	3.1	0.51	1.58	3.1	0.93	2.88	3.1	1.35	4.18	3.1	1.77	5.48
3.84	0.1	0.384	3.1	0.52	1.61	3.1	0.94	2.91	3.1	1.36	4.21	3.1	1.78	5.52
3.74	0.11	0.411	3.1	0.53	1.64	3.1	0.95	2.94	3.1	1.37	4.24	3.1	1.79	5.55
3.65	0.12	0.438	3.1	0.54	1.67	3.1	0.96	2.97	3.1	1.38	4.28	3.1	1.8	5.58
3.58	0.13	0.465	3.1	0.55	1.7	3.1	0.97	3	3.1	1.39	4.31	3.1	1.81	5.61
3.51	0.14	0.492	3.1	0.56	1.73	3.1	0.98	3.04	3.1	1.4	4.34	3.1	1.82	5.64
3.46	0.15	0.519	3.1	0.57	1.77	3.1	0.99	3.07	3.1	1.41	4.37	3.1	1.83	5.67
3.41	0.16	0.546	3.1	0.58	1.8	3.1	1	3.1	3.1	1.42	4.4	3.1	1.84	5.7
3.37	0.17	0.574	3.1	0.59	1.83	3.1	1.01	3.13	3.1	1.43	4.43	3.1	1.85	5.73
3.34	0.18	0.601	3.1	0.6	1.86	3.1	1.02	3.16	3.1	1.44	4.46	3.1	1.86	5.76
3.31	0.19	0.629	3.1	0.61	1.89	3.1	1.03	3.19	3.1	1.45	4.49	3.1	1.87	5.8
3.28	0.2	0.657	3.1	0.62	1.92	3.1	1.04	3.22	3.1	1.46	4.52	3.1	1.88	5.83
3.26	0.21	0.685	3.1	0.63	1.95	3.1	1.05	3.25	3.1	1.47	4.55	3.1	1.89	5.86
3.24	0.22	0.713	3.1	0.64	1.98	3.1	1.06	3.28	3.1	1.48	4.59	3.1	1.9	5.89
3.22	0.23	0.741	3.1	0.65	2.01	3.1	1.07	3.31	3.1	1.49	4.62	3.1	1.91	5.92
3.21	0.24	0.77	3.1	0.66	2.04	3.1	1.08	3.35	3.1	1.5	4.65	3.1	1.92	5.95
3.19	0.25	0.798	3.1	0.67	2.07	3.1	1.09	3.38	3.1	1.51	4.68	3.1	1.93	5.98
3.18	0.26	0.827	3.1	0.68	2.11	3.1	1.1	3.41	3.1	1.52	4.71	3.1	1.94	6.01
3.17	0.27	0.856	3.1	0.69	2.14	3.1	1.11	3.44	3.1	1.53	4.74	3.1	1.95	6.04
3.16	0.28	0.885	3.1	0.7	2.17	3.1	1.12	3.47	3.1	1.54	4.77	3.1	1.96	6.07
3.15	0.29	0.915	3.1	0.71	2.2	3.1	1.13	3.5	3.1	1.55	4.8	3.1	1.97	6.11
3.15	0.3	0.944	3.1	0.72	2.23	3.1	1.14	3.53	3.1	1.56	4.83	3.1	1.98	6.14
3.14	0.31	0.974	3.1	0.73	2.26	3.1	1.15	3.56	3.1	1.57	4.86	3.1	1.99	6.17
3.14	0.32	1	3.1	0.74	2.29	3.1	1.16	3.59	3.1	1.58	4.9	3.1	2	6.2
3.13	0.33	1.03	3.1	0.75	2.32	3.1	1.17	3.62	3.1	1.59	4.93	3.1	2.01	6.23
3.13	0.34	1.06	3.1	0.76	2.35	3.1	1.18	3.66	3.1	1.6	4.96	3.1	2.02	6.26
3.12	0.35	1.09	3.1	0.77	2.38	3.1	1.19	3.69	3.1	1.61	4.99	3.1	2.03	6.29
3.12	0.36	1.12	3.1	0.78	2.42	3.1	1.2	3.72	3.1	1.62	5.02	3.1	2.04	6.32
3.12	0.37	1.15	3.1	0.79	2.45	3.1	1.21	3.75	3.1	1.63	5.05	3.1	2.05	6.35
3.11	0.38	1.18	3.1	0.8	2.48	3.1	1.22	3.78	3.1	1.64	5.08	3.1	2.06	6.38
3.11	0.39	1.21	3.1	0.81	2.51	3.1	1.23	3.81	3.1	1.65	5.11	3.1	2.07	6.42
3.11	0.4	1.24	3.1	0.82	2.54	3.1	1.24	3.84	3.1	1.66	5.14	3.1	2.08	6.45
3.11	0.41	1.27	3.1	0.83	2.57	3.1	1.25	3.87	3.1	1.67	5.17	3.1	2.09	6.48
3.11	0.42	1.3	3.1	0.84	2.6	3.1	1.26	3.9	3.1	1.68	5.21	3.1	2.1	6.51

APPENDIX II *b*)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 80% POWER FOR N = 80.

80% Power, N= 80

N_1 = 40, N_2 = 40, $\beta = 0.2$

HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
6.26	0.01	0.06	1.95	0.43	0.84	1.92	0.86	1.65	1.92	1.29	2.48	1.92	1.72	3.31
4.35	0.02	0.09	1.95	0.44	0.86	1.92	0.87	1.67	1.92	1.3	2.5	1.92	1.73	3.32
3.63	0.03	0.11	1.94	0.45	0.87	1.92	0.88	1.69	1.92	1.31	2.52	1.92	1.74	3.34
3.23	0.04	0.13	1.94	0.46	0.89	1.92	0.89	1.71	1.92	1.32	2.54	1.92	1.75	3.36
2.98	0.05	0.15	1.94	0.47	0.91	1.92	0.9	1.73	1.92	1.33	2.56	1.92	1.76	3.38
2.8	0.06	0.17	1.94	0.48	0.93	1.92	0.91	1.75	1.92	1.34	2.58	1.92	1.77	3.4
2.67	0.07	0.19	1.94	0.49	0.95	1.92	0.92	1.77	1.92	1.35	2.59	1.92	1.78	3.42
2.56	0.08	0.21	1.94	0.5	0.97	1.92	0.93	1.79	1.92	1.36	2.61	1.92	1.79	3.44
2.48	0.09	0.22	1.93	0.51	0.99	1.92	0.94	1.81	1.92	1.37	2.63	1.92	1.8	3.46
2.41	0.1	0.24	1.93	0.52	1.01	1.92	0.95	1.83	1.92	1.38	2.65	1.92	1.81	3.48
2.36	0.11	0.26	1.93	0.53	1.02	1.92	0.96	1.85	1.92	1.39	2.67	1.92	1.82	3.5
2.31	0.12	0.28	1.93	0.54	1.04	1.92	0.97	1.86	1.92	1.4	2.69	1.92	1.83	3.52
2.27	0.13	0.3	1.93	0.55	1.06	1.92	0.98	1.88	1.92	1.41	2.71	1.92	1.84	3.54
2.24	0.14	0.31	1.93	0.56	1.08	1.92	0.99	1.9	1.92	1.42	2.73	1.92	1.85	3.56
2.21	0.15	0.33	1.93	0.57	1.10	1.92	1.00	1.92	1.92	1.43	2.75	1.92	1.86	3.57
2.18	0.16	0.35	1.93	0.58	1.12	1.92	1.01	1.94	1.92	1.44	2.77	1.92	1.87	3.59
2.15	0.17	0.37	1.93	0.59	1.14	1.92	1.02	1.96	1.92	1.45	2.79	1.92	1.88	3.61
2.13	0.18	0.38	1.93	0.6	1.16	1.92	1.03	1.98	1.92	1.46	2.81	1.92	1.89	3.63
2.11	0.19	0.4	1.93	0.61	1.18	1.92	1.04	2.00	1.92	1.47	2.83	1.92	1.9	3.65
2.1	0.2	0.42	1.93	0.62	1.19	1.92	1.05	2.02	1.92	1.48	2.84	1.92	1.91	3.67
2.08	0.21	0.44	1.93	0.63	1.21	1.92	1.06	2.04	1.92	1.49	2.86	1.92	1.92	3.69
2.07	0.22	0.46	1.93	0.64	1.23	1.92	1.07	2.06	1.92	1.5	2.88	1.92	1.93	3.71
2.06	0.23	0.47	1.93	0.65	1.25	1.92	1.08	2.08	1.92	1.51	2.9	1.92	1.94	3.73
2.05	0.24	0.49	1.93	0.66	1.27	1.92	1.09	2.09	1.92	1.52	2.92	1.92	1.95	3.75
2.04	0.25	0.51	1.93	0.67	1.29	1.92	1.1	2.11	1.92	1.53	2.94	1.92	1.96	3.77
2.03	0.26	0.53	1.92	0.68	1.31	1.92	1.11	2.13	1.92	1.54	2.96	1.92	1.97	3.79
2.02	0.27	0.54	1.92	0.69	1.33	1.92	1.12	2.15	1.92	1.55	2.98	1.92	1.98	3.81
2.01	0.28	0.56	1.92	0.7	1.35	1.92	1.13	2.17	1.92	1.56	3.00	1.92	1.99	3.82
2.00	0.29	0.58	1.92	0.71	1.37	1.92	1.14	2.19	1.92	1.57	3.02	1.92	2.00	3.84
2.00	0.3	0.6	1.92	0.72	1.39	1.92	1.15	2.21	1.92	1.58	3.04	1.92	2.01	3.86
1.99	0.31	0.62	1.92	0.73	1.4	1.92	1.16	2.23	1.92	1.59	3.06	1.92	2.02	3.88
1.98	0.32	0.64	1.92	0.74	1.42	1.92	1.17	2.25	1.92	1.6	3.08	1.92	2.03	3.90
1.98	0.33	0.65	1.92	0.75	1.44	1.92	1.18	2.27	1.92	1.61	3.09	1.92	2.04	3.92
1.98	0.34	0.67	1.92	0.76	1.46	1.92	1.19	2.29	1.92	1.62	3.11	1.92	2.05	3.94
1.97	0.35	0.69	1.92	0.77	1.48	1.92	1.2	2.31	1.92	1.63	3.13	1.92	2.06	3.96
1.97	0.36	0.71	1.92	0.78	1.5	1.92	1.21	2.33	1.92	1.64	3.15	1.92	2.07	3.98
1.96	0.37	0.73	1.92	0.79	1.52	1.92	1.22	2.34	1.92	1.65	3.17	1.92	2.08	4.00
1.96	0.38	0.74	1.92	0.8	1.54	1.92	1.23	2.36	1.92	1.66	3.19	1.92	2.09	4.02
1.96	0.39	0.76	1.92	0.81	1.56	1.92	1.24	2.38	1.92	1.67	3.21	1.92	2.1	4.04
1.95	0.4	0.78	1.92	0.82	1.58	1.92	1.25	2.4	1.92	1.68	3.23	1.92	2.11	4.06
1.95	0.41	0.8	1.92	0.83	1.6	1.92	1.26	2.42	1.92	1.69	3.25	1.92	2.12	4.07
1.95	0.42	0.82	1.92	0.84	1.61	1.92	1.27	2.44	1.92	1.7	3.27	1.92	2.13	4.09
			1.92	0.85	1.63	1.92	1.28	2.46	1.92	1.71	3.29	1.92	2.14	4.11

APPENDIX II *c*)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 80% POWER FOR N = 100.

80% Power, N= 100

N_1 = 50, N_2 = 50, $\beta = 0.2$

HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
5.48	0.01	0.05	1.81	0.43	0.78	1.79	0.86	1.54	1.79	1.29	2.3	1.79	1.72	3.07
3.88	0.02	0.08	1.81	0.44	0.8	1.79	0.87	1.55	1.79	1.3	2.32	1.79	1.73	3.09
3.26	0.03	0.1	1.81	0.45	0.81	1.79	0.88	1.57	1.79	1.31	2.34	1.79	1.74	3.11
2.93	0.04	0.12	1.81	0.46	0.83	1.79	0.89	1.59	1.79	1.32	2.36	1.79	1.75	3.13
2.71	0.05	0.14	1.81	0.47	0.85	1.79	0.9	1.61	1.79	1.33	2.38	1.79	1.76	3.14
2.56	0.06	0.15	1.8	0.48	0.87	1.79	0.91	1.63	1.79	1.34	2.39	1.79	1.77	3.16
2.44	0.07	0.17	1.8	0.49	0.88	1.79	0.92	1.64	1.79	1.35	2.41	1.79	1.78	3.18
2.35	0.08	0.19	1.8	0.5	0.9	1.79	0.93	1.66	1.79	1.36	2.43	1.79	1.79	3.2
2.28	0.09	0.21	1.8	0.51	0.92	1.79	0.94	1.68	1.79	1.37	2.45	1.79	1.8	3.21
2.22	0.1	0.22	1.8	0.52	0.94	1.79	0.95	1.7	1.79	1.38	2.46	1.79	1.81	3.23
2.18	0.11	0.24	1.8	0.53	0.95	1.79	0.96	1.71	1.79	1.39	2.48	1.79	1.82	3.25
2.14	0.12	0.26	1.8	0.54	0.97	1.79	0.97	1.73	1.79	1.4	2.5	1.79	1.83	3.27
2.1	0.13	0.27	1.8	0.55	0.99	1.79	0.98	1.75	1.79	1.41	2.52	1.79	1.84	3.29
2.07	0.14	0.29	1.8	0.56	1.01	1.79	0.99	1.77	1.79	1.42	2.54	1.79	1.85	3.3
2.04	0.15	0.31	1.79	0.57	1.02	1.79	1	1.79	1.79	1.43	2.55	1.79	1.86	3.32
2.02	0.16	0.32	1.79	0.58	1.04	1.79	1.01	1.8	1.79	1.44	2.57	1.79	1.87	3.34
2	0.17	0.34	1.79	0.59	1.06	1.79	1.02	1.82	1.79	1.45	2.59	1.79	1.88	3.36
1.98	0.18	0.36	1.79	0.6	1.08	1.79	1.03	1.84	1.79	1.46	2.61	1.79	1.89	3.38
1.96	0.19	0.37	1.79	0.61	1.09	1.79	1.04	1.86	1.79	1.47	2.63	1.79	1.9	3.39
1.95	0.2	0.39	1.79	0.62	1.11	1.79	1.05	1.88	1.79	1.48	2.64	1.79	1.91	3.41
1.94	0.21	0.41	1.79	0.63	1.13	1.79	1.06	1.89	1.79	1.49	2.66	1.79	1.92	3.43
1.92	0.22	0.42	1.79	0.64	1.15	1.79	1.07	1.91	1.79	1.5	2.68	1.79	1.93	3.45
1.91	0.23	0.44	1.79	0.65	1.16	1.79	1.08	1.93	1.79	1.51	2.7	1.79	1.94	3.46
1.9	0.24	0.46	1.79	0.66	1.18	1.79	1.09	1.95	1.79	1.52	2.71	1.79	1.95	3.48
1.89	0.25	0.47	1.79	0.67	1.2	1.79	1.1	1.96	1.79	1.53	2.73	1.79	1.96	3.5
1.88	0.26	0.49	1.79	0.68	1.22	1.79	1.11	1.98	1.79	1.54	2.75	1.79	1.97	3.52
1.88	0.27	0.51	1.79	0.69	1.23	1.79	1.12	2	1.79	1.55	2.77	1.79	1.98	3.54
1.87	0.28	0.52	1.79	0.7	1.25	1.79	1.13	2.02	1.79	1.56	2.79	1.79	1.99	3.55
1.86	0.29	0.54	1.79	0.71	1.27	1.79	1.14	2.04	1.79	1.57	2.8	1.79	2	3.57
1.86	0.3	0.56	1.79	0.72	1.29	1.79	1.15	2.05	1.79	1.58	2.82	1.79	2.01	3.59
1.85	0.31	0.57	1.79	0.73	1.31	1.79	1.16	2.07	1.79	1.59	2.84	1.79	2.02	3.61
1.85	0.32	0.59	1.79	0.74	1.32	1.79	1.17	2.09	1.79	1.6	2.86	1.79	2.03	3.63
1.84	0.33	0.61	1.79	0.75	1.34	1.79	1.18	2.11	1.79	1.61	2.88	1.79	2.04	3.64
1.84	0.34	0.63	1.79	0.76	1.36	1.79	1.19	2.13	1.79	1.62	2.89	1.79	2.05	3.66
1.83	0.35	0.64	1.79	0.77	1.38	1.79	1.2	2.14	1.79	1.63	2.91	1.79	2.06	3.68
1.83	0.36	0.66	1.79	0.78	1.39	1.79	1.21	2.16	1.79	1.64	2.93	1.79	2.07	3.7
1.83	0.37	0.68	1.79	0.79	1.41	1.79	1.22	2.18	1.79	1.65	2.95	1.79	2.08	3.71
1.82	0.38	0.69	1.79	0.8	1.43	1.79	1.23	2.2	1.79	1.66	2.96	1.79	2.09	3.73
1.82	0.39	0.71	1.79	0.81	1.45	1.79	1.24	2.21	1.79	1.67	2.98	1.79	2.1	3.75
1.82	0.4	0.73	1.79	0.82	1.47	1.79	1.25	2.23	1.79	1.68	3	1.79	2.11	3.77
1.82	0.41	0.74	1.79	0.83	1.48	1.79	1.26	2.25	1.79	1.69	3.02	1.79	2.12	3.79
1.81	0.42	0.76	1.79	0.84	1.5	1.79	1.27	2.27	1.79	1.7	3.04	1.79	2.13	3.8
			1.79	0.85	1.52	1.79	1.28	2.29	1.79	1.71	3.05	1.79	2.14	3.82

APPENDIX II *d*)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 80% POWER FOR N = 200.

80% Power, N= 200

N_1 = 100, N_2 = 100, $\beta = 0.2$

HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
3.79	0.01	0.038	1.52	0.43	0.654	1.5	0.86	1.29	1.5	1.29	1.93	1.5	1.72	2.57
2.83	0.02	0.057	1.52	0.44	0.669	1.5	0.87	1.3	1.5	1.3	1.95	1.5	1.73	2.59
2.45	0.03	0.074	1.52	0.45	0.683	1.5	0.88	1.32	1.5	1.31	1.96	1.5	1.74	2.6
2.24	0.04	0.09	1.52	0.46	0.698	1.5	0.89	1.33	1.5	1.32	1.98	1.5	1.75	2.62
2.11	0.05	0.105	1.52	0.47	0.713	1.5	0.9	1.35	1.5	1.33	1.99	1.5	1.76	2.63
2.01	0.06	0.121	1.51	0.48	0.727	1.5	0.91	1.36	1.5	1.34	2.01	1.5	1.77	2.65
1.94	0.07	0.136	1.51	0.49	0.742	1.5	0.92	1.38	1.5	1.35	2.02	1.5	1.78	2.66
1.88	0.08	0.151	1.51	0.5	0.756	1.5	0.93	1.39	1.5	1.36	2.04	1.5	1.79	2.68
1.84	0.09	0.165	1.51	0.51	0.771	1.5	0.94	1.41	1.5	1.37	2.05	1.5	1.8	2.69
1.8	0.1	0.18	1.51	0.52	0.786	1.5	0.95	1.42	1.5	1.38	2.07	1.5	1.81	2.71
1.77	0.11	0.195	1.51	0.53	0.8	1.5	0.96	1.44	1.5	1.39	2.08	1.5	1.82	2.72
1.74	0.12	0.209	1.51	0.54	0.815	1.5	0.97	1.45	1.5	1.4	2.1	1.5	1.83	2.74
1.72	0.13	0.223	1.51	0.55	0.83	1.5	0.98	1.47	1.5	1.41	2.11	1.5	1.84	2.75
1.7	0.14	0.238	1.51	0.56	0.844	1.5	0.99	1.48	1.5	1.42	2.13	1.5	1.85	2.77
1.68	0.15	0.252	1.51	0.57	0.859	1.5	1	1.5	1.5	1.43	2.14	1.5	1.86	2.78
1.67	0.16	0.267	1.51	0.58	0.874	1.5	1.01	1.51	1.5	1.44	2.16	1.5	1.87	2.8
1.65	0.17	0.281	1.51	0.59	0.889	1.5	1.02	1.53	1.5	1.45	2.17	1.5	1.88	2.81
1.64	0.18	0.295	1.51	0.6	0.903	1.5	1.03	1.54	1.5	1.46	2.19	1.5	1.89	2.83
1.63	0.19	0.309	1.5	0.61	0.918	1.5	1.04	1.56	1.5	1.47	2.2	1.5	1.9	2.84
1.62	0.2	0.324	1.5	0.62	0.933	1.5	1.05	1.57	1.5	1.48	2.22	1.5	1.91	2.86
1.61	0.21	0.338	1.5	0.63	0.947	1.5	1.06	1.59	1.5	1.49	2.23	1.5	1.92	2.87
1.6	0.22	0.352	1.5	0.64	0.962	1.5	1.07	1.6	1.5	1.5	2.25	1.5	1.93	2.89
1.59	0.23	0.367	1.5	0.65	0.977	1.5	1.08	1.62	1.5	1.51	2.26	1.5	1.94	2.9
1.59	0.24	0.381	1.5	0.66	0.992	1.5	1.09	1.63	1.5	1.52	2.28	1.5	1.95	2.92
1.58	0.25	0.395	1.5	0.67	1.01	1.5	1.1	1.65	1.5	1.53	2.29	1.5	1.96	2.93
1.57	0.26	0.409	1.5	0.68	1.02	1.5	1.11	1.66	1.5	1.54	2.31	1.5	1.97	2.95
1.57	0.27	0.424	1.5	0.69	1.04	1.5	1.12	1.68	1.5	1.55	2.32	1.5	1.98	2.96
1.56	0.28	0.438	1.5	0.7	1.05	1.5	1.13	1.69	1.5	1.56	2.34	1.5	1.99	2.98
1.56	0.29	0.452	1.5	0.71	1.07	1.5	1.14	1.71	1.5	1.57	2.35	1.5	2	2.99
1.56	0.3	0.467	1.5	0.72	1.08	1.5	1.15	1.72	1.5	1.58	2.37	1.5	2.01	3.01
1.55	0.31	0.481	1.5	0.73	1.1	1.5	1.16	1.74	1.5	1.59	2.38	1.5	2.02	3.02
1.55	0.32	0.495	1.5	0.74	1.11	1.5	1.17	1.75	1.5	1.6	2.4	1.5	2.03	3.04
1.54	0.33	0.51	1.5	0.75	1.13	1.5	1.18	1.77	1.5	1.61	2.41	1.5	2.04	3.05
1.54	0.34	0.524	1.5	0.76	1.14	1.5	1.19	1.78	1.5	1.62	2.43	1.5	2.05	3.07
1.54	0.35	0.539	1.5	0.77	1.15	1.5	1.2	1.8	1.5	1.63	2.44	1.5	2.06	3.08
1.54	0.36	0.553	1.5	0.78	1.17	1.5	1.21	1.81	1.5	1.64	2.46	1.5	2.07	3.1
1.53	0.37	0.567	1.5	0.79	1.18	1.5	1.22	1.83	1.5	1.65	2.47	1.5	2.08	3.11
1.53	0.38	0.582	1.5	0.8	1.2	1.5	1.23	1.84	1.5	1.66	2.49	1.5	2.09	3.13
1.53	0.39	0.596	1.5	0.81	1.21	1.5	1.24	1.86	1.5	1.67	2.5	1.5	2.1	3.14
1.53	0.4	0.611	1.5	0.82	1.23	1.5	1.25	1.87	1.5	1.68	2.52	1.5	2.11	3.16
1.53	0.41	0.625	1.5	0.83	1.24	1.5	1.26	1.89	1.5	1.69	2.53	1.5	2.12	3.17
1.52	0.42	0.64	1.5	0.84	1.26	1.5	1.27	1.9	1.5	1.7	2.54	1.5	2.13	3.19
			1.5	0.85	1.27	1.5	1.28	1.92	1.5	1.71	2.56	1.5	2.14	3.2

APPENDIX III *a*)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 90% POWER FOR N = 30.

90% Power, N= 30

N_1 = 15, N_2 = 15, $\beta = 0.1$

HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
14	0.01	0.1401	3.87	0.43	1.67	3.87	0.86	3.33	3.88	1.29	5	3.88	1.72	6.67
9.22	0.02	0.1843	3.87	0.44	1.7	3.87	0.87	3.37	3.88	1.3	5.04	3.88	1.73	6.71
7.43	0.03	0.2229	3.87	0.45	1.74	3.87	0.88	3.41	3.88	1.31	5.08	3.88	1.74	6.74
6.47	0.04	0.2588	3.87	0.46	1.78	3.87	0.89	3.45	3.88	1.32	5.12	3.88	1.75	6.78
5.87	0.05	0.2933	3.87	0.47	1.82	3.87	0.9	3.49	3.88	1.33	5.15	3.88	1.76	6.82
5.45	0.06	0.327	3.87	0.48	1.86	3.87	0.91	3.53	3.88	1.34	5.19	3.88	1.77	6.86
5.15	0.07	0.3603	3.87	0.49	1.9	3.87	0.92	3.56	3.88	1.35	5.23	3.88	1.78	6.9
4.92	0.08	0.3933	3.87	0.5	1.94	3.87	0.93	3.6	3.88	1.36	5.27	3.88	1.79	6.94
4.74	0.09	0.4262	3.87	0.51	1.98	3.87	0.94	3.64	3.88	1.37	5.31	3.88	1.8	6.98
4.59	0.1	0.4591	3.87	0.52	2.01	3.87	0.95	3.68	3.88	1.38	5.35	3.88	1.81	7.02
4.47	0.11	0.4922	3.87	0.53	2.05	3.87	0.96	3.72	3.88	1.39	5.39	3.88	1.82	7.05
4.38	0.12	0.5255	3.87	0.54	2.09	3.87	0.97	3.76	3.88	1.4	5.43	3.88	1.83	7.09
4.3	0.13	0.5589	3.87	0.55	2.13	3.87	0.98	3.8	3.88	1.41	5.46	3.88	1.84	7.13
4.23	0.14	0.5927	3.87	0.56	2.17	3.87	0.99	3.84	3.88	1.42	5.5	3.88	1.85	7.17
4.18	0.15	0.6267	3.87	0.57	2.21	3.87	1	3.87	3.88	1.43	5.54	3.88	1.86	7.21
4.13	0.16	0.661	3.87	0.58	2.25	3.87	1.01	3.91	3.88	1.44	5.58	3.88	1.87	7.25
4.09	0.17	0.6956	3.87	0.59	2.28	3.87	1.02	3.95	3.88	1.45	5.62	3.88	1.88	7.29
4.06	0.18	0.7305	3.87	0.6	2.32	3.87	1.03	3.99	3.88	1.46	5.66	3.88	1.89	7.33
4.03	0.19	0.7657	3.87	0.61	2.36	3.87	1.04	4.03	3.88	1.47	5.7	3.88	1.9	7.36
4.01	0.2	0.8012	3.87	0.62	2.4	3.87	1.05	4.07	3.88	1.48	5.74	3.88	1.91	7.4
3.99	0.21	0.837	3.87	0.63	2.44	3.87	1.06	4.11	3.88	1.49	5.77	3.88	1.92	7.44
3.97	0.22	0.873	3.87	0.64	2.48	3.87	1.07	4.15	3.88	1.5	5.81	3.88	1.93	7.48
3.95	0.23	0.9093	3.87	0.65	2.52	3.87	1.08	4.18	3.88	1.51	5.85	3.88	1.94	7.52
3.94	0.24	0.9458	3.87	0.66	2.56	3.87	1.09	4.22	3.88	1.52	5.89	3.88	1.95	7.56
3.93	0.25	0.9826	3.87	0.67	2.59	3.87	1.1	4.26	3.88	1.53	5.93	3.88	1.96	7.6
3.92	0.26	1.02	3.87	0.68	2.63	3.87	1.11	4.3	3.88	1.54	5.97	3.88	1.97	7.64
3.91	0.27	1.06	3.87	0.69	2.67	3.87	1.12	4.34	3.88	1.55	6.01	3.88	1.98	7.67
3.91	0.28	1.09	3.87	0.7	2.71	3.87	1.13	4.38	3.88	1.56	6.05	3.88	1.99	7.71
3.9	0.29	1.13	3.87	0.71	2.75	3.87	1.14	4.42	3.88	1.57	6.09	3.88	2	7.75
3.9	0.3	1.17	3.87	0.72	2.79	3.87	1.15	4.46	3.88	1.58	6.12	3.88	2.01	7.79
3.89	0.31	1.21	3.87	0.73	2.83	3.87	1.16	4.49	3.88	1.59	6.16	3.88	2.02	7.83
3.89	0.32	1.24	3.87	0.74	2.87	3.87	1.17	4.53	3.88	1.6	6.2	3.88	2.03	7.87
3.89	0.33	1.28	3.87	0.75	2.9	3.87	1.18	4.57	3.88	1.61	6.24	3.88	2.04	7.91
3.88	0.34	1.32	3.87	0.76	2.94	3.87	1.19	4.61	3.88	1.62	6.28	3.88	2.05	7.95
3.88	0.35	1.36	3.87	0.77	2.98	3.87	1.2	4.65	3.88	1.63	6.32	3.88	2.06	7.98
3.88	0.36	1.4	3.87	0.78	3.02	3.87	1.21	4.69	3.88	1.64	6.36	3.88	2.07	8.02
3.88	0.37	1.44	3.87	0.79	3.06	3.87	1.22	4.73	3.88	1.65	6.4	3.88	2.08	8.06
3.88	0.38	1.47	3.87	0.8	3.1	3.87	1.23	4.77	3.88	1.66	6.43	3.88	2.09	8.1
3.88	0.39	1.51	3.87	0.81	3.14	3.87	1.24	4.8	3.88	1.67	6.47	3.88	2.1	8.14
3.88	0.4	1.55	3.87	0.82	3.18	3.87	1.25	4.84	3.88	1.68	6.51	3.88	2.11	8.18
3.88	0.41	1.59	3.87	0.83	3.21	3.87	1.26	4.88	3.88	1.69	6.55	3.88	2.12	8.22
3.88	0.42	1.63	3.87	0.84	3.25	3.87	1.27	4.92	3.88	1.7	6.59	3.88	2.13	8.25
			3.87	0.85	3.29	3.87	1.28	4.96	3.88	1.71	6.63	3.88	2.14	8.29

APPENDIX III *b*)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 90% POWER FOR N = 80.

90% Power, N= 80

N_1 = 40, N_2 = 40, $\beta = 0.1$

HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
7.2	0.01	0.072	2.18	0.43	0.9364	2.16	0.86	1.85	2.16	1.29	2.78	2.16	1.72	3.71
4.99	0.02	0.0998	2.18	0.44	0.9574	2.16	0.87	1.88	2.16	1.3	2.8	2.16	1.73	3.73
4.14	0.03	0.1242	2.17	0.45	0.9783	2.16	0.88	1.90	2.16	1.31	2.82	2.16	1.74	3.75
3.67	0.04	0.1469	2.17	0.46	0.9994	2.16	0.89	1.92	2.16	1.32	2.85	2.16	1.75	3.77
3.37	0.05	0.1687	2.17	0.47	1.02	2.16	0.90	1.94	2.16	1.33	2.87	2.16	1.76	3.8
3.16	0.06	0.1898	2.17	0.48	1.04	2.16	0.91	1.96	2.16	1.34	2.89	2.16	1.77	3.82
3.01	0.07	0.2105	2.17	0.49	1.06	2.16	0.92	1.98	2.16	1.35	2.91	2.16	1.78	3.84
2.89	0.08	0.2309	2.17	0.5	1.08	2.16	0.93	2.01	2.16	1.36	2.93	2.16	1.79	3.86
2.79	0.09	0.251	2.17	0.51	1.1	2.16	0.94	2.03	2.16	1.37	2.95	2.16	1.8	3.88
2.71	0.1	0.271	2.17	0.52	1.13	2.16	0.95	2.05	2.16	1.38	2.98	2.16	1.81	3.9
2.64	0.11	0.2908	2.16	0.53	1.15	2.16	0.96	2.07	2.16	1.39	3	2.16	1.82	3.93
2.59	0.12	0.3106	2.16	0.54	1.17	2.16	0.97	2.09	2.16	1.4	3.02	2.16	1.83	3.95
2.54	0.13	0.3303	2.16	0.55	1.19	2.16	0.98	2.11	2.16	1.41	3.04	2.16	1.84	3.97
2.5	0.14	0.35	2.16	0.56	1.21	2.16	0.99	2.13	2.16	1.42	3.06	2.16	1.85	3.99
2.46	0.15	0.3697	2.16	0.57	1.23	2.16	1.00	2.16	2.16	1.43	3.08	2.16	1.86	4.01
2.43	0.16	0.3894	2.16	0.58	1.25	2.16	1.01	2.18	2.16	1.44	3.11	2.16	1.87	4.03
2.41	0.17	0.409	2.16	0.59	1.27	2.16	1.02	2.20	2.16	1.45	3.13	2.16	1.88	4.05
2.38	0.18	0.4287	2.16	0.6	1.3	2.16	1.03	2.22	2.16	1.46	3.15	2.16	1.89	4.08
2.36	0.19	0.4485	2.16	0.61	1.32	2.16	1.04	2.24	2.16	1.47	3.17	2.16	1.9	4.1
2.34	0.2	0.4682	2.16	0.62	1.34	2.16	1.05	2.26	2.16	1.48	3.19	2.16	1.91	4.12
2.32	0.21	0.488	2.16	0.63	1.36	2.16	1.06	2.29	2.16	1.49	3.21	2.16	1.92	4.14
2.31	0.22	0.5079	2.16	0.64	1.38	2.16	1.07	2.31	2.16	1.5	3.23	2.16	1.93	4.16
2.29	0.23	0.5277	2.16	0.65	1.4	2.16	1.08	2.33	2.16	1.51	3.26	2.16	1.94	4.18
2.28	0.24	0.5477	2.16	0.66	1.42	2.16	1.09	2.35	2.16	1.52	3.28	2.16	1.95	4.21
2.27	0.25	0.5677	2.16	0.67	1.45	2.16	1.10	2.37	2.16	1.53	3.3	2.16	1.96	4.23
2.26	0.26	0.5877	2.16	0.68	1.47	2.16	1.11	2.39	2.16	1.54	3.32	2.16	1.97	4.25
2.25	0.27	0.6078	2.16	0.69	1.49	2.16	1.12	2.42	2.16	1.55	3.34	2.16	1.98	4.27
2.24	0.28	0.6279	2.16	0.7	1.51	2.16	1.13	2.44	2.16	1.56	3.36	2.16	1.99	4.29
2.23	0.29	0.6481	2.16	0.71	1.53	2.16	1.14	2.46	2.16	1.57	3.39	2.16	2	4.31
2.23	0.3	0.6684	2.16	0.72	1.55	2.16	1.15	2.48	2.16	1.58	3.41	2.16	2.01	4.34
2.22	0.31	0.6887	2.16	0.73	1.57	2.16	1.16	2.50	2.16	1.59	3.43	2.16	2.02	4.36
2.22	0.32	0.7091	2.16	0.74	1.6	2.16	1.17	2.52	2.16	1.6	3.45	2.16	2.03	4.38
2.21	0.33	0.7295	2.16	0.75	1.62	2.16	1.18	2.54	2.16	1.61	3.47	2.16	2.04	4.4
2.21	0.34	0.75	2.16	0.76	1.64	2.16	1.19	2.57	2.16	1.62	3.49	2.16	2.05	4.42
2.2	0.35	0.7705	2.16	0.77	1.66	2.16	1.20	2.59	2.16	1.63	3.52	2.16	2.06	4.44
2.2	0.36	0.7911	2.16	0.78	1.68	2.16	1.21	2.61	2.16	1.64	3.54	2.16	2.07	4.46
2.19	0.37	0.8117	2.16	0.79	1.7	2.16	1.22	2.63	2.16	1.65	3.56	2.16	2.08	4.49
2.19	0.38	0.8324	2.16	0.8	1.73	2.16	1.23	2.65	2.16	1.66	3.58	2.16	2.09	4.51
2.19	0.39	0.8531	2.16	0.81	1.75	2.16	1.24	2.67	2.16	1.67	3.6	2.16	2.1	4.53
2.18	0.4	0.8739	2.16	0.82	1.77	2.16	1.25	2.70	2.16	1.68	3.62	2.16	2.11	4.55
2.18	0.41	0.8947	2.16	0.83	1.79	2.16	1.26	2.72	2.16	1.69	3.64	2.16	2.12	4.57
2.18	0.42	0.9156	2.16	0.84	1.81	2.16	1.27	2.74	2.16	1.7	3.67	2.16	2.13	4.59
			2.16	0.85	1.83	2.16	1.28	2.76	2.16	1.71	3.69	2.16	2.14	4.62

APPENDIX III *c*)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 90% POWER FOR N = 100.

90% Power, N= 100

N_1 = 50, N_2 = 50, $\beta = 0.1$

HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
6.29	0.01	0.0629	2	0.43	0.8593	1.97	0.86	1.7	1.97	1.29	2.55	1.97	1.72	3.4
4.42	0.02	0.0885	2	0.44	0.8784	1.97	0.87	1.72	1.97	1.3	2.57	1.97	1.73	3.42
3.7	0.03	0.111	1.99	0.45	0.8976	1.97	0.88	1.74	1.97	1.31	2.59	1.97	1.74	3.44
3.3	0.04	0.1321	1.99	0.46	0.9167	1.97	0.89	1.76	1.97	1.32	2.61	1.97	1.75	3.46
3.05	0.05	0.1523	1.99	0.47	0.9359	1.97	0.9	1.78	1.97	1.33	2.63	1.97	1.76	3.48
2.86	0.06	0.1719	1.99	0.48	0.9552	1.97	0.91	1.8	1.97	1.34	2.65	1.97	1.77	3.49
2.73	0.07	0.1911	1.99	0.49	0.9745	1.97	0.92	1.82	1.97	1.35	2.67	1.97	1.78	3.51
2.63	0.08	0.21	1.99	0.5	0.9937	1.97	0.93	1.84	1.97	1.36	2.69	1.97	1.79	3.53
2.54	0.09	0.2287	1.99	0.51	1.01	1.97	0.94	1.86	1.97	1.37	2.7	1.97	1.8	3.55
2.47	0.1	0.2473	1.99	0.52	1.03	1.97	0.95	1.88	1.97	1.38	2.72	1.97	1.81	3.57
2.42	0.11	0.2657	1.98	0.53	1.05	1.97	0.96	1.9	1.97	1.39	2.74	1.97	1.82	3.59
2.37	0.12	0.2841	1.98	0.54	1.07	1.97	0.97	1.92	1.97	1.4	2.76	1.97	1.83	3.61
2.33	0.13	0.3024	1.98	0.55	1.09	1.97	0.98	1.93	1.97	1.41	2.78	1.97	1.84	3.63
2.29	0.14	0.3206	1.98	0.56	1.11	1.97	0.99	1.95	1.97	1.42	2.8	1.97	1.85	3.65
2.26	0.15	0.3389	1.98	0.57	1.13	1.97	1	1.97	1.97	1.43	2.82	1.97	1.86	3.67
2.23	0.16	0.3571	1.98	0.58	1.15	1.97	1.01	1.99	1.97	1.44	2.84	1.97	1.87	3.69
2.21	0.17	0.3753	1.98	0.59	1.17	1.97	1.02	2.01	1.97	1.45	2.86	1.97	1.88	3.71
2.19	0.18	0.3935	1.98	0.6	1.19	1.97	1.03	2.03	1.97	1.46	2.88	1.97	1.89	3.73
2.17	0.19	0.4117	1.98	0.61	1.21	1.97	1.04	2.05	1.97	1.47	2.9	1.97	1.9	3.75
2.15	0.2	0.4299	1.98	0.62	1.23	1.97	1.05	2.07	1.97	1.48	2.92	1.97	1.91	3.77
2.13	0.21	0.4482	1.98	0.63	1.25	1.97	1.06	2.09	1.97	1.49	2.94	1.97	1.92	3.79
2.12	0.22	0.4665	1.98	0.64	1.27	1.97	1.07	2.11	1.97	1.5	2.96	1.97	1.93	3.81
2.11	0.23	0.4848	1.98	0.65	1.29	1.97	1.08	2.13	1.97	1.51	2.98	1.97	1.94	3.83
2.1	0.24	0.5032	1.98	0.66	1.31	1.97	1.09	2.15	1.97	1.52	3	1.97	1.95	3.85
2.09	0.25	0.5216	1.98	0.67	1.32	1.97	1.1	2.17	1.97	1.53	3.02	1.97	1.96	3.87
2.08	0.26	0.54	1.98	0.68	1.34	1.97	1.11	2.19	1.97	1.54	3.04	1.97	1.97	3.89
2.07	0.27	0.5584	1.98	0.69	1.36	1.97	1.12	2.21	1.97	1.55	3.06	1.97	1.98	3.91
2.06	0.28	0.5769	1.98	0.7	1.38	1.97	1.13	2.23	1.97	1.56	3.08	1.97	1.99	3.93
2.05	0.29	0.5955	1.98	0.71	1.4	1.97	1.14	2.25	1.97	1.57	3.1	1.97	2	3.95
2.05	0.3	0.6141	1.98	0.72	1.42	1.97	1.15	2.27	1.97	1.58	3.12	1.97	2.01	3.97
2.04	0.31	0.6327	1.98	0.73	1.44	1.97	1.16	2.29	1.97	1.59	3.14	1.97	2.02	3.99
2.04	0.32	0.6514	1.98	0.74	1.46	1.97	1.17	2.31	1.97	1.6	3.16	1.97	2.03	4.01
2.03	0.33	0.6701	1.98	0.75	1.48	1.97	1.18	2.33	1.97	1.61	3.18	1.97	2.04	4.03
2.03	0.34	0.6888	1.98	0.76	1.5	1.97	1.19	2.35	1.97	1.62	3.2	1.97	2.05	4.05
2.02	0.35	0.7076	1.98	0.77	1.52	1.97	1.2	2.37	1.97	1.63	3.22	1.97	2.06	4.07
2.02	0.36	0.7264	1.98	0.78	1.54	1.97	1.21	2.39	1.97	1.64	3.24	1.97	2.07	4.09
2.01	0.37	0.7453	1.98	0.79	1.56	1.97	1.22	2.41	1.97	1.65	3.26	1.97	2.08	4.11
2.01	0.38	0.7642	1.98	0.8	1.58	1.97	1.23	2.43	1.97	1.66	3.28	1.97	2.09	4.13
2.01	0.39	0.7832	1.97	0.81	1.6	1.97	1.24	2.45	1.97	1.67	3.3	1.97	2.1	4.15
2.01	0.4	0.8021	1.97	0.82	1.62	1.97	1.25	2.47	1.97	1.68	3.32	1.97	2.11	4.17
2	0.41	0.8212	1.97	0.83	1.64	1.97	1.26	2.49	1.97	1.69	3.34	1.97	2.12	4.19
2	0.42	0.8402	1.97	0.84	1.66	1.97	1.27	2.51	1.97	1.7	3.36	1.97	2.13	4.21
			1.97	0.85	1.68	1.97	1.28	2.53	1.97	1.71	3.38	1.97	2.14	4.23

APPENDIX III *d*)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 90% POWER FOR N = 200.

90% Power, N= 200

N_1 = 100, N_2 = 100, $\beta = 0.1$

HR	h_1	h_2	HR	h_1	h_2	HR	h_1	h_2	HR	h_1	h_2	HR	h_1	h_2
4.3	0	0.043	1.63	0.43	0.6993	1.6	0.86	1.38	1.6	1.29	2.06	1.6	1.72	2.75
3.2	0	0.063	1.62	0.44	0.7148	1.6	0.87	1.39	1.6	1.3	2.08	1.6	1.73	2.77
2.7	0	0.082	1.62	0.45	0.7304	1.6	0.88	1.41	1.6	1.31	2.1	1.6	1.74	2.79
2.5	0	0.099	1.62	0.46	0.7459	1.6	0.89	1.43	1.6	1.32	2.11	1.6	1.75	2.8
2.3	0.1	0.116	1.62	0.47	0.7615	1.6	0.9	1.44	1.6	1.33	2.13	1.6	1.76	2.82
2.2	0.1	0.132	1.62	0.48	0.777	1.6	0.91	1.46	1.6	1.34	2.14	1.6	1.77	2.83
2.1	0.1	0.148	1.62	0.49	0.7926	1.6	0.92	1.47	1.6	1.35	2.16	1.6	1.78	2.85
2.1	0.1	0.164	1.62	0.5	0.8083	1.6	0.93	1.49	1.6	1.36	2.18	1.6	1.79	2.87
2	0.1	0.18	1.62	0.51	0.8239	1.6	0.94	1.51	1.6	1.37	2.19	1.6	1.8	2.88
2	0.1	0.195	1.61	0.52	0.8395	1.6	0.95	1.52	1.6	1.38	2.21	1.6	1.81	2.9
1.9	0.1	0.211	1.61	0.53	0.8552	1.6	0.96	1.54	1.6	1.39	2.22	1.6	1.82	2.91
1.9	0.1	0.226	1.61	0.54	0.8709	1.6	0.97	1.55	1.6	1.4	2.24	1.6	1.83	2.93
1.9	0.1	0.241	1.61	0.55	0.8865	1.6	0.98	1.57	1.6	1.41	2.26	1.6	1.84	2.95
1.8	0.1	0.256	1.61	0.56	0.9022	1.6	0.99	1.59	1.6	1.42	2.27	1.6	1.85	2.96
1.8	0.2	0.272	1.61	0.57	0.918	1.6	1	1.60	1.6	1.43	2.29	1.6	1.86	2.98
1.8	0.2	0.287	1.61	0.58	0.9337	1.6	1.01	1.62	1.6	1.44	2.3	1.6	1.87	2.99
1.8	0.2	0.302	1.61	0.59	0.9494	1.6	1.02	1.63	1.6	1.45	2.32	1.6	1.88	3.01
1.8	0.2	0.317	1.61	0.6	0.9652	1.6	1.03	1.65	1.6	1.46	2.34	1.6	1.89	3.03
1.8	0.2	0.332	1.61	0.61	0.9809	1.6	1.04	1.66	1.6	1.47	2.35	1.6	1.9	3.04
1.7	0.2	0.347	1.61	0.62	0.9967	1.6	1.05	1.68	1.6	1.48	2.37	1.6	1.91	3.06
1.7	0.2	0.363	1.61	0.63	1.01	1.6	1.06	1.70	1.6	1.49	2.38	1.6	1.92	3.07
1.7	0.2	0.378	1.61	0.64	1.03	1.6	1.07	1.71	1.6	1.5	2.4	1.6	1.93	3.09
1.7	0.2	0.393	1.61	0.65	1.04	1.6	1.08	1.73	1.6	1.51	2.42	1.6	1.94	3.11
1.7	0.2	0.408	1.61	0.66	1.06	1.6	1.09	1.74	1.6	1.52	2.43	1.6	1.95	3.12
1.7	0.3	0.423	1.61	0.67	1.08	1.6	1.1	1.76	1.6	1.53	2.45	1.6	1.96	3.14
1.7	0.3	0.438	1.61	0.68	1.09	1.6	1.11	1.78	1.6	1.54	2.47	1.6	1.97	3.15
1.7	0.3	0.454	1.6	0.69	1.11	1.6	1.12	1.79	1.6	1.55	2.48	1.6	1.98	3.17
1.7	0.3	0.469	1.6	0.7	1.12	1.6	1.13	1.81	1.6	1.56	2.5	1.6	1.99	3.19
1.7	0.3	0.484	1.6	0.71	1.14	1.6	1.14	1.82	1.6	1.57	2.51	1.6	2	3.2
1.7	0.3	0.499	1.6	0.72	1.15	1.6	1.15	1.84	1.6	1.58	2.53	1.6	2.01	3.22
1.7	0.3	0.515	1.6	0.73	1.17	1.6	1.16	1.86	1.6	1.59	2.55	1.6	2.02	3.23
1.7	0.3	0.53	1.6	0.74	1.19	1.6	1.17	1.87	1.6	1.6	2.56	1.6	2.03	3.25
1.7	0.3	0.545	1.6	0.75	1.2	1.6	1.18	1.89	1.6	1.61	2.58	1.6	2.04	3.27
1.7	0.3	0.561	1.6	0.76	1.22	1.6	1.19	1.90	1.6	1.62	2.59	1.6	2.05	3.28
1.7	0.4	0.576	1.6	0.77	1.23	1.6	1.2	1.92	1.6	1.63	2.61	1.6	2.06	3.3
1.6	0.4	0.591	1.6	0.78	1.25	1.6	1.21	1.94	1.6	1.64	2.63	1.6	2.07	3.31
1.6	0.4	0.607	1.6	0.79	1.27	1.6	1.22	1.95	1.6	1.65	2.64	1.6	2.08	3.33
1.6	0.4	0.622	1.6	0.8	1.28	1.6	1.23	1.97	1.6	1.66	2.66	1.6	2.09	3.35
1.6	0.4	0.637	1.6	0.81	1.3	1.6	1.24	1.98	1.6	1.67	2.67	1.6	2.1	3.36
1.6	0.4	0.653	1.6	0.82	1.31	1.6	1.25	2.00	1.6	1.68	2.69	1.6	2.11	3.38
1.6	0.4	0.668	1.6	0.83	1.33	1.6	1.26	2.02	1.6	1.69	2.71	1.6	2.12	3.39
1.6	0.4	0.684	1.6	0.84	1.35	1.6	1.27	2.03	1.6	1.7	2.72	1.6	2.13	3.41
			1.6	0.85	1.36	1.6	1.28	2.05	1.6	1.71	2.74	1.6	2.14	3.43

APPENDIX IV *a*)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 95% POWER FOR N = 30.

95% Power, *N*= 30

N_1 = 15, N_2 = 15, $\beta = 0.05$

HR	h_1	h_2
15.6	0.01	0.1563
10.4	0.02	0.2078
8.42	0.03	0.2527
7.37	0.04	0.2947
6.71	0.05	0.3353
6.25	0.06	0.3751
5.92	0.07	0.4146
5.68	0.08	0.4541
5.49	0.09	0.4938
5.34	0.1	0.5337
5.22	0.11	0.5741
5.12	0.12	0.6148
5.05	0.13	0.656
4.98	0.14	0.6978
4.93	0.15	0.74
4.89	0.16	0.7826
4.86	0.17	0.8258
4.83	0.18	0.8694
4.81	0.19	0.9134
4.79	0.2	0.9578
4.77	0.21	1
4.76	0.22	1.05
4.75	0.23	1.09
4.74	0.24	1.14
4.74	0.25	1.18
4.73	0.26	1.23
4.73	0.27	1.28
4.72	0.28	1.32
4.72	0.29	1.37
4.72	0.3	1.42
4.72	0.31	1.46
4.71	0.32	1.51
4.71	0.33	1.56
4.71	0.34	1.6
4.71	0.35	1.65
4.71	0.36	1.7
4.71	0.37	1.74
4.71	0.38	1.79
4.71	0.39	1.84
4.71	0.4	1.88
4.71	0.41	1.93
4.71	0.42	1.98
4.71	0.43	2.02
4.71	0.44	2.07
4.71	0.45	2.12
4.71	0.46	2.17
4.71	0.47	2.21
4.71	0.48	2.26
4.71	0.49	2.31
4.71	0.5	2.35
4.71	0.51	2.4
4.71	0.52	2.45
4.71	0.53	2.5
4.71	0.54	2.54
4.71	0.55	2.59
4.71	0.56	2.64
4.71	0.57	2.68
4.71	0.58	2.73
4.71	0.59	2.78
4.71	0.6	2.83
4.71	0.61	2.87
4.71	0.62	2.92
4.71	0.63	2.97
4.71	0.64	3.01
4.71	0.65	3.06
4.71	0.66	3.11
4.71	0.67	3.16
4.71	0.68	3.2
4.71	0.69	3.25
4.71	0.7	3.3
4.71	0.71	3.34
4.71	0.72	3.39
4.71	0.73	3.44
4.71	0.74	3.49
4.71	0.75	3.53
4.71	0.76	3.58
4.71	0.77	3.63
4.71	0.78	3.67
4.71	0.79	3.72
4.71	0.8	3.77
4.71	0.81	3.82
4.71	0.82	3.86
4.71	0.83	3.91
4.71	0.84	3.96
4.71	0.85	4
4.71	0.86	4.05
4.71	0.87	4.1
4.71	0.88	4.15
4.71	0.89	4.19
4.71	0.9	4.24
4.71	0.91	4.29
4.71	0.92	4.33
4.71	0.93	4.38
4.71	0.94	4.43
4.71	0.95	4.48
4.71	0.96	4.52
4.71	0.97	4.57
4.71	0.98	4.62
4.71	0.99	4.66
4.71	1	4.71
4.71	1.01	4.76
4.71	1.02	4.81
4.71	1.03	4.85
4.71	1.04	4.9
4.71	1.05	4.95
4.71	1.06	4.99
4.71	1.07	5.04
4.71	1.08	5.09
4.71	1.09	5.14
4.71	1.1	5.18
4.71	1.11	5.23
4.71	1.12	5.28
4.71	1.13	5.32
4.71	1.14	5.37
4.71	1.15	5.42
4.71	1.16	5.47
4.71	1.17	5.51
4.71	1.18	5.56
4.71	1.19	5.61
4.71	1.2	5.66
4.71	1.21	5.7
4.71	1.22	5.75
4.71	1.23	5.8
4.71	1.24	5.84
4.71	1.25	5.89
4.71	1.26	5.94
4.71	1.27	5.99
4.71	1.28	6.03
4.71	1.29	6.08
4.71	1.30	6.13
4.71	1.31	6.17
4.71	1.32	6.22
4.71	1.33	6.27
4.71	1.34	6.31
4.71	1.35	6.36
4.71	1.36	6.41
4.71	1.37	6.46
4.71	1.38	6.5
4.71	1.39	6.55
4.71	1.40	6.6
4.71	1.41	6.64
4.71	1.42	6.69
4.71	1.43	6.74
4.71	1.44	6.78
4.71	1.45	6.83
4.71	1.46	6.88
4.71	1.47	6.92
4.71	1.48	6.97
4.71	1.49	7.02
4.71	1.50	7.06
4.71	1.51	7.11
4.71	1.52	7.16
4.71	1.53	7.21
4.71	1.54	7.25
4.71	1.55	7.3
4.71	1.56	7.35
4.71	1.57	7.39
4.71	1.58	7.44
4.71	1.59	7.49
4.71	1.60	7.53
4.71	1.61	7.58
4.71	1.62	7.63
4.71	1.63	7.67
4.71	1.64	7.72
4.71	1.65	7.77
4.71	1.66	7.81
4.71	1.67	7.86
4.71	1.68	7.91
4.71	1.69	7.95
4.7	1.70	8
4.7	1.71	8.04
4.7	1.72	8.09
4.7	1.73	8.14
4.7	1.74	8.18
4.7	1.75	8.23
4.7	1.76	8.28
4.7	1.77	8.32
4.7	1.78	8.37
4.7	1.79	8.42
4.7	1.8	8.46
4.7	1.81	8.51
4.7	1.82	8.56
4.7	1.83	8.6
4.7	1.84	8.65
4.7	1.85	8.7
4.7	1.86	8.74
4.7	1.87	8.79
4.7	1.88	8.84
4.7	1.89	8.89
4.7	1.9	8.93
4.7	1.91	8.98
4.7	1.92	9.03
4.7	1.93	9.07
4.7	1.94	9.12
4.7	1.95	9.17
4.7	1.96	9.21
4.7	1.97	9.26
4.7	1.98	9.31
4.7	1.99	9.35
4.7	2	9.4
4.7	2.01	9.45
4.7	2.02	9.5
4.7	2.03	9.54
4.7	2.04	9.59
4.7	2.05	9.64
4.7	2.06	9.68
4.7	2.07	9.73
4.7	2.08	9.78
4.7	2.09	9.82
4.7	2.1	9.87
4.7	2.11	9.92
4.7	2.12	9.96
4.7	2.13	10
4.7	2.14	10.1

APPENDIX IV *b*)

ESTIMATED ***HR-h*₂** COMBINATION NEEDED TO ACHIEVE 95% POWER FOR N = 80.

95% Power, N= 80														
N_1 = 40, N_2 = 40, $\beta = 0.05$														
HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
7.99	0.01	0.0799	2.40	0.4	1	1.6	0.9	1.4	2.4	1.3	3.1	2.4	1.7	4.1
5.53	0.02	0.1106	2.40	0.4	1.1	1.6	0.9	1.4	2.4	1.3	3.1	2.4	1.7	4.1
4.58	0.03	0.1374	2.39	0.5	1.1	1.6	0.9	1.4	2.4	1.3	3.1	2.4	1.7	4.1
4.06	0.04	0.1622	2.39	0.5	1.1	1.6	0.9	1.4	2.4	1.3	3.1	2.4	1.8	4.2
3.72	0.05	0.1859	2.39	0.5	1.1	1.6	0.9	1.4	2.4	1.3	3.2	2.4	1.8	4.2
3.48	0.06	0.2089	2.39	0.5	1.2	1.6	0.9	1.5	2.4	1.3	3.2	2.4	1.8	4.2
3.31	0.07	0.2314	2.39	0.5	1.2	1.6	0.9	1.5	2.4	1.4	3.2	2.4	1.8	4.2
3.17	0.08	0.2536	2.39	0.5	1.2	1.6	0.9	1.5	2.4	1.4	3.2	2.4	1.8	4.3
3.06	0.09	0.2755	2.39	0.5	1.2	1.6	0.9	1.5	2.4	1.4	3.3	2.4	1.8	4.3
2.97	0.1	0.2973	2.39	0.5	1.2	1.6	1	1.5	2.4	1.4	3.3	2.4	1.8	4.3
2.9	0.11	0.3189	2.39	0.5	1.3	1.6	1	1.5	2.4	1.4	3.3	2.4	1.8	4.3
2.84	0.12	0.3405	2.39	0.5	1.3	1.6	1	1.6	2.4	1.4	3.3	2.4	1.8	4.4
2.78	0.13	0.362	2.38	0.6	1.3	1.6	1	1.6	2.4	1.4	3.4	2.4	1.8	4.4
2.74	0.14	0.3835	2.38	0.6	1.3	1.6	1	1.6	2.4	1.4	3.4	2.4	1.9	4.4
2.7	0.15	0.405	2.38	0.6	1.4	1.6	1	1.6	2.4	1.4	3.4	2.4	1.9	4.4
2.67	0.16	0.4265	2.38	0.6	1.4	1.6	1	1.6	2.4	1.4	3.4	2.4	1.9	4.5
2.64	0.17	0.448	2.38	0.6	1.4	1.6	1	1.6	2.4	1.5	3.5	2.4	1.9	4.5
2.61	0.18	0.4696	2.38	0.6	1.4	1.6	1	1.7	2.4	1.5	3.5	2.4	1.9	4.5
2.59	0.19	0.4913	2.38	0.6	1.5	1.6	1	1.7	2.4	1.5	3.5	2.4	1.9	4.5
2.56	0.2	0.513	2.38	0.6	1.5	1.6	1.1	1.7	2.4	1.5	3.5	2.4	1.9	4.6
2.55	0.21	0.5347	2.38	0.6	1.5	1.6	1.1	1.7	2.4	1.5	3.6	2.4	1.9	4.6
2.53	0.22	0.5565	2.38	0.6	1.5	1.6	1.1	1.7	2.4	1.5	3.6	2.4	1.9	4.6
2.51	0.23	0.5784	2.38	0.7	1.6	1.6	1.1	1.7	2.4	1.5	3.6	2.4	1.9	4.6
2.5	0.24	0.6004	2.38	0.7	1.6	1.6	1.1	1.7	2.4	1.5	3.6	2.4	2	4.6
2.49	0.25	0.6224	2.38	0.7	1.6	1.6	1.1	1.8	2.4	1.5	3.6	2.4	2	4.7
2.48	0.26	0.6445	2.38	0.7	1.6	1.6	1.1	1.8	2.4	1.5	3.7	2.4	2	4.7
2.47	0.27	0.6667	2.38	0.7	1.6	1.6	1.1	1.8	2.4	1.6	3.7	2.4	2	4.7
2.46	0.28	0.689	2.38	0.7	1.7	1.6	1.1	1.8	2.4	1.6	3.7	2.4	2	4.7
2.45	0.29	0.7113	2.38	0.7	1.7	1.6	1.1	1.8	2.4	1.6	3.7	2.4	2	4.8
2.45	0.3	0.7337	2.38	0.7	1.7	1.6	1.2	1.8	2.4	1.6	3.8	2.4	2	4.8
2.44	0.31	0.7562	2.38	0.7	1.7	1.6	1.2	1.9	2.4	1.6	3.8	2.4	2	4.8
2.43	0.32	0.7788	2.38	0.7	1.8	1.6	1.2	1.9	2.4	1.6	3.8	2.4	2	4.8
2.43	0.33	0.8014	2.38	0.8	1.8	1.6	1.2	1.9	2.4	1.6	3.8	2.4	2	4.9
2.42	0.34	0.8241	2.38	0.8	1.8	1.6	1.2	1.9	2.4	1.6	3.9	2.4	2.1	4.9
2.42	0.35	0.8468	2.38	0.8	1.8	1.6	1.2	1.9	2.4	1.6	3.9	2.4	2.1	4.9
2.42	0.36	0.8696	2.38	0.8	1.9	1.6	1.2	1.9	2.4	1.6	3.9	2.4	2.1	4.9
2.41	0.37	0.8925	2.38	0.8	1.9	1.6	1.2	2	2.4	1.7	3.9	2.4	2.1	5
2.41	0.38	0.9154	2.38	0.8	1.9	1.6	1.2	2	2.4	1.7	4	2.4	2.1	5
2.41	0.39	0.9384	2.38	0.8	1.9	1.6	1.2	2	2.4	1.7	4	2.4	2.1	5
2.4	0.4	0.9615	2.38	0.8	2	1.6	1.3	2	2.4	1.7	4	2.4	2.1	5
2.4	0.41	0.9845	2.38	0.8	2	1.6	1.3	2	2.4	1.7	4	2.4	2.1	5.1
2.4	0.42	1.01	2.38	0.8	2	1.6	1.3	2	2.4	1.7	4.1	2.4	2.1	5.1
			2.38	0.9	2	1.6	1.3	2.1	2.4	1.7	4.1	2.4	2.1	5.1

APPENDIX IV *c*)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 95% POWER FOR N = 100.

95% Power, N= 100

N_1 = 50, N_2 = 50, $\beta = 0.05$

HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
6.97	0.01	0.0697	2.17	0.43	0.9339	2.15	0.86	1.85	2.15	1.29	2.77	2.15	1.72	3.7
4.89	0.02	0.0977	2.17	0.44	0.9547	2.15	0.87	1.87	2.15	1.3	2.8	2.15	1.73	3.72
4.07	0.03	0.1222	2.17	0.45	0.9757	2.15	0.88	1.89	2.15	1.31	2.82	2.15	1.74	3.74
3.63	0.04	0.145	2.17	0.46	0.9966	2.15	0.89	1.91	2.15	1.32	2.84	2.15	1.75	3.76
3.34	0.05	0.1668	2.17	0.47	1.02	2.15	0.9	1.94	2.15	1.33	2.86	2.15	1.76	3.79
3.13	0.06	0.188	2.16	0.48	1.04	2.15	0.91	1.96	2.15	1.34	2.88	2.15	1.77	3.81
2.98	0.07	0.2087	2.16	0.49	1.06	2.15	0.92	1.98	2.15	1.35	2.9	2.15	1.78	3.83
2.86	0.08	0.2291	2.16	0.5	1.08	2.15	0.93	2	2.15	1.36	2.93	2.15	1.79	3.85
2.77	0.09	0.2492	2.16	0.51	1.1	2.15	0.94	2.02	2.15	1.37	2.95	2.15	1.8	3.87
2.69	0.1	0.2692	2.16	0.52	1.12	2.15	0.95	2.04	2.15	1.38	2.97	2.15	1.81	3.89
2.63	0.11	0.289	2.16	0.53	1.14	2.15	0.96	2.06	2.15	1.39	2.99	2.15	1.82	3.92
2.57	0.12	0.3088	2.16	0.54	1.17	2.15	0.97	2.09	2.15	1.4	3.01	2.15	1.83	3.94
2.53	0.13	0.3285	2.16	0.55	1.19	2.15	0.98	2.11	2.15	1.41	3.03	2.15	1.84	3.96
2.49	0.14	0.3482	2.16	0.56	1.21	2.15	0.99	2.13	2.15	1.42	3.05	2.15	1.85	3.98
2.45	0.15	0.3678	2.16	0.57	1.23	2.15	1	2.15	2.15	1.43	3.08	2.15	1.86	4
2.42	0.16	0.3875	2.16	0.58	1.25	2.15	1.01	2.17	2.15	1.44	3.1	2.15	1.87	4.02
2.40	0.17	0.4072	2.16	0.59	1.27	2.15	1.02	2.19	2.15	1.45	3.12	2.15	1.88	4.04
2.37	0.18	0.4268	2.15	0.6	1.29	2.15	1.03	2.22	2.15	1.46	3.14	2.15	1.89	4.07
2.35	0.19	0.4465	2.15	0.61	1.31	2.15	1.04	2.24	2.15	1.47	3.16	2.15	1.9	4.09
2.33	0.2	0.4663	2.15	0.62	1.34	2.15	1.05	2.26	2.15	1.48	3.18	2.15	1.91	4.11
2.31	0.21	0.4861	2.15	0.63	1.36	2.15	1.06	2.28	2.15	1.49	3.21	2.15	1.92	4.13
2.30	0.22	0.5059	2.15	0.64	1.38	2.15	1.07	2.3	2.15	1.5	3.23	2.15	1.93	4.15
2.29	0.23	0.5257	2.15	0.65	1.4	2.15	1.08	2.32	2.15	1.51	3.25	2.15	1.94	4.17
2.27	0.24	0.5457	2.15	0.66	1.42	2.15	1.09	2.34	2.15	1.52	3.27	2.15	1.95	4.2
2.26	0.25	0.5656	2.15	0.67	1.44	2.15	1.1	2.37	2.15	1.53	3.29	2.15	1.96	4.22
2.25	0.26	0.5856	2.15	0.68	1.46	2.15	1.11	2.39	2.15	1.54	3.31	2.15	1.97	4.24
2.24	0.27	0.6057	2.15	0.69	1.49	2.15	1.12	2.41	2.15	1.55	3.33	2.15	1.98	4.26
2.24	0.28	0.6258	2.15	0.7	1.51	2.15	1.13	2.43	2.15	1.56	3.36	2.15	1.99	4.28
2.23	0.29	0.646	2.15	0.71	1.53	2.15	1.14	2.45	2.15	1.57	3.38	2.15	2	4.3
2.22	0.3	0.6662	2.15	0.72	1.55	2.15	1.15	2.47	2.15	1.58	3.4	2.15	2.01	4.32
2.21	0.31	0.6865	2.15	0.73	1.57	2.15	1.16	2.5	2.15	1.59	3.42	2.15	2.02	4.35
2.21	0.32	0.7069	2.15	0.74	1.59	2.15	1.17	2.52	2.15	1.6	3.44	2.15	2.03	4.37
2.20	0.33	0.7273	2.15	0.75	1.61	2.15	1.18	2.54	2.15	1.61	3.46	2.15	2.04	4.39
2.20	0.34	0.7477	2.15	0.76	1.64	2.15	1.19	2.56	2.15	1.62	3.48	2.15	2.05	4.41
2.19	0.35	0.7682	2.15	0.77	1.66	2.15	1.2	2.58	2.15	1.63	3.51	2.15	2.06	4.43
2.19	0.36	0.7887	2.15	0.78	1.68	2.15	1.21	2.6	2.15	1.64	3.53	2.15	2.07	4.45
2.19	0.37	0.8093	2.15	0.79	1.7	2.15	1.22	2.62	2.15	1.65	3.55	2.15	2.08	4.48
2.18	0.38	0.83	2.15	0.8	1.72	2.15	1.23	2.65	2.15	1.66	3.57	2.15	2.09	4.5
2.18	0.39	0.8507	2.15	0.81	1.74	2.15	1.24	2.67	2.15	1.67	3.59	2.15	2.1	4.52
2.18	0.4	0.8714	2.15	0.82	1.76	2.15	1.25	2.69	2.15	1.68	3.61	2.15	2.11	4.54
2.18	0.41	0.8922	2.15	0.83	1.79	2.15	1.26	2.71	2.15	1.69	3.64	2.15	2.12	4.56
2.17	0.42	0.913	2.15	0.84	1.81	2.15	1.27	2.73	2.15	1.7	3.66	2.15	2.13	4.58
			2.15	0.85	1.83	2.15	1.28	2.75	2.15	1.71	3.68	2.15	2.14	4.6

APPENDIX IV *d*)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 95% POWER FOR N = 200.

95% Power, N= 200

N_1 = 100, N_2 = 100, $\beta = 0.05$

HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
4.73	0.01	0.0473	1.72	0.43	0.7392	1.69	0.86	1.46	1.69	1.29	2.18	1.69	1.72	2.91
3.46	0.02	0.0692	1.72	0.44	0.7556	1.69	0.87	1.47	1.69	1.3	2.2	1.69	1.73	2.93
2.96	0.03	0.0887	1.72	0.45	0.7721	1.69	0.88	1.49	1.69	1.31	2.22	1.69	1.74	2.95
2.68	0.04	0.1071	1.71	0.46	0.7885	1.69	0.89	1.51	1.69	1.32	2.24	1.69	1.75	2.96
2.49	0.05	0.1247	1.71	0.47	0.805	1.69	0.9	1.52	1.69	1.33	2.25	1.69	1.76	2.98
2.37	0.06	0.1419	1.71	0.48	0.8214	1.69	0.91	1.54	1.69	1.34	2.27	1.69	1.77	3
2.27	0.07	0.1588	1.71	0.49	0.8379	1.69	0.92	1.56	1.69	1.35	2.29	1.69	1.78	3.01
2.19	0.08	0.1754	1.71	0.5	0.8545	1.69	0.93	1.58	1.69	1.36	2.3	1.69	1.79	3.03
2.13	0.09	0.1918	1.71	0.51	0.871	1.69	0.94	1.59	1.69	1.37	2.32	1.69	1.8	3.05
2.08	0.1	0.2081	1.71	0.52	0.8875	1.69	0.95	1.61	1.69	1.38	2.34	1.69	1.81	3.07
2.04	0.11	0.2243	1.71	0.53	0.9041	1.69	0.96	1.63	1.69	1.39	2.35	1.69	1.82	3.08
2	0.12	0.2405	1.71	0.54	0.9207	1.69	0.97	1.64	1.69	1.4	2.37	1.69	1.83	3.1
1.97	0.13	0.2565	1.7	0.55	0.9373	1.69	0.98	1.66	1.69	1.41	2.39	1.69	1.84	3.12
1.95	0.14	0.2725	1.7	0.56	0.9539	1.69	0.99	1.68	1.69	1.42	2.4	1.69	1.85	3.13
1.92	0.15	0.2885	1.7	0.57	0.9706	1.69	1	1.69	1.69	1.43	2.42	1.69	1.86	3.15
1.9	0.16	0.3045	1.7	0.58	0.9872	1.69	1.01	1.71	1.69	1.44	2.44	1.69	1.87	3.17
1.88	0.17	0.3204	1.7	0.59	1	1.69	1.02	1.73	1.69	1.45	2.46	1.69	1.88	3.18
1.87	0.18	0.3363	1.7	0.6	1.02	1.69	1.03	1.74	1.69	1.46	2.47	1.69	1.89	3.2
1.85	0.19	0.3523	1.7	0.61	1.04	1.69	1.04	1.76	1.69	1.47	2.49	1.69	1.9	3.22
1.84	0.2	0.3682	1.7	0.62	1.05	1.69	1.05	1.78	1.69	1.48	2.51	1.69	1.91	3.23
1.83	0.21	0.3841	1.7	0.63	1.07	1.69	1.06	1.8	1.69	1.49	2.52	1.69	1.92	3.25
1.82	0.22	0.4001	1.7	0.64	1.09	1.69	1.07	1.81	1.69	1.5	2.54	1.69	1.93	3.27
1.81	0.23	0.416	1.7	0.65	1.1	1.69	1.08	1.83	1.69	1.51	2.56	1.69	1.94	3.29
1.8	0.24	0.432	1.7	0.66	1.12	1.69	1.09	1.85	1.69	1.52	2.57	1.69	1.95	3.3
1.79	0.25	0.4479	1.7	0.67	1.14	1.69	1.1	1.86	1.69	1.53	2.59	1.69	1.96	3.32
1.78	0.26	0.4639	1.7	0.68	1.15	1.69	1.11	1.88	1.69	1.54	2.61	1.69	1.97	3.34
1.78	0.27	0.48	1.7	0.69	1.17	1.69	1.12	1.9	1.69	1.55	2.63	1.69	1.98	3.35
1.77	0.28	0.496	1.7	0.7	1.19	1.69	1.13	1.91	1.69	1.56	2.64	1.69	1.99	3.37
1.77	0.29	0.5121	1.7	0.71	1.2	1.69	1.14	1.93	1.69	1.57	2.66	1.69	2	3.39
1.76	0.3	0.5281	1.7	0.72	1.22	1.69	1.15	1.95	1.69	1.58	2.68	1.69	2.01	3.4
1.76	0.31	0.5442	1.7	0.73	1.24	1.69	1.16	1.96	1.69	1.59	2.69	1.69	2.02	3.42
1.75	0.32	0.5604	1.7	0.74	1.26	1.69	1.17	1.98	1.69	1.6	2.71	1.69	2.03	3.44
1.75	0.33	0.5765	1.7	0.75	1.27	1.69	1.18	2	1.69	1.61	2.73	1.69	2.04	3.46
1.74	0.34	0.5927	1.7	0.76	1.29	1.69	1.19	2.02	1.69	1.62	2.74	1.69	2.05	3.47
1.74	0.35	0.6089	1.7	0.77	1.31	1.69	1.2	2.03	1.69	1.63	2.76	1.69	2.06	3.49
1.74	0.36	0.6251	1.7	0.78	1.32	1.69	1.21	2.05	1.69	1.64	2.78	1.69	2.07	3.51
1.73	0.37	0.6413	1.7	0.79	1.34	1.69	1.22	2.07	1.69	1.65	2.79	1.69	2.08	3.52
1.73	0.38	0.6576	1.7	0.8	1.36	1.69	1.23	2.08	1.69	1.66	2.81	1.69	2.09	3.54
1.73	0.39	0.6739	1.69	0.81	1.37	1.69	1.24	2.1	1.69	1.67	2.83	1.69	2.1	3.56
1.73	0.4	0.6902	1.69	0.82	1.39	1.69	1.25	2.12	1.69	1.68	2.85	1.69	2.11	3.57
1.72	0.41	0.7065	1.69	0.83	1.41	1.69	1.26	2.13	1.69	1.69	2.86	1.69	2.12	3.59
1.72	0.42	0.7229	1.69	0.84	1.42	1.69	1.27	2.15	1.69	1.7	2.88	1.69	2.13	3.61
			1.69	0.85	1.44	1.69	1.28	2.17	1.69	1.71	2.9	1.69	2.14	3.62

APPENDIX V a)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 99% POWER FOR N = 30.

99% Power, N= 30

N_1 = 15, N_2 = 15, $\beta = 0.01$

HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
18.79	0.01	0.1879	6.93	0.43	2.98	6.93	0.86	5.96	6.77	1.29	8.74	6.72	1.72	11.56
12.78	0.02	0.2555	6.93	0.44	3.05	6.93	0.87	6.03	6.77	1.3	8.8	6.72	1.73	11.63
10.52	0.03	0.3156	6.93	0.45	3.12	6.93	0.88	6.1	6.77	1.31	8.87	6.72	1.74	11.69
9.32	0.04	0.373	6.93	0.46	3.19	6.93	0.89	6.17	6.77	1.32	8.93	6.72	1.75	11.76
8.59	0.05	0.4297	6.93	0.47	3.26	6.93	0.9	6.24	6.76	1.33	9	6.72	1.76	11.83
8.11	0.06	0.4866	6.93	0.48	3.33	6.93	0.91	6.3	6.76	1.34	9.06	6.72	1.77	11.9
7.78	0.07	0.5443	6.93	0.49	3.4	6.93	0.92	6.37	6.76	1.35	9.12	6.72	1.78	11.96
7.54	0.08	0.6031	6.93	0.5	3.47	6.92	0.93	6.44	6.76	1.36	9.19	6.72	1.79	12.03
7.37	0.09	0.6632	6.93	0.51	3.53	6.92	0.94	6.51	6.75	1.37	9.25	6.72	1.80	12.1
7.25	0.1	0.7247	6.93	0.52	3.6	6.92	0.95	6.57	6.75	1.38	9.32	6.72	1.81	12.16
7.16	0.11	0.7874	6.93	0.53	3.67	6.92	0.96	6.64	6.75	1.39	9.38	6.72	1.82	12.23
7.09	0.12	0.8513	6.93	0.54	3.74	6.91	0.97	6.71	6.75	1.4	9.45	6.72	1.83	12.3
7.05	0.13	0.9162	6.93	0.55	3.81	6.91	0.98	6.77	6.75	1.41	9.51	6.72	1.84	12.36
7.01	0.14	0.982	6.93	0.56	3.88	6.91	0.99	6.84	6.74	1.42	9.58	6.72	1.85	12.43
6.99	0.15	1.05	6.93	0.57	3.95	6.90	1	6.9	6.74	1.43	9.64	6.72	1.86	12.5
6.97	0.16	1.12	6.93	0.58	4.02	6.90	1.01	6.97	6.74	1.44	9.71	6.72	1.87	12.57
6.96	0.17	1.18	6.93	0.59	4.09	6.89	1.02	7.03	6.74	1.45	9.77	6.72	1.88	12.63
6.95	0.18	1.25	6.93	0.6	4.16	6.89	1.03	7.1	6.74	1.46	9.84	6.72	1.89	12.7
6.94	0.19	1.32	6.93	0.61	4.23	6.89	1.04	7.16	6.74	1.47	9.9	6.72	1.90	12.77
6.94	0.2	1.39	6.93	0.62	4.3	6.88	1.05	7.23	6.74	1.48	9.97	6.72	1.91	12.84
6.94	0.21	1.46	6.93	0.63	4.37	6.88	1.06	7.29	6.74	1.49	10	6.72	1.92	12.9
6.93	0.22	1.53	6.93	0.64	4.44	6.87	1.07	7.35	6.73	1.5	10.1	6.72	1.93	12.97
6.93	0.23	1.59	6.93	0.65	4.51	6.87	1.08	7.42	6.73	1.51	10.2	6.72	1.94	13.04
6.93	0.24	1.66	6.93	0.66	4.58	6.86	1.09	7.48	6.73	1.52	10.2	6.72	1.95	13.1
6.93	0.25	1.73	6.93	0.67	4.65	6.86	1.1	7.54	6.73	1.53	10.3	6.72	1.96	13.17
6.93	0.26	1.8	6.93	0.68	4.71	6.85	1.11	7.61	6.73	1.54	10.4	6.72	1.97	13.24
6.93	0.27	1.87	6.93	0.69	4.78	6.85	1.12	7.67	6.73	1.55	10.4	6.72	1.98	13.31
6.93	0.28	1.94	6.93	0.7	4.85	6.84	1.13	7.73	6.73	1.56	10.5	6.72	1.99	13.37
6.93	0.29	2.01	6.93	0.71	4.92	6.84	1.14	7.8	6.73	1.57	10.6	6.72	2.00	13.44
6.93	0.3	2.08	6.93	0.72	4.99	6.84	1.15	7.86	6.73	1.58	10.6	6.72	2.01	13.51
6.93	0.31	2.15	6.93	0.73	5.06	6.83	1.16	7.92	6.73	1.59	10.7	6.72	2.02	13.58
6.93	0.32	2.22	6.93	0.74	5.13	6.83	1.17	7.99	6.73	1.6	10.8	6.72	2.03	13.64
6.93	0.33	2.29	6.93	0.75	5.2	6.82	1.18	8.05	6.73	1.61	10.8	6.72	2.04	13.71
6.93	0.34	2.36	6.93	0.76	5.27	6.81	1.19	8.11	6.73	1.62	10.9	6.72	2.05	13.78
6.93	0.35	2.42	6.93	0.77	5.34	6.81	1.2	8.17	6.72	1.63	11	6.72	2.06	13.85
6.93	0.36	2.49	6.93	0.78	5.41	6.81	1.21	8.23	6.72	1.64	11	6.72	2.07	13.91
6.93	0.37	2.56	6.93	0.79	5.48	6.80	1.22	8.3	6.72	1.65	11.1	6.72	2.08	13.98
6.93	0.38	2.63	6.93	0.8	5.55	6.80	1.23	8.36	6.72	1.66	11.2	6.72	2.09	14.05
6.93	0.39	2.7	6.93	0.81	5.62	6.79	1.24	8.42	6.72	1.67	11.2	6.72	2.10	14.12
6.93	0.4	2.77	6.93	0.82	5.69	6.79	1.25	8.49	6.72	1.68	11.3	6.72	2.11	14.18
6.93	0.41	2.84	6.93	0.83	5.76	6.78	1.26	8.55	6.72	1.69	11.4	6.72	2.12	14.25
6.93	0.42	2.91	6.93	0.84	5.82	6.78	1.27	8.61	6.72	1.7	11.4	6.72	2.13	14.32
			6.93	0.85	5.89	6.78	1.28	8.68	6.72	1.71	11.5	6.72	2.14	14.39

APPENDIX V *b*)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 99% POWER FOR N = 80.

99% Power, N= 80

N_1 = 40, N_2 = 40, $\beta = 0.01$

HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
9.49	0.01	0.0949	2.9	0.43	1.25	2.89	0.86	2.49	2.89	1.29	3.73	2.89	1.72	4.98
6.58	0.02	0.1317	2.9	0.44	1.28	2.89	0.87	2.52	2.89	1.3	3.76	2.89	1.73	5.01
5.45	0.03	0.1634	2.9	0.45	1.3	2.89	0.88	2.55	2.89	1.31	3.79	2.89	1.74	5.04
4.82	0.04	0.1927	2.9	0.46	1.33	2.89	0.89	2.57	2.89	1.32	3.82	2.89	1.75	5.06
4.41	0.05	0.2207	2.9	0.47	1.36	2.89	0.9	2.6	2.89	1.33	3.85	2.89	1.76	5.09
4.13	0.06	0.2478	2.9	0.48	1.39	2.89	0.91	2.63	2.89	1.34	3.88	2.89	1.77	5.12
3.92	0.07	0.2743	2.9	0.49	1.42	2.89	0.92	2.66	2.89	1.35	3.91	2.89	1.78	5.15
3.76	0.08	0.3005	2.9	0.5	1.45	2.89	0.93	2.69	2.89	1.36	3.93	2.89	1.79	5.18
3.63	0.09	0.3264	2.9	0.51	1.48	2.89	0.94	2.72	2.89	1.37	3.96	2.89	1.8	5.21
3.52	0.1	0.3522	2.89	0.52	1.51	2.89	0.95	2.75	2.89	1.38	3.99	2.89	1.81	5.24
3.44	0.11	0.3779	2.89	0.53	1.53	2.89	0.96	2.78	2.89	1.39	4.02	2.89	1.82	5.27
3.36	0.12	0.4036	2.89	0.54	1.56	2.89	0.97	2.81	2.89	1.4	4.05	2.89	1.83	5.3
3.3	0.13	0.4293	2.89	0.55	1.59	2.89	0.98	2.83	2.89	1.41	4.08	2.89	1.84	5.33
3.25	0.14	0.455	2.89	0.56	1.62	2.89	0.99	2.86	2.89	1.42	4.11	2.89	1.85	5.35
3.21	0.15	0.4808	2.89	0.57	1.65	2.89	1	2.89	2.89	1.43	4.14	2.89	1.86	5.38
3.17	0.16	0.5067	2.89	0.58	1.68	2.89	1.01	2.92	2.89	1.44	4.17	2.89	1.87	5.41
3.13	0.17	0.5326	2.89	0.59	1.71	2.89	1.02	2.95	2.89	1.45	4.2	2.89	1.88	5.44
3.1	0.18	0.5587	2.89	0.6	1.74	2.89	1.03	2.98	2.89	1.46	4.22	2.89	1.89	5.47
3.08	0.19	0.5849	2.89	0.61	1.76	2.89	1.04	3.01	2.89	1.47	4.25	2.89	1.9	5.5
3.06	0.2	0.6113	2.89	0.62	1.79	2.89	1.05	3.04	2.89	1.48	4.28	2.89	1.91	5.53
3.04	0.21	0.6377	2.89	0.63	1.82	2.89	1.06	3.07	2.89	1.49	4.31	2.89	1.92	5.56
3.02	0.22	0.6643	2.89	0.64	1.85	2.89	1.07	3.1	2.89	1.5	4.34	2.89	1.93	5.59
3	0.23	0.6911	2.89	0.65	1.88	2.89	1.08	3.12	2.89	1.51	4.37	2.89	1.94	5.61
2.99	0.24	0.7179	2.89	0.66	1.91	2.89	1.09	3.15	2.89	1.52	4.4	2.89	1.95	5.64
2.98	0.25	0.7449	2.89	0.67	1.94	2.89	1.1	3.18	2.89	1.53	4.43	2.89	1.96	5.67
2.97	0.26	0.772	2.89	0.68	1.97	2.89	1.11	3.21	2.89	1.54	4.46	2.89	1.97	5.7
2.96	0.27	0.7993	2.89	0.69	2	2.89	1.12	3.24	2.89	1.55	4.49	2.89	1.98	5.73
2.95	0.28	0.8266	2.89	0.7	2.02	2.89	1.13	3.27	2.89	1.56	4.51	2.89	1.99	5.76
2.95	0.29	0.8541	2.89	0.71	2.05	2.89	1.14	3.3	2.89	1.57	4.54	2.89	2	5.79
2.94	0.3	0.8816	2.89	0.72	2.08	2.89	1.15	3.33	2.89	1.58	4.57	2.89	2.01	5.82
2.93	0.31	0.9093	2.89	0.73	2.11	2.89	1.16	3.36	2.89	1.59	4.6	2.89	2.02	5.85
2.93	0.32	0.9371	2.89	0.74	2.14	2.89	1.17	3.38	2.89	1.6	4.63	2.89	2.03	5.88
2.92	0.33	0.9649	2.89	0.75	2.17	2.89	1.18	3.41	2.89	1.61	4.66	2.89	2.04	5.9
2.92	0.34	0.9929	2.89	0.76	2.2	2.89	1.19	3.44	2.89	1.62	4.69	2.89	2.05	5.93
2.92	0.35	1.02	2.89	0.77	2.23	2.89	1.2	3.47	2.89	1.63	4.72	2.89	2.06	5.96
2.91	0.36	1.05	2.89	0.78	2.26	2.89	1.21	3.5	2.89	1.64	4.75	2.89	2.07	5.99
2.91	0.37	1.08	2.89	0.79	2.29	2.89	1.22	3.53	2.89	1.65	4.77	2.89	2.08	6.02
2.91	0.38	1.11	2.89	0.8	2.31	2.89	1.23	3.56	2.89	1.66	4.8	2.89	2.09	6.05
2.91	0.39	1.13	2.89	0.81	2.34	2.89	1.24	3.59	2.89	1.67	4.83	2.89	2.1	6.08
2.91	0.4	1.16	2.89	0.82	2.37	2.89	1.25	3.62	2.89	1.68	4.86	2.89	2.11	6.11
2.9	0.41	1.19	2.89	0.83	2.4	2.89	1.26	3.65	2.89	1.69	4.89	2.89	2.12	6.14
2.9	0.42	1.22	2.89	0.84	2.43	2.89	1.27	3.67	2.89	1.7	4.92	2.89	2.13	6.17
			2.89	0.85	2.46	2.89	1.28	3.7	2.89	1.71	4.95	2.89	2.14	6.19

APPENDIX V *c*)

ESTIMATED ***HR*-h_2** COMBINATION NEEDED TO ACHIEVE 99% POWER FOR N = 100.

99% Power, N= 100														
N_1 = 50, N_2 = 50, $\beta = 0.01$														
HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
8.25	0.01	0.0825	2.56	0.43	1.1	2.54	0.86	2.19	2.54	1.29	3.28	2.55	1.72	4.38
5.78	0.02	0.1156	2.56	0.44	1.12	2.54	0.87	2.21	2.54	1.3	3.31	2.55	1.73	4.4
4.81	0.03	0.1442	2.56	0.45	1.15	2.54	0.88	2.24	2.54	1.31	3.33	2.55	1.74	4.43
4.27	0.04	0.1707	2.55	0.46	1.17	2.54	0.89	2.26	2.54	1.32	3.36	2.55	1.75	4.45
3.92	0.05	0.1959	2.55	0.47	1.2	2.54	0.9	2.29	2.54	1.33	3.38	2.55	1.76	4.48
3.67	0.06	0.2203	2.55	0.48	1.22	2.54	0.91	2.32	2.54	1.34	3.41	2.55	1.77	4.51
3.49	0.07	0.2442	2.55	0.49	1.25	2.54	0.92	2.34	2.54	1.35	3.44	2.55	1.78	4.53
3.35	0.08	0.2677	2.55	0.5	1.28	2.54	0.93	2.37	2.54	1.36	3.46	2.55	1.79	4.56
3.23	0.09	0.291	2.55	0.51	1.3	2.54	0.94	2.39	2.54	1.37	3.49	2.55	1.8	4.58
3.14	0.1	0.3141	2.55	0.52	1.33	2.54	0.95	2.42	2.54	1.38	3.51	2.55	1.81	4.61
3.06	0.11	0.3371	2.55	0.53	1.35	2.54	0.96	2.44	2.54	1.39	3.54	2.55	1.82	4.63
3	0.12	0.36	2.55	0.54	1.38	2.54	0.97	2.47	2.54	1.4	3.56	2.55	1.83	4.66
2.95	0.13	0.3829	2.55	0.55	1.4	2.54	0.98	2.49	2.54	1.41	3.59	2.55	1.84	4.68
2.9	0.14	0.4057	2.55	0.56	1.43	2.54	0.99	2.52	2.55	1.42	3.61	2.55	1.85	4.71
2.86	0.15	0.4286	2.55	0.57	1.45	2.54	1	2.54	2.55	1.43	3.64	2.55	1.86	4.73
2.82	0.16	0.4516	2.55	0.58	1.48	2.54	1.01	2.57	2.55	1.44	3.66	2.55	1.87	4.76
2.79	0.17	0.4746	2.55	0.59	1.5	2.54	1.02	2.6	2.55	1.45	3.69	2.55	1.88	4.79
2.76	0.18	0.4976	2.55	0.6	1.53	2.54	1.03	2.62	2.55	1.46	3.72	2.55	1.89	4.81
2.74	0.19	0.5207	2.55	0.61	1.55	2.54	1.04	2.65	2.55	1.47	3.74	2.55	1.9	4.84
2.72	0.2	0.5439	2.55	0.62	1.58	2.54	1.05	2.67	2.55	1.48	3.77	2.55	1.91	4.86
2.7	0.21	0.5672	2.55	0.63	1.6	2.54	1.06	2.7	2.55	1.49	3.79	2.55	1.92	4.89
2.68	0.22	0.5905	2.55	0.64	1.63	2.54	1.07	2.72	2.55	1.5	3.82	2.55	1.93	4.91
2.67	0.23	0.614	2.55	0.65	1.65	2.54	1.08	2.75	2.55	1.51	3.84	2.55	1.94	4.94
2.66	0.24	0.6375	2.55	0.66	1.68	2.54	1.09	2.77	2.55	1.52	3.87	2.55	1.95	4.96
2.64	0.25	0.6611	2.55	0.67	1.71	2.54	1.1	2.8	2.55	1.53	3.89	2.55	1.96	4.99
2.63	0.26	0.6849	2.55	0.68	1.73	2.54	1.11	2.82	2.55	1.54	3.92	2.55	1.97	5.01
2.62	0.27	0.7087	2.54	0.69	1.76	2.54	1.12	2.85	2.55	1.55	3.94	2.55	1.98	5.04
2.62	0.28	0.7326	2.54	0.7	1.78	2.54	1.13	2.88	2.55	1.56	3.97	2.55	1.99	5.07
2.61	0.29	0.7565	2.54	0.71	1.81	2.54	1.14	2.9	2.55	1.57	4	2.55	2	5.09
2.6	0.3	0.7806	2.54	0.72	1.83	2.54	1.15	2.93	2.55	1.58	4.02	2.55	2.01	5.12
2.6	0.31	0.8048	2.54	0.73	1.86	2.54	1.16	2.95	2.55	1.59	4.05	2.55	2.02	5.14
2.59	0.32	0.829	2.54	0.74	1.88	2.54	1.17	2.98	2.55	1.6	4.07	2.55	2.03	5.17
2.59	0.33	0.8533	2.54	0.75	1.91	2.54	1.18	3	2.55	1.61	4.1	2.55	2.04	5.19
2.58	0.34	0.8777	2.54	0.76	1.93	2.54	1.19	3.03	2.55	1.62	4.12	2.55	2.05	5.22
2.58	0.35	0.9021	2.54	0.77	1.96	2.54	1.2	3.05	2.55	1.63	4.15	2.55	2.06	5.24
2.57	0.36	0.9266	2.54	0.78	1.98	2.54	1.21	3.08	2.55	1.64	4.17	2.55	2.07	5.27
2.57	0.37	0.9512	2.54	0.79	2.01	2.54	1.22	3.1	2.55	1.65	4.2	2.55	2.08	5.3
2.57	0.38	0.9759	2.54	0.8	2.04	2.54	1.23	3.13	2.55	1.66	4.23	2.55	2.09	5.32
2.57	0.39	1	2.54	0.81	2.06	2.54	1.24	3.16	2.55	1.67	4.25	2.55	2.1	5.35
2.56	0.4	1.03	2.54	0.82	2.09	2.54	1.25	3.18	2.55	1.68	4.28	2.55	2.11	5.37
2.56	0.41	1.05	2.54	0.83	2.11	2.54	1.26	3.21	2.55	1.69	4.3	2.55	2.12	5.4
2.56	0.42	1.07	2.54	0.84	2.14	2.54	1.27	3.23	2.55	1.7	4.33	2.55	2.13	5.42
			2.54	0.85	2.16	2.54	1.28	3.26	2.55	1.71	4.35	2.55	2.14	5.45

APPENDIX V *d*)

ESTIMATED *HR*-h_2 COMBINATION NEEDED TO ACHIEVE 99% POWER FOR N = 200.

99% Power, N= 200

N_1 = 100, N_2 = 100, $\beta = 0.01$

HR	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2	*HR*	h_1	h_2
5.54	0.01	0.0554	1.91	0.43	0.8222	1.89	0.86	1.62	1.89	1.29	2.44	1.89	1.72	3.25
4.02	0.02	0.0804	1.91	0.44	0.8405	1.89	0.87	1.64	1.89	1.3	2.45	1.89	1.73	3.27
3.41	0.03	0.1022	1.91	0.45	0.8588	1.89	0.88	1.66	1.89	1.31	2.47	1.89	1.74	3.29
3.07	0.04	0.1226	1.91	0.46	0.8772	1.89	0.89	1.68	1.89	1.32	2.49	1.89	1.75	3.3
2.84	0.05	0.1422	1.91	0.47	0.8956	1.89	0.9	1.7	1.89	1.33	2.51	1.89	1.76	3.32
2.69	0.06	0.1612	1.9	0.48	0.914	1.89	0.91	1.72	1.89	1.34	2.53	1.89	1.77	3.34
2.57	0.07	0.1798	1.9	0.49	0.9324	1.89	0.92	1.74	1.89	1.35	2.55	1.89	1.78	3.36
2.48	0.08	0.1981	1.9	0.5	0.9508	1.89	0.93	1.76	1.89	1.36	2.57	1.89	1.79	3.38
2.4	0.09	0.2161	1.9	0.51	0.9693	1.89	0.94	1.78	1.89	1.37	2.59	1.89	1.8	3.4
2.34	0.1	0.2341	1.9	0.52	0.9878	1.89	0.95	1.79	1.89	1.38	2.61	1.89	1.81	3.42
2.29	0.11	0.2519	1.9	0.53	1.01	1.89	0.96	1.81	1.89	1.39	2.62	1.89	1.82	3.44
2.25	0.12	0.2696	1.9	0.54	1.02	1.89	0.97	1.83	1.89	1.4	2.64	1.89	1.83	3.46
2.21	0.13	0.2873	1.9	0.55	1.04	1.89	0.98	1.85	1.89	1.41	2.66	1.89	1.84	3.47
2.18	0.14	0.3049	1.9	0.56	1.06	1.89	0.99	1.87	1.89	1.42	2.68	1.89	1.85	3.49
2.15	0.15	0.3224	1.9	0.57	1.08	1.89	1	1.89	1.89	1.43	2.7	1.89	1.86	3.51
2.13	0.16	0.34	1.9	0.58	1.1	1.89	1.01	1.91	1.89	1.44	2.72	1.89	1.87	3.53
2.1	0.17	0.3576	1.89	0.59	1.12	1.89	1.02	1.93	1.89	1.45	2.74	1.89	1.88	3.55
2.08	0.18	0.3751	1.89	0.6	1.14	1.89	1.03	1.95	1.89	1.46	2.76	1.89	1.89	3.57
2.07	0.19	0.3927	1.89	0.61	1.16	1.89	1.04	1.96	1.89	1.47	2.78	1.89	1.9	3.59
2.05	0.2	0.4102	1.89	0.62	1.17	1.89	1.05	1.98	1.89	1.48	2.79	1.89	1.91	3.61
2.04	0.21	0.4278	1.89	0.63	1.19	1.89	1.06	2	1.89	1.49	2.81	1.89	1.92	3.63
2.02	0.22	0.4454	1.89	0.64	1.21	1.89	1.07	2.02	1.89	1.5	2.83	1.89	1.93	3.65
2.01	0.23	0.463	1.89	0.65	1.23	1.89	1.08	2.04	1.89	1.51	2.85	1.89	1.94	3.66
2	0.24	0.4807	1.89	0.66	1.25	1.89	1.09	2.06	1.89	1.52	2.87	1.89	1.95	3.68
1.99	0.25	0.4983	1.89	0.67	1.27	1.89	1.1	2.08	1.89	1.53	2.89	1.89	1.96	3.7
1.98	0.26	0.516	1.89	0.68	1.29	1.89	1.11	2.1	1.89	1.54	2.91	1.89	1.97	3.72
1.98	0.27	0.5338	1.89	0.69	1.3	1.89	1.12	2.11	1.89	1.55	2.93	1.89	1.98	3.74
1.97	0.28	0.5516	1.89	0.7	1.32	1.89	1.13	2.13	1.89	1.56	2.95	1.89	1.99	3.76
1.96	0.29	0.5694	1.89	0.71	1.34	1.89	1.14	2.15	1.89	1.57	2.96	1.89	2	3.78
1.96	0.3	0.5872	1.89	0.72	1.36	1.89	1.15	2.17	1.89	1.58	2.98	1.89	2.01	3.8
1.95	0.31	0.6051	1.89	0.73	1.38	1.89	1.16	2.19	1.89	1.59	3	1.89	2.02	3.82
1.95	0.32	0.623	1.89	0.74	1.4	1.89	1.17	2.21	1.89	1.6	3.02	1.89	2.03	3.83
1.94	0.33	0.6409	1.89	0.75	1.42	1.89	1.18	2.23	1.89	1.61	3.04	1.89	2.04	3.85
1.94	0.34	0.6589	1.89	0.76	1.44	1.89	1.19	2.25	1.89	1.62	3.06	1.89	2.05	3.87
1.93	0.35	0.6769	1.89	0.77	1.46	1.89	1.2	2.27	1.89	1.63	3.08	1.89	2.06	3.89
1.93	0.36	0.695	1.89	0.78	1.47	1.89	1.21	2.28	1.89	1.64	3.1	1.89	2.07	3.91
1.93	0.37	0.713	1.89	0.79	1.49	1.89	1.22	2.3	1.89	1.65	3.12	1.89	2.08	3.93
1.92	0.38	0.7312	1.89	0.8	1.51	1.89	1.23	2.32	1.89	1.66	3.13	1.89	2.09	3.95
1.92	0.39	0.7493	1.89	0.81	1.53	1.89	1.24	2.34	1.89	1.67	3.15	1.89	2.1	3.97
1.92	0.4	0.7675	1.89	0.82	1.55	1.89	1.25	2.36	1.89	1.68	3.17	1.89	2.11	3.99
1.92	0.41	0.7857	1.89	0.83	1.57	1.89	1.26	2.38	1.89	1.69	3.19	1.89	2.12	4
1.91	0.42	0.8039	1.89	0.84	1.59	1.89	1.27	2.4	1.89	1.7	3.21	1.89	2.13	4.02
			1.89	0.85	1.61	1.89	1.28	2.42	1.89	1.71	3.23	1.89	2.14	4.04