Journal of Modern Applied Statistical Methods

Volume 17 | Issue 1 Article 7

2018

Sample Size for Non-Inferiority Tests for One Proportion: A Simulation Study

Özlem Güllü
Department of Statistics, University of Ankara, Turkey, ozlem.gullu@gmail.com

Mustafa Agah Tekindal
University of Selçuk, Konya, Turkey, matekindal@gmail.com

Sample Size for Non-Inferiority Tests for One Proportion: A Simulation Study

Cover Page Footnote

The study was presented as oral presentation as follows identifier "Sample size for non-inferiority tests for one proportion: A simulation study". Second International Researchers, Statisticians and Young Statisticians Congress Abstract Book s.64, 4-8 May 2016, Hacettepe University, Ankara.

Journal of Modern Applied Statistical Methods
May 2018, Vol. 17, No. 1, eP2475
doi: 10.22237/jmasm/1525132800

בס"ד

ISSN 1538 − 9472

Sample Size for Non-Inferiority Tests for One Proportion: A Simulation Study

Özlem Güllü
University of Ankara
Ankara, Turkey

Mustafa Agah Tekindal
University of Selçuk
Konya, Turkey

The objective of non-inferiority trials is to demonstrate the efficiency of a novel treatment whether it is acceptably less or more efficient than a control or active (existing) treatment. They are employed in situations where, when compared to the active treatment, the novel treatment is to be advantageous with higher rates of reliability, compatibility, cost-efficiency, etc. Odds ratio is the most significant measure used in investigating the size of efficiency of treatments relative to one another. The purpose of the study is to calculate and evaluate the sample size under different scenarios based on three different test statistics in non-inferiority trials for one proportion via Monte Carlo simulations.

Keywords: Clinical trial, non-inferiority trials, odds ratio, power, sample size

Introduction

In clinical trials, the aim is to display whether the use of a novel drug or a novel medical instrument will be efficient and reliable. It is a widespread practice that a treatment is compared with a control group or a placebo group. One such practice is the employment of non-inferiority trials. Non-inferiority trials involve testing the effectiveness of a novel treatment that is acceptably less/more effective than a control or active (existing) treatment. They are performed in situations where compared to the active (existing) treatment, the novel treatment is to be advantageous with higher rates of reliability, compatibility, cost-efficiency, etc. In order to ensure reliability, these trials should be designed in accordance with correct statistical methods. A proper scientific study needs to follow certain steps, such as formulating hypotheses, applying the appropriate test statistic, determining the sample size, collecting the data, analyzing the data, and finally interpreting the data. Sample size is one of the most important factors that impact the reliability and

doi: 10.22237/jmasm/1525132800 | Accepted: April 10, 2017; Published: June 7, 2018.
Correspondence: Özlem Güllü, ozlem.gullu@gmail.com

correctness of a clinical trial. It plays an essential role in ensuring the validity, correctness, reliability, and integrity of the targeted clinical trial (Chow, Shao, & Wang, 2008).

Power analysis is the most frequently applied method used to calculate the sample size. Power analysis refers to the calculation of the required sample size that can yield the clinically/statistically significant difference and thus provide the expected power under conditions where Type-I error is invariant. A designed clinical trial is expected to have adequate power at an appropriate significance level. Generally, the power value is expected to be over 80%. If the power of the employed test is low, that test may fail to detect a difference that really exists (Schlotzhauer, 2007; Alkan, Terzi, & Alkan, 2015). There are many studies within the literature regarding the calculation of the adequate sample size (Alkan et al., 2015; Desu & Raghavarao, 1990; Julious, Campbell, & Altman, 1999; Machin, Campbell, Tan, & Tan, 2009; Tekindal & Yazıcı, 2016; Demirel, Oruç, & Gürler, 2016).

Hahn (2012) noted sample size is highly sensitive with respect to the expected effects within treatment and control groups. A much larger sample size is needed in order to analyze the situations where the novel treatment is much less effective than the control group, whereas a smaller sample size is sufficient in case the novel treatment is a bit more effective than the control group. As the non-inferiority margin increases, the required sample size decreases. On the other hand, it was also concluded that the exaggeration of this ratio reduces the power of the test.

Walker and Nowacki (2010) reported the non-inferiority margin is directly influential on the sample size. They produced different sample sizes with non-inferiority margins ranging from 0.06 to 0.12 with values increasing at 0.01 units. When the power of the test was 80% and the non-inferiority margin was set as 0.06, the required sample size was calculated as 26,186, whereas the required sample size decreased to 535 with 0.12 non-inferiority margin under the same conditions. In conclusion, they demonstrated that small changes in non-inferiority margin may lead to bigger changes in the sample size.

Assuming $\alpha = 0.05$ and baseline proportion as 0.5, Tunes-da-Silva (2008) calculated the required sample size to reach the power of test at 80% and 90%. As the non-inferiority margin decreased, the sample size to meet the target power of both tests increased. In addition, they analyzed the relationship between non-inferiority odds ratio and baseline proportion, and found as the baseline proportion changes, non-inferiority odds ratio changes as well. In this respect, they emphasized that the necessity of using the appropriate proportion specified by the clinicians.

The objective of this study is to calculate and assess the proper sample size for a sample rate at non-inferiority trials via three different test statistics (exact test, *Z* test, and *Z*-test with continuity correction) under different scenarios.

Methodology

The Type-I error was set at 0.05; baseline proportion was 0.50; and different non-inferiority odds ratios (0.75, 0.80, 0.85, 0.90, 0.95, 0.99) were considered. P_{Odds} was calculated for odds ratios 0.1875, 0.2, 0.2125, 0.225, 0.2375, and 0.2475. The data were derived from a binomial distribution ($p = 0.5$) with different non-inferiority odds ratios (0.75, 0.80, 0.85, 0.90, 0.95, 0.99) via increasing the sample size from 10 to 500 by 1 to calculate the power of the test. Having rendered 10000 repetitions for each scenario via Monte Carlo simulation method, the results were further evaluated. The power of the test calculated via using PASS Version 11 (Hintze, 2011).

Non-Inferiority Trials

In clinical trials, the dual character displaying response variable is commonly used in particular for testing the effectiveness of a drug or a medical instrument, or for comparing the treatment groups. In classical hypothesis testing, the ratios obtained from the novel and the active (existing) treatment groups are compared to see if there is a statistically or clinically significant difference. Nevertheless, the researchers may want to prefer the novel treatment to the active (existing) treatment only under the conditions where the former being less costly and having less adverse effects. Likewise, in certain studies, the use of placebo may not be ethical. Hence, a need to detect whether the novel treatment is either equal or non-inferior to the existing treatment emerges. These studies are referred as non-inferiority/equivalence studies and their analyses require simple modifications within the classical hypotheses. For instance, assume that the success rate of an existing treatment on a certain disease is 70%. However, this treatment is expensive, and sometimes displays serious adverse effects. Therefore, the researchers have developed a novel treatment, and it is ready for testing. One of the leading questions to be answered is whether the new treatment will be as good as the existing one. In other words, will at least 70% of the treated subjects positively respond to the novel treatment? The novel treatment may be chosen even if it is less effective than the existing one. In this case, there is a need to determine to what extent the novel treatment can be less effective. Determined by the researchers, this value is called

the non-inferiority margin. The determination of the non-inferiority margin, δ, is the most critical step in equivalence/non-inferiority testing.

Being the maximum acceptable extent of clinical non-inferiority of an experimental treatment, the non-inferiority margin δ must be prospectively defined. One approach to specifying the margin is based on clinical significance, which can obviously be subjective. Sometimes it is possible to choose a margin for declaring non-inferiority of a treatment, in which that treatment ends up having no effect or even a detrimental effect (Hahn, 2012).

The International Conference on Harmonisation (ICH) documents offer two guidelines (ICH, 2000; D'Agostino, Massora, & Sullivan, 2003):

1) The determination of the margin in a non-inferiority trial is based on both statistical reasoning and clinical judgement, and should reflect uncertainties in the evidence on which the choice is based, and should be suitably conservative.
2) This non-inferiority margin cannot be greater than the smallest effect size that the active drug would be reliably expected to have compared with placebo in the setting of a placebo-controlled trial.

Testing for Non-Inferiority using Odds Ratio

Let P represent the proportion responding as a success. That is to say, P is the actual probability of a success in a binomial experiment. In a non-inferiority experiment, the baseline proportion is the response rate of the active treatment. Furthermore, P_0 represents the response proportion that is tested in the null hypothesis, H_0.

Non-inferiority trials are the studies showing that the novel treatment is clinically less different/effective than the existing treatment. Let PN represent the smallest value of P that still results in the conclusion that the novel treatment is non-inferior to the current treatment. The relevant hypothesis equation is given in (1):

$$H_0 : P \leq PN \quad \text{vs} \quad H_1 : P > PN \tag{1}$$

For the analysis of the non-inferiority trials, three different methods, namely difference, ratio, and odds ratio (OR), are applied. In this study, OR, which is the most frequently used method to reveal the effectiveness of two treatment methods, is employed (Wang & Chow, 2007).

The odds of an event are calculated by dividing the event risk by the non-event risk. Thus the odds ratio for P_1 and P_0 is defined as

$$\text{OR} = \frac{O_1}{O_0} = \frac{P_1(1-P_0)}{P_0(1-P_1)} \tag{2}$$

In practice, the log-scaled odds ratio is defined as $\theta = \log(\text{OR})$. An estimator of θ can be obtained as

$$\begin{aligned} \hat{\theta} &= \log(\text{OR}) \\ \text{OR} &= \frac{\hat{P}_1(1-\hat{P}_0)}{\hat{P}_0(1-\hat{P}_1)} \end{aligned} \tag{3}$$

Testing the non-inferiority hypotheses for the odds ratio,

$$\text{H}_0 : \theta \le \delta \quad \text{vs} \quad \text{H}_1 : \theta > \delta \tag{4}$$

where δ is the noninferiority or superiority margin on the log-scale. Define the following test statistic

$$T = (\hat{\theta} - \delta)\left[\frac{1}{n_1\hat{P}_1(1-\hat{P}_1)} + \frac{1}{n_0\hat{P}_0(1-\hat{P}_0)}\right]^{-1/2} \tag{5}$$

For a given significance level α, the null hypothesis would be rejected if $T > z_\alpha$. On the other hand, under the alternative hypothesis, the power of the above test can be approximated by

$$\varphi\left((\theta - \delta)\left[\frac{1}{n_1P_1(1-P_1)} + \frac{1}{n_0P_0(1-P_0)}\right]^{-1/2} - z_\alpha\right) \tag{6}$$

Power and Sample Size Non-Inferiority Using Odds Ratio

Power refers to the probability of establishing the true research hypothesis. Power analysis can also be defined as the calculation of the necessary sample size to

achieve the targeted power. Selection of the adequate sample size depends on the clinically significant difference, the targeted power, the pre-defined significance level, and the relevant hypotheses within the scope of the study. Besides, the non-inferiority margin is also a directly influential factor on the sample size in non-inferiority trials. The calculation of adequate sample size regarding non-inferiority using odds ratio is given in equations (7) and (8) (Wang & Chow, 2007).

Power

The sample size needed for achieving the power of $1-\beta$ can be obtained by solving the following equation

$$(\theta-\delta)\left[\frac{1}{n_1P_1(1-P_1)}+\frac{1}{n_0P_0(1-P_0)}\right]^{-1/2}-z_{\alpha/2}=z_{\beta} \tag{7}$$

Sample Size

Assuming that $n_1 / n_0 = K$,

$$\begin{aligned} n_1 &= Kn_0 \\ n_0 &= \frac{(z_\alpha+z_\beta)^2}{(\theta-\delta)^2}\left[\frac{1}{KP_1(1-P_1)}+\frac{1}{P_0(1-P_0)}\right] \end{aligned} \tag{8}$$

Results

Assuming that Type-I error is 0.05 and baseline proportion is 0.50, data were produced with different non-inferiority odds ratios (0.75, 0.80, 0.85, 0.90, 0.95, 0.99) at different sample sizes from 10 to 500. The cases when the power of the test reach 80% while non-inferiority odds ratio is 0.75 are displayed in Tables 1-3 and Figures 1-3.

Table 1 and Figure 1 indicate that the power of the test exceeds 80% only when the non-inferiority odds ratio is 0.75. The power of the test decreases in other proportions. Table 2 and Figure 2 display that the power of the test reaches and exceeds 80% when the non-inferiority odds ratios are 0.75 and 0.80. The power of the test decreases in other proportions. Table 3 and Figure 3 show that the power

of the test happens and exceeds 80% only when the non-inferiority odds ratios are 0.75 and 0.80. The power of the test decreased in other proportions.

Conclusions

Novel treatments are developed due to technological advances in medicine. Even though they have similar or less effectiveness compared to the active (existing) treatments, the novel treatments are preferred as long as they provide more benefits. In some occasions, the active (existing) treatment may be costlier or having severe adverse effects. Furthermore, the use of placebo may not be ethical or the active (existing) treatment may be controversial. In such cases, non-inferiority tests are frequently employed. In designing non-inferiority trials, the trial should be well understood in advance and possible inconveniences should be taken into account. For these studies, the selection of the non-inferiority margin and the determination of the sample size are very important.

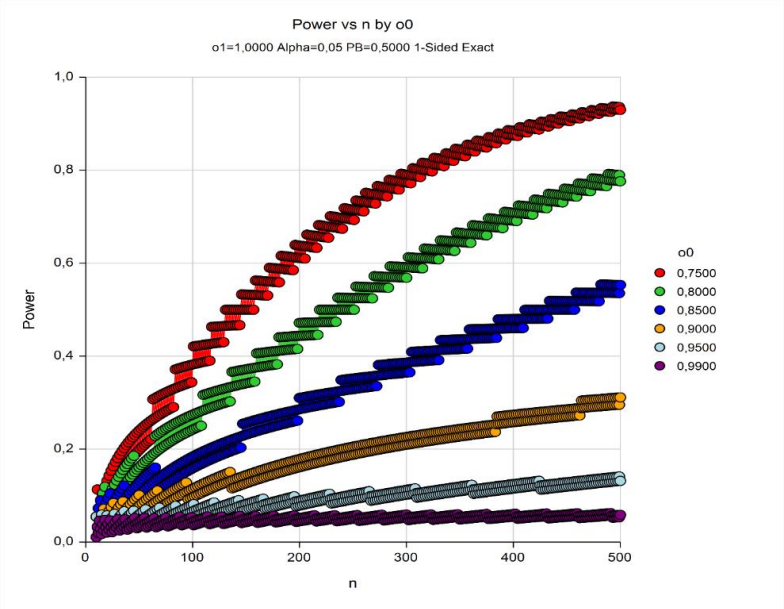

Figure 1. Results of simulation for exact test

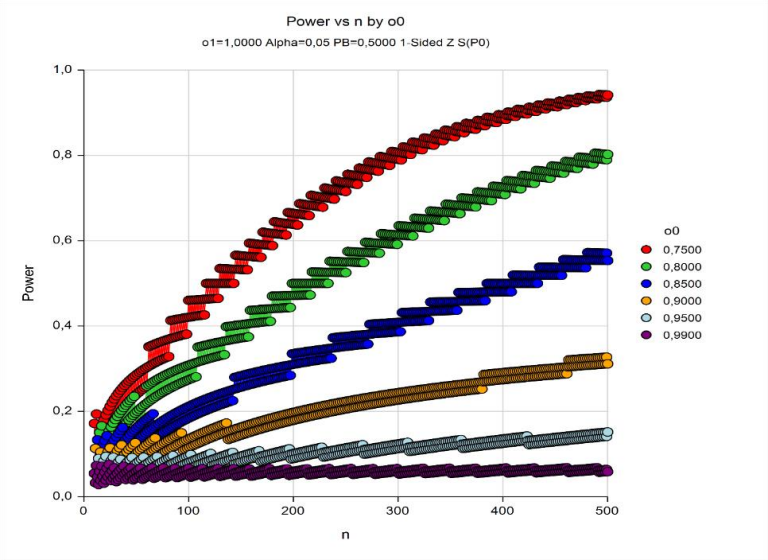

Figure 2. Results of simulation for *Z* test

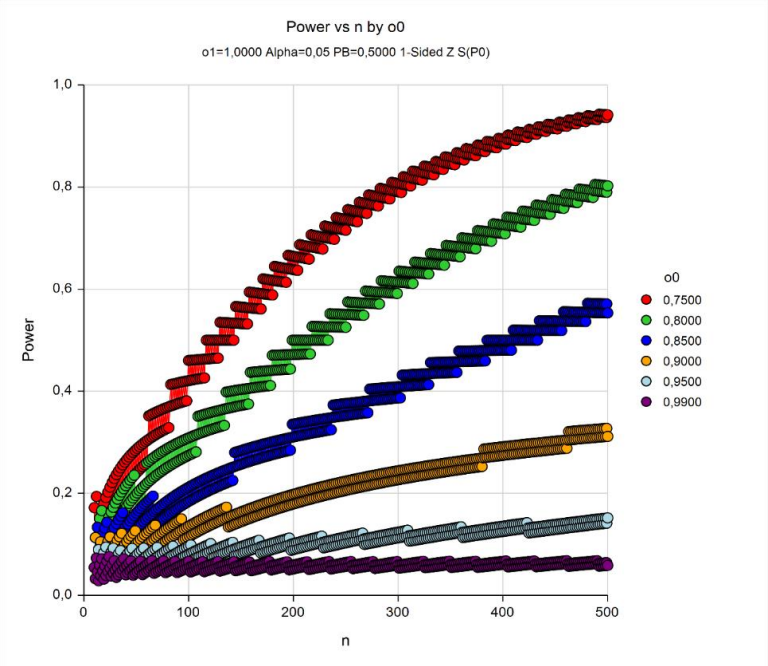

Figure 3. Results of simulation for *Z* test with continuity correction

In this study, the appropriate sample sizes for one proportion in non-inferiority trials are calculated via three different test statistics. The results derived from all three test statistics were very close to one another. Therefore, it can be concluded that the non-inferiority odds ratio is directly influential on determining the proper sample size. In addition, in parallel to the findings of the previous literature, in our study the exaggeration of the non-inferiority odds ratio also leads to loss of power for the test. In this respect, this ratio should be determined with special care to ensure the appropriate sample size.

Studies involving the comparison of effectiveness of two groups are common in medicine and veterinary. In this study, taking into accounts odds ratio which is the most frequently applied method to compare the effectiveness of two, the appropriate sample sizes for non-inferiority trials are calculated at 80% power and 0.05 significance levels. The calculated values are given in practical tables to make it easier for the researchers those intend to employ the method. In addition, the accuracy of the results will definitely be higher in the studies that are to be conducted with proper sample sizes determined according to tables provided in this study.

References

Alkan, N., Terzi, Y., & Alkan, B. B. (2015). Power analysis and sample size calculation for logrank test. *IAAOJ, Scientific Science, 3*(2), 19-28. Retrieved from http://dergipark.gov.tr/download/article-file/367794

Chow, S. C., Shao, J., & Wang, H. (2008). *Sample size calculations in clinical research* (2nd ed.). New York, NY: Chapman and Hall/CRC. doi: 10.1201/9781584889830

D'Agostino, R. B., Massora, M. J., & Sullivan, M. L. (2003). Non-inferiority trials: design concepts and issues – The encounters of academic consultants in statistics. *Statistics in Medicine, 22*(2), 169-186. doi: 10.1002/sim.1425

Demirel, N., Oruç, Ö. E., & Gürler, S. (2016). Practical approaches for determination of sample size in paired case control studies. *Türkiye Klinikleri Biyoistatistik Dergisi, 8*(1), 36-44. doi: 10.5336/biostatic.2015-47261

Desu, M. M., & Raghavarao, D. (1990). *Sample size methodology*. Boston, MA: Academic Press. doi: 10.1016/B978-0-12-212165-4.50009-7

Hahn, S. (2012). Understanding noninferiority trial. *Korean Journal of Pediatrics, 55*(11), 403-407. doi: 10.3345/kjp.2012.55.11.403

Hintze, J. (2011). PASS 11 sample size [computer software]. NCSS, LLC: Kaysville, UT.

International Conference on Harmonisation. (2000). *Guidance on choice of control group and related design and conduct issues in clinical trials (ICH E 10)*. Bethesda, MD: United States Food and Drug Administration.

Julious, S. A., Campbell, M. J., & Altman, D. G. (1999). Estimating sample sizes for continuous, binary, and ordinal outcomes in paired comparisons: Practical hints. *Journal of Biopharmaceutical Statistics, 9*(2), 241-251. doi: 10.1081/bip-100101174

Machin, D., Campbell, M. J., Tan, S. B., & Tan, S. H. (2009). *Sample size tables for clinical studies* (3rd ed.). West Sussex, UK: Wiley-Blackwell. doi: 10.1002/9781444300710

Schlotzhauer, S. D. (2007). Elementary statistics using JMP. Cary, NC: SAS Institute, Inc.

Tekindal, M. A., & Yazıcı, A. C. (2016). Williams test required sample size for determining the minimum effective dose. *Türkiye Klinikleri Biyoistatistik Dergisi, 8*(1), 53-81. doi: 10.5336/biostatic.2015-46401

Tunes-da-Silva, G. (2008). Methods for equivalence and noninferiority testing. *Biology of Blood and Marrow Transplantation, 15*(1), 120-127. doi: 10.1016/j.bbmt.2008.10.004

Walker, E., & Nowacki, A. S. (2010). Understanding equivalence and noninferiority testing. *Journal of General Internal Medicine, 26*(2), 192-196. doi: 10.1007/s11606-010-1513-8

Wang, H., & Chow, S. C. (2007). Sample size calculation for comparing proportions. In R. D'Agostino, J. Massaro, & L. Sullivan (Eds.), *Wiley encyclopedia of clinical trials*. Hoboken, NJ: John Wiley & Sons, Inc. doi: 10.1002/9780471462422.eoct005

Appendix A. Tables

Table 1. Results of power analysis of one proportion non-inferiority for exact test

Power	*N*	Non-Inf OR	Actual OR	Baseline prop. (PB)	Target alpha	Actual alpha	Beta
0.2399	50	0.7500	1.0000	0.5000	0.0500	0.0421	0.7601
0.3822	100	0.7500	1.0000	0.5000	0.0500	0.0410	0.6178
0.5325	150	0.7500	1.0000	0.5000	0.0500	0.4675	0.4675
0.6381	200	0.7500	1.0000	0.5000	0.0500	0.0466	0.3619
0.7153	250	0.7500	1.0000	0.5000	0.0500	0.0443	0.2847
0.7735	300	0.7500	1.0000	0.5000	0.0500	0.0412	0.2265
0.8044	**306**	**0.7500**	**1.0000**	**0.5000**	**0.0500**	**0.0490**	**0.1956**
0.8451	350	0.7500	1.0000	0.5000	0.0500	0.0474	0.1549
0.8749	400	0.7500	1.0000	0.5000	0.0500	0.0426	0.1251
0.9142	450	0.7500	1.0000	0.5000	0.0500	0.0468	0.0858
0.9300	500	0.7500	1.0000	0.5000	0.0500	0.0416	0.0700
0.1611	50	0.8000	1.0000	0.5000	0.0500	0.0374	0.8389
0.2421	100	0.8000	1.0000	0.5000	0.0500	0.0346	0.7579
0.3416	150	0.8000	1.0000	0.5000	0.0500	0.0379	0.6584
0.4718	200	0.8000	1.0000	0.5000	0.0500	0.0496	0.5282
0.5252	250	0.8000	1.0000	0.5000	0.0500	0.0445	0.4748
0.5687	300	0.8000	1.0000	0.5000	0.0500	0.0393	0.4313
0.6458	350	0.8000	1.0000	0.5000	0.0500	0.0434	0.3542
0.7088	400	0.8000	1.0000	0.5000	0.0500	0.0465	0.2912
0.7602	450	0.8000	1.0000	0.5000	0.0500	0.0487	0.2398
0.7922	**489**	**0.8000**	**1.0000**	**0.5000**	**0.0500**	**0.0494**	**0.2078**
0.7764	500	0.8000	1.0000	0.5000	0.0500	0.0416	0.2236
0.1013	50	0.8500	1.0000	0.5000	0.0500	0.0321	0.8987
0.1841	100	0.8500	1.0000	0.5000	0.0500	0.0433	0.8159
0.2313	150	0.8500	1.0000	0.5000	0.0500	0.0417	0.7687
0.3104	200	0.8500	1.0000	0.5000	0.0500	0.0500	0.6896
0.3290	250	0.8500	1.0000	0.5000	0.0500	0.0420	0.6710
0.3864	300	0.8500	1.0000	0.5000	0.0500	0.0449	0.6136
0.4363	350	0.8500	1.0000	0.5000	0.0500	0.0464	0.5637
0.4801	400	0.8500	1.0000	0.5000	0.0500	0.0469	0.5199
0.5188	450	0.8500	1.0000	0.5000	0.0500	0.0468	0.4812
0.5534	500	0.8500	1.0000	0.5000	0.0500	0.0462	0.4466
0.1013	50	0.9000	1.0000	0.5000	0.0500	0.0497	0.8987
0.0967	100	0.9000	1.0000	0.5000	0.0500	0.0338	0.9033
0.1442	150	0.9000	1.0000	0.5000	0.0500	0.0439	0.8558
0.1790	200	0.9000	1.0000	0.5000	0.0500	0.0480	0.8210
0.2055	250	0.9000	1.0000	0.5000	0.0500	0.0489	0.7945
0.2265	300	0.9000	1.0000	0.5000	0.0500	0.0481	0.7735
0.2436	350	0.9000	1.0000	0.5000	0.0500	0.0464	0.7564

Table 1 (continued).

Power	*N*	Non-Inf OR	Actual OR	PB	Target alpha	Actual alpha	Beta
0.2579	400	0.9000	1.0000	0.5000	0.0500	0.0442	0.7421
0.2700	450	0.9000	1.0000	0.5000	0.0500	0.0418	0.7300
0.3114	500	0.9000	1.0000	0.5000	0.0500	0.0474	0.6886
0.0595	50	0.9500	1.0000	0.5000	0.0500	0.0408	0.9405
0.0666	100	0.9500	1.0000	0.5000	0.0500	0.0394	0.9334
0.0825	150	0.9500	1.0000	0.5000	0.0500	0.0443	0.9175
0.0895	200	0.9500	1.0000	0.5000	0.0500	0.0439	0.9105
0.0920	250	0.9500	1.0000	0.5000	0.0500	0.0414	0.9080
0.1126	300	0.9500	1.0000	0.5000	0.0500	0.0488	0.8874
0.1094	350	0.9500	1.0000	0.5000	0.0500	0.0437	0.8906
0.1251	400	0.9500	1.0000	0.5000	0.0500	0.0481	0.8749
0.1193	450	0.9500	1.0000	0.5000	0.0500	0.0425	0.8807
0.1318	500	0.9500	1.0000	0.5000	0.0500	0.0453	0.8682
0.0325	50	0.9900	1.0000	0.5000	0.0500	0.0300	0.9675
0.0443	100	0.9900	1.0000	0.5000	0.0500	0.0398	0.9557
0.0430	150	0.9900	1.0000	0.5000	0.0500	0.0377	0.9570
0.0518	200	0.9900	1.0000	0.5000	0.0500	0.0447	0.9482
0.0568	250	0.9900	1.0000	0.5000	0.0500	0.0483	0.9432
0.0594	300	0.9900	1.0000	0.5000	0.0500	0.0498	0.9406
0.0487	350	0.9900	1.0000	0.5000	0.0500	0.0399	0.9513
0.0605	400	0.9900	1.0000	0.5000	0.0500	0.0494	0.9395
0.0598	450	0.9900	1.0000	0.5000	0.0500	0.0482	0.9402
0.0587	500	0.9900	1.0000	0.5000	0.0500	0.0467	0.9413

Table 2. Results of power analysis of one proportion non-inferiority for *Z* test

Power	*N*	Non-Inf OR	Actual OR	PB	Target alpha	Actual alpha	Beta
0.2399	50	0.7500	1.0000	0.5000	0.0500	0.0421	0.7601
0.4602	100	0.7500	1.0000	0.5000	0.0500	0.0618	0.5398
0.5325	150	0.7500	1.0000	0.5000	0.0500	0.0465	0.4675
0.6381	200	0.7500	1.0000	0.5000	0.0500	0.0466	0.3619
0.7153	250	0.7500	1.0000	0.5000	0.0500	0.0443	0.2847
0.8091	**294**	**0.7500**	**1.0000**	**0.5000**	**0.0500**	**0.0562**	**0.1909**
0.8067	300	0.7500	1.0000	0.5000	0.0500	0.0525	0.1933
0.8451	350	0.7500	1.0000	0.5000	0.0500	0.0474	0.1549
0.8944	400	0.7500	1.0000	0.5000	0.0500	0.0526	0.1056
0.9142	450	0.7500	1.0000	0.5000	0.0500	0.0468	0.0858
0.9413	500	0.7500	1.0000	0.5000	0.0500	0.0502	0.0587
0.1611	50	0.8000	1.0000	0.5000	0.0500	0.0374	0.8389
0.3086	100	0.8000	1.0000	0.5000	0.0500	0.0529	0.6914
0.4033	150	0.8000	1.0000	0.5000	0.0500	0.0534	0.5967
0.4718	200	0.8000	1.0000	0.5000	0.0500	0.0496	0.5282
0.5252	250	0.8000	1.0000	0.5000	0.0500	0.0445	0.4748
0.6136	300	0.8000	1.0000	0.5000	0.0500	0.0502	0.3864
0.6847	350	0.8000	1.0000	0.5000	0.0500	0.0542	0.3153
0.7088	400	0.8000	1.0000	0.5000	0.0500	0.0465	0.7088
0.7602	450	0.8000	1.0000	0.5000	0.0500	0.0487	0.2398
0.8051	**488**	**0.8000**	**1.0000**	**0.5000**	**0.0500**	**0.0546**	**0.1949**
0.8022	500	0.8000	1.0000	0.5000	0.0500	0.0502	0.1978
0.1611	50	0.8500	1.0000	0.5000	0.0500	0.0586	0.8389
0.1841	100	0.8500	1.0000	0.5000	0.0500	0.0433	0.8159
0.2839	150	0.8500	1.0000	0.5000	0.0500	0.0585	0.7161
0.3104	200	0.8500	1.0000	0.5000	0.0500	0.0500	0.6896
0.3760	250	0.8500	1.0000	0.5000	0.0500	0.0546	0.6240
0.3864	300	0.8500	1.0000	0.5000	0.0500	0.0449	0.6136
0.4363	350	0.8500	1.0000	0.5000	0.0500	0.0464	0.5637
0.4801	400	0.8500	1.0000	0.5000	0.0500	0.0469	0.5199
0.5188	450	0.8500	1.0000	0.5000	0.0500	0.0468	0.4812
0.5534	500	0.8500	1.0000	0.5000	0.0500	0.0462	0.4466
0.1013	50	0.9000	1.0000	0.5000	0.0500	0.0497	0.8987
0.1356	100	0.9000	1.0000	0.5000	0.0500	0.0518	0.8644
0.1442	150	0.9000	1.0000	0.5000	0.0500	0.0439	0.8558
0.1790	200	0.9000	1.0000	0.5000	0.0500	0.0480	0.8210
0.2055	250	0.9000	1.0000	0.5000	0.0500	0.0489	0.7945
0.2265	300	0.9000	1.0000	0.5000	0.0500	0.0481	0.7735
0.2436	350	0.9000	1.0000	0.5000	0.0500	0.0464	0.7564
0.2912	400	0.9000	1.0000	0.5000	0.0500	0.0544	0.7088
0.3021	450	0.9000	1.0000	0.5000	0.0500	0.0509	0.6979
0.3114	500	0.9000	1.0000	0.5000	0.0500	0.0474	0.6886
0.0595	50	0.9500	1.0000	0.5000	0.0500	0.0408	0.9405
0.0967	100	0.9500	1.0000	0.5000	0.0500	0.0597	0.9033

Table 2 (continued).

Power	*N*	Non-Inf OR	Actual OR	PB	Target alpha	Actual alpha	Beta
0.0825	150	0.9500	1.0000	0.5000	0.0500	0.0443	0.9175
0.0895	200	0.9500	1.0000	0.5000	0.0500	0.0439	0.9105
0.1147	250	0.9500	1.0000	0.5000	0.0500	0.0540	0.8853
0.1126	300	0.9500	1.0000	0.5000	0.0500	0.0488	0.8874
0.1308	350	0.9500	1.0000	0.5000	0.0500	0.0545	0.8692
0.1251	400	0.9500	1.0000	0.5000	0.0500	0.0481	0.8749
0.1391	450	0.9500	1.0000	0.5000	0.0500	0.0517	0.8609
0.1518	500	0.9500	1.0000	0.5000	0.0500	0.0545	0.8482
0.0595	50	0.9900	1.0000	0.5000	0.0500	0.0554	0.9405
0.0666	100	0.9900	1.0000	0.5000	0.0500	0.0603	0.9334
0.0603	150	0.9900	1.0000	0.5000	0.0500	0.0533	0.9397
0.0518	200	0.9900	1.0000	0.5000	0.0500	0.0447	0.9482
0.0568	250	0.9900	1.0000	0.5000	0.0500	0.0483	0.9432
0.0594	300	0.9900	1.0000	0.5000	0.0500	0.0498	0.9406
0.0605	350	0.9900	1.0000	0.5000	0.0500	0.0500	0.9395
0.0605	400	0.9900	1.0000	0.5000	0.0500	0.0494	0.9395
0.0598	450	0.9900	1.0000	0.5000	0.0500	0.0482	0.9402
0.0587	500	0.9900	1.0000	0.5000	0.0500	0.0467	0.9413

Table 3. Results of power analysis of one proportion non-inferiority for *Z* test with continuity correction

Power	*N*	Non-Inf OR	Actual OR	PB	Target alpha	Actual alpha	Beta
0.2399	50	0.7500	1.0000	0.5000	0.0500	0.0421	0.7601
0.3822	100	0.7500	1.0000	0.5000	0.0500	0.0410	0.6178
0.5325	150	0.7500	1.0000	0.5000	0.0500	0.0465	0.4675
0.6381	200	0.7500	1.0000	0.5000	0.0500	0.0466	0.3619
0.7153	250	0.7500	1.0000	0.5000	0.0500	0.0443	0.2847
0.8083	**296**	**0.7500**	**1.0000**	**0.5000**	**0.0500**	**0.0549**	**0.1917**
0.8067	300	0.7500	1.0000	0.5000	0.0500	0.0525	0.1933
0.8451	350	0.7500	1.0000	0.5000	0.0500	0.0474	0.1549
0.8944	400	0.7500	1.0000	0.5000	0.0500	0.0526	0.1056
0.9142	450	0.7500	1.0000	0.5000	0.0500	0.0468	0.0858
0.9413	500	0.7500	1.0000	0.5000	0.0500	0.0502	0.0587
0.2399	50	0.8000	1.0000	0.5000	0.0500	0.0670	0.7601
0.3086	100	0.8000	1.0000	0.5000	0.0500	0.0529	0.6914
0.4033	150	0.8000	1.0000	0.5000	0.0500	0.0534	0.5967
0.4718	200	0.8000	1.0000	0.5000	0.0500	0.0496	0.5282
0.5252	250	0.8000	1.0000	0.5000	0.0500	0.0445	0.4748
0.6136	300	0.8000	1.0000	0.5000	0.0500	0.0502	0.3864
0.6847	350	0.8000	1.0000	0.5000	0.0500	0.0542	0.3153
0.7088	400	0.8000	1.0000	0.5000	0.0500	0.0465	0.2912
0.7602	450	0.8000	1.0000	0.5000	0.0500	0.0487	0.2398
0.8046	**490**	**0.8000**	**1.0000**	**0.5000**	**0.0500**	**0.0538**	**0.1954**
0.8022	500	0.8000	1.0000	0.5000	0.0500	0.0502	0.1978
0.1611	50	0.8500	1.0000	0.5000	0.0500	0.0586	0.8389
0.1841	100	0.8500	1.0000	0.5000	0.0500	0.0433	0.8159
0.2839	150	0.8500	1.0000	0.5000	0.0500	0.0585	0.7161
0.3104	200	0.8500	1.0000	0.5000	0.0500	0.0500	0.6896
0.3760	250	0.8500	1.0000	0.5000	0.0500	0.0546	0.6240
0.3864	300	0.8500	1.0000	0.5000	0.0500	0.0449	0.6136
0.4363	350	0.8500	1.0000	0.5000	0.0500	0.0464	0.5637
0.4801	400	0.8500	1.0000	0.5000	0.0500	0.0469	0.5199
0.5188	450	0.8500	1.0000	0.5000	0.0500	0.0468	0.4812
0.5534	500	0.8500	1.0000	0.5000	0.0500	0.0462	0.4466
0.1013	50	0.9000	1.0000	0.5000	0.0500	0.0497	0.8987
0.1356	100	0.9000	1.0000	0.5000	0.0500	0.0518	0.8644
0.1442	150	0.9000	1.0000	0.5000	0.0500	0.0439	0.8558
0.1790	200	0.9000	1.0000	0.5000	0.0500	0.0480	0.8210
0.2055	250	0.9000	1.0000	0.5000	0.0500	0.0489	0.7945
0.2265	300	0.9000	1.0000	0.5000	0.0500	0.0481	0.7735
0.2436	350	0.9000	1.0000	0.5000	0.0500	0.0464	0.7564
0.2912	400	0.9000	1.0000	0.5000	0.0500	0.0544	0.7088
0.3021	450	0.9000	1.0000	0.5000	0.0500	0.0509	0.6979
0.3114	500	0.9000	1.0000	0.5000	0.0500	0.0474	0.6886
0.0595	50	0.9500	1.0000	0.5000	0.0500	0.0408	0.9405

Table 3 (continued).

Power	*N*	Non-Inf OR	Actual OR	PB	Target alpha	Actual alpha	Beta
0.0967	100	0.9500	1.0000	0.5000	0.0500	0.0597	0.9033
0.0825	150	0.9500	1.0000	0.5000	0.0500	0.0443	0.9175
0.0895	200	0.9500	1.0000	0.5000	0.0500	0.0439	0.9105
0.1147	250	0.9500	1.0000	0.5000	0.0500	0.0540	0.8853
0.1126	300	0.9500	1.0000	0.5000	0.0500	0.0488	0.8874
0.1308	350	0.9500	1.0000	0.5000	0.0500	0.0545	0.8692
0.1251	400	0.9500	1.0000	0.5000	0.0500	0.0481	0.8749
0.1391	450	0.9500	1.0000	0.5000	0.0500	0.0517	0.8609
0.1518	500	0.9500	1.0000	0.5000	0.0500	0.0545	0.8482
0.0595	50	0.9900	1.0000	0.5000	0.0500	0.0554	0.9405
0.0666	100	0.9900	1.0000	0.5000	0.0500	0.0603	0.9334
0.0603	150	0.9900	1.0000	0.5000	0.0500	0.0533	0.9397
0.0518	200	0.9900	1.0000	0.5000	0.0500	0.0447	0.9482
0.0568	250	0.9900	1.0000	0.5000	0.0500	0.0483	0.9432
0.0594	300	0.9900	1.0000	0.5000	0.0500	0.0498	0.9406
0.0605	350	0.9900	1.0000	0.5000	0.0500	0.0500	0.9395
0.0605	400	0.9900	1.0000	0.5000	0.0500	0.0494	0.9395
0.0598	450	0.9900	1.0000	0.5000	0.0500	0.0482	0.9402
0.0587	500	0.9900	1.0000	0.5000	0.0500	0.0467	0.9413