



Contents lists available at ScienceDirect

Statistics and Probability Letters

journal homepage: www.elsevier.com/locate/stapro

The IM-based method for testing the non-inferiority of odds ratio in matched-pairs design

Hua Jin^{a,*}, Song Li^a, Yaolan Jin^b^a School of Mathematical Science, South China Normal University, Guangzhou 510631, PR China^b Department of Mathematics, University of Waterloo, Canada

ARTICLE INFO

Article history:

Received 22 May 2015

Received in revised form 15 November 2015

Accepted 15 November 2015

Available online 22 November 2015

Keywords:

Inferential model

Non-inferiority

Odds ratio

Type I error

Power

ABSTRACT

We construct an exact test for the non-inferiority of odds ratio based on the inferential model, which is a valid prior-free probabilistic inference method. Simulation studies suggest that our new test can be a competitive alternative to two asymptotic tests.

© 2015 Elsevier B.V. All rights reserved.

1. Introduction

The problem of testing the non-inferiority in matched-pairs design with binary responses is a common issue in medical research. Current methods for evaluation of equivalence or non-inferiority based on binary outcome include those proposed by Lu and Bean (1995), Nam (1997), Tango (1998), Hsueh et al. (2001), Liu et al. (2002), Sidik (2003), Lloyd and Moldovan (2008), Chen and Jin (2012), Zhong et al. (2012) for difference in proportions or those proposed by Lachenbruch and Lynch (1998), Nam and Blackwelder (2002), Tang et al. (2003), Jin et al. (2014) for the relative risk defined as the ratio of proportions.

However, difference in proportions and relative risk are often used as measures of risk association for comparing different treatments in prospective clinical trials, but they cannot be applied to assess equivalence or non-inferiority of risk or disease outcomes in retrospective studies. On the other hand, odds ratio is the most widely used measure of risk association that can be used in both prospective and retrospective studies. Then, Liu et al. (2005) proposed non-inferiority testing in matched-pairs design based on odds ratio.

For the sake of convenience, we only consider prospective studies in this paper. The results obtained from the prospective matched-pair design can be equally applied to the retrospective matched-pair studies.

For a prospective matched-pair study, the results of N subjects can be presented in a 2×2 table as given in Table 1, where a , b , c and d are respectively the observed numbers of pairs with outcomes (1, 1), (1, 2), (2, 1) and (2, 2), a and d are referred to the concordant pairs, b and c are called discordant pairs. In addition, let p_{11} , p_{12} , p_{21} and p_{22} be corresponding probabilities of the pairs.

* Corresponding author.

E-mail address: jinh1@163.com (H. Jin).

Table 1
Data structure 2×2 table for a prospective matched-pair study.

Exposed (treatment)	Unexposed (control)		Total
	Response (1)	Non-response (2)	
Response (1)	a (p_{11})	b (p_{12})	$a + b$ (p_{1+})
Non-response (2)	c (p_{21})	d (p_{22})	$c + d$ (p_{2+})
Total	$a + c$ (p_{+1})	$b + d$ (p_{+2})	N (1)

Under the assumption of a constant conditional marginal odds ratio for all values of the matching covariate, the conditional marginal odds ratio can be expressed in terms of the ratio of the population averaged discordant probabilities as [Lachin \(2000\)](#):

$$\delta = p_{12}/p_{21}. \quad (1.1)$$

If the objective of a prospective clinical trial is to verify whether the efficacy of the new treatment is no worse than that of the standard treatment within a pre-specified clinically meaningful margin δ_0 , $0 < \delta_0 < 1$, the hypothesis of non-inferiority can be formulated as

$$H_0 : \delta \leq \delta_0 \text{ VS. } H_1 : \delta > \delta_0. \quad (1.2)$$

[Liu et al. \(2005\)](#) proposed two methods to test the hypotheses in (1.2). The one is called the delta method, and the corresponding test statistic is

$$Z_D = \frac{\ln(\hat{\delta}) - \ln(\delta_0)}{\sqrt{\frac{1}{b} + \frac{1}{c}}}, \quad (1.3)$$

where $\hat{\delta} = b/c$, which is the estimate of parameter δ . The other one is the score test method, and the test statistic is

$$Z_S = \frac{b - \delta_0 c}{\sqrt{\delta_0(b + c)}}. \quad (1.4)$$

Both of them are considered to be asymptotically standard normal under the null hypothesis $\delta = \delta_0$. So the corresponding decision rules may not be exact in the sense that the sizes of the tests could be larger than they are claimed to be.

In this paper, we construct an exact test for the non-inferiority of odds ratio of the matched-pairs design based on the inferential model (IM), which is a valid prior-free probabilistic inference method proposed by [Martin and Liu \(2013a,b\)](#). The IMs do not require a prior to be specified, yet they produce probabilistic inferential results that have desirable frequency properties. It can provide exact inference, which is desirable in medical statistics. There should be a general advantage to the IM approach over other existing methods that are justified by asymptotic theory and, furthermore, the opportunities for improvement are greater in discrete problems like the one considered in this paper.

The remainder of the paper is structured as follows: Section 2 presents our new test based on the inferential model. In Section 3, we carry out simulation studies to compare our test to the two asymptotic tests. In Section 4, we treat a real data example for illustration. Some conclusions are presented in the last section.

2. Inferential model for non-inferiority

In this section, we use the inferential model to test the hypotheses in (1.2). We can transfer the null hypothesis $H_0 : \delta \leq \delta_0$ to the assertion $\mathcal{A} = \{\delta : \delta \leq \delta_0\}$. If evidence in data suggests that assertion \mathcal{A} is false, then we will reject the null hypothesis that \mathcal{A} is true.

The IM construction starts with an association, a formula for the data-generating mechanism, which involves the model parameters and a collection of unobservable auxiliary variables. In this case, the observable data is a 2 by 2 table of counts. However, efficient inference in discrete problems is challenging. It is difficult to find a closed form to express the relationship between the data and the model parameters and unobservable auxiliary variables. In the sequel, we follow the conditional IM argument in [Martin and Liu \(2015a\)](#) to define an association for $\delta = \frac{p_{12}}{p_{21}}$ based on the minimal sufficient statistic.

Let (X_{12}, X_{21}) be the random variables corresponding to the observed data (b, c) , then (X_{12}, X_{21}) is the minimal sufficient statistic for the parameters (p_{12}, p_{21}) , on which our parameter of interest δ depends only. The joint probability density function is

$$P\{X_{12} = b, X_{21} = c\} = \frac{n!}{b!c!(n-b-c)!} p_{12}^b p_{21}^c (1 - p_{12} - p_{21})^{n-b-c}$$

Download English Version:

<https://daneshyari.com/en/article/1151327>

Download Persian Version:

<https://daneshyari.com/article/1151327>

[Daneshyari.com](https://daneshyari.com)