科技部補助專題研究計畫成果報告

期末報告

成本效果機率在臨床試驗之廣義檢定與應用

- 計 畫 類 別 : 個別型計畫
- 計畫編號: MOST 103-2314-B-040-008-
- 執行期間: 103年08月01日至104年10月31日
- 執行單位:中山醫學大學護理學系(所)
- 計畫主持人: 李其融
- 共同主持人:林彩玉
- 計畫參與人員: 大專生-兼任助理人員:廖妍雅 大專生-兼任助理人員:曾東鋐
- 報告附件:出席國際會議研究心得報告及發表論文

處理方式:

- 1. 公開資訊:本計畫涉及專利或其他智慧財產權,2年後可公開查詢
- 2.「本研究」是否已有嚴重損及公共利益之發現:否
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中華民國 105 年 01 月 30 日

- 中 文 摘 要 : 在健康經濟學、公共衛生與健康科學的領域裡,成本效果分析經常 在臨床試驗中用以評估不同治療方式或不同介入方式的成本效果。 成本效果增量比、增量淨效益、增量淨健康效益、成本效果可接受 曲線等指標都是一般最常使用的分析工具。成本效果比較機率是另 一種分析工具,它是以機率分配來比較不同治療方式的成本效果比 。在實務上,成本資料經常為偏斜分配,但上述的分析工具都是以 平均數為基礎進行推論,平均數卻對於極端值相當敏感,但對成本 效果機率卻影響有限。在此計畫中,我們以比較成本效果機率來探 討偏斜分配對不同評估成本效果工具的影響;並在臨床試驗樣本數 有限的情況下,提出廣義樞紐量估計法建立確切的有母數推論,並 模擬隨機分派臨床試驗成本效果資料進行模擬分析與有限樣本之探 討。
- 中 文 關 鍵 詞 : 成本效果比較機率, 偏斜分配, 廣義樞紐量, 廣義推論, 隨機分派臨床 試驗
- 英文摘要: In health economics, public health and health science, the cost-effectiveness analysis is a type of economic evaluation that examines the costs-effectiveness of two competing treatments or interventions. The costeffectiveness data are usually collected from randomized clinical trial. Traditionally, the incremental costeffectiveness ratio (ICER) and its derivative measures, incremental net benefit, incremental net health benefit, and cost-effectiveness acceptability curve, are used to be analytic indices for cost-effectiveness analysis. The probability of comparative cost-effectiveness (PCCE) is another measure, which expresses the chance that the cost spent per effect for a case is cheap enough to overcome that for a control. Unlike the ICER and derivative measures of ICER that are constructed by mean cost and mean effectiveness, the probability of cost-effectiveness is not sensitive to extreme value. In this project, we discussed the influence of skewed distribution and symmetric distribution for ICER, derivative measures of ICER and PCCE. Consider the limited sample size in clinical trials we proposed an exact parametric inference for PCCE based on the concept of generalized pivotal quantities. Finally simulation studies conducted in finite sample sizes based on the design of randomized control trial.
- 英文關鍵詞: probability of comparative cost-effectiveness, skewed distribution, generalized pivotal quantity, generalized inference, randomized clinical trial

科技部補助專題研究計畫成果報告

(□期中進度報告/ ☑期末報告)

成本效果機率在臨床試驗之廣義檢定與應用

計畫類別: ☑個別型計畫 □整合型計畫 計畫編號: MOST103-2314- B-040-008-執行期間: 103 年 8 月 1 日至 104 年 10 月 31 日

執行機構及系所:中山醫學大學護理系

計畫主持人:李其融

共同主持人:林彩玉

計畫參與人員:曾東鋐、廖妍雅

本計畫除繳交成果報告外,另含下列出國報告,共1份: □執行國際合作與移地研究心得報告 ☑出席國際學術會議心得報告

期末報告處理方式:

1.公開方式:

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☑涉及專利或其他智慧財產權,□一年☑二年後可公開查詢

- 2.「本研究」是否已有嚴重損及公共利益之發現:☑否□是
- 「本報告」是否建議提供政府單位施政參考 ☑否 □是, (請列舉 提供之單位;本部不經審議,依勾選逕予轉送)

中華民國 105 年1月30日

一、中英文摘要與關鍵詞

• 中文摘要

在健康經濟學、公共衛生與健康科學的領域裡,成本效果分析經常在臨床試驗 中用以評估不同治療方式或不同介入方式的成本效果。成本效果增量比、增量淨效 益、增量淨健康效益、成本效果可接受曲線等指標都是一般最常使用的分析工具。成 本效果比較機率是另一種分析工具,它是以機率分配來比較不同治療方式的成本效果 比。在實務上,成本資料經常為偏斜分配,但上述的分析工具都是以平均數為基礎進 行推論,平均數卻對於極端值相當敏感,但對成本效果機率卻影響有限。在此計畫 中,我們以比較成本效果機率來探討偏斜分配對不同評估成本效果工具的影響;並在 臨床試驗樣本數有限的情況下,提出廣義樞紐量估計法建立確切的有母數推論,並模 擬隨機分派臨床試驗成本效果資料進行模擬分析與有限樣本之探討。

• 英文摘要

In health economics, public health and health science, the cost-effectiveness analysis is a type of economic evaluation that examines the costs-effectiveness of two competing treatments or interventions. The cost-effectiveness data are usually collected from randomized clinical trial. Traditionally, the incremental cost-effectiveness ratio (ICER) and its derivative measures, incremental net benefit, incremental net health benefit, and cost-effectiveness acceptability curve, are used to be analytic indices for cost-effectiveness analysis. The probability of comparative cost-effectiveness (PCCE) is another measure, which expresses the chance that the cost spent per effect for a case is cheap enough to overcome that for a control. Unlike the ICER and derivative measures of ICER that are constructed by mean cost and mean effectiveness, the probability of cost-effectiveness is not sensitive to extreme value. In this project, we discussed the influence of skewed distribution and symmetric distribution for ICER, derivative measures of ICER and PCCE. Consider the limited sample size in clinical trials we proposed an exact parametric inference for PCCE based on the concept of generalized pivotal quantities. Finally simulation studies conducted in finite sample sizes based on the design of randomized control trial.

• 關鍵詞

中文:成本效果比較機率,偏斜分配,廣義樞紐量,廣義推論,隨機分派臨床試驗 英文: probability of comparative cost-effectiveness, skewed distribution, generalized pivotal quantity, generalized inference, randomized clinical trial 二、報告內容

• Introduction

In health economics, public health and health science, the cost-effectiveness analysis is a form of economic evaluation that examines the costs-effectiveness of competing treatments or interventions over the past several decades (Van Hout, Al et al. 1994, Briggs and Fenn 1998). Traditionally, the incremental cost-effectiveness ratio (ICER) and its derivative measures, incremental net benefit (INB) and cost-effectiveness acceptability curve (CEAC), are used to be analytic indices for cost-effectiveness analysis (Willan and Briggs 2006). The series of measures draw attention to compare the difference of cost and the difference of effectiveness between two competing treatments. Although, the measures could be more relevant to health economics and policy decision (O'Hagan and Stevens 2002), they have several disadvantages: 1) when the value of effectiveness difference is close to zero, the ICER is meaningless, 2) the magnitude of negative ICER could be misleading, 3) the INB has no natural interpretation when the effectiveness isn't measured by money, and 4) mean cost and mean effectiveness are both sensitive to skewed data, and 5) a subjective or political cutoff is generally need in ICER, INB and CEAC (Dinh and Zhou 2006, Bang and Zhao 2012, Bang and Zhao 2012).

The cost-effectiveness data are usually collected from randomized clinical trial. In randomized clinical trials, a many-to-one comparison, that compares several treatments with a control, is the most common setup (Dilba, Bretz et al. 2004, Gutjahr and Brannath 2013). However limited statistical approaches have been developed for the evaluation of many-to-one comparison in cost-effectiveness analysis. In the study we propose to use the probability of cost-effectiveness in this problem. The probability of cost-effectiveness expresses the chance of gaining net benefit based on the probability distribution of cost-effectiveness ratio. This probability similar to the area under receiver operating characteristic (ROC) curve is use to evaluate the cost-effectiveness between two competing treatments (Willan 2001). The ROC curve has become a popular tool for evaluating the ability of measure to discriminate case and control in clinical trials (Pepe 2004), although it is a individual measure (O'Hagan and Stevens 2002). Unlike ICER and its derivative measures that are constructed by mean cost and mean effectiveness, the probability of cost-effectiveness is not sensitive to extreme value.

Second, we provide a generalized-pivotal-quantity (GPQ) approach to construct exact interval estimation for the many-to-one comparison. The GPQ approach is used to develop a

generalized confidence interval (GCI) for specific parameters containing nuisance parameters (Weerahandi 1993), and it is frequently used to obtain confidence intervals in situations where conventional methods are difficult to apply or fail to provide good solutions. The GCI estimation has been recently proven successful in many applications like the bioequivalence study (McNally, Iyer et al. 2003), the ROC curve analysis (Li, Liao et al. 2008, Li, Liao et al. 2008), the construction of tolerance intervals (Liao, Lin et al. 2005, Lin and Liao 2006, Lin, Liao et al. 2008), and the multivariate analysis of variance (Gamage, Mathew et al. 2004, Li 2009). The definition and properties of probability of cost-effectiveness and the GCI are presented in following section. Finally simulation results demonstrate that our proposed interval estimation provides not only sufficient probability coverage but also reasonable expected length.

• 研究方法

Let us consider a two-armed intervention study first. Denote that (C_j, E_j) are vectors of two random variable, the cost incurred and the effect achieved, on intervention *j* where j = 1 for case and j = 0 for control. The cost-to-effect ratio C_j/E_j is a measure of costeffectiveness for intervention *j* (Siegel, Laska et al. 1996). Therefore, the probability of comparative cost-effectiveness (PCCE) is formulated as

$$\pi_{10} = P\left(\frac{C_1}{E_1} < \frac{C_0}{E_0}\right).$$

It presents the chance that the cost spent per effect for a case is cheap enough to overcome that for a control. In addition, it may be mentioned that π_{10} equals the area under the ROC curve (AUC) for diagnostic test or biomarkers with continuous outcome. Over recent years, it has been increasingly used in biomedical informatics, machine learning, data mining, and health economics (Lasko, Bhagwat et al. 2005, Laking, Lord et al. 2006). Consider the skewness of the cost and effectiveness. We assume that (C_j , E_j) have independent bivariate lognormal distributions for j = 0, 1, and denote that

$$\begin{bmatrix} X_j \\ Y_j \end{bmatrix} = \begin{bmatrix} \ln C_j \\ \ln E_j \end{bmatrix} \sim N(\boldsymbol{\mu}_j, \boldsymbol{\Sigma}_j), \text{ where } \boldsymbol{\mu}_j = \begin{bmatrix} \boldsymbol{\mu}_{Xj} \\ \boldsymbol{\mu}_{Yj} \end{bmatrix} \text{ and } \boldsymbol{\Sigma}_j = \begin{bmatrix} \sigma_{Xj}^2 & \sigma_{XYj} \\ \sigma_{XYj} & \sigma_{Yj}^2 \end{bmatrix}.$$

Then the PCCE π_{10} can be showed as

$$\pi_{10} = P(D_1 < D_0)$$
$$= \Phi\left(\frac{\delta_0 - \delta_1}{\sqrt{\tau_0^2 + \tau_1^2}}\right)$$

where $D_j = X_j - Y_j \sim N(\delta_j, \tau_j^2)$, $\delta_j = \mu_{Xj} - \mu_{Yj}$, $\tau_j^2 = \sigma_{Xj}^2 + \sigma_{Yj}^2 - 2\sigma_{XYj}$, and $\Phi(\cdot)$ is the cumulative distribution function of standard normal distribution.

In a three-armed study, the intervention *j* equals 1 for treatment 1, equals 2 for treatment 2, and equals 0 for control. The PCCE for intervention *k* and control is denoted by π_{k0} for k = 1, 2. Then the probability $\theta = \pi_{20} - \pi_{10}$ evaluates the probability difference of comparing two treatments to a control. Suppose that (C_j, E_j) for j = 0, 1, 2 follow independent bivariate lognormal distributions. The probability of two-to-one comparison is

$$\begin{aligned} \theta &= \pi_{20} - \pi_{10} \\ &= P(D_2 < D_0) - P(D_1 < D_0) \\ &= \Phi\left(\frac{\delta_0 - \delta_2}{\sqrt{\tau_0^2 + \tau_2^2}}\right) - \Phi\left(\frac{\delta_0 - \delta_1}{\sqrt{\tau_0^2 + \tau_1^2}}\right). \end{aligned}$$
(1)

Now we propose a GPQ-based approach to develop exact confidence interval for the difference of PCCEs. Suppose that $\{(X_{ij}, Y_{ij}) = (\ln C_{ij}, \ln E_{ij}), i = 1, ..., n_j, j = 0, 1, 2\}$ is a random sample from $N(\mu_j, \Sigma_j)$ for j = 0, 1, 2, then $\{D_{ij} = X_{ij} - Y_{ij}, i = 1, ..., n_j, j = 0, 1, 2\}$ is a random sample from $N(\delta_j, \tau_j^2)$. The maximum likelihood estimators of δ_j and τ_j^2 are given by

$$\overline{D}_{j} = \overline{X}_{j} - \overline{Y}_{j} \sim N\left(\delta_{j}, \frac{\tau_{j}^{2}}{n_{j}}\right) \text{ and}$$
$$S_{Dj}^{2} = S_{Xj}^{2} + S_{Yj}^{2} - 2S_{XYj} \sim \frac{\tau_{j}^{2}}{n_{j} - 1}\chi_{n_{j}-1}^{2},$$

where \overline{D}_j are sample means and $S_{D_j}^2$ are sample variance. We use the concept of GPQ to construct confidence interval for π_{10} , π_{20} and θ . According to (1), the GPQs for δ_j and τ_j^2 can be defined respectively as

$$R_{\delta_j} = \overline{d}_j - (\overline{D}_j - \delta_j) \sqrt{\frac{s_{D_j}^2}{S_{D_j}^2}} = \overline{d}_j - Z_j \sqrt{\frac{R_{\tau_j^2}}{n_j}} \quad \text{and}$$

$$R_{\tau_j^2} = \frac{s_{D_j}^2 \tau_j^2}{S_{D_j}^2} = \frac{(n_j - 1)s_{D_j}^2}{U_j},$$
(2)

where \bar{d}_j and $s_{D_j}^2$ are observed \bar{D}_j and observed $S_{D_j}^2$, and Z_j and U_j are mutually independent for all *j*. From (2), we can verify that the distributions of and does not depend on any unknown parameters, and. Thus GPQs for π_{10} , π_{20} and θ are given by

$$R_{\pi_{k_0}} = \Phi\left(\frac{R_{\delta_0} - R_{\delta_k}}{\sqrt{R_{\tau_0^2} + R_{\tau_k^2}}}\right) \text{ for } k = 1, 2, \text{ and } R_{\theta} = R_{\pi_{20}} - R_{\pi_{10}}.$$
(3)

Set the confidence coefficient α , a $(1-\alpha)$ % generalized confidence interval for π_{k0} can be easily estimated by the $100(\alpha/2)$ th and $100(1-\alpha/2)$ th percentiles of the distribution of $R_{\pi_{k0}}$ which can be simulated by the Monte Carlo approach. Using the same approach, a generalized confidence interval for θ also can be established from the distribution of R_{θ} on three-armed RCT. Based on the concept of GPQ, we can use the Bonferroni correction or Šidák correction to construct a $(1-\alpha)$ % simultaneous confidence region for $\{R_{\pi_{k0}}, k = 1, 2, ..., K\}$ when $K \ge 3$. However we will not show the finite sample properties for the simultaneous confidence region in this project.

• 模擬分析

Simulation studies are conducted to examine finite sample properties of the proposed methods based on GPQs. Consider a three-armed RCT. The data of logarithm of cost-to-effect ratio $\{D_{ij}, i = 1, ..., n_j, j = 0, 1, 2\}$ are generated from $N(\delta_j, \tau_j^2)$. The sample size are specified as follows: $n_0 = n_1 = n_2 = n = 5, 10, 20, 50, 100$. Without loss of generality, all variances of D_j are the same and fixed at 1, and the mean of control D_0 is fixed at 0. The probability differences $\theta = \pi_{20} - \pi_{10}$ are consider for 0, 0.05, 0.1, and 0.2, and the ranges of π_{10} are set from 0.5-0.9. For each specified parameter combination, the data are independently generated 2500 times. The simulated results of coverage probabilities and ranges of confidence interval for θ are displayed in Table 1 and Figure 1, and the coverage probabilities of confidence interval for π_{10} are showed in Table 2.

The simulation results lead us to the following conclusions. For all of the simulation results, our proposed approach empirically adequately provides sufficient coverage probabilities at the nominal confidence level 95 per cent, especially when the sample size $n \ge 10$. Under the same parameter setting for θ , the expected lengths are shorter when the value of π_{10} is closer to 1 (boundary).

• 結論與建議

In this study, we present two GPQ-based methods to construct a confidence interval for the PCCE and PCCE comparison. The performance of our proposed method has been examined empirically by simulation studies. We find that the coverage probabilities are sufficiently close to the nominal level. Hence the proposed GPQ-based approach is suitable for the probabilities of comparable cost-effectiveness and their comparisons.

When number of intervention is greater than three, the simultaneous confidence region also can be constructed in our proposed procedure and Bonferroni or Šidák corrections. However these corrections are conservative approximations as the number of intervention is large. Further research is needed for using the concept of GPQs to construct the exact simultaneous confidence region for several π_{k0} . In addition, censoring that is a common feature in follow-up studies should be properly accounted in analysis of cost, effectiveness, or the probability of comparative cost-effectiveness. This is also one of topics for further study.

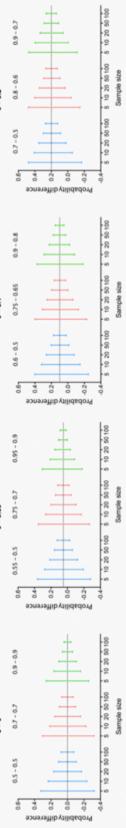
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$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	e	s	0.9600	0.9620	0.9620	0.9584	0.957		0.9708	0.9616	0.9620	0.9708	0.9640	0.9592	0.9656
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$\begin{bmatrix} 0.9468 & 0.9576 & 0.9566 & 0.9508 & 0.9464 & 0.9532 & 0.9488 & 0.9572 \\ 0.9532 & 0.9428 & 0.9452 & 0.9452 & 0.9500 & 0.9488 & 0.9444 & 0.9560 \\ \hline 0.9428 & 0.9428 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9464 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9464 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9464 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9488 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9464 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9488 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9566 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9660 \\ \hline 0.9444 & 0.9560 & 0.9468 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9464 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9464 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9464 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9444 & 0.9560 & 0.9464 & 0.9444 & 0.9560 \\ \hline 0.9444 & 0.9560 & 0.9444 & 0.9444 & 0.9560 & 0.9444 & 0.9464 & 0.9464 & 0.9444 & 0.9464 & 0.9464 & 0.9444 & 0.9464 & 0.9464 & 0.9444 & 0.9464 & 0.9464 & 0.9464 & 0.9464 & 0.9444 & 0.9464 & 0.9464 & 0.9464 & 0.9464 & 0.9444 & 0.9464 & 0.9464 & 0.9464 & 0.9464 & 0.9444 & 0.9464 & 0.9$		20	0.9560	0.9564	0.9524	0.9548	0.956		0.9596	0.9484	0.9424	0.9556	0.9508	0.9500	0.9568
0.9532 0.9428 0.9452 0.9500 0.9488 0.9560 a=0.05 a=0.05 a=0.05 a=0.05 a=0.05 a=0.05 a=0.1 a=0.1 a=0.1 a=0.1 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.4 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.2 a=0.4 a=0.2 a=0.2 a=0.2 a=0.4 a=0.2 a=0.2 a=0.4 a=0.2 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5 a=0.5		8	0.9496	0.9416	0.9488	0.9468	0.957		0.9556	0.9508	0.9464	0.9532	0.9488	0.9572	0.9484
8=0.05 8=0.05 8=0.05 0.05-0.5 0.25-0.5 0.05-0		100	0.9480	0.9552	0.9496	0.9532	0.942		0.9452	0.9528	0.9500	0.9488	0.9444	0.9560	0.9480
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Figure 1. T	he empirical r	range of 95% confide	ence interval for 6	$0 = m_{20} - m_{10}$										
06 05-0.5 0.7-0.7 0.9-0.8 0.5 0.5-0.5 0.5-0.5 0.5-0.5 0.5-0.5 0.3-0.6 04 04 05 05 0.5-0.5 0.5-0.5 0.5-0.5 0.5-0.5 0.3-0.6 04 05 05 05 0.5 0.5-0.5 0.5-0.5 0.5-0.5 0.3-0.6 05 04 05 05 0.5 0.5-0.5 0.5-0.5 0.3-0.6 04 05 05 05 05 0.5 0.5 0.5 05 04 1 1 1 1 1 05 1 1 1 1 1 1 05 05 05 05 05 05 0.5				0=0			0 = 0.(05			0 = 0.1			0 = 0.2	
04- 1				0.7 - 0.7	0.9 - 0.9				6.0 - 56.1	-		8.9 - 0.8			0.9-0.7
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				-	. 1			-	iiffen	~			iffen 02	-	+



ble 2. T	he empirical	coverage probabil	silities of 95% confidence	ance interval for m ₁₀		
	T ₁₀	66:0	0.95	0.9	0.7	0.5
e	5	0.9580	0.9604	0.9620	0.9760	0.9728
	10	0.9496	0.9564	0.9588	0.9596	0.9608
	20	0.9576	0.9560	0.9548	0.9468	0.9568
	20	0.9480	0.9552	0.9524	0.9484	0.9460
	100	0.9520	0.9580	0.9484	0.9540	0.9504

科技部補助專題研究計畫成果報告自評表

請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或 應用價值(簡要敘述成果所代表之意義、價值、影響或進一步發展之可能 性)、是否適合在學術期刊發表或申請專利、主要發現(簡要敘述成果是 否有嚴重損及公共利益之發現)或其他有關價值等,作一綜合評估。

- 請就研究內容與原計畫相符程度、達成預期目標情況作一綜合評估
 ☑達成目標
 □未達成目標(請說明,以100字為限)
 □實驗失敗
 □因故實驗中斷
 □其他原因
 3. 研究成果在學術期刊發表或申請專利等情形:
 論文:□已發表 ☑未發表之文稿□撰寫中□無
 專利:□已獲得□申請中□無
 - 技轉:□已技轉□洽談中□無

其他:(以100字為限)

3. 請依學術成就、技術創新、社會影響等方面,評估研究成果之學術或 應用價值(簡要敘述成果所代表之意義、價值、影響或進一步發展之 可能性),如已有嚴重損及公共利益之發現,請簡述可能損及之相關程 度(以 500 字為限)

研究結果與原計畫相符,並已達成原計畫內預期完成之目標,此研究結果具學術價值,除了參加一場國際會議之海報發表外,亦延伸致相關主題,於同場國際會議中發表。此外,本研究結果已撰寫完成並 投稿至SCI的學術期刊。

參與之研究之工作人員除了學習有系統地探討文獻外,更學習成本 效果分析之評估指標、成果效果分析之估計方法、廣義區間估計與廣 義檢定、模擬計算、程式撰寫。在資料處理端,也精熟龐大資料的篩 選與整理,相信會對日後相關的工作奠定良好的能力基礎。

科技部補助專題研究計畫出席國際學術會議心得報告

日期:105年1月28日

計畫編號	MOST103-2314- B-04	-008-						
計畫名稱	成本效果機率在臨床	試驗之廣義檢	定與應用					
出國人員 姓名	李其融	服務機構 及職稱	中山醫學大學護理系					
會議時間	104年8月8日至	104 年 8 月 8 日至 @iiii Washington State Convention						
曾	104年8月13日 Center, Seattle, US							
會議名稱	(中文) 2015 聯合統言 (英文) 2015 Joint Stat		5S					
發表題目	(中文) 比較多對一成 (英文) On the Exact Ir in Probability of	nterval Estimat	ion for the Many-to-One Comparisons					

一、參加會議經過

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在本次會議中,我們以海報報告的方式發表「On the Exact Interval Estimation for the Many-to-One Comparisons in Probability of Cost-Effectiveness」,探討的主 題有二:一、以機率的方式建立新的成本效果評估指標;二、利用建立的成本 效果機率提供多組成本效果機率的比較方法與廣義區間估計。透過模擬計算, 我們發現我們所提出的方法在有限樣本下在覆蓋率上都具有良好的表現。並於 海報報告時,與 Ching-Ray Yu、Wei-Wen Hsu 等多位學者討論我們的研究成果。 特別感謝廣義區間估計的專家 Kalimuthu Krishnamoorthy,對於我們的研究給予 重要的理路觀點與應用上的建議。

另外與林彩玉教授聯合發表「Testing Equality of Average Cost-Effectiveness Ratios in Multiple Treatments」,該研究主題獲得藥廠研究員的青睐,互相表示合作意願。

1

此外本人亦參加了許多口頭發表場次,如 Causal Inference、Statistics Education Through Online Education、From Consulting to Collaboration to Leadership: Increasing the Impact of Statistical Practice、New and Diverse Applications of Cost-Effective Two-Phase Sampling Designs、ROC and Multi-Reader Studies for Diagnostic Devices、Innovations in Design and Analysis of Clinical Trials 等等,以 瞭解與成本效果、臨床試驗、統計教學、統計諮詢等目前研究與教學相關議題 的進展,以及與諮詢常碰到的實務問題在統計上最新的解決方法。除了聽講者 發表研究成果外,也學習講者的報告風格與提問與應答的技巧,受益不少。

會議中除了論文發表外,還有統計圖書攤位的新書發表、統計軟體攤位的產品 介紹等,非常熱鬧。會議前之歡迎晚會與會議期間除了與外國學者交流外,亦 遇見國內師長與學者,並與之討論研究成果或工作經驗,相談甚歡。

二、與會心得

感謝科技部提供本人出國參加國際會議的補助,此次會議是本人第一次參與 JSM 國際會議,見識到北美地區最大研討會的規模、學術交流與產業交流的價 值,獲得許多寶貴之經驗,雖然本人選擇以海報張貼的方式參與會議,但仍然 受到國內外學者的建議與指教。同時,在聆聽其它場次的口頭報告中,了解各 國學者目前關心統計理論、統計實務的問題,以及產學專家學者所提出的解決 方法,並且觀摩他們報告的方式與技巧。

在這次會議中,除了參加與我研究議題相關的口頭報告場次外,也參加了與我 工作上經常碰到的資料庫分析等場次活動,瞭解目前在應用領域上最新的問題, 以及統計上可提供的思考與可解決的方法,讓我在未來的諮詢工作上可對諮詢 者提供不一樣的處理方法與研究方向。

三、發表論文全文或摘要

ABSTRACT. In health economics, public health and health science, the cost-effectiveness analysis is a type of economic evaluation that examines the costs-effectiveness of two competing treatments or interventions. However limited statistical approaches have been developed for the evaluation comparing more than two treatments. The probability of cost-effectiveness is an measure, which expresses the chance of gaining net benefit based on the probability distribution of cost-effectiveness ratio. Unlike the incremental cost-effectiveness ratio (ICER) and its derivative measures that are constructed by mean cost and mean effectiveness, the probability of cost-effectiveness is not sensitive to extreme value. In this study we propose to use the concept of generalized pivotal quantities to construct exact interval estimation for the many-to-one comparison (several experimental treatments are

compared with a control treatment) in the probability of cost-effectiveness. Simulation results demonstrate that our proposed interval estimation provides not only sufficient probability coverage but also reasonable expected length. Numerical examples using published data sets of illustrate the proposed method.

四、建議

參加此次的會議不僅僅增加統計上的國際視野,也見識了 JSM 的規模與討論議 題的多樣性。在學術上,瞭解各領域應用統計方法的現況與統計專家學者提出 最新的思維與解決方法,並於討論中引發不同的思考。在實務上,有別於國內 之統計研討會,有公共衛生、政府、民間企業、天文等應用統計領域專家參與 其中,並且熱烈討論,也從企業關心的實質問題引導至學術學者解決。因此建 議國內學者,特別如同本人一樣是國內博士班畢業或是未曾出國留學或出國作 研究的研究者,能多參加歐美之大型國際會議,相信對國內統計之學術研究及 產業推展會有正面的幫助,也會刺激研究者向外吸取知識與拓展視野的渴望。

五、攜回資料名稱及內容

- 會議議程手冊:研討會發表論文之活動場次、時間、發表人、摘要,主辦與協 辦單位、人員。
- 2. 研討會紀念側背包一只,其他軟體商、書商、生技公司之紀念品。
- 3. 與研究領域相關之重要專家學者之聯絡方式。

六、其他

會前歡迎晚會



海報報告



會場、與會者合影



科技部補助專題研究計畫出席國際學術會議心得報告

日期:105年1月28日

計畫編號	MOST103-2314- B-040)-008-					
計畫名稱	成本效果機率在臨床	試驗之廣義檢	定與應用				
出國人員 姓名	李其融	李其融 服務機構 中山醫學大學護理系					
合详时明	104年8月8日至	104 年 8 月 8 日至 @iiii Washington State Convention					
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會議中除了論文發表外,還有統計圖書攤位的新書發表、統計軟體攤位的產品 介紹等,非常熱鬧。會議前之歡迎晚會與會議期間除了與外國學者交流外,亦 遇見國內師長與學者,並與之討論研究成果或工作經驗,相談甚歡。

二、與會心得

感謝科技部提供本人出國參加國際會議的補助,此次會議是本人第一次參與 JSM 國際會議,見識到北美地區最大研討會的規模、學術交流與產業交流的價 值,獲得許多寶貴之經驗,雖然本人選擇以海報張貼的方式參與會議,但仍然 受到國內外學者的建議與指教。同時,在聆聽其它場次的口頭報告中,了解各 國學者目前關心統計理論、統計實務的問題,以及產學專家學者所提出的解決 方法,並且觀摩他們報告的方式與技巧。

在這次會議中,除了參加與我研究議題相關的口頭報告場次外,也參加了與我 工作上經常碰到的資料庫分析等場次活動,瞭解目前在應用領域上最新的問題, 以及統計上可提供的思考與可解決的方法,讓我在未來的諮詢工作上可對諮詢 者提供不一樣的處理方法與研究方向。

三、發表論文全文或摘要

ABSTRACT. In health economics, public health and health science, the cost-effectiveness analysis is a type of economic evaluation that examines the costs-effectiveness of two competing treatments or interventions. However limited statistical approaches have been developed for the evaluation comparing more than two treatments. The probability of cost-effectiveness is an measure, which expresses the chance of gaining net benefit based on the probability distribution of cost-effectiveness ratio. Unlike the incremental cost-effectiveness ratio (ICER) and its derivative measures that are constructed by mean cost and mean effectiveness, the probability of cost-effectiveness is not sensitive to extreme value. In this study we propose to use the concept of generalized pivotal quantities to construct exact

interval estimation for the many-to-one comparison (several experimental treatments are compared with a control treatment) in the probability of cost-effectiveness. Simulation results demonstrate that our proposed interval estimation provides not only sufficient probability coverage but also reasonable expected length. Numerical examples using published data sets of illustrate the proposed method.

四、建議

參加此次的會議不僅僅增加統計上的國際視野,也見識了 JSM 的規模與討論議 題的多樣性。在學術上,瞭解各領域應用統計方法的現況與統計專家學者提出 最新的思維與解決方法,並於討論中引發不同的思考。在實務上,有別於國內 之統計研討會,有公共衛生、政府、民間企業、天文等應用統計領域專家參與 其中,並且熱烈討論,也從企業關心的實質問題引導至學術學者解決。因此建 議國內學者,特別如同本人一樣是國內博士班畢業或是未曾出國留學或出國作 研究的研究者,能多參加歐美之大型國際會議,相信對國內統計之學術研究及 產業推展會有正面的幫助,也會刺激研究者向外吸取知識與拓展視野的渴望。

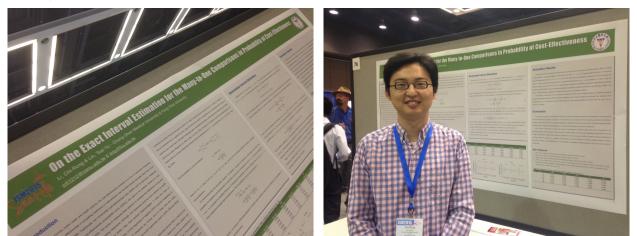
五、攜回資料名稱及內容

- 會議議程手冊:研討會發表論文之活動場次、時間、發表人、摘要,主辦與協 辦單位、人員。
- 2. 研討會紀念側背包一只,其他軟體商、書商、生技公司之紀念品。
- 3. 與研究領域相關之重要專家學者之聯絡方式。
- 六、其他

會前歡迎晚會



海報報告



會場、與會者合影



科技部補助計畫衍生研發成果推廣資料表

日期:2016/01/28

	計畫名稱:成本效果機率在臨床試驗之廣義	檢定與應用
科技部補助計畫	計畫主持人:李其融	
	計畫編號: 103-2314-B-040-008-	學門領域: 公共衛生及環境醫學
	無研發成果推廣資料	4

103年度專題研究計畫研究成果彙整表

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填	研討會/工作坊			0			
項 目	電子報、網站			0			
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科技部補助專題研究計畫成果報告自評表

請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或應用價值(簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性)、是否適 合在學術期刊發表或申請專利、主要發現或其他有關價值等,作一綜合評估。

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1.	請就研究內容與原計畫相符程度、達成預期目標情況作一綜合評估 ■達成目標 □未達成目標(請說明,以100字為限) □實驗失敗 □因故實驗中斷 □其他原因 說明:
2.	研究成果在學術期刊發表或申請專利等情形: 論文:□已發表 ■未發表之文稿 □撰寫中 □無 專利:□已獲得 □申請中 ■無 技轉:□已技轉 □洽談中 ■無 其他:(以100字為限)
3.	請依學術成就、技術創新、社會影響等方面,評估研究成果之學術或應用價值 (簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性)(以 500字為限) 研究結果與原計畫相符,並已達成原計畫內預期完成之目標,此研究結果具學 術價值,除了參加一場國際會議之海報發表外,亦延伸致相關主題,於同場國 際會議中發表。此外,本研究結果已撰寫完成並投稿至SCI的學術期刊。 參與之研究之工作人員除了學習有系統地探討文獻外,更學習成本效果分析之 評估指標、成果效果分析之估計方法、廣義區間估計與廣義檢定、模擬計算、 程式撰寫。在資料處理端,也精熟龐大資料的篩選與整理,相信會對日後相關 的工作奠定良好的能力基礎。