EFFECT SIZES OF FIXED AND RANDOM EFFECTS MODEL IN META-ANALYSIS

by

FOO CHUAN HUI

Dissertation submitted in partial fulfillment of the requirements for the degree of Master of Science in Statistics

April 2010

ACKNOWLEDGEMENTS

First and foremost, I would like to express my deepest gratitude to my thesis supervisor, Associate Professor Dr. Low Heng Chin, for her invaluable guidance, relentless contribution of ideas, suggestions, constant advice and patience throughout my study.

I also gratefully acknowledge the Ministry of Higher Education of Malaysia and the Universiti Pendidikan Sultan Idris for providing me the financial assistance during my master study. Further, I would like to express my sincere appreciation to the School of Mathematical Sciences as well as the library of USM for providing various facilities and references.

I would like to convey my heartfelt gratitude to my father, Foo Ah Chye, and my mother, Yew Soo Ngou, for being the pillars of my strength. Their greatest contribution, sacrifice, constant prayers, patience and endless encouragement all this while are certainly the greatest motivation to inspire me to do my very best. Thanks also to all my friends and course mates for lending me their friendship and moral support.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

KESAN SAIZ TERHADAP MODEL KESAN TETAP DAN RAWAK DALAM ANALISIS-META

ABSTRAK

Dalam beberapa dekad yang lalu, analisis-meta telah berkembang dengan pesat dalam pelbagai bidang pengajian untuk meningkatkan kualiti penyelidikan yang sebelumnya menerusi tinjauan kuantitatif. Tinjauan kuantitatif mengukur saiz kesan daripada kajian-kajian secara menyeluruh. Oleh itu, objektif disertasi ini ialah menentukan kaedah penghitungan saiz kesan bagi keadaan yang berbeza dalam analisis meta. Terdapat dua penemuan kunci bagi kajian ini adalah seperti berikut: Pertamanya, kaedah *vote-counting* akan digunakan sekiranya penganggaran saiz kesan tidak didapati. Seterusnya, kaedah kesan tetap dan kesan rawak akan digunakan untuk menganggarkan saiz kesan gabungan sekiranya saiz kesan dapat dihitung. Sebanyak 55 ujikaji rawak berkawal pada rawatan Tamoxifen diberi kepada pesakit-pesakit kanser payudara peringkat awal yang diamati berdasarkan kes-kes kambuh serta kes-kes kematian masing-masing. Kemudian, data tersebut dianalisa dengan menggunakan perisian statistik terkini dan canggih, Comprehensive Meta-Analysis (CMA) versi 2.0. CMA didapati bermanfaat dan berinteraktif dalam proses analisis meta. Pilihan dan penerbitan yang bersifat 'bias' harus dielakkan demi menghasilkan analisis meta yang lebih berkualiti.

ABSTRACT

Over a few decades ago, meta-analysis has rapidly developed in various fields of studies to improve the quality of previous research by quantitative review. Quantitative review assesses an overall magnitude of the effect from multiple studies. Hence, the objective in this dissertation is to determine the methods of finding effect sizes for different conditions in meta-analysis. Two key findings of this study are as follows: Firstly, vote-counting method will be applied if the effect size estimates are not available. Next, fixed effects and random effects methods will be used in combining the effect size estimates when effect size estimates can be calculated. 55 Randomised Controlled Trials (RCTs) on Tamoxifen treatment for early breast cancer patients are observed according to recurrences and mortality cases, respectively. The data is then analysed by using the latest statistical software, Comprehensive Meta-Analysis (CMA) version 2.0. CMA is found to be beneficial and interactive in the process of meta-analysis. The selection bias as well as the publication bias should be avoided in order to produce better quality meta-analysis.

CHAPTER 1
INTRODUCTION

1.1 Introduction To Meta-Analysis

Gene V. Glass is the first person to develop the term "meta-analysis" and to demonstrate its use in 1976. Meta-analysis is the integration of data from a large number of research studies through statistical analysis, thus providing conclusions in the simpler forms of relationship to the large collection of studies. It can also be defined as the combination of findings from multiple studies and the deficiencies of information are re-analyzed to give a systematic and plausible conclusion. Meta-analysis can be classified into two different types of systematic review: (1) qualitative review, and (2) quantitative review.

Meta-analytic process provides the gathered information from past research findings. Through this, it enables us to discover what are the requirements and even the drawbacks as a guideline for future research. As long as there is a preliminary study, numerous questions can be resolved with the existence of meta-analysis procedures. The study of the relationship can be carried out by using meta-analysis despite the primary studies which did not go through the process. In addition, meta-analysis is able to rectify inaccurate results such as the misrepresented effects of sampling error, inconsistent findings and other measurement inaccuracies. Meta-analytic study is very useful because of its power in the relationship between variables, the correlation between independent variables (variety of treatments) and the efficiency of the interventions (therapy, counselling).

Meta-analysis is known to be an exclusive element due to the effect size which enables the degree of findings to be calculated. The three most regularly applied measures of effect sizes include standardized mean differences, the product-moment correlation r, (Rosenthal, 1991) and the odds ratio (Fleiss, 1994; Haddock *et al.*, 1998). The purpose of meta-analysis is to comprehend the variation of effect size whenever it diverges greatly from study to study. We then use the one-way analysis of variance (ANOVA) to investigate categorical moderators.

Moderator variable is said to be an interaction either in the form of a qualitative or quantitative variable that changes the direction of the correlation between the independent and dependent variables (Holmbeck, 1997). A moderator can intensify or even weaken treatment effect. If the moderator variable is excluded from the studies, it will be dangerous for those who are undergoing improper treatment and even will reduce the power of statistical testing (Kraemer *et al.*, 2001).

Meta-analysis is a way to identifying, synthesizing and accumulating the findings of particular studies, has been widely performed in randomized controlled trials (RCT) which plays an important role in an intervention. Employee training programs, leadership development programs, performance management systems, and organizational development interventions used meta-analysis and found it to be a useful and effective approach.

Systematic reviews may not necessarily include a statistical synthesis called meta-analysis. They take into account the same studies within combination results which are thereby considered a meaningful finding. To be specific, meta-analysis is an optional element (subset) of a systematic review, which uses a specific statistical method to combine the individual studies' findings (see Figure 1.1).

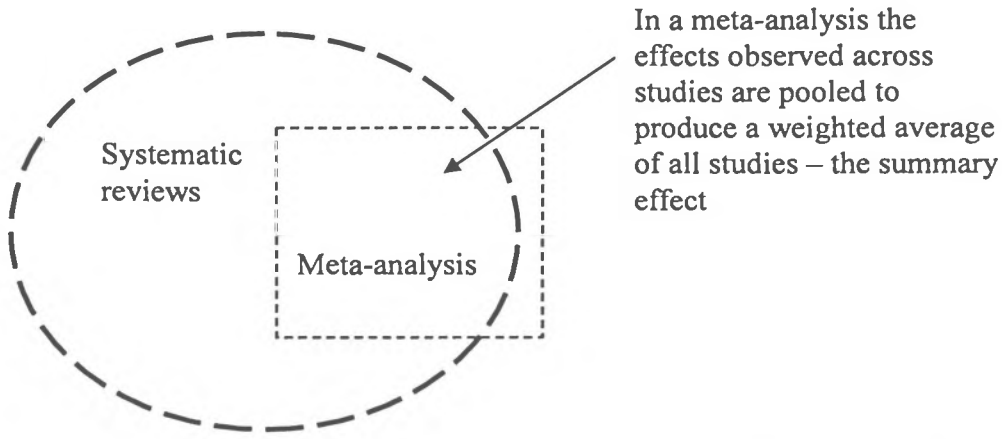

Figure 1.1: Systematic reviews versus Meta-analysis (source: Arvanitis et al., 2004)

The reasons for using meta-analysis are to (i) find out the existence of an effect, (ii) identify the degree of an effect, (iii) ensure the usefulness of moderator variable for an effect, and (iv) overcome the discrepancy in a research. Through meta-analytic studies, the intervention effect can be estimated more thoroughly if further and additional information is provided. Many primary studies vary in characteristics. With meta-analysis, it allows the differences in effect estimates to be examined. The purposes of the meta-analysis can be diverse subject to the need of the investigator. The focus can be on finding the population mean of correlation between variables, some estimating the variance of the population distribution or others that require both the mean and variance for statistical computation.

The importance of meta-analysis is not merely for those who use its procedures or techniques but there is greater impact for researchers who seriously investigate different types of meta-analysis for the sake of research purposes. From a large number of studies, each of them is treated as a data source for meta-analysis. Upon assessment, the impact of various statistical methods will be identified

respectively. Therefore, chronological development is considerably crucial for the findings.

Table 1.1 compares the advantages and disadvantages in meta-analysis. In terms of advantages, meta-analysis enables a large number of studies summarize through systematic review. It can detect the relationships whereby the others could not, and solve the limitations of previous study. By quantitative analysis for outcomes in multiple domains, meta-analysis is able to obtain more accurate findings.

For disadvantages, the author requires much effort and expertise to combine a great number of studies for a specific topic. A meta-analysis weak summary produces erratic research or more often it is called "garbage in, garbage out".

Table 1.1 Comparison between strengths and weaknesses of meta-analysis

STRENGTHS	WEAKNESSES
Summarize the research findings on a big-scale	Publication bias - More likely to publish positive significant result rather than negative ones
Curb the troubles faced by traditional narrative reviews - Analyze the impact of moderating variables	Greater effort for the cumulative findings
Able to investigate small or moderate relationships ambiguous in previous studies	Meta-analysis has results with a combination of "poorly" designed studies and "good" studies
Increase the precision of effects summary - discipline and transparency	Only deals with main effects - interaction effects via moderator analyses
Manage to increase power - identify significant effects	Different subjects, variables, and measuring method produce illogical conclusions

1.2 Research Fields in Meta-analysis

Since the 1970s, the applications of meta-analysis in psychological, educational, behavioural, and medical interventions have focused on investigating

the effectiveness of each study's treatment respectively. More than three hundred meta-analysis had been reviewed by Lipsey & Wilson (1993) involving the research areas in mental health interventions, counselling and psychoeducational interventions, health related psychological and educational treatment, work or organizational interventions, and educational interventions.

1.2.1 Impact on Theory Development

The development of theory relies on the observations in behaviour and social sciences. In the 1970s, behavioural scientists were seeking for quantitative summaries based on the techniques in meta-analysis in their research literature. Having a good understanding of the empirical relationship among variables is the key to build up theories. The purpose of the studies would not succeed without a strong relationship among variables. Only those with highly correlated variable can proceed to the further interactive or moderator-based theories. From the theory itself, it indicates an explanation prior to the meta-analytic findings. Guzzo, Jackson, and Katzell (1986) criticized this because the theory depends on the strong relationship variable and it is not developed directly from meta-analysis.

Science seeks for explanation all the time, and explanation renders the causal. If the data of behavior and social sciences match with one of the methods, either path analysis (Hunter & Gerbing, 1982) or structural equation modelling (SEM) then the method can be utilized to examine causal theories.

1.2.2 Impact on Psychology

The ability of meta-analysis is to establish a deduction once the new knowledge is learnt through different studies based on quantitative review. On top of that, meta-

analysis can even come out with new discovery which could hardly be explained from any individual study.

The major review journal in psychology is Psychological Bulletin. Fixed-effect methods are the most common model used in Psychological Bulletin. In fact, random effects model could be more appropriate to be used since it assumes all studies are from different populations while fixed effects model assumes that all studies from a single population. So, fixed effects model is always the first choice because it is easier and its findings are much better compared to traditional narrative review, but the accuracy of the findings would be doubtful.

1.2.3 Impact on Medical Field

According to Hunt (1997), if we make a comparison between behavioural & social sciences and medical research, medical research uses more meta-analysis. This phenomena is noticeably seen in the leading medical journals namely New England Journal of Medicine as well as the Journal of the American Medical Association (approximately 962 to 1411 meta-analyses are recorded in medical literature by 1995; Moher & Olkin, 1995). For medical research, the researchers will not know exactly whether the applicants are receiving the treatments or the placebo in a random allocation. This method is the most frequent mode in medical research, so-called the Randomized Controlled Trial (RCT). Unfortunately, the test that is usually being implemented is based on a small sample size, and so the population effect sizes are always small as well. Despite the same treatment is applied for different RCTs, yet it yields a contradictory outcome in each study.

Thomas Chalmers is the pioneer who suggested the application of meta-analysis in medical research. After doing a survey on meta-analysis and statistical

research on different diseases, Chalmers *et al.* (1977) who first used the drug based on different treatments, diseases and various areas of medical practice came to the conclusion that a great number of lives would have been saved as long as the application of meta-analysis is applied and contained chronologically in previous medical research literature. Moreover, the Cochrane Collaboration is another method for Chalmers to be put into practice. It is necessary to update the newest findings in RCT as the development in medical research findings has saved numerous lives.

1.2.4 Impact on other disciplines

Meta-analysis is equally essential for marketing, sociology, finance and even wildlife management research study. Political science is starting to make use of meta-analysis (Pinello, 1999) whereas meta-analysis in economics is now receiving increasing attention, too (Stanley, 2001). In social sciences, a strategy is being developed similar to the method accomplished in the medical field, the Campbell Collaboration (Boruch, 2005).

1.3 Types of Meta-analysis

In qualitative literature review, a researcher combines a set of studies and makes a narrative review. The researcher interprets the findings of the studies in words, rather than mathematical description. Nevertheless, the conclusions of narrative review have always been inconsistent from one literature to the other. By the mid-1990s, quantitative literature review which focuses on effect sizes is used in meta-analysis to avoid the problems of qualitative reviews. The authors review articles by choosing an effect size from the previous research finding. After that

meta-analysis is used to describe the overall magnitude (strong or weak) of the effect from a large number of studies based on different situations.

Lately, meta-analytic summaries for primary research papers have been used widely. Meta-analysis is used to provide information about the constancy of an overall relationship among the studies being carried out. Compared to a complete study for quantitative literature review, meta-analytic summaries could be much easier based on a single analysis from different studies.

1.4 Meta-analysis Procedures

The following flow chart shows the basic steps on conducting meta-analysis. Firstly, we need to have the problem statement, and then collect information in a systematic way by reviewing literature from printed research papers or electronic journals (published and unpublished), read through each literature's method and analysis.

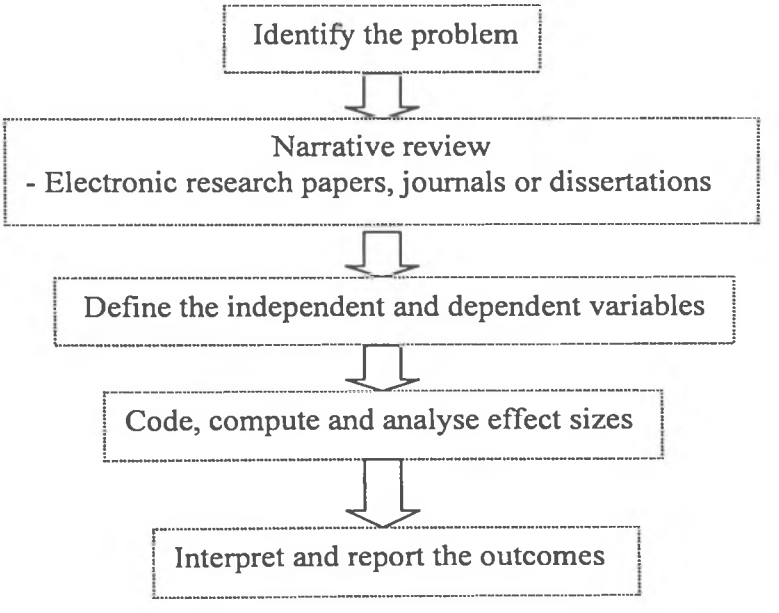

Figure 1.2 Steps of conducting meta-analysis

Next, we specify the independent and dependent variables of interest (effects of radiotherapy treatment on cancer patients). Once we have identified the objective of the study, we code every data accordingly and analyze the data set to evaluate the magnitude of the effect sizes. Finally, we interpret the results based on the output of data analysis.

Meta-analysis is based on the concept of effect size as defined by Glass (1976). In short, effect size (ES) is the difference between the mean of the experimental group and the mean of the control group divided by the standard deviation of the control group. Meta-analysis combines the effects throughout the studies in order to increase the precision of the overall mean effect. If the difference between the null and alternative means (ES) is greater, the more precise the test is. Those appropriate measures that are applicable in calculating ES are (a) central tendency, (b) pre-post contrast, (c) group contrast, and (d) association between variables.

1.5 Introduction to fixed effect versus random effect models

The major task of many meta-analyses is to forecast how far the effect size varies from each other through the values of moderating variables. The two most ordinary categories of theoretical models in meta-analysis are fixed effect and random effect models depending on the magnitude of heterogeneity in the studies. For the fixed effects methods, we say the population is homogeneous. In this case, the estimated effect sizes are fixed. On the other hand, random effects methods with the heterogeneous population vary within studies and between studies.

The fixed-effect models estimate a common population parameter generated by every effect size from the individual studies. This can be interpreted as a constant

effect size will occur throughout the studies, except for the differences from observations due to sampling error.

The meta-analysts are allowed to place the confidence interval around the estimated population mean effect size both in fixed-effect and random-effect analyses. The confidence interval for the random effect model will be wider than the ones for the fixed effect model, given a set of effect sizes (Lipsey & Wilson, 2001). The fixed-effect analysis is selected despite the random effect case is more suitable to be used as its computation is not so complicated. Decision making on either select fixed-effects models or random-effects models is the main concern when drawing a conclusion from the findings (National Research Council, 1992). Lately, there is a suggestion that the assumptions made by random-effects models are more rational, in general, than those made by fixed-effects models (Hunter & Schmidt, 2000).

The random-effect model assumes that there is variation in population effect size rather than it is a constant. It assumes a random sampling from a multiple population. In fact the random sampling is assumed from a single population for a fixed-effect model. As a result, some of the parameter estimates will vary from the others.

1.6 Objective

To determine methods of finding effect sizes in meta-analysis.

1.7 Format of dissertation

This thesis is divided into five chapters. Chapter 1 is gives the introduction on meta-analysis, a brief discussion about the contemporary development of meta-analysis in different research of studies, objective as well as the format of the

dissertation. Chapter 2 focuses on the literature review that is related to meta-analysis. It commences with an introduction to meta-analysis. The origin of meta-analysis since 1904 until the current development of meta-analysis in various fields of studies will be included. Moreover, a brief discussion on effect size estimates, and meta-analysis methods for different research of studies are reviewed.

Chapter 3 presents the methodology. The methods of finding effect size estimate in different circumstances are introduced. A brief discussion on the measurement of clinical intervention is given.

Chapter 4 includes a case study with a set of secondary data set from clinical trials. Comprehensive Meta-Analysis (CMA) 2.0 statistical software is used to analyze the data. This chapter will emphasize on the usage of CMA in conducting meta-analysis. The outcomes of the data will be evaluated and interpreted.

Conclusion and further research relevant to the meta-analysis will be discussed in Chapter 5. The main contributions as well as the limitation of the findings are included.