University of Southern Queensland

Statistical Methodology for Ordinal Data in Meta-Analysis

A Dissertation submitted by
Md. Belal Hossain
B.Sc.(Hons), M.Sc.

For the degree of
Doctor of Philosophy

2011
Abstract

Meta-analysis combines results from several independent studies. Different methods are available to carry out meta-analyses for binary and continuous outcomes. The effect measures used for binary outcomes are odds ratio (OR), relative risk (RR), risk difference (RD), arcsine difference (AS), hazard ratio (HR) etc. For continuous outcomes mean difference (MD) and standardised mean difference (SMD) are used in meta-analysis. However, there are many medical and health studies in which the outcome variables are measured on an ordinal categorical scale with more than two categories. These categories are non-numerically valued, usually levels. In a typical ordinal categorical data there may be $L$ categories $C_1, C_2, \ldots, C_L$ ($C_1$ is the best and $C_L$ the worst or vice versa) and $J$ comparison groups $G_1, G_2, \ldots, G_J$. Hence the count data for such studies are represented by a $J \times L$ contingency table. As a special case when there are two comparison groups in randomised controlled trials (RCTs), we set a $2 \times L$ contingency table. As a result, the ordinary OR, log OR or RR can not be used directly without splitting the $2 \times L$ ($L > 2$) contingency table into $2 \times 2$ tables.

Among other effect measures for ordinal data there are local and global odds ratios (Dale, 1984), cumulative odds ratios, continuation odds ratio (Agresti, 2010) etc. The local odds ratio measures local association for a specific outcome category not for the whole study. The global odds ratio is
a measure of ratios of the quadrant probabilities \((J = L \geq 4)\). Whereas in RCTs there are only two comparison groups \((J = 2)\) namely the treatment and control groups. The cumulative odds ratios provide a comparison of pairs of levels of the explanatory variable with respect to their entire conditional distribution of the dependent variable. As a result, these measures are not appropriate in meta-analysis with RCTs.

The data from studies with several ordered categories are analysed by various methods in meta-analysis. Some methods require specific model assumptions while others collapse the \(2 \times L\) \((L > 2)\) contingency table into \(2 \times 2\) tables for measuring the effect size. For example, the proportional odds model (Whitehead et al., 2001) requires a proportionality assumption and there is no well defined variance estimate of the pooled estimator for the sample size weight method (Edwardes and Baltzan, 2000) that uses general odds ratio \((OR_G)\) as an effect measure.

Therefore we need a method in meta-analysis that can be used for estimating the effect size without any loss of information by merging categories and is not restricted to any model assumptions.

We propose generalised odds ratio (GOR) as an effect measure for ordinal categorical outcomes in meta-analysis (Agresti, 1980). For confidence intervals (CI) of the individual study effects and meta-analysis we employ independent multinomial distribution approach. A general fixed and a random effects models are developed using GOR in meta-analysis for ordinal categorical outcomes.

Heterogeneity is one of the most problematic aspects in many meta-analyses. We have demonstrated a method to remedy the problem of heterogeneity in meta-analysis for ordinal data. Following Saleh (2006) a quasi-empirical Bayes method (QEBM) is developed using predicted generalised
odds ratio (PGOR) for heterogeneous ordinal categorical outcomes. This method identifies the extreme studies and improves the meta-analysis in the presence of heterogeneity. Three different meta-analyses on several studies with different degree of heterogeneity are presented. The first example is of individual patients data (IPD) on tacrine trials with Alzheimer’s disease, the second example is of misoprostol trials with insignificant heterogeneity and the third example is from simulation studies with significant heterogeneity. The three examples clearly illustrate detailed implementation process and usefulness of the proposed method.

We apply and compare GOR with OR as an effect measure for binary outcomes in meta-analysis. Three alternative methods for combining results from binary outcomes are presented for meta-analysis. The first method is a sample size weight method (Edwardes and Baltzan, 2000) for binary outcomes using OR_G. The other two methods employ GOR as an effect measure for binary outcomes in meta-analysis. We present results by analysing six RCTs from meta-analysis of D1 versus D2 gastrectomy for gastric adenocarcinoma (Memon et al., 2011).

This study also proposes GOR as an effect measure and presents method in meta-analysis for latent continuous outcomes. GOR is simple and it has straightforward interpretation. It can be used for more than two treatment groups as well. Hence GOR is a very useful effect measure in meta-analysis not only for multilevel ordinal categorical outcomes but also for binary and latent continuous outcomes.
Certification of Dissertation

I certify that the ideas, experimental work, results, analyses, software and conclusions reported in this dissertation are entirely my own effort, except otherwise acknowledged. I also certify that the work is original and has not been previously submitted for any other award, except where otherwise acknowledged.

........................................
Signature of Candidate
Date

ENDORSEMENT

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Signature of Supervisor
Date
Acknowledgements

First of all I express my sincere gratitude to Almighty for the completion of this thesis.

I sincerely thank my reverend principal supervisor, Dr Shahjahan Khan, for introducing the research topic, well structured direction, and continuous encouragement to work on this research project. This thesis would not have been completed without his expert guidance, generous support, flexible working time for me and motivation. I thank him for his academic support, arranging financial assistance and providing collaboration opportunities with his research associates in Queensland Health. I am highly benefitted from his excellent professional leadership in enriching my academic experience and collaboration. I also thank his family for kind support from the very beginning in my stay in Australia.

I would like to thank my co-supervisor, Dr Muhammed Ashraf Memon for his invaluable comments and suggestions on this thesis and other projects we worked together.

Special thanks to the University of Southern Queensland and University of Dhaka, Bangladesh for supporting my PhD study, Dept. of Maths & Computing for providing opportunities to work as a tutor/marker, and Australian Centre for Sustainable Catchments (ACSC) for sponsoring my conference travels.
I would like to thank Dr Richard Watson and Dr Stijn Dekeyser, the Heads of Department of Mathematics & Computing, University of Southern Queensland, for offering me teaching related contracts. Those really helped me to enrich my academic career. I also thank Dr Ashley Plank, Ms Christine McDonald and Ms Taryn Swan for welcoming me as a team member of the statistics group. It was a pleasure working with the Data Analysis teaching team and a huge number of students and sharing ideas on social forum. Do you know ‘How many eggs there should be in the hearty breakfast when you finish the exams?’ I do.

My sincere thanks go to the administrative staff of the Department of Maths & Computing, especially Helen Nkansah and Kris Lyon, the Office of the Research and Higher Degrees, the Faculty of Sciences, the Library, the ICT services for quick technical and administrative assistances.

Finally, big applause to my family members who sat me free for three years and took all the responsibilities on themselves to enable me to complete this thesis. Thank you perhaps have no use to them but thank you any way.

Last but not the least, I express my gratitude to my colleagues in University of Dhaka.
## List of Abbreviations

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<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>CI</td>
<td>confidence interval</td>
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<tr>
<td>df</td>
<td>degrees of freedom</td>
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<td>GOR</td>
<td>generalised odds ratio</td>
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<td>LOR</td>
<td>log odds ratio</td>
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<td>MLE</td>
<td>maximum likelihood estimator</td>
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<tr>
<td>OR</td>
<td>odds ratio</td>
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<td>ORG</td>
<td>general odds ratio</td>
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<td>PGOR</td>
<td>predicted generalised odds ratio</td>
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<td>PTE</td>
<td>preliminary test estimator</td>
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<tr>
<td>QEBM</td>
<td>quasi-empirical Bayes method</td>
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<td>RCTs</td>
<td>randomised controlled trials</td>
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<td>RR</td>
<td>relative risk</td>
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