University of Southern Queensland

Statistical Methodology for Ordinal Data in Meta-Analysis

A Dissertation submitted by

Md. Belal Hossain

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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 2×2 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 2×2 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 ($\mathrm{OR_G}$) 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.

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Signature of Candidate Date

ENDORSEMENT

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Signature of Supervisor Date

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List of Abbreviations

CI	confidence interval
df	degrees of freedom
GOR	generalised odds ratio
LOR	log odds ratio
MLE	maximum likelihood estimator
OR	odds ratio
OR_G	general odds ratio
PGOR	predicted generalised odds ratio
PTE	preliminary test estimator
QEBM	quasi-empirical Bayes method
RCTs	randomised controlled trials
RR	relative risk

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