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Technical Review
Number 8

Meta-regression Approaches: What, Why, When, and How?

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No. 290-97-0001

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AHRQ Publication No. 04-0033
March 2004

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Suggested Citation:

Morton SC, Adams JL, Suttorp MJ, Shekelle PG. Meta-regression Approaches: What, Why, When, and How? Technical Review 8 (Prepared by Southern California–RAND Evidence-based Practice Center, under Contract No 290-97-0001). AHRQ Publication No. 04-0033. Rockville, MD: Agency for Healthcare Research and Quality. March 2004.

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. This report on *Meta-regression Approaches: What, Why, When and How?* was requested and funded by the National Center for Complementary and Alternative Medicine. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this technical review. They may be sent to: Director, Center for Outcomes and Evidence, Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850.

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The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services of a particular drug, device, test, treatment, or other clinical service.

Acknowledgments

We gratefully acknowledge the participation and constructive feedback provided by these expert panelists:

- Dr. Jesse Berlin, University of Pennsylvania School of Medicine
- Dr. William DuMouchel, AT&T Research
- Dr. Vic Hasselblad, Duke Clinical Research Institute
- Dr. Joseph Lau, Division of Clinical Care Research, New England Medical Center
- Dr. Thomas Louis, RAND, Washington, DC
- Dr. Martin McIntosh, Biostatistics Department, University of Washington and Fred Hutchinson Cancer Research Center
- Dr. Ingram Olkin, Department of Statistics, Stanford University
- Dr. Allan Sampson, Department of Statistics, University of Pittsburgh
- Dr. Chris Schmid, Tufts University School of Medicine, New England Medical Center

Dr. Jesse Berlin from the University of Pennsylvania School of Medicine and Dr. Thomas Louis from RAND (now at Johns Hopkins) reviewed the draft report. In addition, Southern California EPC staff not on the study team also reviewed the draft report. We gratefully acknowledge the assistance of these referees.

***Note**: Acknowledgments are made with the explicit statement that this does not constitute endorsement of the report.*

Structured Abstract

Objective. The broad objective of this report is to compare and contrast via simulation five meta-regression approaches that model the heterogeneity among study treatment effects: fixed effects with and without covariates; random effects with and without covariates; and control rate meta-regression.

Methodology. We conducted a systematic review of MEDLINE®, HealthSTAR, EMBASE, MANTIS, SciSearch®, Social SciSearch®, Allied and Complementary Medicine, the Current Index to Statistics, and the Methodology Register of the Cochrane Library from the inception of each database through March 2001 using the search terms "metaregress-" or "meta" within two words of "regress-." We supplemented these searches with articles identified by experts, and by searching the reference lists of all relevant articles found. We constructed a statistical notation generally applicable to different meta-regression methods. We convened a one-day panel of nine experts, and elicited their recommendations for the practice of meta-regression and implementation of our simulation study. We implemented a large-scale simulation to compare and contrast the five meta-regression techniques.

Main Results. We identified and categorized 85 publications on meta-regression. We presented scenarios for which meta-regression might be informative, and expressed the most common meta-regression models in a common notation. Our expert panel made several recommendations regarding the simulation parameters. The panel also identified the need for outreach by the methodological community to the user community in advising how to conduct, interpret, and present meta-regression analyses, including the development of software and diagnostic aids to assess models.

The simulation was a complete factorial design including all possible 7,776 combinations of the simulation parameters. The results were evaluated using an analysis-of-variance (ANOVA) model relating the simulation parameters to the bias in the estimation of the additive treatment effect. Across the five different meta-regression methods, six terms in a three-way ANOVA model were found to be practically important as they captured contributions to the bias of 10% or greater on average.

Conclusions. Our simulation results produced specific guidelines for meta-regression practitioners that may be summarized in the key message that the causes of heterogeneity should be explored via the inclusion of covariates at both the person level and study level. Based on our comparison of bias across approaches, either fixed effects or random effects methods can be used to support this exploration. In terms of future simulation research, we need to increase the variability in sample sizes, explore correlations between study outcome rates and covariates at both the study and person level, and evaluate within-study variation for person-level covariate(s). We now have in place a simulation methodology, a common notation, and a supportive panel of national experts to enable and guide our continued work in this area. The research presented in this report has already impacted the application of meta-regression in several alternative medicine settings, and improved our ability to synthesize and understand these therapies.

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Appendixes for this report are provided electronically at http://www.ahrq.gov/clinic/epcindex.htm. Scroll through the topic list to select this report.