Automated Meta-Analysis in Medical Research: A Causal Learning Perspective

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Background and Motivation
- Meta-analysis is a systematic approach for obtaining a summary result by analyzing previously published experimental studies
- Conventional meta-analysis is extremely inefficient and vulnerable to human bias
- Recent advances in NLP have sought to automate the initial steps to detect potential biases (predefined by the Cochrane risk of bias tool) and outcome (therapeutic association) from scientific publications
- Causal inference seeks to understand the causal relationship between risks of bias and the outcome
- The task of inferring summary therapeutic association is reduced to an interventional question: What will the therapeutic association be if no risk of biases are observed in the studies?

Problem Definition
- Given the Cochrane risks of bias \( A \in \{0,1\}^D \) and the therapeutic association \( Y \in \{0,1,2\} \) extracted by NLP systems from individual RCTs
  - 0/1 in \( A \) denotes low/high risk of bias in a domain
  - 0/1/2 in \( Y \) denotes negative, no, and positive therapeutic association
- The goal of automated meta-analysis is to infer the summary therapeutic association between a treatment (a drug) and the outcome (a disease) given \( A \) and \( Y \)

Multiple Causal Inference for Automated Meta-Analysis (MCMA)

1. Research Challenges:
   - Out-of-Sample Distribution. No access to RCTs where there is no risks of bias in the training data
   - Unmeasured Factors. Unmeasured factors can lead to conflicting therapeutic associations observed in different RCTs, e.g., bias from domain expertise
   - Uncertainty in NLP Systems. NLP systems can make mistakes, especially when they are applied to data collected from specialized domains

2. Causal Assumptions:
   - Stable Unit Treatment Value Assumption (SUTVA)
   - Positivity
   - No unobserved single-cause confounders

3. Inference Algorithm:

Experiments
Empirical evaluation for automated meta-analysis on real-world data is extremely challenging. We verify our methods on both synthetic and semi-synthetic data.

1. Synthetic Experiments:
   - With embedded causal knowledge, MCMA does not hurt the performance on predicting individual therapeutic associations potentially influenced by risks of bias and hidden confounders
   - Prediction performance of both standard classifiers and MCMA tend to degrade as we introduce more confounding noise

2. Semi-Synthetic Experiments:
   - We collected scientific papers on meta-analysis from PubMed and Cochrane Library databases
   - We used statistics from real-world RCTs to parameterize the simulation to augment data
   - We obtained results similar to those from synthetic experiments

This work was conducted under the auspices of the IBM Science for Social Good initiative.