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 $\boldsymbol{A} \in \{0,1\}^D$ and the therapeutic association $Y \in \{0,1,2\}$ extracted by NLP systems from individual RCTs
  - $0/1$ in $\boldsymbol{A}$ 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 $\boldsymbol{A}$ and Y

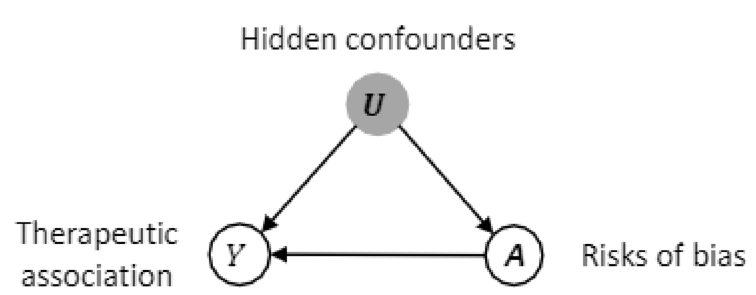
Multiple Causal Inference for Automated Meta-Analysis (MCMA)

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:

Substitute Confounder Inference → Fit a latent variable model, e.g., Probabilistic PCA

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Predictive Check → Check the performance of the latent-variable model

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Causal Effect Estimation → Augment data with inferred hidden confounder $\boldsymbol{z}$ and fit the outcome model

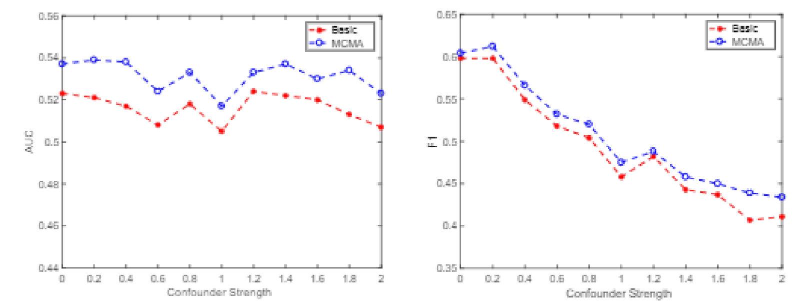
$$f(\boldsymbol{a}, \boldsymbol{z}) = \beta^T \boldsymbol{a} \pm \gamma^T \boldsymbol{z}$$

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



(a) AUC score. (b) F1 score.

- MCMA outperforms Basic multi-class classifiers on predicting *summary* therapeutic association, corroborating its effectiveness

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.

ACM CHIL Workshop 2021