Interactive Visual Exploration of Pairwise Meta-Analysis Results

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Figure 1: The screenshot of our system that shows: (a) a filter panel showing the options for scenario customization; (b) an outcome list displays the available safety outcomes and the number of records in each grade according to the scenario specified in the filter panel; and (c) a result panel showing the forest plots of the pairwise meta-analysis result.

ABSTRACT

Pairwise Meta-analysis (PMA) is a widely used tool for evidence synthesizing in clinical research and practice. However, it's challenging to explore the PMA results for clinicians and researchers as complexity of clinical questions increase involving a huge number of studies and outcomes. Thus, we propose an interactive web-based visual analytics system to support users on the PMA result exploration and analysis.

Index Terms: Applied computing - Life and medical sciences -Health informatics; Human-centered computing - Visualization

1 INTRODUCTION

Cancer is a significant health problem, and its treatment can lead to physical and psychological issues which affect a patient's quality of life directly. A comprehensive summary of the benefit and harm outcomes of the treatment plan will not only help researchers improve drug development, but also help clinicians make clinical decisions for patient care [1]. Clinical decision making requires clinicians and patients to discuss data about potentials benefits and harms using totality of existing evidence. Therefore, to summarize

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the findings and synthesize evidence for important clinical questions, pairwise meta-analyses (PMAs) are used to get precise estimates of treatment effects.

However, presenting the results from meta-analysis when there are many outcomes synthesized from massive clinical datasets is challenging [2]. For example, we conducted a systematic review and meta-analysis involving more than 150 studies synthesizing evidence for more than 300 outcomes across more than a dozen cancer types (Fig. 1). It is difficult to present the PMA result in an easy-to-use way to facilitate further exploration and usage.

To address this limitation, we propose a visual analytics system to facilitate the PMA result exploration. Using this system, clinicians and patients can visualize the relevant data for shared decision making. Our main contribution is the design and implementation of an interactive visual analytic system for exploring results in an ongoing PMA project.

2 TASK ANALYSIS AND DESIGN REQUIREMENTS

Our design process began with a series of informal discussions and interviews with the domain experts on PMA at Mayo Clinic. Two of the authors are our internal collaborators with rich experience in PMAs. The other three collaborators are likewise engaged in a variety of PMAs. Due to the complexity of the PMA needs from the clinical question, we built a prototype system to validate the concepts and collect feedbacks based on an ongoing PMA project "Toxicity of Immune Checkpoint Inhibitor". With the initial task analysis and feedbacks on the prototype system, we identified the following domain goals for end-users when exploring safety outcomes as the initial step to start our visual design.

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Figure 2: The architecture of our proposed system

T.1 How to best present safety and toxicity results for a given outcome from a particular drug? To decide whether a treatment is efficacious and safe, a PMA is conducted to synthesize the evidence for each clinical outcome. Some of the outcomes are more important than others in different clinical scenarios, hence each outcome must be presented individually to meet the clinical needs of different users.

T.2 How to best summarize the evidence across a range of outcomes to assess the overall performance of a drug? There are usually many safety outcomes related to a treatment plan, and the information about all safety outcomes is concerned for treatment decisions. Thus, the results should be summarized in a unified view for shared decision making between patients and clinicians. Thus, dynamic presentation is necessary to accommodate the presentation of complex analyses in a user-friendly manner.

Based on these two tasks described above, we identified the following design requirements.

R.1 Interactive exploration. The system needs to provide flexible options to help users customize the scenario and conduct PMA (T.1 and T.2). At the same time, due to the inter-connections between scenarios, study attributes, safety outcomes, and PMA parameters, the system should be able to correlate these elements automatically to support interactive exploration of PMA results.

R.2 Exploration of different settings. Clinicians would like to know how the PMA result changes according to different variables (T.1). The system needs to be able to support dynamic selection and display the corresponding results.

3 SYSTEM OVERVIEW

As shown in Fig. 2, our proposed system's architecture consists of three major modules: the data pipeline, the PMA service, and the visualization frontend.

Once new studies are available, the data pipeline will collect the meta data from PubMed, Ovid, and ClinicalTrials.gov. The raw data will be processed, and the outcomes will be extracted, then saved into a central database.

To conduct PMA, we use R packages (meta and dmetar) as the backend and use Python packages (pandas and rpy2) to converts the input (e.g., the outcome records extracted from studies) into predefined format dataset to meet the requirements of those R packages. To support flexible analysis, we wrappers the PMA backend as a web service to serve instant analysis requests (R.2).

The visualization frontend provides users with coordinated interactive views to support PMA result exploration and real-time PMA on customized scenario. The visualization frontend is built on D3.js, AlaSQL.js, and Vue.js.

4 VISUALIZATION AND INTERACTIVE DESIGNS

Our system provides multiple linked views to support the PMA result exploration. The interface shows a filter panel (Fig. 1(a)), an outcome list (Fig. 1(b)) and a PMA result panel (Fig. 1(c)).

The filter panel is a dynamic form providing the coordinated options for users to decide clinical scenario for analysis (R.1). Once

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Decreas	ed appetite	93	84 -		OR 0.85			
🗅 Dehydra	tion	14	6 2	Weight loss	(0.51 to 1.44)	41 per 1000	48 per 1000	7 less per 1000
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Figure 3: The screenshot of our system in the comparison mode shows: (a) outcome list in a multi-selection mode; and (b) the outcome table containing the selected outcomes

the scenario is decided, the filter options are converted into a query for filtering studies, and the outcome list is updated according to the filtered studies (Fig. 1(b)).

The outcome list is a tree-like table, in which each row indicates a safety outcome. The three cells after outcome name represents its three levels. When clicking the cell, a PMA request will be sent to the PMA service. Once the PMA result returns, the result panel will be updated and show the forest plots (Fig. 1(c)).

In addition, the outcome list could be set to comparison mode to support multi-selection of outcomes. As shown in Fig. 3, users could select multiple outcomes and categorized them by grade into a table for comparison. The outcome name and result detail are clickable to show more options for further exploration (R.1).

5 DISCUSSION

To adequately test the efficacy of our system, we iteratively designed and developed the system with weekly feedback from our domain experts. The designs are tested on an ongoing PMA project of "Toxicity of Immune Checkpoint Inhibitor" during the development. At present, we did not carry out formal user tests since it is still in an early stage. Our domain experts appreciated the interactive designs and were able to effectively use the system to explore the PMA results. In addition, they commented that the PMA results could be further used in shared clinical decision making, which is helpful for clinical practice.

6 CONCLUSION AND FUTURE WORKS

In this work, we present a visual analytics system which tightly integrates the PMA and information visualization techniques to support clinicians and researchers. Since our system is still in early stage, and there could be more visual designs and features to support further exploration, we will keep developing the features and the visual design for further exploration of the PMA results. Our work has the potential to transform how synthesized evidence is presented to patients for shared decisions making and to guideline developers and policy makers.

REFERENCES

- J. H. Elliott *et al.*, "Living systematic review: 1. Introduction—the why, what, when, and how," *Journal of Clinical Epidemiology*, vol. 91, pp. 23–30, Nov. 2017
- [2] R. van de Schoot *et al.*, "An open-source machine learning framework for efficient and transparent systematic reviews," *Nature Machine Intelligence*, vol. 3, no. 2, Art. no. 2, Feb. 2021