Visual Exploration of the Pairwise Meta-analysis of Toxicity of Immune Checkpoint Inhibitors

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Abstract

Clinicians often struggle to translate the evidence synthesized by meta-analysis to care of their patients. An interactive and clinically meaningful presentation of results from a pairwise meta-analysis (PWMA) can immensely facilitate the interpretation of evidence in research and clinical practice. Therefore, we proposed a web-based interactive tool that allows clinicians to access the toxicity profiles of immune checkpoint inhibitors in cancer patients tailored to a specific clinical encounter.

Introduction and Background

Systematic reviews and meta-analyses (SRMAs) are widely used to summarize estimates of treatment effects by pooling evidence from randomized controlled trials[1]. Often, even with high-quality SRMAs, there is a translation gap, as clinicians cannot take the published evidence and apply it directly to clinical practice. For example, often clinicians are interested in identifying the toxicity of immune checkpoint inhibitors (ICIs) for a specific clinical setting. However, the published analyses are too narrow or too broad for the specific clinical question. Further, with the rapid influx of evidence, the data is outdated soon after publication.

While several applications are available for managing systematic reviews (Covidence, DistillerSR, RevMan) and conducting meta-analyses (STATA, SAS, JASP, Excel, and OpenMetaAnalysis), these are restricted to personal, local use and cannot be directly employed for online, interactive exploration of the results. Hence, to address these limitations, we propose a serverless real-time web-based interactive tool to provide an interactive and dynamic assessment of toxicity profiles of immune checkpoint inhibitors in cancer patients.

Here, we demonstrate the feasibility of our web-based interactive tool presenting the data from a living meta-analysis of immune checkpoint inhibitors for the treatment of cancer patients. This tool allows visualization of data from a living meta-analysis of more than 150 clinical trials evaluating ICI agents across several different cancer types reporting approximately 300 different adverse events. The goal of this tool is to provide the most up-to-date evidence to clinicians and patients for shared decision-making in a user-friendly manner at the point of care.

Methods

As shown in Figure 1a, the user interface (UI) and core modules are built on frontend JavaScript libraries (e.g., Vue.js, D3.js, AlaSQL, etc.), which operates in a web browser runtime. All the data used for PWMA are loaded into an in-browser database to prevent network transmission upon filter selections in the UI. We developed a lightweight JavaScript PWMA module that can run in the user's local web browser, which is optimized for specific real-time PWMA tasks, such as the fixed effect meta-analysis with treatment-effects expressed as odds ratio. In addition, we adopted a serverless architecture to design the system, which removes the need for a traditional always-on server[3]. As no server is involved, no time is spent on data transfer between the browser and server, and the user interface can get instant PWMA results for visualization.

Following the agile software development process and Munzner nested model[4], we summarized the task requirements and design rationales by interviewing domain experts to guide the development. **Figure 1b** shows a screenshot of our proposed system which consists of a range of filters for clinically relevant comparisons. The system consists of multiple panels, including (A) a list of adverse events (**Figure 1-b1**), (B) a comparison view (**Figure 1-b2**) outlining the details of selected adverse events, and finally (C) a forest plot (**Figure 1-b3**), which presents the summary effect estimate and dispersion across studies for a specific adverse event of interest. The selection of adverse events can be dynamically updated using the list of adverse events (**Figure 1-b1**). The system also provides the flexibility to select multiple adverse events simultaneously, using same or different sets of filters and measures of effect which users can utilize for a dynamic assessment of toxicity.

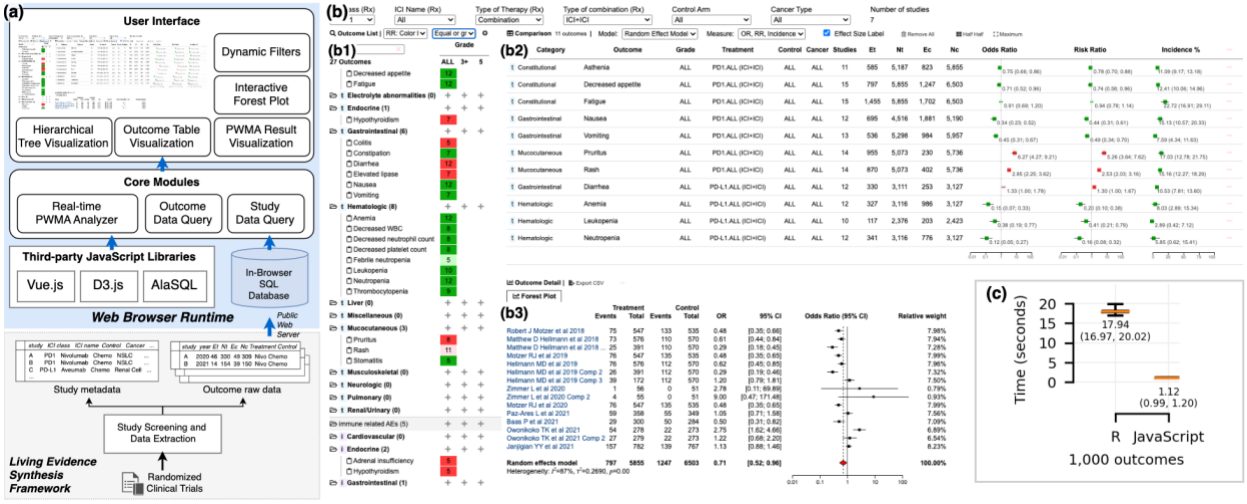

Figure 1. (a) The serverless architecture of our proposed tool. All calculation and visualization functions are implemented in the web browser's runtime, removing the need for an always-on server. (b) The screenshot of the user interface of our proposed tool includes (b1) an adverse event list showing the estimated effects of categorized adverse events, (b2) a comparison view showing the detailed PWMA results of the selected adverse events, and (b3) a forest plot showing the pooled effect and spread of the studies included in a specific adverse event. (c) Comparing the time cost of PWMA calculation of 1,000 outcomes in R and JavaScript.

Results

We conducted a preliminary experiment by randomly sampling 1000 adverse events from the living meta-analysis and estimating the summary effect using the fixed-effects model. The forest plot generated (Figure 1c) visually represents the summary odds ratios for selected adverse events and their corresponding confidence intervals. We found that the JavaScript-based PWMA module performed significantly faster than the conventional R-based module, achieving near-instantaneous results. This rapid processing enabled real-time exploration and immediate feedback for each clinical query, demonstrating the system's potential to handle large-scale data in real-time.

We also conducted a pilot usability test with a small group of clinicians and methodologists specializing in oncology and evidence-based medicine. Participants particularly appreciated the system's capacity to handle multiple comparisons and its user-friendly interface, which allowed them to quickly filter and interpret data from numerous clinical trials. The tool's real-time feedback on various toxicity outcomes, combined with its intuitive layout, enabled them to form evidence-based conclusions about the relative safety profiles of ICIs in different clinical contexts. While the results of the preliminary usability test were promising, formal and systematic testing involving a larger group of users is still needed. Such tests would focus on evaluating both the effectiveness and efficiency of the tool in clinical practice.

Discussion and Planned work

At present, our tool can visualize more than 300 adverse events related to immune checkpoint inhibitors in patients with cancer at a single interactive interface. Our domain experts suggested that it would be helpful to summarize similar information in a companion summary of findings table that includes certainty of evidence assessment. In addition, they suggested emphasizing the adverse events more frequently reported than the others and adding more filters to reduce the number of adverse events in the list. In the future, we envision adding more interactive designs to provide an in-depth exploration of the adverse events of immune checkpoint inhibitors and build more meta-analysis functions in JavaScript to support more PWMA of multiple clinical outcomes.

References

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