Searching Clinical Trial Registries in Systematic Literature Reviews (SLR): Which and Why?

MSR231

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Background

- The systematic literature review (SLR) process requires comprehensive searches of published and grey literature. Grey literature refers to information from other sources that are not commercially published in peer-reviewed journals, such as conference proceedings, dissertations, government publications, and policy papers.[1]
- Trial registries such as ClinicalTrials.gov (CTG), the World Health Organization-International Clinical Trials Registry Platform (WHO-ICTRP), and the European Union Drug Regulating Authorities Clinical Trials Database (EudraCT) are widely used as sources of grey literature for SLRs. These registries record a range of interventional study data, including those that may not have been published in peer-reviewed journals. Searching such registries during the SLR process aligns with recommendations from the Cochrane Handbook for Systematic Reviews of Interventions version 6.5.[2]
- Clinical trials in the US are usually registered in CTG, and those in Europe in EudraCT. Drivers for registering studies specifically in the International Standard Randomised Controlled Trial Number (ISRCTN) registry are less obvious, inviting questions about whether, or to what extent, it could be a unique additional source of grey literature.

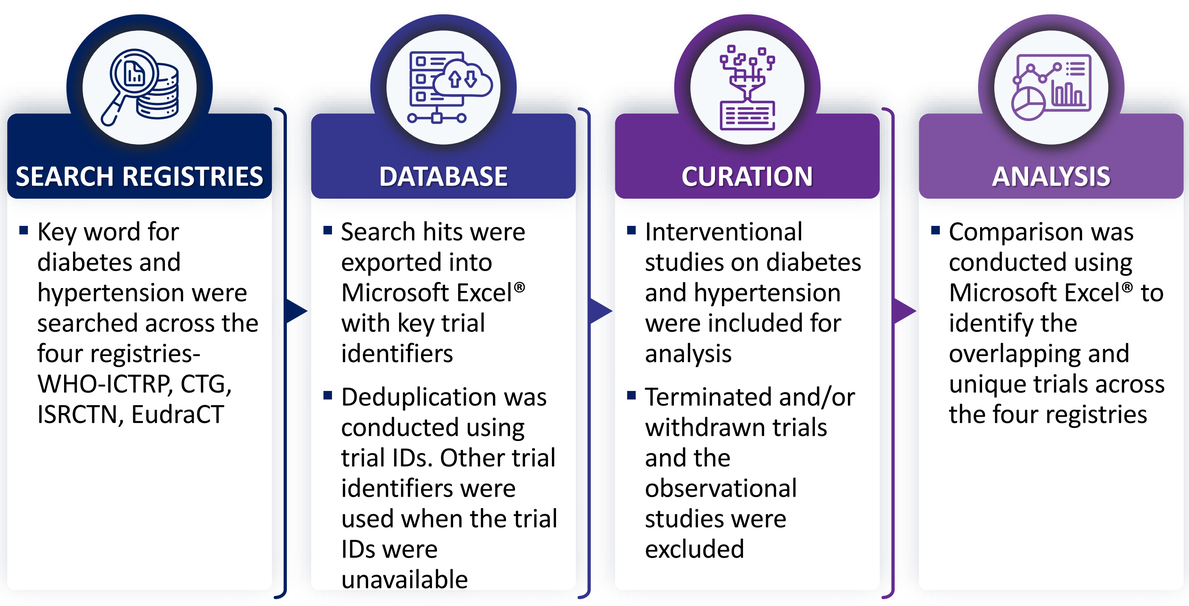
Objectives

- The objective of this comparative analysis was to examine the overlap of identified clinical trials across four clinical trial registries—CTG, WHO-ICTRP, EudraCT, and ISRCTN—focusing specifically on two primary disease areas: diabetes and hypertension. Diabetes and hypertension were chosen because of the large numbers of registered trials relating to these conditions. We also aimed to evaluate the degree of uniqueness with ISRCTN to determine its potential as a source of grey literature for SLRs.

Methods

- Targeted searches were conducted using keywords “diabetes,” “diabetes mellitus,” and “hypertension” across CTG, WHO-ICTRP, EudraCT, and ISRCTN. The searches for diabetes and hypertension were conducted in June 2024 and October 2024, respectively.
- Search results were exported to Microsoft Excel® and contained the following trial identifiers (when available): National Clinical Trial Number; Study Title; Study URL; Study Status; Brief Summary; Conditions; Interventions; Sponsor; Collaborators; Phases; Study Type; Study Design; Other Identifiers (IDs); Start Date; Primary Completion Date; Completion Date; and Locations.
- Only interventional studies that specifically targeted hypertension or diabetes were included in the analysis. Trials related to complications of hypertension, comorbidities, or other associated conditions were excluded. Additionally, observational and non-interventional studies, as well as trials with a “terminated” or “withdrawn” status, were removed from the analysis.
- Duplicate entries within each trial registry were identified and removed using trial IDs (where available) or study titles and secondary identifiers.
- A comparison analysis was performed using primary trial IDs, titles, and secondary IDs in Microsoft Excel® to identify overlapping trials across the four registries and the unique number of trials found in ISRCTN in comparison with the other registries.

Figure 1. Study Methodology



Abbreviations: CTG = ClinicalTrials.gov; EudraCT = European Union Drug Regulating Authorities Clinical Trials Database; ID = identifier; ISRCTN = International Standard Randomised Controlled Trial Number; WHO-ICTRP = the World Health Organization-International Clinical Trials Registry Platform

Results

- After deduplication and curation of the search results, the total number of trials on diabetes included for the comparison analysis was 21,623 from WHO-ICTRP, 12,437 from CTG, 1,414 from EudraCT, and 938 from ISRCTN. The total for hypertension was 10,595 from WHO-ICTRP, 4,554 from CTG, 711 from EudraCT, and 226 from ISRCTN.
- For diabetes, WHO-ICTRP included 100% of trials registered in CTG, 84% of those in EudraCT, and 86% of those in ISRCTN. A comparison of CTG with other registries showed minimal overlap: 6% with ISRCTN and <1% with EudraCT. Also, only 1.8% of trials from ISRCTN overlapped with the EudraCT-registered trials.
- For hypertension, WHO-ICTRP included 99.3% of trials registered in CTG, 86% of those in EudraCT, and 100% of those in ISRCTN. In comparison, CTG included 4% of the trials registered in ISRCTN and 2% of those in EudraCT. Also, only 6% of the trials in ISRCTN were also registered in EudraCT.
- Of the diabetes trials collectively registered across the four registries, 106 were listed only in ISRCTN. For hypertension, ISRCTN included 204 trials not registered in CTG or EudraCT.

Table 1. Overlap between trial registries

DIABETES				HYPERTENSION			
WHO-ICTRP (N=21623)				**WHO-ICTRP (N=10595)**			
100%	**CTG (N=12437)**			99.3%	**CTG (N=4554)**		
84%	<1%	**EudraCT (N=1414)**		86%	2%	**EudraCT (N=711)**	
86%	6%	1.8%	**ISRCTN (N=938)**	100%	4%	6%	**ISRCTN (N=226)**

For each comparison, the lower-positioned trial registry provides the denominator for the cited % e.g. “For diabetes, WHO-ICTRP identified 100% of the trials registered in CTG.”

Abbreviations: CTG = ClinicalTrials.gov; EudraCT = European Union Drug Regulating Authorities Clinical Trials Database; ISRCTN = International Standard Randomised Controlled Trial Number; WHO-ICTRP = the World Health Organization-International Clinical Trials Registry Platform

Limitations

- The analysis focused solely on diabetes and hypertension, which could limit the generalizability of the findings to other diseases.
- Differences in the representation of registry data and the frequency of status updates may impact the accuracy of comparisons. Generally, the variations in data formats, terminology, or categorization methods may lead to misunderstandings or misinterpretations when analyzing the information.

Conclusions

- While CTG, WHO-ICTRP, and EudraCT are key grey literature sources for SLRs to identify clinical trials, our findings suggest that ISRCTN provides significant, unique trial-related information inclusion, which could enhance overall completeness of related SLRs.
- Future research examining the specific value that ISRCTN contributes to the evidence base for common and rare diseases could offer significant advantages to researchers.

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Disclosures

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