

Systematic inclusion of clinical trial information as informative priors for quantitative safety signal detection in spontaneous reporting systems



Integrating clinical trial information marginally but consistently improved performance, which can reduce review burden. Further gains may be possible by refining the methodology, especially the mapping of unstructured product information between the two data sources

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Background

- Quantitative signal detection in post-marketing spontaneous reporting systems (SRSs) is crucial for drug safety surveillance. However, traditional disproportionality analyses do not include safety insights from clinical trials (CTs).¹
- While ClinicalTrials.gov is the largest public registry of CTs, its safety data consists of non-standardized, investigator-reported text that complicates systematic analysis. The recent ClinicalTrials.gov Transformation Database pipeline² transforms this raw data by aligning adverse events (AEs) to the standard MedDRA terminology. This crucial step allows CT safety insights to be systematically integrated into post-marketing surveillance.
- This study proposes a Bayesian dynamic borrowing approach that integrates CT data using a robustified meta-analytic predictive (MAP) prior within a Bayesian hierarchical model, aiming to enhance AE signal detection in SRSs.

Aim



To evaluate the impact of integrating summary CT data on disproportionality analysis performance.

Methods

ClinicalTrials.gov

Product-event pair (PE):³ Information Component (IC) estimates from summary counts of AEs per arm within CTs

CTIC

- For each specific PE, IC estimates from CTs are used to create a MAP prior.
- This prior is then combined with FAERS data (2015–2019) for the same pair within a Bayesian model to generate statistical alerts.

product name
reported name
active moiety in group title or description

Mapping between ClinicalTrials.gov and FAERS

CTs exclusion:

- CT arms mapped to several products
- arms mapped to both "placebo" and a product
- CTs lacking at least one exposed arm and one placebo arm

Performance evaluation

Traditional IC⁴ vs

CTIC

Published reference set³

- 88 products approved between 2014 and 2017

48

products included in the evaluation

Results

96293

PE reported in FAERS – 88 products

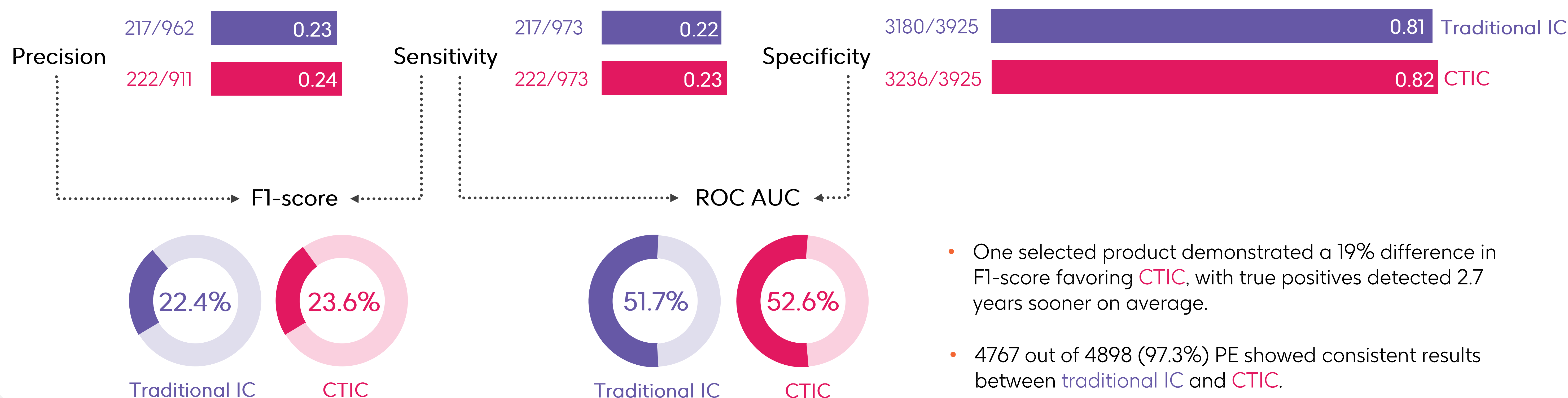
5697 (5.9%)

FAERS PE with available data in ClinicalTrials.gov – 48 products

4898 (5.1%)

Reference PE with available data in ClinicalTrials.gov and FAERS

Traditional IC vs CTIC



Abbreviations

CTIC, clinical trial information component; FAERS, US Food and Drug Administration Adverse Event Reporting System; MedDRA, Medical Dictionary for Regulatory Activities; ROC AUC, receiver operating characteristics area under curve.

References

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Data Sharing Statement

The data that support the findings of this study are available from the corresponding author (FH), upon reasonable request.

Authors' contributions

Study concept and design: FH, JP, GP, and AB. Data acquisition: FH and JP. Data analysis: FH and JP. Data interpretation: FH, JP, GP, and AB.

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