How Could the Appraisal Tools of Real-world Evidence be Applied for the Decision-making in Health Technology Assessment: a Mixed-methods Review and Thematic Analysis

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Background & Objective

- Non-randomized studies (NRS) have become a popular data source in health technology assessment (HTA).

- Given the concerns on NRS quality, HTA decision-makers have called for comprehensive NRS guidance. One way of issuing guidance is to apply NRS appraisal tools, which are commonly used in epidemiological studies.

- **Objective:** we aim to identify existing appraisal tools for NRSs with interventions, and to provide recommendations on how to select a tool.

Method

Identification of appraisal tools with three approaches

Approach one: *Systematic search of articles in Medline*
- Timeline: 2019 – now;
- Search strategy: ED Andrea et al. (2021)

Approach two: *Snowballing approach, according to Wohlin (2016)*
- Website that supports the snowballing approach: Connected Papers;
- Starting from two identified reviews of appraisal tools: ED Andrea et al. (2021) & J. Quigley et al. (2019).

Approach three: *Searching for appraisal tools on the websites of European HTA agencies, EMA , and US FDA*
- HTA agencies identified from the website of the INAHTA (International Network of Agencies for Health Technology Assessment);
- Four search terms: Critical appraisal, Quality, Risk of bias, Methodology;

Eligibility criteria

(1) Appraisal tools can be applied to non-randomized studies;
(2) Appraisal tools were designed for interventions, rather than exposures;
(3) An appraisal tool was excluded if it was designed for secondary research only, such as a systematic review or cost-effectiveness analysis.

Thematic analysis

- Identification of items that represent quality of non-randomized studies: consensus of the research team;
- Evaluation on whether an identified appraisal tool mentioned the items;
- Evaluation on how (i.e., related to reporting or risk of bias) and to what extent (i.e., with or without clear explanation on the item);
- Software: NVIVO 12.

CONCLUSION

- The RWE appraisal tools have great potential to be applied as guidance for HTA decision-making, but their applicability is limited by the great heterogeneity in how they address the concerns of HTA decision-makers.
- To improve the tool applicability for HTA decision-making, an effective strategy may be developed to select or adapt these tools.
- To achieve this, HTA decision-makers may need to be involved in the development and implementation process of appraisal tools, and to reach consensus by collaborating more closely with tool developers and HTA guideline developers.

RESULTS

Table 1. List of items (1-27)

#	Item	#	Item
1	Study objective	14	Length of follow-up (intervention)
2	Protocol	15	Outcome selection (outcome)
3	Study design	16	Definition (Outcome)
4	Ethical approval	17	Measurement (Outcome)
5	Sample size calculation/Power	18	Blinding (Outcome)
6	Eligibility criteria	19	Data source (Data collection)
7	Patients	20	Missing data (Data collection)
8	Participation rate	21	Loss to follow-up (Data collection)
9	Baseline characteristics	22	Description (Data analysis)
10	Selection (Intervention)	23	Sensitivity (Data analysis)
11	Definition (Intervention)	24	Confounding (Data Analysis)
12	Measurement (Intervention)	25	Are all the results included (results)
13	Blinding (intervention)	26	SPIN (Results)
		27	Conflict of interest

Table 2. How the appraisal tools fill in each item

Rows (appraisal tools): RELEVANT, RAMboMan, MMAT, CASP Case-control, CASP Cohort, SURE, JBI_Case-Control, JBI_Case-series, JBI_Cohort, ROBINS-I, ISPOR-AMCP-NPC, GRACE, NIH-NHLBI, HEB Wales, RoBANS, RTI-Item Bank, SIGN Case-control, SIGN Cohort, Montreal, STROBE, TREND, ACROBAT-NRSI, MINORS, GRADE publication bias, Rangel, EPHPP (Thomas), Atluri, Bishop, Blagojevic, Genaiy, Glasgow University, Tseng, Weightman, Wells (NOS), Quality Criteria Checklist, NICE checklist, IHE quality appraisal tool, AXIS tool, AHRQ, Pluye, Heller, Gagnier, Faillie, Manchikanti, Handu, Viswanathan, Young, ISPE, ENCePP Checklist, CONSORT, RECORD, ISPOR-ISPE, OSTEBA, Kennedey.

Legend:
- With detailed explanations for both methodology and reporting
- With brief explanations for both methodology and reporting
- With detailed explanations for only reporting
- With brief explanations for only reporting
- With detailed explanations for only methodology
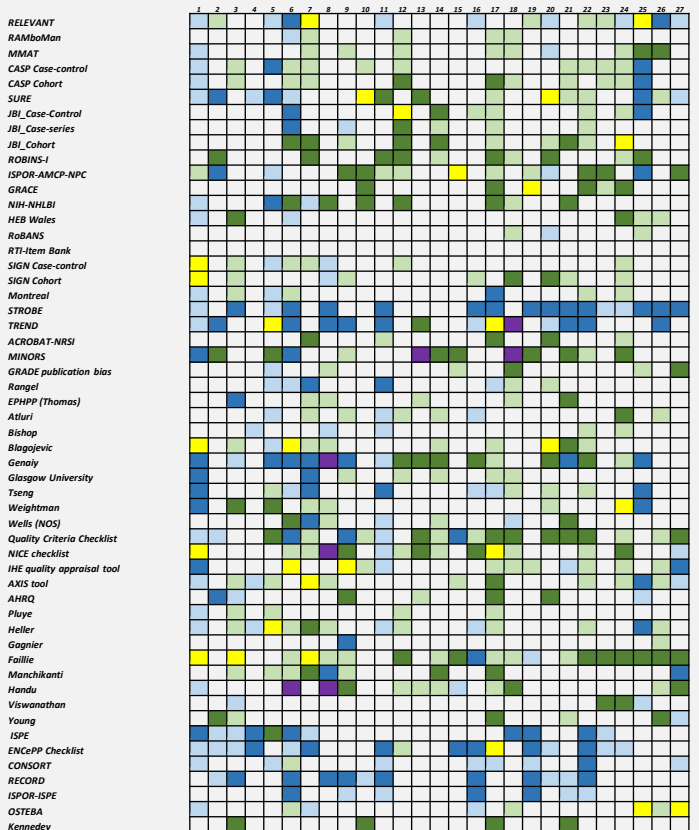- With brief explanations for only methodology

Reference

Wohlin C. Second-generation systematic literature studies using snowballing. InProceedings of the 20th International Conference on Evaluation and Assessment in Software Engineering 2016 Jun 1 (pp. 1-6).
D'Andrea E, et al. How well can we assess the validity of non-randomised studies of medications? A systematic review of assessment tools. BMJ open. 2021 Mar 1;11(3):e043961.
Quigley JM, et al. Critical appraisal of nonrandomized studies—a review of recommended and commonly used tools. Journal of Evaluation in Clinical Practice. 2019 Feb;25(1):44-52.