Evaluating Risk of Bias and Applicability in Meta-analyses of Individual Participant Data

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Background: Assessing risk of bias and applicability (RoB) of included studies is critical for interpreting meta-analysis (MA) results. RoB tools for diagnostic, prognostic, and prediction studies include QUADAS-2 and PROBAST. However, individual participant data meta-analyses (IPD-MAs) differ from aggregate-data MAs in that in IPD-MA, datasets may include additional information, eligibility criteria may differ from the original publications, and definitions for index tests/predictors and reference standards/outcomes can be standardized across studies. Thus, tailored RoB tools may be needed.

Aims: To review how RoB is currently assessed in IPD-MAs, and to examine QUADAS-2 and PROBAST, with the goal of developing IPD-MA extensions for each tool.

Methods: We reviewed RoB assessments in IPD-MAs published in the last 12 months. We then examined how QUADAS-2 (and in-progress extensions) and PROBAST items might be evaluated in an IPD-MA context; noting which items might be removed, edited, or added; and hypothesized how results may be incorporated into IPD-MA analyses.

Results: We observed that current IPD-MAs rarely and inconsistently evaluate RoB, and most do not incorporate RoB judgements into analyses. Our findings indicate using QUADAS-2 and PROBAST to assess RoB of IPD datasets themselves, rather than study publications. Certain items may need to be coded at the participant level (e.g., timing between index test/predictor and reference standard/outcome), whereas others (e.g., quality of diagnostic tool) may apply uniformly to an included study. Most analysis items (e.g., pre-specification of thresholds and variables for analysis) may not be relevant, as IPD-MA researchers perform the analyses themselves. RoB results may be incorporated into analyses by conducting subgroup analyses among studies and participants with overall low RoB or by conducting formal interaction analyses with item-level RoB responses.

Conclusions: Development and dissemination of IPD-MA extensions for QUADAS-2 and PROBAST will lead to improved RoB assessments in IPD-MAs of diagnostic, prognostic, and prediction studies.

Keywords
Risk of bias, applicability, QUADAS-2, PROBAST, individual participant data meta-analysis