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Testing a tool for assessing the risk of bias for nonrandomized studies showed moderate reliability and promising validity

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Abstract

Objectives: To develop and validate a new risk-of-bias tool for nonrandomized studies (NRSs).

Study Design and Setting: We developed the Risk of Bias Assessment Tool for Nonrandomized Studies (RoBANS). A validation process with 39 NRSs examined the reliability (interrater agreement), validity (the degree of correlation between the overall assessments of RoBANS and Methodological Index for Nonrandomized Studies [MINORS], obtained by plotting the overall risk of bias relative to effect size and funding source), face validity with eight experts, and completion time for the RoBANS approach.

Results: RoBANS contains six domains: the selection of participants, confounding variables, the measurement of exposure, the blinding of the outcome assessments, incomplete outcome data, and selective outcome reporting. The interrater agreement of the RoBANS tool except the measurement of exposure and selective outcome reporting domains ranged from fair to substantial. There was a moderate correlation between the overall risks of bias determined using RoBANS and MINORS. The observed differences in effect sizes and funding sources among the assessed studies were not correlated with the overall risk of bias in these studies. The mean time required to complete RoBANS was approximately 10 min. The external experts who were interviewed evaluated RoBANS as a ''fair'' assessment tool.

Conclusions: RoBANS shows moderate reliability, promising feasibility, and validity. The further refinement of this tool and larger validation studies are required.

Keywords: Risk of bias; Nonrandomized studies; Systematic reviews; Reliability; Validity; Validation studies

1. Introduction

A systematic review can be defined as a ''scientific investigation that focuses on a specific question and uses explicit, prespecified scientific methods to identify, select, assess, and summarize the findings of similar but separate studies'' [1]. When undertaking systematic reviews, the risk of bias for the included studies should be formally assessed because this factor has a substantial impact on estimates of treatment effects and may affect the validity of systematic reviews [2].

The design of the studies that are included in systematic reviews plays a major role in determining the reliability and the validity of the estimates of treatment effects. The randomized controlled trial (RCT) is widely regarded as the design of choice for assessing the effectiveness of health care interventions [2]. However, some questions of interest cannot be answered by a review of randomized trials, and some interventions cannot be randomized or are extremely unlikely to be studied in randomized trials. For example, evidence of certain effects, such as long-term and rare

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Authors' contributions: S.Y.K. designed and conducted the study and wrote the manuscript. S.Y.K., S.S.S., and S.K.H. developed the new tool and its instructions. H.J.S., Y.J.L., and J.E.P. participated in validating the new tool. B.H.J. and H.J.S. assisted in the performance of the study. All of the authors contributed to the conception and design of the study and read and approved the final manuscript.

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What is new?

Key findings

- We developed the Risk of Bias Assessment tool for Nonrandomized Studies (RoBANS), which contains six domains: the selection of participants, confounding variables, the measurement of exposure, the blinding of the outcome assessments, incomplete outcome data, and selective outcome reporting.

What this adds to what was known?

- RoBANS shows moderate reliability, promising feasibility, and validity.

What is the implication and what should change now?

- This tool should be widely evaluated to confirm its reliability and validity. The tool should be updated and refined as new information is generated regarding factors that affect the risk of bias for nonrandomized studies.

outcomes, or outcomes that were not considered important when major randomized trials were conducted, cannot be adequately investigated in randomized trials. In these contexts, review authors may be justified in including nonrandomized studies (NRSs) [3].

The Cochrane Collaboration introduced a tool to assess the risk of bias for RCTs [3], and this tool has been widely used. This tool was not developed to address NRSs, and certain domains of this tool are not necessarily appropriate for NRSs. However, the general structure of the tool and its assessments appear to be useful templates to follow during the assessment of the risk of bias for NRSs [3].

Many instruments for assessing the risk of bias for NRSs have been created, and these instruments were systematically reviewed by Deeks et al. [4]. In their review, these authors started with 182 tools. After reducing this number to a shortlist of 14 tools, they identified 6 tools that possess potential utility for systematic reviews [5−10], although none of the examined tools had been formally validated. The Methodological Index for Non-Randomized Studies (MINORS) is the only quality assessment tool for NRSs that has been validated [11]. However, MINORS has several limitations with respect to systematic reviews; in particular, this tool is scale based and may therefore be unfit for certain study designs, such as the before-and-after design.

The objectives of this study were to develop and validate a new risk-of-bias tool for assessing NRSs in systematic reviews.

2. Methods

2.1. Development

A team of three experts (S.Y.K., S.S.S., and S.K.H.) in the field of evidence-based medicine was formed to develop a new risk-of-bias tool for assessing NRSs in systematic reviews. The authors reviewed previous risk-of-bias tools for NRSs used in systematic reviews that were developed by Deeks et al. [4] and West et al. [12] and examined similar tools that have been used by various organizations, such as the National Institute for Health and Clinical Excellence (which uses this type of tool to provide public health guidance) [13] and the US Preventive Services Task Force [14]. The main principles that guided the tool development process in this study were the desires for an instrument that (1) is applicable for use across various study designs; (2) is in compliance with the algorithm of study design classification (Design Algorithm for the Medical Literature of Intervention [DAMI]); (3) can be applied to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach; and (4) is compatible with the Cochrane risk-of-bias tool. DAMI is an algorithm tool that our team has previously developed in accordance with these principles [15]. These principles were again adhered to during our development of Risk of Bias Assessment Tool for Non-randomized Studies (RoBANS). In other words, we applied the same types of risk-of-bias analysis for both RoBANS and DAMI but modified the bias domains for RoBANS to render the tool suitable for NRSs. The bias domains that are evaluated in RoBANS are shown in Table 1.

As in the Cochrane risk-of-bias tool, the bias types in RoBANS are selection, performance, detection, attrition, and reporting biases. However, the domains of selection and performance biases were modified to include the selection of participants, confounding variables, and the measurement of exposure. We also created a detailed risk-of-bias domain and criteria for judging the risk of bias for each domain. Similar to Cochrane Risk of Bias, RoBANS is outcome-based checklists. In particular, the domains of blinding of outcome assessments and incomplete outcome data can be treated as outcome-based evaluations.

RoBANS was developed after a careful consideration of advice from a wide variety of experts, including systematic review experts, statisticians, epidemiologists, and clinical practitioners.

2.2. Validation

To validate RoBANS, three researchers (J.E.P., Y.J.L., and H.J.S.) assessed samples of 39 NRSs from four systematic reviews. Three of the chosen systematic reviews [16−18] were health technology assessments that had been performed by the National Evidence-based Healthcare Collaborating Agency, and the remaining systematic review was an assessment that was published by the Cochrane Database of Systematic Reviews that included NRSs [19]. Three reviewers