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## COMMENTARY

# The Risk of Bias in Vaccine Effectiveness (RoB-VE) project: introduction to a methodological initiative to improve risk-of-bias assessment and reporting in vaccine effectiveness research

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## Abstract

**Background and Objective:** Vaccine effectiveness (VE) studies are essential for informing immunization policy and public health decision-making. However, the observational nature of most VE studies introduces unique methodological challenges, including biases that are not adequately addressed by existing risk-of-bias (RoB) tools. The Risk of Bias in Vaccine Effectiveness (RoB-VE) project is an international, multiphase methodological research initiative aimed at improving the quality, transparency, interpretability, and reporting of VE research.

**Discussion:** Funded by the Canadian Institutes of Health Research and supported by many global partners, the project seeks to generate a comprehensive toolkit for VE studies. This includes an RoB assessment resource tailored to VE study designs and a complementary reporting guideline to enhance consistency in VE study reporting. The project follows an evidence-informed approach, beginning with a review of the literature to inform tool development, and progressing through interest holder engagement, modified

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Delphi consensus, usability testing, and beta validation. This introductory paper outlines the rationale, scope, and methodology of the RoB-VE project. These efforts aim to strengthen the methodological foundation of VE research and support more reliable evidence synthesis and policy development. © 2025 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).

**Keywords:** Vaccination; Observational studies; Evidence synthesis methods; Quality appraisal; Critical appraisal; Study quality

### Plain Language Summary

VE studies measure how well vaccines work in real-world scenarios. These studies are essential for shaping vaccination recommendations. To assess the validity of VE studies, it is necessary to carry out an RoB assessment, which involves looking at different aspects of the study (eg, data collection methods, how participants are recruited, etc.) that have the potential to yield misleading results. Existing RoB assessment tools do not fully capture issues particularly relevant to VE studies and inconsistent reporting limits their usefulness. To address this, we are conducting the RoB-VE project. This project aims to improve the quality, transparency, interpretability, and reporting of VE research through the development, validation, and dissemination of a robust and user-friendly RoB assessment tool, specifically tailored for assessing VE studies. Our methodology involves a comprehensive multistep process based on established approaches. A broad range of international participants with diverse expertise and profiles will be engaged along the way to refine and finalize the tool. After pilot testing the beta version of the tool and making further refinements, we aim to deliver version 1 of the tool, which will undergo a large-scale application phase to assess its reliability and usefulness. Additionally, we will develop a reporting guideline to enhance the completeness of reporting of VE studies. This introductory paper outlines the rationale, scope, and methodology of the RoB-VE project. This project will elevate the standards of evidence synthesis, ultimately contributing to more reliable, transparent, and impactful research in the critical field of VE evaluation.

Vaccine effectiveness (VE) studies are a cornerstone of public health decision-making [1]. They provide critical evidence on how well vaccines perform in real-world settings [2], across diverse populations, and under varying conditions. These studies inform national immunization programs, guide global health policy, and shape public trust in vaccines. Yet, the credibility of VE evidence depends not only on the data collected but also on the methodological rigor and transparent reporting with which studies are designed, conducted, and interpreted.

Unlike randomized controlled trials, underpinning vaccine efficacy, VE studies are often phase 4/postimplementation studies and observational in nature. They rely on a broad host of designs such as cohort studies, case-control studies, test-negative designs, regression discontinuity approaches, among others [3]. Each of these designs introduces potential risks of biases (RoBs) (ie, systematic errors or flaws)—some common to all observational research, others unique to the context of vaccination, for example, the healthy vaccinee bias [4,5] and healthcare-seeking behavior bias according to vaccination status [3]. Assessment of quality of VE studies requires careful consideration of biases uniquely operationalized and specific to VE research and how these potential biases manifest themselves in the particular study design employed. The World Health Organization (WHO) has published useful

guidance on assessing COVID-19 VE, which includes descriptions of biases relevant for COVID-19 VE studies, the study designs that are impacted, and how the bias may affect the VE estimate (eg, direction and magnitude) [3]. However, there is a need for tailored guidance for assessment of RoB in VE studies that can be applied irrespective of the pathogen or vaccine of interest.

Despite the widespread use of VE studies in systematic reviews and policy documents, there is currently no dedicated, validated tool for assessing RoB in this body of evidence. Existing tools—such as the Newcastle-Ottawa Scale or Risk Of Bias In Nonrandomized Studies—of Interventions (ROBINS-I) [6,7]—offer general frameworks for evaluating observational studies, but they often fail to provide the operational guidance required to capture the nuances of VE research. Moreover, there is variability in how RoB tools are used across reviews in general [8], possibly leading to variability in how VE evidence is appraised, synthesized, and interpreted.

To address this gap, we launched the RoB-VE project (funded by the Canadian Institutes of Health Research)—a multi-year initiative designed to improve the quality, transparency, interpretability, and reporting of VE research. The protocol is registered on the Open Science Framework [9]. The RoB-VE Project brings together an international consortium of methodologists, epidemiologists, vaccinologists,

public health professionals, and members of the public. The project is endorsed by leading organizations including the WHO, the World Association of Medical Editors (WAME), the Canadian Immunization Research Network (CIRN), the Canadian Association for Immunization Research, Evaluation and Education (CAIRE), and the EQUATOR Network.

Our goal is to design, validate, and disseminate a comprehensive toolkit for VE research. This includes an RoB-VE assessment resource, tailored specifically to VE studies, and a complementary reporting guideline to standardize and improve the clarity and consistency of VE study reporting. Together, these resources will support researchers, reviewers, and policy decision-makers in generating and using VE evidence that is methodologically sound, transparent, and trustworthy.

The RoB-VE project is being developed through a collaborative, evidence-informed process that acknowledges the unique complexity of VE research, thus ensuring that the resulting resource is both usable across the diverse range of VE study designs and contexts and is practical. Rather than presupposing the need for an entirely new tool, we are allowing the data and input from key interest holders to guide whether the final product will be a novel instrument, an adaptation or extension of an existing RoB assessment tool, or specific tailored guidance to appropriately operationalize the unique RoB in this context. Inclusivity, diversity, and equity are central to our process: we are engaging researchers, policy decision-makers, and members of the public, to ensure the toolkit is relevant, accessible, and responsive to the needs of those who generate and use VE evidence. By embedding these values throughout the project, we aim to produce a toolkit, that is, technically robust, widely applicable, and trusted by the global VE community. The [Figure](#) provides a visual overview of the six major phases of the RoB-VE Project.

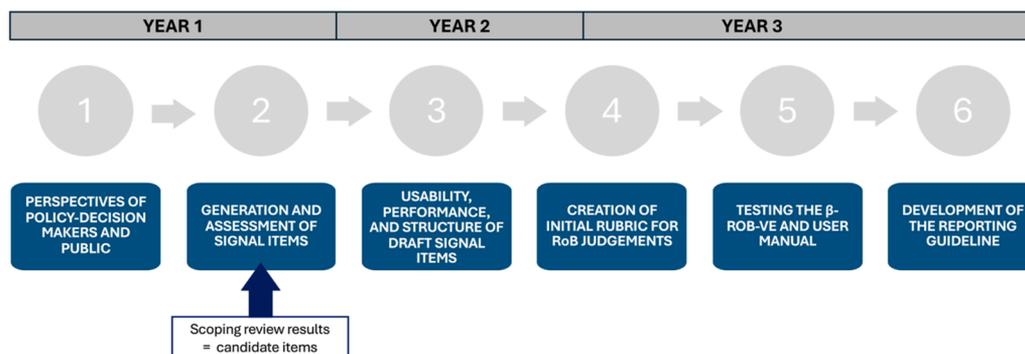
We will initiate the RoB-VE program by conducting focus groups with members of the public (eg, caregivers of children, older adults, and underrepresented groups)

and policy decision-makers to explore their information needs and expectations regarding VE research (Step 1). The insights gained will inform both the technical content and the knowledge translation strategy of the project. Input from these groups may also shape specific features of the toolkit, such as checklist items that promote clarity and transparency in VE reporting.

Next, we will initiate a survey-based Delphi process to refine and validate the candidate signal items identified through a literature review (Step 2). These items—representing potential sources of bias and their operationalization that is specific to VE studies—evaluated by a panel of vaccine experts and methodologists who will be identified from VE studies or systematic reviews, the WHO SAGE group, vaccine research networks, and from collaborator nominations and various working groups (eg, Cochrane). Through multiple rounds of online surveys, the panel will assess the relevance, clarity, and completeness of each item. This process will culminate in a draft version of the RoB-VE tool, which may emerge as a standalone instrument, an extension to an existing tool, or tailored guidance.

The draft tool will then undergo structured testing to assess its usability, performance, and internal structure (Step 3). A random sample of VE studies, with representation across study designs, will be independently reviewed by VE experts and methodologists using the draft RoB-VE. We will measure inter-rater reliability, internal consistency, and the conceptual coherence of the signal items. Usability will also be assessed through surveys capturing their experiences with the tool, including the clarity of instructions, ease of use, and appropriateness of the response scale.

Following this, we will develop a rubric (scoring guide) to direct overall RoB judgments (Step 4). This rubric will be informed by data generated from applying the draft tool to primary VE studies included in exemplar systematic reviews. It will describe how responses to individual signal items should be synthesized to arrive at an overall judgment of low, moderate, or high RoB. The broader research team



**Figure.** The RoB-VE project: This figure outlines the six main steps we will undertake to develop the RoB-VE toolkit, which includes the RoB-VE assessment resource and the VE reporting guideline. RoB-VE, Risk of Bias in Vaccine Effectiveness.

will iteratively review and refine the rubric through consensus-building exercises.

Once the rubric is finalized, we will proceed to beta-testing of the RoB-VE tool and its accompanying user manual (Step 5). A group of systematic review experts will apply the tool to one of ten review packages, consisting of a systematic review of VE studies and the underlying studies, and provide structured feedback on its components. Testing will involve ten systematic review packages. This phase will allow us to assess the tool's performance in real-world conditions and to make final refinements based on user input, ensuring that the tool is methodologically sound, practically useful, and user-friendly. The outcome of this phase will be the release of the RoB-VE version 1.

In the final phase of the project (Step 6), we will develop a reporting guideline for primary VE studies using standard methods [10]. This guideline will be informed by the validated signal items, expert input, and existing reporting guidelines. It will serve as a practical resource for researchers designing and reporting VE studies, promoting greater transparency and methodological consistency. The complete RoB-VE toolkit, including both the RoB-VE version 1 and the VE reporting guideline, will be made publicly available on the project website.

The RoB-VE toolkit is intended to support researchers at various stages of the research process. As part of our knowledge dissemination plan, we will host webinars, workshops, and training sessions to support researchers in using the tools. The RoB-VE version 1 will improve the quality and consistency of RoB assessments in systematic reviews of VE studies. The VE reporting guideline will assist researchers both at the design stage and at reporting stage to improve planning and strengthen reporting of primary VE studies [11]. These tools, if given to peer reviewers by journal editors [12], will support them in the peer-review process by simplifying and standardizing the process of evaluating VE studies. In addition, use of these tools in VE studies, leading to more relevant and transparent evaluations of quality, will thereby support policy-makers in making decisions regarding how much a particular VE study should be depended on. More broadly, our project will contribute to a deeper understanding of how bias manifests in VE research and how it can be mitigated through better design, reporting, and appraisal practices.

By involving members of the public in shaping the toolkit and its dissemination strategy, the RoB-VE Project also aims to improve scientific literacy and foster trust between researchers and the communities they serve. We are committed to promoting the initiative widely and encouraging international engagement in tool development and dissemination. As with any methodological resource, we anticipate the toolkit will evolve over time. We will remain attentive to feedback from users and responsive to the changing needs of the VE research community throughout the development process and beyond.

## CRediT authorship contribution statement

**Cassandra Laurie:** Writing – review & editing, Writing – original draft, Project administration, Methodology. **Pablo Alonso Coello:** Writing – review & editing, Methodology. **Ivan D. Florez:** Writing – review & editing, Methodology. **Maxime Lê:** Writing – review & editing, Methodology. **David Moher:** Writing – review & editing, Methodology. **Manish Sadarangani:** Writing – review & editing, Methodology. **Maria E. Sundaram:** Writing – review & editing, Methodology. **George Wells:** Writing – review & editing, Methodology. **Krista Wilkinson:** Writing – review & editing, Methodology. **Kerry Dwan:** Writing – review & editing, Methodology. **Scott A. Halperin:** Writing – review & editing, Methodology. **Stuart G. Nicholls:** Writing – review & editing, Methodology. **Barnaby C. Reeves:** Writing – review & editing, Methodology. **Hugh Sharma Waddington:** Writing – review & editing, Methodology. **Beverley Shea:** Writing – review & editing, Methodology. **Melissa Brouwers:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization. **Giorgia Sulis:** Writing – review & editing, Writing – original draft, Project administration, Methodology, Funding acquisition, Conceptualization.

## Declaration of competing interest

D. Moher is on the editorial board of the *Journal of Clinical Epidemiology*. The remaining authors have no conflicts of interest to disclose.

## Data availability

No data was used for the research described in the article.

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