



# Development of a risk of bias assessment tool specifically for meta-analysis of trials for surgical site infection

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## Introduction

Surgical site infection (SSI) presents a significant impact to patients, communities and healthcare. SSI rates, as high as 20%, after surgery, are associated with higher morbidity, prolonged hospital stays and increased hospital costs.<sup>1</sup> SSI can be due to multiple different reasons including patient- and operative level factors.<sup>2</sup> With increasingly new clinical trials ongoing to address SSIs, the development of a robust and specific risk of bias (RoB) assessment tool tailored for SSIs is essential for conducting accurate meta-analyses. Meta-analyses on high-quality randomised controlled trials (RCTs) to produce reliable and generalizable results. However, identifying these high-quality RCTs remains challenging, since the current Risk of Bias-2 tool is not specific to surgery. Therefore, we aimed to summarise development of an adapted SSI-specific Risk of Bias-2 (RoB-2) tool. Further, we aim to highlight its potential applications to guide future conduct of meta-analysis that informs clinical practice guidelines and policy.

## Methods

We have presented the initial stages of development and pilot use in a published meta-analysis.<sup>3</sup> Here, we provide the full details and final tool and included only the essential domains, in order to place enable more widespread use. To develop an adapted SSI-specific Risk of Bias-2, we undertook a four-staged consensus process with a group of surgeons and methodologists with expertise in international SSI trials. Selected experts included chief investigators, trial statisticians, trial methodologists, health technology assessment experts and guideline panel members that have been directly involved in SSI trials within the last 5-years. This included representation from the NIHR Global Health Research Unit on Global Surgery, the Wound Research Network (WREN), the Royal College of Surgeons of England, African Surgical Outcomes Study group, National Institute of Clinical Excellence (NICE) SSI guidelines committee, Birmingham Surgical Trials Consortium, a WHO Perioperative Care Collaborating centre, the WHO Surgical Site Infection prevention guidelines panel. This new tool is designed to be a shorter and more focused version, maintaining the critical elements necessary for assessing the quality of RCTs in the context of SSIs.

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Table 1. Summary of essential domains and areas of bias within the SSI-specific Risk of Bias-2 tool

	Type of bias	Definition of low risk	Assessment
Random sequence generation	Selection	Randomisation of patients using validated methodology, which included centralised, computer-based, or web-based sequence generation but excluded mechanical methods that could potentially be manipulated, such as shuffling of cards; quasi-randomisation or randomisation based on surgeons' judgement, preference, or availability were excluded	Low risk: valid randomisation methodology; high risk: none or unclear randomisation methodology
Allocation concealment	Selection	Acceptable method for assigning participants to comparison groups without risk of previous knowledge of an upcoming allocation; low-risk methods include central allocation and randomly mixed block sizes	Low risk: valid allocation methodology; high risk: none or unclear allocation methodology
Baseline differences between intervention groups	Selection	No significant differences between the baseline demographics of the intervention and control groups; recognition, analysis, and control of baseline differences between groups	Low risk: analysis and appropriate control for baseline differences; high risk: little or no recognition or control for baseline differences, or both
Analysis of groups to which they were randomly assigned	Attrition	Complete reporting of follow-up of all patients, including protocol deviations, deaths, and loss to follow-up; an intention-to-treat analysis is highly desirable; modification for loss to follow-up (i.e., patients who did not complete 30-day follow-up) or in those for whom a wound could not be assessed, or in those who did not have surgery after randomisation, was still considered low risk; exclusion of patients in whom wounds could be assessed (e.g. incorrect allocation) and per-protocol only analysis without adequate description of patients lost to follow-up were considered to be high risk	Low risk: intention-to-treat analysis performed, or full reporting of protocol deviations and loss to follow-up; high risk: no intention-to-treat analysis performed or incomplete reporting
Missing outcome data	Loss to follow-up	Acceptable level of loss to follow-up is <20% in patients who survived at 30 days; sensitivity analysis around missing outcome data is preferable to demonstrate that missing results do not affect the overall outcome of the analysis	Low risk: loss to follow-up <20%; high risk: loss to follow-up ≥20%
Blinding of outcome assessors	Detection	As diagnosis of SSI is a structured but subjective assessment, and blinding of outcome assessors is essential, appropriate training of the outcome assessor should also be provided	Low risk: blinded outcome assessor; high risk: unblinded, untrained outcome assessor
Quality assurance of outcome assessment	Outcome definition	A formal definition of SSI was used	Low risk: valid definition stated; high risk: definition not stated, or invalid
Quality assurance of outcome assessment	Follow-up period pre-defined	Follow-up intervals were pre-defined and standardised for each participant	Low risk: follow-up defined; high risk: follow-up not defined

## Results

The four-staged consensus process identified ten domains which are important to assessment of RCT's evaluating interventions to reduce SSI. These domains contain ten areas of bias, which were mapped out to the Cochrane RoB-2 tool, in which SSI-specific quality criteria were included where possible. Of the ten

domains, one was new (quality assurance of outcome assessment) and nine were adapted from different aspects of the Cochrane tool through a four-stage process.

From these ten, eight were prioritised as essential and taken forward into the final adapted SSI-specific RoB-2 tool. The eight essential key domains are listed in



Table 1. Two domains were classed as desirable, which were blinding of surgeons and blinding of patients, because they were non-discriminatory towards a high-quality or low-quality assessment. Although desirable for all RCTs, blinding of the surgeon delivering an intraoperative intervention is difficult (ie, because they are performing the index operation); to lower the risk of bias in SSI trials, ideally, the unblinded surgeon will not perform the outcome assessment. Although blinding patients to the intervention is useful, it might not be possible in all interventions in reducing SSI and, therefore, not pragmatic for future conduct of SSI trials.

## Discussion

The development of this SSI-specific RoB-2 tool addresses a significant gap in the current methodologies for evaluating RCTs in the context of SSIs. Current RoB-2 tools often fall short in several domains when applied to SSI studies, necessitating a tailored approach.<sup>4</sup> The utility of this tool extends beyond the assessment of existing studies. It can also serve as a valuable resource in the design of new RCTs focused on SSIs. By highlighting areas in the conduct and reporting of randomised trials, this tool can guide researchers design studies of high-quality. This proactive approach can ultimately lead to higher quality evidence being generated in the field of SSI research.

Moreover, the adoption of this tool in future meta-analyses can enhance the reliability and generalisability of their findings. This is because this tool provides standardisation in the assessment of clinical trials, allowing both researchers and policymakers to better understand what has been done. Importantly, high-quality RCTs are the cornerstone of robust meta-analyses, and this tool provides a means to systematically and consistently identify such studies.<sup>5</sup> As a result, meta-analyses that utilise this tool are likely to produce more accurate and meaningful conclusions, which can inform clinical practice and policy decisions related to SSI prevention and management.

The development of this SSI-specific RoB-2 assessment tool is an important step towards improving the quality of future clinical trials and meta-analyses. By focusing on the unique aspects of SSIs and streamlining the assessment process, this tool provides a practical and rigorous means of evaluating the quality of RCTs. Its application in both the assessment of existing studies and the design of new trials holds the potential to significantly improve the quality of evidence in SSI research, ultimately leading to better patient outcomes

and more effective infection control strategies.

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