Table 25.3.a. Bias domains included in the ROBINS-I tool

Bias domain	Category of bias	Explanation
Pre-intervention domains		
Bias due to confounding	Confounding	Baseline confounding occurs when one or more prognostic variables (factors that predict the outcome of interest) also predict the intervention received at baseline. ROBINS-I can also address time-varying confounding, which occurs when post-baseline prognostic factors affect the intervention received after baseline.
Bias in selection of participants into the study	Selection bias	When exclusion of some eligible participants, the initial follow-up time of some participants, or some outcome events is related to both intervention and outcome, an association between intervention and outcome may arise even if the true effect is null. This bias is distinct from confounding. A specific example is bias due to inclusion of prevalent users rather than new users of an intervention.
At-intervention domain		
Bias in classification of interventions	Information bias	Bias introduced by either differential or non-differential misclassification of intervention status. Non-differential misclassification is unrelated to the outcome and usually biases the estimated intervention effect toward the null. Differential misclassification occurs when misclassification of intervention status is related to the outcome or risk of the outcome.
Post-intervention domains		
Bias due to deviations from intended interventions	Confounding	Bias arising from systematic differences between intervention and comparator groups in the care provided that represent deviations from the intended intervention(s). Assessment depends on the effect of interest (effect of assignment to intervention versus effect of adherence to intervention).
Bias due to missing data	Selection bias	Bias arising when follow-up data are missing for individuals initially included and followed (e.g. differential loss to follow-up related to prognostic factors), or when individuals are excluded due to missing information on intervention status or other variables such as confounders.
Bias in measurement of the outcome	Information bias	Bias introduced by differential or non-differential errors in outcome measurement. This can occur if outcome assessors are aware of intervention status, if different assessment methods are used across intervention groups, or if measurement error is related to intervention status or effects.
Bias in selection of the reported result	Reporting bias	Selective reporting of results from among multiple outcome measurements, analyses, or subgroups in a manner that depends on the findings.

Table 25.4.a. Bias domains included in the ROBINS-I tool for follow-up studies, with a summary of the issues addressed

Bias domain	Issues addressed
Bias due to confounding	Whether: • the review author should consider baseline confounding only, or both baseline confounding and time-varying confounding (arising in studies in which follow-up time is split according to the intervention being received); • all important confounding domains were controlled for; • the confounding domains were measured validly and reliably by the variables available; and • appropriate analysis methods were used to control for the confounding.
Bias in selection of participants into the study	Whether: • selection of participants into the study (or into the analysis) was based on participant characteristics observed after the start of intervention; • (if applicable) these characteristics were associated with intervention and influenced by outcome (or a cause of the outcome); • start of follow-up and start of intervention were the same; and • (if applicable) adjustment techniques were used to correct for the presence of selection biases.
Bias in classification of interventions	Whether: • intervention status was classified correctly for all (or nearly all) participants; • information used to classify intervention groups was recorded at the start of the intervention; and • classification of intervention status could have been influenced by knowledge of the outcome or risk of the outcome.
Bias due to deviations from intended interventions	*When the review authors' interest is in the effect of assignment to intervention (see Section 25.3.3):* Whether: • there were deviations from the intended intervention because of the experimental context (i.e. deviations that do not reflect usual practice); and, if so, whether they were balanced between groups and likely to have affected the outcome. *When the review authors' interest is in the effect of adhering to intervention (see Section 25.3.3):* Whether: • important co-interventions were balanced across intervention groups; • failures in implementing the intervention could have affected the outcome and were unbalanced across intervention groups; • study participants adhered to the assigned intervention regimen and if not whether non-adherence was unbalanced across intervention groups; and • (if applicable) an appropriate analysis was used to estimate the effect of adhering to the intervention.

Bias due to missing data	Whether: • the number of participants omitted from the analysis due to missing outcome data was small; • the number of participants omitted from the analysis due to missing data on intervention status was small; • the number of participants omitted from the analysis due to missing data on other variables needed for the analysis was small; • (if applicable) there was evidence that the result was not biased by missing outcome data; and • (if applicable) missingness in the outcome was likely to depend on the true value of the outcome (e.g. because of different proportions of missing outcome data, or different reasons for missing outcome data, between intervention groups).
Bias in measurement of the outcome	Whether: • the method of measuring the outcome was inappropriate; • measurement or ascertainment of the outcome could have differed between intervention groups; • outcome assessors were aware of the intervention received by study participants; and • (if applicable) assessment of the outcome could have been influenced by knowledge of intervention received; and whether this was likely.
Bias in selection of the reported result	Whether: • the numerical result being assessed is likely to have been selected, on the basis of the results, from multiple outcome measurements within the outcome domain; • the numerical result being assessed is likely to have been selected, on the basis of the results, from multiple analyses of the data; and • the numerical result being assessed is likely to have been selected, on the basis of the results, from multiple subgroups of a larger cohort.

Table 25.5.a Bias domains included in the ROBINS-I tool for (uncontrolled) before-after studies, with a summary of the issues addressed

Bias domain	Additional or different issues addressed compared with follow-up studies
Bias due to confounding	Whether: • measurements of outcomes were made at sufficient pre-intervention time points to permit characterization of pre-intervention trends and patterns; • there are extraneous events or changes in context around the time of the intervention that could have influenced the outcome; and • the study authors used an appropriate analysis method that accounts for time trends and patterns, and controls for all the important confounding domains.
Bias in selection of participants into the study	The issues are similar to those for follow-up studies. For studies that prospectively follow a specific group of units from pre-intervention to post-intervention, selection bias is unlikely. For repeated cross-sectional surveys of a population, there is the potential for selection bias even if the study is prospective.
Bias in classification of interventions	Whether specification of the distinction between pre-intervention time points and post-intervention time points could have been influenced by the outcome data.
Bias due to deviations from intended interventions	*Assuming the review authors' interest is in the effect of assignment to intervention (see Section 25.3.3):* Whether the effects of any preparatory (pre-interruption) phases of the intervention were appropriately accounted for.
Bias due to missing data	Whether outcome data were missing for whole clusters (units of multiple individuals) as well as for individual participants.
Bias in measurement of the outcome	Whether: • methods of outcome assessment were comparable before and after the intervention; and • there were changes in systematic errors in measurement of the outcome coincident with implementation of the intervention.
Bias in selection of the reported result	The issues are the same as for follow-up studies.

Table 25.6.a Bias domains included in the ROBINS-I tool for controlled before-after studies, with a summary of the issues addressed

Bias domain	Additional or different issues addressed compared with follow-up studies
Bias due to confounding	Whether: • measurements of outcomes were made at sufficiently many time points, in both the intervention and comparator groups, to permit characterization of pre-intervention trends and patterns; • any extraneous events or changes in context around the time of the intervention that could have influenced the outcome were experienced equally by both intervention groups; and • pre-intervention trends and patterns in outcomes were analysed appropriately and found to be similar across the intervention and comparator groups.
Bias in selection of participants into the study	The issues are similar to those for follow-up studies. For repeated cross-sectional surveys of a population, there is the potential for selection bias if changes in the types of participants/units included in repeated surveys differ between intervention and comparator groups.
Bias in classification of interventions	Whether classification of time points as before versus after intervention could have been influenced by post-intervention outcome data.
Bias due to deviations from intended interventions	*Assuming the review authors' interest is in the effect of assignment to intervention (see Section 25.3.3):* The issues are the same as for follow-up studies.
Bias due to missing data	Whether outcome data were missing for whole clusters as well as for individual participants.
Bias in measurement of the outcome	Whether: • methods of outcome assessment were comparable across intervention groups and before and after the intervention; and • there were changes in systematic errors in measurement of the outcome coincident with implementation of the intervention.
Bias in selection of the reported result	The issues are the same as for follow-up studies.