Revised Cochrane risk-of-bias tool for randomized trials (RoB 2)

TEMPLATE FOR COMPLETION

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on behalf of the RoB2 Development Group

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| **Study details**   |  |  | | --- | --- | | **Reference** | Chung, J., Mundy, M. E., Hunt, I., Coxon, A., Dyer, K. R., & McKenzie, S. (2021). An evaluation of an online brief mindfulness-based intervention in higher education: A pilot conducted at an Australian university and a British university. Frontiers in psychology, 12, 752060. https://doi.org/10.3389/fpsyg.2021.752060 |   **Study design**   |  |  | | --- | --- | | □ | Individually-randomized parallel-group trial | | □ | Cluster-randomized parallel-group trial | | □ | Individually randomized cross-over (or other matched) trial |   **For the purposes of this assessment, the interventions being compared are defined as**   |  |  |  |  | | --- | --- | --- | --- | | Experimental: | Brief MBI | Comparator: | Waitlist control |  |  |  | | --- | --- | | **Specify which outcome is being assessed for risk of bias** | WEMWBS (Warwick-Edinburgh Mental Well-Being Scale) 14-item scale (Tennant et al., 2007), due to an error only 12 items were used. |  |  |  | | --- | --- | | **Specify the numerical result being assessed.** In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed. | Pre and post-measures of the WEMWBS for the Brief MBI and Waitlist control group, table 2. P.7 in journal article. |   **Is the review team’s aim for this result…?**   |  |  | | --- | --- | | □ | to assess the effect of *assignment to intervention* (the ‘intention-to-treat’ effect) | | X | to assess the effect of *adhering to intervention* (the ‘per-protocol’ effect) |   **If the aim is to assess the effect of *adhering to intervention***, select the deviations from intended intervention that should be addressed (at least one must be checked):  X occurrence of non-protocol interventions  □ failures in implementing the intervention that could have affected the outcome  X non-adherence to their assigned intervention by trial participants  **Which of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply)**  X Journal article(s) with results of the trial + supplementary materials  □ Trial protocol  □ Statistical analysis plan (SAP)  □ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)  □ Company-owned trial registry record (e.g. GSK Clinical Study Register record)  □ “Grey literature” (e.g. unpublished thesis)  □ Conference abstract(s) about the trial  □ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)  □ Research ethics application  □ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)  □ Personal communication with trialist  □ Personal communication with the sponsor |

## Risk of bias assessment

Responses underlined in green are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

**Domain 1: Risk of bias arising from the randomization process**

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| **Signalling questions** | **Comments** | **Response options** |
| **1.1 Was the allocation sequence random?** | “For each subject unit and year level (e.g. psychology, first year), one of the study modes (e.g. online) was allocated to the control condition, and the other study mode (e.g. on-campus) was allocated to the intervention condition. When allocating subject units to the study conditions, the research team ensured that an approximately equal number of students were enrolled in each of the study modes and subject units, and that in the overall participant population, an approximately equal number of potential participants were allocated to the control and intervention conditions.”  1.2 “Potential participants were invited to self-enrol in the LMS site created for this study. The explanatory statement was provided which detailed the nature of the research study evaluating a brief, online mindfulness intervention. The explanatory statement indicated to students which experimental condition they would receive (wait-list control or intervention), were provided a brief and general definition of mindfulness, were informed of the type of mindfulness activities, the duration of the intervention and study, and finally the types of questions asked in the survey. Participants then provided consent and completed the baseline (T1) survey via an online survey platform.” | N  Answer ‘Yes’ if a random component was used in the sequence generation process. Examples include computer-generated random numbers.  Answer ‘No’ if no random element was used in generating the allocation sequence or the sequence is predictable.  Answer ‘No information’ if the only information about randomization methods is a statement that the study is randomized. |
| **1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?** | N  Answer ‘Yes’ if the trial used any form of remote or centrally administered method to allocate interventions to participants, where the process of allocation is controlled by internet-based randomization service providers.  Answer ‘No’ if there is reason to suspect that the enrolling investigator or the participant had knowledge of the forthcoming allocation. |
| **1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?** | Despite the following: “Full datasets were obtained for 69 participants in the control group, and 83 participants in the intervention group. Full random allocation and stratification were not possible, yet baseline comparisons revealed participants were well matched (see Table 1). Majority of the sample (96%) was psychology students. The demographics and characteristics of the sample are shown in Table 1.”  The 148 participants were assigned to the waitlist control and 279 participants to the intervention group. Thus, randomisation indicates substantial differences in group sizes. | Y  Answer ‘Yes’ if there are imbalances that indicate problems with the randomization process, including:  (1) substantial differences between intervention group sizes, compared with the intended allocation ratio; or  (2) a substantial excess in statistically significant differences in baseline characteristics between intervention groups, beyond that expected by chance; or  (3) imbalance in one or more key prognostic factors, or baseline measures of outcome variables, that is very unlikely to be due to chance and for which the between-group difference is big enough to result in bias in the intervention effect estimate. |
| **Risk-of-bias judgement** |  | High |
| Optional: What is the predicted direction of bias arising from the randomization process? | Experimental group contains a significantly higher nr of participants which leads to an increased chance of finding a significant effect. | Favours experimental |

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of adhering to intervention*)

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| **Signalling questions** | **Comments** | **Response options** |
| **2.1. Were participants aware of their assigned intervention during the trial?** | “Potential participants were invited to self-enrol in the LMS site created for this study. The explanatory statement was provided which detailed the nature of the research study evaluating a brief, online mindfulness intervention. The explanatory statement indicated to students which experimental condition they would receive (wait-list control or intervention), were provided a brief and general definition of mindfulness, were informed of the type of mindfulness activities, the duration of the intervention and study, and finally the types of questions asked in the survey. Participants then provided consent and completed the baseline (T1) survey via an online survey platform.”  2.2 Intervention delivered using digital platform. | Y |
| **2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?** | N |
| **2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across intervention groups?** | There is no information on whether there were any non-protocol interventions and whether these were balanced across intervention groups. | NI |
| **2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the outcome?** |  | NA |
| **2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected participants’ outcomes?** | “The independent samples t-tests conducted between participants who completed the study and those that withdrew (i.e. did not complete the follow-up survey) yield no evidence that participants differed significantly on any of outcome measures of WEMWBS, PSS and MAAS (see Supplementary Material 1)  Specifically, in regard to KCL attrition and its stark contrast compared to MU attrition, we  suggest that this can largely be explained by contextual factors with mindfulness and wellbeing being a normalised concept at MU. At MU, mindfulness has been long established for student and staff wellbeing as it was introduced in the early 2000s by Assoc. Prof. Craig Hassed. Since then mindfulness has been part of the core curriculum in medical programmes at the university for over 20 years and has also been incorporated into other disciplines, such as psychology. In comparison, KCL was in the early stages of developing and implementing their Student Mental Health and Wellbeing Strategic Plan at this time of this research.” | PN |
| **2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of adhering to the intervention?** | A completers only analysis appears to have been used, there’s no justification: “The main outcome variable of interest was the difference between scores at follow-up compared to baseline (i.e. T2 scores − T1 scores), computed for each outcome variable, which we  refer to as ‘change’. Change was examined in regard to the size (i.e. the size of the units between the two-time points) and direction (i.e. changes that were positive or negative in outcome value). Change values that were positive indicated increased scores, and negative change values indicated decreased scores on the outcome measure. Independent t-tests were used to compare group differences on all binary predictor variables on levels of change in wellbeing, stress and mindfulness between T1 and T2. Hedge’s g was used to calculate effect size and is recommended when sample sizes are small and unequal. For the main analysis and to explore the impact of the intervention on participants levels of wellbeing, stress and mindfulness, a series of regression models were applied. The models predicted the variation of change in outcome between T1 and T2 accounted for by theintervention and participant demographics and characteristics. Baseline levels of the outcome variable at T1 were used as a covariate in the models. Our primary focus is on reporting the variance accounted for by the condition; however, we  also present the full model that explains the variance accounted for by various variables.” | PN |
| **Risk-of-bias judgement** |  | High |
| Optional: What is the predicted direction of bias due to deviations from intended interventions? |  | Unpredictable |

Domain 3: Missing outcome data

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| **Signalling questions** | **Comments** | **Response options** |
| **3.1 Were data for this outcome available for all, or nearly all, participants randomized?** | See figure 1.:  A total of 427 participants were randomised, 148 participants to baseline and 279 to the intervention group. A total of 79 dropped out in the control group and 196 in the intervention group. | N  The appropriate study population for an analysis of the intention to treat effect is all randomized participants.“Nearly all” should be interpreted as that the number of participants with missing outcome data is sufficiently small that their outcomes, whatever they were, could have made no important difference to the estimated effect of intervention. For continuous outcomes, availability of data from 95% of the participants will often be sufficient. |
| **3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?** | There is no evidence that the result was not biased by missing outcome data. | N  Evidence that the result was not biased by missing outcome data may come from: (1) analysis methods that correct for bias; or (2) sensitivity analyses showing that results are little changed under a range of plausible assumptions about the relationship between missingness in the outcome and its true value. However, imputing the outcome variable, either through methods such as ‘last-observation-carried-forward’ or via multiple imputation based only on intervention group, should not be assumed to correct for bias due to missing outcome data. |
| **3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?** | No reasons for missing outcome data other than participants dropping out were reported. Analysis indicate that there were differences in condition, age and study mode for the outcome measure:  “Group differences by participant characteristics and demographics on change in WEMWBS, PSS and MAAS scores, between T1 and T2, were explored (see Supplementary Material 3).”  Supplementary material 3 indicates there were no significant differences at baseline between the participants that did and did not drop out based on mental well-being, perceived stress and mindfulness levels.  “Significant group differences were found in condition, age and study mode for each of the three outcome measures. Non-significant group differences were found for the remaining variables (institution, gender, level, meditation or mindfulness experience).” | Y  If loss to follow up, or withdrawal from the study, could be related to participants’ health status, then it is possible thatmissingness in the outcome was influenced by its true value. However, if all missing outcome data occurred for documented reasons that are unrelated to the outcome then the risk of bias due to missing outcome data will be low (for example, failure of a measuring device or interruptions to routine data collection).In time-to-event analyses, participants censored during trial follow-up, for example because they withdrew from the study, should be regarded as having missing outcome data, even though some of their follow up is included in the analysis. Note that such participants may be shown as included in analyses in CONSORT flow diagrams. |
| **3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?** | Y  Reasons for answering ‘Yes’ are:  1.Differences between intervention groups in the proportions of missing outcome data.  2.Reported reasons for missing outcome data provide evidence that missingness in the outcome depends on its true value.  3.Reported reasons for missing outcome data differ between the intervention groups.  4.The circumstances of the trial make it likely that missingness in the outcome depends on its true value. For example, in trials of interventions to treat schizophrenia it is widely understood that continuing symptoms make drop out more likely.  Answer ‘No’ if the analysis accounted for participant characteristics that are likely to explain the relationship between missingness in the outcome and its true value. |
| **Risk-of-bias judgement** |  | High |
| Optional: What is the predicted direction of bias due to missing outcome data? |  | Unpredictable |

Domain 4: Risk of bias in measurement of the outcome

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| **Signalling questions** | **Comments** | **Response options** |
| **4.1 Was the method of measuring the outcome inappropriate?** | Despite the measurement not being fully administered, the study provides evidence of its validity when not obtaining 2 out of 14 items. Although it is interesting to note that their validity is higher than the validity of the original scale. Thus, some concerns about the validity of this measurement remain. It is also unknown whether the summed average will be sensitive enough for intervention effects compared to the summed score as the range differs from 14-74 (original scale) to 1-5 (current study).  “Warwick-Edinburgh Mental Wellbeing Scale The Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) is a 14-item scale measuring wellbeing over the past 2weeks (Tennant et  al., 2007). Items are measured on a 5-point Likert scale from 1=none of the time to 5=all of the time. Due to a procedural error, participants in the MU sample completed 12 items in the WEMWBS (excluding items 12 & 13). To appropriately combine and compare MU and KCL datasets, items were summed and averaged (rather than using a summed score). Higher average WEMWBS scores indicate increased wellbeing. Cronbach’s alpha has been reported as 0.89–0.91 in university student and population samples, as well as high test-retest reliability (α=0.82; Tennant et  al., 2007). Cronbach’s alpha for MU sample based on 12 items was 0.89, and at KCL with 14 items was 0.90. Both samples demonstrated high internal consistency.” | PY  Answer ‘Yes’ or ‘Probably yes’ if the method of measuring the outcome is inappropriate, for example because:  (1) it is unlikely to be sensitive to plausible intervention effects (e.g. important ranges of outcome values fall outside levels that are detectable using the measurement method); or  (2) the measurement instrument has been demonstrated to have poor validity. |
| **4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?** | It was automatically administered using a digital questionnaire. | N  Comparable methods of outcome measurement (data collection) involve the same measurement methods and thresholds, used at comparable time points. Differences between intervention groups may arise because of ‘diagnostic detection bias’ in the context of passive collection of outcome data, or if an intervention involves additional visits to a healthcare provider, leading to additional opportunities for outcome events to be identified. |
| **4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?** | Participants (assessors) were aware of their intervention received: “participants were aware of the study condition they had been allocated to”. | Y  Answer ‘No’ if outcome assessors were blinded to intervention status. For participant-reported outcomes, the outcome assessor is the study participant. |
| **4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?** |  | Y  Knowledge of the assigned intervention could influence participant-reported outcomes (such as level of pain), observer-reported outcomes involving some judgement, and intervention provider decision outcomes. They are unlikely to influence observer-reported outcomes that do not involve judgement, for example all-cause mortality. |
| **4.5 If Y/PY/NI to 4.4:** **Is it likely that assessment of the outcome was influenced by knowledge of intervention received?** | PN  This question distinguishes between situations in which (i) knowledge of intervention status could have influenced outcome assessment but there is no reason to believe that it did (assessed as ‘Some concerns’) from those in which (ii) knowledge of intervention status was likely to influence outcome assessment (assessed as ‘High’). When there are strong levels of belief in either beneficial or harmful effects of the intervention, it is more likely that the outcome was influenced by knowledge of the intervention received. Examples may include patient-reported symptoms in trials of homeopathy, or assessments of recovery of function by a physiotherapist who delivered the intervention. |
| **Risk-of-bias judgement** |  | High |
| Optional: What is the predicted direction of bias in measurement of the outcome? |  | Unpredictable |

Domain 5: Risk of bias in selection of the reported result

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| **Signalling questions** | **Comments** | **Response options** |
| **5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?** | Couldn’t find/obtain any pre-specified analysis plan or pre-registration of the study. | NI  If the researchers’ pre-specified intentions are available in sufficient detail, then planned outcome measurements and analyses can be compared with those presented in the published report(s). To avoid the possibility of selection of the reported result, finalization of the analysis intentions must precede availability of unblinded outcome data to the trial investigators. |
| **Is the numerical result being assessed likely to have been selected, on the basis of the results, from...** |  |  |
| **5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?** | All measures and outcome timepoints for each group have been reported. | PN  Answer ‘Yes’ or ‘Probably yes’ if:  There is clear evidence (usually through examination of a trial protocol or statistical analysis plan) that a domain was measured in multiple eligible ways, but data for only one or a subset of measures is fully reported (without justification), and the fully reported result is likely to have been selected on the basis of the results. Selection on the basis of the results can arise from a desire for findings to be newsworthy, sufficiently noteworthy to merit publication, or to confirm a prior hypothesis. For example, trialists who have a preconception, or vested interest in showing, that an experimental intervention is beneficial may be inclined to report outcome measurements selectively that are favourable to the experimental intervention.  Answer ‘No’ or ‘Probably no’ if:  There is clear evidence (usually through examination of a trial protocol or statistical analysis plan) that all eligible reported results for the outcome domain correspond to all intended outcome measurements.  Or  There is only one possible way in which the outcome domain can be measured (hence there is no opportunity to select from multiple measures).  or  Outcome measurements are inconsistent across different reports on the same trial, but the trialists have provided the reason for the inconsistency and it is not related to the nature of the results.  Answer ‘No information’ if:  Analysis intentions are not available, or the analysis intentions are not reported in sufficient detail to enable an assessment. |
| **5.3 ... multiple eligible analyses of the data?** | There’s no pre-specified analysis plan, there’s also no information on how exactly they would/did handle missing data – thus it is unknown if multiple eligible (ITT and PP analysis) were performed and one of the outcomes were chosen. There being more than one eligible way to analyse the data. | NI  There is clear evidence (usually through examination of a trial protocol or statistical analysis plan) that a measurement was analysed in multiple eligible ways, but data for only one or a subset of analyses is fully reported (without justification), and the fully reported result is likely to have been selected on the basis of the results. |
| **Risk-of-bias judgement** |  | Some concerns |
| Optional: What is the predicted direction of bias due to selection of the reported result? |  | Unpredictable |

Overall risk of bias

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| **Risk-of-bias judgement** |  | High |
| Optional: What is the overall predicted direction of bias for this outcome? |  | Favours experimental |



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