# Blinding in randomised clinical trials of psychological interventions: a retrospective study of published trial reports

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## Abstract

**Objectives** To study the extent of blinding in randomised clinical trials of psychological interventions and the interpretative considerations if randomised clinical trials are not blinded.

**Design** Retrospective study of trial reports published in six high impact factor journals within the field of psychiatry in 2017 and 2018.

**Setting** Trial reports published in World Psychiatry, JAMA Psychiatry, Lancet Psychiatry, American Journal of Psychiatry, British Journal of Psychiatry, or Psychotherapy and Psychosomatics.

**Main outcome measures** Blinding status of participants, treatment providers, outcome assessors, data managers, the data safety and monitoring committee, statisticians and conclusion makers, if trialists rejected the null hypothesis on the primary outcome measure, and if trialists discussed the potential bias risk from lack of blinding in the published trial report.

**Results** 63 randomised clinical trials of psychological interventions were identified. None (0%; 95% CI 0% to 5.75%) of the trials reported blinding of all possible key persons. 37 (58.7%; 95% CI 46.42% to 70.04%) trials reported blinding of outcome assessors. Two (3.2%; 95% CI 0.87% to 10.86%) trials reported blinding of participants. Two (3.2%; 95% CI 0.87% to 10.86%) trials reported blinding of data managers. Three (4.8%; 95% CI 1.63% to 13.09%) trials reported blinding of statisticians. None of the trials reported blinding of treatment providers, the data safety and monitoring committee, and conclusion makers. 45 (71.4%; 95% CI 59.30% to 81.10%) trials rejected the null hypothesis on the primary outcome(s). 13 (20.7%; 95% CI 12.48% to 32.17%) trials discussed the potential bias risk from lack of blinding in the published trial report.

**Conclusions** Blinding of key persons involved in randomised clinical trials of psychological interventions is rarely sufficiently documented. The possible interpretative limitations are only rarely considered. There is a need of randomised clinical trials of psychological interventions with documented blinding attempts of all possible key persons.

## Summary box

**What is already known about this subject?**

- Participants, treatment providers, outcome assessors, data managers, the data safety and monitoring committee, statisticians and conclusion makers must ideally be blinded to protect against bias in any trial. The extent of blinding of all possible key persons has not been studied in randomised clinical trials of psychological interventions.

**What are the new findings?**

- Blinding of key persons is rarely reported or implemented in randomised clinical trials of psychological intervention, and only few trialists consider the bias risk this may have caused. Therefore, there is a risk that previous randomised clinical trials of psychological interventions generally may have overestimated the beneficial effects and underestimated the harmful effects of the experimental interventions being studied.

**How might it impact clinical practice in the forseeable future?**

- Randomised clinical trials of psychological interventions with attempts of blinding of key persons are needed and can help to identify effective psychological interventions at low risk of harm.

## Introduction

Blinding in randomised clinical trials refers to the methodological principle of preventing bias by withholding information about allocation status from individuals or groups.[1] Several studies have demonstrated that lack of blinding is responsible for biased treatment estimates.[2–12] For example, meta-analyses of trials with and without reports of blinding of participants and outcome assessors have indicated an overestimation of the beneficial effects of the studied interventions in trials

without blinding.[7–9] These results were confirmed in a metaepidemiological study of 228 Cochrane meta-analyses, in which exaggerated effect estimates were found in trials without blinded participants, personnel and outcome assessors.[10] However, a new metaepidemiological study investigating 142 Cochrane reviews with both blinded and non-blinded trials on any topic was recently published without showing effects of blinding.[13] Both metaepidemiological studies included, but were not limited to, psychosocial and behavioural interventions. The latter study conflicts with the previously described studies, as it indicated no evidence of a difference in estimated treatment effect between trials with and without blinded participants, healthcare providers and outcome assessors.[13 14] Nevertheless, this study may have been at risk of type II errors as it only included approximately half the number of meta-analyses compared with the metaepidemiological study by Savović *et al*.[10] Furthermore, the authors concluded that risk of bias due to lack of blinding should be carefully considered.[13] For a detailed comparison of the two metaepidemiological studies, see online supplemental file 1. Based on previous evidence, blinding should remain a methodological safeguard in randomised clinical trials.[13–15] It may be argued that blinding of key persons in a trial does not affect the bias risk of 'hard' outcomes, such as mortality. However, a large metaepidemiological study did not observe consistently different bias for subjective outcomes compared with mortality.[10] If the method of measurement of the hard outcome is insufficiently performed and described, blinding may theoretically matter. For example, if mortality is not systematically assessed, for example, by looking in all participants' medical journals or person registries, if these are available, then the outcome may be biased if outcome assessors are not blinded. Therefore, trialists should continue to make every effort to incorporate possible blinding procedures into their trial designs regardless of the type of outcome, and readers of trial reports should look for reports of which key persons were blinded to avoid potentially biased conclusions.[16 17]

Trial participants, treatment providers, outcome assessors, data managers, the data safety and monitoring committee, statisticians and conclusion makers should ideally all be blinded to minimise the risk of biased trial results regardless of the type of studied interventions.[6 18–20]

In box 1, we describe how all these key persons may be blinded in randomised clinical trials of psychological interventions.

Because of the difficulties of blinding participants and treatment providers in randomised clinical trials of psychological interventions, it is important to assess the extent of blinding of these and other more easily blinded key trials persons in the current literature. Further, the extent of blinding of key persons involved in a randomised clinical trial of psychological interventions has not yet been systematically studied. The objective of the present study is to evaluate the extent of blinding in trials and the interpretative considerations if the trials are not blinded in six high impact factor journals.

## Methods

### Search strategy

Two investigators (SJ, FWF) independently searched for randomised clinical trials of psychological interventions (eg, psychodynamic therapy, cognitive–behavioural therapy, or mentalisation-based therapy) for any type of psychiatric disorder published in 2017 or 2018 on the websites of six high-journal impact factor psychiatric journals:

- *World Psychiatry*: https://www.wpanet.org/english.

**Box 1 How to blind key persons in randomised clinical trials of psychological interventions**

**Blinding of trial participants and treatment providers (performance bias)**

Trial participants and treatment providers are more difficult to blind in randomised clinical trials of psychological interventions compared with pharmacological trials, which typically achieve blinding with matching placebo pills.[95 106] However, there is evidence that most participants and treatment providers in pharmacological trials break blind.[107 108] Despite the obvious challenges of implementing blinding procedures for participants and treatment providers, it is theoretically and perhaps also practically possible to blind both participants and treatment providers in randomised clinical trials of psychological interventions. Motivated potential therapists who have no or limited knowledge about psychotherapy could be trained and supervised in psychotherapy techniques without knowing the exact type of psychotherapy, and participants with no prior experience with psychotherapy may be kept blinded throughout the trial if they are not informed about the specific therapy (the name of the psychotherapy tradition, etc). However, it is plausible that blinding of participants and treatment providers will compromise the effects of the active ingredients of the psychological intervention. Effective delivery of a particular psychological intervention may require extensive training, which would be difficult to implement with the blinding intact.

**Blinding of outcome assessors (detection bias)**

In randomised clinical trials of psychological interventions, implementing efficient blinding procedures for outcome assessors is relatively simple; non-blinded participants may be instructed to withhold information about allocation status when assessed by an independent assessor.[18] Efforts to avoid unblinding furthermore include locating the outcome assessors separately from treatment providers, and to assign new outcome assessors in cases of unintentional unblinding.

Whenever psychological trials deal with effects on participant-reported outcomes (eg, symptoms, mood, quality of life), the interpretation of potential intervention effects becomes marred with lack of blinding, because the participant, who is often unblinded, is the outcome assessor.

**Blinding of data managers**

Blinding of data managers can be achieved by having blinded research personnel handle data entry, data coding and data cleaning. When data are collected in paper participant report forms (PRFs), transferring of data from paper to the electronic database should be performed by blinded research personnel, and data should then be validated by double entry. When using electronic PRFs, blinded data entry can be achieved by having blinded outcome assessors enter data directly

Continued

**Box 1 Continued**

into the electronic database, for example, while interviewing the participant. Once data collection is complete, the coding and cleaning of data should be performed with intervention groups concealed from the data manager.

**Blinding of the data safety and monitoring committee**
The data safety and monitoring committee should receive a blinded data set on a prespecified time point during data collection and based on the results of the interim analyses decide if the trial should stop or carry on. The data safety and monitoring committee may request unblinded data throughout the trial period, but the initial data analyses should be blinded to protect against bias in decision-making.

**Blinding of statisticians**
Bias may also be introduced during the statistical analysis of the trial results through the selective use and reporting of statistical tests.[109] This may be a conscious or unconscious process spurred by trialists or statisticians eager to see a certain result.[16] The best method to avoid this potential bias is first to publish a detailed statistical analysis plan before the analyses begin along with a protocol predefining the trial methodology in detail. Second, the statistician should be kept blinded until the entire statistical analysis has been completed.[110] The statistician should receive data from the data manager with the intervention groups concealed as, for example, 'A' and 'B' and should perform the predefined analyses while the blinding is intact.

**Blinding of conclusion makers**
Blinding of conclusion makers can be done by having the trial steering committee receiving blinded statistical analyses from the blinded statistician with interventions coded as, for example, A and B. The steering committee should then write and agree on two abstracts: one based on the assumption that the experimental intervention is 'A', and another based on the assumption that the experimental intervention is 'B'. Once the steering committee has written and agreed on the two abstracts, the blinding may be broken.[110 111] This procedure could reduce the likelihood of post-hoc rationalisation of results in any trial not limited to psychological interventions.

- *JAMA Psychiatry*: https://jamanetwork.com/journals/jamapsychiatry.
- *American Journal of Psychiatry*: https://ajp.psychiatryonline.org/.
- *British Journal of Psychiatry*: https://www.cambridge.org/core/journals/the-british-journal-of-psychiatry.
- *Lancet Psychiatry*: https://www.thelancet.com/journals/lanpsy/home.
- *Psychotherapy and Psychosomatics*: https://www.karger.com/Journal/Home/223864.

We chose these peer-reviewed journals due to their high impact factor (ranging from 7.2 to 34.0 in Web of Science for the year 2018). The time period was chosen randomly to provide an overview of the current practise. The two investigators (SJ, FWF) independently screened titles and abstracts for the two selected publication years. Full texts were retrieved for all trial reports if these were judged to be eligible, or if further information were needed to assess eligibility. Any discrepancies were resolved through discussion or, if required, through discussion with a third investigator (JCJ).

### Eligibility criteria

We included any randomised clinical trial (as defined by trialists) assessing the effects of psychological interventions for any psychiatric disorder, that is, we included (1) trials comparing two or more psychological interventions with each other, (2) trials comparing psychological interventions with non-psychological interventions (eg, drugs, no intervention, or wait-list), and (3) trials assessing the effects of a psychological intervention without a treatment provider (eg, virtual reality exposure therapy with virtual therapists or computerised cognitive–behavioural therapy). In the latter group of trials, the domain 'blinding of treatment providers' was classified as 'not applicable'.

### Data extraction

Two independent investigators (SJ, FWF) extracted data and performed risk-of-bias assessments. Any disagreements were resolved through discussion or, if required, they consulted a third investigator (JCJ). For each trial, we extracted if the following key persons were described as blinded to treatment allocation: (1) participants; (2) treatment providers; (3) outcome assessors (for the primary outcome); (4) data managers; (5) the data safety and monitoring committee; (6) statisticians; and (7) conclusion makers. We also extracted if trialists rejected the null hypothesis when reporting results on their primary outcome(s) at maximum follow-up, and if trialists discussed the potential bias risk from lack of blinding of the psychological intervention in the published report. Both the published trial reports and any online supplemental materials were used for data extraction.

### Assessment of risk of bias in included trials

For each key person, risk of bias was evaluated using the following criteria:

- *Low risk of bias*: if it was mentioned that the key person was blinded, and this was sufficiently described.
- *Uncertain risk of bias*: if it was not mentioned if the key person in the trial was blinded or the blinding procedures were insufficiently described.
- *High risk of bias*: if no blinding or incomplete blinding of the key person was described.

### Statistical analysis

Descriptive data were summarised as proportions with 95% CIs using Stata V.16[21] command 'prtest' using the Wilson method.[22] The CI refers to the level of uncertainty. The 95% CI represents that in a hypothetical indefinite data collection, the interval estimate will contain the true value in 95% of the samples.

### Patient and public involvement

Patients and members of the public were not involved in this research because it was designed to answer a methodological challenge that was not directly dependent on patient priorities or experiences. The methodological expertise required to plan the study, analyse the results and write the manuscript was dependent on specialist knowledge. Hence, we did not try to identify patients

or members of the public with these specialties for cooperation on this manuscript.

## Results

A total of 63 randomised clinical trials of psychological interventions were identified.[23–85] Characteristics of the included trials may be found in online supplemental file 2. An overview of results can be found in tables 1 and 2.

### Blinding of all possible parties

None (0%; 95% CI 0% to 5.75%) of the identified trials reported blinding of all possible parties, that is, the 'true' proportion of trials with blinding of all possible parties is probably between 0% and 5.75%.

### Blinding of participants

Two (3.2%; 95% CI 0.87% to 10.86%) of the 63 trials reported adequate blinding of participants[24 67] (table 1). One trial compared the effects of internet-delivered cognitive–behavioural therapy with internet patient education.[24] There were no treatment providers involved. The other trial compared the effects of gaze-contingent versus gaze-non-contingent music reward therapy.[67] In both trials, participants were blinded to their allocated intervention, as they theoretically could not distinguish the experimental condition from the control. The remaining trials either did not adequately report if blinding of participants was performed and the bias risk was then rated as 'unclear', or they reported that participants were unblinded and the bias risk for was then rated as 'high'.

### Blinding of treatment providers

None (0%; 95% CI 0% to 5.83%) of the 62 applicable trials reported blinding of treatment providers (table 1). One trial was not applicable for assessment in this domain, as both interventions were purely internet delivered, and thus did not have any treatment providers.[24] The remaining trials either did not adequately report if blinding of treatment providers was performed, and the bias risk was then rated as unclear, or they reported that treatment providers were unblinded, and the bias risk for was then rated as high.

### Blinding of outcome assessors

37 (58.7%; 95% CI 46.42% to 70.04%) of the 63 trials reported adequate blinding of outcome assessors on the primary outcome (table 1). The remaining trials either did not adequately report if blinding of outcome assessors was performed, and the bias risk was then rated as unclear, or they reported that outcome assessors were unblinded, and the bias risk for was then rated as high. When the primary outcome was purely participant reported, the risk of bias was equivalent to the risk of bias for the participant domain, for example, the outcome assessor domain was assessed as high, if the participant was unblinded while filling in the questionnaire. If trialists assessed more than one primary outcome, and these were assessed at different risks of bias, we chose the primary outcome with the highest risk of bias.

### Blinding of data managers

Two (3.2%; 95% CI 0.87% to 10.86%) of the 63 trials reported adequate blinding of data managers[48 62] (table 1). One trial reported that: "[d]ata coding, data entry, and data cleaning were done by individuals masked to treatment allocation".[48] The other trial reported that "…data managers were masked to study allocation".[62] Two trials reported that the data manager was unblinded.[68 81] The

**Table 1** Risk-of-bias assessment of blinding status in 63 randomised clinical trials of psychological interventions

| | Participants (n=63) | Treatment providers (n=62)* | Outcome assessors (n=63) | Data managers (n=63) | Data Safety and Monitoring Committee (n=20)† | Statisticians (n=63) | Conclusion makers (n=63) |
|---|---|---|---|---|---|---|---|
| Number of trials at low risk of bias | 2 (3.2%; 95% CI† 0.87% to 10.86%) | 0 (0%; 95% CI 0% to 5.83%) | 37 (58.7%; 95% CI 46.42% to 70.04%) | 2 (3.2%; 95% CI 0.87% to 10.86%) | 0 (0%; 95% CI 0% to 16.11%) | 3 (4.8%; 95% CI 1.63% to 13.09%) | 0 (0%; 95% CI 0% to 5.75%) |
| Number of trials at unclear risk of bias | 21 (33.3%; 95% CI 22.95% to 45.63%) | 29 (46.8%; 95% CI 34.91% to 59.02%) | 9 (14.3%; 95% CI 7.7% to 24.97%) | 59 (93.7%; 95% CI 84.78% to 97.50%) | 20 (100%; 95% CI 83.89% to 1%) | 57 (90.5%; 95% CI 80.74% to 95.56%) | 62 (98.4%; 95% CI 91.54% to 99.72%) |
| Number of trials at high risk of bias | 40 (63.5%; 95% CI 51.15% to 74.28%) | 33 (53.2%; 95% CI 40.98% to 65.09%) | 17 (27.0%; 95% CI 17.58% to 39.03%) | 2 (3.2%; 95% CI 0.87% to 10.86%) | 0 (0%; 95% CI 0% to 16.11%) | 3 (4.8%; 95% CI 1.63% to 13.09%) | 1 (1.6%; 95% CI 0.28% to 8.46%) |

*One trial was not eligible for assessment, as the interventions were computer delivered and thus did not include any treatment providers.
†Forty-three trials were not eligible for assessment, as they did not include a data safety and monitoring committee.

Table 2 Handling of results in non-blinded trials

| | Rejection of null hypothesis (n=63) | Discussion of bias risk in published report (n=63) |
|---|---|---|
| Number of trials | 45 (71.4%; 95% CI 59.30% to 81.10%) | 13 (20.6%; 95% CI 12.48% to 32.17%) |

bias risk for this domain was then rated as high. The remaining trials did not mention if blinding of data managers was performed and the bias risk was then rated as unclear.

### Blinding of the data safety and monitoring committee

None (0%; 95% CI 0% to 16.11%) of the 20 eligible trials reported blinding of the data safety and monitoring committee (table 1). Forty-three trials were not eligible for assessment in this domain, as they did not include a data safety and monitoring committee. In the 20 eligible trials, the blinding status of the data safety and monitoring committee was not described and the bias risk was then rated as unclear.

### Blinding of statisticians

Three (4.8%; 95% CI 1.63% to 13.09%) of the 63 trials reported adequate blinding of statisticians during data analysis[25 76 81] (table 1). One trial reported that "[i]ndependent statisticians analysing the results were masked to group for the initial analyses".[76] The second trial reported that "The research assistant for data analysis was blinded in respect of the group allocation results".[81] The third trial reported that "the trial statistician was blinded to the allocated treatments during the analysis of the primary outcome".[25] Three trials reported that the statistician was unblinded while analysing data.[34 39 47] The bias risk for this domain was then rated as high. The remaining trials did not mention if blinding of statisticians was performed during data analysis, and the bias risk was then rated as unclear.

### Blinding of conclusion makers

None (0%; 95% CI 0% to 5.75%) of the 63 trials reported adequate blinding of conclusion makers (table 1). One trial reported that interpretation of results was performed on unmasked data.[40] The bias risk for this domain was then rated as high. The remaining trials did not mention if blinding of conclusion makers was performed, and the bias risk was then rated as unclear.

### Rejection of null hypothesis

Forty-five (71.4%; 95% CI 59.30% to 81.10%) of the 63 trials rejected the null hypothesis on the primary outcome(s), meaning that statistical superiority of the experimental intervention was found in a superiority trial, equivalence was found in equivalence trials and non-inferiority was found in non-inferiority trials (table 2). We assessed a rejection of the null hypothesis if the trialists rejected the null hypothesis on at least one of the primary outcomes. In 67.5% of the trials that blinded the outcome assessor, the null hypothesis was rejected on the primary outcome. In 76.9% of the trials that did not blind the outcome assessor, or where the blinding status of the outcome assessor was unclear, the null hypothesis was rejected on the primary outcome.

### Discussion of bias risk due to lack of blinding in the published trial report

Thirteen (20.6%; 95% CI 12.48% to 32.17%) of the 63 trials discussed the potential bias risk from lack of blinding in the published trial report[24 25 29 31 39 49 56 57 60 62 67 70 84] (table 2). Seven trials discussed the bias risk from lack of participant blinding.[24 25 31 49 56 60 67] Two trials discussed the bias risk from lack of therapist blinding.[29 84] Two trials discussed the bias risk from lack of outcome assessor blinding.[57 70] One trial discussed the bias risk from lack of researcher blinding.[39] One trial discussed the bias risk from lack of 'full blinding'.[62]

## Discussion

Blinding of all possible key persons is rarely reported as adequate in randomised clinical trials of psychological interventions. Some key persons are more frequently blinded than others. In the present study of trials published in high impact factor journals, 58.7% of the included trials reported adequate blinding of outcome assessors. Participants, treatment providers, data managers, the data safety and monitoring committee, statisticians and conclusion makers were typically either not blinded (high risk of bias) or it was unclear whether blinding was performed (unclear risk of bias). However, it may be inappropriate to assume inadequate blinding merely based on inadequate reporting. Several studies indicate that trialists often do not report blinding procedures even when such procedures have been adequately implemented.[86–88] Nevertheless, accurate reporting of blinding efforts and discussions of lack of blinding may reduce the risk of biased conclusions. In the present study, only 20.6% of the trials discussed the potential bias risk from unsuccessful or lack of blinding in the published trial report. This makes it difficult for readers to judge the quality of the research. 71.4% of the trials rejected their null hypothesis on their primary outcome. Considering our findings, there is a risk that previous randomised clinical trials of psychological interventions may have overestimated the beneficial effects and underestimated the harmful effects of the experimental interventions being studied due to bias risks associated with lack of blinding.[2–9] There may be reasons to believe that unblinded trial key persons may, consciously or unconsciously, fail to acknowledge harmful effects of the interventions. A non-blinded trial person who has a certain interest in a result, for example a psychotherapist with many years of experience and expertise in a given psychological intervention, might give less attention to harmful effects because of his or hers underlying beliefs. Likewise, an unblinded participant who is told that the psychological intervention is effective and without any harms might either not register or fail to report harmful effects.

The present study has limitations. First, we did not publish a protocol and a statistical analysis plan prior to this retrospective study of published trial reports. Second, we may have missed important trials with sufficient blinding due to our selection of journals. However, journals with high journal impact factor are known to have lower risks of bias compared to journals with lower journal impact factor.[89 90] Hence, there is a possibility that the included trials from the selected journals may have underestimated the true bias risk arising from lack of blinding, and that blinding is in fact even less frequently performed or reported if trials from journals with lower journal impact factor had also been included. Third, we only looked at psychological interventions although other intervention areas (eg, pharmacological interventions) may have comparable problems with blinding.

It may be argued that it is difficult or impossible to blind all relevant key persons in a randomised clinical trial. In pharmacological trials, participants may experience adverse events (or lack of adverse events) which may break their blinding.[91–94] In non-pharmacological trials, for example, surgical trials, it is challenging to perform sham interventions for blinding purposes.[95–97] Nevertheless, blinding of all possible key persons have been attempted in previous trials.[98 99] It is possible that the blinding of some of

the key persons in these trials was not successful, but adequate blinding was attempted. It has been debated whether it may be possible to test the success of blinding by having, for example, the outcome assessors guess the participant's allocated intervention on completion of the assessment interview.[94 100 101] However, it is generally recommended *not* to assess whether blinding procedures were successful, because these tests lack validity, as they cannot distinguish blindness from hunches about harms, adverse effects or efficacy.[92 100 102]

Whether or not blinding of participants and treatment providers is a bias risk that needs to be controlled for in randomised clinical trials of psychological interventions must be discussed. In trials investigating psychotherapy (as opposed to drug trials), it is argued that it is redundant to control for self-confirming response expectancies, given that expectancy change is a legitimate, potentially effective psychological variable.[103–105] For example, changing expectations is a core feature of cognitive–behavioural therapy. Thus, one could argue that it would be counterproductive to attempt adequate blinding of participants and treatment providers, as it would diminish the effective ingredients of the interventions being studied. Furthermore, there would be substantial practical problems in such trial, as it would require training of motivated potential therapists with no or limited prior experience in psychotherapy, who would then deliver the intervention without knowing the exact type of psychotherapy tradition while maintaining blinding. Likewise, it would require recruitment of participants with no prior experience and knowledge of psychotherapy traditions.

Despite this apparent obstacle, one could argue that it is appropriate to expect bias due to non-blinded participants. Research in non-psychological interventions has demonstrated that non-blinded participants may experience and report symptoms differently from blinded ones, because of response bias (when participants report symptoms according to what they think will please the investigators) and because of positive response expectancy from receiving a treatment considered to be superior.[1 103 104] In a randomised clinical trial, this could result in participants (consciously or unconsciously) giving exaggerated reports of symptom relief merely because the treatment providers or outcome assessors are perceived as caring and interested in their well-being. It may also produce accurate reports of greater symptom relief, because of self-confirming response expectancies.[103] A systematic review found that non-blinded participants generated more optimistic self-reported estimates of intervention effects compared with blinded ones.[7] There is no reason to believe, that these processes would not also translate to randomised clinical trials of psychological interventions. Non-blinded participants in psychological trials may, for example, search the internet for information about the psychological intervention they receive, which may influence their outcomes, because they develop an allegiance to the specific psychological tradition. This can become particularly challenging in the case of participant-reported outcomes, for example, symptoms or quality of life, where the participant is also the outcome assessor.[18]

In randomised clinical trials of psychological interventions, it may also be appropriate to expect bias due to non-blinded treatment providers.[1] Therapists are often highly trained and supervised in delivering a specific psychological intervention, and they will then probably expect this intervention to be superior to treatment as usual given their personal investment. This expectation may influence the participants' outcomes, if the therapists disclose their allegiance to the participants. It may even influence the participants' outcomes even if the therapists do not disclose their allegiance, given that expectation of improvement can alter therapists' behaviours in ways that alter the effectiveness of the treatment.

It is possible to design a psychotherapy trial attempting to blind participants and treatment providers. The first step would be to randomise motivated potential therapists with no or limited knowledge of psychotherapy to receive either blinded or non-blinded training and supervision and subsequently deliver blinded or non-blinded psychotherapy. If the number of therapists is high enough, it will be possible to assess if attempts of blinded psychotherapy would yield different intervention effects compared with psychotherapy delivered by non-blinded therapists, and hence whether attempting blinding of therapists and participants compromises the active ingredients of psychotherapy. If no evidence of a difference is found, the second step would be to design a randomised clinical trial in which two psychotherapy traditions were compared with attempts of blinding of all possible key persons. Of course, such trial would have limitations, for example, effective delivery of the psychological intervention would potentially require extensive training of the therapists, which would be difficult to implement within a trial period while keeping the blinding intact. Thus, there would be a risk that the lower amount of training would reduce generalisability of the findings. Recruiting participants with no or limited knowledge and experience about psychological interventions could also reduce generalisability. Furthermore, the proposed methods to blind the participants could theoretically work only in trials with an 'active' control group. If the control group is standard care, there would be a risk that the participants would recognise the provided care from previous experience. Nevertheless, it may be argued that the benefits in terms of complete blinding may not exceed the limitations arising from low generalisability. Until evidence has shown that blinding does not significantly affect the results, we believe that blinding of all possible parties should ideally be attempted in randomised clinical trials of psychological interventions.

## Conclusions

Blinding of key persons involved is rarely documented in randomised clinical trials of psychological interventions, and only few trialists consider the bias risk this may have caused in trials published in high impact factor journals. Therefore, there is a risk that previous randomised clinical trials of psychological interventions generally may have overestimated the beneficial effects and underestimated the harmful effects of the experimental interventions being studied. There is a need of randomised clinical trials assessing the effects of psychological interventions with attempts of blinding of all possible key persons. If blinding is not possible to implement, or is not adequately reported, readers should consider the possible implications when interpreting the trial results. Future randomised clinical trials of psychological interventions should improve implementation and reporting of blinding status, particularly of trial persons who are easily blinded, that is, data managers, the data safety and monitoring committee, statisticians and conclusion makers.

**Contributors** SJ, CG, and JCJ initiated the study and wrote the first manuscript draft. SJ and FWF independently retrieved relevant trial reports from the selected databases, performed risk of bias assessments, and statistical analyses with ongoing supervision from CG, SS, IK, and JCJ. All authors read, commented on and approved the final manuscript.

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