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SAS macro programme for Bang's Blinding Index to assess and visualise the success of blinding in randomised controlled trials

Zongshi Qin ,[1] Yongpei Yu,[1] Hongqiu Gu,[2] Dongdong Shi,[3] Zhen Wang ,[3] Jiani Wu,[4] Toshiaki Furukawa,[5] Yangfeng Wu[1]

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For numbered affiliations see end of article.

Correspondence to
Professor Jiani Wu;
jiani_wu@aliyun.com

Professor Toshiaki Furukawa;
furukawa@kuhp.kyoto-u.ac.jp

Professor Yangfeng Wu;
wuyf@bjmu.edu.cn

ABSTRACT

This paper aims to present a Statistical Analysis Software (SAS) macro %BBIplus, offering estimation and visualisation methods for the Bang's Blinding Index (BBI) for randomised controlled trials (RCTs) with various designs. We developed the SAS macro programme %BBIplus to facilitate the implementation of BBI. This user-friendly programme allows for easy and rapid estimation and visualisation of BBI across different scenarios, including pairwise comparison RCTs with two arms, double-dummy design RCTs with three arms and factorial design RCTs with four arms. The programme requires no pre-existing data set, and users only need to input the number of individuals of correct, uncertain or wrong guesses in each intervention or control group. We illustrate the functionality of %BBIplus using blinding assessment data from three previously published RCTs: BBR (adjunctive berberine reduces antipsychotic-associated weight gain and metabolic syndrome in patients with schizophrenia: a randomised controlled trial), SELECT-TDCS (the sertraline versus electrical current therapy for treating depression clinical study: results from a factorial, randomised controlled trial) and ELECT-TDCS (trial of electrical direct-current therapy versus escitalopram for depression) studies. The programme estimates the BBI for each arm, providing point estimates, 95% CI and associated p values. Additionally, %BBIplus can visualise the estimations through forest plots and make the judgement for the success of blinding easily and rapidly. This tool caters to the needs of clinical trial investigators, offering a comprehensive solution for estimating and visualising the blinding index under various RCT designs.

INTRODUCTION

Randomised controlled trials (RCTs) with double-blinding are considered the gold standard in clinical research, offering a robust framework to assess the efficacy of interventions. Within the RCT procedure, blinding plays a vital role in minimising biases, especially in trials using patient-reported outcome measures. Without proper blinding, the effect of interventions may be prone to overestimation.[1] Effective blinding ensures that observed outcomes can be attributed solely to the intervention, mitigating preconceived expectations or biases.

Despite the critical role of blinding, systematic reviews and meta-analyses have indicated a lack of reporting and assessment of blinding in RCTs.[2–5] Traditional methods of blinding assessment, such as participant or investigator questionnaires, are subjective and susceptible to biases. Existing statistical methods, such as χ^2, basically test the independence of two variables (guesses and assignments); they provide p values for statistical testing but not a numerical measure of blinding itself. Kappa statistics measure agreement rather than disagreement, which makes it hard to judge whether the blinding is successful. Recognising the need for more rigorous evaluation, quantitative measures are encouraged.[6] The Bang Blinding Index (BBI), introduced by Bang, presents a quantitative measure for assessing blinding success.[7] It incorporates participants' correct and incorrect guesses, along with uncertainties in making the guess. BBI offers an objective means for researchers to assess the success of blinding, enhancing the validity of trial results.[8 9] Although BBI is increasingly applied in the blinding assessment of RCTs, its application can be challenging due to its lack of being a visualisation-friendly tool, leading to misinterpretations in the results of blinding assessments. Herein, we introduce a Statistical Analysis Software (SAS macro, %BBIplus, designed for efficient and customisable BBI calculations. It offers an update to visualisation for BBI calculation and expands to accommodate multiple group designs with illustrative examples.[3 10 11]

METHODS

The assumptions of BBI

The primary purpose of BBI is to quantitatively evaluate the effectiveness of blinding. BBI assumes that in the absence of any unblinding, participants will guess their treatment group at random. For instance, in a two-arm trial (treatment vs placebo), participants would have a 50% chance of guessing correctly purely by chance. The assumption also implies that each participant's guess is independent of others' guesses. This means that the blinding effectiveness is evaluated based on individual guesses without considering potential patterns or correlations between different participants' guesses. If the blinding is effective, the proportion of correct guesses should align closely with the expected proportion under random guessing. A higher-than-expected proportion of correct guesses suggests potential unblinding, meaning participants might have received cues or information that helped them correctly identify their treatment allocation. Conversely, a lower-than-expected proportion of correct guesses could indicate systematic bias or misinformation.

Estimation of BBI

	True arm	
Guessed	Treatment	Control
Treatment	N_{11}	N_{21}
Control	N_{12}	N_{22}
Do not know	N_{13}	N_{23}

$$\widehat{BBI_n} = (2\widehat{r_{n|n}} - 1) \times \left(\frac{N_{n1}+N_{n2}}{N_{n1}+N_{n2}+N_{n3}}\right)$$

Where

$$\widehat{r_{n|n}} = \frac{N_{nn}}{N_{n1}+N_{n2}}$$

As a statistical measure designed to assess the success of blinding in clinical trials, the estimation of BBI has been previously described in detail.[7] In short, the BBI estimates the proportion of individuals who guess their treatment assignment correctly in the n^{th} treatment arm. Each arm of a trial will, therefore, have its own BBI value, which is a continuous value and takes on a value between −1 and 1. If the BBI equals 1, it means that all responses are correct, and complete unblinding is inferred. If the BBI equals −1, then all responses are incorrect, and complete blinding is inferred, although this may indicate unblinding in the opposite direction (eg, opposite guessing). If the BBI equals 0, then half of the guesses are correct and half of the guesses are incorrect, inferring random guessing. In general, if the BBI takes on value from −0.2 to 0.2, blinding is considered to be successful. Unblinding (or opposite guessing) may be claimed if the relevant limit of the 95% CI does not cover 0.

Parameter input for %BBIplus

The %BBIplus macro comprises three distinct modules: %BBI2, %BBI3 and %BBI4. Each module is tailored to handle specific scenarios, with %BBI2 designed for two-arm studies, %BBI3 for three-arm studies and %BBI4 for four-arm studies. The environment for this macro is based on SAS V.9.4 (SAS Institute, Cary, North Carolina, USA). The SAS code used in this study is provided as supplementary material (see online supplemental files 1, 2). Table 1 outlines the diverse scenarios covered by this macro, accommodating cases and methodologies involving two or more groups. The flexibility of the %BBIplus macro allows users to specify the data frame based on the unique characteristics of their study design. The key parameters of the macro are summarised in table 2.

Creating contingency tables

To create a contingency table, we will employ the SAS software Freq procedure to create the R × C table, with the true arm (Row) listed on the top of the table and the guessed intervention (Column) listed on the left of the table. This step simply creates the contingency table for the descriptive data, including the number of people and the proportion of each cell.

Estimating the p value for each arm

This assumption was tested and confirmed in SAS by using the SAS software CDF (Cumulative Distribution Function), which calculates the cumulative probability under the binomial distribution. Under this assumption, a comparison was made between the subjects' guesses

Table 1 Supported scenarios by %BBIplus

Macro	Design	Arms	Scenario
%BBI2	Pairwise comparison	2	Group 1: berberine Group 2: placebo[10]
%BBI3	Double dummy	3	Group 1: escitalopram+sham tDCS Group 2: active tDCS+placebo Group 3: placebo plus sham tDCS[11]
%BBI4	Factorial	4	Group 1: sham tDCS+placebo Group 2: sham tDCS+sertraline Group 3: active tDCS+placebo Group 4: active tDCS+sertraline[12]

tDCS, transcranial direct-current stimulation

Table 2 Parameters required by %BBIpl

Parameter	Description
AR	People who were allocated to A group and Rightly guess
AW	People who were allocated to A group and Wrongly guess
AU	People who were allocated to A group and chose Unknown
A_{all}	Sum of AR, AW and AU
BR	People who were allocated to B group and Rightly guess
BW	People who were allocated to B group and Wrongly guess
BU	People who were allocated to B group and chose Unknown
B_{all}	Sum of BR, BW and BU
CR	People who were allocated to C group and Rightly guess
CW	People who were allocated to C group and Wrongly guess
CU	People who were allocated to C group and chose Unknown
C_{all}	Sum of CR, CW and CU
DR	People who were allocated to D group and Rightly guess
DW	People who were allocated to D group and Wrongly guess
DU	People who were allocated to D group and chose Unknown
D_{all}	Sum of DR, DW and DU

and the null hypothesis that the trial was successfully blinded (BBI = 0). A one-tailed test was employed to evaluate the statistical significance of BBI, as the hypothesis assumes a directional effect, specifically testing whether the observed BBI deviates significantly in the direction indicating unblinding.

Visualisation

To visualise the results, we will employ the SAS software SGPLOT procedure to illustrate the BBI and its 95% CI by using the forest plot. A forest plot arrays BBIs and 95% CIs for multiple arms. A vertical reference line (x=0) is typically plotted at the null hypothesis, with the statistical significance of an individual point and whiskers compared with that reference line. The 95% CI for herein estimated BBI is two-sided. To intuitively understand the blinding feasibility progression, a traffic light system was employed in the plots. Here, the BBI falling within the range of −0.2 to 0.2 is depicted in green, indicating a successful blinding. BBI falling within the ranges of −0.3 to −0.2 and 0.2 to 0.3 are represented in yellow, indicating an acceptable blinding status. BBI falling within −1.0 to −0.3 and 0.3 to 1.0 are represented in red, indicating a failure blinding.

Table 3 Responses of assessment of blinding in the BBR study

	True arm		
Guessed, n (%)	Berberine	Placebo	Total
Berberine	7 (9.2)	9 (11.8)	16 (21.1)
Placebo	8 (10.5)	12 (15.8)	20 (26.3)
Unknown	22 (28.9)	18 (23.7)	40 (52.6)
Total	37 (48.7)	39 (51.3)	76 (100)

BBR, adjunctive berberine reduces antipsychotic-associated weight gain and metabolic syndrome in patients with schizophrenia: a randomised controlled trial.

EXAMPLES

The BBR study as an example of the two-arm design of RCT

BBR (adjunctive berberine reduces antipsychotic-associated weight gain and metabolic syndrome in patients with schizophrenia: a randomised controlled trial) study is a two-arm RCT comparing berberine with placebo for patients with schizophrenia suffering from a metabolic syndrome. A total of 120 patients were randomly allocated to two groups: the berberine group and the placebo group.[10] To assess the success of blinding, patients were asked to guess whether they had received berberine or placebo after treatment in week 12. The responses of participants are summarised in table 3. Overall, 76 (63.3%) participants responded to the credibility assessment question. Among them, 40 (52.6%) participants were unsure of their treatment allocation; 7 (9.2%) participants in the berberine group and 12 (15.8%) participants in the placebo group believed that they received berberine treatment. The Blinding Index (BI) for the berberine group (Arm 1) was estimated to be −0.03 (95% CI −0.20 to 0.15, p=0.602), while the BI for the placebo group (Arm 2) was 0.08 (95% CI −0.12 to 0.27, p=0.255). These results indicate the successful blinding of both groups, as the BIs fall within the range (−0.2 to 0.2), suggesting that participants' guesses align with random chance and supporting the credibility of the blinding procedure for both treatment arms. Figure 1 illustrates the forest plot depicting the BBIs and their corresponding 95% CIs for the two arms in the BBR study.

The ELECT-TDCS study as an example of the three-arm design of RCT

The ELECT-TDCS (trial of electrical direct-current therapy versus escitalopram for depression) study compared the efficacy of transcranial direct current stimulation (tDCS) with that of the selective serotonin-reuptake inhibitor escitalopram in patients with major depressive disorder.[11] A total of 245 patients underwent randomisation, with 91 being assigned to escitalopram plus sham tDCS, 94 to active tDCS plus placebo and 60 to placebo plus sham tDCS. To assess the integrity of trial-group blinding, patients were asked to guess which intervention they had received. The responses of participants are summarised in table 4. Regarding the level of active tDCS

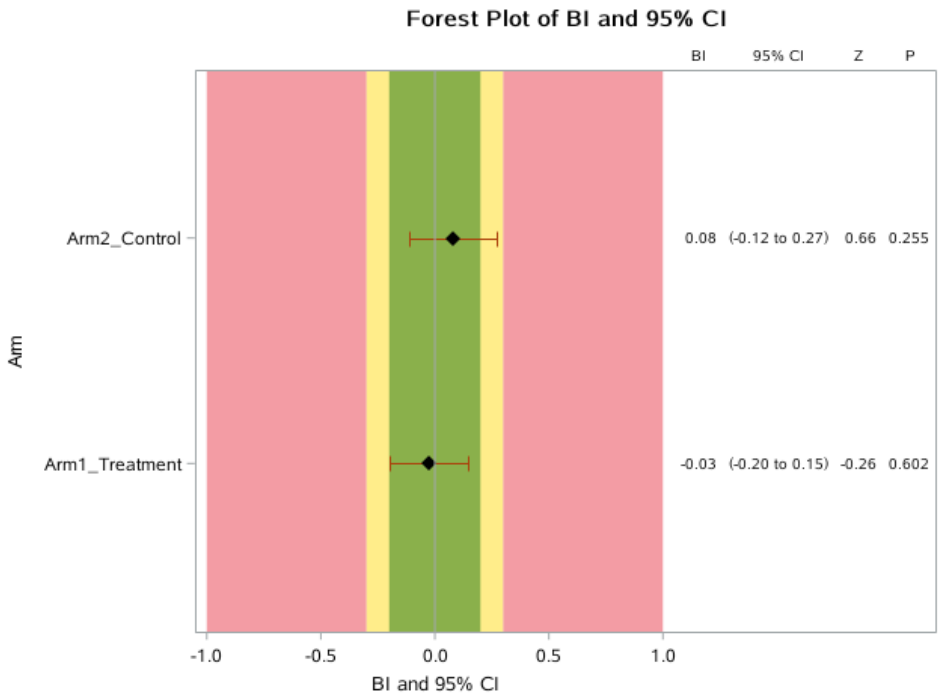

Figure 1 The forest plot of BBIs and their 95% CIs for two arms in the BBR study. The green, yellow and red margins represent successful, acceptable and unsuccessful blinding, respectively. The diamond marks the BBI, and the error bars show the 95% CI for each BBI. Both BIs for Arm 1 (–0.03) and Arm 2 (0.08) are close to 0, indicating successful blinding in both arms. BBI, Bang's Blinding Index; BBR, adjunctive berberine reduces antipsychotic-associated weight gain and metabolic syndrome in patients with schizophrenia: a randomised controlled trial; BI, Blinding Index.

versus sham tDCS, the BI for the placebo plus active tDCS group (Arm 1) is 0.08 (95% CI –0.15 to 0.30, p=0.289) and the BI for the escitalopram plus sham tDCS group (Arm 2) is 0.00 (95% CI –0.19 to 0.19, p=0.500), and the BI for the placebo plus sham tDCS group (Arm 3) is –0.26 (95% CI –0.45 to –0.07, p=0.989). The blinding success for level 1 in this RCT can be accepted overall; it showed that subjects in Arm 3 (placebo plus sham tDCS) are slightly more likely to report they received the active tDCS, but this tendency was within chance variation. Regarding the level of escitalopram versus placebo, the BI for the placebo plus active tDCS group (Arm 1) is 0.62 (95% CI 0.45 to 0.80, p<0.001) and the BI for the escitalopram plus sham tDCS group (Arm 2) is –0.06 (95% CI –0.25 to 0.14, p=0.682), and the BI for the placebo plus sham tDCS group (Arm 3) is 0.56 (95% CI 0.40 to 0.72, p<0.001). This finding indicates for Arm 1 and Arm 3 in level 2, the subjects tend to be unblinded, with people receiving the placebo correctly guessing that they received the placebo.

Table 4 Responses of assessment of blinding in the ELECT-TDCS study

	True arm			
Guessed, n (%)	Placebo+tDCS	Escitalopram+sham tDCS	Placebo+sham tDCS	Total
Level 1: active tDCS versus sham tDCS				
Active tDCS	28 (14.2)	36 (18.3)	46 (23.4)	110 (55.8)
Sham tDCS	24 (12.2)	36 (18.3)	27 (13.7)	87 (44.2)
Unknown	NA	NA	NA	NA
Total	52 (26.4)	72 (36.5)	73 (37.1)	197 (100)
Level 2: escitalopram versus placebo				
Placebo	43 (21.7)	38 (19.2)	57 (28.8)	138 (69.7)
Escitalopram	10 (5.1)	34 (17.2)	16 (8.1)	60 (30.3)
Unknown	NA	NA	NA	NA
Total	53 (26.8)	72 (36.4)	73 (36.9)	198 (100)

ELECT-TDCS, trial of electrical direct-current therapy versus escitalopram for depression; NA, not applicable; tDCS, transcranial direct-current stimulation.

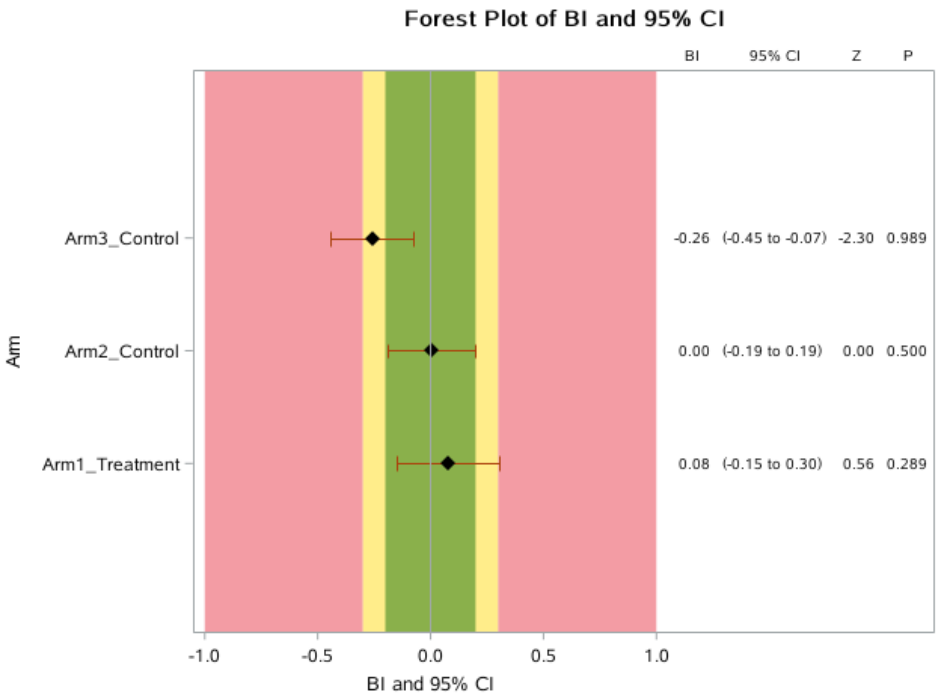

Figure 2 The forest plot of BBIs and 95% CIs of the three arms for level 1 (tDCS vs sham tDCS) in the ELECT-TDCS study. The green, yellow and red margins represent successful, acceptable and unsuccessful blinding, respectively. The diamond marks the BBI, and the error bars show the 95% CI for each BBI. In the non-pharmacological intervention level (active tDCS vs sham tDCS, see table 4), the BIs for Arm 1 and Arm 2 are close to 0, indicating successful blinding in these two arms. The negative BI (–0.26) for Arm 3 suggests an opposite guess by the participants, but it is still considered acceptable. BBI, Bang's Blinding Index; BI, Blinding Index; ELECT-TDCS, trial of electrical direct-current therapy versus escitalopram for depression; tDCS, transcranial direct current stimulation.

Figures 2 and 3 illustrate the forest plot depicting the BBIs and their corresponding 95% CIs for the three arms in the BBR study.

The SELECT-TDCS study as an example of the four-arm design of RCT

The SELECT-TDCS (the sertraline versus electrical current therapy for treating depression clinical study: results from a factorial, randomised controlled trial) study is a factorial, randomised controlled trial in which 120 patients were randomised using a 2×2 design to sertraline/placebo and active/sham tDCS, constituting four groups: sham tDCS plus placebo, sham tDCS plus sertraline, active tDCS plus placebo and active tDCS plus sertraline.[12] To assess the integrity of trial-group blinding, patients were asked to guess which intervention they had received. The responses of participants are summarised in table 5. Note that the data structure here is not like the example of ELECT-TDCS (table 4). The presented data for each arm of table 5 were combined by two treatment groups and started by two levels. As a result, the BI for sham tDCS (Arm 1) is −0.27 (95% CI −0.49 to −0.04, p=0.973), the BI for active tDCS (Arm 2) is 0.66 (95% CI 0.49 to 0.83, p<0.001), the BI for placebo (Arm 3) is 0.50 (95% CI 0.30 to 0.70, p<0.001) and the BI for sertraline (Arm 4) is 0.16 (95% CI −0.07 to 0.39, p=0.126). The finding indicates for Arm 2 (active tDCS plus placebo/sertraline) and Arm 3 (active tDCS/sham tDCS plus placebo), the subjects tended to be unblinded and correctly guessed that they were on active tDCS (for people in Arm 2) or on placebo (for people in Arm 3), respectively. Figure 4 illustrates the forest plot depicting the BBIs and their corresponding 95% CIs for the four arms in the BBR study.

DISCUSSION

Blinding is considered to be an important feature of RCTs that minimises the potential influence of patients' and clinicians' expectations on possible benefits and harms associated with the intervention, and it remains essential for subjective outcomes such as patient-reported outcomes.[13] When unblinded, participants may introduce bias through the use of other effective interventions, differential reporting of symptoms and psychological or biological effects of receiving a placebo, although debates persist on the magnitude of blinding's impact on RCT results.[14–16] The unsuccessful blinding will lead to magnitude effects between intervention and placebo, as placebo effects involve molecular biological effects.[17] At this stage, researchers should be encouraged to conduct blinding assessments when they report the results in RCTs.[4 5 18] Currently, psychiatric studies have significant potential to improve adherence to reproducibility and transparency practices regarding study protocols and statistical

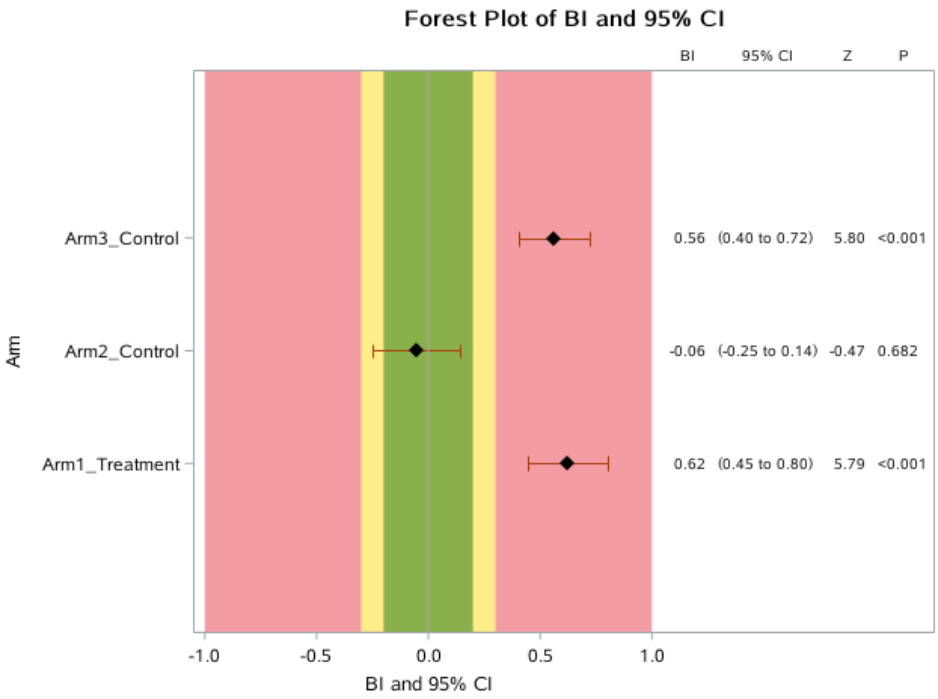

Figure 3 The forest plot of BBIs and 95% CIs of the three arms for level 2 (escitalopram vs placebo) in the ELECT-TDCS study. The green, yellow and red margins represent successful, acceptable and unsuccessful blinding, respectively. The diamond marks the BBI, and the error bars show the 95% CI for each BBI. In the pharmacological intervention level (active escitalopram vs placebo, see table 4), the BBI for Arm 2 (–0.06) is close to 0, indicating successful blinding. However, the BBIs for Arm 1 (0.62) and Arm 3 (0.56) suggest correct guesses by participants, indicating unsuccessful blinding. BBI, Bang's Blinding Index; BI, Blinding Index; ELECT-TDCS, trial of electrical direct-current therapy versus escitalopram for depression.

Table 5 Responses of assessment of blinding in the SELECT-TDCS study

	True arm				
Guessed, n (%)	Sham tDCS+ placebo/sertraline	Active tDCS+placebo/ sertraline	Active/sham tDCS+ placebo	Active/sham tDCS+sertraline	Total
Level 1: active tDCS versus sham tDCS					
Sham tDCS	18 (17.6)	9 (8.8)	NA	NA	27 (26.5)
Active tDCS	31 (30.4)	44 (43.1)	NA	NA	75 (73.5)
Unknown	NA	NA	NA	NA	
Total	49 (48.0)	53 (52.0)	NA	NA	102 (100)
Level 2: sertraline versus placebo					
Placebo	NA	NA	39 (38.2)	21 (20.6)	60 (58.8)
Sertraline	NA	NA	13 (12.7)	29 (28.4)	42 (41.2)
Unknown	NA	NA	NA	NA	
Total	NA	NA	52 (51.0)	50 (49.0)	102 (100)

NA, not applicable; SELECT-TDCS, the sertraline versus electrical current therapy for treating depression clinical study: results from a factorial, randomised controlled trial; tDCS, transcranial direct-current stimulation.

analysis plans.[19] However, the blinding assessment still lacks performance.[20]

While descriptive statistics provide useful insights into blinding data, they emphasise the number of participants who correctly or wrongly guess the allocation of groups. Previous studies have developed packages for software like R (package BI: Blinding Assessment Indexes for Randomised, Controlled, Clinical Trials) and Stata (module BLINDING: Stata module to compute blinding indexes) to assess blinding in pairwise comparison design RCTs with two arms using BBI; a comparable method for SAS is currently unavailable. This paper introduces an SAS macro, %BBIplus, designed to estimate the success of blinding in RCTs. In contrast to existing packages,[21] %BBIplus expands its applicability from two-arm RCTs to multi-arm configurations, encompassing three-arm double-dummy designed RCTs and four-arm factorial

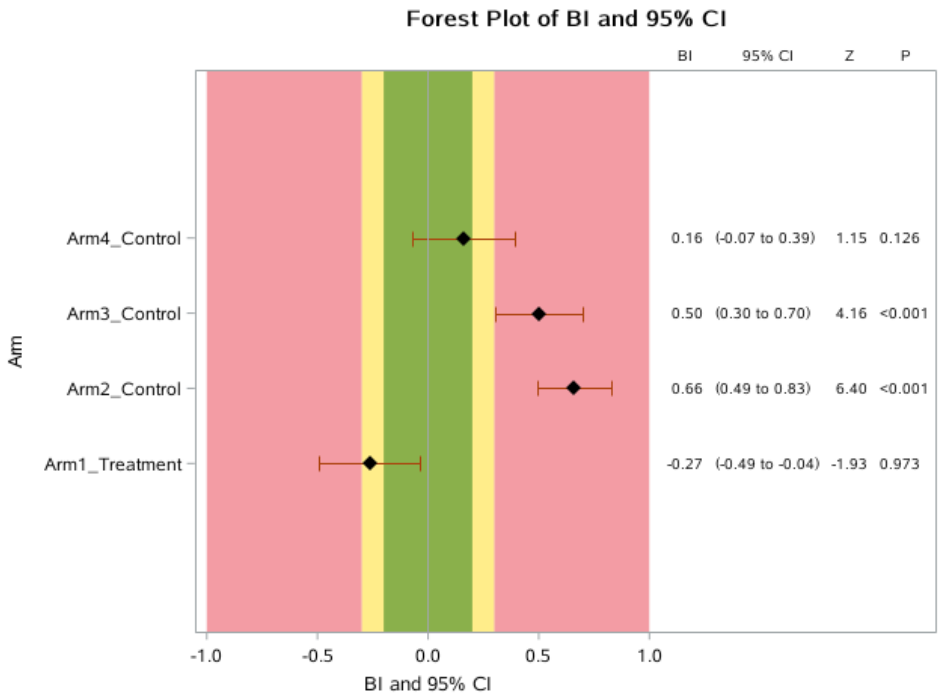

Figure 4 The forest plot of BBIs and 95% CIs for four arms in the SELECT-TDCS study. The green, yellow and red margins represent successful, acceptable and unsuccessful blinding, respectively. The diamond marks the BBI, and the error bars show the 95% CI for each BBI. In the non-pharmacological intervention level (active tDCS vs sham tDCS, see table 5), the BBI for Arm 1 is -0.27, indicating an opposite guess by the participants, but it is still considered acceptable blinding, the BI for Arm 2 is 0.66, suggesting correct guesses by participants and unsuccessful blinding. In the pharmacological intervention level (sertraline vs placebo, see table 5), the BBI for Arm 3, similar to Arm 2, is 0.50, indicating unsuccessful blinding, and the BI for Arm 4 is 0.16, indicating a successful blinding. BBI, Bang's Blinding Index; BI, Blinding Index; SELECT-TDCS, the sertraline versus electrical current therapy for treating depression clinical study: results from a factorial, randomised, controlled trial; tDCS, transcranial direct current stimulation.

designed RCTs. Notably, the macro incorporates a forest plot for visualisation of BBI calculation, enhancing interpretability. Three illustrative examples (BBR, SELECT-TDCS and ELECT-TDCS) demonstrate the application of %BBIplus in various scenarios.

Compared with the χ^2 test, which is mainly based on p values to judge the success of blinding, BBI provides a more specific method, and the judgement is dependent on the effect size. However, the limitations of the assumptions of BBI should be noted. In reality, participants may not always guess the assignment randomly. They might have had perceived effects, had access to information or held personal biases that influenced their guesses. This can affect the accuracy of the BBI in reflecting true blinding effectiveness. In addition, a binary selection category for participants (sure or unknown) limited nuanced responses such as the subject's response of 'somewhat believe'. Third, the BBI can be sensitive to the sample size. In small trials, the index may not accurately reflect the effectiveness of blinding due to random variations. Fourth, the BBI does not provide information on why blinding might have failed. It simply indicates that it might not be effective without explaining the reasons or mechanisms behind the failure. Last, this macro cannot meet all designs of clinical trials, such as n-of-1 trials and master protocol trials. Further methodological research on the blinding assessment is still needed.

CONCLUSION

Blinding is a crucial methodological feature of RCTs, particularly in psychiatric research where patient-reported outcome measures are involved. Effective blinding prevents biased assessment and minimises the chance of co-interventions. In this paper, we have developed an SAS tool tailored for clinical trial investigators and statisticians. Using data from three psychiatric studies—BBR, ELECT-TDCS and SELECT-TDCS, which include pharmacological, non-pharmacological and combination interventions—we have offered a comprehensive solution for estimating and visualising the blinding index across different RCT designs.

Author affiliations
[1]Peking University Clinical Research Institute, Beijing, China
[2]Department of Neurology and China National Clinical Research Center for Neurological Diseases, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
[3]Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai, China
[4]Department of Acupuncture and Neurology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China

[5]Department of Health Promotion and Human Behavior, Kyoto University Graduate School of Medicine and School of Public Health, Kyoto, Japan

Contributors ZQ: conceptualisation, formal analysis, investigation, writing—original draft, writing—review and editing, visualisation, project administration, funding acquisition. YY: methodology, writing—review and editing. HG: methodology, writing—review and editing. DS: methodology, writing—review and editing. ZW: methodology, writing—review and editing. JW: conceptualisation, investigation, writing—original draft, writing—review and editing. TF: methodology, writing—review and editing, supervision. YW: methodology, writing—review and editing, supervision.

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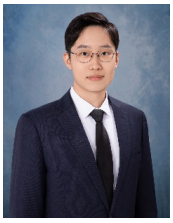
ORCID iDs
Zongshi Qin http://orcid.org/0000-0001-5888-461X
Zhen Wang http://orcid.org/0000-0003-4319-5314

REFERENCES

1 Chan AW, Tetzlaff JM, Gotzsche PC, *et al*. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346:e7586.
2 Scott AJ, Sharpe L, Colagiuri B. A systematic review and meta-analysis of the success of blinding in antidepressant RCTs. *Psychiatry Res* 2022;307:114297.
3 Baethge C, Assall OP, Baldessarini RJ. Systematic review of blinding assessment in randomized controlled trials in schizophrenia and affective disorders 2000-2010. *Psychother Psychosom* 2013;82:152–60.
4 Lin Y-H, Sahker E, Shinohara K, *et al*. Assessment of blinding in randomized controlled trials of antidepressants for depressive disorders 2000-2020: a systematic review and meta-analysis. *EClinMed* 2022;50:101505.
5 Tajika A, Furukawa TA, Shinohara K, *et al*. Blinding successfulness in antipsychotic trials of acute treatment for schizophrenia: a systematic review. *BMJ Ment Health* 2023;26:e300654.
6 Kolahi J, Bang H, Park J. Towards a proposal for assessment of blinding success in clinical trials: up-to-date review. *Community Dent Oral Epidemiol* 2009;37:477–84.
7 Bang H. Random guess and wishful thinking are the best blinding scenarios. *Contemp Clin Trials Commun* 2016;3:117–21.
8 Colagiuri B, Sharpe L, Scott A. The blind leading the not-so-blind: a meta-analysis of blinding in pharmacological trials for chronic pain. *J Pain* 2019;20:489–500.
9 Tambiah JRS, Simsek I, Swearingen CJ, *et al*. Comparing patient-reported outcomes from sham and saline-based placebo injections for knee osteoarthritis: data from a randomized clinical trial of lorecivivint. *Am J Sports Med* 2022;50:630–6.
10 Chan M, Qin Z, Man S-C, *et al*. Adjunctive berberine reduces antipsychotic-associated weight gain and metabolic syndrome in patients with schizophrenia: a randomized controlled trial. *Psychiatry Clin Neurosci* 2022;76:77–85.
11 Brunoni AR, Moffa AH, Sampaio-Junior B, *et al*. Trial of electrical direct-current therapy versus escitalopram for depression. *N Engl J Med* 2017;376:2523–33.
12 Brunoni AR, Valiengo L, Baccaro A, *et al*. The sertraline vs. electrical current therapy for treating depression clinical study: results from a factorial, randomized, controlled trial. *JAMA Psychiatry* 2013;70:383–91.
13 Chow SC, Chow SS, Pong A. Review of current controversial issues in clinical trials. *Gen Psychiatr* 2021;34:e100540.
14 Hróbjartsson A, Emanuelsson F, Skou Thomsen AS, *et al*. Bias due to lack of patient blinding in clinical trials. A systematic review of trials randomizing patients to blind and nonblind sub-studies. *Int J Epidemiol* 2014;43:1272–83.
15 Moustgaard H, Clayton GL, Jones HE. Impact of blinding on estimated treatment effects in randomised clinical trials: meta-epidemiological study. *BMJ* 2020;368:l6802.
16 Drucker AM, Chan AW. Blindsided: challenging the dogma of masking in clinical trials. *BMJ* 2020;368:m229.
17 Cai L, He L. Placebo effects and the molecular biological components involved. *Gen Psychiatr* 2019;32:e100089.
18 Schulz KF, Altman DG, Moher D, *et al*. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c332.
19 Sherry CE, Pollard JZ, Tritz D, *et al*. Assessment of transparent and reproducible research practices in the psychiatry literature. *Gen Psychiatr* 2020;33:e100149.
20 Cheng Y, Liu H, Yuan R, *et al*. Effectiveness of pharmacogenomics on the response and remission of treatment-resistant depression: a meta-analysis of randomised controlled trials. *Gen Psychiatr* 2023;36:e101050.
21 Kim J, Park JJ, Bang H, *et al*. Blinding assessment: one step forward. *Dent Hypotheses* 2021;12:169–73.



Zongshi Qin received his PhD degree from Li Ka Shing Faculty of Medicine, The University of Hong Kong, China in 2022. Currently, he is working at Peking University Clinical Research Institute as a postdoc fellow in China. As the principal investigator, he is funded by the National Natural Science Foundation, the China Postdoctoral Science Foundation, and the International Postdoctoral Exchange Fellowship Program. His main research interests include the methodology of clinical trials and translational medical research of neuromodulation and neuropsychiatric disease.