Evaluation of Probiotic Studies Based On The Revised Cochrane Risk-Of-Bias Tool For Randomized Crossover Trials

Date of Evaluation: 15 August 2022

Tool adapted from: Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Eldridge SM, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019; **366**: l4898.

Website: https://sites.google.com/site/riskofbiastool/welcome/rob-2-0-tool?authuser=0

Details of Study

Name of Study	Non-viable Lactobacillus reuteri DSMZ 17648 (Pylopass) as a new approach to Helicobacter pylori control in humans
Study Design	Randomized Crossover Trial
Probiotic(s) Studied	Lactobacillus reuteri DSMZ17648
Conclusion on Efficacy	Uncertain
Reference	Mehling H, Busjahn A. Non-viable Lactobacillus reuteri DSMZ 17648 (Pylopass) as a new approach to Helicobacter pylori control in humans. Nutrients. 2013;5(8):3062-73. Epub 2013/08/07. doi: 10.3390/nu5083062. (Link to Article)

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 1a: Risk of bias arising from the randomization process

Signalling questions	Response options
1.1 Was the allocation sequence random?	Y / PY / PN / N / NI
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y / PY / PN / N / NI
1.3 Did baseline differences between intervention groups at the start of the first period suggest a problem with the randomization process?	Y / PY / PN / N / NI
Risk-of-bias judgement	Low / High / Some concerns

Domain S: Risk of bias arising from period and carryover effects

Signalling questions	Response options
S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal?	Y / PY / PN / N / NI
S.2 If N/PN/NI to S.1: Were period effects accounted for in the analysis?	NA / Y / PY / PN / N / NI
S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period?	Y / PY / PN / N / NI
Risk-of-bias judgement	Low / High / Some concerns

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

Signalling questions	Response options
2.1. Were participants aware of their assigned intervention during each period of the trial?	Y / PY / PN / N / NI
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during each period of the trial?	Y / PY / PN / N / NI
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?	NA / Y / PY / PN / N / NI
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y / PY / PN / N / NI
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA / Y / PY / PN / N / NI
Risk-of-bias judgement	Low / High / Some concerns

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

Signalling questions	Response options
2.1. Were participants aware of their assigned intervention during each period of the trial?	Y / PY / PN / N / NI
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during each period of the trial?	Y / PY / PN / N / NI
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced between interventions?	NA / Y / PY / PN / N / NI
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the outcome?	NA / Y / PY / PN / N / NI
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected participants' outcomes?	NA / Y / PY / PN / N / NI
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?	NA / Y / PY / PN / N / NI
Risk-of-bias judgement	Low / High / Some concerns

Domain 3: Risk of bias due to missing outcome data

Signalling questions	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y / PY / PN / N / NI
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	NA / Y / PY / PN / N
3.3 If N/PN to 3.2 Could missingness in the outcome depend on its true value?	NA / Y / PY / PN / N / NI
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA / Y / PY / PN / N / NI
Risk-of-bias judgement	Low / High / Some concerns

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Response options
4.1 Was the method of measuring the outcome inappropriate?	Y / PY / PN / N / NI
4.2 Could measurement or ascertainment of the outcome have differed between interventions within each sequence?	Y / PY / PN / N / NI
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	NA / Y / PY / PN / N / NI
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA / Y / PY / PN / N / NI
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA / Y / PY / PN / N / NI
Risk-of-bias judgement	Low / High / Some concerns

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

Signalling questions	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?	Y / PY / PN / N / NI
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?	Y / PY / PN / N / NI
5.3 ... multiple eligible analyses of the data?	Y / PY / PN / N / NI
5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified?	Y / PY / PN / N / NI
Risk-of-bias judgement	Low / High / Some concerns

Overall risk of bias

Risk-of-bias judgement	Comments: ● Only stated study was randomized, no information about the randomization method. ● No information on carryover effects.	Low / High / Some concerns