

Study	Risk of bias domains							Overall
	D1	D2	D3	D4	D5	D6	D7	
Chumpitazi, B.P. et al. 2014	-	-	+	?	X	-	+	X
Baranguan Castro, M.L. et al. 2019	-	X	+	+	X	-	X	X
Wintermeyer, P. et al. 2012	-	X	+	+	+	-	-	X
Escobar, J. Et al. 2014	X	-	+	-	-	-	X	X

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
X Serious
- Moderate
+ Low
? No information

Figure S1. Risk of bias of the eligible non-RCTs/single arm clinical trials using the Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) [32] tool.

		Risk of bias domains for crossover RCTs						
		D1	D2	D3	D4	D5	D6	Overall
Study	Chumpitazi, B.P. et al, 2015							
	Francavilla, R. et al, 2018							
	Gremse, D.A. et al. 2003							

D1: 1) bias due to randomization process
 D2: 2) Bias arising from period and carryover effects
 D3: 2) Bias due to deviations from intended intervention
 D4: 3) Bias due to missing outcome data
 D5: 4) Bias in measurement of the outcome
 D6: 5) bias in selection of the reported results

Judgement
 Some concerns
 Low

Figure S2. Risk of bias of the eligible RCTs with crossover design using the Cochrane Risk of Bias Tool (ROB-2) [35] tool for crossover trials.

Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Dogan, G. et al. 2020	+	-	-	+	+	-
Boradyn, K.M.; et al. 2020	+	+	+	+	?	+
Nogay, N.H. et al. 2021	-	+	+	-	+	-
Piwowarczyk, A. et al. 2020	+	+	+	+	+	+
Ghalichi, F. et al. 2016	-	-	+	+	+	-
Al-Biltagi, M. et al. 2022	-	+	+	+	+	-
Wirth, S. et al. 2014	+	+	-	+	+	-
Gijsbers, R. et al. 2012	-	-	+	-	-	-

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
- Some concerns
+ Low
? No information

Figure S3. Risk of bias of the eligible RCTs using the Cochrane Risk of Bias Tool (ROB-2) [34].

References:

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