
























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							
		<div>D1: 1) bias due to randomization process D2: S 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</div>						<div>Judgement  Some concerns  Low</div>

**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.

	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Study	Dogan, G. et al. 2020					
	Boradyn, K.M.; et al. 2020					
	Nogay, N.H. et al. 2021					
	Piowarczyk, A. et al. 2020					
	Ghalichi, F. et al. 2016					
	Al-Biltagi, M. et al. 2022					
	Wirth, S. et al. 2014					
	Gijssbers, R. et al. 2012					
<p>Domains:</p> <p>D1: Bias arising from the randomization process.</p> <p>D2: Bias due to deviations from intended intervention.</p> <p>D3: Bias due to missing outcome data.</p> <p>D4: Bias in measurement of the outcome.</p> <p>D5: Bias in selection of the reported result.</p>						
<p>Judgement</p> <p> Some concerns</p> <p> Low</p> <p> No information</p>						

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

## References:

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