Supplementary

Table S1 OHAT risk of bias assessment for 18 included studies

Study	1	2	3	4	5	6	7	8	9	10	11	Total (out of 44)
Rohlmann *et al.* (1995)	1	1	1	2	4	1	3	3	3	3	3	25
Rohlmann *et al.* (1997)	1	1	3	2	4	1	4	4	3	3	3	29
Rohlmann *et al.* (1997)	1	1	1	2	4	1	3	3	3	3	3	25
Rohlmann *et al.* (1998)	1	1	1	2	4	1	3	3	3	3	3	25
Rohlmann *et al.* (1999)	1	1	1	2	4	1	4	4	4	4	4	30
Rohlmann *et al.* (2000)	1	1	1	2	4	1	4	4	4	4	4	30
Szivek *et al.* (2005)	1	1	1	2	4	1	3	3	3	3	3	25
Rohlmann *et al.* (2008)	1	1	1	2	4	1	4	4	4	4	4	30
Rohlmann *et al.* (2008)	1	1	1	2	4	1	4	4	4	4	4	30
Rohlmann *et al.* (2010)	1	1	1	2	4	1	4	4	4	4	4	30
Rohlmann *et al.* (2011)	1	1	2	2	4	1	4	4	4	4	4	31
Rohlmann *et al.* (2012)	1	1	2	1	4	1	4	4	4	4	4	30
Rohlmann *et al.* (2013)	1	1	2	2	4	1	4	4	4	4	4	31
Rohlmann *et al.* (2013)	1	1	2	2	4	1	4	4	4	4	4	31
Rohlmann *et al.* (2014)	1	1	2	3	4	1	4	4	4	4	4	32
Dreischarf *et al.* (2015)	2	1	2	3	4	1	4	4	4	4	4	33
Damm *et al.* (2017)	2	1	4	3	4	1	4	4	4	4	4	35
Barri *et al.* (2021)	2	2	4	3	4	2	4	4	4	4	4	37

Each study is given a score out of 4 (1= definitely high risk of bias, 2= probably high risk of bias, 3= probably low risk of bias, 4= definitely low risk of bias). There are 11 questions across seven bias domains as detailed below—Selection bias: (I) Was administered dose or exposure level adequately randomized? (II) Was allocation to study groups adequately concealed? (III) Did selection of study participants result in appropriate comparison groups? Confounding bias: (IV) Did the study design or analysis account for important confounding and modifying variables? Performance bias: (V) Were experimental conditions identical across study groups? (VI) Were the research personnel and human subjects blinded to the study group during the study? Attrition/exclusion bias: (VII) Were outcome data complete without attrition or exclusion from analysis? (VIII) Can we be confident in the exposure characterization? (IX) Can we be confident in the outcome assessment? Selective reporting bias: (X) Were all measured outcomes reported? Other bias: (XI) Were there no other potential threats to internal validity (e.g., statistical methods were appropriate, and researchers adhered to the study protocol)? OHAT, the Office of Health Assessment and Translation.

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