

Appendix table 1: The quality of the included studies assessed using the Cochrane Collaboration Risk of Bias Tool.¹³

Study, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Participants screened for AHR	Washout period between treatments	Adequate sample size*
Molphy et al. 2019 [58]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	At least 7 days	4360
Merlini et al., 2019 [57]	Low risk	Low risk	High risk	Unclear risk	Low risk	Low risk	Unclear risk	48 hours	14
Hafedh et al., 2019 [56]	Unclear risk	Low risk	High risk	Unclear risk	Low risk	Low risk	High risk	Not reported	131
Laurent et al., 2018 [55]	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	High risk	At least 4 days	663
Ekstrom et al., 2018 [54]	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	High risk	2 to 14 days of interval	866
Molphy et al., 2017 [53]	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk	At least 7 days	15447600
Halabchi et al., 2017 [52]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	1 week	489
Hostrup et al., 2016 [61]	Unclear risk	Low risk	High risk	Unclear risk	Low risk	Low risk	Low risk	na	3532
Koch et al., 2015 [51]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	3 to 14 days	392
Koch et al., 2015 [50]	Unclear risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk	3 to 14 days	698
Koch et al., 2015 [49]	Unclear risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk	3 to 14 days	1108
Hostrup et al., 2015 [60]	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	High risk	na	16
Karlsen et al., 2014 [48]	Low risk	Low risk	High risk	Unclear risk	Low risk	Low risk	High risk	3 days	9168
Hostrup et al., 2014 [47]	Low risk	Low risk	High risk	Unclear risk	Low risk	Low risk	High risk	3 days	649
Dickinson et al., 2014a [59]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	na	194
Dickinson et al., 2014b [46]	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Separate days	514
Sanchez et al., 2013 [45]	Unclear risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk	1 week	496
Decorte et al., 2013 [44]	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	High risk	4 days to 3 weeks	28
Elers et al., 2012 [43]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	High risk	1 week	392
Beloka et al., 2011 [42]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	High risk	Overnight	No difference
Andersen et al. 2009, [41]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Separate days	282
Sporer et al., 2008 [40]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	At least 3 days	651
Descorte et al., 2008 [39]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	High risk	3 days to 3 weeks	883
Tjorhom et al., 2007 [38]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	2 to 8 days	4876

Riiser et al., 2006 [37]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	2 to 7 days	1081
Van Baak et al., 2004 [36]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	4 to 14 days.	123
Stewart et al., 2002 [35]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	At least 1 wk.	76919
Collomp et al., 2002 [34]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	3 days	124
Collomp et al., 2000a [29]	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	High risk	2 days to 3 weeks	7883
Collomp et al., 2000b [30]	Low Risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	On two different days	2430
Goubault et al., 2001 [33]	Unclear risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	High risk	Approximately 1 week	9
Carlsen et al., 2001 [32]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	4 weeks	124
Van Bak et al., 2000 [31]	Unclear risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk	3-4 weeks	26
Sue-Chu et al., 1999 [28]	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	At least 2 days	15517
Sandsund et al., 1998 [27]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	At least 1 day	1949
Larsson et al., 1997 [26]	Unclear risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Low risk	24 hours.	1005
Carlsen et al., 1997 [25]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	On three different days	209
Norris et al., 1996 [24]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	At least 24 hours	3210
Heir et al., 1995 [22]	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	2 to 7 days	323
Unnithan et al., 1994 [22]	Unclear risk	Low risk	High risk	Unclear risk	Low risk	Low risk	Low risk	At least 2 days	429
Fleck et al., 1993 [21]	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	1 day	796
Morton et al., 1992 [20]	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	4 to 10 days	284822
Meeuwisse et al. 1992 [19]	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Approximately 1 week	316
Violante et al., 1989 [18]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	High risk	Not reported	1823
Bedi et al 1988 [16]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	At least 1 week	75
Booth et al., 1988 [17]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	High risk	7 days	1303
McKenzie et al. 1983[58]	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	na	411

* Adequate sample size assessed by calculation of the sample size (pairwise comparisons between placebo and beta2-agonist) required for the effect to obtain an alpha of 0.05 and a beta of 0.2 [43]. na: not applicable, as it is a parallel trial. AHR: airway hyperresponsiveness. No difference: no difference in effect between groups.