

Table 1: Characteristics of the 22 randomized clinical trials included in the systematic review:

Study	Medications Evaluated	Duration of trial/ no randomized	Definition of AECOPD	Patients who prematurely stopped study meds retained in trial?	Temporal independence established?/ Blinded adjudication of events?	Outcomes Reported: Proportions having ≥ 1 exacerbation, Mean exac/pt-y, or both.	Weighted statistical approach used?	Over-dispersion accounted for?
Mahler, AmJRCCM 2002(37)	F/S, Salmeterol,	24 weeks N = 691	Event-based	Yes	No/No	Proportions	N/A*	N/A*
Szafranski, ERJ 2003(38)	B/F, Formoterol,	12 months N= 812	Event-based	No	No/No	Mean exacerbations/ pt-y	Yes	Yes
Calverley, Lancet 2003(39)	F/S, Salmeterol	12 months N= 1465	Event-based	No	No/No	Mean exacerbations/ pt-y	Yes	No
Calverley, ERJ 2003(40)	B/F, Formoterol,	12 months N = 1022	Event-based	No	No/No	Mean exacerbations/ pt-y	Yes	Yes
Hanania, Chest 2003(41)	F/S, Salmeterol	24 weeks N= 723	Event-based	No	No/No	Proportions	N/A	N/A
Dal Negro, PulmPharm & Therap. 2003(42)	F/S, Salmeterol, Theophylline	52 weeks N = 18	Event-based	N/A (no dropouts)	No/No	Mean exacerbations/ pt-y	N/A (no dropouts)	No
Wouters, Thorax 2005(43)	F/S, Salmeterol with Fluticasone withdrawal	52 weeks N = 373	Event-based	No	Temporal independence established for mild exacerbations only/ No	Mean exacerbations/ pt-y	No	No
Kardos, AmJRCCM 2006(44)	F/S, Salmeterol	44 weeks N = 994	Event-based	No	No/No	Mean exacerbations/ pt-y	Yes	No
Casaburi, ERJ 2002(45)	Tiotropium	52 weeks N = 921	Symptom-based	No	No/No	Both	No	No
Vincken, ERJ 2002(46)	Tiotropium, Ipratropium	52 weeks N = 535	Symptom-based	No	No/No	Both	No	No
Brusasco, Thorax 2003(47)	Tiotropium, Salmeterol	24 weeks N = 1207	Symptom-based	No	No/No	Both	No	No
Niewoehner, Annals Int Med 2005(48)	Tiotropium	24 weeks N = 1829	Event-based	Yes	No/No	Both	No	No
Briggs, PulmPharm & Therap. 2005(49)	Tiotropium, Salmeterol	12 weeks N = 653	Symptom-based	No	No/No	Both	No	No
Dusser, ERJ 2006(50)	Tiotropium	52 weeks N = 1010	Event-based	No	No/No	Both	No	No
Beeh, Pneumologie 2006(51)	Tiotropium	12 weeks N = 1639	Event-based	Yes	No/No	Proportions	N/A	N/A

Van Noord, ERJ 2000(30)	Salmeterol, Ipratropium	12 weeks N = 144	Event-based	Yes	No/No	Proportions	N/A	N/A
ZuWallack, Chest 2001(31)	Salmeterol, Theophylline	12 weeks N = 943	Event-based	Yes	No/No	Proportions	N/A	N/A
Rennard, AmJRCCM 2003(32)	Salmeterol, Ipratropium	12 weeks N = 405	Event-based	No	No/No	Proportions	N/A	N/A
Chapman, CRJ 2002(33)	Salmeterol, Ipratropium	24 weeks N = 408	Event-based	Yes	No/No	Proportions	N/A	N/A
Rossi, Chest 2002(34)	Formoterol, Theophylline	12 months N = 854	Symptom- based for mild exacerbations Event-based for moderate and severe.	No	No/No	Proportions	N/A	N/A
Celli, Resp Med 2003(35)	Salmeterol, Sibenaedet	12 weeks N = 1368	Event-based	Unclear	No/No	Proportions	N/A	N/A
Stockley, Thorax 2006(36)	Salmeterol	12 months N = 634	Event-based	No	No/No	Both	No	No

*Use of a weighted statistical technique and correction of over-dispersion is applicable only to those studies that reported mean exacerbations/patient-year

F/S = fluticasone/salmeterol

B/F= budesonide/formoterol