Table 21: Clinical evidence profile: Comparison 1.1. Mannitol versus placebo

0 114							No. of a		F65			
Quality	y assessmen	t					No of pa	atients	Effect			
No of studi	Design	Risk of	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration	Mannit ol	Contro I	Relativ e	Absolute		
es		bias				S			(95%			Impor
									ČI)		Quality	tance
FEV ₁ %	6 predicted (repeated	l measures, ch	ange from ba	seline) (follo	ow-up 2 weeks:	range of	scores: 0	-100: Bet	ter indicated b	v higher value	s)

Quality	assessmen	t					No of pa	atients	Effect			
No of studi es	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Mannit ol	Contro I	Relativ e (95% CI)	Absolute	Quality	Impor tance
1 (Jaqu es 2008)	randomise d trials ¹	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	none	3	6	-	MD 3.95 higher (0.96 to 6.94 higher)	LOW	CRITI CAL
FEV ₁ %	predicted (repeated	measures, ch	ange from ba	aseline) (follo	ow-up 2 months	; range o	f scores:	0-100; B	etter indicated	by higher valu	ies)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	no serious imprecisio n	none	361	239	-	MD 2.98 higher (1.04 to 4.92 higher)	MODERATE	CRITI CAL
FEV ₁ %	predicted (repeated	measures, ch	ange from ba	aseline) (follo	ow-up 4 months	; range o	f scores:	0-100; B	etter indicated	by higher valu	ies)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	none	361	239	-	MD 3.26 higher (1.16 to 5.35 higher)	LOW	CRITI CAL
FEV ₁ %	predicted (repeated	measures, ch	ange from ba	aseline) (follo	ow-up 6 months	; range o	f scores:	0-100; B	etter indicated	by higher valu	ies)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	none	361	239	-	MD 3.89 higher (1.69 to 6.08 higher)	LOW	CRITI CAL

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Quality	y assessmen	t					No of pa	atients	Effect			
No of studi	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Mannit ol	Contro I	Relativ e (95% CI)	Absolute	Quality	Impor tance
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	none	Total nui children young pe 258 (Nur each gro reported	and eople: mber in oup not	-	MD 2.64 higher (0.73 lower to 6.02 higher)	LOW	CRITI CAL
	% predicted in ted by higher			eople (repea	ted measure	s, change from	baseline)	(follow-u	ıp 4 mon	ths; range of s	scores: 0-100; I	Better
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	none	Total nui children young pe 258 (Nur each gro reported	and eople: mber in oup not	-	MD 1.34 higher (2.42 lower to 5.10 higher)	LOW	CRITI CAL
-	% predicted in		, , ,	eople (repea	ted measure	s, change from	baseline)	(follow-u	ıp 6 mon	ths; range of s	scores: 0-100; I	Better
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	none	Total nui children young pe 258 (Nur each gro reported	and eople: mber in oup not	-	MD 3.03 higher (0.78 lower to 6.84 higher)	LOW	CRITI CAL
FEV ₁ % values		n adults	(repeated mea	sures, chang	je from base	line) (follow-up	2 months	; range o	f scores:	0-100; Better	indicated by hi	igher
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	none	Total nui adults: 3 (Number group no reported	17 in each ot	-	MD 3.72 higher (0.82 to 6.64 higher)	LOW	CRITI CAL

No of studi es	/ assessmen Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	No of pa Mannit ol	Contro	Relativ e (95% CI)	Absolute	Quality	Impor tance
FEV ₁ % values	•	n adults	(repeated mea	sures, chang	e from base	line) (follow-up	4 months	; range o	f scores:	0-100; Better	indicated by h	igher
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	none	Total nui adults: 3 (Number group no reported	s17 r in each ot	-	MD 4.23 higher (0.98 to 7.48 higher)	LOW	CRITI CAL
FEV ₁ % values	•	n adults	(repeated mea	sures, chang	e from base	line) (follow-up	6 months	s; range o	of scores:	0-100; Better	indicated by h	igher
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	none	Total nur adults: 3 (Number group no reported	s17 r in each ot	-	MD 5.74 higher (2.36 to 9.13 higher)	LOW	CRITI CAL
Time to	o first protoc	ol define	ed pulmonary	exacerbation	(follow-up:	6 months)						
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ⁴	none	0/361 (0%)	0/239 (0%)	HR 0.7 (0.48 to 1.02)	-	LOW	CRITI CAL
Numbe	er of children	and you	ung people wit	h protocol de	efined exace	rbations (proxy	for time t	o next ex		on) (follow-up	6 months)	
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ⁵	none	No. particip ants with exacer bations	No. partici pants with exacer bation	RR 0.62 (0.35 to 1.09)	-	LOW	CRITI CAL

Quality	/ assessmen	ıt					No of pa	atients	Effect			
No of studi es	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Mannit ol	Contro I	Relativ e (95% CI)	Absolute	Quality	Impor tance
							not reporte d. Total N of particip ants: 154	s not reporte d. Total N of partici pants: 105				
Numbe	er of adults w	vith prot	ocol defined ex	xacerbations	(proxy for ti	me to next exac	erbation)	(follow-u	ıp: 6 mor	nths)		
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ⁵	none	No. particip ants with exacer bations not reporte d. Total N of particip ants: 207	No. partici pants with exacer bation s not reporte d. Total N of partici pants: 134	RR 0.76 (0.52 to 1.13)	-	LOW	CRITI CAL
Numbe	er of patients	needing	g additional IV	antibiotics (f	ollow-up 6 m	nonths)						
2 (Aitke n 2012,	randomise d trials	no seriou s risk of bias	serious ⁶	serious ²	serious ⁵	none	165/36 1 (45.7%)	134/23 9 (56.1%)	RR 0.81 (0.63 to 1.04)	107 fewer per 1000 (from 28 fewer to 168 fewer)	VERY LOW	CRITI CAL

Quality	/ assessmen	t					No of pa	atients	Effect			
No of studi	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Mannit ol	Contro I	Relativ e (95% CI)	Absolute	Quality	Impor tance
Bilton 2011)								56%		106 fewer per 1000 (from 28 fewer to 168 fewer)		
Quality values		QOL res	spiratory doma	in (change fr	om baseline) (follow-up 4 m	onths; ra	nge of so	ores: 0-1	00; Better indi	cated by highe	er
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	serious ⁷	serious ²	serious ³	none	292	215	-	MD 1.66 lower (5.66 lower to 2.34 higher)	VERY LOW	IMPO RTAN T
Quality		QOL res	spiratory doma	in (change fr	om baseline	(follow-up 6 m	onths; ra	nge of so	ores: 0-1	00; Better indi	cated by highe	er
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	very serious ⁸	very serious2	very serious ⁹	none	268	197	-	MD 1.53 lower (12.11 lower to 9.05 higher)	VERY LOW	IMPO RTAN T
Quality		QOL vit				low-up 4 month			: 0-100; E			
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	None	207	154	-	MD 3.42 higher (0.21 lower to 7.04 higher)	LOW	IMPO RTAN T
Quality	of life - CF	QOL vit	ality domain (c	hange from b	aseline) (fol	low-up 6 month	s; range	of scores	: 0-100; E	Better indicate	d by higher val	lues)

Quality	/ assessmen	t					No of pa	atients	Effect			
No of studi	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Mannit ol	Contro I	Relativ e (95% CI)	Absolute	Quality	Impor tance
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	None	187	138	-	MD 4.84 higher (0.86 to 8.82 higher)	LOW	IMPO RTAN T
Quality	of life - CFC	QOL phy	sical domain (change from	baseline) (fo	ollow-up 4 mont	hs; range	of score	es: 0-100;	Better indicat	ed by higher va	alues)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	no serious imprecisio n	None	291	214	-	MD 1.8 lower (4.72 lower to 1.11 higher)	MODERATE	IMPO RTAN T
Quality	of life - CFC	QOL phy	sical domain (change from	baseline) (fo	ollow-up 6 mont	hs; range	of score	s: 0-100;	Better indicat	ed by higher va	alues)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	serious ¹⁰	serious ²	very serious ⁹	none	268	197	-	MD 0.66 higher (6.2 lower to 7.52 higher)	VERY LOW	IMPO RTAN T
Quality	of life - CFC	QOL em	otion domain	(change from	baseline) (fo	ollow-up 4; rang	ge of scor	es: 0-100	; Better i	ndicated by hi	gher values)	
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	no serious imprecisio n	None	292	214	-	MD 2.11 lower (4.56 lower to 0.34 higher)	MODERATE	IMPO RTAN T

Quality	/ assessmen	t					No of pa	atients	Effect			
No of studi	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Mannit ol	Contro I	Relativ e (95% CI)	Absolute	Quality	Impor tance
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	no serious imprecisio n	None	269	196	-	MD 1.27 lower (3.74 lower to 1.2 higher)	MODERATE	IMPO RTAN T
Quality	of life - CF	QOL eati	ing domain (ch	ange from ba	aseline) (follo	ow-up 4 months	; range o	f scores:	0-100; B	etter indicated	l by higher valu	ıes)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	no serious imprecisio n	None	292	213	-	MD 0.81 higher (1.96 lower to 3.58 higher)	MODERATE	IMPO RTAN T
Quality	of life - CF	QOL eati	ing domain (ch	ange from ba	aseline) (follo	ow-up 6 months	; range o	f scores:	0-100; B	etter indicated	l by higher valu	ıes)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	no serious imprecisio n	None	269	197	-	MD 0.68 higher (2.29 lower to 3.65 higher)	MODERATE	IMPO RTAN T
Quality	y of life - CF	QOL hea	lth domain (cl	nange from b	aseline) (foll	low-up 4 weeks	range of	scores:	0-100; Be	etter indicated	by higher valu	es)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	no serious imprecisio n	None	208	152	-	MD 0.43 lower (4.18 lower to 3.32 higher)	MODERATE	IMPO RTAN T

No of studies Posign Risk of bias Design Risk of trials Position	Quality	, assessmen	t					No of pa	atients	Effect			
(Aitke d trials serious s risk of bias 2012, and of bias 2012) Quality of life – CFQOL social domain (change from baseline) (follow-up 4 weeks; range of scores: 0-100; Better indicated by higher value and the serious serious inconsistenc by a serious inconsistenc by a serious of bias 2012, and of b	studi	Design	of				consideration		Contro I	e (95%	Absolute	Quality	Impor tance
2 randomise d trials seriou seriou serious inconsistenc y serious inconsistenc y no serious imprecisio n serious serious serious serious serious inconsistenc y no serious imprecisio n no serious ser	(Aitke n 2012, Bilton		seriou s risk of	inconsistenc	serious ²	imprecisio	None	186	139	-	lower (4.14 lower to	MODERATE	IMPO RTAN T
(Aitke n s risk of bias lower (3.7 lower to 1.3 low	Quality	of life - CF	QOL soc	ial domain (ch	ange from ba	seline) (follo	ow-up 4 weeks;	range of	scores: 0	-100; Bet	tter indicated l	oy higher value	s)
2 randomise d trials serious s	(Aitke n 2012, Bilton		seriou s risk of	inconsistenc	serious ²	imprecisio	None	292	212	-	lower (3.7 lower to 1.3	MODERATE	IMPO RTAN T
(Aitke n s risk of bias Serious serious Se	Quality	of life - CF	QOL soc	ial domain (ch	ange from ba	seline) (follo	ow-up 6 months	; range o	f scores:	0-100; B	etter indicated	by higher valu	ies)
2 randomise d trials no serious serious² serious³ None 290 210 - MD 3.1 LOW lower (6.49 lower to 0.29 higher)	(Aitke n 2012, Bilton		seriou s risk of		serious ²	serious ³	None	268	197	-	lower (6.66 lower to	VERY LOW	IMPO RTAN T
(Aitke d trials seriou inconsistenc s risk y lower to 0.29 higher) Bilton	Quality	of life - CF	QOL boo	ly domain (cha	nge from bas	seline) (follo	w-up 4 months;	range of	scores: ()-100; Be	tter indicated	by higher value	es)
2011)	(Aitke n 2012, Bilton		seriou s risk of	inconsistenc	serious ²	serious ³	None	290	210	-	lower (6.49 lower to	LOW	IMPO RTAN T

Quality	/ assessmen	t					No of pa	atients	Effect			
No of studi es	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Mannit ol	Contro I	Relativ e (95% CI)	Absolute	Quality	Impor tance
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	no serious imprecisio n	None	266	195	-	MD 1.19 lower (4.51 lower to 2.13 higher)	MODERATE	IMPO RTAN T
Quality	of life - CFC	OL role	domain (chan	ge from base	line) (follow-	-up 4 months; ra	ange of so	cores: 0-	100; Bette	er indicated by	/ higher values	s)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	no serious imprecisio n	None	207	151	7	MD 1.22 higher (2.21 lower to 4.66 higher)	MODERATE	IMPO RTAN T
Quality	of life - CFC	OL role	domain (chan	ge from base	line) (follow-	-up 6 months; ra	ange of so	cores: 0-	100; Bette	er indicated by	/ higher values	;)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	serious ¹²	serious ²	serious ³	None	186	138	-	MD 1.30 lower (45.79 lower to 3.19 higher)	VERY LOW	IMPO RTAN T
Quality	of life - CFC	OL dige	estion domain	change from	baseline) (fo	ollow-up 4 mon	ths; range	e of score	es: 0-100	Better indica	ted by higher v	alues)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	no serious imprecisio n	none	292	213	-	MD 1.49 lower (4.77 lower to 1.78 higher)	MODERATE	IMPO RTAN T

Quality	/ assessmen	t					No of pa	atients	Effect			
No of studi	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Mannit ol	Contro I	Relativ e (95% CI)	Absolute	Quality	Impor tance
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	None	268	197	-	MD 1.07 lower (5.04 lower to 2.9 higher)	LOW	IMPO RTAN T
Quality	of life - CFC	QOL weig	ght domain (ch	ange from ba	aseline) (follo	ow-up 4 months	s; range o	f scores:	0-100; B	etter indicated	l by higher valu	ıes)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	None	207	153	-	MD 4.23 lower (10.28 lower to 1.83 higher)	LOW	IMPO RTAN T
Quality	of life - CFC	QOL weig	ght domain (ch	ange from ba	aseline) (follo	ow-up 6 months	s; range o	f scores:	0-100; B	etter indicated	l by higher valu	ıes)
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	serious ³	None	186	139	-	MD 3.27 lower (9.84 lower to 3.31 higher)	LOW	IMPO RTAN T
Advers	se events: ha	emopty	sis (mild) (follo	w-up 2 week	s)							
1 (Jaqu es 2008)	randomise d trials ¹	no seriou s risk of bias	no serious inconsistenc y	serious ²	not calculable a	None	(0%)	8 (0%)	RR not estima ble ^b	0 events in each group	MODERATE	IMPO RTAN T
Advers	se events: ha	emopty	sis (severe) (fo	llow-up 2 we	eks)							
				serious ²		None	1	8			VERY LOW	

No of studies 1 randomise (Jaqu es 2008) Adverse events: Brandomise (Bilto d trials n 2011) Adverse events: Have a continuous des continuous de continuous des continuous de continuous des continuous de contin	no seriou s risk	no serious riou inconsistenc sk y s hospasm (mild) (for no serious riou inconsistenc	Indirectnes s	very serious ⁹ onths) not calculable	Other consideration s	Mannit ol 2(5.3%)	Contro I 2(5.3%)	Relativ e (95% CI) RR 1 (0.15 to 6.74)	O fewer per 1000 (from 45 fewer to 302 more)	Quality	Impor tance IMPO RTAN T
(Jaqu d trials¹ es 2008) Adverse events: Br 1 randomise (Bilto d trials n 2011) Adverse events: Ha 2 randomise (Aitke d trials n 2012, Bilton	seriou s risk of bias ronchos no seriou s risk	riou inconsistenc sk y s hospasm (mild) (for no serious riou inconsistenc	· · · · · · · · · · · · · · · · · · ·	onths) not calculable	None	0/177)	(0.15 to 6.74)	1000 (from 45 fewer to 302 more)		RTAN
1 randomise d trials n 2011) Adverse events: Have a d trials n 2012, Bilton	no seriou s risk	no serious iou inconsistenc	· · · · · · · · · · · · · · · · · · ·	not calculable	None		0/118	DD not	0		
(Bilto n 2011) Adverse events: Have a randomise d trials n 2012, Bilton	seriou s risk	riou inconsistenc	serious ²	calculable	None		0/118	DD not	0		
2 randomise (Aitke d trials n 2012, Bilton	of bias	S				(0%)	(0%)	RR not estima ble ^b	0 events in each group	MODERATE	IMPO RTAN T
(Aitke d trials n 2012, Bilton	aemopty	optysis (mild) (follo	ow-up 6 mont	:hs)							
	no seriou s risk of	riou inconsistenc	serious ²	very serious ⁹	None	6/361 (1.7%)	2/239 (0.84%)	RR 1.73 (0.26 to	6 more per 1000 (from 6 fewer to 89 more)	VERY LOW	IMPO RTAN T
	bias	s					0.9%	11.62)	7 more per 1000 (from 7 fewer to 96 more)		
Adverse events: Br	ronchos	hospasm (moderat	te) (follow-up	6 months)							
1 randomise (Bilto d trials n 2011)	no seriou	no serious riou inconsistenc sk y	serious ²	very serious ⁹	None	1/177 (0.56%)	0/118 (0%)	RR 2.01 (0.03 to 133.11)	-	VERY LOW	IMPO RTAN T

Quality assessment							No of patients		Effect			
No of studi es	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Mannit ol	Contro I	Relativ e (95% CI)	Absolute	Quality	Impor tance
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	very serious ⁹	None	10/361 (2.8%)	1/239 (0.42%)	RR 4.66 (0.5 to 43.49)	15 more per 1000 (from 2 fewer to 178 more)	VERY LOW	IMPO RTAN T
								0.4%		15 more per 1000 (from 2 fewer to 170 more)		
Advers	se events: Br	onchos	pasm (severe)	(follow-up 6 i	months)							
1 (Bilto n 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	very serious ⁹	none	1/177 (0.56%)	0/118 (0%)	RR 2.01 (0.03 to 133.11)	-	VERY LOW	IMPO RTAN T
Advers	se events: Ha	emopty	sis (severe) (fo	ollow-up 6 mc	onths)							
2 (Aitke n 2012,	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	very serious ⁹	none	3/361 (0.83%)	1/239 (0.42%)	RR 1.55 (0.13 to 18.99)	2 more per 1000 (from 4 fewer to 75 more)	VERY LOW	IMPO RTAN T
Bilton 2011)								0.4%		2 more per 1000 (from 3 fewer to 72 more)		
Adverse events: Bronchospasm in children and young people (follow-up 6 months)												
1 (Bilto n 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	not calculable a	None	0/63 (0%)	0/42 (0%)	RR not estima ble ^b	0 events in each group	MODERATE	IMPO RTAN T

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Quality assessment						No of patients		Effect				
No of studi es	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Mannit ol	Contro I	Relativ e (95% CI)	Absolute	Quality	Impor tance
Advers	se events in a	adults: E	Bronchospasm	in adults (fo	llow-up 6 mo	onths)						
1 (Bilto n 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	very serious ⁹	None	No. particip ants with bronch ospas m not reporte d. Total N of particip ants: 114	No. partici pants with bronch ospas m not reporte d. Total N of partici pants: 76	RR 3.35 (0.16 to 71.50)	-	VERY LOW	IMPO RTAN T
Advers	se events: Ha	aemopty	sis in children	and young p	eople (follow	v-up 6 months)						
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	very serious ⁹	none	No. particip ants with haemo ptysis not reporte d. Total N of particip ants: 154	No. partici pants with haemo ptysis not reporte d. Total N of partici pants: 105	RR 5.48 (0.69 to 43.50)	-	VERY LOW	IMPO RTAN T

Quality No of studi es	/ assessmen Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	No of pa Mannit ol	atients Contro I	Effect Relativ e (95% CI)	Absolute	Quality	Impor tance
2 (Aitke n 2012, Bilton 2011)	randomise d trials	no seriou s risk of bias	no serious inconsistenc y	serious ²	very serious ⁹	none	No. particip ants with haemo ptysis not reporte d. Total N of particip ants: 207	No. partici pants with haemo ptysis not reporte d. Total N of partici pants: 134	RR 1.83 (0.64 to 5.23)	-	VERY LOW	IMPO RTAN T

Abbreviations: CFQOL: cystic fibrosis quality of life questionnaire; CI: confidence interval; FEV₁: forced expiratory volume in 1 second; HR: hazard ratio; MD: mean difference; RR: risk ratio

- 1 Cross-over design
- 2 The quality of the evidence was downgraded by 1 as the participants in the trial underwent a tolerance test at screening. Those who failed were not entered in the study, and this limits the generalisability of the results to the general CF population.
- 3 The quality of the evidence was downgraded by 1 as the 95% CI crossed 1 clinical MID
- 4 The quality of the evidence was downgraded by 1, as the 95% CI crossed the null effect
- 5 The quality of the evidence was downgraded by 1 as the 95% CI crossed 1 default MID
- 6 The quality of the evidence was downgraded by 1 due to moderate heterogeneity (12=59%)
- 7 The quality of the evidence was downgraded by 1 due to moderate heterogeneity (12=37%).
- 8 The quality of the evidence was downgraded by 2 due to high heterogeneity (I2=89%)
- 9 The quality of the evidence was downgraded by 2 as the 95% CI crossed 2 default MIDs
- 10 The quality of the evidence was downgraded by 1 due to high heterogeneity (I2=77%). It was not downgraded further as both studies showed no differences between groups.
- 11 The quality of the evidence was downgraded by 2 due to high heterogeneity (I2=70%). Studies show conflicting results.
- 12 The quality of the evidence was downgraded by 1 due to moderate heterogeneity (I2=41%)
- a Imprecision not calculable because risk ratio could not be estimated as there were 0 events in each group
- b Risk ratio not estimable because there were 0 events in each group