

Table 26: Clinical evidence profile: Comparison 3.1. Nebulised sodium chloride (> 3% concentration) versus placebo (0.9% to 0.12%) or low-concentration (≤ 3%)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High concentration (>3% sodium chloride)	Low concentration (≤3% sodium chloride)	Relative (95% CI)	Absolute		
Failed to regain pre-exacerbation FEV₁% predicted (follow-up: at hospital discharge; range of scores: 0-100; Better indicated by higher values)												
1 (Dentice 2016)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	17/67 (25.4%)	28/65 (43.1%)	RR 0.59 (0.36 to 0.97)	177 fewer per 1000 (from 13 fewer to 276 fewer)	MODERATE	CRITICAL
Lung function: % change in FEV₁ (follow-up 2 weeks; range of scores: 0-100; Better indicated by higher values)												
1 (Gupta 2012)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	15	15	-	MD 14.35 lower (27.8 to 0.9 lower)	MODERATE	CRITICAL
Lung function: % change in FEV₁ (follow-up 4 weeks; range of scores: 0-100; Better indicated by higher values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High concentration (>3% sodium chloride)	Low concentration (≤3% sodium chloride)	Relative (95% CI)	Absolute		
2 (Gupta 2012, Mainz 2016)	randomised trials ²	very serious ³	very serious ⁴	no serious indirectness	very serious ⁵	none	75	78	-	MD 4.92 lower (17.69 lower to 7.86 higher)	VERY LOW	CRITICAL
Lung function: % change in FEV₁ (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1 (Elkins 2006)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	76	73	-	MD 4.1 higher (0.08 lower to 8.28 higher)	MODERATE	CRITICAL
Lung function: % change in FEV₁ (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values)												
1 (Elkins 2006)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	75	65	-	MD 5.37 higher (1.03 to 9.71 higher)	MODERATE	CRITICAL
Lung function: % change in FEV₁ (follow-up 36 weeks; range of scores: 0-100; Better indicated by higher values)												
1 (Elkins)	randomised trials	no serious	no serious inconsistency	no serious indirectness	serious ¹	none	69	65	-	MD 3.63 higher	MODERATE	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High concentration (>3% sodium chloride)	Low concentration (≤3% sodium chloride)	Relative (95% CI)	Absolute		
2006)		risk of bias								(1.56 lower to 8.82 higher)		
Lung function: % change in FEV₁ (follow-up 48 weeks; range of scores: 0-100; Better indicated by higher values)												
1 (Elkins 2006)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	68	66	-	MD 2.31 higher (2.72 lower to 7.34 higher)	MODERATE	CRITICAL
Time to first pulmonary exacerbation (follow-up: > 1 year)												
2 (Dentice 2016, Rosenfeld 2012)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ⁶	none	225	228	HR 0.92 (0.74 to 1.14)	-	MODERATE	CRITICAL
Number of days of treatment for a pulmonary exacerbation (follow-up 48 weeks; Better indicated by lower values)												
1 (Rosenfeld)	randomised trials	no serious risk	no serious inconsistency	no serious indirectness	no serious imprecision	none	158	163	-	MD 1.11 higher (0.89	HIGH	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High concentration (>3% sodium chloride)	Low concentration (≤3% sodium chloride)	Relative (95% CI)	Absolute		
2012)		of bias								to 1.33 higher)		
Change in quality of life following treatment – CFQOL, physical domain (follow-up 7 days; range of scores: 0-100; Better indicated by higher values)												
1 (Dentice 2016)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	67	65	-	MD 2.00 higher (3.12 lower to 7.12 higher)	MODERATE	IMPORTANT
Change in quality of life following treatment – CFQOL, burden domain (follow-up 7 days; range of scores: 0-100; Better indicated by higher values)												
1 (Dentice 2016)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	65	-	MD 0.00 higher (4.78 lower to 4.78 higher)	HIGH	IMPORTANT
Change in quality of life following treatment – CFQOL, health domain (follow-up 7 days; range of scores: 0-100; Better indicated by higher values)												
1 (Dentice)	randomised trials	no serious risk	no serious inconsistency	no serious indirectness	serious ¹	none	67	65	-	MD 2.00 lower (8.15 lower)	MODERATE	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High concentration (>3% sodium chloride)	Low concentration (≤3% sodium chloride)	Relative (95% CI)	Absolute		
2016)		of bias								to 4.15 higher)		
Change in quality of life following treatment – CFQOL, respiratory domain (follow-up 7 days; range of scores: 0-100; Better indicated by higher values)												
1 (Dentice 2016)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	67	65	-	MD 1.00 higher (4.99 lower to 6.99 higher)	MODERATE	IMPORTANT
Change in quality of life following treatment – CFQOL, physical domain (at hospital discharge; range of scores: 0-100; Better indicated by higher values)												
1 (Dentice 2016)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	67	65	-	MD 2.00 higher (4.15 lower to 8.15 higher)	MODERATE	IMPORTANT
Change in quality of life following treatment – CFQOL, burden domain (at hospital discharge; range of scores: 0-100; Better indicated by higher values)												
1 (Dentice)	randomised trials	no serious risk	no serious inconsistency	no serious indirectness	serious ¹	none	67	65	-	MD 2.00 higher (4.04 lower)	MODERATE	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High concentration (>3% sodium chloride)	Low concentration (≤3% sodium chloride)	Relative (95% CI)	Absolute		
2016)		of bias								to 8.04 higher)		
Change in quality of life following treatment – CFQOL, health domain (at hospital discharge; range of scores: 0-100; Better indicated by higher values)												
1 (Dentice 2016)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	67	65	-	MD 2.00 higher (4.99 lower to 8.99 higher)	MODERATE	IMPORTANT
Change in quality of life following treatment – CFQOL, respiratory domain (at hospital discharge; range of scores: 0-100; Better indicated by higher values)												
1 (Dentice 2016)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	67	65	-	MD 2.00 lower (8.67 lower to 4.67 higher)	MODERATE	IMPORTANT
Quality of life: CFQ parent, CFQ-R respiratory (follow-up 4 week; range of scores: 0-100; Better indicated by higher values)												
1 (Amin 2010)	randomised trials ⁷	no serious risk	no serious inconsistency	no serious indirectness	serious ¹	none	20		-	MD 5.9 higher (3.1 lower)	MODERATE	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High concentration (>3% sodium chloride)	Low concentration (≤3% sodium chloride)	Relative (95% CI)	Absolute		
		of bias								to 14.9 higher)		
Quality of life: CFQ 14+, CFQ-R respiratory (follow-up 4 weeks; Better indicated by higher values)												
1 (Amin 2010)	randomised trials ⁷	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious ⁵	none	20		-	MD 5.2 higher (7 lower to 17.4 higher)	LOW	IMPORTANT
Change in quality of life: CFQ-R parents (follow-up 48 weeks; range of scores: 0-100; Better indicated by higher values)												
1 (Elkins 2006)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious ⁵	none	34	33	-	MD 1.13 lower (7.49 lower to 5.23 higher)	LOW	IMPORTANT
Change in quality of life: CFQ-R 14+ (follow-up 48 weeks; range of scores: 0-100; Better indicated by higher values)												
1 (Elkins 2006)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	46	46	-	MD 7.77 higher (1.86 to 13.68 higher)	MODERATE	IMPORTANT
Change in quality of life: CFQ-R respiratory domain (follow-up 48 weeks; range of scores: 0-100; Better indicated by higher values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High concentration (>3% sodium chloride)	Low concentration (≤3% sodium chloride)	Relative (95% CI)	Absolute		
1 (Rosenthal 2012)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	158	163	-	MD 3.3 higher (0 to 6.6 higher)	MODERATE	IMPORTANT

Abbreviations: CFQ-R: cystic fibrosis questionnaire revised; CI: confidence interval; FEV₁: forced expiratory volume in 1 second; HR: hazard ratio, MD: mean difference; RR: risk ratio

1 The quality of the evidence was downgraded by 1 as the 95% CI crossed 1 clinical MID

2 Mainz 2016: Cross-over study

3 The quality of the study was downgraded by 1 due to unclear risk of bias in relation to random sequence generation, allocation concealment and selective reporting in 1 study

4 The quality of the evidence was downgraded by 2 due to serious inconsistency (I²=77%)

5 The quality of the evidence was downgraded by 2 as the 95% CI crossed 2 clinical MIDs

6 The quality of the evidence was downgraded by 1 as the 95% CI crossed the null effect

7 Amin 2010: cross-over study