Quality assessment						No of patients		Effect			
Design	Risk of bias	Inconsistenc y	Indirectne ss	Imprecisi on	Other consideration s	Acetylcystei ne	Place bo	Relati ve (95% CI)	Absolu te	Quality	Importanc e
Lung function: change in FEV1 (% predicted) (follow-up 4 weeks; range of scores: 0-100; Better indicated by higher values)											
randomise d trials	very serio us ¹	no serious inconsistenc y	no serious indirectnes s	serious ²	none	10	9	-	MD 3.51 higher (0.65 lower to 7.67 higher)	VERY LOW	CRITICAL
unction: cha	inge in l	FEV1 (% predic	cted) (follow-	up 12 weeks	s; range of sco	res: 0-100; Bet	ter indic	ated by h	nigher val	ues)	
randomise d trials	no serio us risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious ³	none	10	11	-	MD 5 higher (10.84 lower to 20.84 higher)	LOW	CRITICAL
unction: cha	nge in l	FEV ₁ (% predic	ted) (follow-	up 24 weeks	s; range of sco	res: 0-100; Bet	ter indic	ated by h	nigher val	ues)	
randomise d trials	no serio us risk of bias	no serious inconsistenc y	no serious indirectnes s	serious ²	none	36	34	-	MD 4.4 higher (0.83 to 7.97 higher)	MODERAT E	CRITICAL
	Design unction: cha randomise d trials unction: cha randomise d trials unction: cha randomise d trials	Design Risk of bias unction: cha-ge in I randomise d trials very serio us ¹ unction: cha-ge in I randomise d trials no serio us risk of bias unction: cha-ge in I randomise d trials no serio us risk of bias unction: cha-ge in I randomise d trials no serio us risk of bias unction: cha-ge in I randomise d trials no serio us risk of bias	Design Risk of bias Inconsistenc y unction: change in FEV1 (% prediction of trials no serious inconsistenc y aunction: change in FEV1 (% prediction of trials no serious inconsistenc y unction: change in FEV1 (% prediction of trials no serious inconsistenc y unction: change in FEV1 (% prediction of trials no serious inconsistenc y randomise d trials no serious inconsistenc y unction: change in FEV1 (% prediction of trials no serious inconsistenc y unction: change in FEV1 (% prediction of trials no serious inconsistenc y unction: change in FEV1 (% prediction of trials no serious inconsistenc y us risk of bias no serious inconsistenc y inconsistenc us risk of bias no serious inconsistenc y	DesignRisk of biasInconsistenc yIndirectne ssunction: change in FEV1 (% predicted) (follow- randomise d trialsvery serio us1no serious inconsistenc yno serious indirectnes sunction: change in FEV1 (% predicted) (follow- randomise d trialsno serio us1no serious indirectnes sunction: change in FEV1 (% predicted) (follow- randomise d trialsno serio us1no serious inconsistenc yno serious indirectnes sunction: change in FEV1 (% predicted) (follow- randomise d trialsno serio us risk of biasno serious inconsistenc yno serious indirectnes sunction: change in FEV1 (% predicted) (follow- randomise d trialsno serio us risk of biasno serious indirectnes s	DesignRisk of biasInconsistenc yIndirectne ssImprecisi onunction: change in FEV1 (% predicted) (follow-up 4 weeks; randomise d trialsvery serio us1no serious inconsistenc yno serious indirectnes sserious2unction: change in FEV1 (% predicted) (follow-up 12 weeks; serio us1no serious inconsistenc yno serious indirectnes sserious2unction: change in FEV1 (% predicted) (follow-up 12 weeks; inconsistenc us risk of biasno serious inconsistenc yno serious indirectnes svery serious indirectnes sunction: change in FEV1 (% predicted) (follow-up 12 weeks; of biasno serious indirectnes svery serious2unction: change in FEV1 (% predicted) (follow-up 24 weeks; of biasno serious indirectnes sserious2unction: change in FEV1 (% predicted) (follow-up 24 weeks; of biasno serious indirectnes sserious2	DesignRisk of biasInconsistenc yIndirectne ssImprecisi onOther consideration sunction: change in FEV1 (% predicted) (follow-up 4 weeks; range of score randomise d trialsno serious inconsistenc yno serious sserious snoneunction: change in FEV1 (% predicted) (follow-up 12 weeks; range of score inconsistenc yno serious sserious2noneunction: change in FEV1 (% predicted) (follow-up 12 weeks; range of score yno serious indirectnes sserious2noneunction: change in FEV1 (% predicted) (follow-up 12 weeks; range of score inconsistenc yno serious indirectnes snonerandomise d trialsno serio us risk of biasno serious inconsistenc yno serious sno serious sunction: change in FEV1 (% predicted) (follow-up 24 weeks; range of score inconsistenc inconsistenc yno serious snoneunction: change in FEV1 (% predicted) (follow-up 24 weeks; range of score inconsistenc indirectnes snone	Design biasRisk of biasInconsistenc yIndirectne ssImprecisi onOther consideration sAcetylcystei neunction: change in randomiseFEV1 (% predicted) (follow-up 4 weeks; range of scores: 0-100; Better inconsistenc yno serious indirectnes sno serious2 serious2none10unction: change in trialsFEV1 (% predicted) (follow-up 12 weeks; range of scores: 0-100; Better indirectnes snone10unction: change in d trialsFEV1 (% predicted) (follow-up 12 weeks; range of scores: 0-100; Better indirectnes snone10unction: change in d trialsno serious inconsistenc us risk of biasno serious sno serious snone10unction: change in randomise d trialsno serious inconsistenc yno serious sno serious snone10unction: change in randomise d trialsFEV1 (% predicted) (follow-up 24 weeks; range of scores: 0-100; Better s10unction: change in randomise d trialsno serious yno serious sno serious2 indirectnes snone36	DesignRisk of biasInconsistenc yIndirectne ssImprecisi onOther consideration sAcetylcystei nePlace bounction: charge in FEV1 (% predicted) (follow-up 4 weeks; range of scores: 0-100; Better indica inconsistenc yno serious indirectnesnone109unction: charge in FEV1 (% predicted) (follow-up 12 weeks; range of scores: 0-100; Better indica indirectnes snone109unction: charge in FEV1 (% predicted) (follow-up 12 weeks; range of scores: 0-100; Better indica indirectnes snone1011unction: charge in FEV1 (% predicted) (follow-up 12 weeks; range of scores: 0-100; Better indica indirectnes snone1011unction: charge in FEV1 (% predicted) (follow-up 12 weeks; range of scores: 0-100; Better indica indirectnes snone1011unction: charge in FEV1 (% predicted) (follow-up 24 weeks; range of scores: 0-100; Better indica indirectnes snone1011unction: charge in FEV1 (% predicted) (follow-up 24 weeks; range of scores: 0-100; Better indica indirectnes snone3634unction: charge in FEV1 (% predicted) (follow-up 24 weeks; range of scores: 0-100; Better indica indirectnes snone3634	DesignRisk of biasInconsistenc yIndirectne ssImprecisi onOther considerationAcetylcystei nePlace boRelati ve (95% CI)unction: charge in FEV: (% predicted) (follow-up 4 weeks; range of scores: 0-100; Better indicated by hi inconsistenc us1no serious inconsistenc yno serious s serious sserious2 serious2none109-unction: charge in FEV: (% predicted) (follow-up 12 weeks; range of scores: 0-100; Better indicated by hi inconsistenc yno serious sserious2 snone109-unction: charge in FEV: (% predicted) (follow-up 12 weeks; range of scores: 0-100; Better indicated by hi inconsistenc yno serious sno serious2 snone1011-randomise d trialsno serio us risk of biasno serious sno serious2 snone1011-unction: charge in FEV: (% predicted) (follow-up 24 weeks; range of scores: 0-100; Better indicated by hi serious311-unction: charge in FEV: (% predicted) (follow-up 24 weeks; range of scores: 0-100; Better indicated by hi serious311-unction: charge in FEV: (% predicted) (follow-up 24 weeks; range of scores: 0-100; Better indicated by hi serious311-unction: charge in FEV: (% predicted)no serious indirectnes sserious2none3634unction: charge in FEV: (% predicted)no serious indirectnes sserious2none3634unction: charge in FEV: (% predicted) <td>Design biasRisk of biasInconsistenc yIndirectne ssImprecisi onOther consideration sAcetylcystei nePlace boRelati ve (% C1)Absolu teunction: charge in FEV, (% predicted) (follow-up 4 weeks; range of scores: 0-100; Better indicated by higher value inconsistenc yno serious indirectnes sno serious2 snone109-MD 3.51 higher (0.65) lower to 7.677 higher)unction: charge in FEV, (% predicted) (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher value snone109-MD 3.51 higher to 0.665 lower to 7.677unction: charge in FEV, (% predicted) (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher value randomise d trialsno serious inconsistenc yno serious indirectnes snone1011-MD 5 higher to 7.677 higher)unction: charge in FEV, (% predicted) (follow-up 24 weeks; 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Table 27: Clinical evidence profile: Comparison 4. Acetylcysteine versus placebo

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Quality assessment						No of patients		Effect				
No of studi es	Design	Risk of bias	Inconsistenc y	Indirectne ss	Imprecisi on	Other consideration s	Acetylcystei ne	Place bo	Relati ve (95% CI)	Absolu te	Quality	Importanc e
1 (Con rad 2015)	randomise d trials	no serio us risk of bias	no serious inconsistenc y	no serious indirectnes s	not calculable 4	none	36	34	-	MD 0.19 higher (0.03 lower to 0.42 higher)	HIGH	IMPORTAN T
Incide	nce of pulmo	onary ex	xacerbations (1	follow-up 24	weeks)							
1 (Con rad 2015)	randomise d trials	no serio us risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious ³	none	15/36 (41.7%)	17/34 (50%)	RR 0.83 (0.5 to 1.39)	85 fewer per 1000 (from 250 fewer to 195 more)	LOW	CRITICAL
Quality	y of life: QFC	Q-R resp	biratory (follow	v-up 24 week	s; range of s	scores: 0-100; I	Better indicate	d by hig	her value	es)		
1 (Con rad 2015)	randomise d trials	no serio us risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious ³	none	36	34	-	MD 0.34 lower (6.3 lower to 5.62 higher)	LOW	IMPORTAN T

Abbreviations: CFQ-R: cystic fibrosis questionnaire revised; CI: confidence interval; FEV1: forced expiratory volume in 1 second; IL-8: interleukin 8; MD: mean difference; RR: risk ratio

1 The quality of the evidence was downgraded by 1 as this is an open trial, and there was unclear randomization and allocation concealment.

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

3 The quality of the evidence was downgraded by 2 as the 95% CI crossed 2 clinical MIDs 4 Imprecision not calculable, as SD for the control group was not available in the study