

Final

Cystic Fibrosis: diagnosis and management

Appendix I

Main appendix document

Forest Plots

25 October 2017

FINAL

*Developed by the National Guideline Alliance, hosted
by the Royal College of Obstetricians and
Gynaecologist*

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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Appendix I: Forest plots

I.1 Diagnosis of cystic fibrosis

Not applicable for this review.

I.2 Information and support

Not applicable to this review.

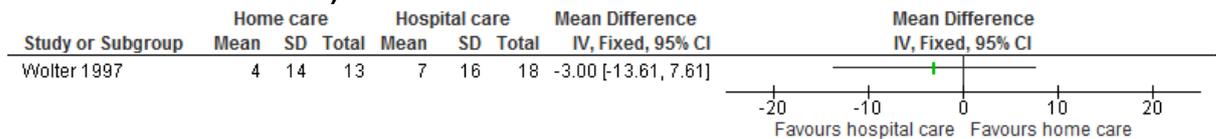
I.3 Service delivery

I.3.1 Service configuration

I.3.1.1 Home-based care

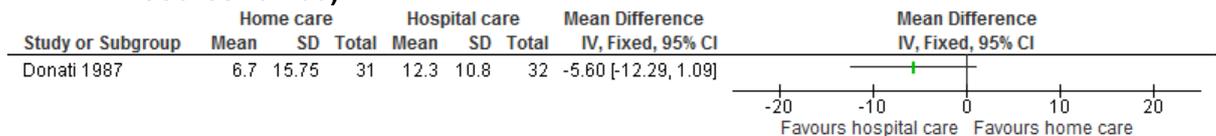
Comparison 1.1: home versus hospital care for the administration of intravenous antibiotics (IV AB) in people with CF experiencing an acute pulmonary exacerbation

Figure 1: Lung function: Change in FEV₁ % predicted at 21 days follow-up (range of scores: 0-100)



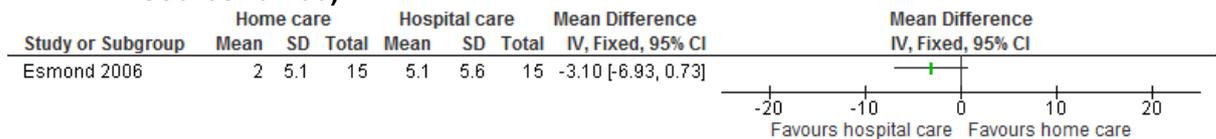
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 2: Lung function: Change in FEV₁ % predicted at 18 days follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 3: Lung function: Change in FEV₁ % predicted at 15 days follow-up (range of scores: 0-100)



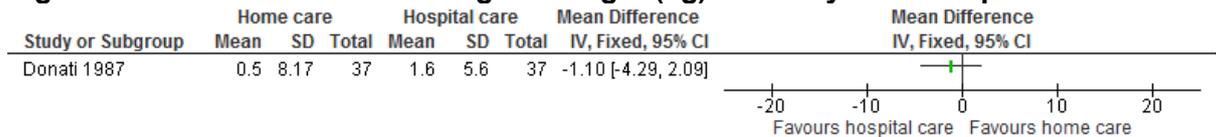
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 4: People starting next course of AB more than 12 weeks after completing the previous course (proxy outcome for time to next exacerbation) at 18 days follow-up



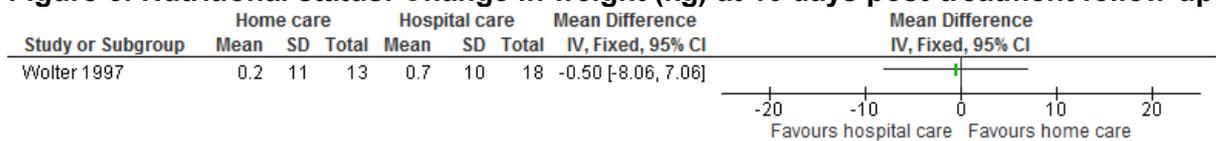
Abbreviations: AB: antibiotics; CI: confidence interval; M-H: Mantel Haenszel;

Figure 5: Nutritional status: Change in weight (kg) at 18 days follow-up



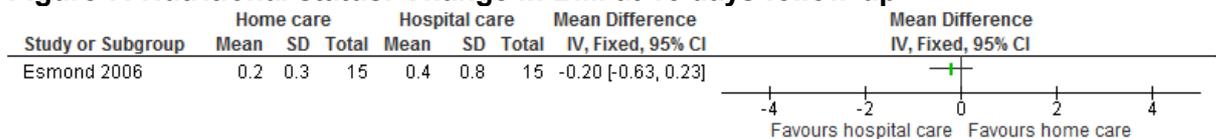
Abbreviations: CI: confidence interval; kg: kilograms; IV: inverse variance; SD: standard deviation;

Figure 6: Nutritional status: Change in weight (kg) at 10 days post-treatment follow-up



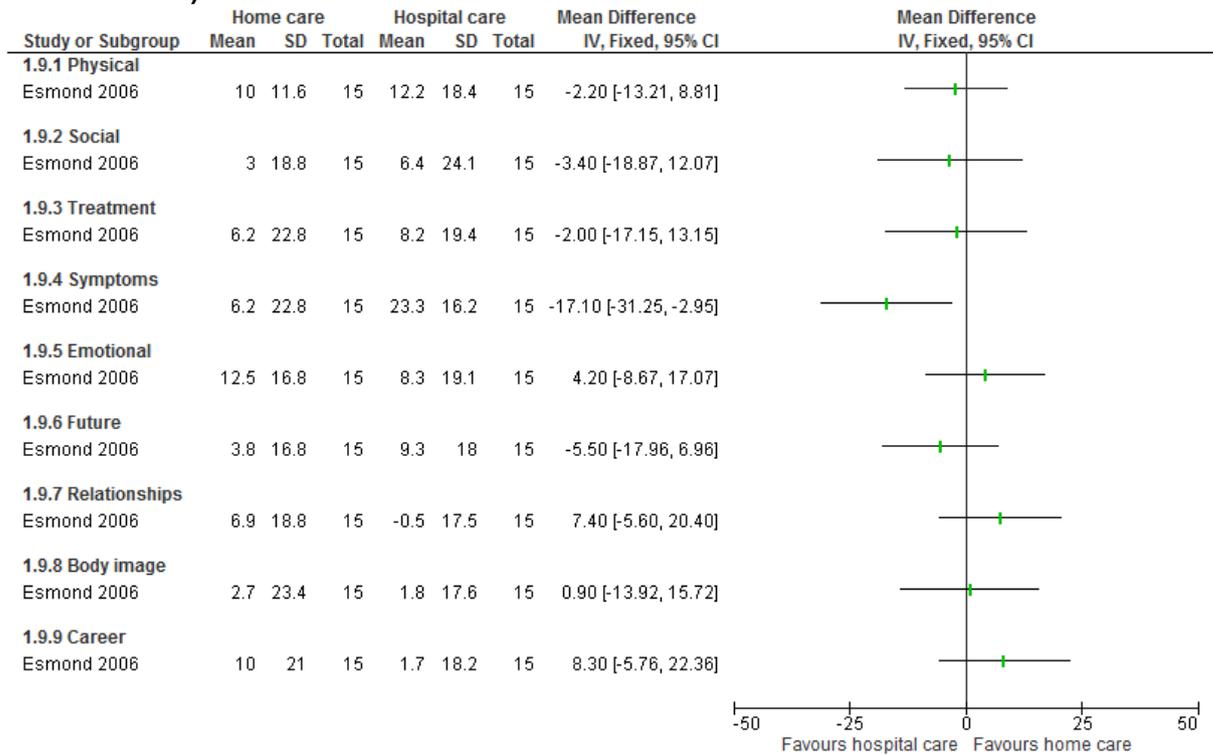
Abbreviations: CI: confidence interval; kg: kilograms; IV: inverse variance; SD: standard deviation;

Figure 7: Nutritional status: Change in BMI at 15 days follow-up



Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation;

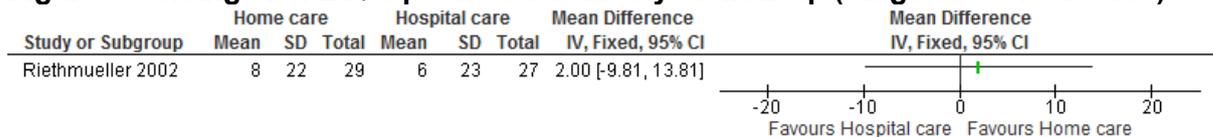
Figure 8: Change in quality of life (CF-QOL) at 15 days follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; CF-QOL: cystic fibrosis quality of life questionnaire; IV: inverse variance; SD: standard deviation

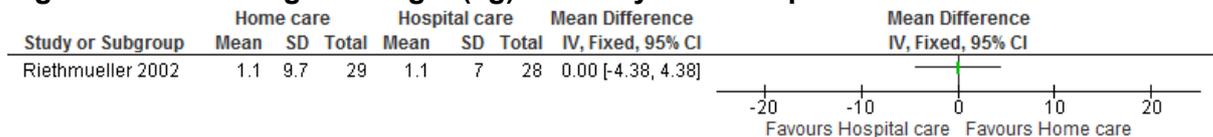
Comparison 1.2. Home versus hospital care for the administration of intravenous antibiotics (IV AB) in people with CF and chronic pulmonary infection with P. Aeruginosa

Figure 9: Change in FEV₁% predicted at 14 days follow-up (range of scores: 0-100)



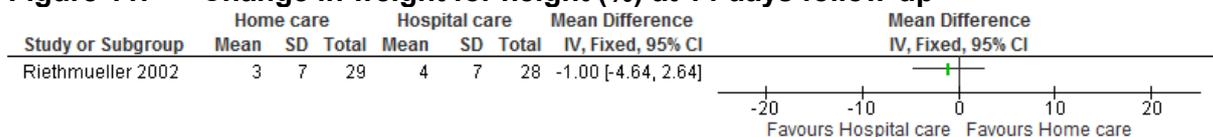
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 10: Change in weight (kg) at 14 days follow-up



Abbreviations: CI: confidence interval; kg: kilograms; SD: standard deviation; IV: inverse variance

Figure 11: Change in weight for height (%) at 14 days follow-up

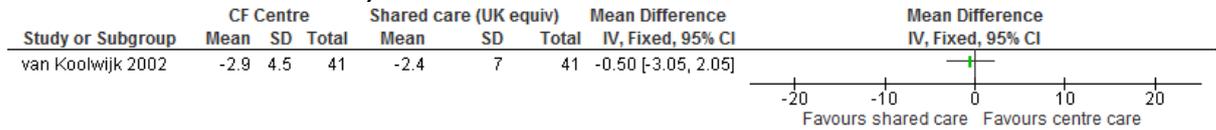


Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

I.3.1.2 CF centre care

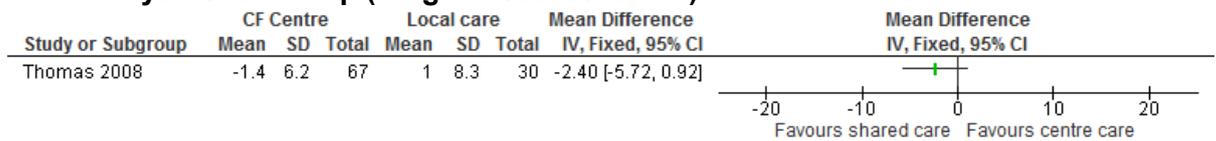
Comparison 2.1. CF centre care versus shared care

Figure 12: Lung function: Change in FEV₁ % predicted at 1 year follow-up (range of scores: 0-100)



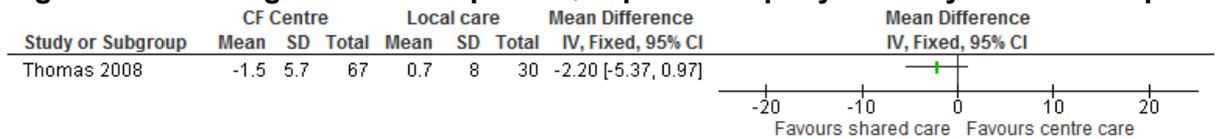
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 13: Lung function: Change from first to last FEV₁ % predicted per year at 3 years follow-up (range of scores: 0-100)



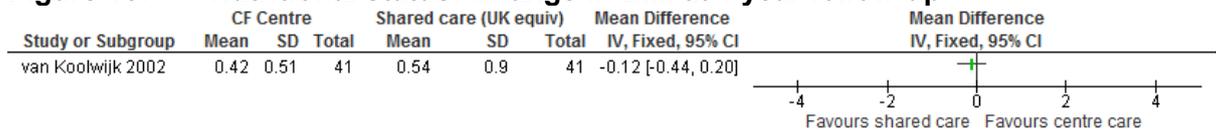
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 14: Lung function: Slope FEV₁ % predicted per year at 3 years follow-up



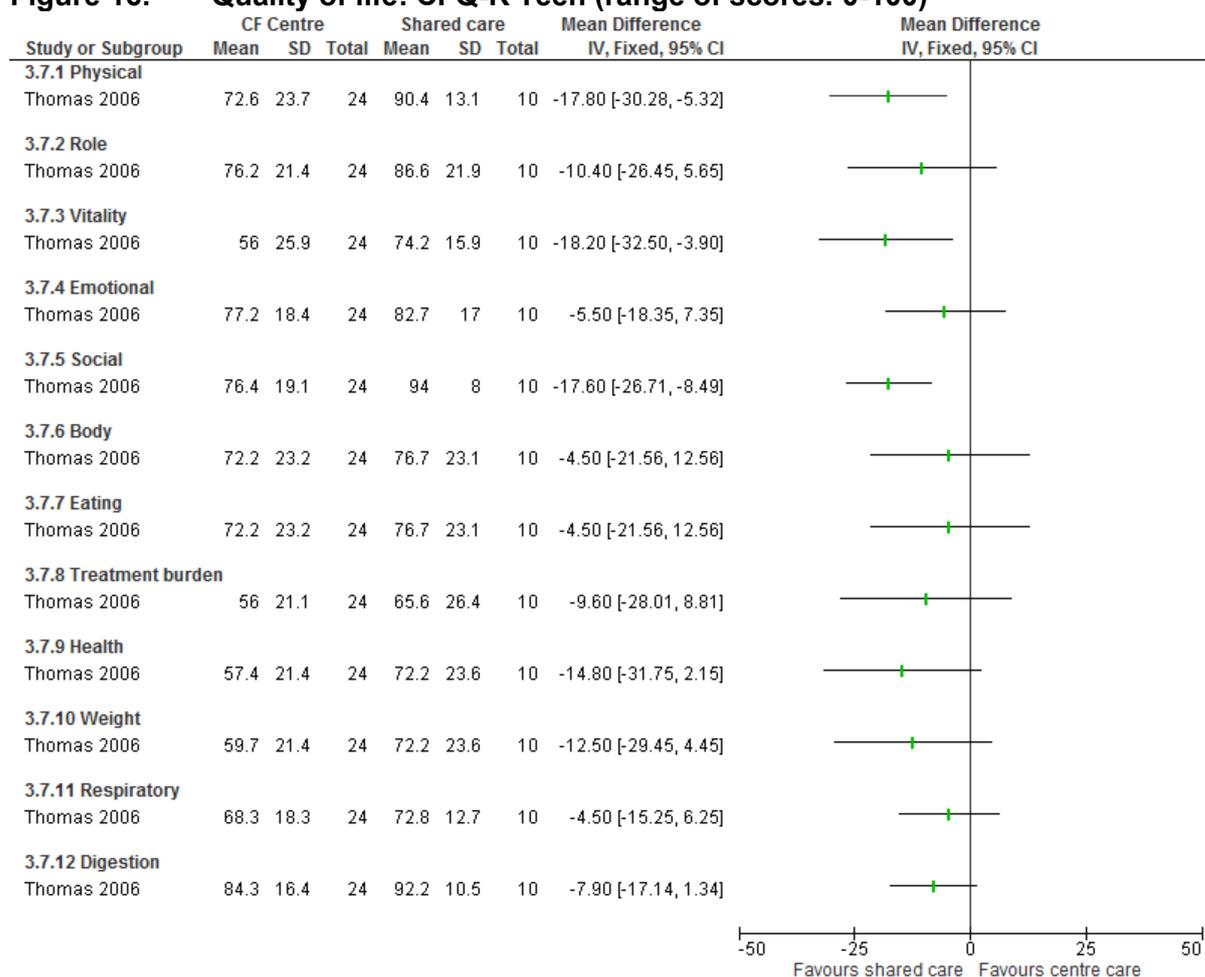
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 15: Nutritional status: Change in BMI at 1 year follow-up



Abbreviations: BMI: body mass index ; CI: confidence interval; IV: inverse variance; SD: standard deviation

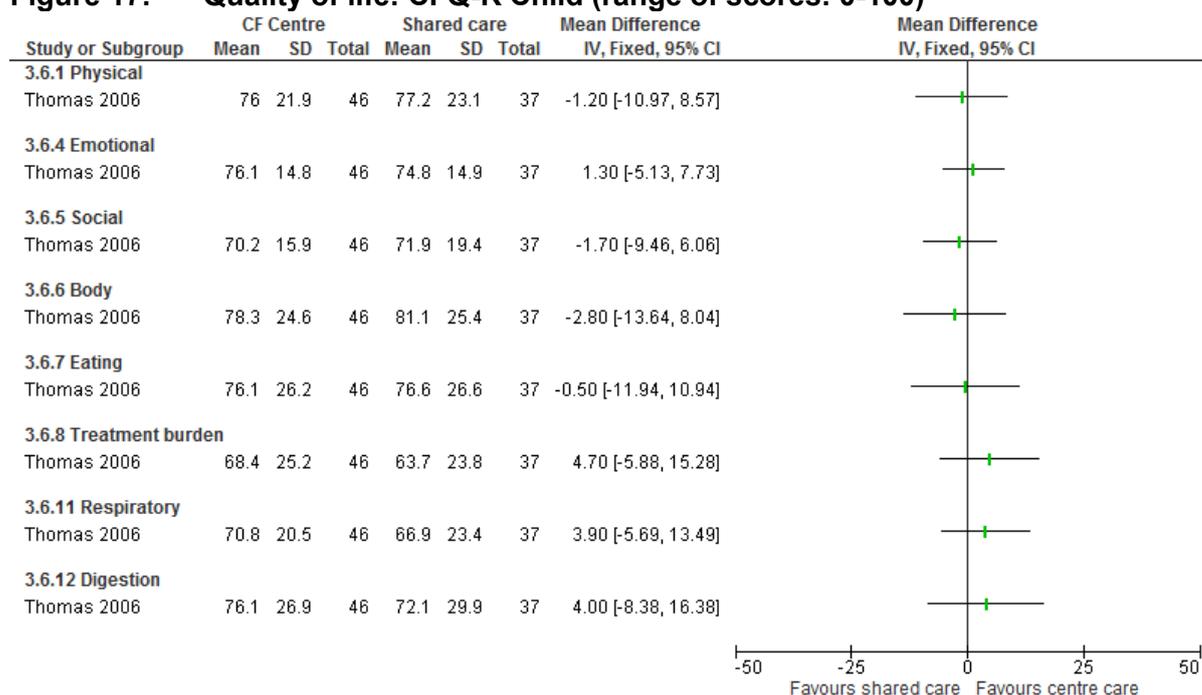
Figure 16: Quality of life: CFQ-R Teen (range of scores: 0-100)



Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation.

Note: Cross-sectional study

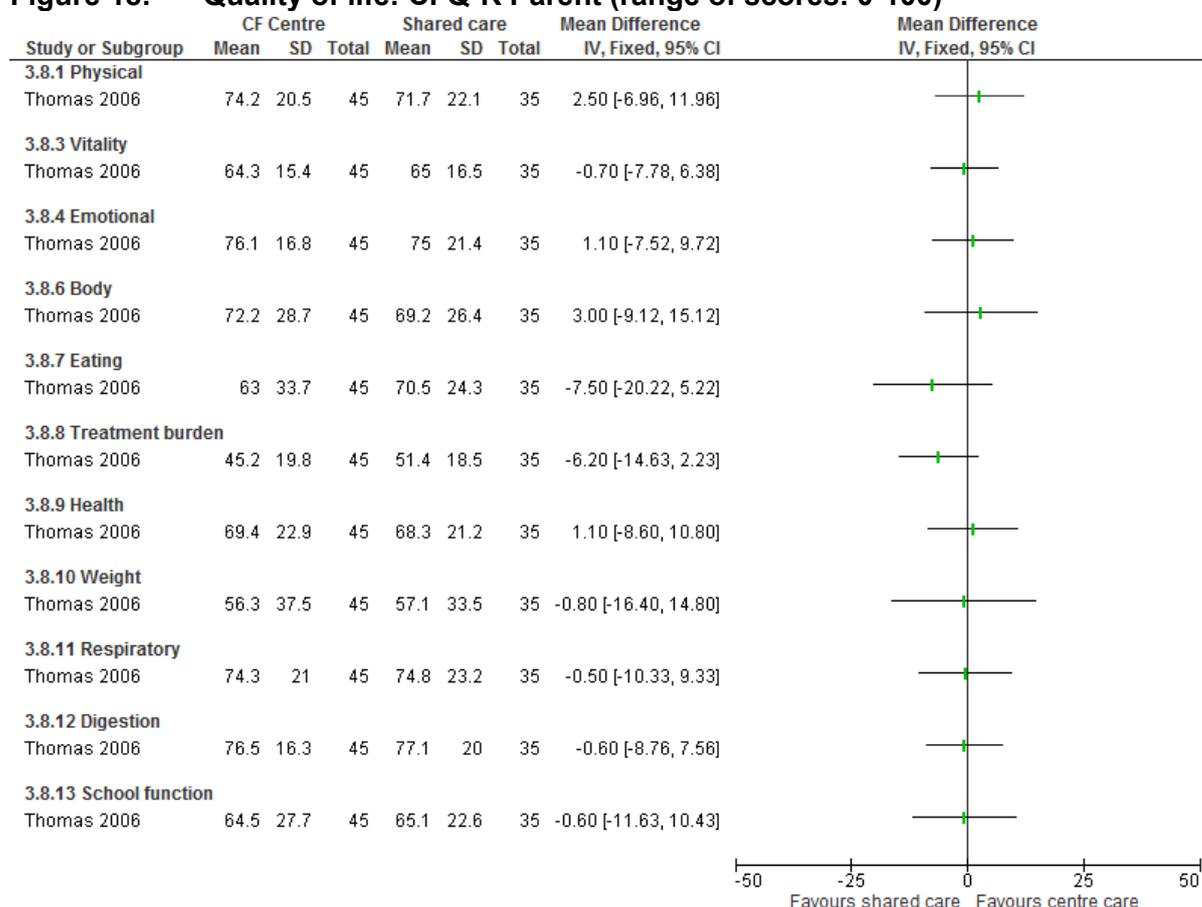
Figure 17: Quality of life: CFQ-R Child (range of scores: 0-100)



Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation.

Note: Cross-sectional study

Figure 18: Quality of life: CFQ-R Parent (range of scores: 0-100)

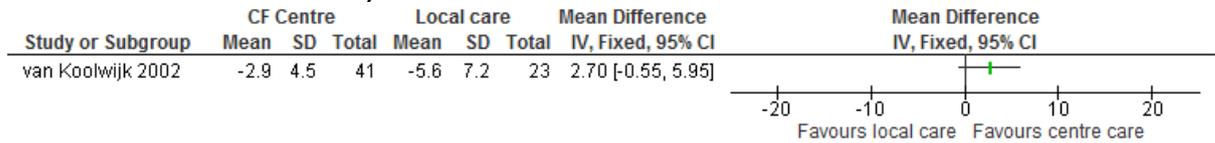


Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation.

Note: Cross-sectional study

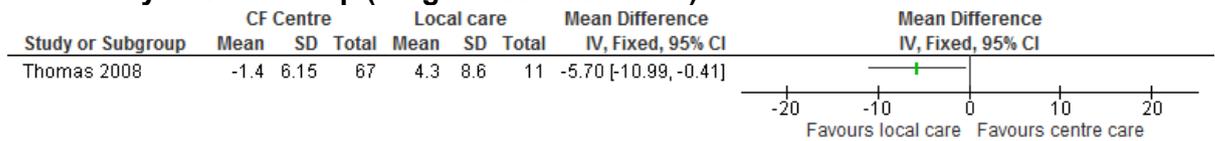
Comparison 2.2. CF centre care versus local care (below CF Trust recommendations)

Figure 19: Lung function: Change in FEV₁ % predicted at 1 year follow-up (range of scores: 0-100)



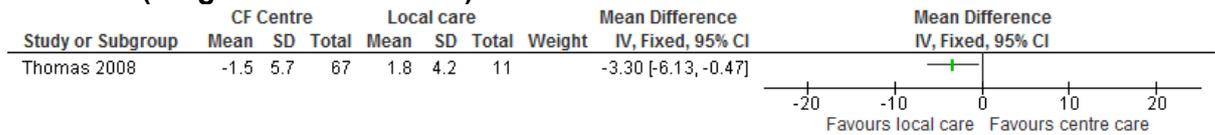
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 20: Lung function: Change from first to last FEV₁ % predicted per year at 3 years follow-up (range of scores: 0-100)



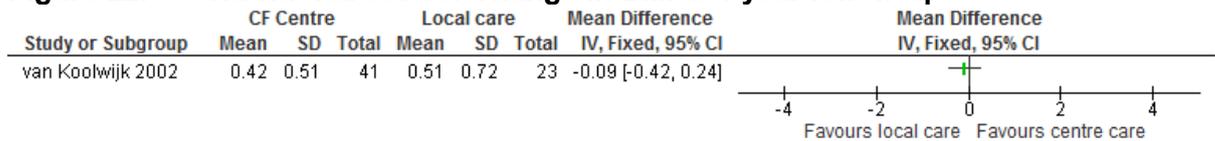
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 21: Lung function: Slope FEV₁ % predicted per year at 3 years follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 22: Nutritional status: Change in BMI at 1 year follow-up



Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation;

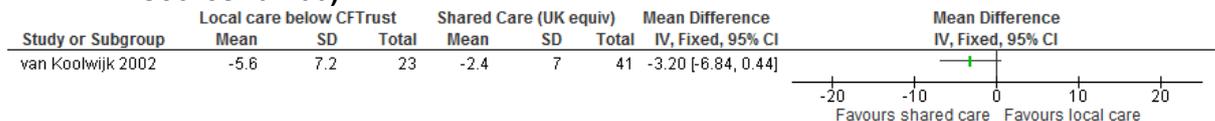
Comparison 2.3. CF centre care versus general clinic (non-CF)

Data could not be plotted.

1.3.1.3 Shared care

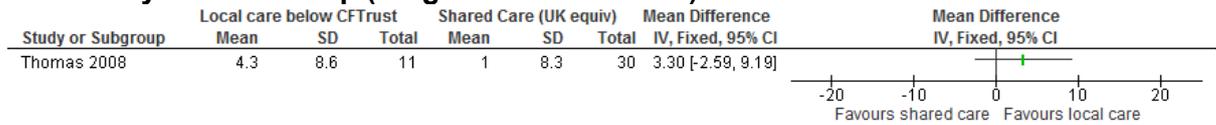
Comparison 3.1. Local care (below CF Trust Standards) versus shared care (UK equivalent)

Figure 23: Lung function: Change in FEV₁ % predicted at 1 year follow-up (range of scores: 0-100)



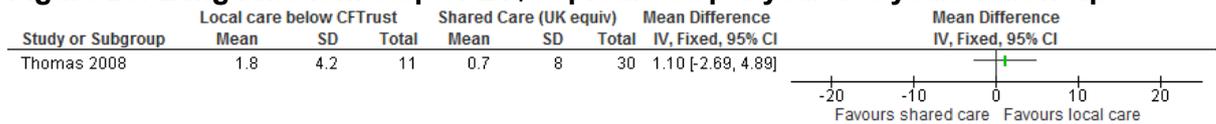
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 24: Lung function: Change from first to last FEV₁% predicted per year at 3 years follow-up (range of scores: 0-100)



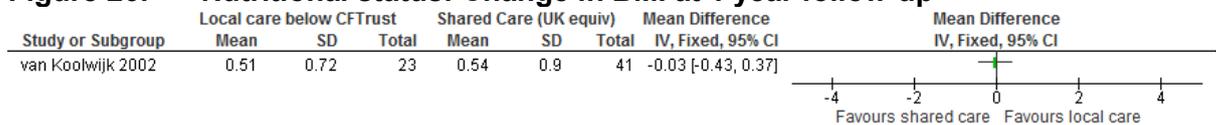
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 25: Lung function: slope FEV₁ % predicted per year at 3 years follow-up



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

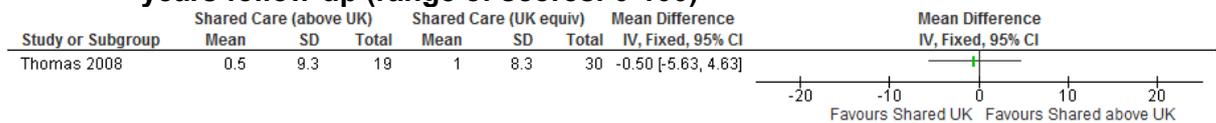
Figure 26: Nutritional status: Change in BMI at 1 year follow-up



Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

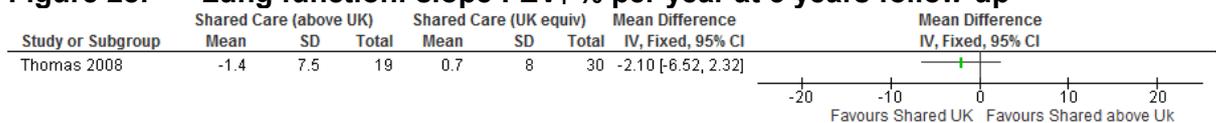
Comparison 3.2 Shared care (above UK standards) versus shared care (UK equivalent)

Figure 27: Lung function: Change from first to last FEV₁ % predicted per year at 3 years follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 28: Lung function: slope FEV₁ % per year at 3 years follow-up

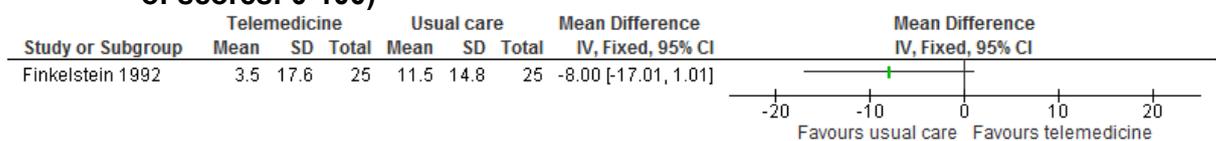


Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

1.3.1.4 Telemedicine

Comparison 4.1. Home monitoring + diary recording versus usual care

Figure 29: Lung function: Change in FEV₁ % predicted at 4 years follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Comparison 4.2. Telemedicine *versus* usual care

Data could not be plotted.

I.3.2 Multidisciplinary teams

Not applicable, as no studies were included in this review.

I.4 Transition

Not applicable to this review.

I.5 Complications of cystic fibrosis

Not applicable to this review.

I.6 Monitoring for pulmonary disease

I.6.1 Review 1. Monitoring for pulmonary disease onset in people with CF without clinical signs or symptoms of lung disease

Comparison 1. Lung function tests *versus* imaging tests

No forest plots available.

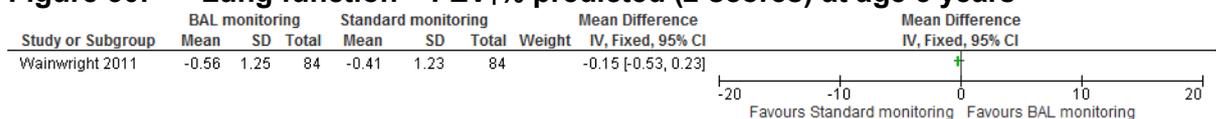
I.6.2 Review 2. Monitoring for evolving pulmonary disease in people with CF with established lung disease

Not applicable, as evidence was found for this review.

I.6.3 Review 3. Monitoring for evolving pulmonary disease in people with CF following an acute pulmonary exacerbation

Comparison 1. Monitoring using bronchoalveolar lavage (BAL) *versus* standard monitoring

Figure 30: Lung function – FEV₁% predicted (z-scores) at age 5 years



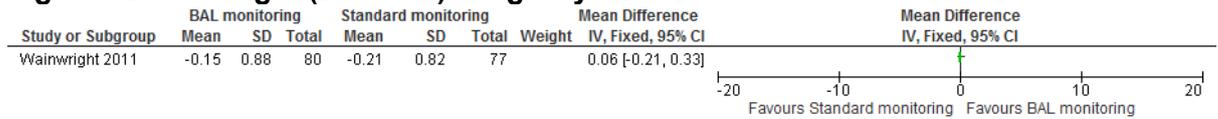
Abbreviations. BAL: bronchoalveolar lavage; CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation. Infants were recruited before age 6 months and followed until age 5 years.

Figure 31: Clearance of the organism from the cultures at age 5 years



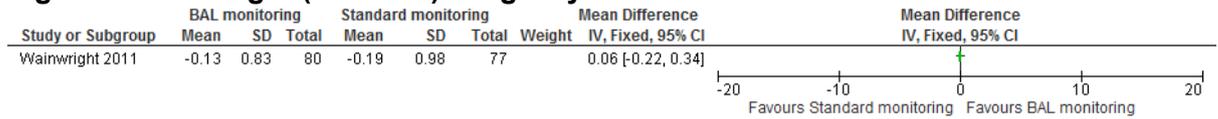
Abbreviations: BAL: bronchoalveolar lavage; M-H: Mantel-Haenszel; CI: confidence interval. Infants were recruited before age 6 months and followed until age 5 years

Figure 32: Weight (z-scores) at age 5 years



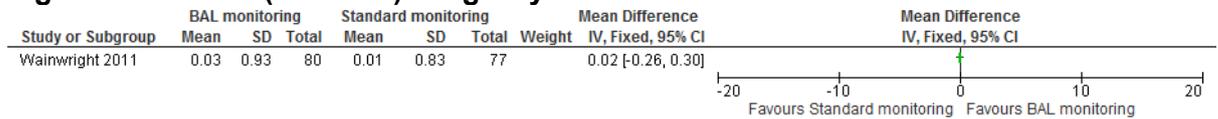
Abbreviations: BAL: bronchoalveolar lavage; SD: standard deviation; IV: inverse variance; CI: confidence interval. Infants were recruited before age 6 months and followed until age 5 years

Figure 33: Height (z-scores) at age 5 years



Abbreviations: BAL: bronchoalveolar lavage; CI: confidence interval; IV: inverse variance; SD: standard deviation. Infants were recruited before age 6 months and followed until age 5 years

Figure 34: BMI (z-scores) at age 5 years



Abbreviations: BAL: bronchoalveolar lavage; BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation. Infants were recruited before age 6 months and followed until age 5 years

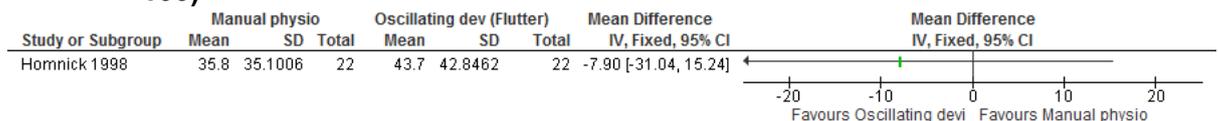
I.7 Airway clearance techniques

Comparison 1. Manual physiotherapy versus no airway clearance techniques

No evidence was found for this comparison.

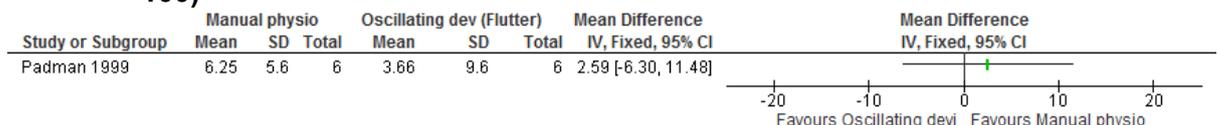
Comparison 2. Manual physiotherapy techniques versus oscillating devices

Figure 35: Change in FEV₁ % predicted after 8.8 days follow-up (range of scores: 0-100)



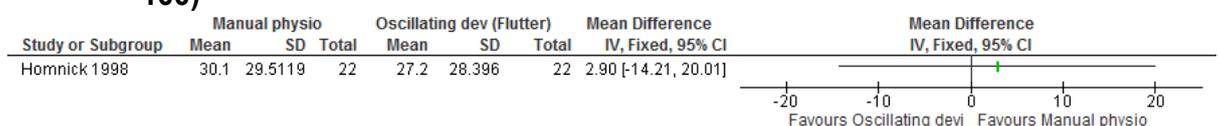
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 36: Change in FEV₁ % predicted at 1 month follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

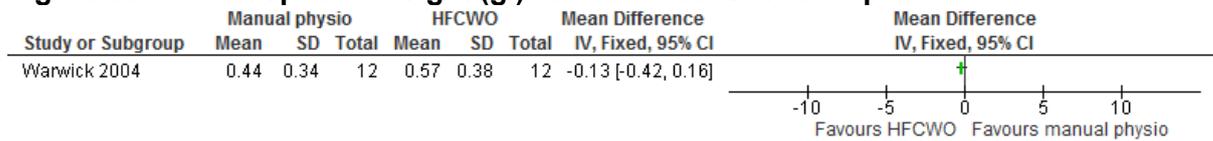
Figure 37: Change in FVC % predicted at 2 weeks follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

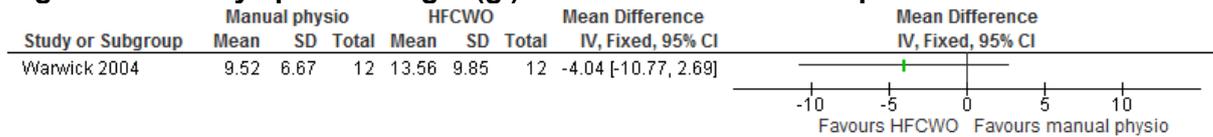
Comparison 3. Manual physiotherapy versus high frequency chest wall oscillation (HFCWO)

Figure 38: Wet sputum weight (g.) at 1 to 2 weeks follow-up



Abbreviations: HFCWO: High Frequency Chest Wall Oscillation; SD: standard deviation; IV: inverse variance; CI: confidence interval

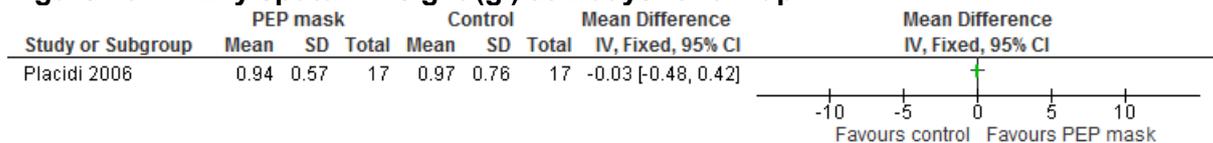
Figure 39: Dry sputum weight (g.) at 1 to 2 weeks follow-up



Abbreviations: HFCWO: High Frequency Chest Wall Oscillation; SD: standard deviation; IV: inverse variance; CI: confidence interval

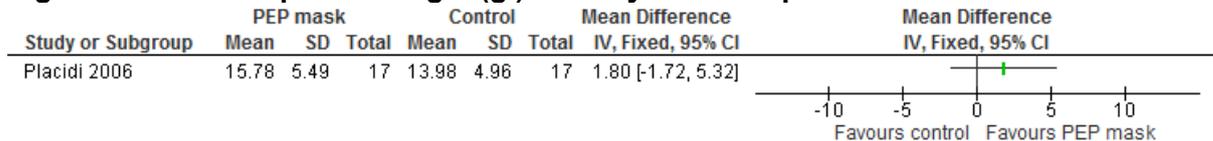
Comparison 4. Positive expiratory pressure mask (PEP) versus no airway clearance technique

Figure 40: Dry sputum weight (g.) at 2 days follow-up



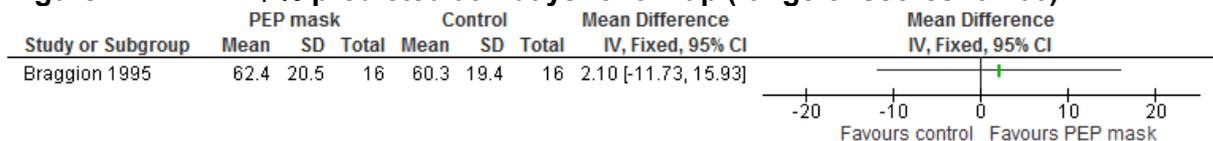
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 41: Wet sputum weight (g.) at 2 days follow-up



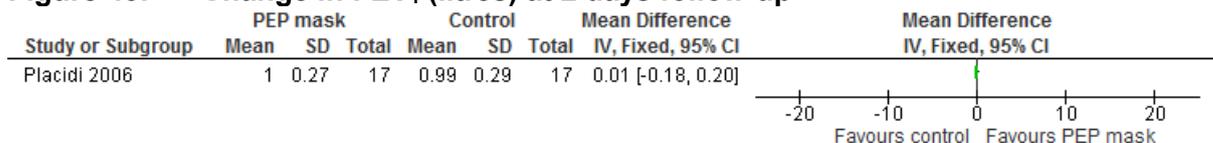
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 42: FEV₁ % predicted at 2 days follow-up (range of scores: 0-100)



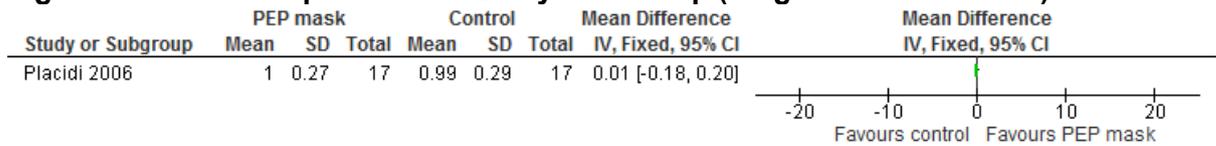
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 43: Change in FEV₁ (litres) at 2 days follow-up



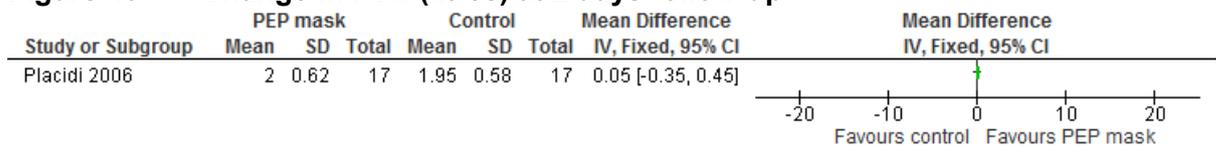
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 44: FVC % predicted at 2 days follow-up (range of scores: 0-100)



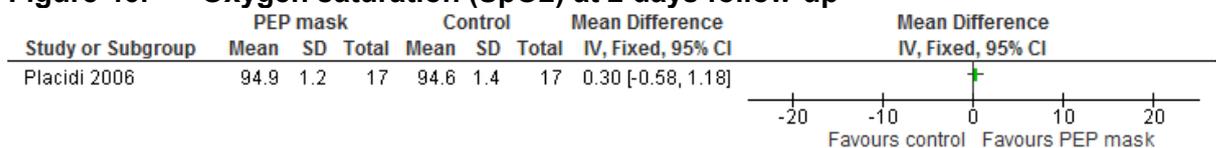
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

Figure 45: Change in FVC (litres) at 2 days follow-up



Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

Figure 46: Oxygen saturation (SpO2) at 2 days follow-up



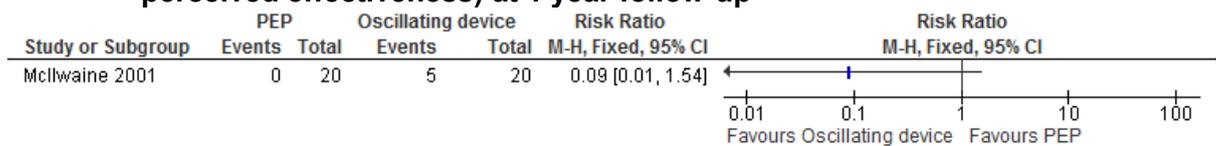
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

Comparison 5. Positive expiratory pressure mask (PEP) versus active cycle of breathing techniques (ACBT)

No evidence was found for this comparison.

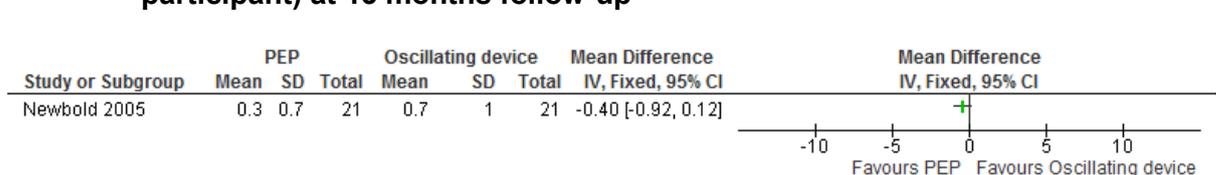
Comparison 6. Positive expiratory pressure mask (PEP) versus oscillating devices

Figure 47: Patient preference (measured as self-withdrawal due to lack of perceived effectiveness) at 1 year follow-up



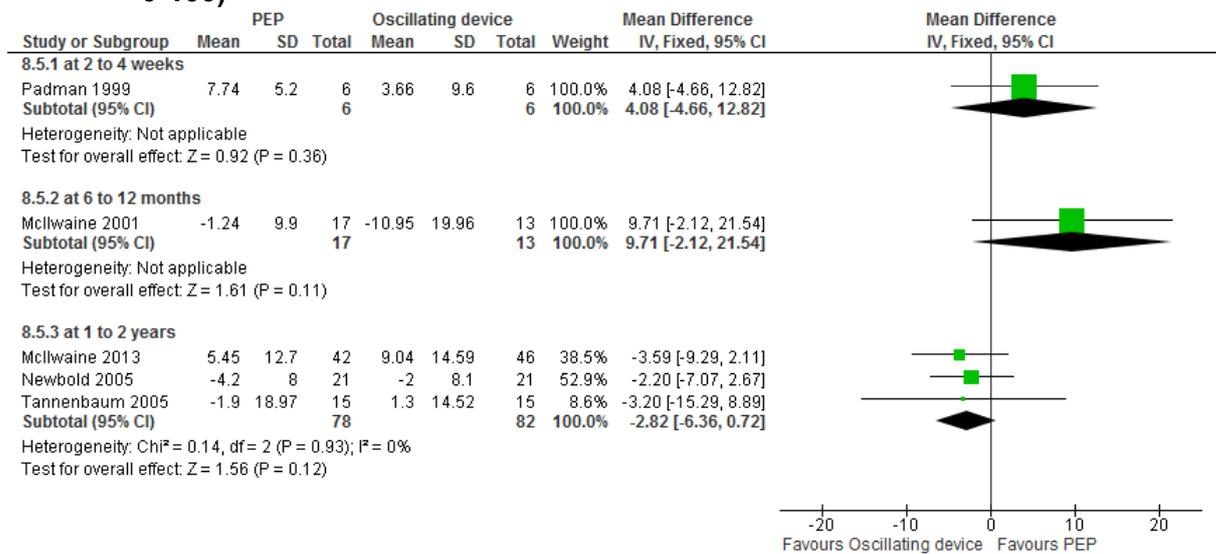
Abbreviations: PEP: positive expiratory pressure mask; M-H: Mantel-Haenszel; CI: confidence interval

Figure 48: Hospitalisations due to respiratory exacerbations (mean number per participant) at 13 months follow-up



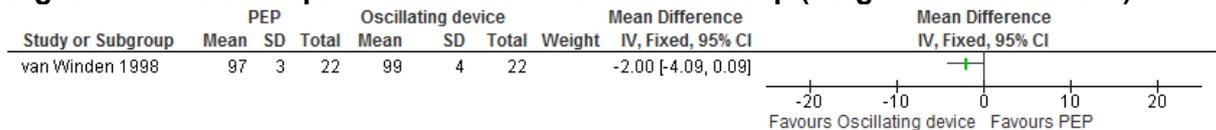
Abbreviations: PEP: positive expiratory pressure mask; SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 49: Change in FEV₁ % predicted at up to 2 years follow-up (range of scores: 0-100)



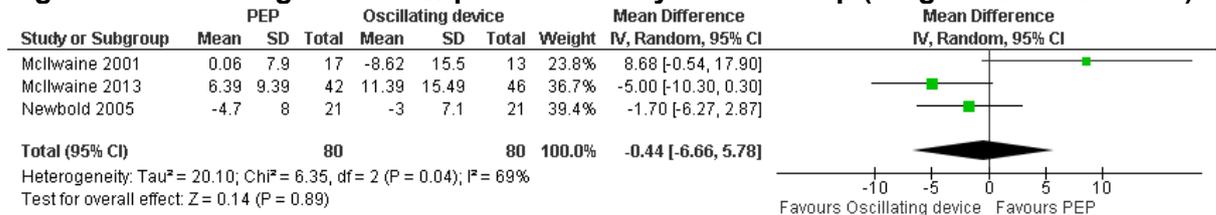
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

Figure 50: FVC % predicted at 2 to 4 weeks follow-up (range of scores: 0-100)



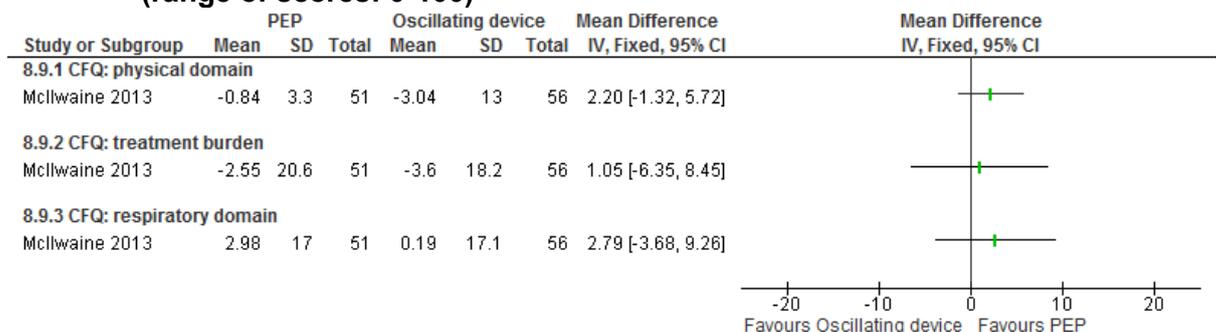
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

Figure 51: Change in FVC % predicted at 1 year follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

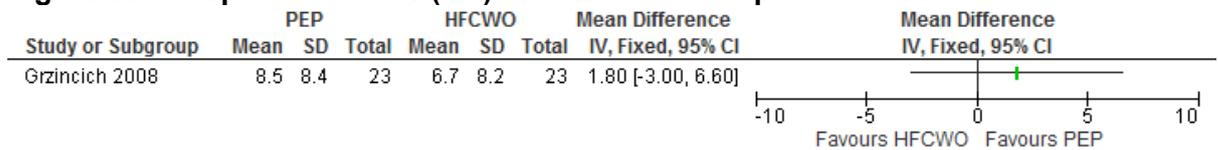
Figure 52: Change in quality of life (measured with CF-QOL) at 1 year follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; CF-QOL: cystic fibrosis quality of life questionnaire; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

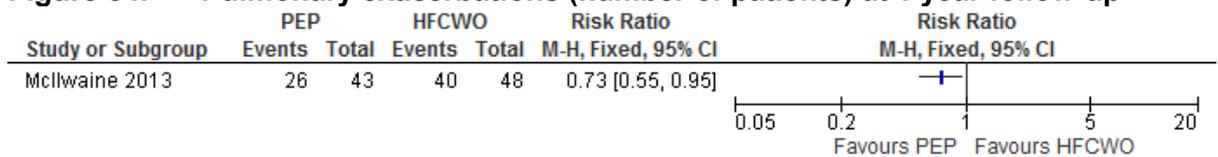
Comparison 7. Positive expiratory pressure mask (PEP) versus high frequency chest wall oscillation (HFCWO)

Figure 53: Sputum volume (ml.) at 1 week follow-up



Abbreviations: PEP: positive expiratory pressure mask; HFCWO: high frequency chest wall oscillation; SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 54: Pulmonary exacerbations (number of patients) at 1 year follow-up



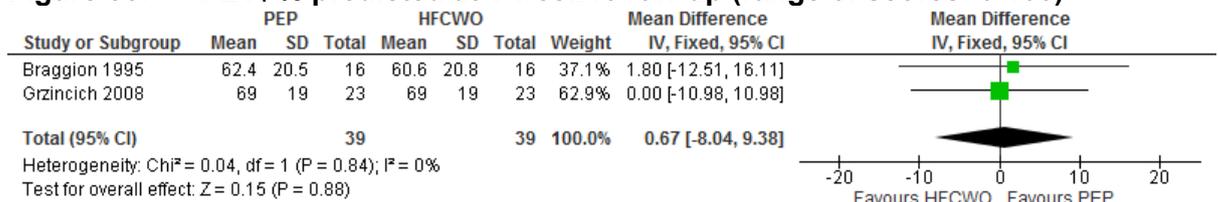
Abbreviations: PEP: positive expiratory pressure mask; HFCWO: high frequency chest wall oscillation; M-H: Mantel-Haenszel; CI: confidence interval

Figure 55: Pulmonary exacerbations (patients requiring antibiotics) at 1 year follow-up



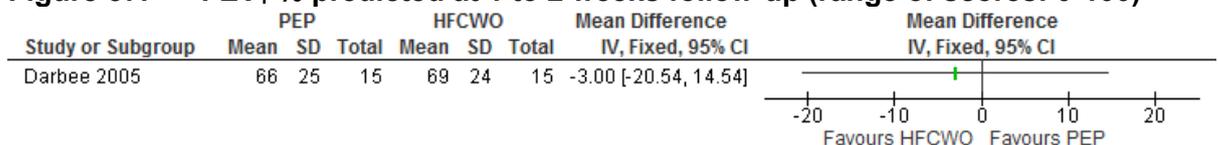
Abbreviations: PEP: positive expiratory pressure mask; HFCWO: high frequency chest wall oscillation; M-H: Mantel-Haenszel; CI: confidence interval

Figure 56: FEV₁ % predicted at 1 week follow-up (range of scores: 0-100)



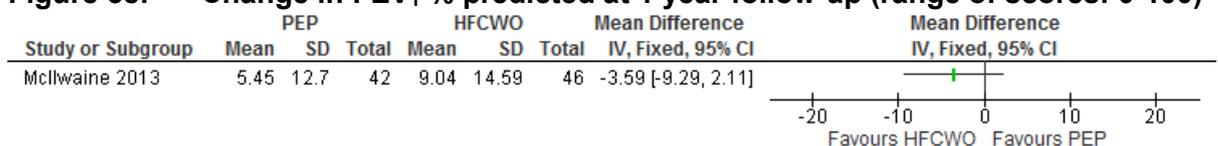
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV₁: forced expiratory volume in 1 second; HFCWO: high frequency chest wall oscillation; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

Figure 57: FEV₁ % predicted at 1 to 2 weeks follow-up (range of scores: 0-100)



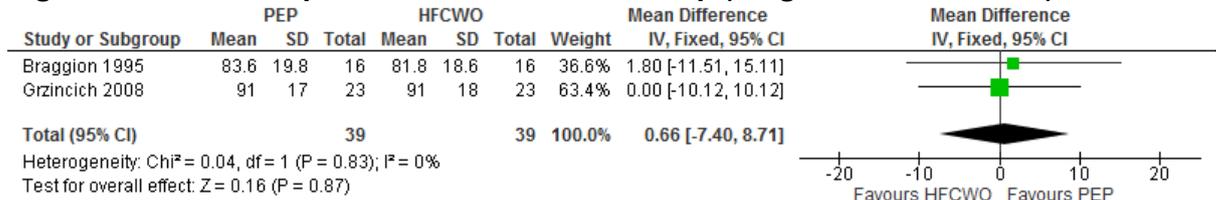
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; HFCWO: high frequency chest wall oscillation; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

Figure 58: Change in FEV₁ % predicted at 1 year follow-up (range of scores: 0-100)



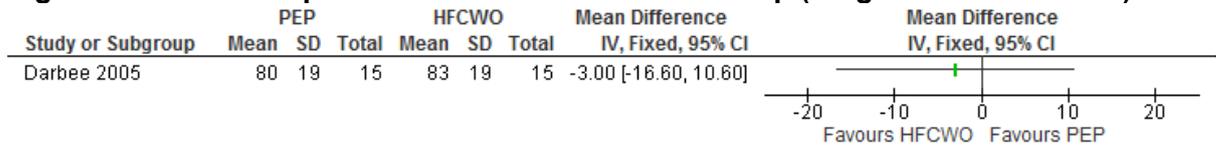
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; HFCWO: high frequency chest wall oscillation; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

Figure 59: FVC % predicted at 1 week follow-up (range of scores: 0-100)



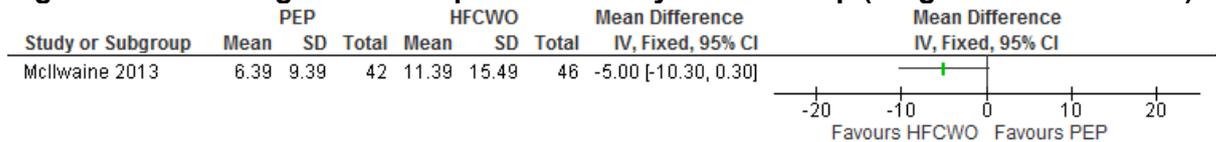
Abbreviations: CI: confidence interval; df: degrees of freedom; FVC: forced vital capacity; HFCWO: high frequency chest wall oscillation; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

Figure 60: FVC % predicted at 1 to 2 weeks follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FVC: forced vital capacity; HFCWO: high frequency chest wall oscillation; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

Figure 61: Change in FVC % predicted at 1 year follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FVC: forced vital capacity; HFCWO: high frequency chest wall oscillation; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

Comparison 8. Active cycle of breathing technique (ACBT) versus no airway clearance technique

No evidence was retrieved for this comparison.

Comparison 9. Active cycle breathing technique (ACBT) versus autogenic drainage (AD)

No evidence was retrieved for this comparison.

Comparison 10. Autogenic drainage (AD) versus no airway clearance technique

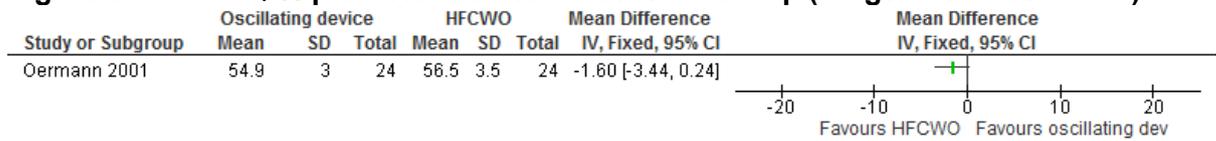
No evidence was retrieved for this comparison.

Comparison 11. Oscillating device versus no airway clearance technique

No evidence was retrieved for this comparison.

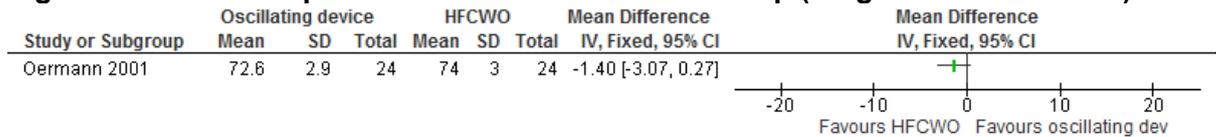
Comparison 12. Oscillating device versus high frequency chest wall oscillation (HFCWO)

Figure 62: FEV₁ % predicted at 2 to 4 weeks follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; HFCWO: high frequency chest wall oscillation; IV: inverse variance; SD: standard deviation

Figure 63: FVC % predicted at 2 to 4 weeks follow-up (range of scores: 0-100)



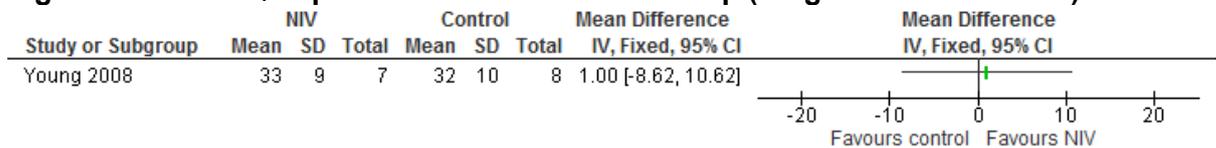
Abbreviations: CI: confidence interval; FVC: forced vital capacity; HFCWO: high frequency chest wall oscillation; IV: inverse variance; SD: standard deviation

Comparison 13. High frequency chest wall oscillation (HFCWO) versus no airway clearance technique

No evidence was found for this comparison.

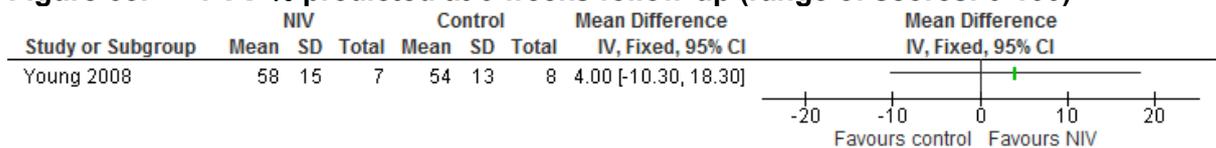
Comparison 14. Non-invasive ventilation (NIV) versus no airway clearance technique

Figure 64: FEV₁ % predicted at 6 weeks follow-up (range of scores: 0-100)



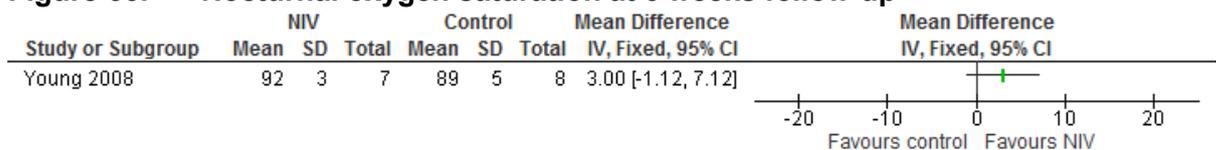
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; NIV: non-invasive ventilation; SD: standard deviation;

Figure 65: FVC % predicted at 6 weeks follow-up (range of scores: 0-100)



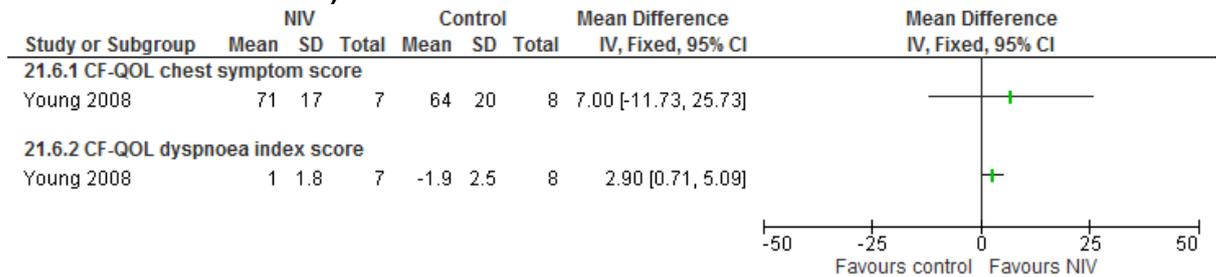
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; NIV: non-invasive ventilation; SD: standard deviation

Figure 66: Nocturnal oxygen saturation at 6 weeks follow-up



Abbreviations: CI: confidence interval; IV: inverse variance; NIV: non-invasive ventilation; SD: standard deviation

Figure 67: Quality of life (CF-QOL questionnaire) at 6 weeks follow-up (range of scores: 0-100)



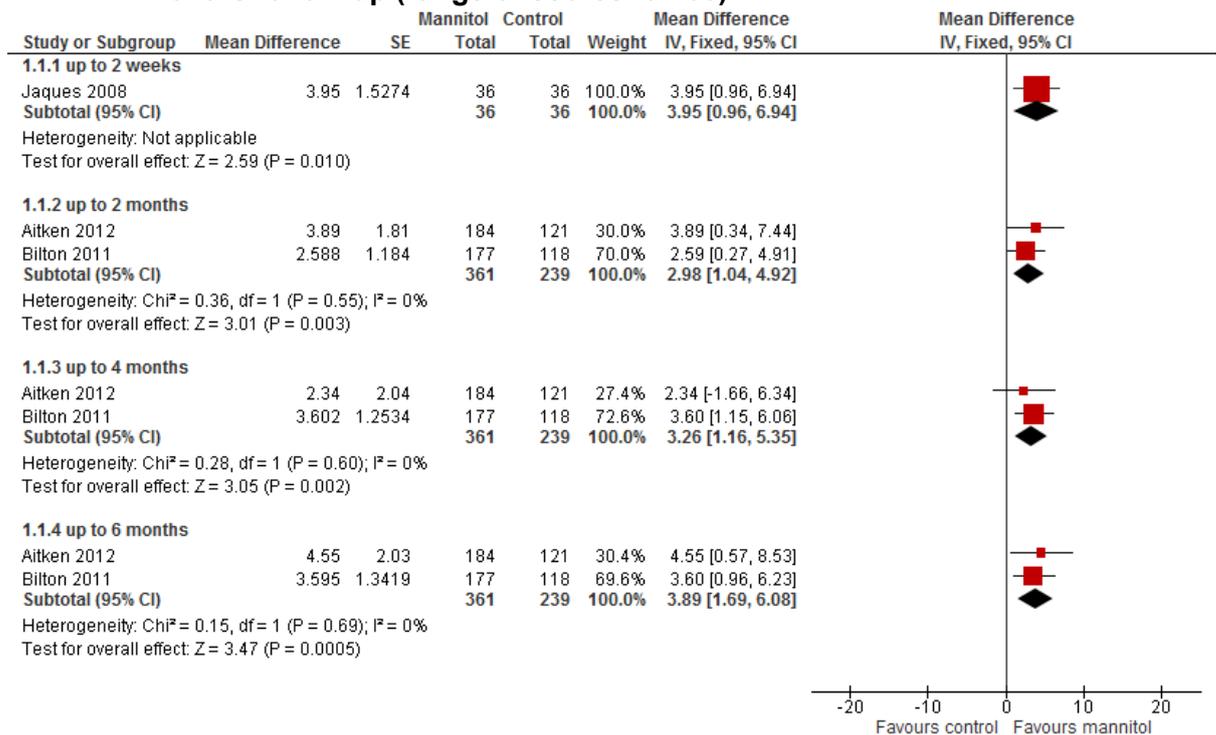
Abbreviations: CI: confidence interval; CF-QOL: cystic fibrosis quality of life questionnaire; IV: inverse variance; NIV: non-invasive ventilation; SD: standard deviation

I.8 Mucoactive agents

I.8.1 Mannitol

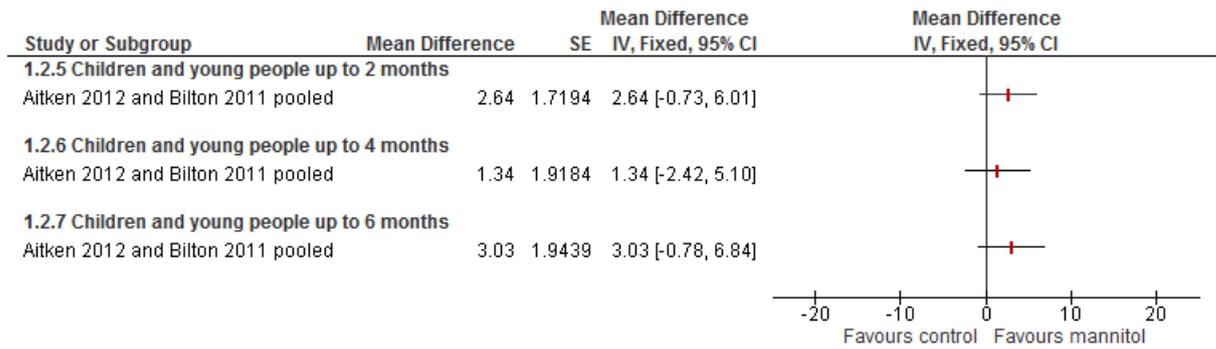
Comparison 1.1. Mannitol versus placebo

Figure 68: Lung function: change in FEV1 % predicted at 2 weeks and 2, 4 & 6 months follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV1: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error

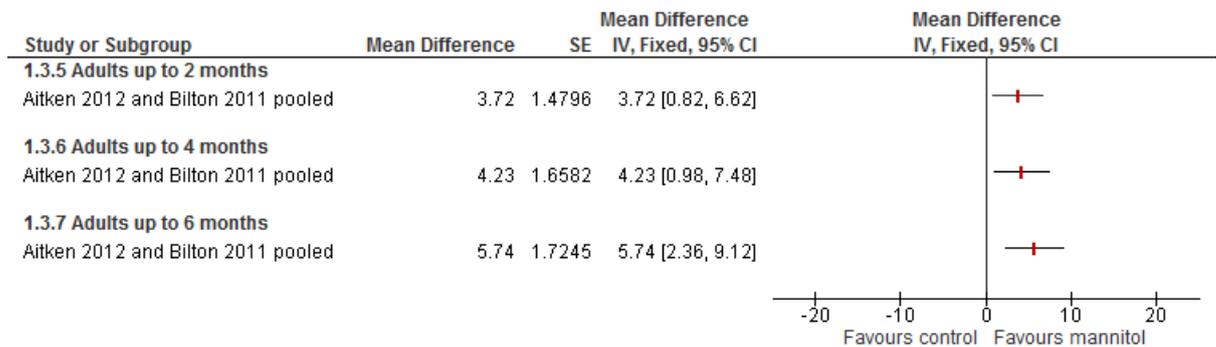
Figure 69: Lung function: change in FEV1 % predicted in children and young people at 2, 4 & 6 months follow-up (range of scores 0-100)



Abbreviations: CI: confidence interval; FEV1: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error

Data was extracted from Cochrane SR Nolan 2015. Data was already pooled for Aitken 2012 and Bilton 2011 studies

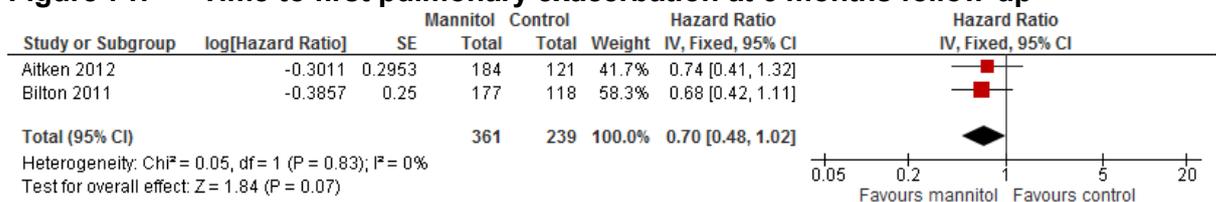
Figure 70: Lung function: change in FEV1 % predicted in adults at 2, 4 & 6 months follow-up (range of scores 0-100)



Abbreviations: CI: confidence interval; FEV1: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error

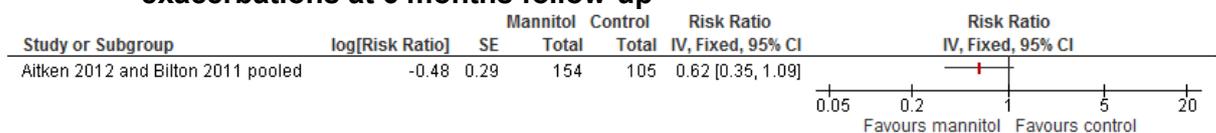
Data was extracted from Cochrane SR Nolan 2015. Data was already pooled for Aitken 2012 and Bilton 2011 studies

Figure 71: Time to first pulmonary exacerbation at 6 months follow-up



Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

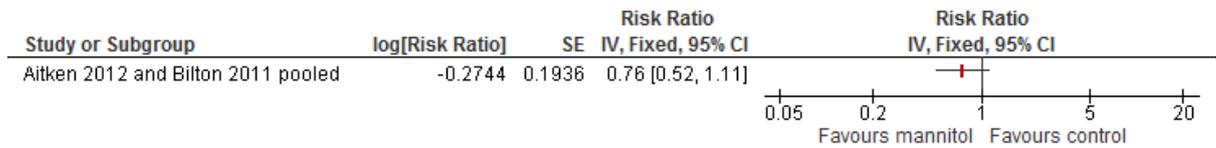
Figure 72: Number of children and young people with protocol defined exacerbations at 6 months follow-up



Abbreviations: IV: inverse variance; SE: standard error

Data was extracted from Cochrane SR Nolan 2015. Data was already pooled for Aitken 2012 and Bilton 2011 studies

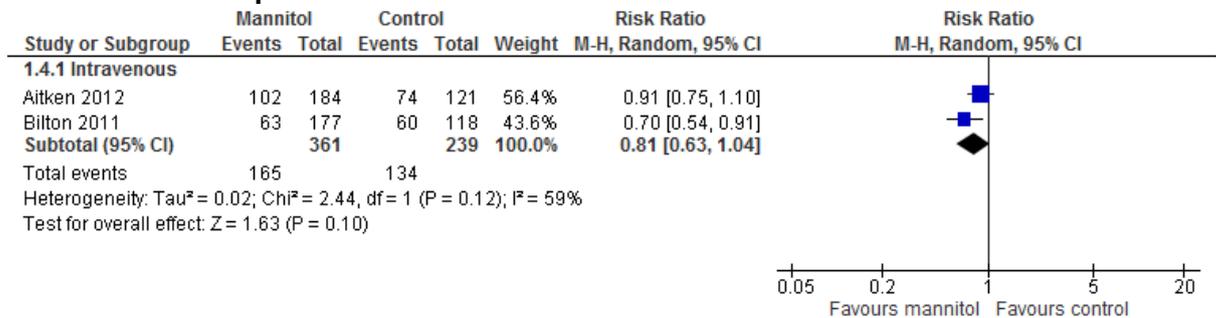
Figure 73: Number of adults with protocol defined exacerbations at 6 months follow-up



Abbreviations: IV: inverse variance; SE: standard error

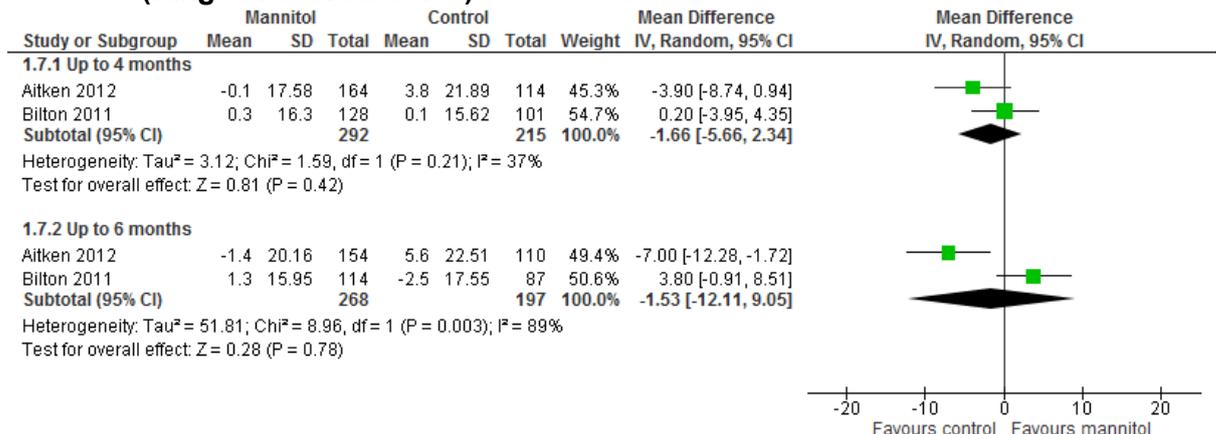
Data was extracted from Cochrane SR Nolan 2015. Data was already pooled for Aitken 2012 and Bilton 2011 studies

Figure 74: Number of patients needing additional IV antibiotics at 6 months follow-up



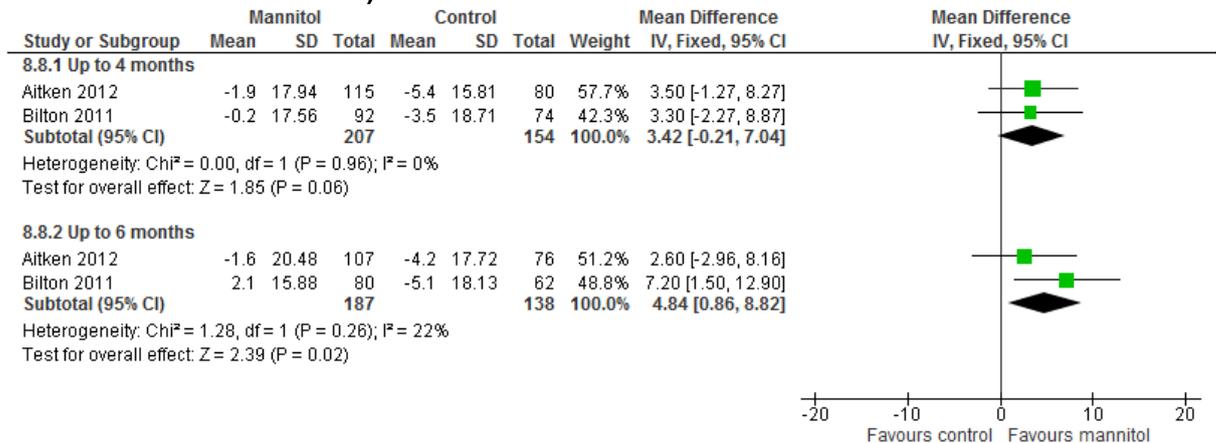
Abbreviations: CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel

Figure 75: Quality of life: change in CFQ-R respiratory at 4 & 6 months follow-up (range of scores: 0-100)



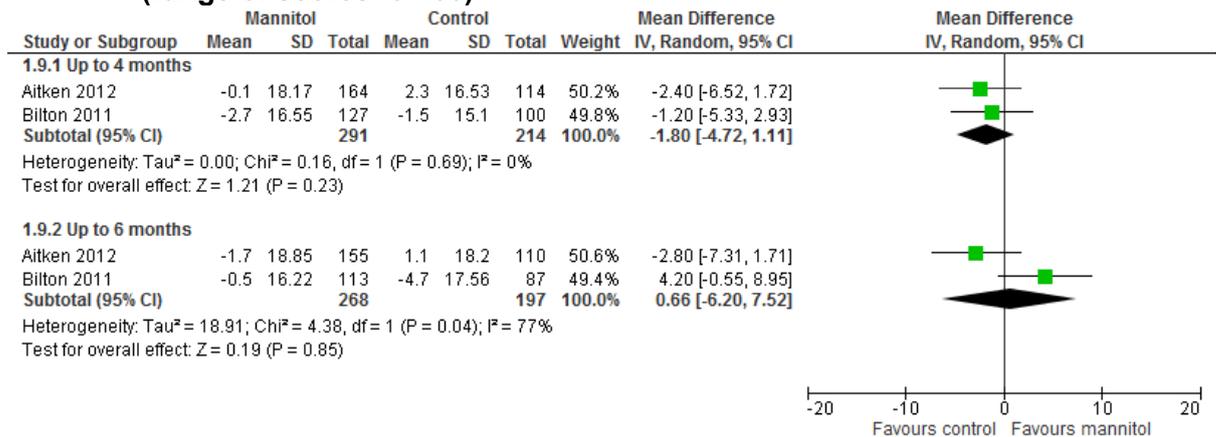
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

Figure 76: Quality of life: change in CFQ-R vitality at 4 & 6 months follow-up (range of scores: 0-100)



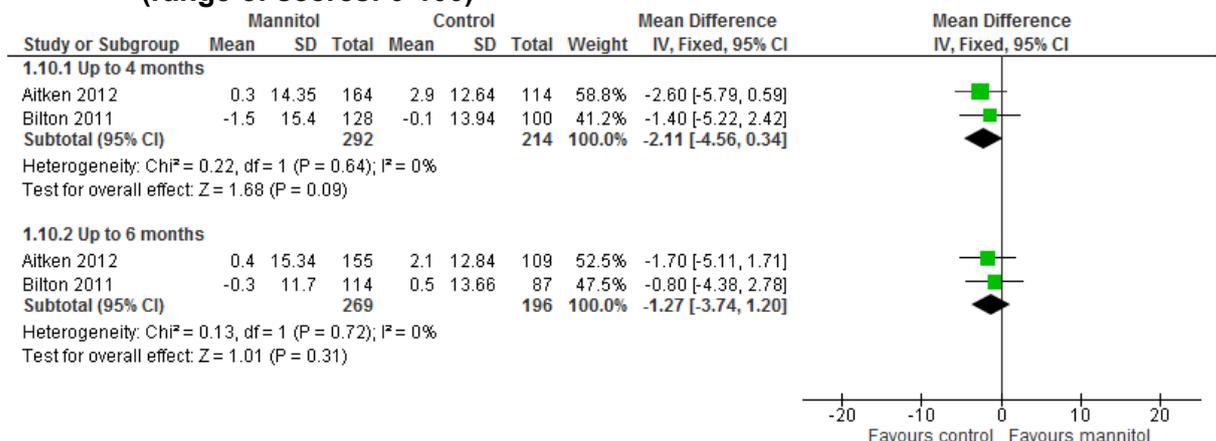
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

Figure 77: Quality of life: change in CFQ-R physical at 4 & 6 months follow-up (range of scores: 0-100)



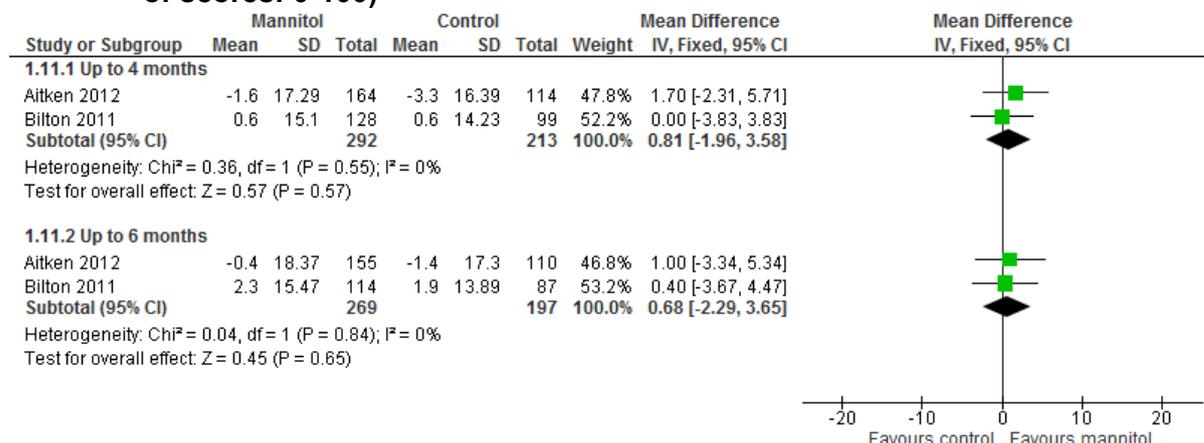
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

Figure 78: Quality of life: change in CFQ-R emotion at 4 & 6 months follow-up (range of scores: 0-100)



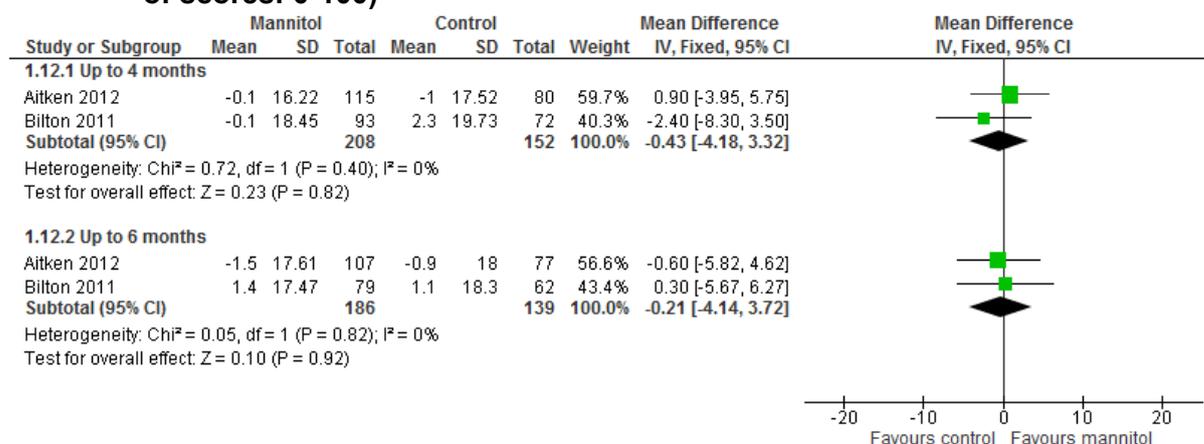
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

Figure 79: Quality of life: change in CFQ-R eating at 4 & 6 months follow-up (range of scores: 0-100)



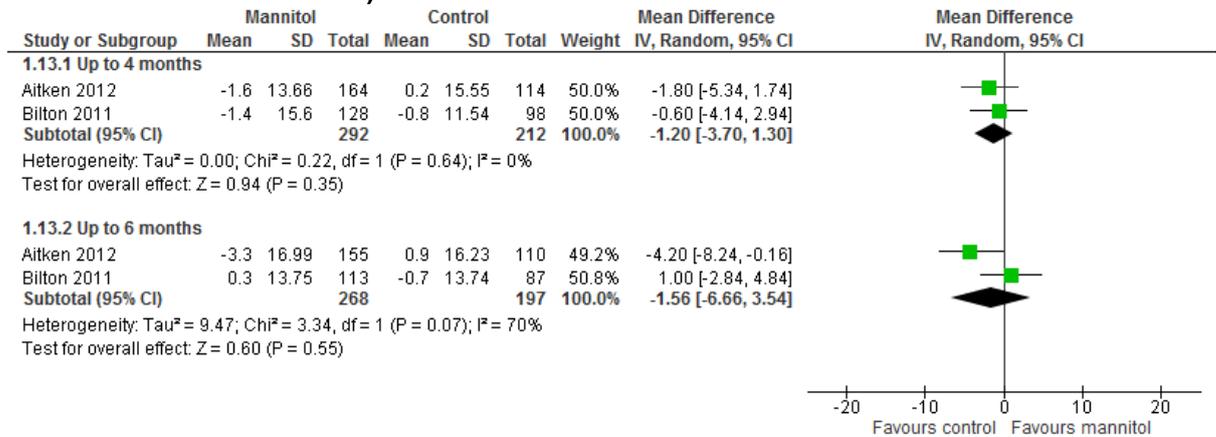
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

Figure 80: Quality of life: change in CFQ-R health at 4 & 6 months follow-up (range of scores: 0-100)



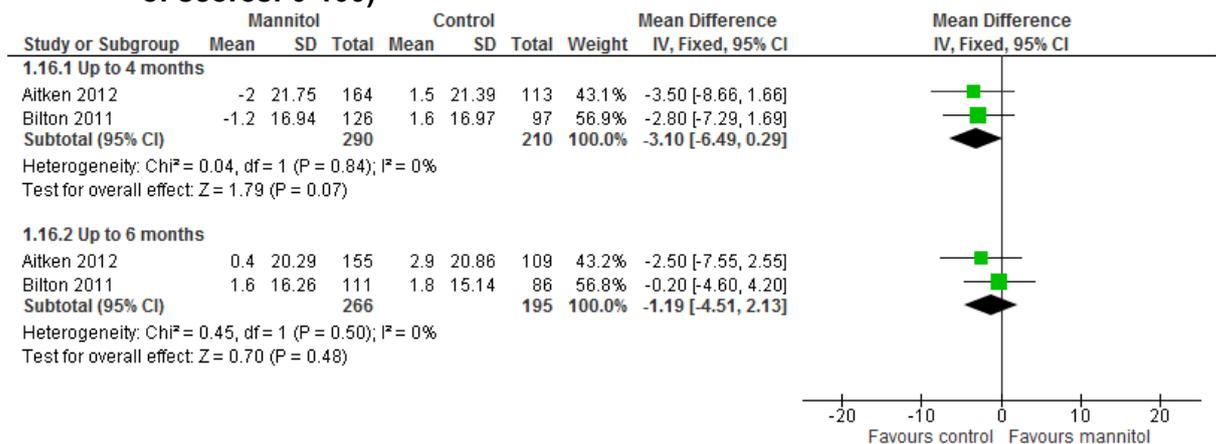
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

Figure 81: Quality of life: change in CFQ-R social at 4 & 6 months follow-up (range of scores: 0-100)



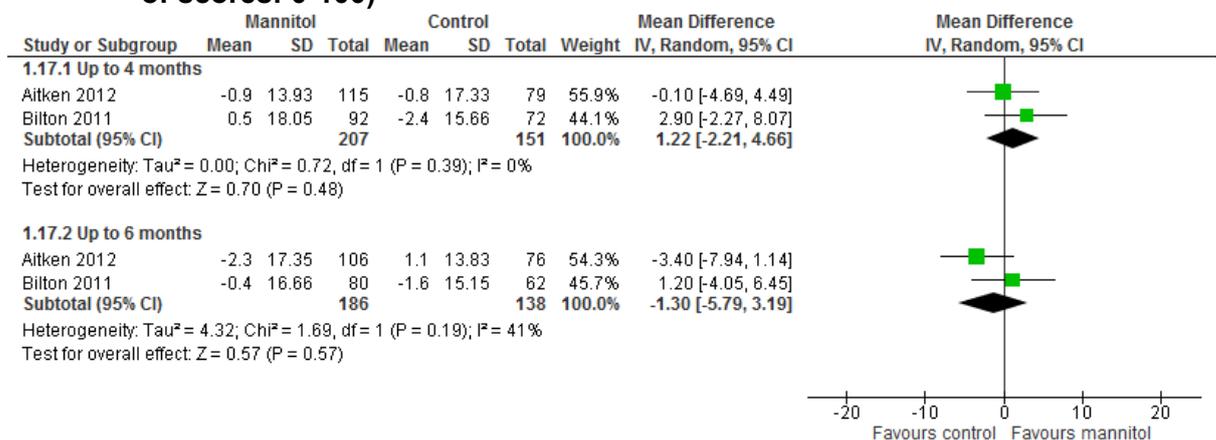
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

Figure 82: Quality of life: change in CFQ-R body at 4 & 6 months follow-up (range of scores: 0-100)



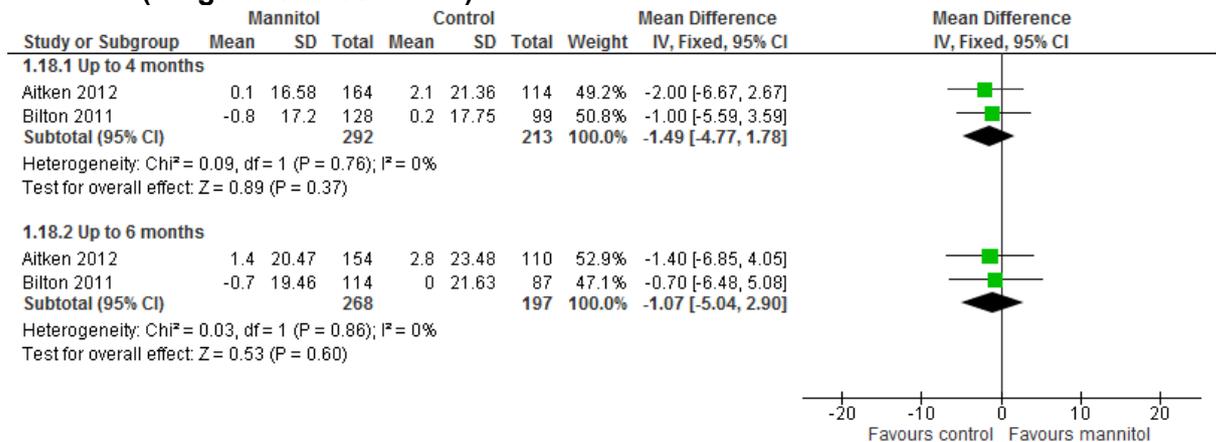
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

Figure 83: Quality of life: change in CFQ-R role at 4 & 6 months follow-up (range of scores: 0-100)



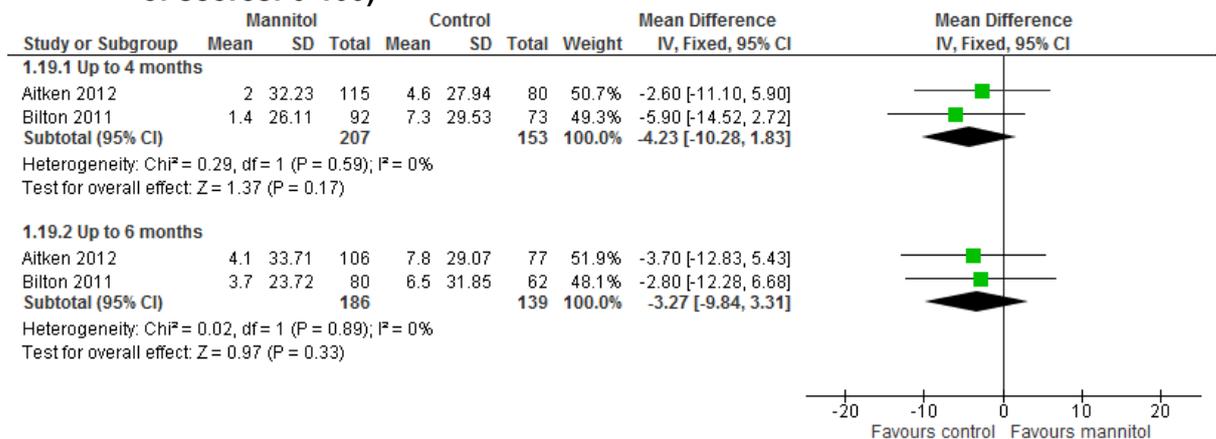
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

Figure 84: Quality of life: change in CFQ-R digestion at 4 & 6 months follow-up (range of scores: 0-100)



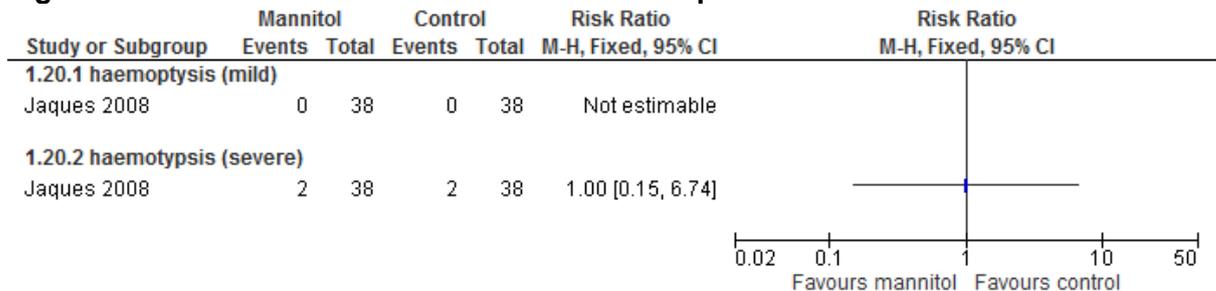
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

Figure 85: Quality of life: change in CFQ-R weight at 4 & 6 months follow-up (range of scores: 0-100)



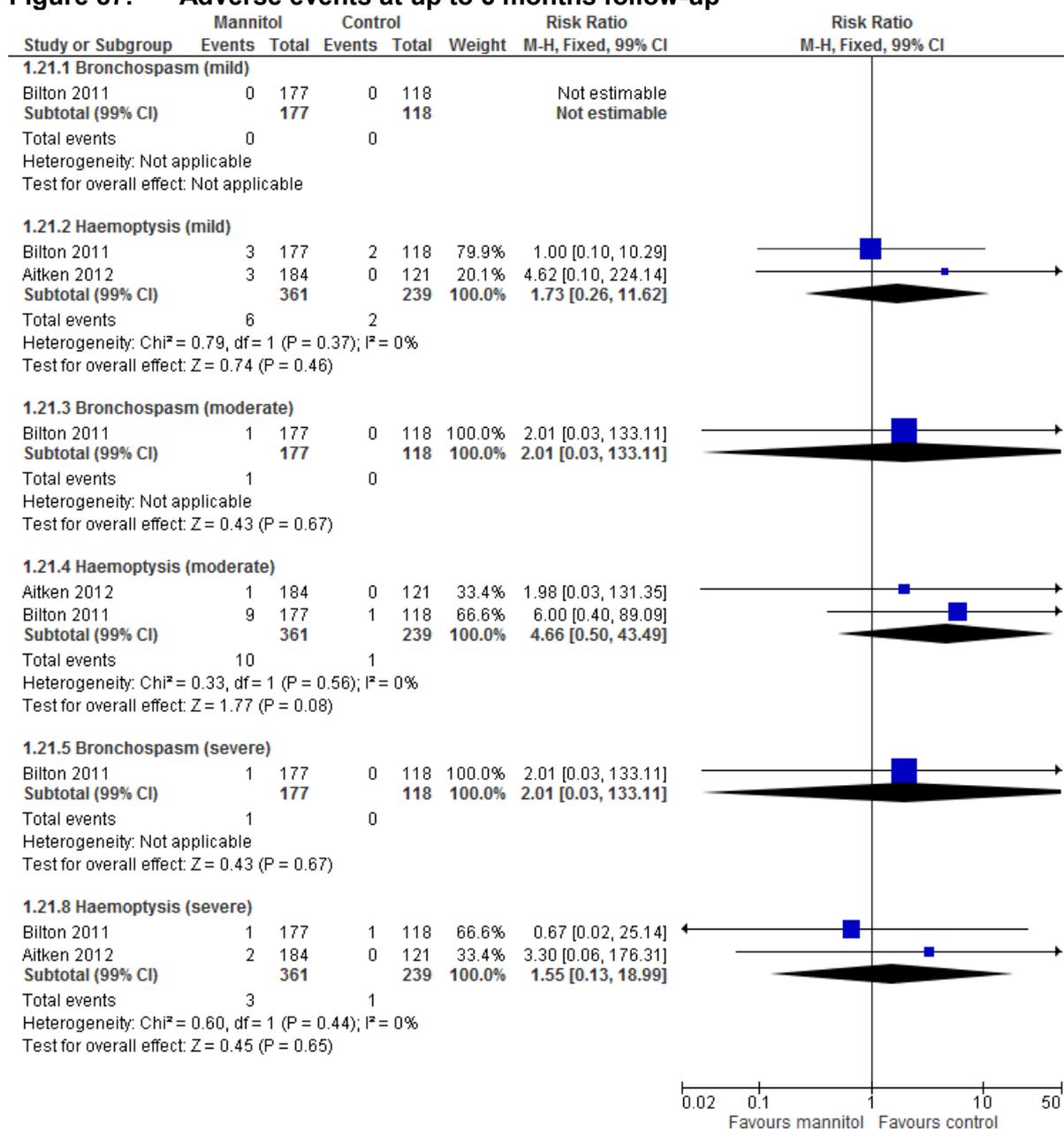
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

Figure 86: Adverse events at 2 weeks follow-up



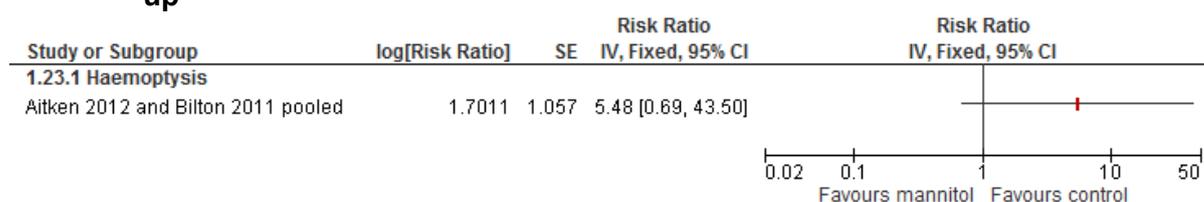
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 87: Adverse events at up to 6 months follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

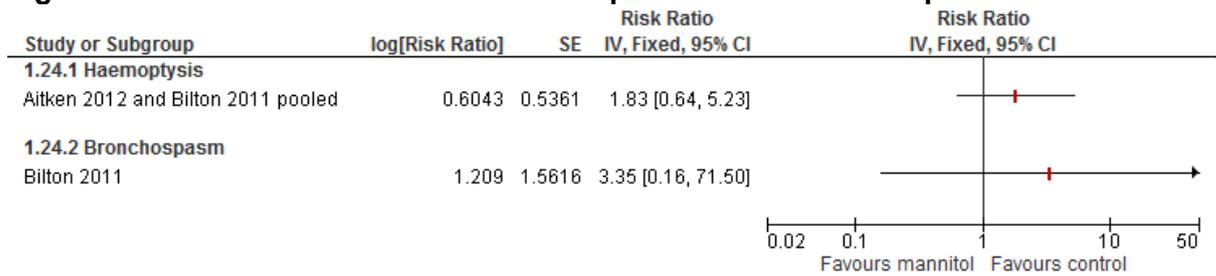
Figure 88: Adverse events in children and young people at up to 6 months follow-up



Abbreviations: IV: inverse variance; SE: standard error

Data was extracted from Cochrane SR Nolan 2015. Data was already pooled for Aitken 2012 and Bilton 2011 studies

Figure 89: Adverse events in adults at up to 6 months follow-up

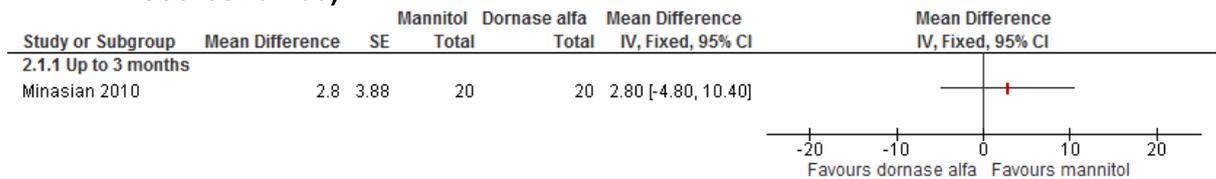


Abbreviations: IV: inverse variance; SE: standard error

Data was extracted from Cochrane SR Nolan 2015. Data was already pooled for Aitken 2012 and Bilton 2011 studies for haemoptysis

Comparison 1.2.1. Mannitol versus Dornase alfa

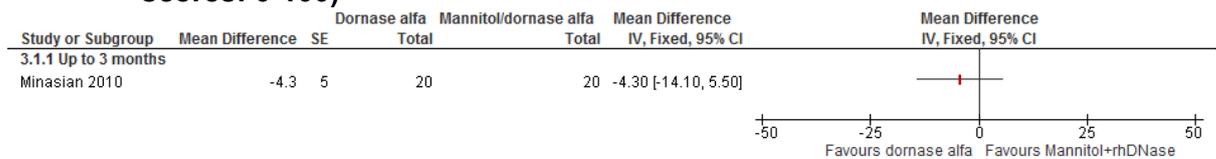
Figure 90: Lung function – FEV₁ % change from baseline up to 3 months (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error

Comparison 1.2.2. Mannitol + Dornase alfa versus Dornase alfa alone

Figure 91: Lung function – FEV₁ % change from baseline up to 3 months (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error

Comparison 1.3: Mannitol versus nebulised sodium chloride

No evidence was found for this comparison.

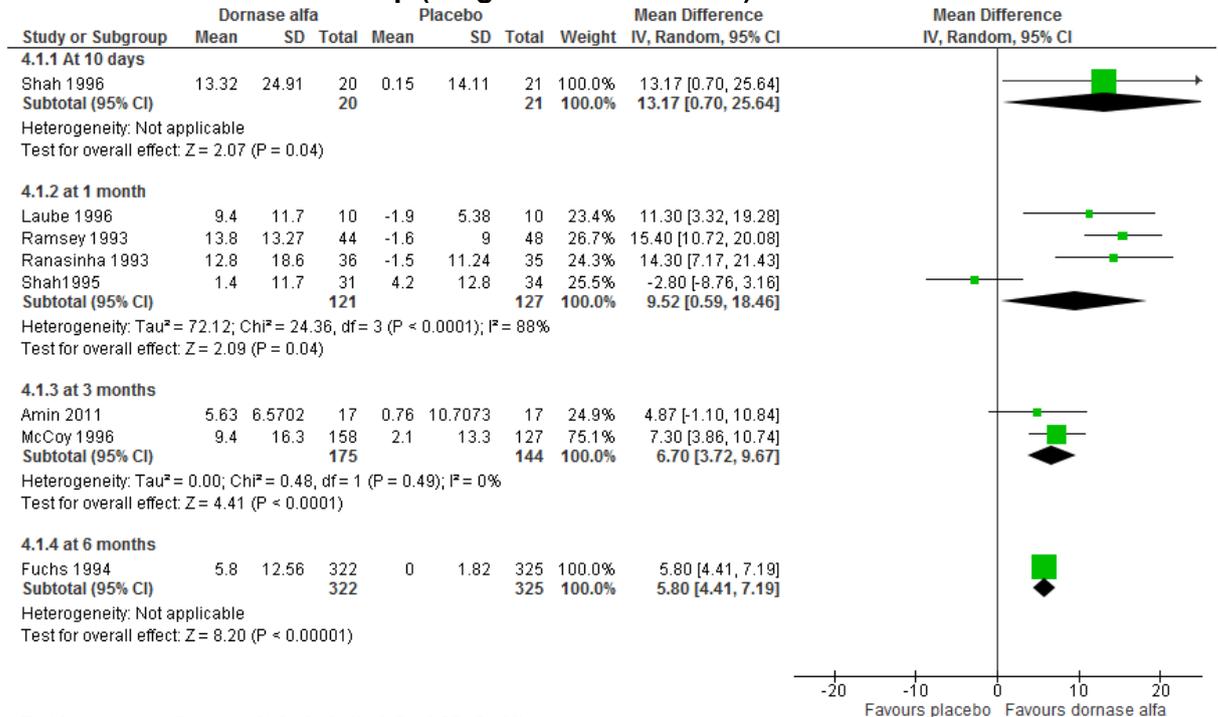
Comparison 1.4. Mannitol versus acetylcysteine

No evidence was found for this comparison.

I.8.2 Dornase alfa

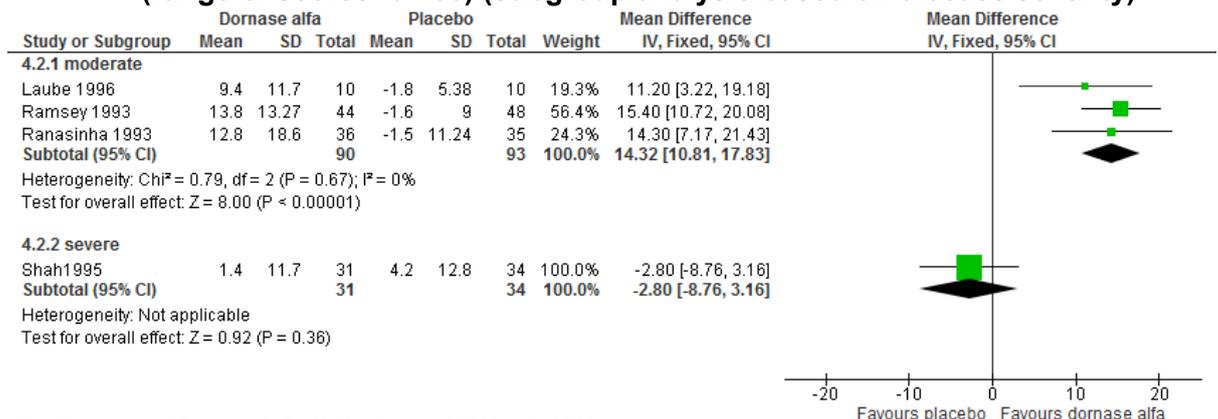
Comparison 2.1. Dornase alfa versus placebo

Figure 92: Lung function: relative mean % change in FEV₁ at 10 days; and at 1, 3 & 6 months follow-up (range of scores: 0-100)



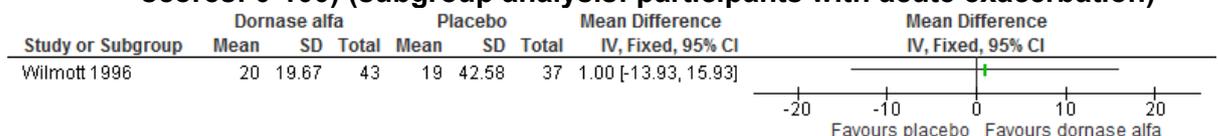
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation.
Note: See sensitivity analysis

Figure 93: Lung function: relative mean % change in FEV₁ at 1 month follow-up (range of scores: 0-100) (subgroup analysis based on disease severity)



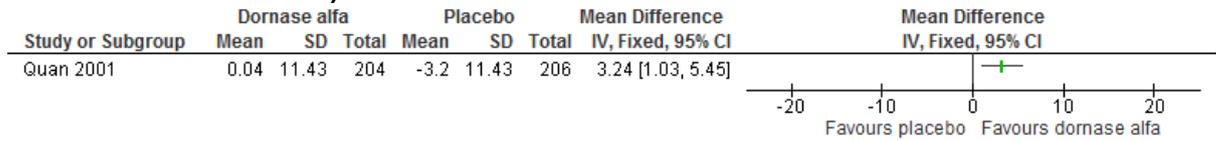
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 94: Lung function: mean % change in FEV₁ at 1 month follow-up (range of scores: 0-100) (subgroup analysis: participants with acute exacerbation)



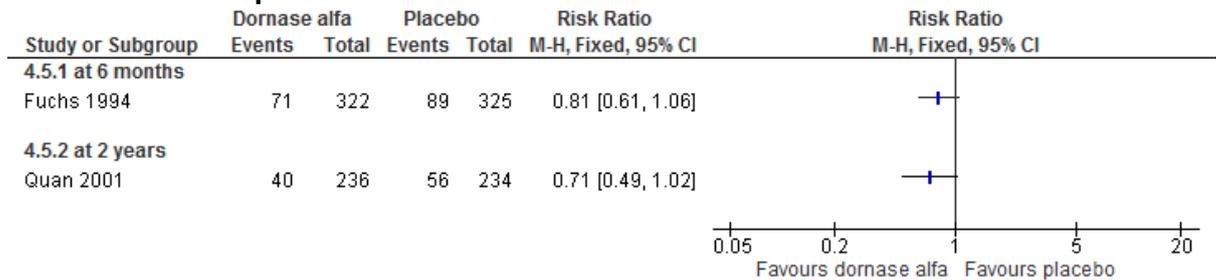
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 95: Lung function: absolute mean % change in FEV₁ at 2 years (range of scores: 0-100)



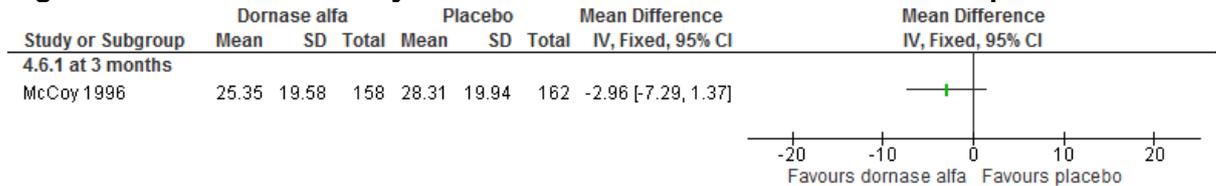
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 96: Number of people experiencing exacerbations at 6 months & 2 years follow-up



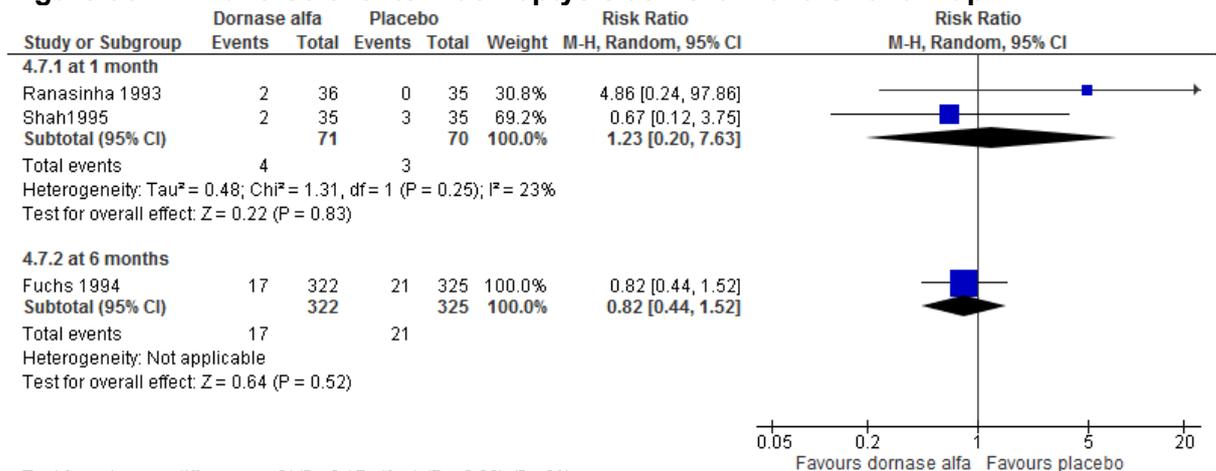
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 97: Number of days of IV antibiotics use at 1 month follow-up



Abbreviations: CI: confidence interval; IV antibiotics: intravenous antibiotics; IV: inverse variance; SD: standard deviation

Figure 98: Adverse events: haemoptysis at 1 & 6 months follow-up



Test for subgroup differences: Chi² = 0.17, df = 1 (P = 0.68), I² = 0%
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 99: Adverse events: voice alteration at 1, 3, 6 months and 2 years follow-up

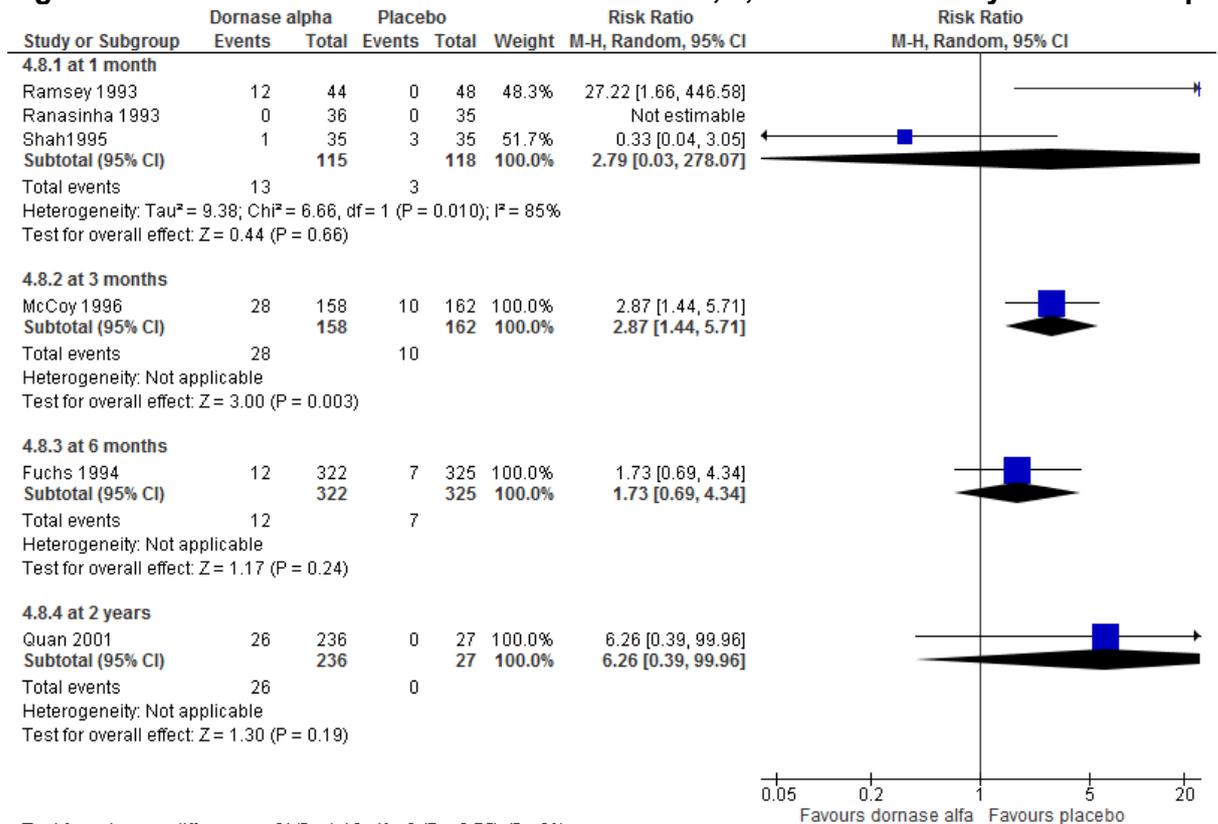
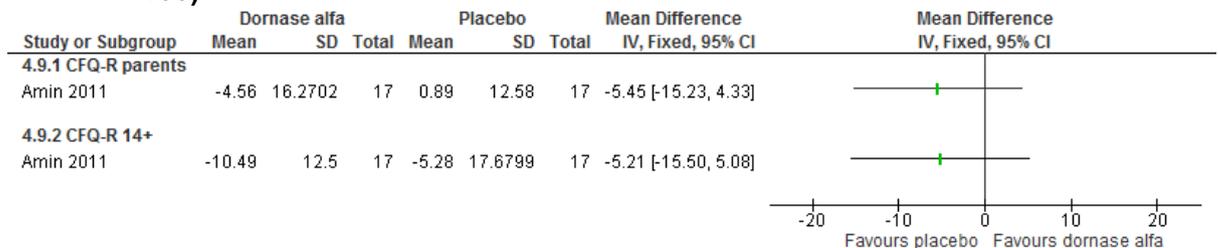


Figure 100: Quality of life (measured with CFQ-R) at 3 months (range of scores: 0-100)



Comparison 2.2. Dornase alfa versus nebulized sodium chloride

Figure 101: Lung function: mean % change in FEV₁ at 3 weeks and 3 months follow-up

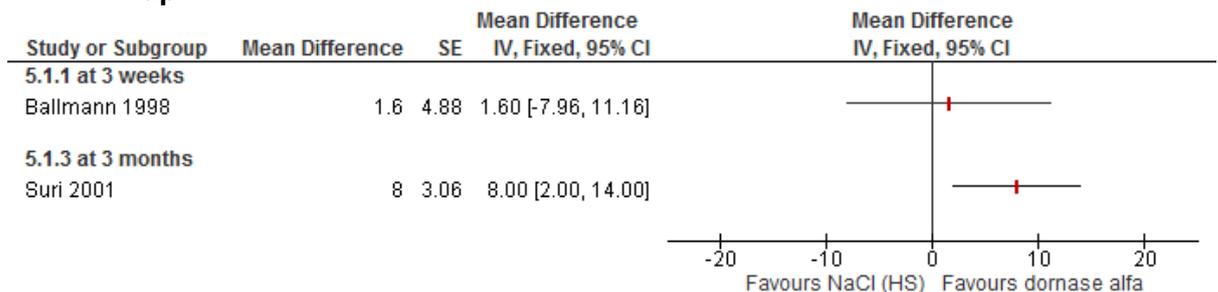
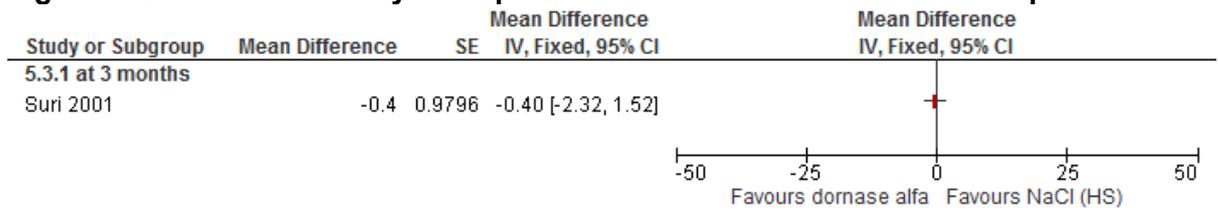


Figure 102: Number of days of inpatient treatment at 3 months follow-up



Abbreviations: CI: confidence interval; IV: inverse variance; NaCl (HS): sodium chloride (hypertonic saline); SE: standard error

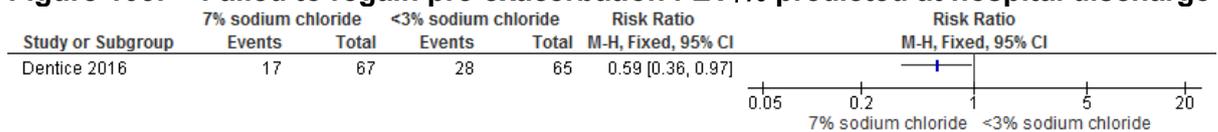
Comparison 2.3. Dornase alfa versus acetylcysteine

No evidence was found for this comparison.

I.8.3 Nebulised sodium chloride

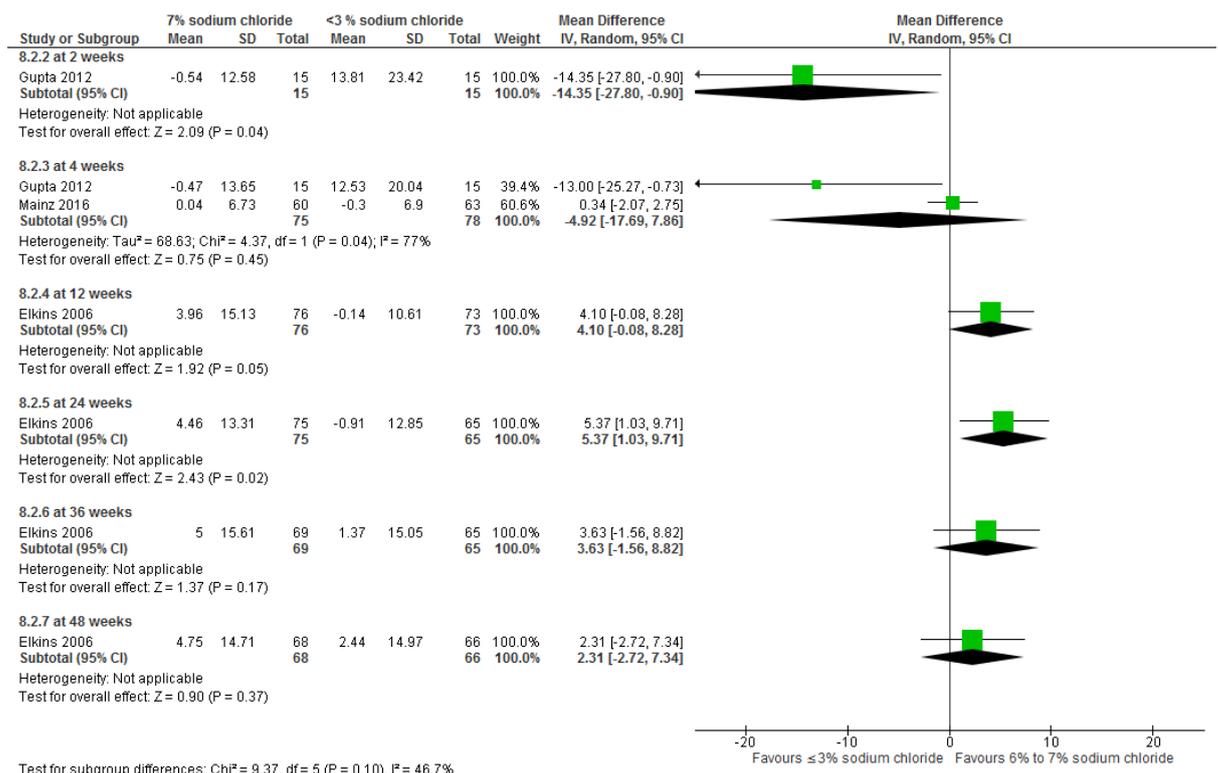
Comparison 3.1. Nebulised sodium chloride (> 3% concentration) versus placebo (0.9% to 0.12%) or low-concentration (≤ 3%)

Figure 103: Failed to regain pre-exacerbation FEV₁% predicted at hospital discharge



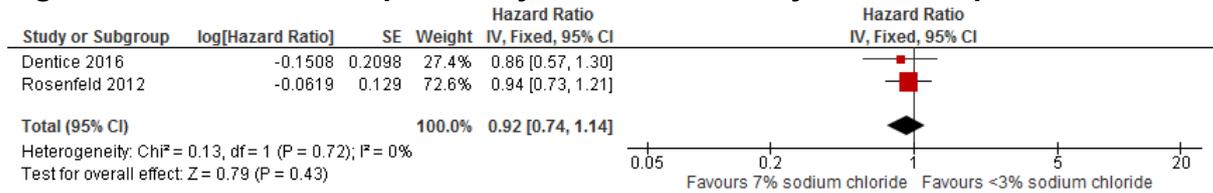
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel. Note: Length of hospital stay was 12 days for the intervention group, and 13 days for the control group. Pre-exacerbation FEV₁% predicted was measured ≈ 6 months before.

Figure 104: Lung function: % change in FEV₁ at 2, 4, 12, 24, 36 & 48 weeks follow-up (range of scores: 0-100)



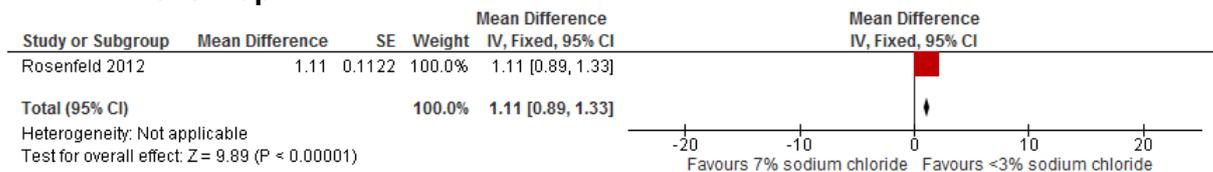
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 105: Time to next pulmonary exacerbation at 1 year follow-up



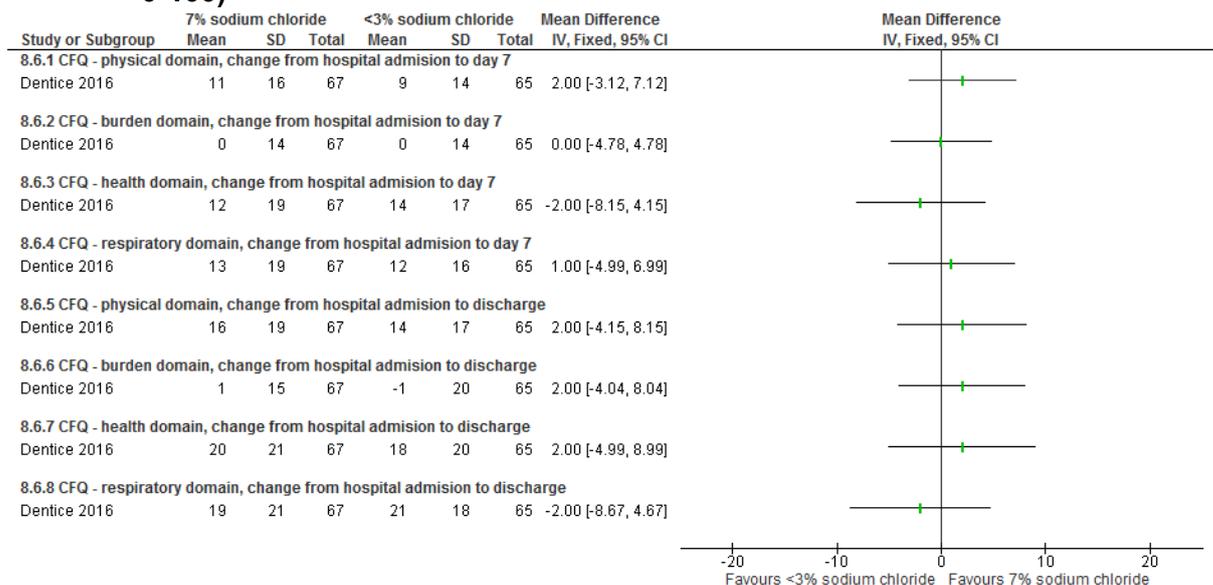
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

Figure 106: Number of days of treatment for a pulmonary exacerbation at 48 weeks follow-up



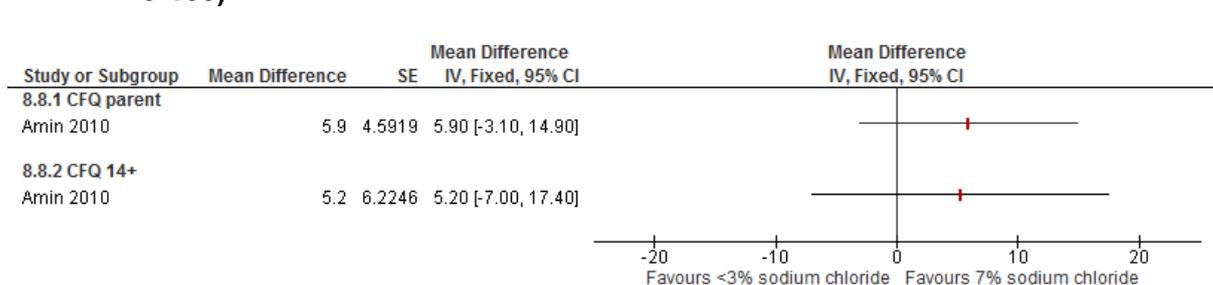
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

Figure 107: Change in quality of life (CF-QOL) following treatment (range of scores: 0-100)



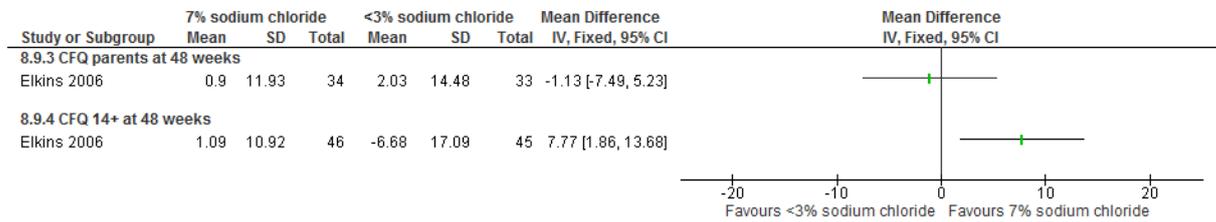
Abbreviations: CI: confidence interval; CF-QOL: cystic fibrosis quality of life questionnaire; IV: inverse variance; SD: standard deviation

Figure 108: Change in quality of life (CFQ-R), at 4 weeks follow-up (range of scores: 0-100)



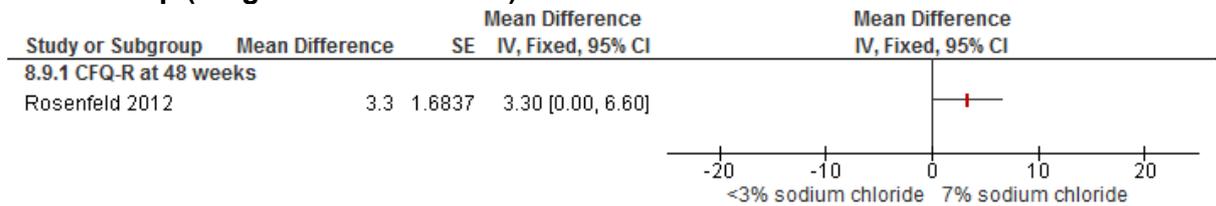
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SE: standard error

Figure 109: Change in quality of life (CFQ-R) at 48 weeks follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

Figure 110: Change in quality of life: CFQ-R respiratory domain, at 48 weeks follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SE: standard error

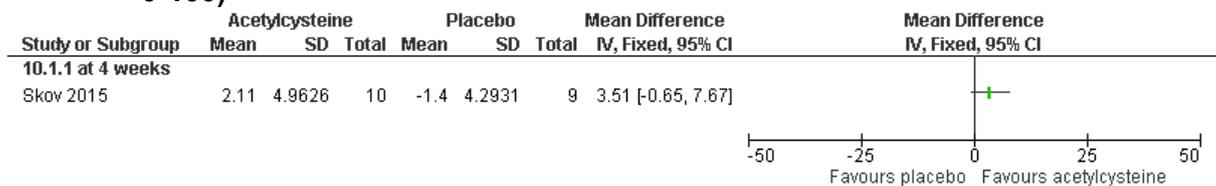
Comparison 3.2. Nebulised sodium chloride versus acetylcysteine

No evidence was found for this comparison.

I.8.4 Acetylcysteine

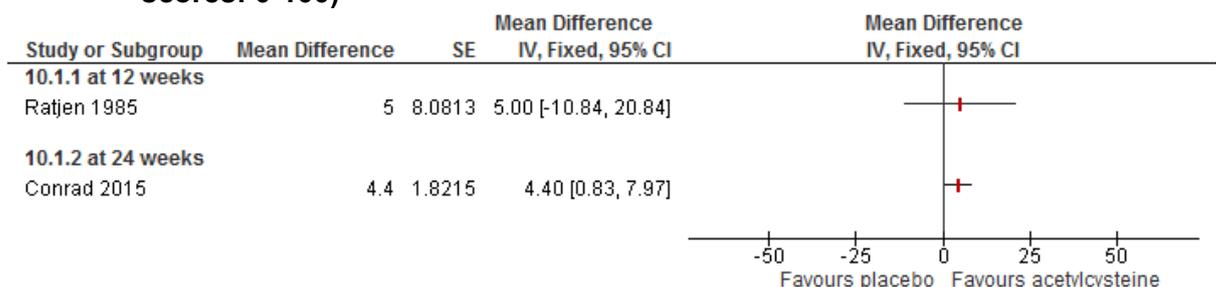
Comparison 4. Acetylcysteine versus placebo

Figure 111: Lung function: change in FEV₁ % predicted at 4 weeks (range of scores: 0-100)



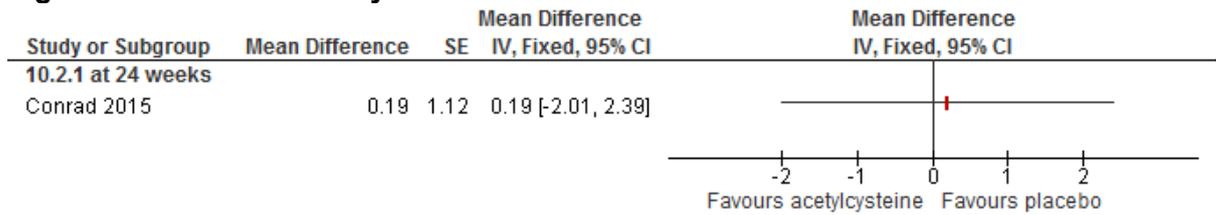
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

Figure 112: Lung function: change in FEV₁ % predicted at 12 and 24 weeks (range of scores: 0-100)



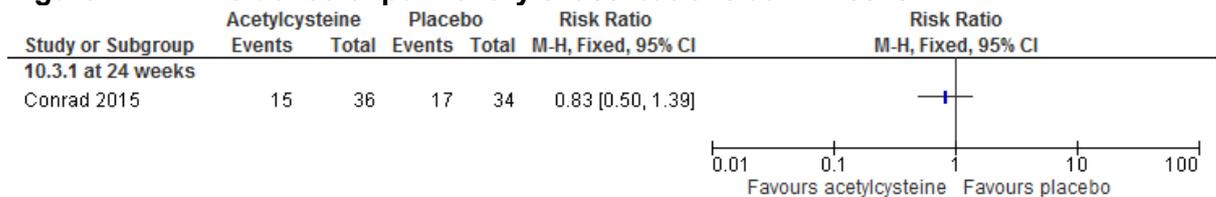
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

Figure 113: Inflammatory markers: IL-8 at 24 weeks



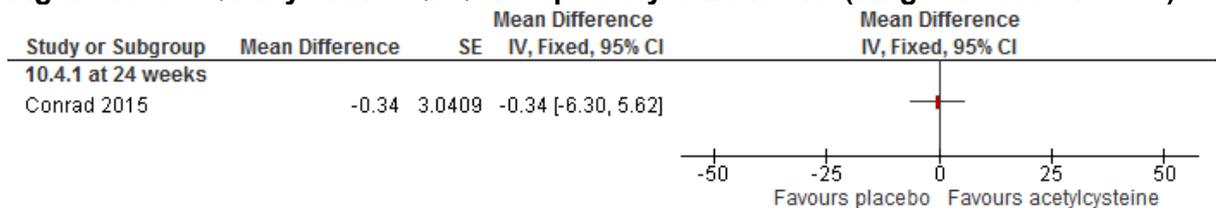
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

Figure 114: Incidence of pulmonary exacerbations at 24 weeks



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 115: Quality of life: QFQ-R respiratory at 24 weeks (range of scores: 0-100)

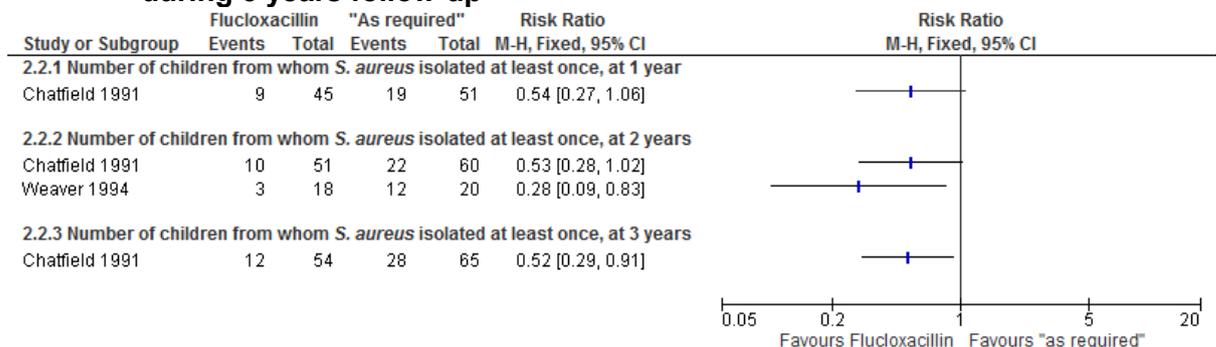


Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SE: standard error

I.9 Pulmonary infection – prophylaxis

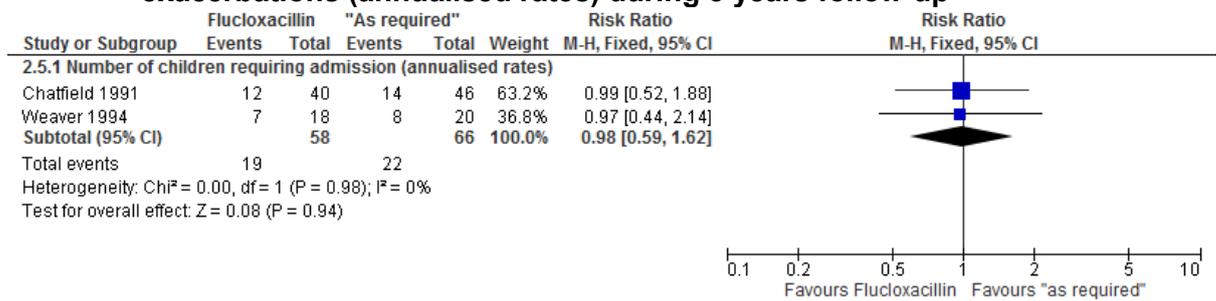
Comparison 1. Continuous oral flucloxacillin versus antibiotics as required

Figure 116: Number of children from whom *S. Aureus* was identified at least once during 3 years follow-up



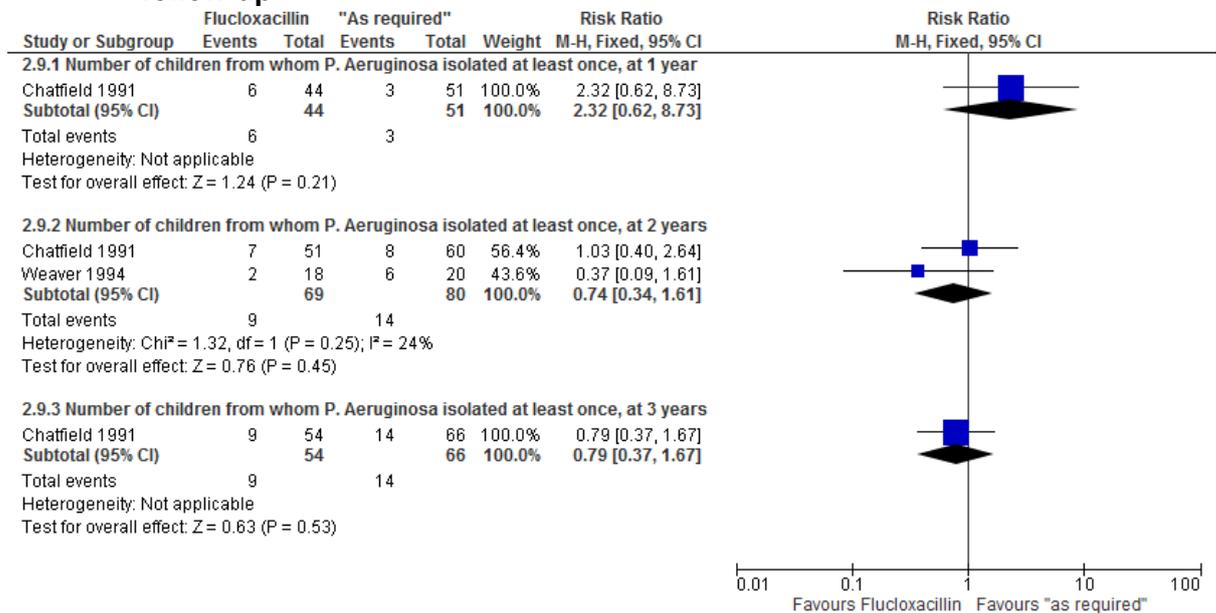
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 117: Number of children admitted to hospital due to pulmonary exacerbations (annualised rates) during 3 years follow-up



Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

Figure 118: Number of children in whom *P. aeruginosa* was identified during 3 years follow-up



Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

Comparison 2. Continuous oral Cephalixin versus antibiotics as required

Figure 119: Number of children from whom *S. aureus* was identified at least once during 6 years follow-up

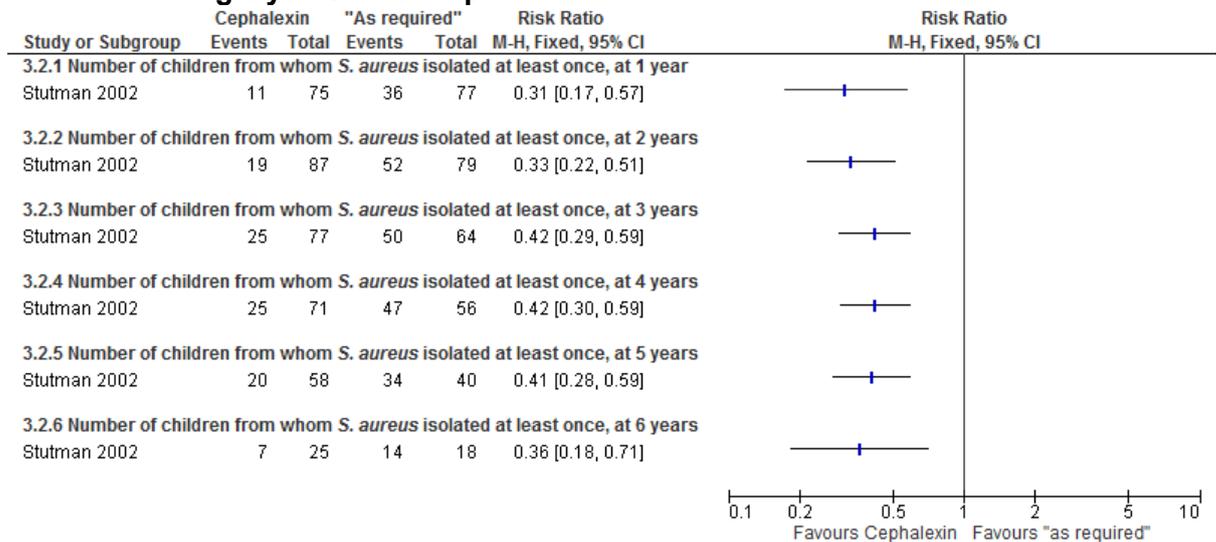


Figure 120: FEV₁ (litres) at 6 years follow-up

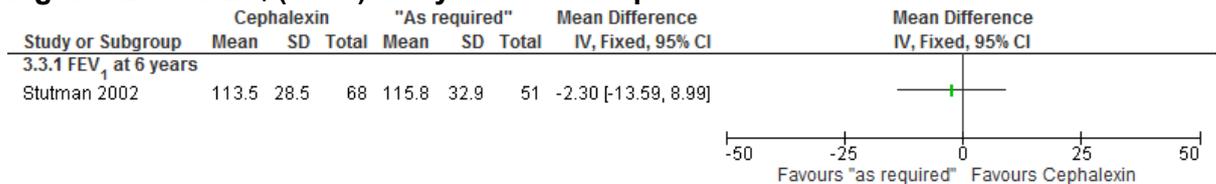


Figure 121: Pulmonary exacerbations (%) during 6 years follow-up

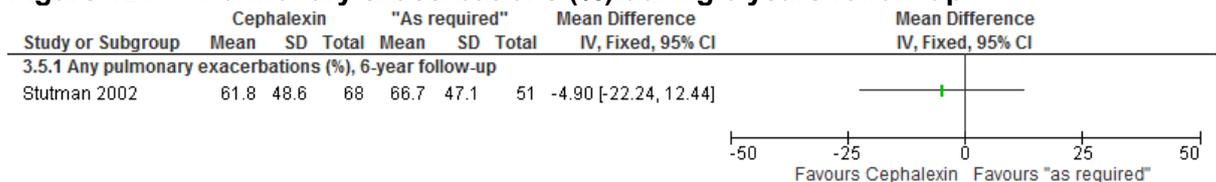
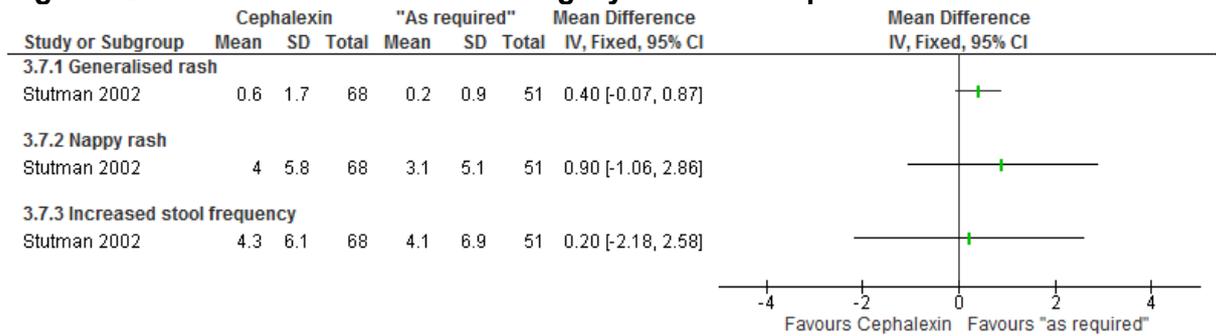


Figure 122: Number of children admitted to hospital due to pulmonary exacerbations (annualised rates) during 6 years follow-up

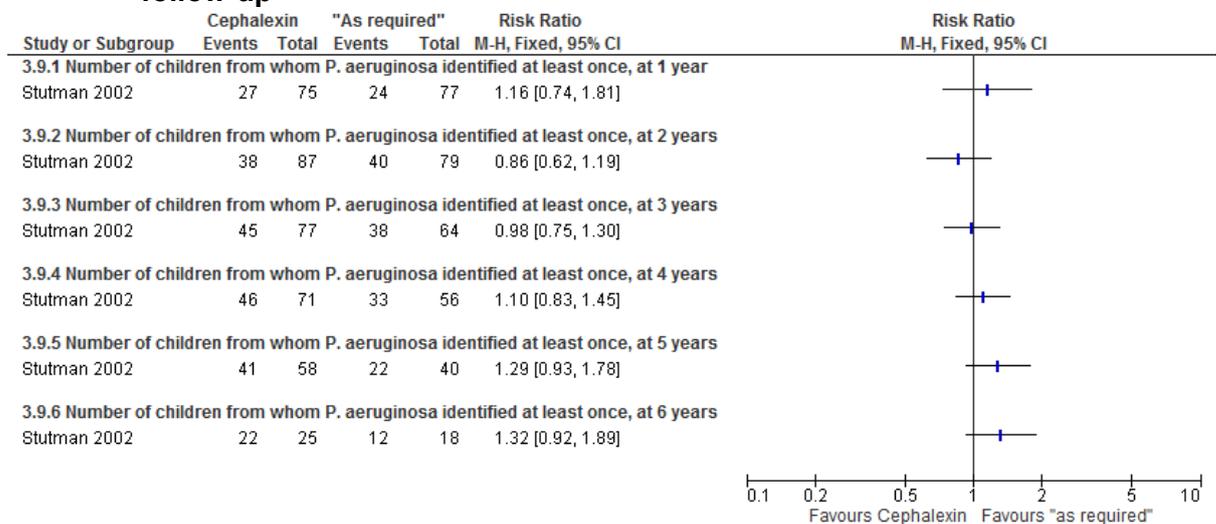


Figure 123: Minor adverse events during 6 years follow-up



Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 124: Number of children in whom *P. Aeruginosa* was identified at 1 to 6 years follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

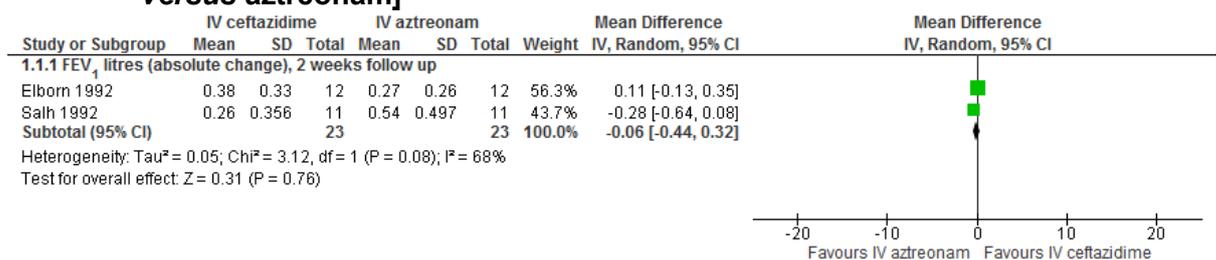
I.10 Pulmonary infection – acute

I.10.1 *Pseudomonas aeruginosa*

I.10.1.1 Antimicrobial treatment for pulmonary exacerbations due to *P. aeruginosa*

Comparison 1. Single IV antibiotic versus single IV antibiotic

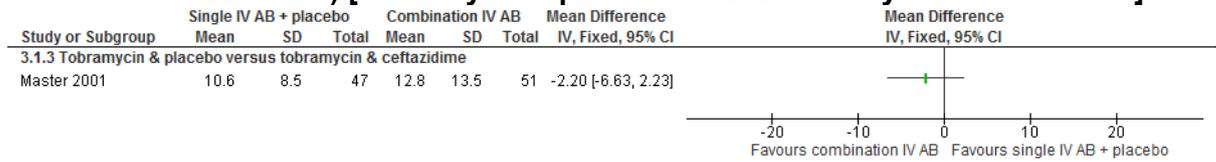
Figure 125: FEV₁ litres (absolute change) at end of 2 week course [ceftazidime versus aztreonam]



Abbreviations: CI: confidence interval; df: degrees of freedom; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

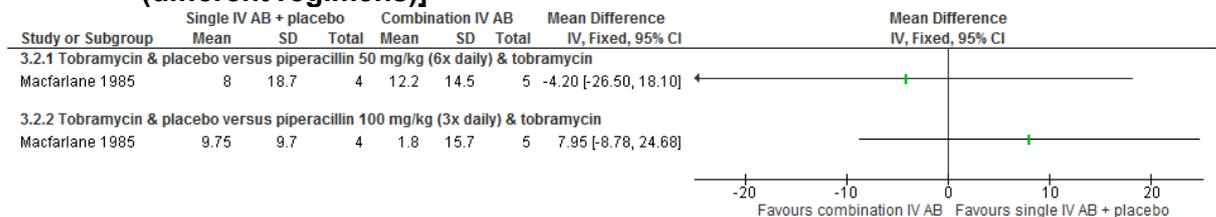
Comparison 2. Single IV antibiotic (with placebo) versus combination IV

Figure 126: FEV₁ % predicted (absolute change) at 10 days follow-up (range of scores: 0-100) [Tobramycin + placebo versus tobramycin + ceftazidime]



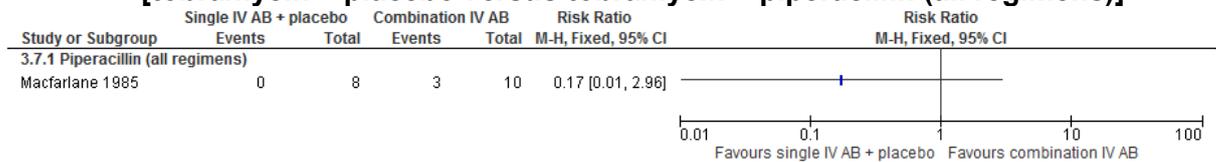
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance (at the top of the plot) or intravenous (at the bottom of the plot); SD: standard deviation

Figure 127: FEV₁ % predicted (relative change) at end of 2 weeks course (range of scores: 0-100) [tobramycin + placebo versus tobramycin + piperacillin (different regimens)]



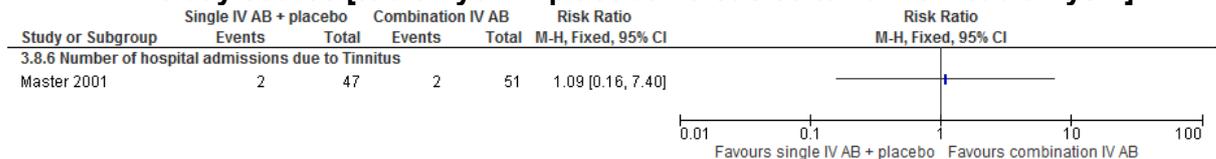
Abbreviations: AB: antibiotics; CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance (at the top of the plot) or intravenous (at the bottom of the plot); SD: standard deviation

Figure 128: Adverse effects: sensitivity reaction at end of 2 weeks course [tobramycin + placebo versus tobramycin + piperacillin (all regimens)]



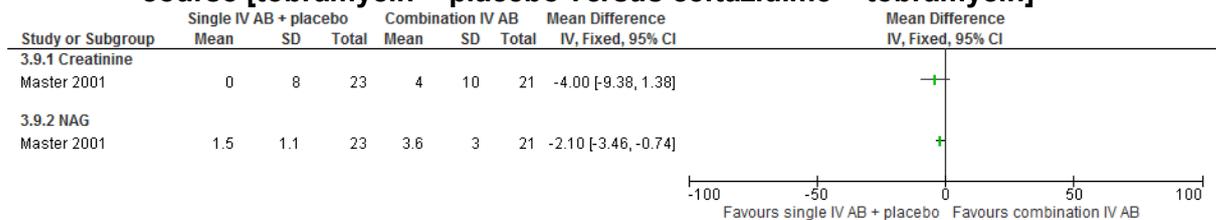
Abbreviations: AB: antibiotics; CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel

Figure 129: Adverse effects: number of hospital admissions due to tinnitus during 10 day course [tobramycin + placebo versus ceftazidime + tobramycin]



Abbreviations: AB: antibiotics; CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel

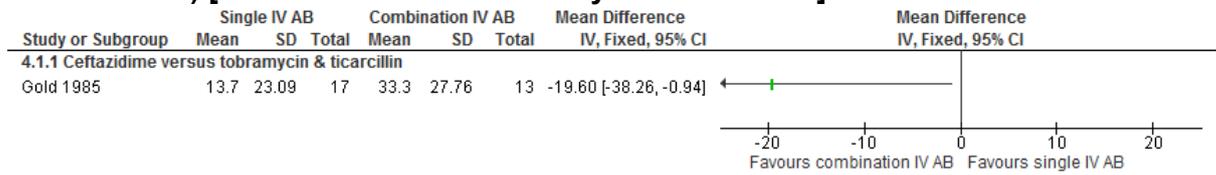
Figure 130: Adverse effects: adverse effects (serum concentrations) during 10 day course [tobramycin + placebo versus ceftazidime + tobramycin]



Abbreviations: AB: antibiotics; CI: confidence interval; IV: inverse variance; IV AB: intravenous antibiotics; SD: standard deviation

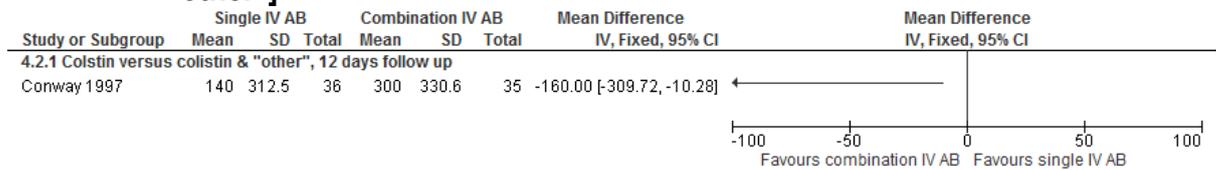
Comparison 3. Single IV antibiotic versus combination IV antibiotic for pulmonary exacerbations with PA

Figure 131: FEV₁ (relative change) at 10 to 14 days follow-up (range of scores: 0-100) [ceftazidime versus tobramycin & ticarcillin]



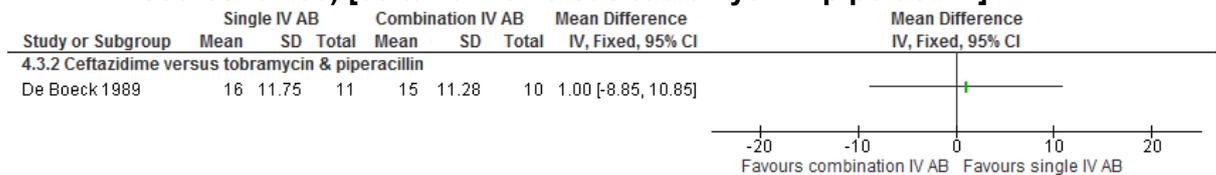
Abbreviations: AB: antibiotics; CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; IV AB: intravenous antibiotics; SD: standard deviation

Figure 132: FEV₁ ml (absolute change) at 12 days follow-up [colistin versus colistin + "other"]



Abbreviations: AB: antibiotics; CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; IV AB: intravenous antibiotics; SD: standard deviation

Figure 133: FEV₁ % predicted (absolute change) at 14 days follow-up (range of scores: 0-100) [ceftazidime versus tobramycin + piperacillin]



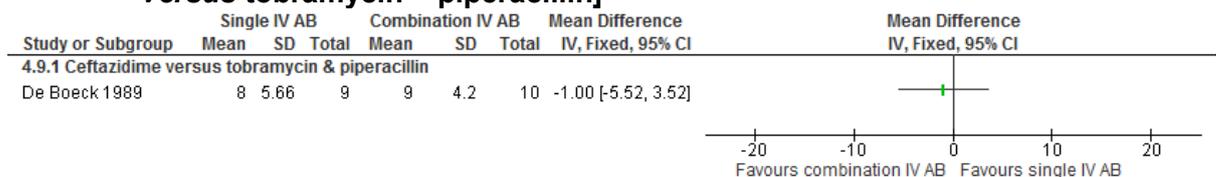
Abbreviations: AB: antibiotics; CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; IV AB: intravenous antibiotics; SD: standard deviation

Figure 134: Eradication: number of people in whom pseudomonas isolates were eradicated at end of course at 10 days follow-up [piperacillin versus piperacillin & tobramycin]



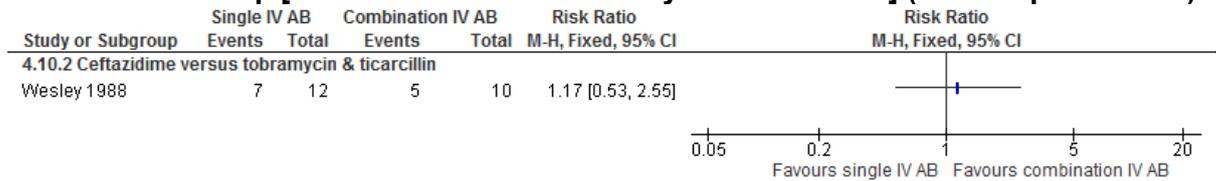
Abbreviations: AB: antibiotics; CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel;

Figure 135: Time to readmission (in months) at 24 to 26 months follow-up [ceftazidime versus tobramycin + piperacillin]



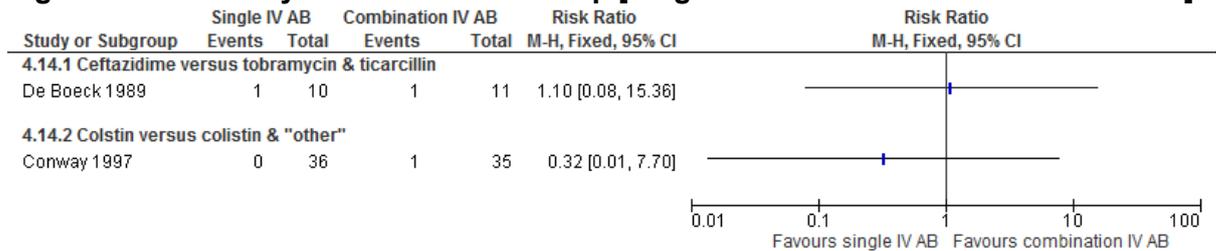
Abbreviations: AB: antibiotics; CI: confidence interval; IV: inverse variance; IV AB: intravenous antibiotics; SD: standard deviation

Figure 136: Number of admissions requiring IV antibiotics or death at 3 months follow-up [ceftazidime versus tobramycin & ticarcillin] (follow-up 3 months)



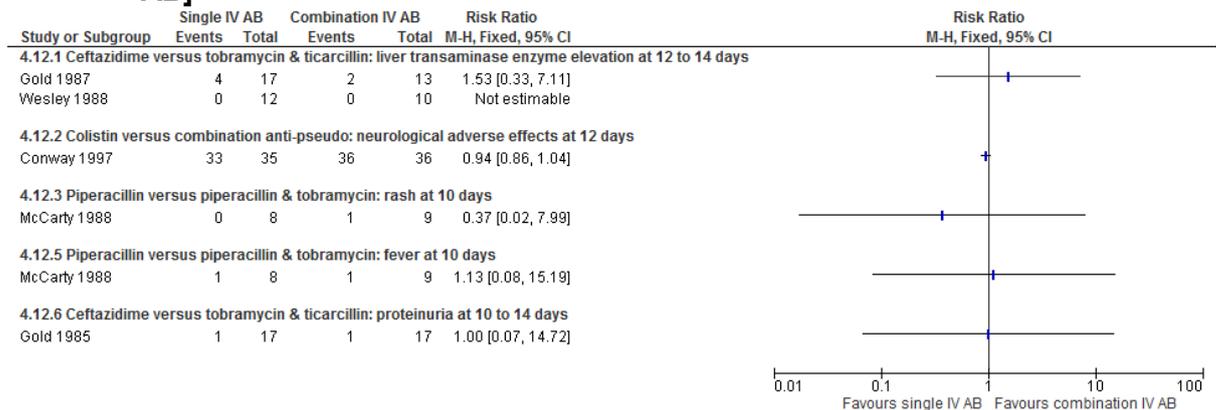
Abbreviations: AB: antibiotics; CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel

Figure 137: Mortality at 4 months follow-up [Single IV AB versus combination IV AB]



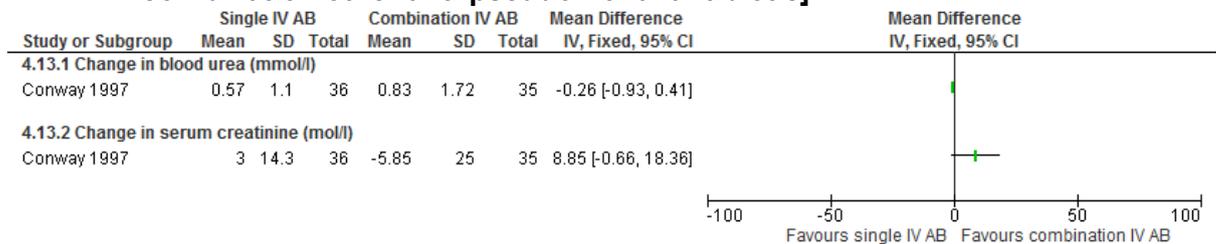
Abbreviations: AB: antibiotics; CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel;

Figure 138: Adverse events at 14 days follow-up [single IV versus combination IV AB]



Abbreviations: AB: antibiotics; CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel

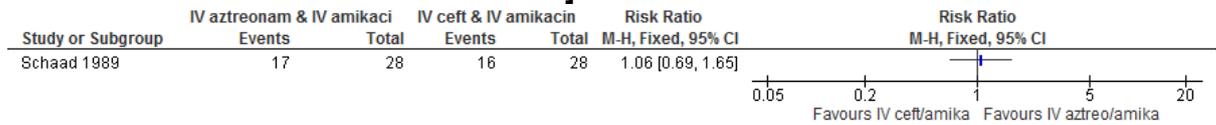
Figure 139: Adverse events: renal toxicity at 12 days follow-up [colistin versus combination other anti-pseudomonal antibiotic]



Abbreviations: AB: antibiotics; CI: confidence interval; IV: inverse variance; IV AB: intravenous antibiotics; SD: standard deviation

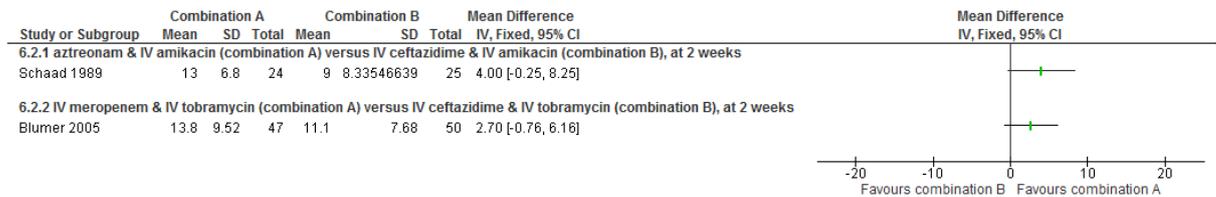
Comparison 4. Combination IV antibiotics versus combination IV antibiotics for pulmonary exacerbations

Figure 140: Eradication of pathogen at 2 weeks follow-up [aztreonam + amikacin versus ceftazidime + amikacin]



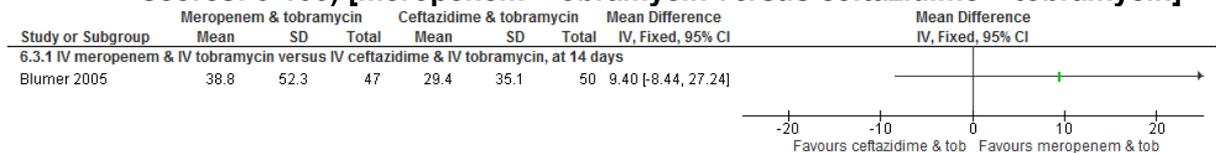
Abbreviations: *aztreo*: aztreonam; *amika*: amikacin; *M-H*: Mantel-Haenszel; *CI*: confidence interval

Figure 141: FEV₁ % predicted (absolute change) at 2 weeks follow-up (range of scores: 0-100) [IV combination A vs IV combination B]



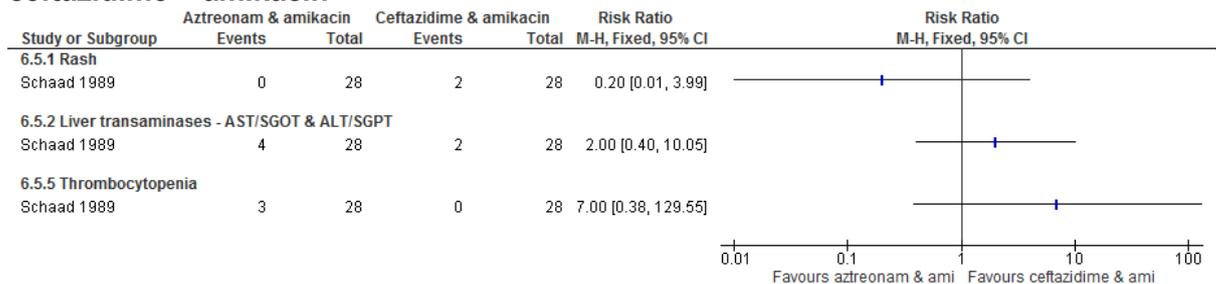
Abbreviations: *amika*: amikacin; *ceft*: ceftazidime; *CI*: confidence interval; *FEV₁*: forced expiratory volume in 1 second; *IV*: inverse variance; *SD*: standard deviation

Figure 142: FEV₁ % predicted (relative change) at 2 weeks follow-up (range of scores: 0-100) [meropenem + obramycin versus ceftazidime + tobramycin]



Abbreviations: *CI*: confidence interval; *FEV₁*: forced expiratory volume in 1 second; *IV*: inverse variance; *SD*: standard deviation; *tob*: tobramycin

Figure 143: Adverse effects at 2 weeks follow-up [aztreonam + amikacin versus ceftazidime + amikacin]



Abbreviations: *ami*: amikacin; *CI*: confidence interval; *M-H*: Mantel-Haenszel;

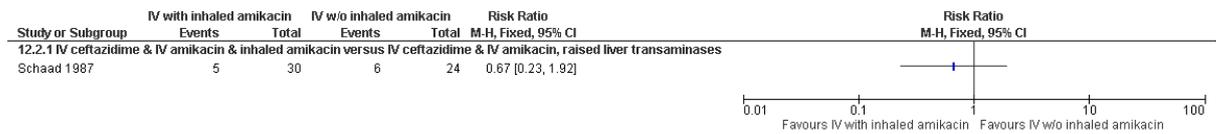
Comparison 5. Two IV antibiotics + inhaled antibiotic versus 2 IV without inhaled antibiotic

Figure 144: Eradication of *P. aeruginosa* at 15 days follow-up [IV ceftazidime + IV amikacin + inhaled amikacin versus IV ceftazidime + IV amikacin]



Abbreviations: *CI*: confidence interval; *IV*: intravenous; *M-H*: Mantel-Haenszel; *w/o*: without

Figure 145: Adverse effects: raised liver transaminases at 4 to 6 weeks follow-up [IV ceftazidime + IV amikacin + inhaled amikacin versus IV ceftazidime + IV amikacin]



Abbreviations: CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel; w/o: without

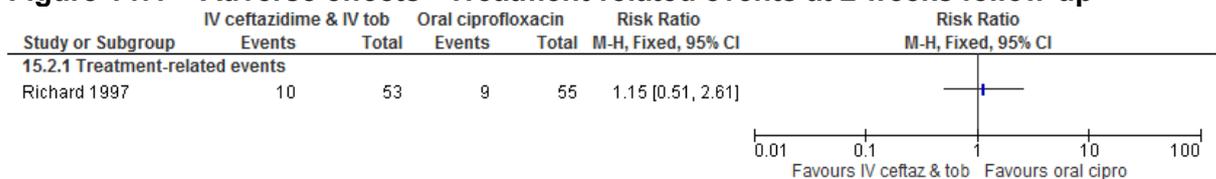
Comparison 6. IV ceftazidime + IV tobramycin versus oral ciprofloxacin

Figure 146: Eradication of P. aeruginosa at 2 weeks follow-up



Abbreviations: ceft: ceftazidime; CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel; tob: tobramycin

Figure 147: Adverse effects - Treatment-related events at 2 weeks follow-up

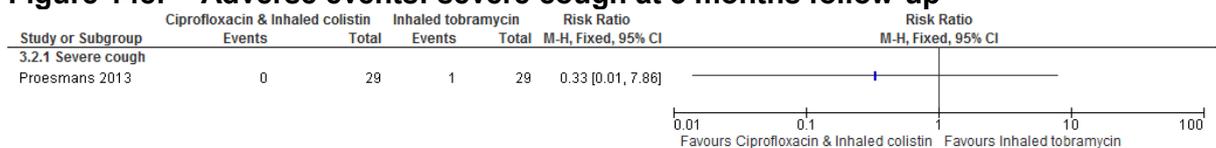


Abbreviations: ceft: ceftazidime; CI: confidence interval; cipro: ciprofloxacin; IV: intravenous; M-H: Mantel-Haenszel; tob: tobramycin

I.10.1.2 Antimicrobial treatment for acute infection with P. aeruginosa

Comparison 7. Oral ciprofloxacin + inhaled colistin versus inhaled tobramycin

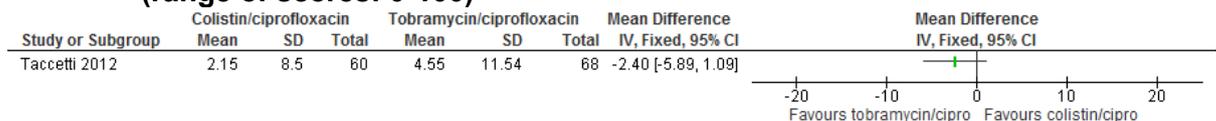
Figure 148: Adverse events: severe cough at 3 months follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

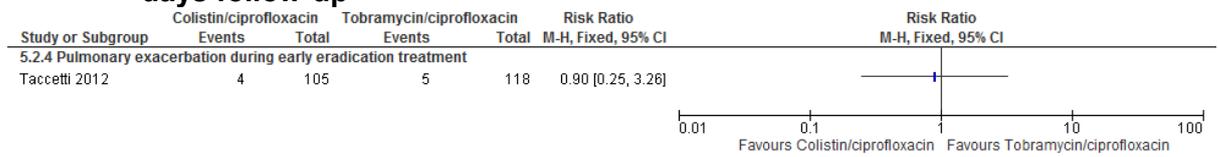
Comparison 8. Inhaled colistin + oral ciprofloxacin versus inhaled tobramycin + oral ciprofloxacin

Figure 149: Relative change in % predicted FEV₁ from baseline at 54 days follow-up (range of scores: 0-100)



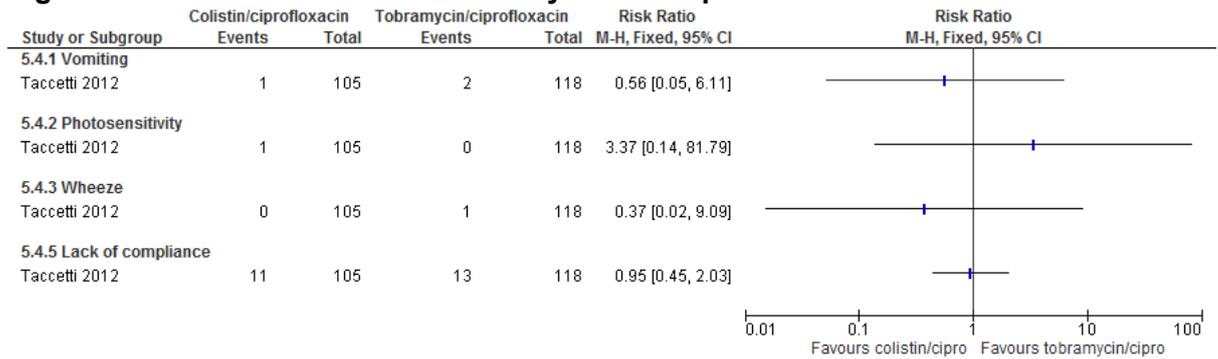
Abbreviations: CI: confidence interval; cipro: ciprofloxacin; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 150: Treatment failure - trial discontinuation due to lack of compliance at 28 days follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel;

Figure 151: Adverse effects at 28 days follow-up



Abbreviations: CI: confidence interval; cipro: ciprofloxacin; M-H: Mantel-Haenszel

I.10.2 Staphylococcus aureus

Not applicable, as no studies were identified for inclusion.

I.10.3 Burkholderia cepacia complex

Not applicable, as no studies were identified for inclusion.

I.10.4 Non-tuberculous mycobacteria

Not applicable, as no studies were identified for inclusion.

I.10.5 Non-identified pathogen

Not applicable, as no studies were identified for inclusion.

I.11 Pulmonary infection – chronic

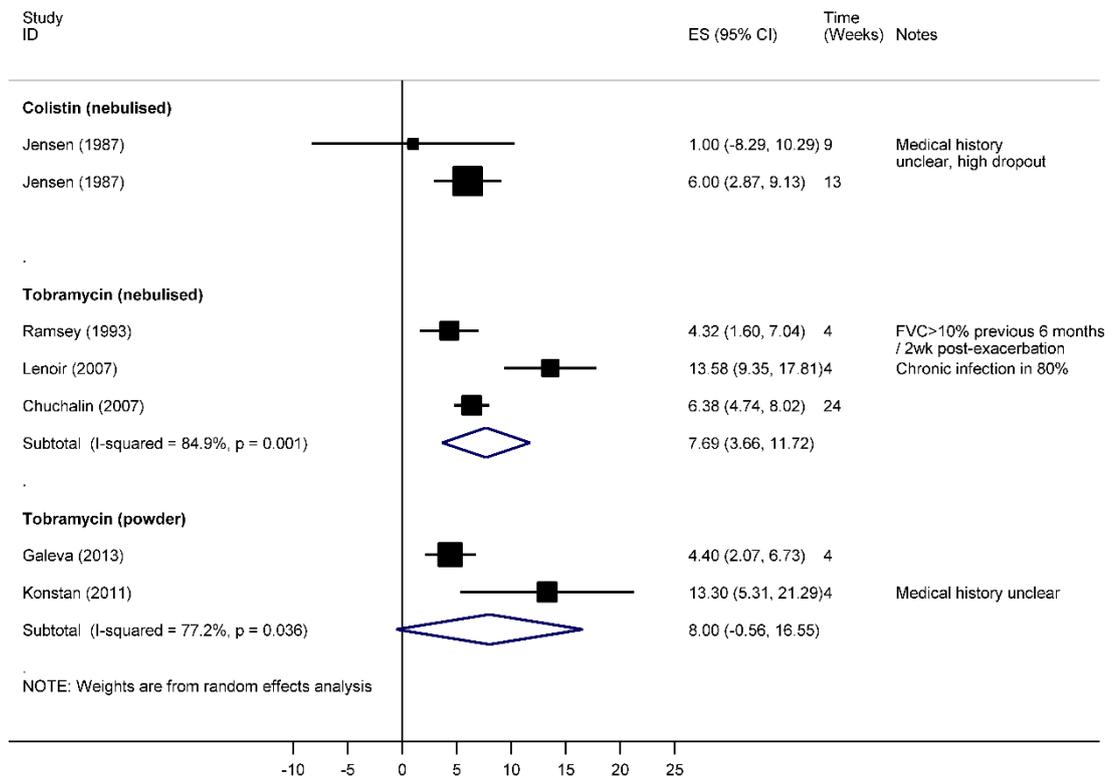
I.11.1 Pseudomonas Aeruginosa

I.11.1.1 NMA outcomes

Outcome 1: NMA FEV₁ % predicted (range of scores: 0-100)

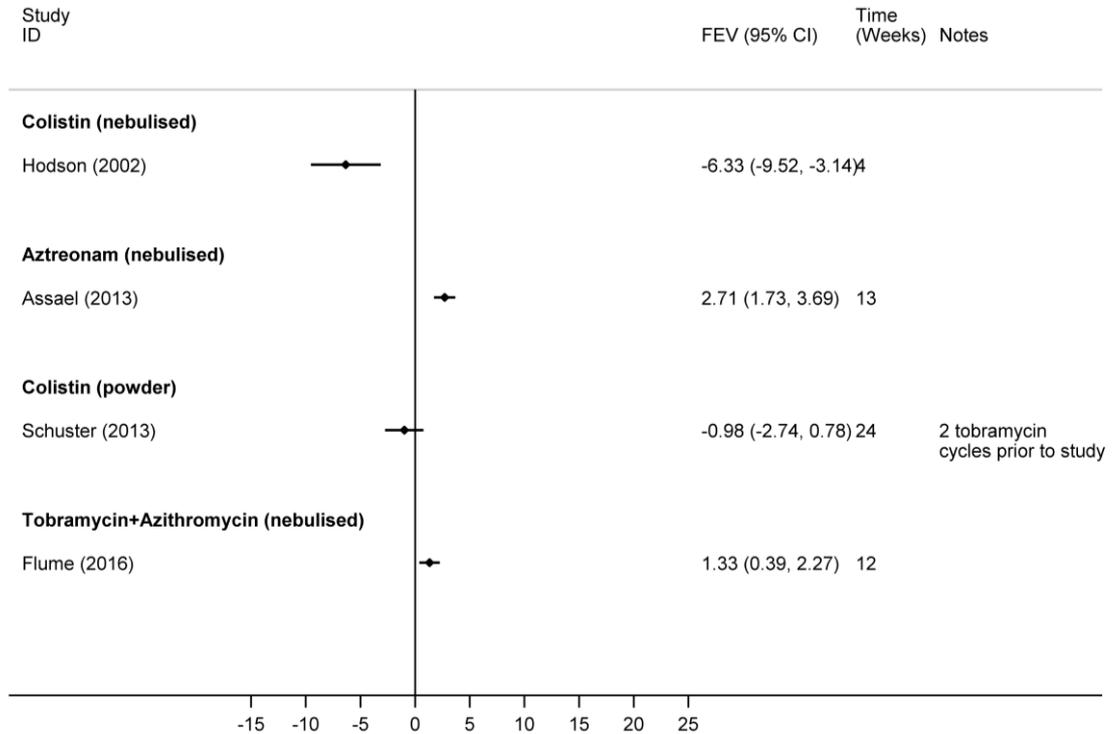
Figure 152: Forest plot showing mean differences (with their 95% CI) of study estimates for interventions *versus* placebo

Treatments versus placebo



Abbreviations: CI: confidence interval; ES: effect size

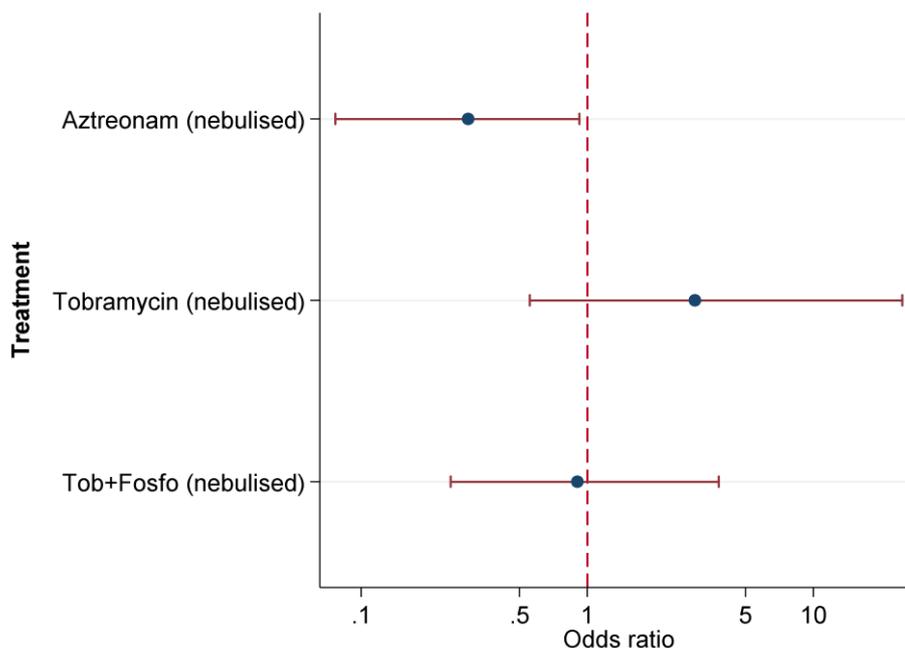
Figure 153: Forest plot showing mean differences (with their 95% CI) of study estimates for interventions versus tobramycin (nebulised)



Abbreviations: CI: confidence interval; FEV: forced expiratory volume

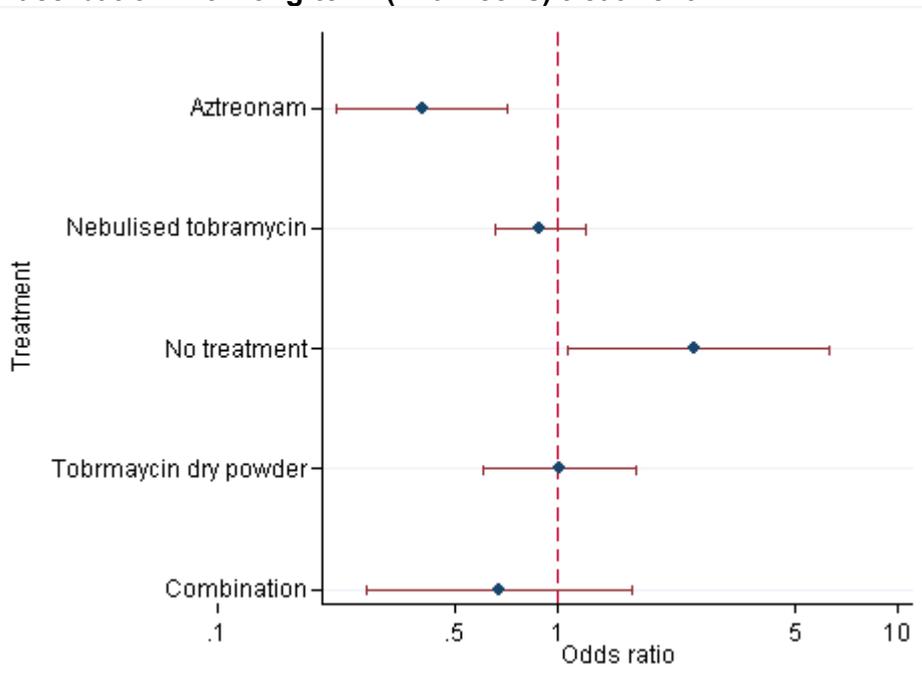
Outcome 2: NMA number of patients experiencing at last one exacerbation

Figure 154: Forest plot showing odds ratios (with their 95% CI) of NMA estimates for each intervention versus placebo for the number of people experiencing at least one exacerbation with short-term (4-10 weeks) treatment



Abbreviations: CI: confidence interval; Fosfo: fosfomycin; Tob: tobramycin. Note: Vertical dashed line shows line of no effect.

Figure 155: Forest plot showing odds ratios (with their 95% CI) of NMA estimates for each intervention versus placebo for the number of people experiencing at least one exacerbation with long-term (>10 weeks) treatment

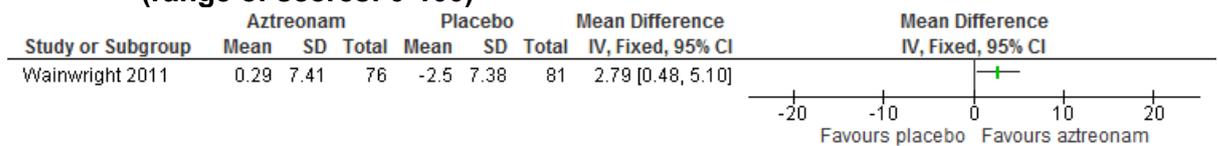


Combination: 28 days aztreonam lysine (nebulised) alternating with 28 days tobramycin (nebulised). Vertical dashed line shows the line of no effect

I.11.1.2 Non-NMA outcomes (pairwise comparisons)

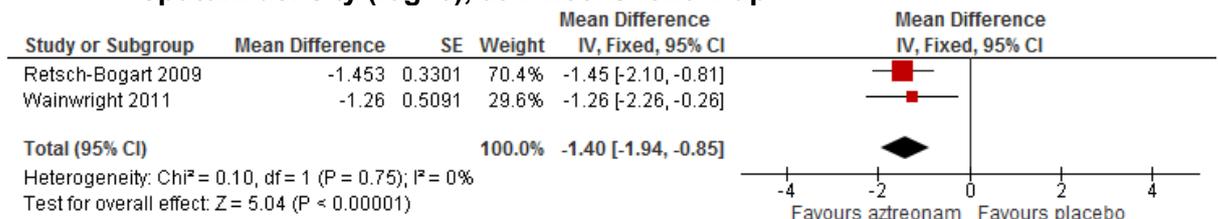
Pairwise comparison 1: Aztreonam lysine versus placebo

Figure 156: Lung function: relative change in FEV₁% predicted at 28 days follow-up (range of scores: 0-100)



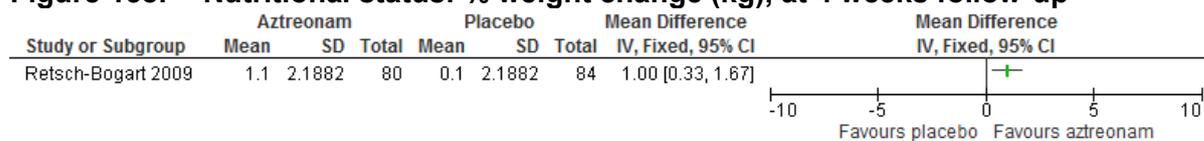
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 157: Suppression of the organism: adjusted mean change in P. aeruginosa sputum density (log₁₀), at 4 weeks follow-up



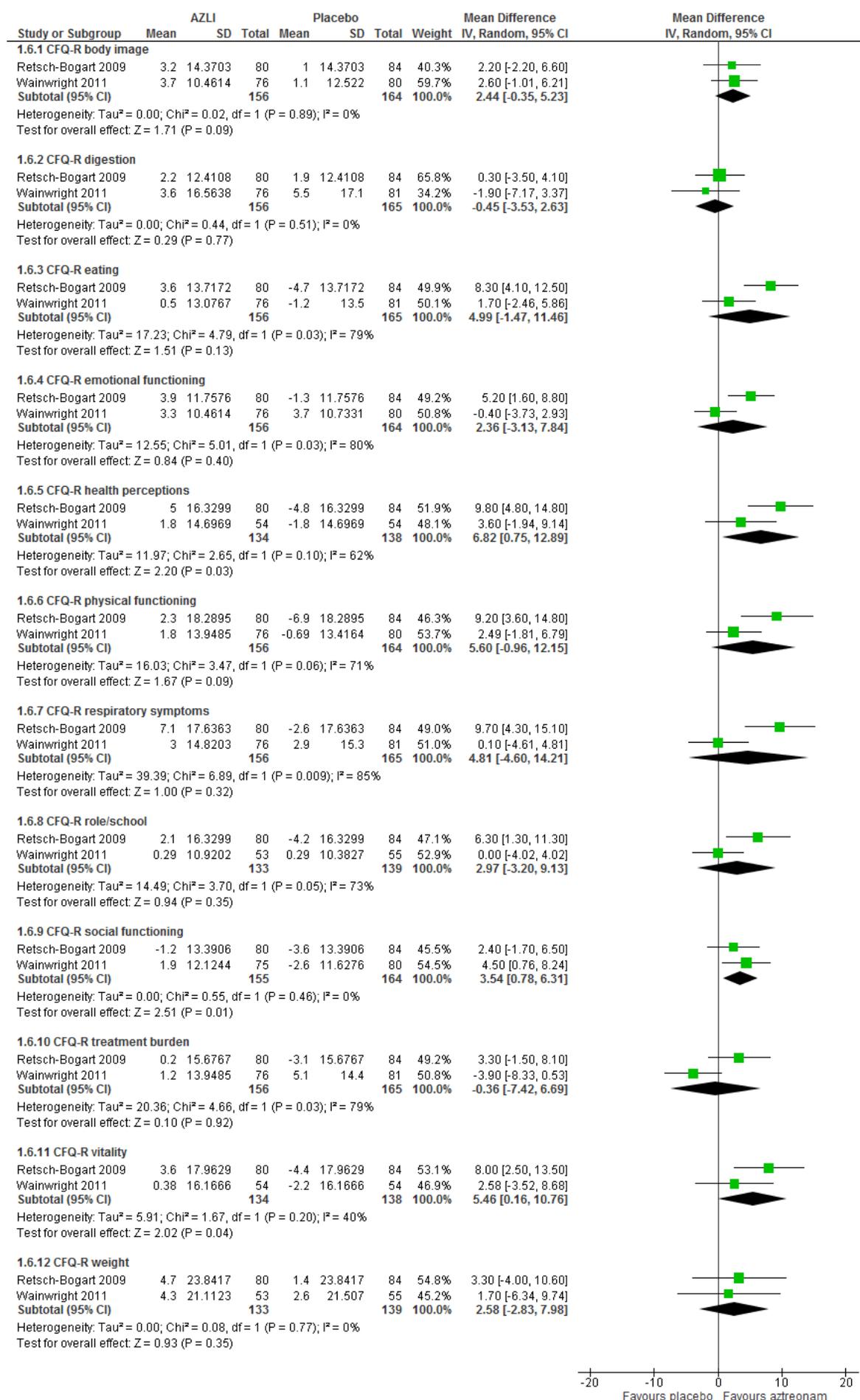
Abbreviations: CI: confidence interval; df: degrees of freedom; IV: inverse variance; SE: standard error

Figure 158: Nutritional status: % weight change (kg), at 4 weeks follow-up



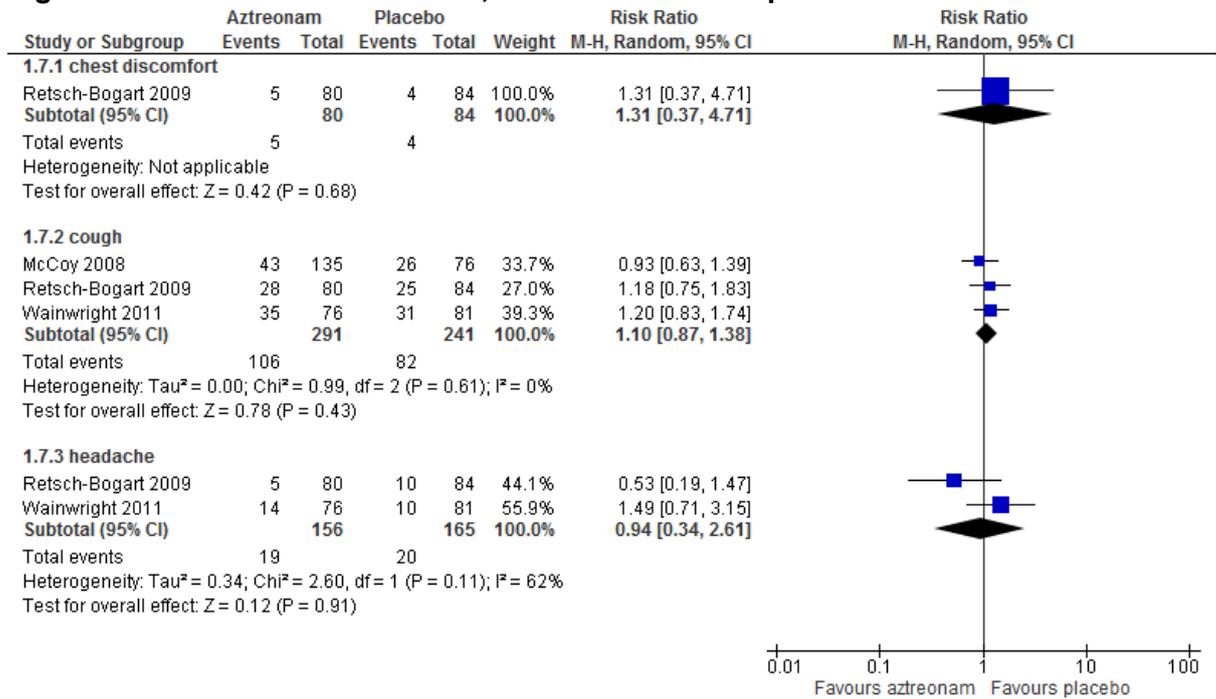
Abbreviations: CI: confidence interval; IV: inverse variance; kg: kilograms; SD: standard deviation

Figure 159: Quality of life: CFQ-R, at 4 weeks follow-up (range of scores: 0-100)



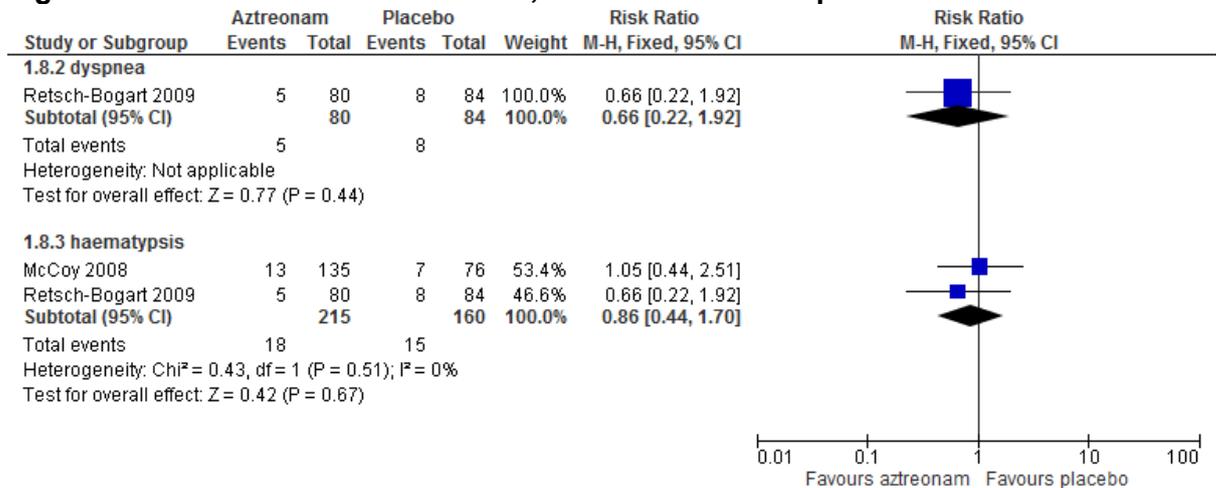
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

Figure 160: Mild adverse events, at 4 weeks follow-up



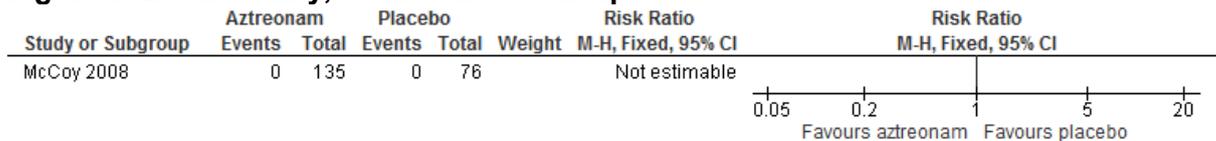
Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

Figure 161: Serious adverse events, at 4 weeks follow-up



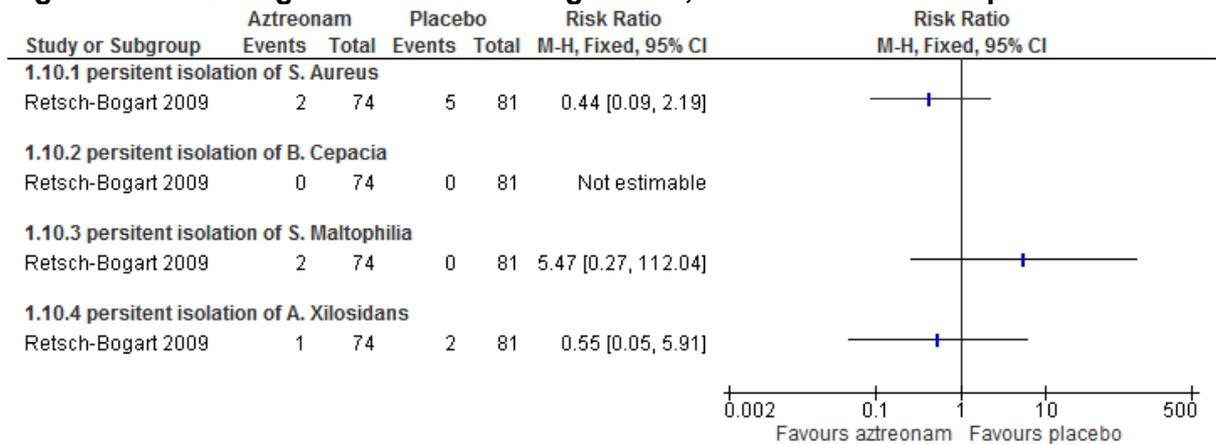
Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

Figure 162: Mortality, at 4 weeks follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel. Not estimable as no deaths were recorded in either group.

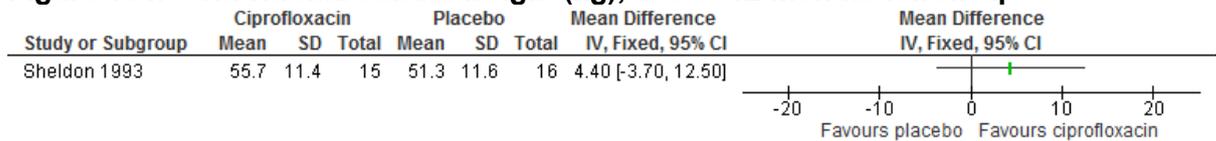
Figure 163: Emergence of resistant organisms, at 42 weeks follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel.

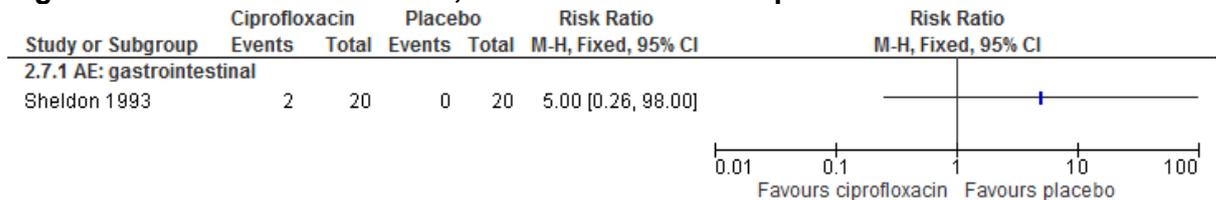
Pairwise comparison 2: Ciprofloxacin versus placebo

Figure 164: Nutritional status: weight (kg), at 6 to 12 months follow-up



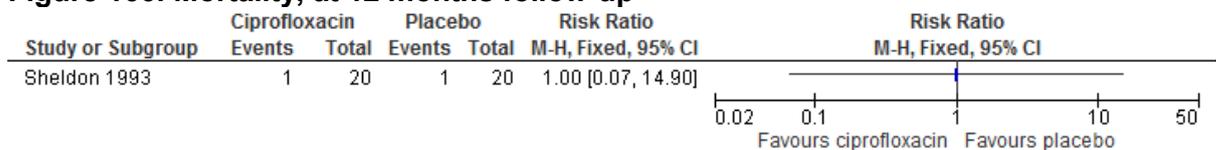
Abbreviations: CI: confidence interval; kg: kilograms; IV: inverse variance; SD: standard deviation

Figure 165: Mild adverse events, at 12 months follow-up



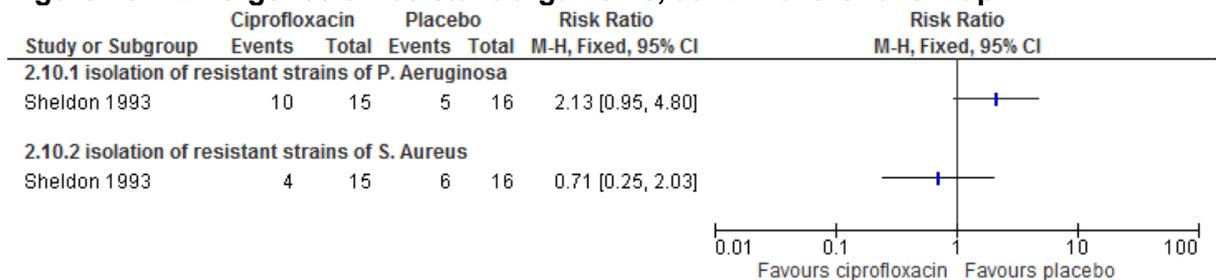
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel.

Figure 166: Mortality, at 12 months follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

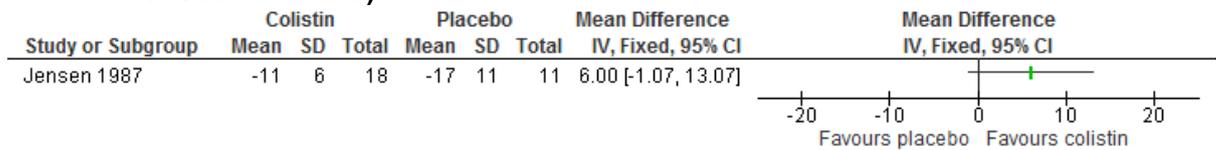
Figure 167: Emergence of resistant organisms, at 12 months follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

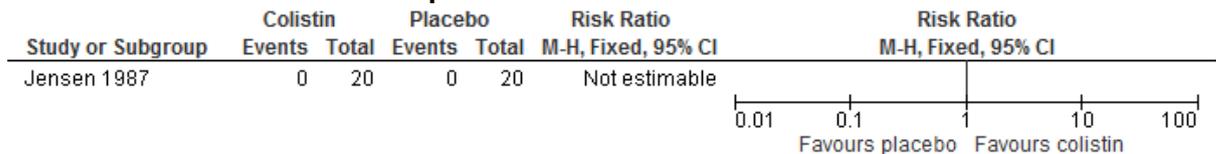
Pairwise comparison 3.1. Colistin versus placebo

Figure 168: Lung function: change in FEV₁ % predicted at 3 months follow-up (range of scores: 0-100)



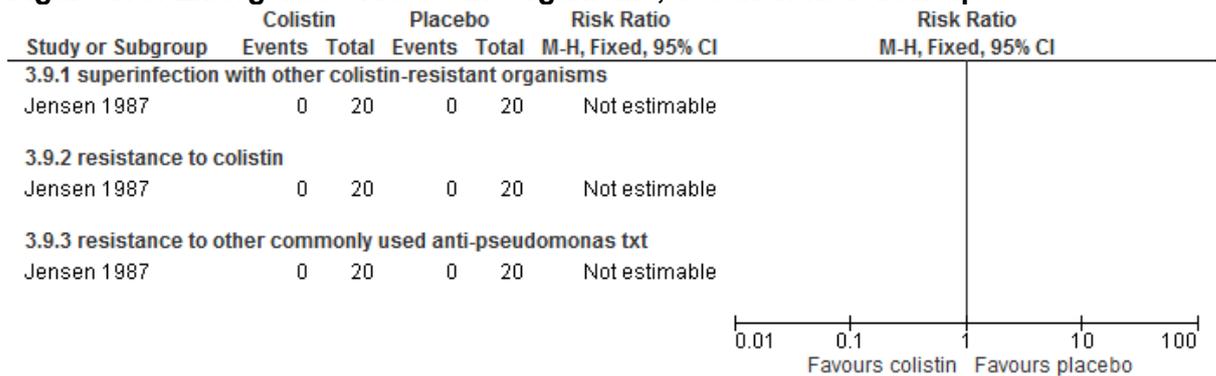
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 169: Suppression of the organism: eradication of the organism from sputum, at 3 months follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel. Data cannot be plotted as there were 0 events in each group.

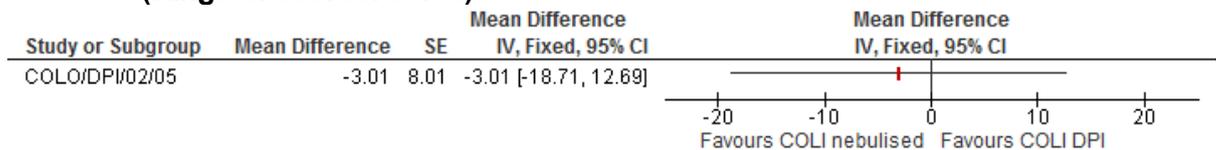
Figure 170: Emergence of resistant organisms, at 3 months follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel. Data cannot be plotted as there were 0 events in each group.

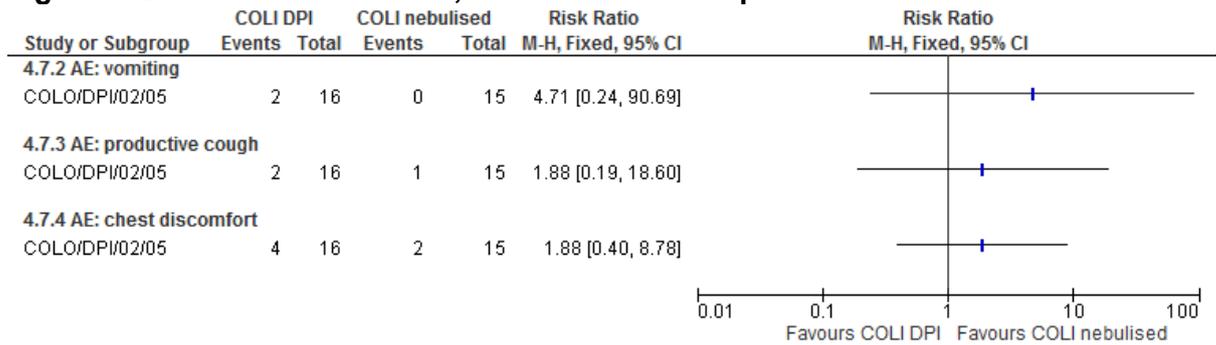
Pairwise comparison 3.2. Colistin inhalation powder (COLO DPI) versus colistin inhalation solution (COLI nebulised)

Figure 171: Lung function: % mean change in FEV₁% predicted at 4 weeks follow-up (range of scores: 0-100)



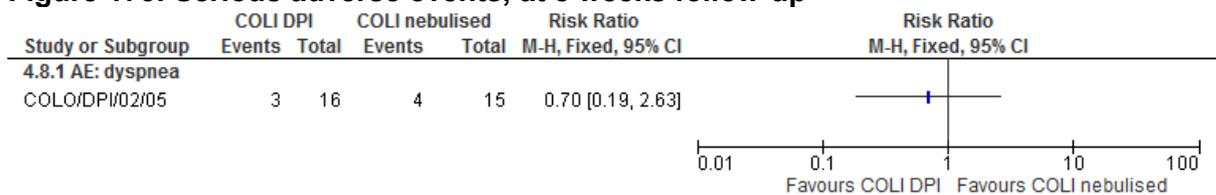
Abbreviations: CI: confidence interval; COLI: colistin; DPI: dry powder inhalation; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error

Figure 172: Mild adverse events, at 8 weeks follow-up



Abbreviations: CI: confidence interval; COLI: colistin; DPI: dry powder inhalation; M-H: Mantel-Haenszel

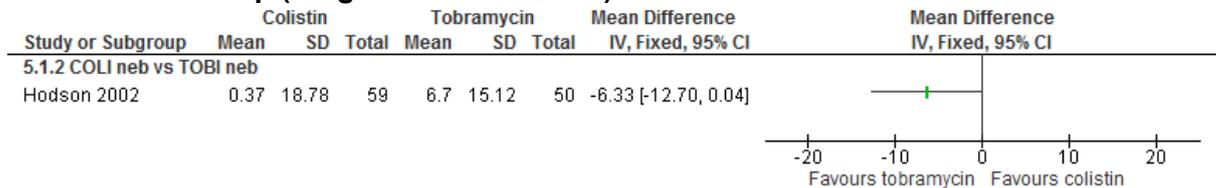
Figure 173: Serious adverse events, at 8 weeks follow-up



Abbreviations: CI: confidence interval; COLI: colistin; DPI: dry powder inhalation; M-H: Mantel-Haenszel

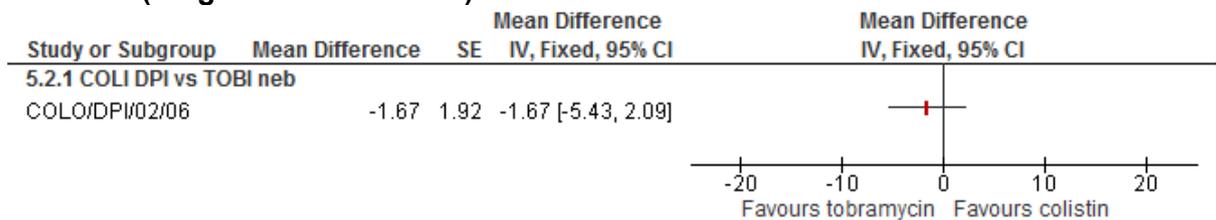
Pairwise comparison 3.3. Colistin versus tobramycin

Figure 174: Lung function: mean % change in FEV₁% predicted at 1 to 3 months follow-up (range of scores: 0-100)



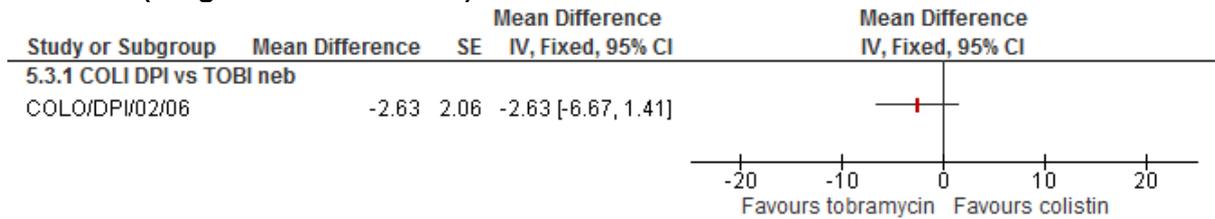
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; Neb: nebulised; SD: standard deviation

Figure 175: Lung function: mean % change in FEV₁% predicted at 4 weeks follow-up (range of scores: 0-100)



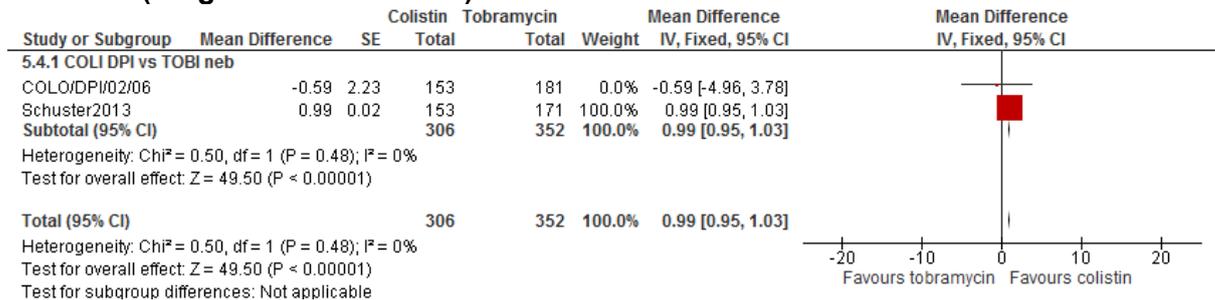
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; Neb: nebulised; SE: standard error

Figure 176: Lung function: mean % change in FEV₁% predicted at 12 weeks follow-up (range of scores: 0-100)



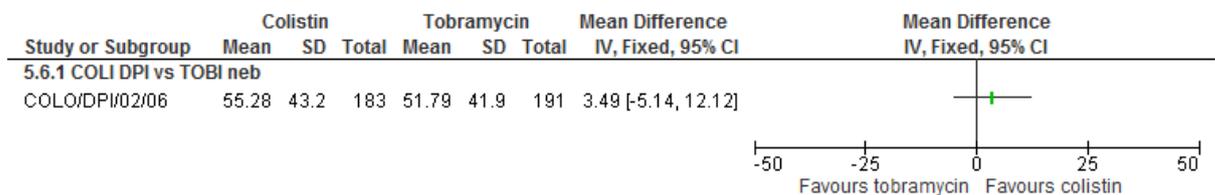
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; Neb: nebulised; SE: standard error

Figure 177: Lung function: mean % change in FEV₁% predicted at 24 weeks follow-up (range of scores: 0-100)



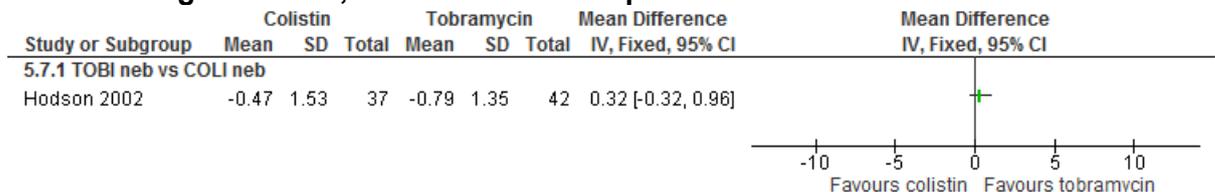
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; Neb: nebulised; SE: standard error

Figure 178: Time to next pulmonary exacerbation: time to first additional anti-pseudomonal treatment (days), at 24 weeks follow-up



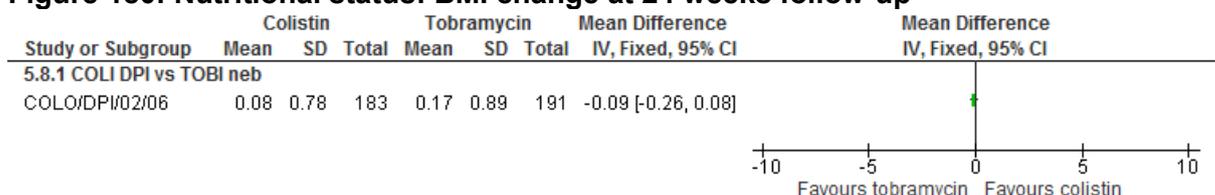
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 179: Suppression of the organism: change in sputum P. aeruginosa density Log₁₀ CFU/ml, at 4 weeks follow-up



Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 180: Nutritional status: BMI change at 24 weeks follow-up



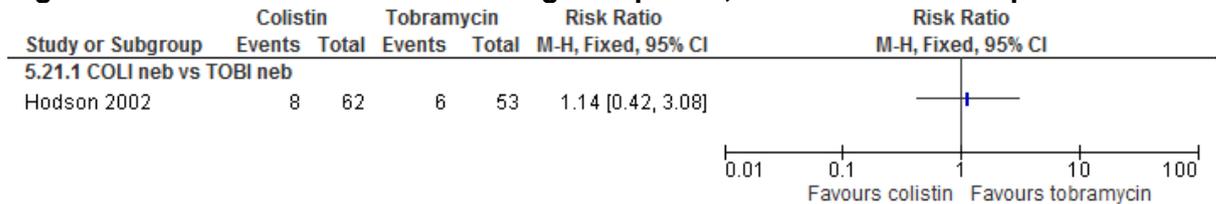
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 181: Quality of life: CFQ-R all domains, at 24 weeks follow-up (range of scores: 0-100)

Data cannot be presented in forest plots, as SD are not reported.

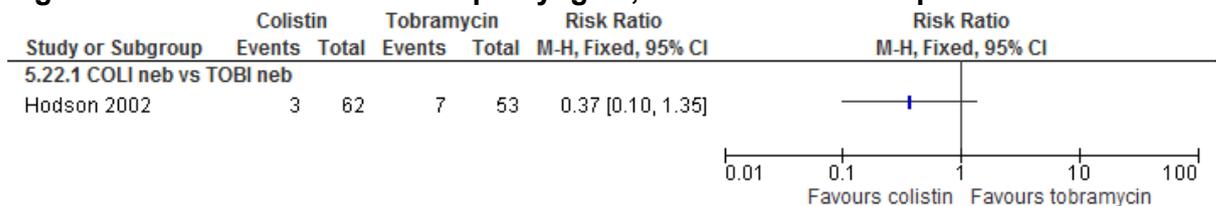
Abbreviations: CFQ-R: cystic fibrosis questionnaire revised

Figure 182: Mild adverse events: change in sputum, at 4 weeks follow-up



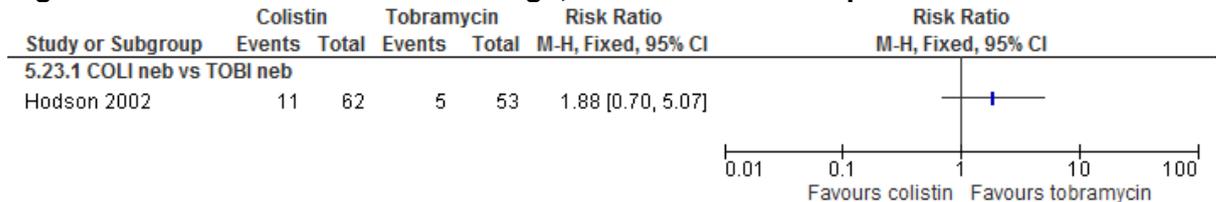
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 183: Mild adverse events: pharyngitis, at 4 weeks follow-up



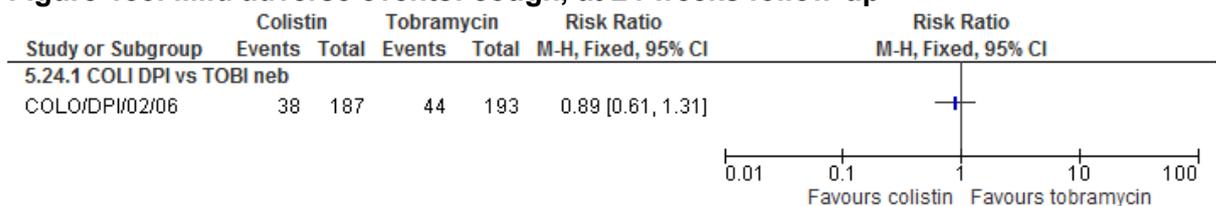
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 184: Mild adverse events: cough, at 4 weeks follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 185: Mild adverse events: cough, at 24 weeks follow-up



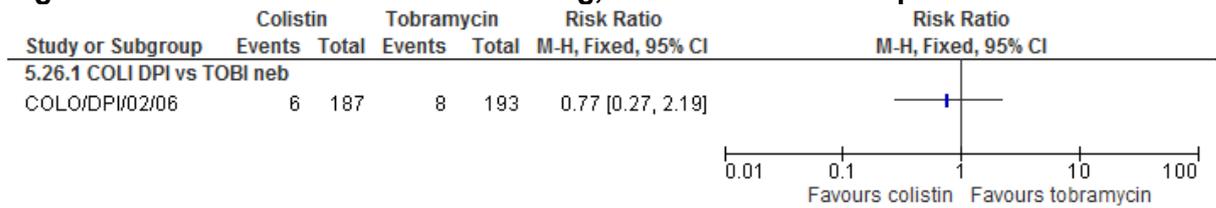
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 186: Mild adverse events: chest discomfort, at 24 weeks follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 187: Mild adverse events: vomiting, at 24 weeks follow-up



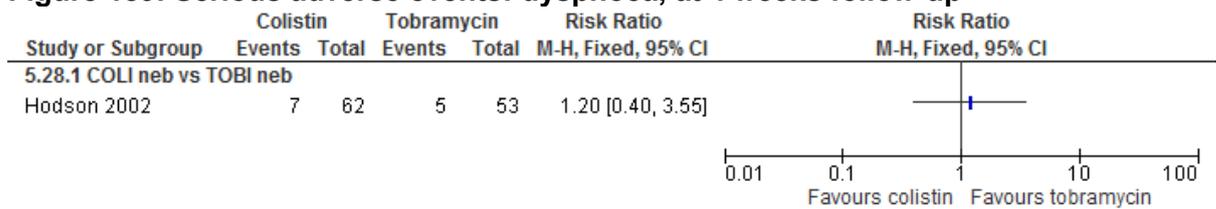
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 188: Serious adverse events: patients with > 1 serious AE, at 4 weeks follow-up



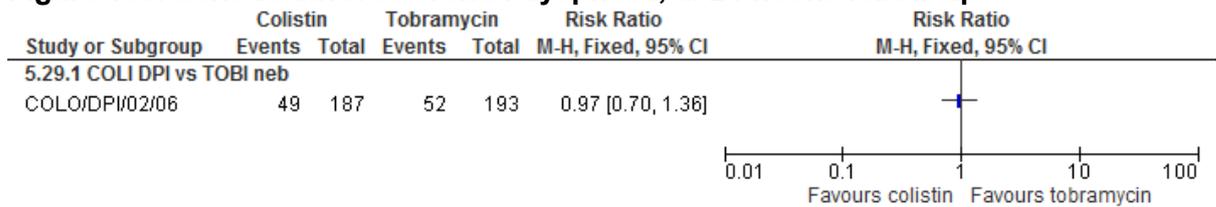
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 189: Serious adverse events: dyspnoea, at 4 weeks follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 190: Serious adverse events: dyspnoea, at 24 weeks follow-up



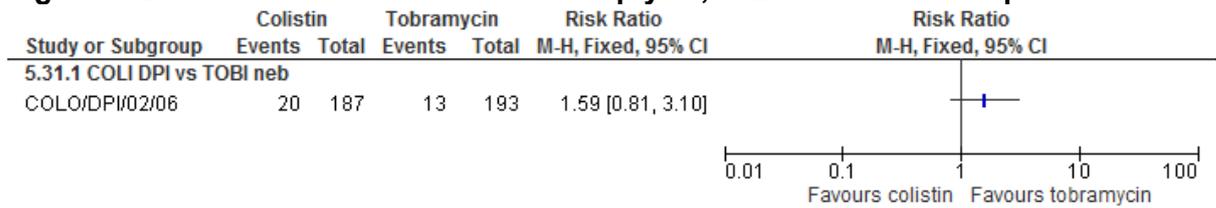
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 191: Serious adverse events: patients withdrawn, at 24 weeks follow-up



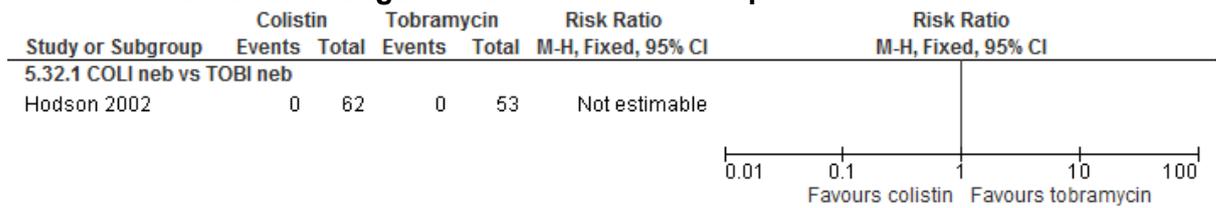
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 192: Serious adverse events: haemoptysis, at 24 weeks follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

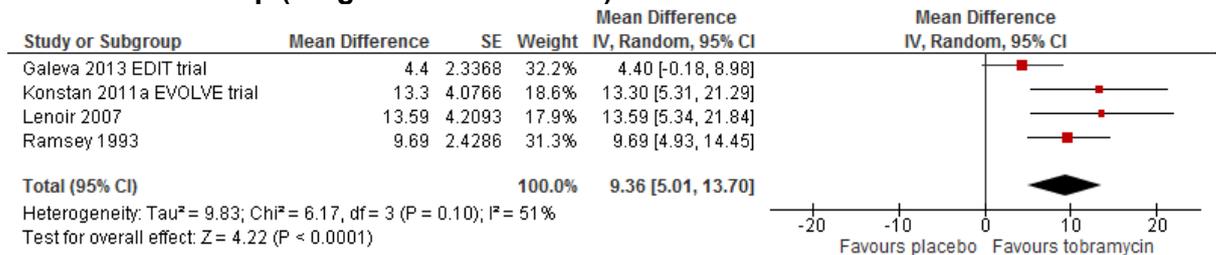
Figure 193: Emergence of resistant organisms: emergence of highly tobramycin-resistant P. Aeruginosa at 4 weeks follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel. Data cannot be plotted, as there were 0 events in each group.

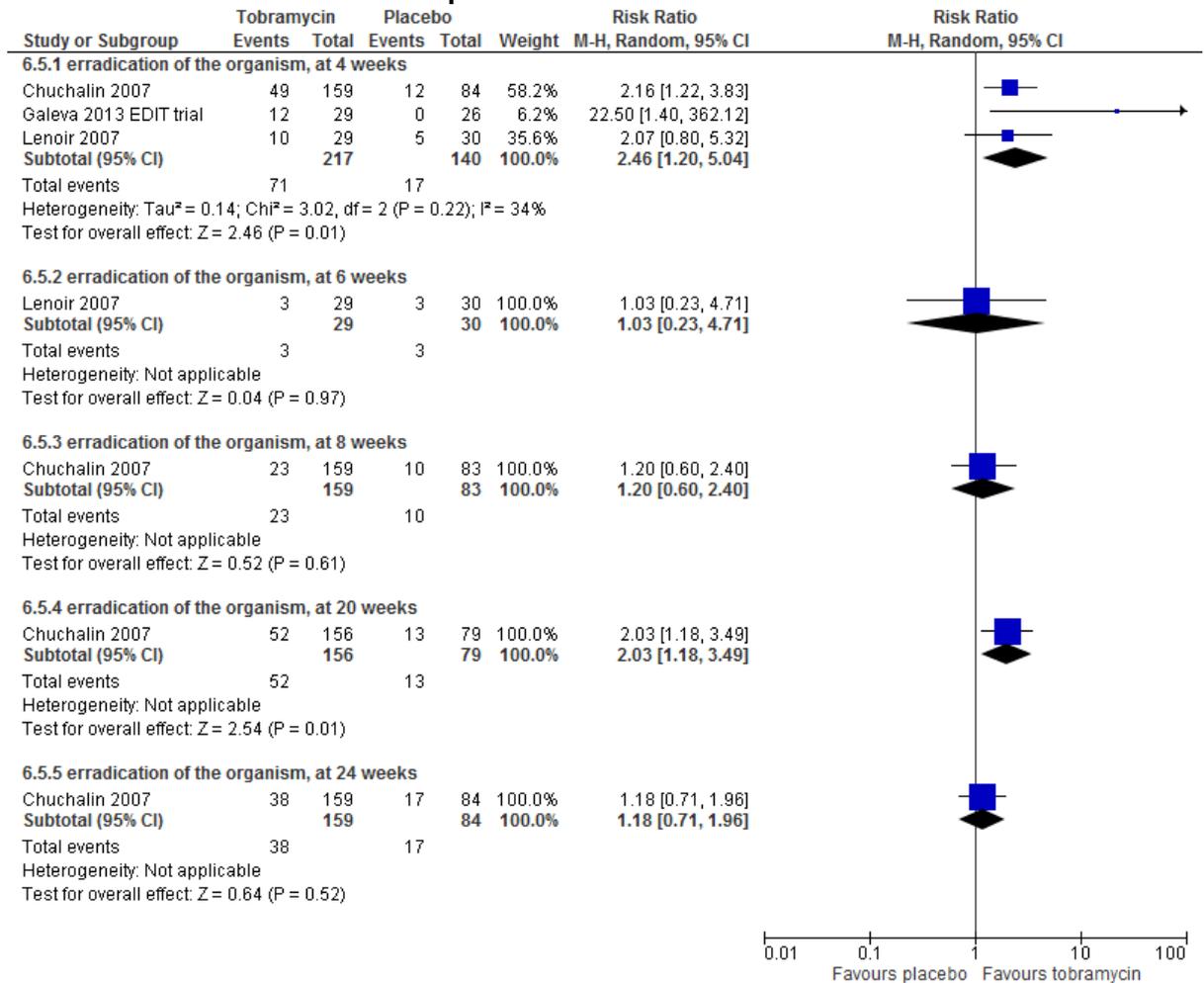
Pairwise comparison 4.1. Tobramycin versus placebo

Figure 194: Lung function: mean % change in FEV₁% predicted at 1 to 3 months follow-up (range of scores: 0-100)



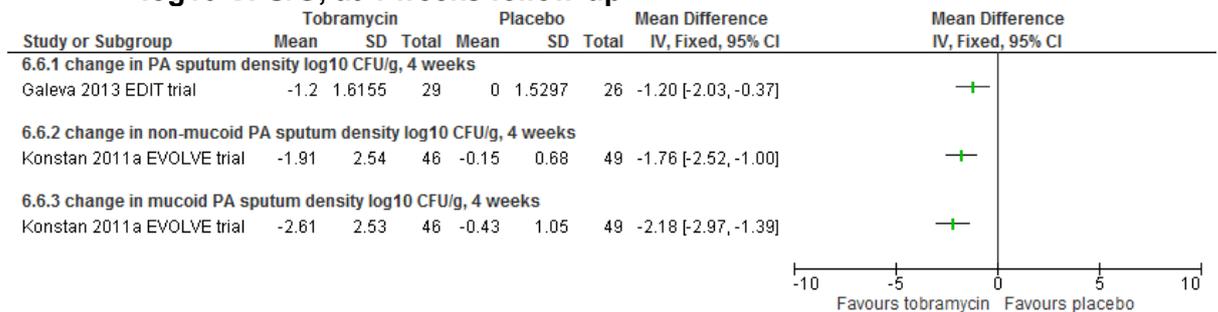
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error

Figure 195: Suppression of the organism: eradication of the organism at 4, 6, 12, 8, 20 and 24 weeks follow-up



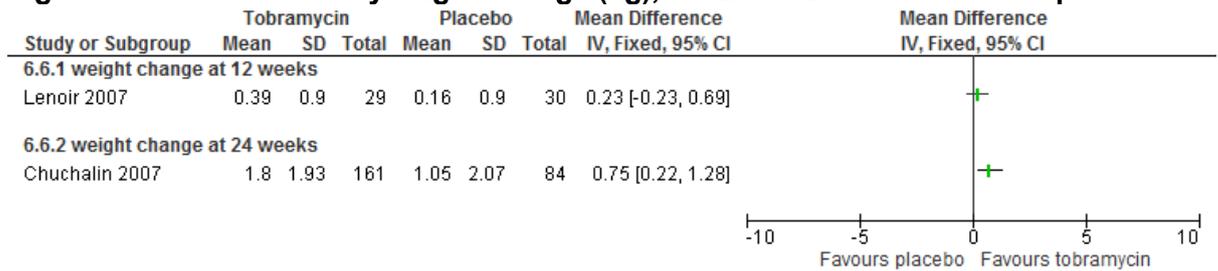
Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

Figure 196: Suppression of the organism: change in P. aeruginosa sputum density log₁₀ CFU/G, at 4 weeks follow-up



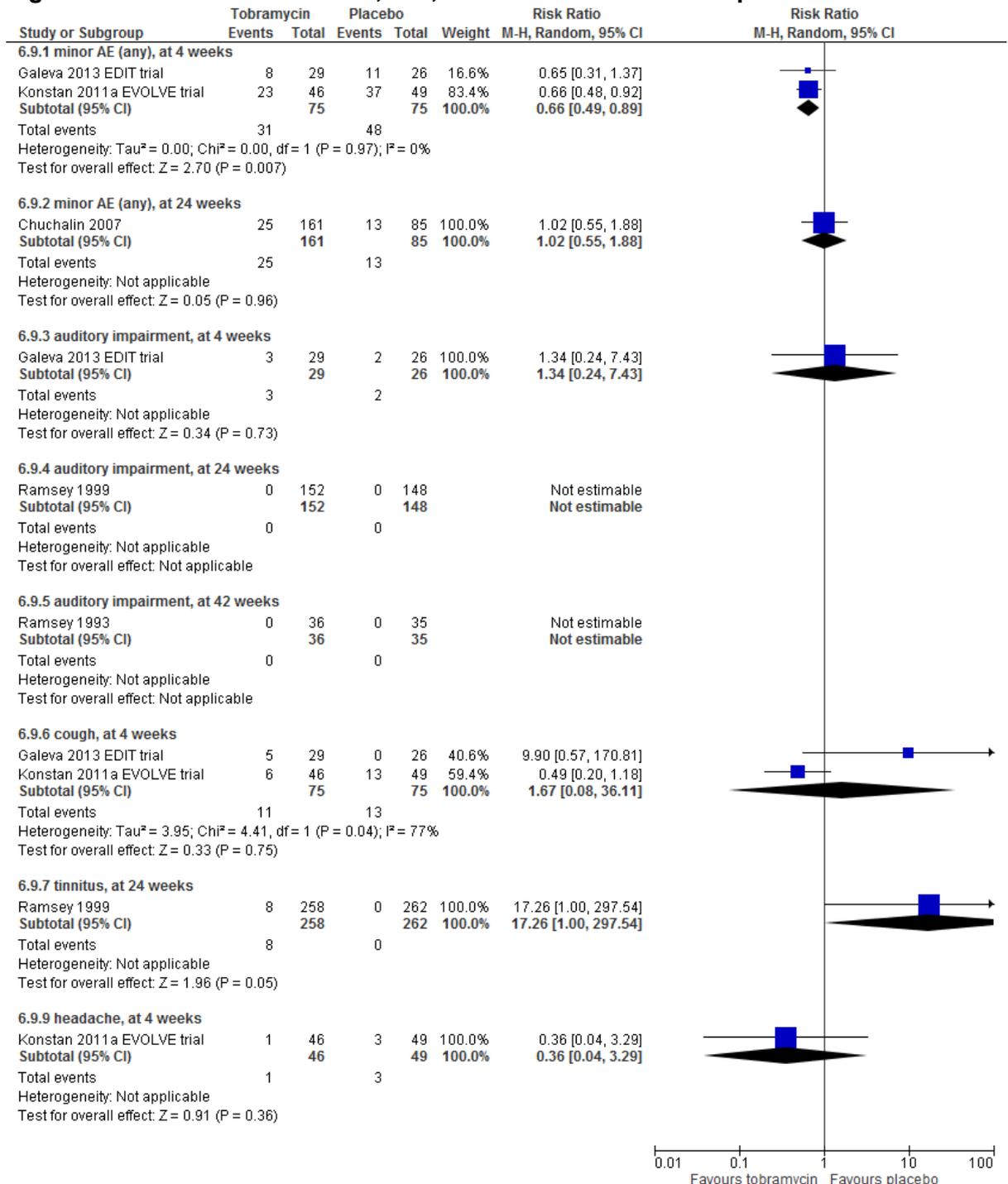
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 197: Nutrition: bodyweight change (kg), at 12 and 24 weeks follow-up



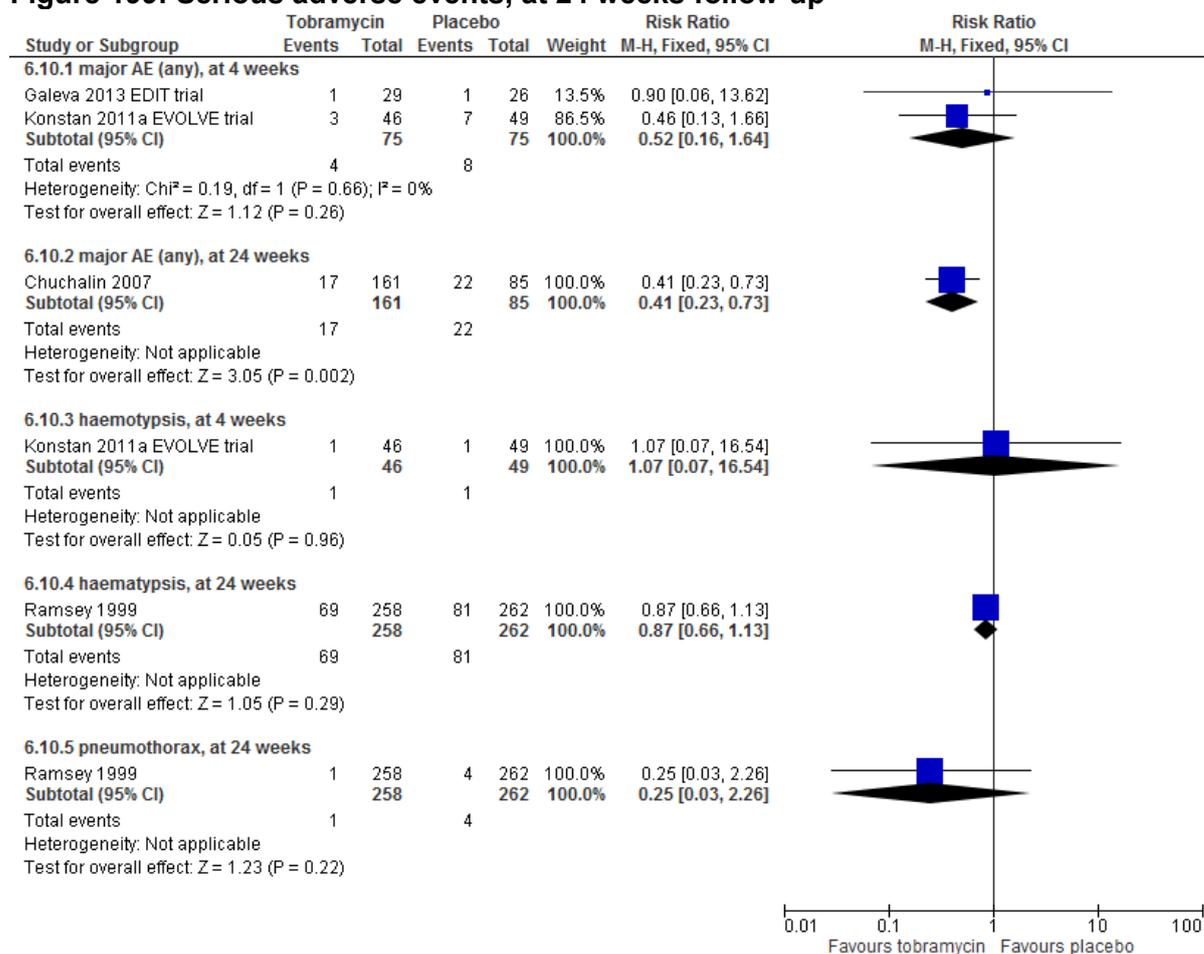
Abbreviations: CI: confidence interval; IV: inverse variance; kg: kilograms; SD: standard deviation

Figure 198: Mild adverse events, at 4, 24 and 42 weeks follow-up



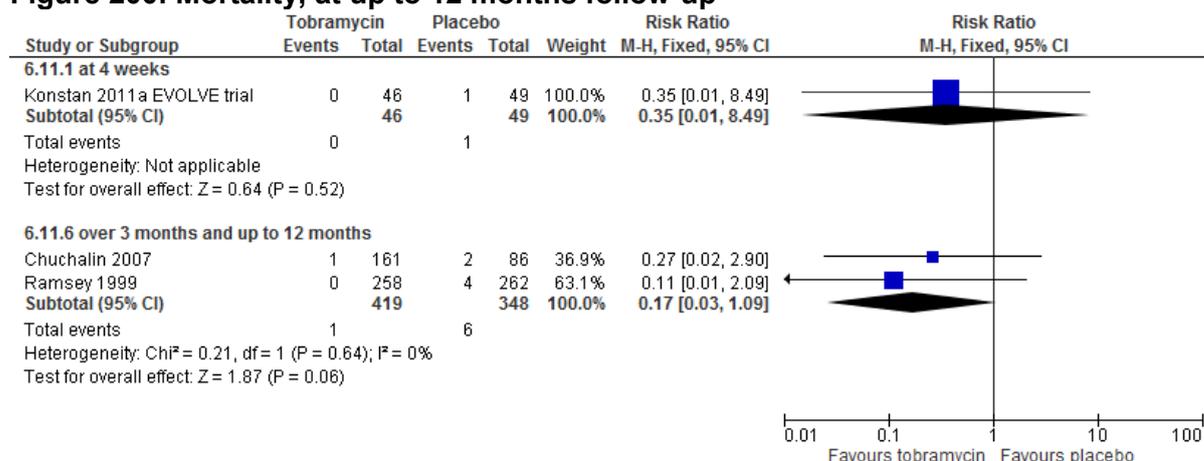
Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

Figure 199: Serious adverse events, at 24 weeks follow-up



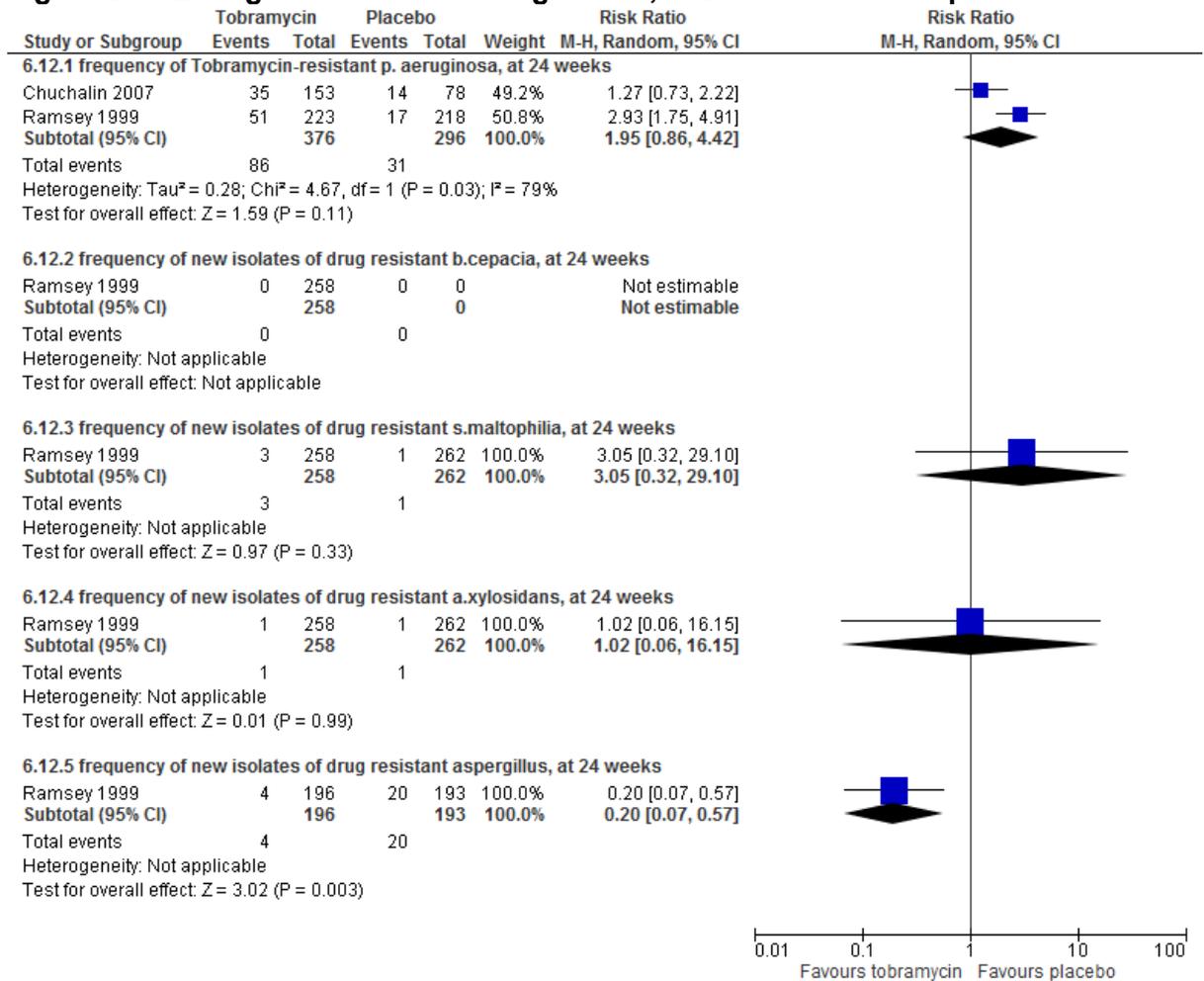
Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

Figure 200: Mortality, at up to 12 months follow-up



Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

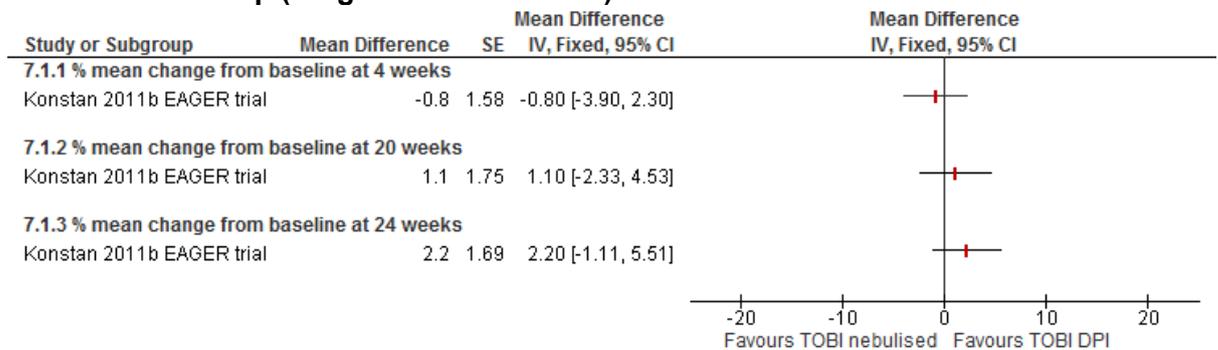
Figure 201: Emergence of resistant organisms, at 24 weeks follow-up



Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

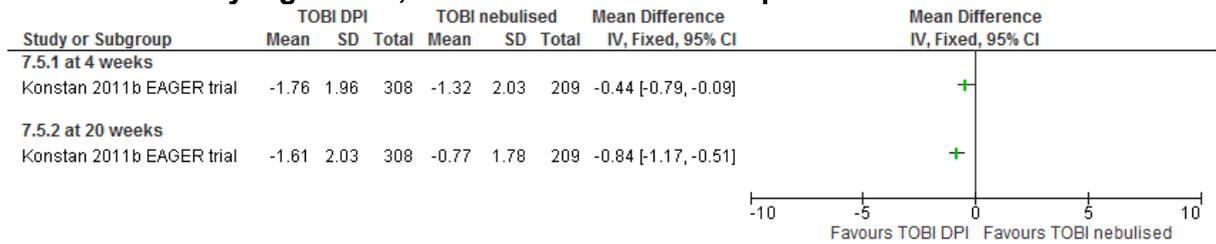
Pairwise comparison 4.2. Tobramycin inhalation powder (TOBI DPI) versus tobramycin inhalation solution (TOBI nebulised)

Figure 202: Lung function: mean change in FEV₁% predicted at 4, 20 and 24 weeks follow-up (range of scores: 0-100)



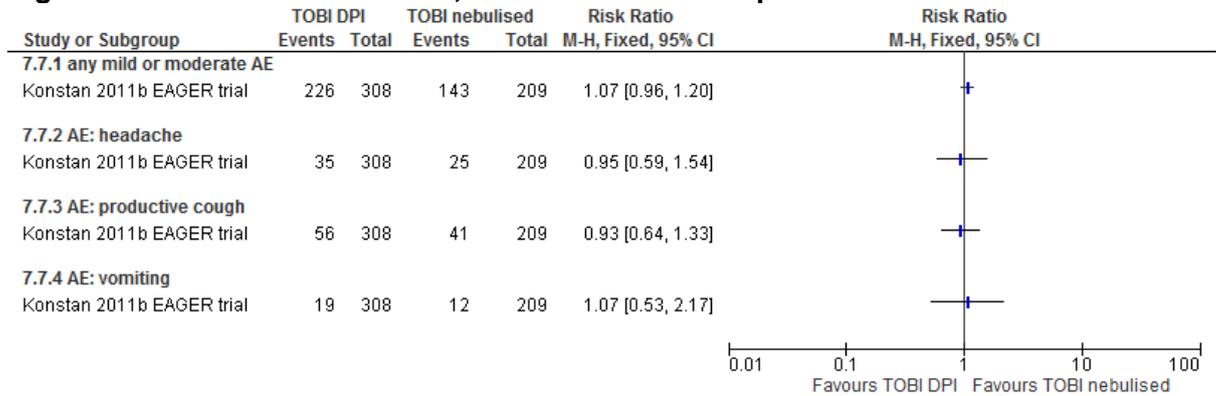
Abbreviations: CI: confidence interval; DPI: dry powder inhalation; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error; TOBI: tobramycin

Figure 203: Suppression of the organism: mean change in *P. aeruginosa* sputum density log₁₀ CFU, at 4 to 20 weeks follow-up



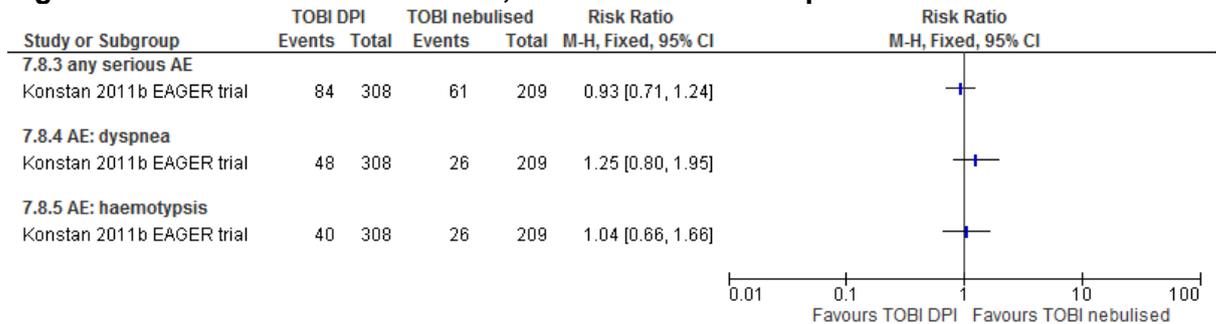
Abbreviations: CI: confidence interval; DPI: dry powder inhalation; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; PA: *Pseudomonas aeruginosa*; SD: standard deviation; TOBI: tobramycin

Figure 204: Mild adverse events, at 24 weeks follow-up



Abbreviations: CI: confidence interval; DPI: dry powder inhalation; M-H: Mantel-Haenszel; TOBI: tobramycin

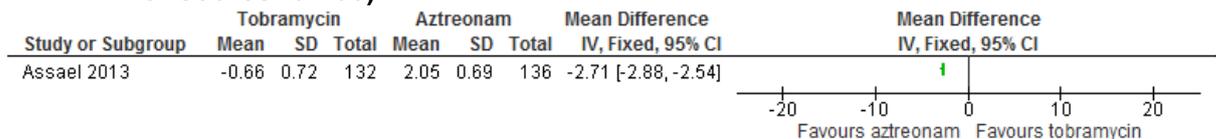
Figure 205: Serious adverse events, at 24 weeks follow-up



Abbreviations: CI: confidence interval; DPI: dry powder inhalation; M-H: Mantel-Haenszel; TOBI: tobramycin

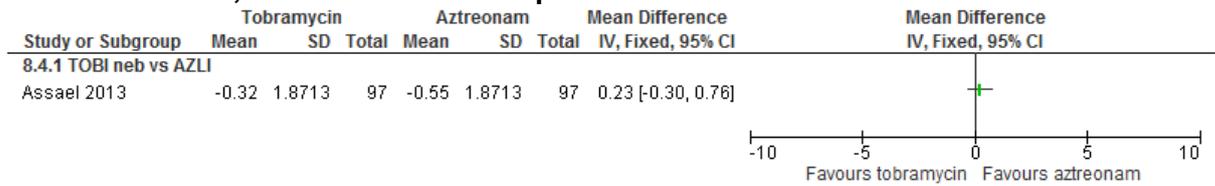
Pairwise comparison 4.3. Tobramycin versus Aztreonam lysine

Figure 206: Lung function: % change in FEV₁% predicted at 3 months follow-up (range of scores: 0-100)



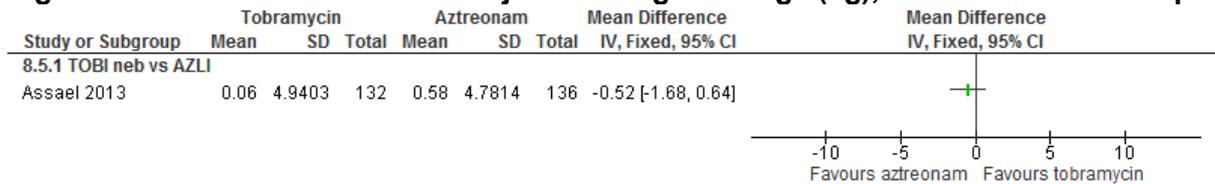
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation. Calculated across 3x28-day treatment courses

Figure 207: Suppression of the organism: adj mean change sputum density log₁₀ PA CFU/G, at 20 weeks follow-up



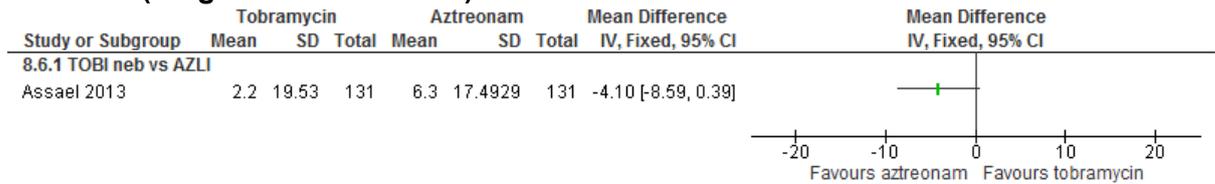
Abbreviations: CI: confidence interval; CFU: colony forming unit; IV: inverse variance; PA: *Pseudomonas aeruginosa*; SD: standard deviation

Figure 208: Nutritional status: % adj mean weight change (kg), at 24 weeks follow-up



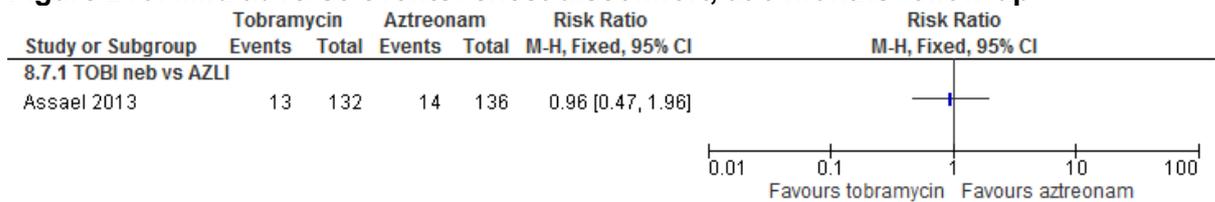
Abbreviations: CI: confidence interval; ; IV: inverse variance; kg: kilograms; SD: standard deviation

Figure 209: Quality of life: CFQ-R respiratory, adj mean change, at 20 weeks follow-up (range of scores: 0-100)



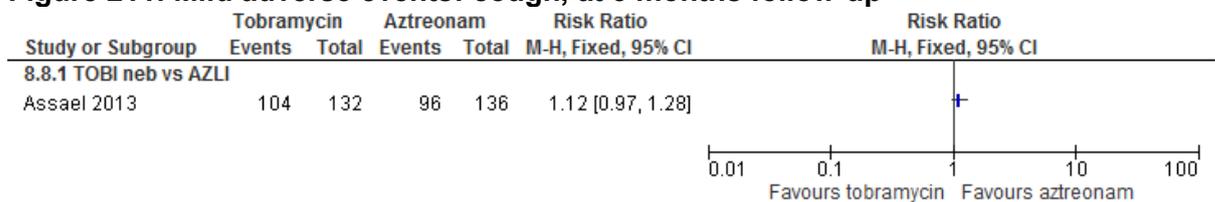
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

Figure 210: Mild adverse events: chest discomfort, at 3 months follow-up



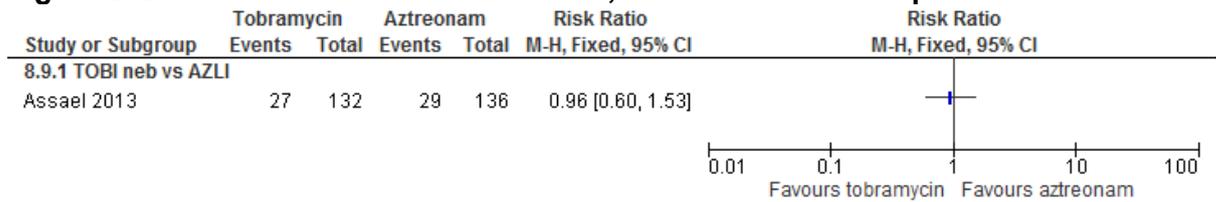
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 211: Mild adverse events: cough, at 3 months follow-up



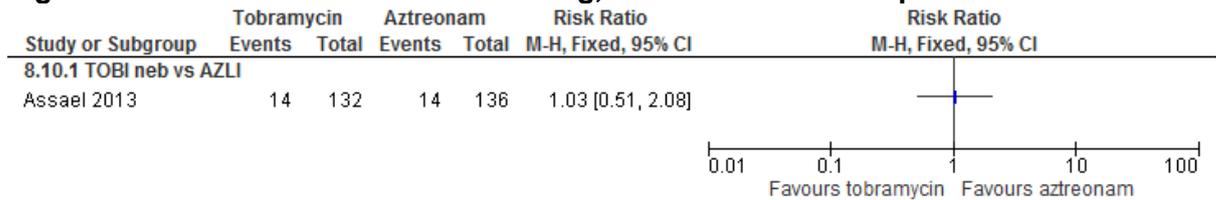
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 212: Mild adverse events: headache, at 3 months follow-up



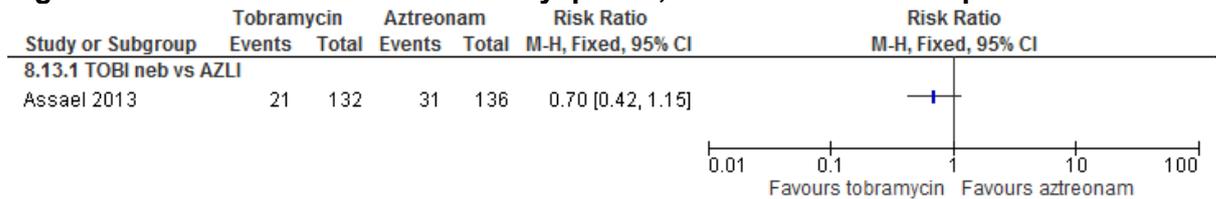
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 213: Mild adverse events: vomiting, at 3 months follow-up



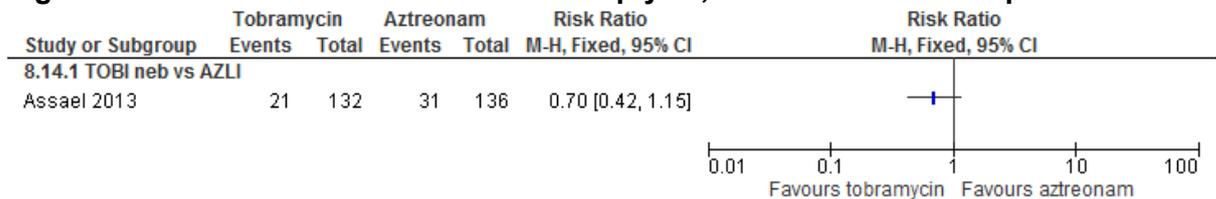
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 214: Serious adverse events: dyspnoea, at 3 months follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

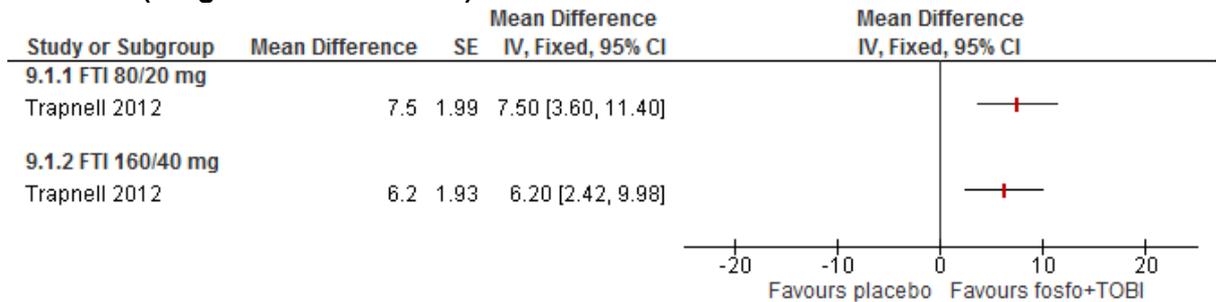
Figure 215: Serious adverse events: haemoptysis, at 3 months follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

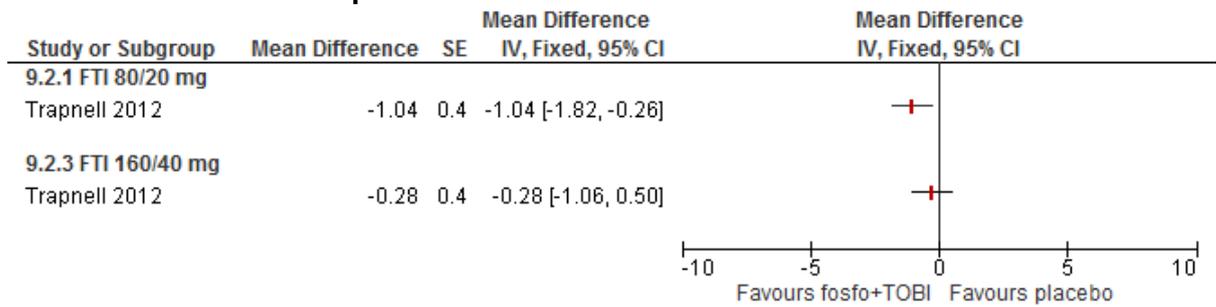
Pairwise comparison 5. Combination of fosfomycin + tobramycin versus placebo

Figure 216: Lung function: relative change in FEV₁% predicted, at 4 weeks follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; fosfo+TOBI: fosfomycin + tobramycin; IV: inverse variance; SE: standard error

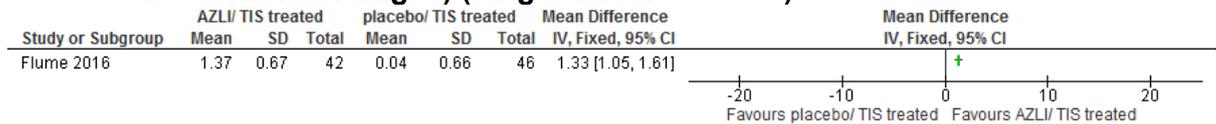
Figure 217: Suppression of the organism: sputum PA density, log 10 CFU/g at 4 weeks follow-up



Abbreviations: fosfo+TOBI: fosfomycin + tobramycin; SE: standard error; IV: inverse variance; CI: confidence interval

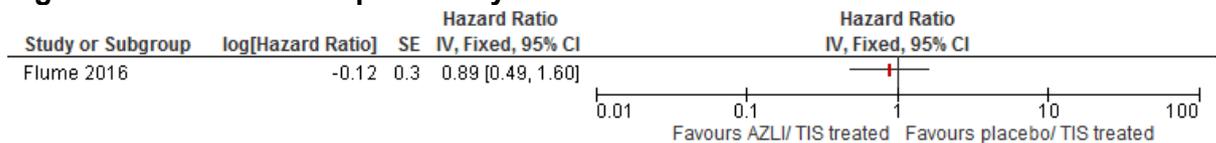
Pairwise comparison 6. Continuous alternating therapy versus intermittent treatment: aztreonam lysine + tobramycin or placebo + tobramycin

Figure 218: Lung function: % change in FEV₁% predicted (values at 4, 12 and 20 weeks were averaged) (range of scores: 0-100)



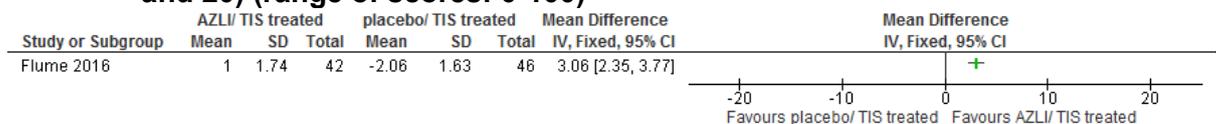
Abbreviations: AZLI: aztreonam lysine; CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation; TIS: tobramycin inhaled solution

Figure 219: Time to next pulmonary exacerbation



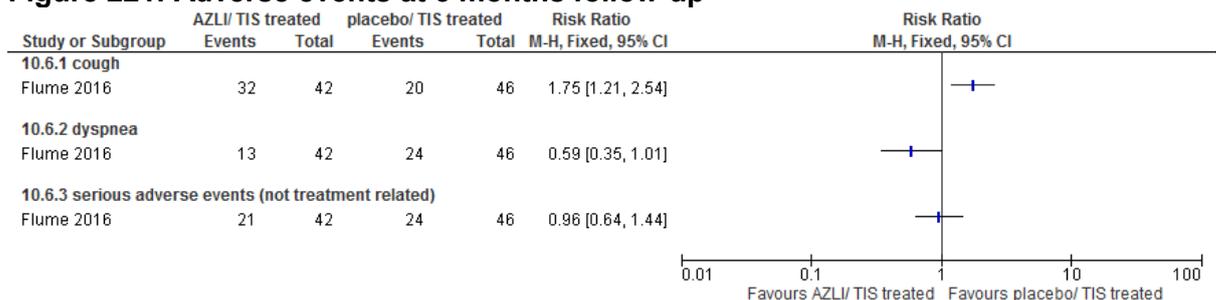
Abbreviations: AZLI: aztreonam lysine; CI: confidence interval; IV: inverse variance; SE: standard error; TIS: tobramycin inhaled solution

Figure 220: Quality of life: change in CFQ-R (scores were averaged from weeks 4, 12 and 20) (range of scores: 0-100)



Abbreviations: AZLI: aztreonam lysine; CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation; TIS: tobramycin inhaled solution

Figure 221: Adverse events at 3 months follow-up



Abbreviations: AZLI: aztreonam lysine; CI: confidence interval; M-H: Mantel-Haenszel; TIS: tobramycin inhaled solution

I.11.2 Staphylococcus Aureus

Not applicable, as no relevant studies were identified.

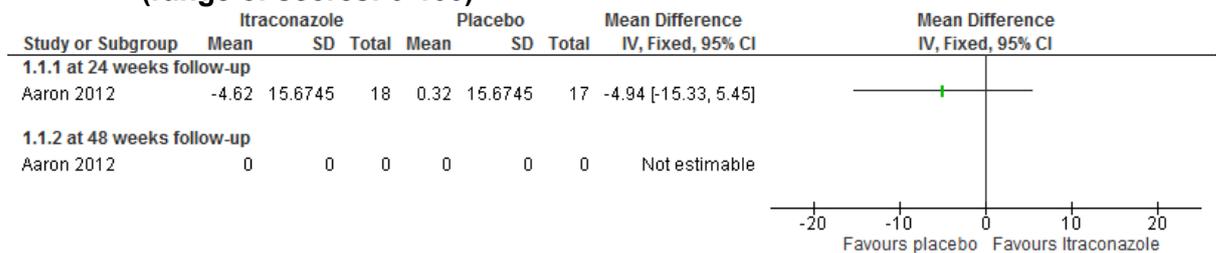
I.11.3 Burkholderia Cepacia Complex

Not applicable, as no relevant studies were identified.

I.11.4 Aspergillus Fumigatus

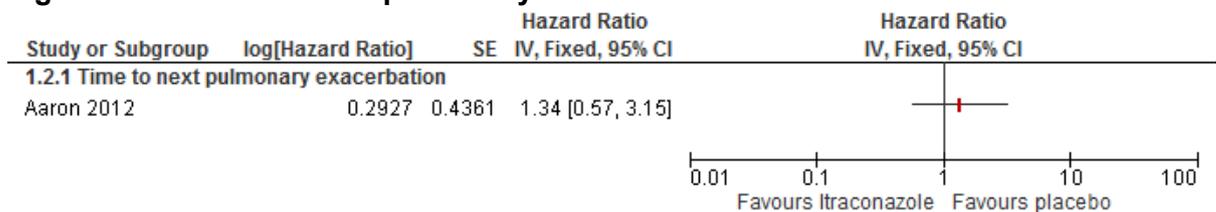
Pairwise comparison 7: Itraconazole versus placebo

Figure 222: Percentage change in FEV₁ from baseline at 24 and 48 weeks follow-up (range of scores: 0-100)



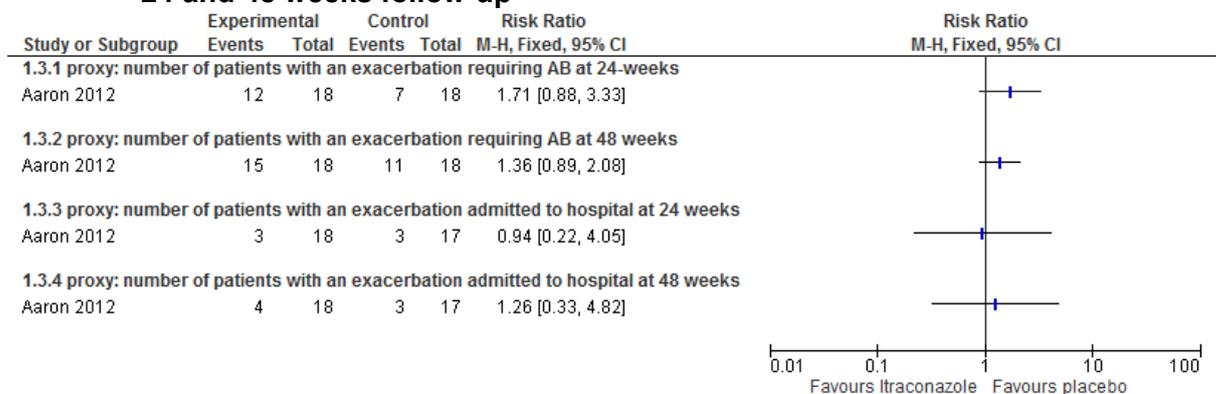
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation. Mean difference (95% CI) at 48-weeks follow-up: -3.71% (-13.26 to 20.28). Not enough data was provided for RevMan.

Figure 223: Time to next pulmonary exacerbation at 24 weeks



Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

Figure 224: Number of pulmonary exacerbations requiring AB or hospitalization, at 24 and 48 weeks follow-up

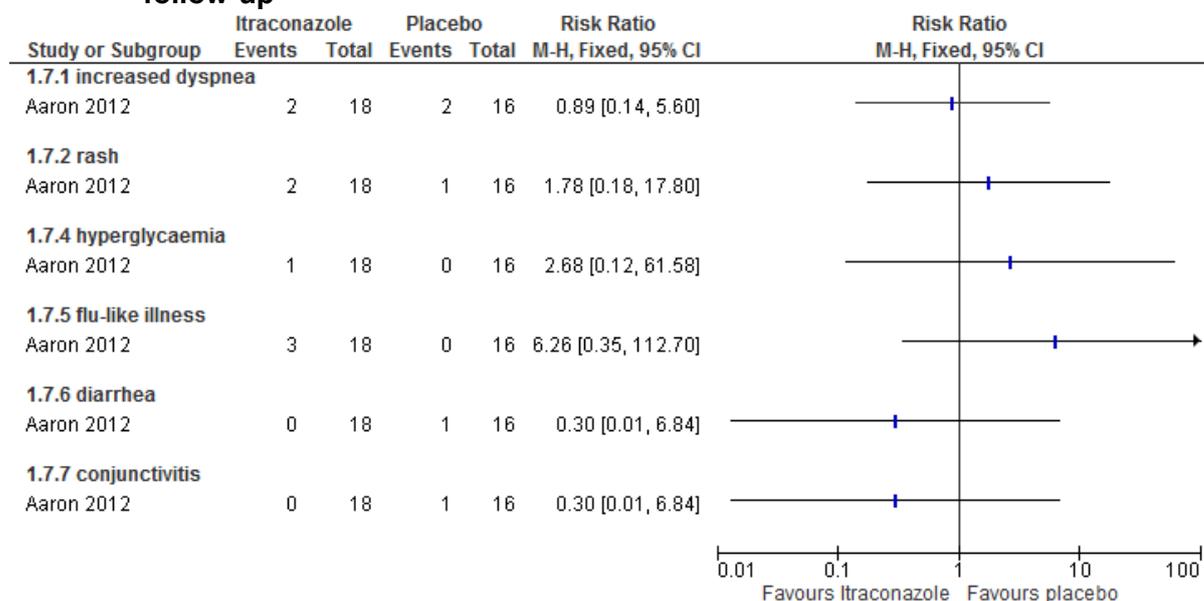


Abbreviations: AB: antibiotics; CI: confidence interval; M-H: Mantel-Haenszel. Proxy outcome.

Figure 225: Quality of life

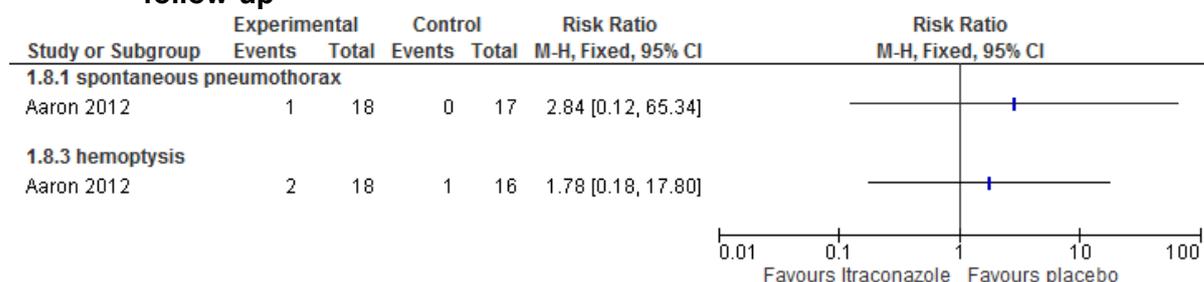
Data could not be plotted.

Figure 226: Number of people experiencing minor adverse events at 24 weeks follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 227: Number of people experiencing major adverse events at 24 weeks follow-up



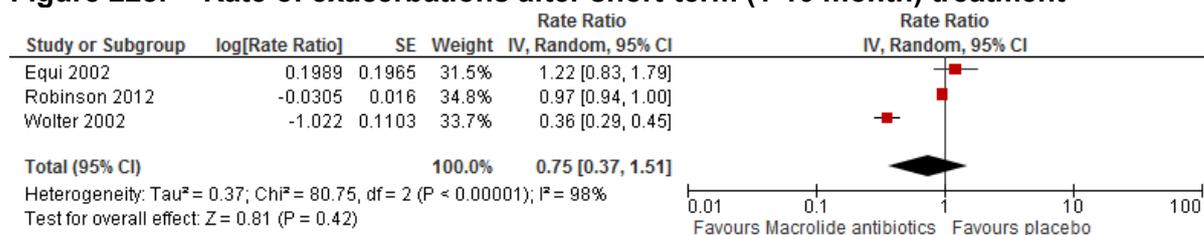
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

I.12 Immunomodulatory agents

I.12.1 NMA outcomes

Pairwise comparison from NMA. Macrolide antibiotics *versus* placebo

Figure 228: Rate of exacerbations after short-term (1-10 month) treatment

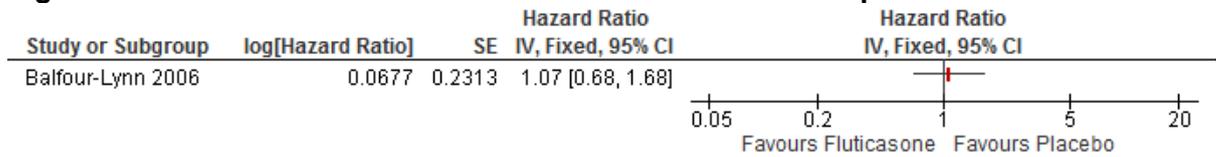


Abbreviations: CI: confidence interval; df: degrees of freedom; IV: inverse variance; SE: standard error

I.12.2 Non-NMA outcomes (pairwise comparisons)

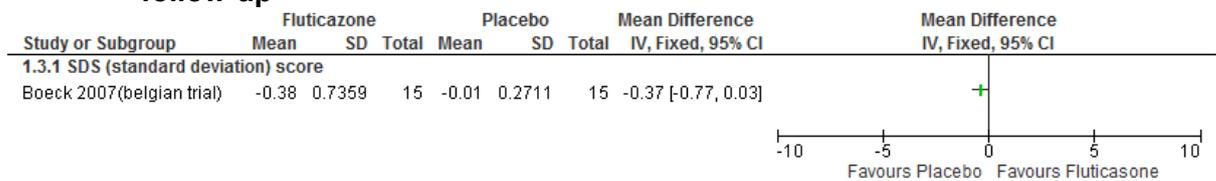
Pairwise comparison 1. Fluticasone versus placebo

Figure 229: Time to next exacerbation at 8 months follow-up



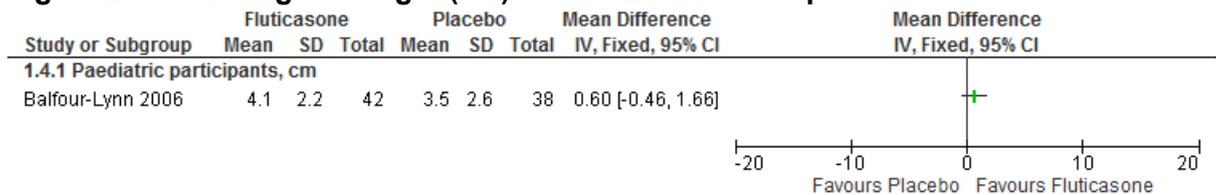
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

Figure 230: Change in height (height standard deviation score) at 0 to 12 months follow-up



Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

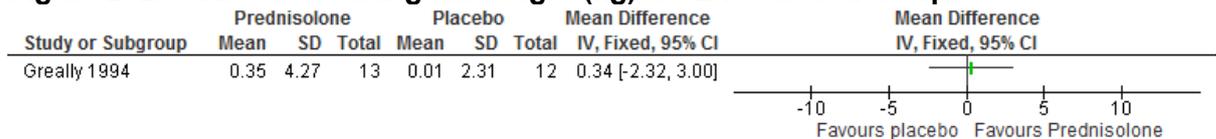
Figure 231: Change in height (cm) at 8 months follow-up



Abbreviations: CI: confidence interval; cm: centimetres; IV: inverse variance; SD: standard deviation

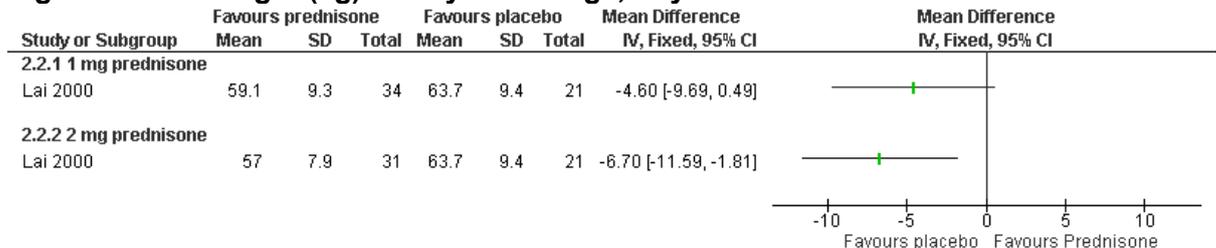
Pairwise comparison 2. Prednisone/ Prednisolone versus placebo

Figure 232: Absolute change in weight (kg) at 12 weeks follow-up



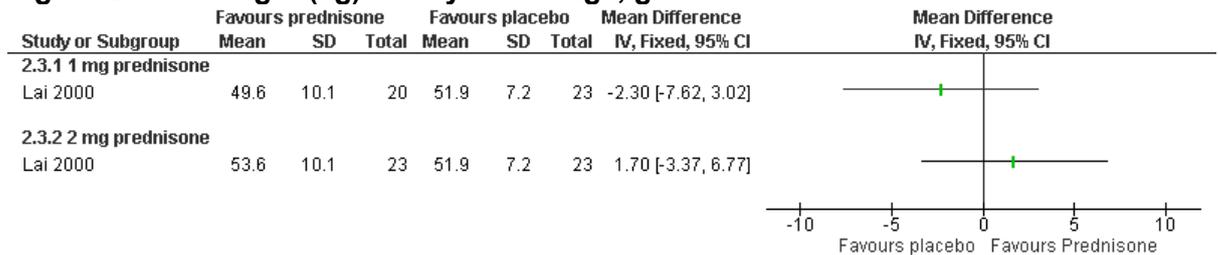
Abbreviations: CI: confidence interval; IV: inverse variance; kg: kilograms; SD: standard deviation. Intervention: 2mg/kg Prednisolone;

Figure 233: Weight (kg) at 18 years of age, boys



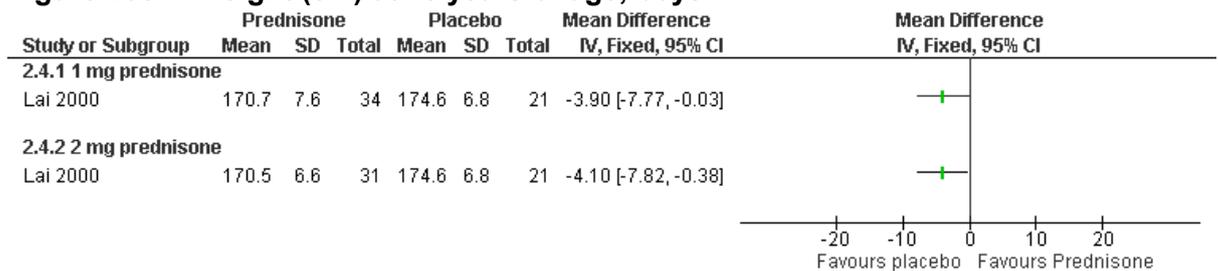
Abbreviations: CI: confidence interval; IV: inverse variance; kg: kilograms; SD: standard deviation

Figure 234: Weight (kg) at 18 years of age, girls



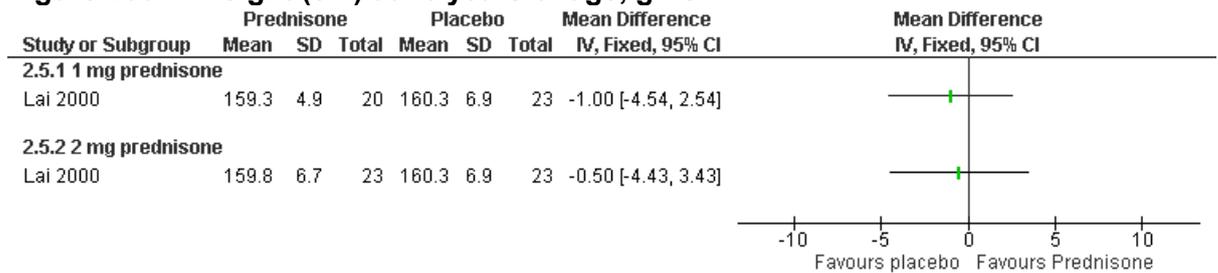
Abbreviations: CI: confidence interval; IV: inverse variance; kg: kilograms; SD: standard deviation

Figure 235: Height (cm) at 18 years of age, boys



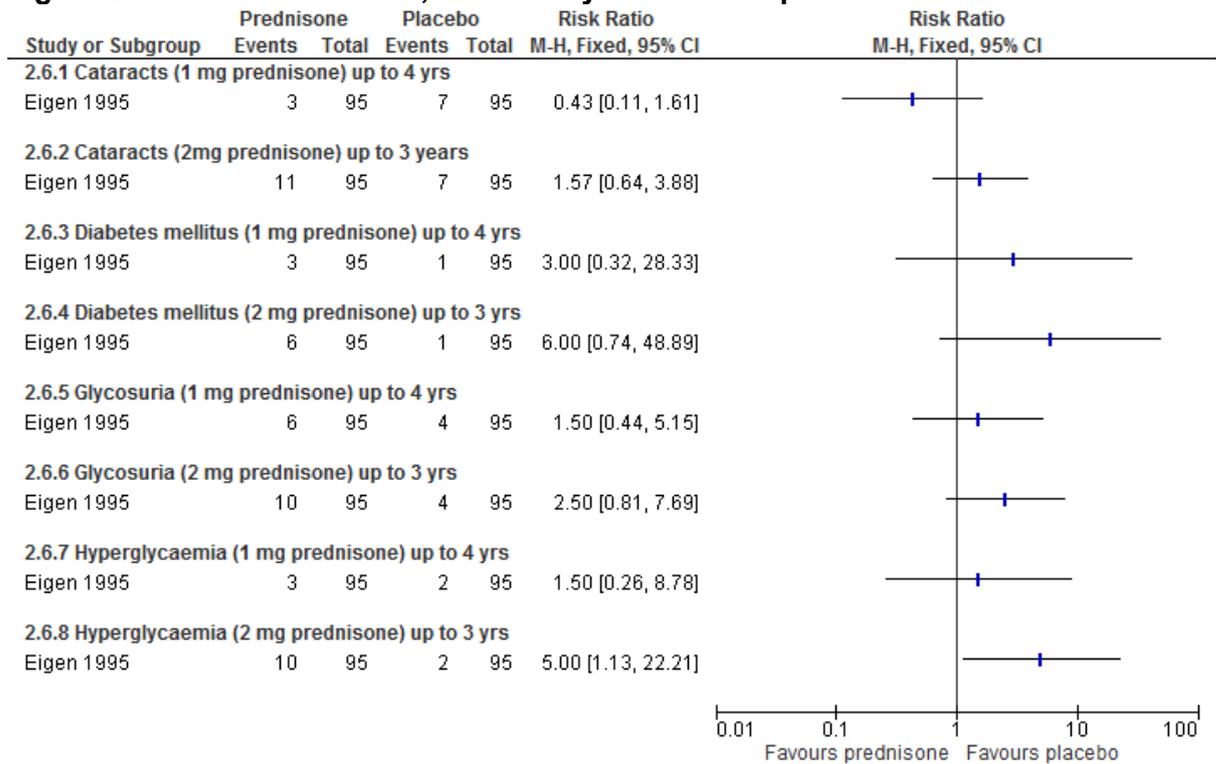
Abbreviations: CI: confidence interval; cm: centimetres; IV: inverse variance; SD: standard deviation

Figure 236: Height (cm) at 18 years of age, girls



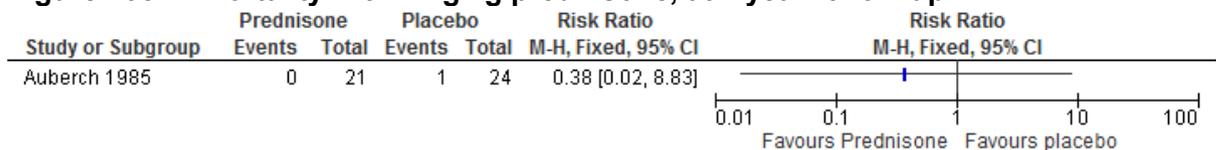
Abbreviations: CI: confidence interval; cm: centimetres; IV: inverse variance; SD: standard deviation

Figure 237: Adverse effects, at 3 and 4 years follow-up



Abbreviations: CI: confidence interval; : M-H: Mantel-Haenszel

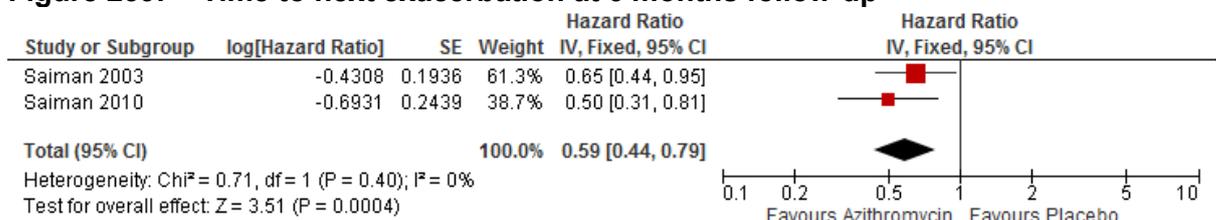
Figure 238: Mortality with 2mg/kg prednisone, at 4 year follow-up



Abbreviations: CI: confidence interval; kg: kilograms; M-H: Mantel-Haenszel; mg: milligrams

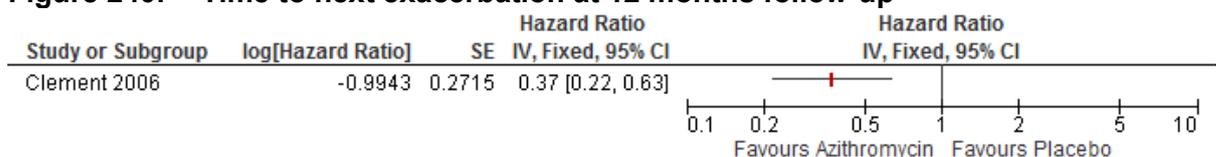
Pairwise comparison 3. Azithromycin versus placebo

Figure 239: Time to next exacerbation at 6 months follow-up



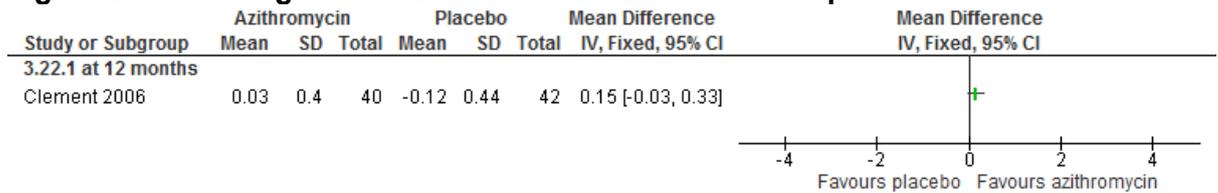
Abbreviations: CI: confidence interval; df: degrees of freedom; IV: inverse variance; SE: standard error

Figure 240: Time to next exacerbation at 12 months follow-up



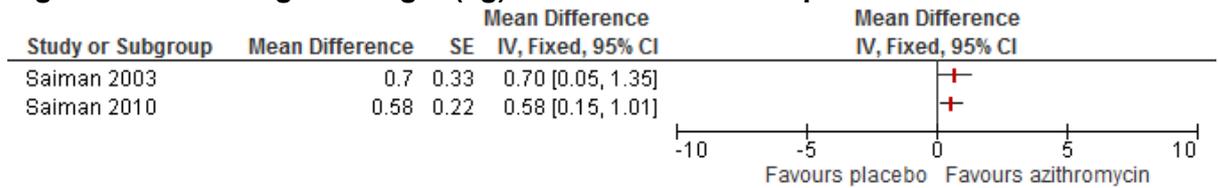
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

Figure 241: Change in BMI z score at 12 months follow-up



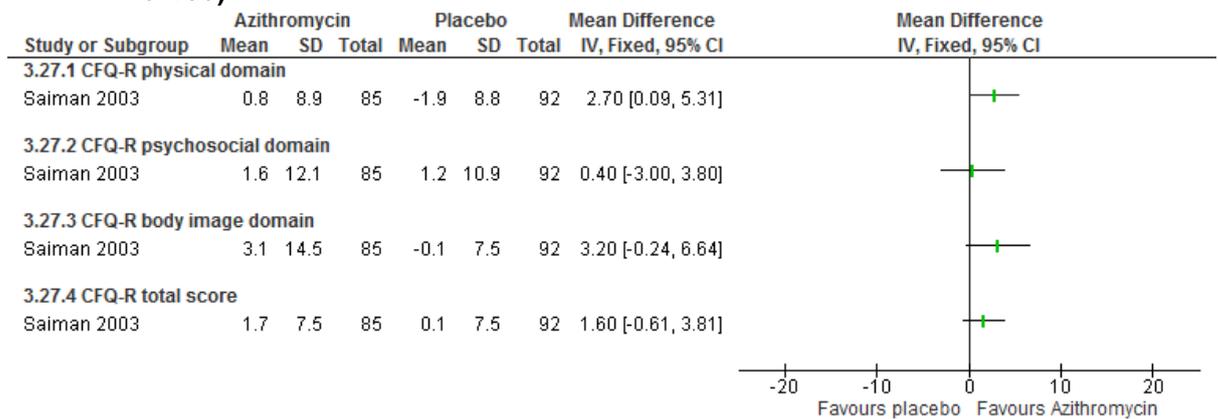
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 242: Change in weight (kg) at 6 months follow-up



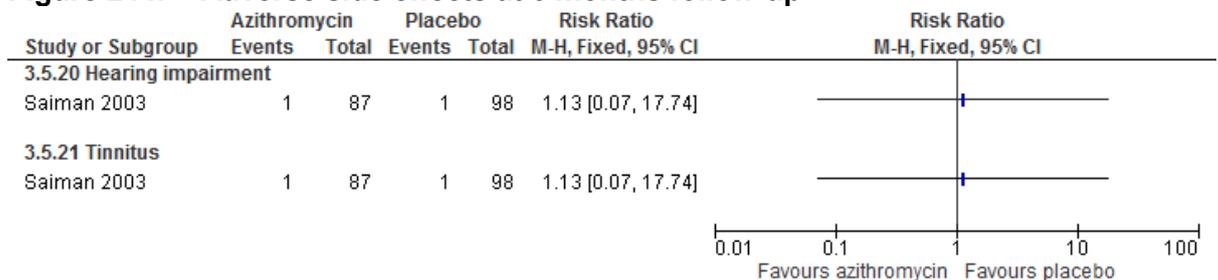
Abbreviations: CI: confidence interval; IV: inverse variance; kg: kilograms; SE: standard error

Figure 243: Change in quality of life (CFQ-R) at 6 months follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

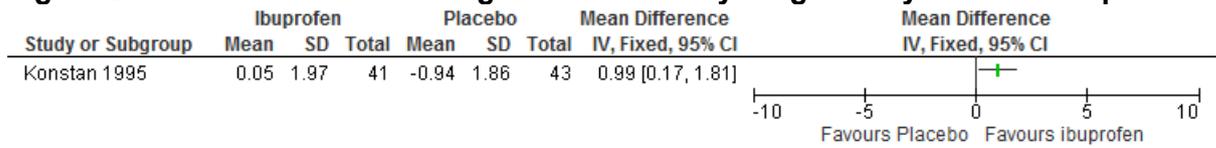
Figure 244: Adverse side effects at 6 months follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

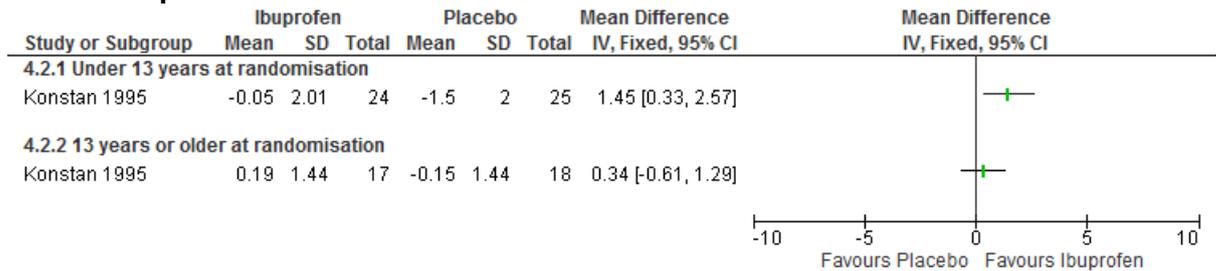
Pairwise comparison 4. Ibuprofen versus placebo

Figure 245: Annual rate of change in % ideal body weight at 4 years follow-up



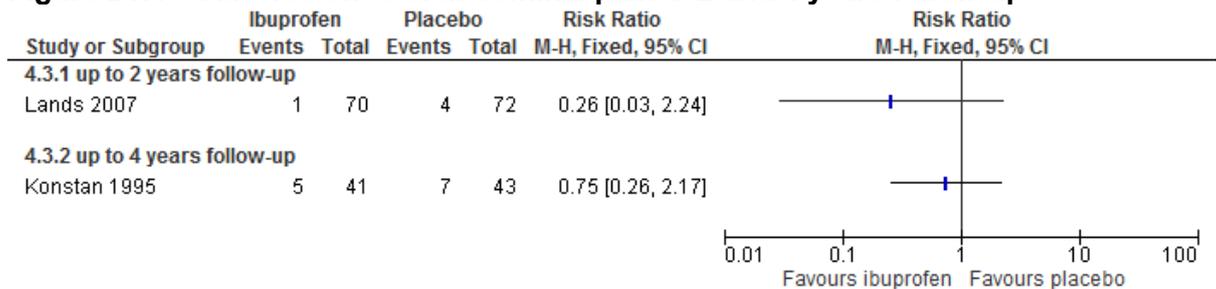
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 246: Annual rate of change in % ideal body weight by age at 4 years follow-up



Abbreviations: CI: Confidence interval; IV: inverse variance; SD: standard deviation

Figure 247: Adverse effects: abdominal pain at 2 and 4 years follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 248: Adverse effects: gastrointestinal bleeding) at 2 years follow-up

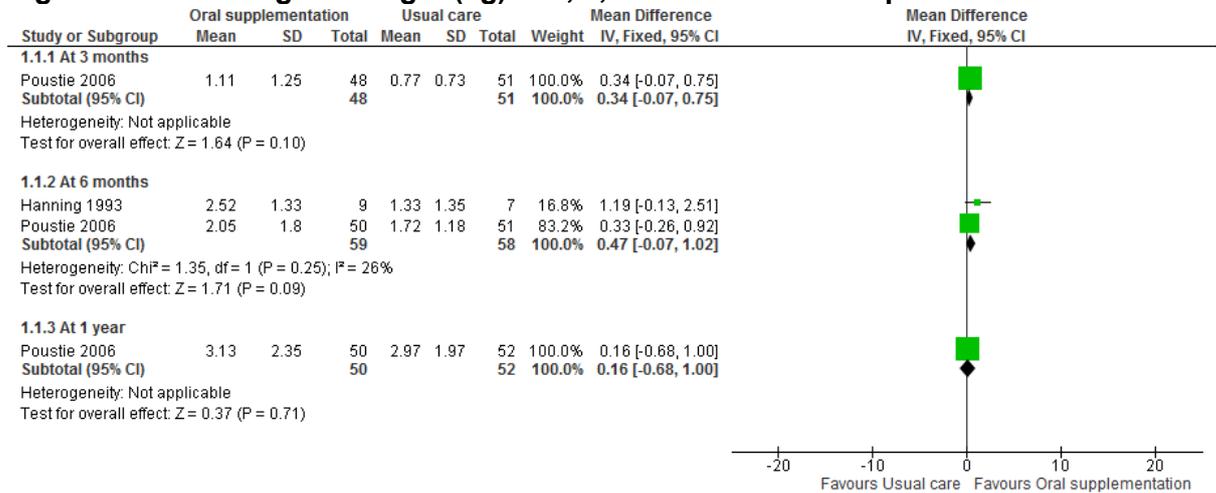


Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

I.13 Nutritional interventions

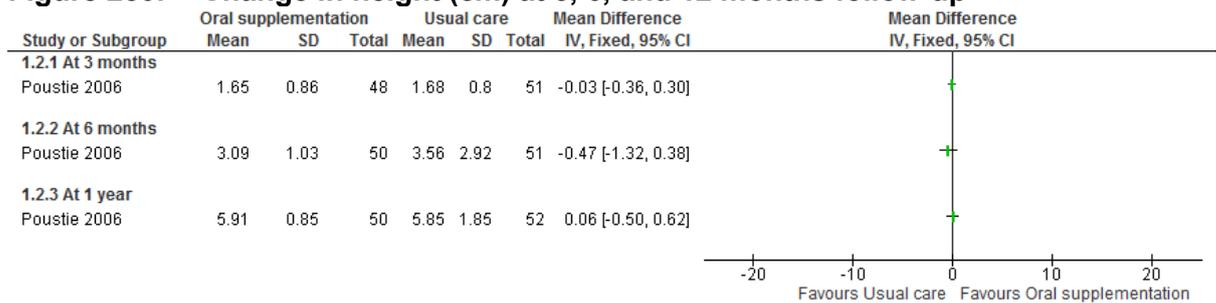
Comparison 1. Oral supplements versus usual care

Figure 249: Change in weight (kg) at 3, 6, 12 months follow-up



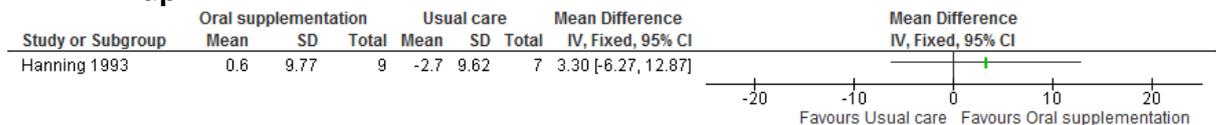
Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 250: Change in height (cm) at 3, 6, and 12 months follow-up



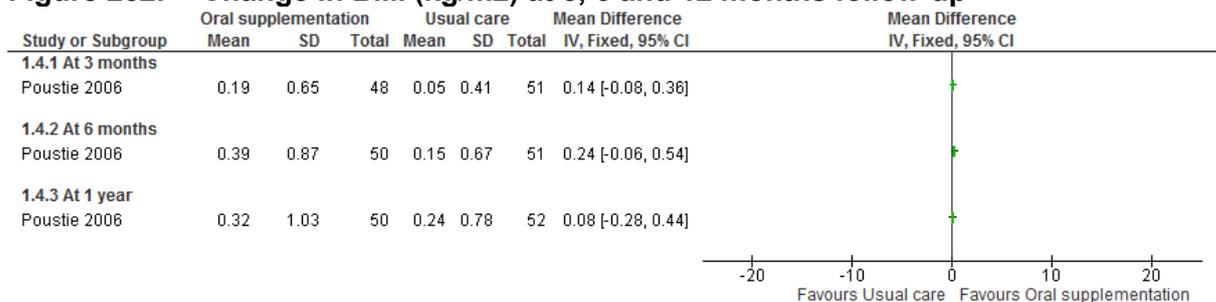
Abbreviations: CI: confidence interval; cm: centimetres; IV: inverse variance; SD: standard deviation;

Figure 251: Change in weight as % expected for age and height at 6 months follow-up



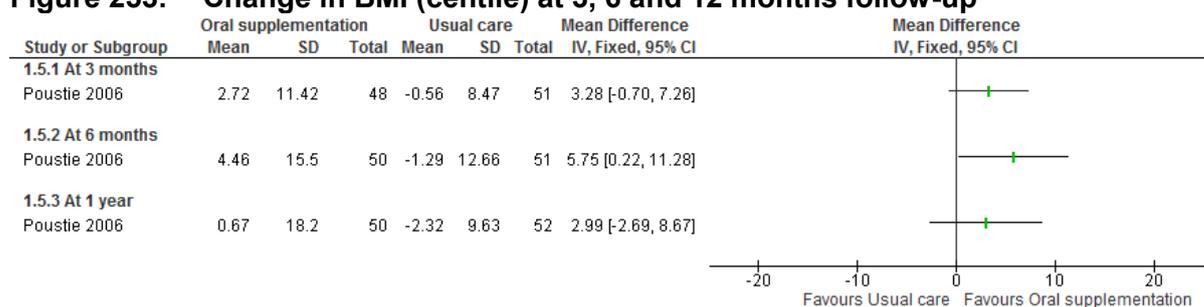
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation;

Figure 252: Change in BMI (kg/m²) at 3, 6 and 12 months follow-up



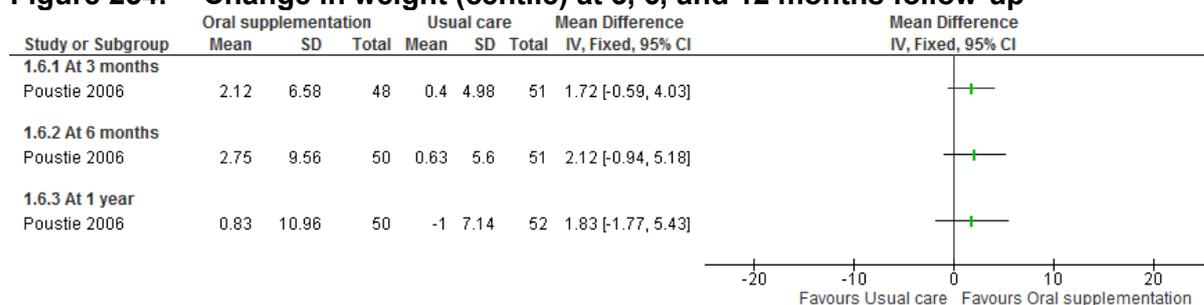
Abbreviations: BMI: body mass index; CI: confidence interval; kg: kilograms; IV: inverse variance; m²: square metres; SD: standard deviation

Figure 253: Change in BMI (centile) at 3, 6 and 12 months follow-up



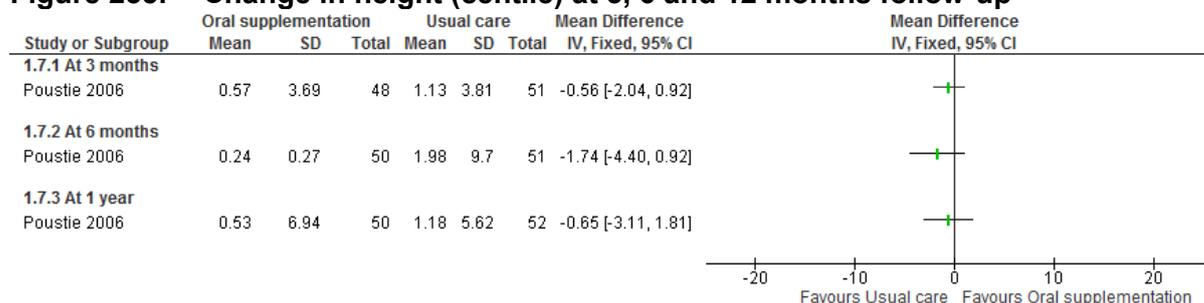
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 254: Change in weight (centile) at 3, 6, and 12 months follow-up



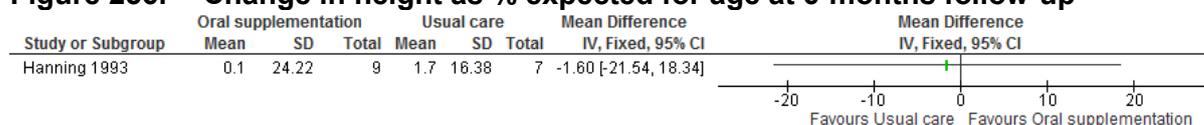
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 255: Change in height (centile) at 3, 6 and 12 months follow-up



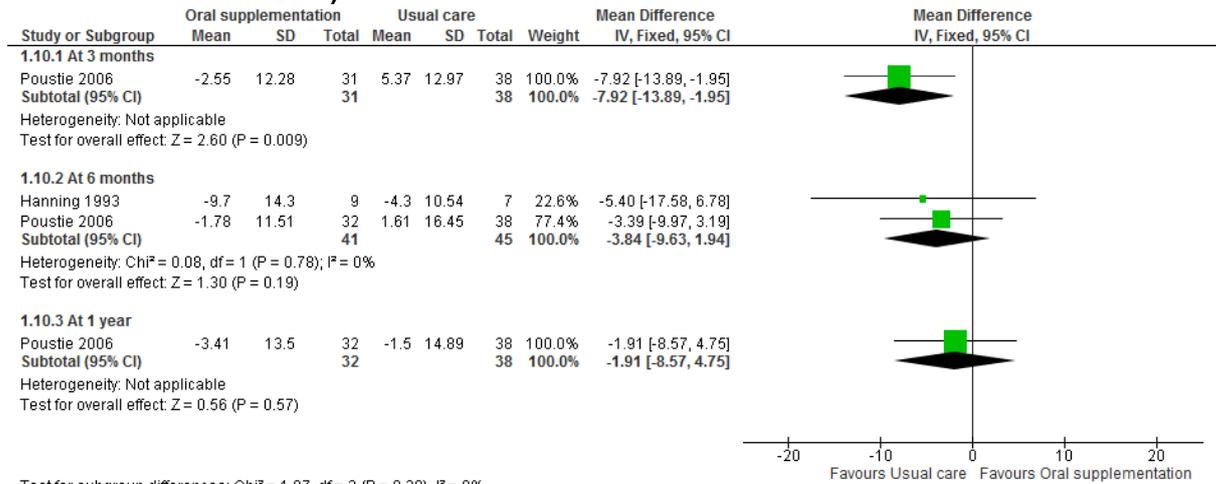
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 256: Change in height as % expected for age at 6-months follow-up



Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 257: Change in FEV₁ % predicted at 3, 6 and 12 months follow-up (range of scores: 0-100)

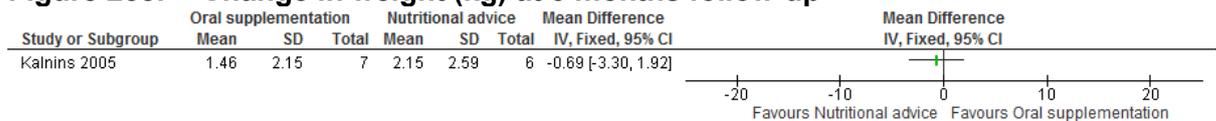


Test for subgroup differences: Chi² = 1.87, df = 2 (P = 0.39), I² = 0%

Abbreviations: CI: confidence interval; df: degrees of freedom; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

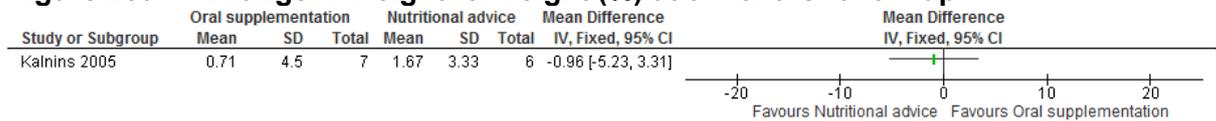
Comparison 1.2 Oral calorie supplementation versus nutritional advice

Figure 258: Change in weight (kg) at 3 months follow-up



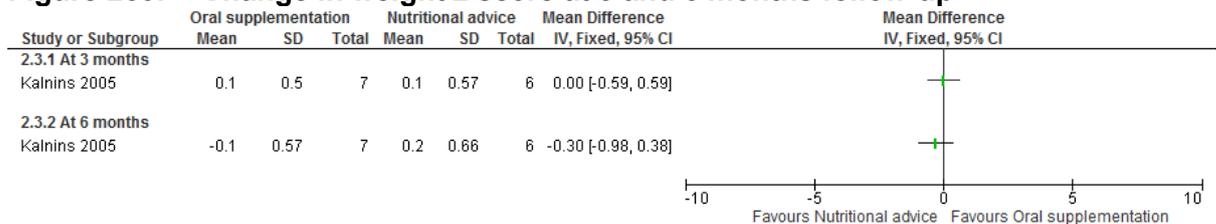
Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 259: Change in weight for height (%) at 3 months follow-up



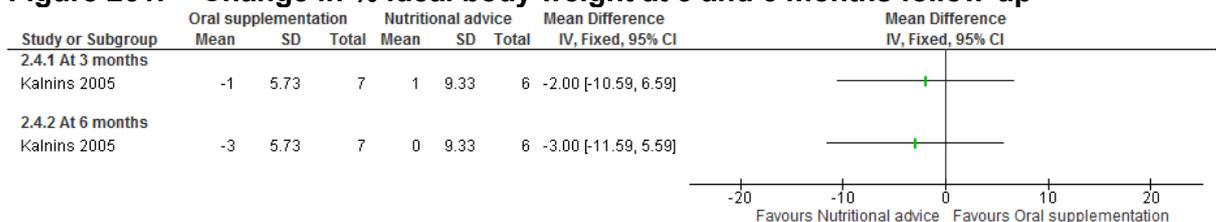
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 260: Change in weight z score at 3 and 6 months follow-up



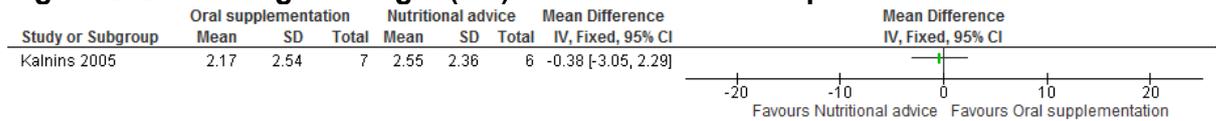
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 261: Change in % ideal body weight at 3 and 6 months follow-up



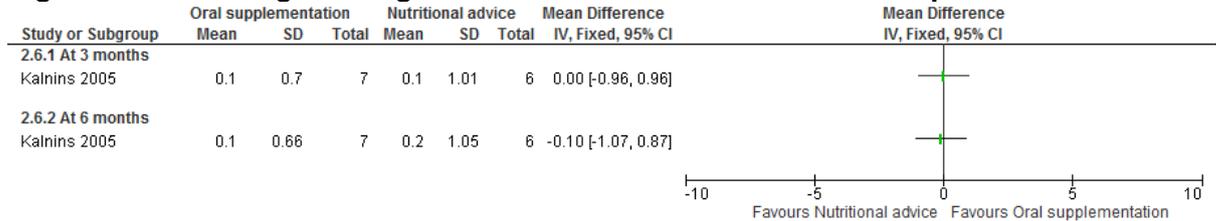
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 262: Change in height (cm) at 3 months follow-up



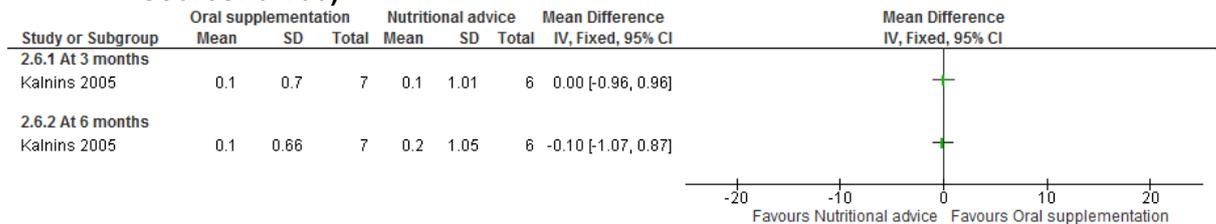
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 263: Change in height z score at 3 and 6 months follow-up



Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

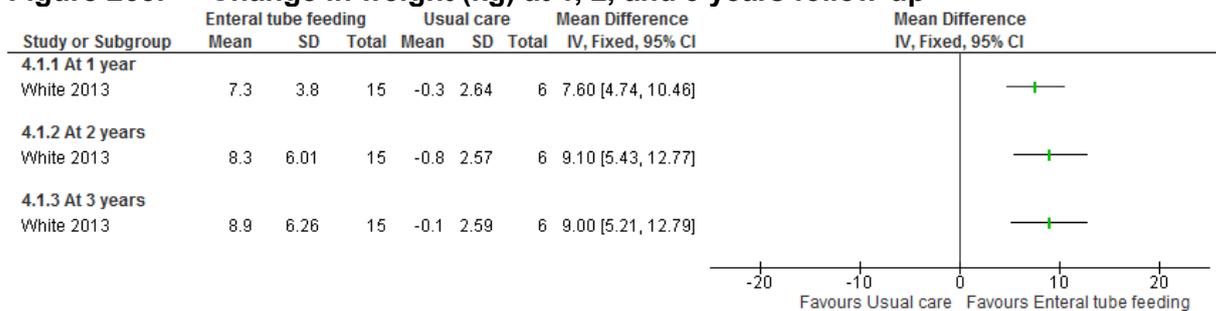
Figure 264: Change in FEV₁ % predicted at 3 and 6 months follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

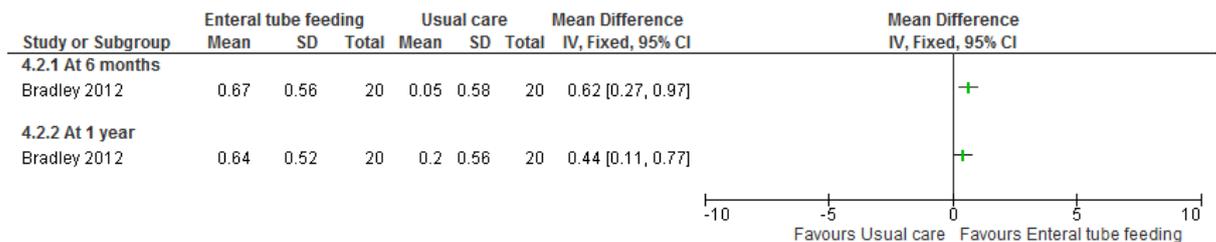
Comparison 2. Enteral tube feeding versus nutritional advice

Figure 265: Change in weight (kg) at 1, 2, and 3 years follow-up



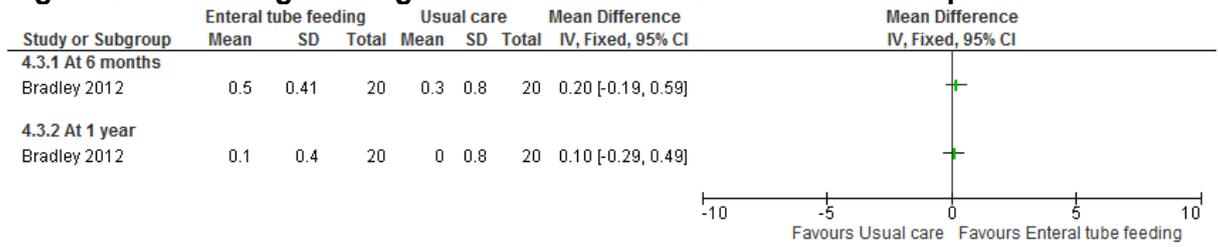
Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 266: Change in weight z score at 6 and 12 months follow-up



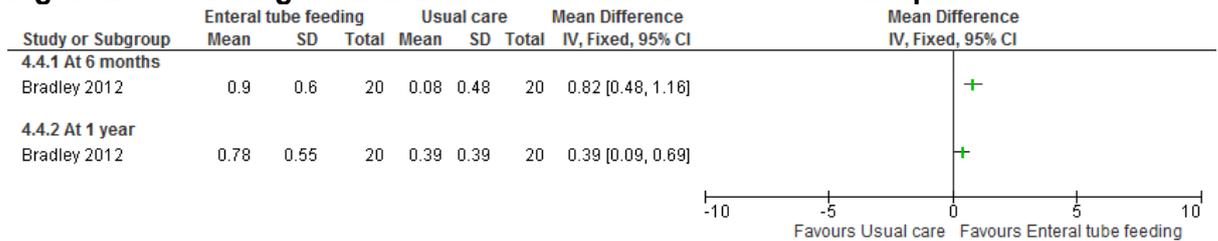
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 267: Change in height z score at 6 and 12 months follow-up



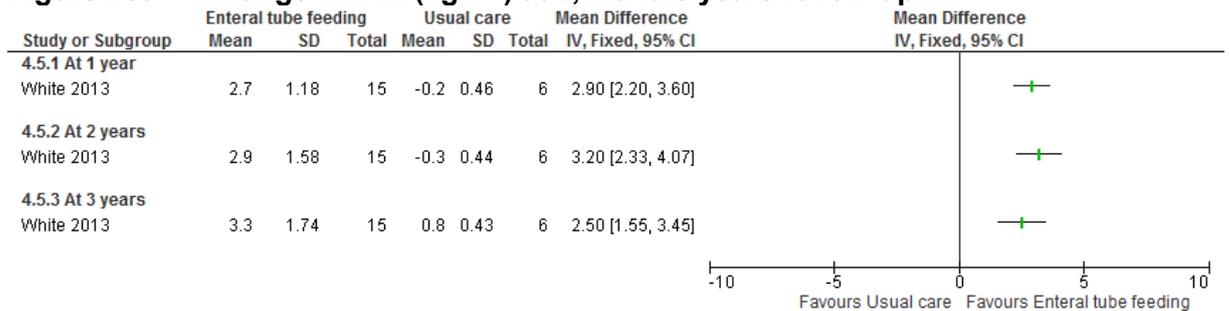
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 268: Change in BMI z score at 6 and 12 months follow-up



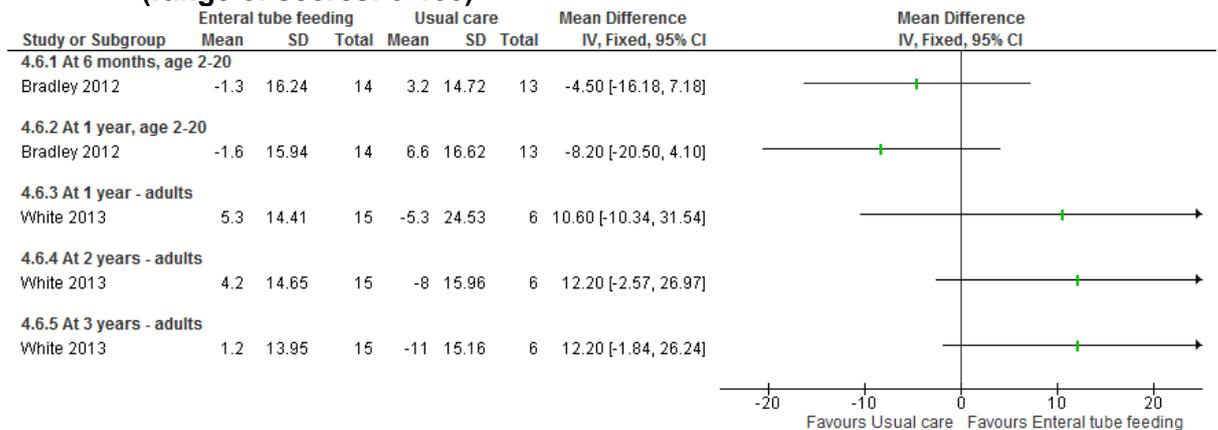
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 269: Change in BMI (kg/m²) at 1, 2 and 3 years follow-up



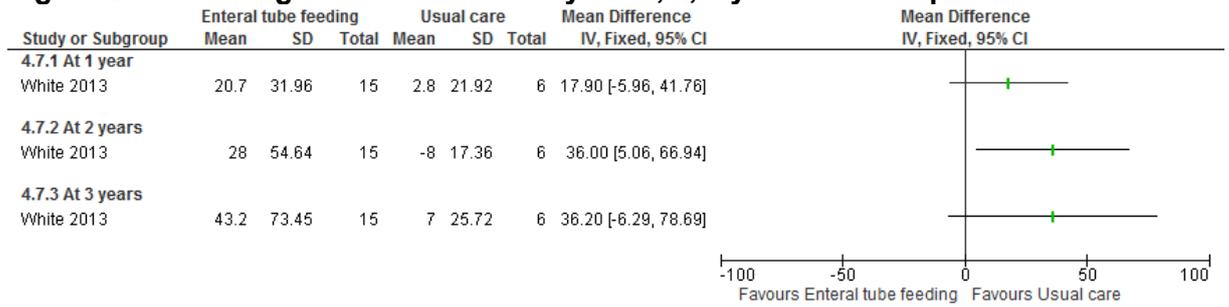
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; kg: kilograms; m²: square metres; SD: standard deviation

Figure 270: Change in FEV₁ % predicted at 6 months and at 1, 2, 3 years follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

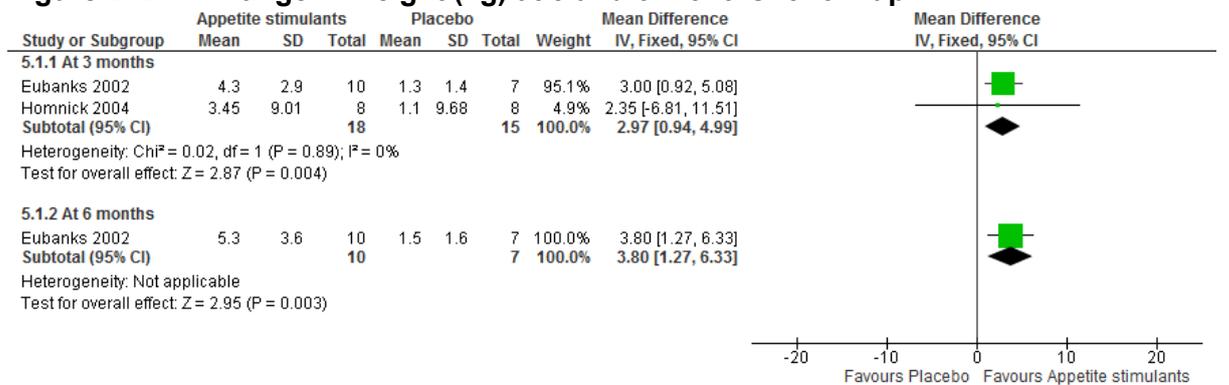
Figure 271: Change in IV treatment days at 1, 2, 3 years follow-up



Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

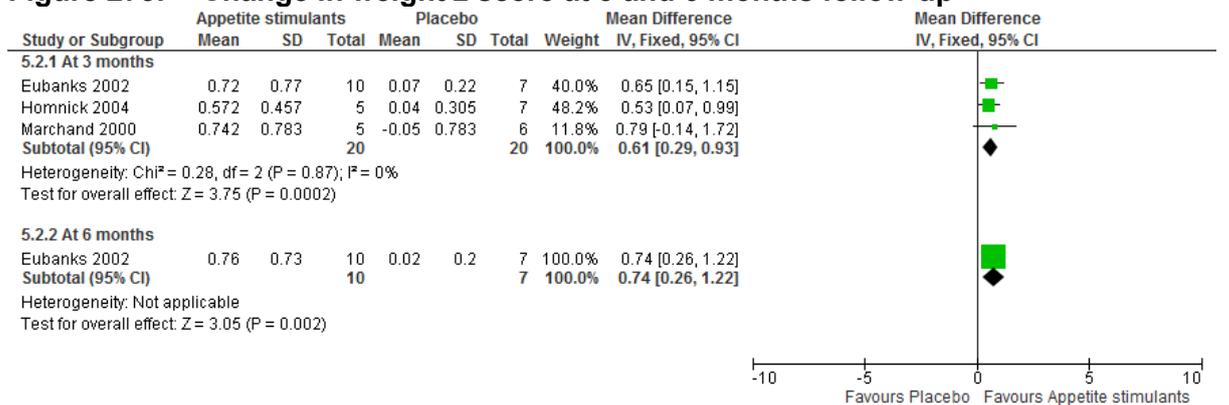
Comparison 3. Appetite stimulants versus placebo

Figure 272: Change in weight (kg) at 3 and 6 months follow-up



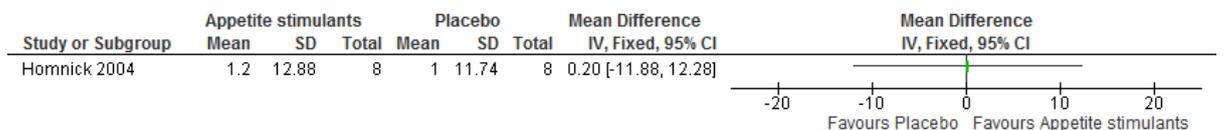
Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval; df: degrees of freedom

Figure 273: Change in weight z score at 3 and 6 months follow-up



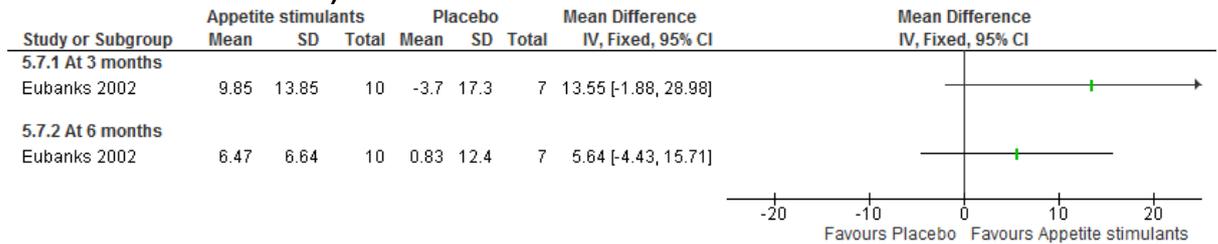
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval; df: degrees of freedom

Figure 274: Change in height (cm) at 3 months follow-up



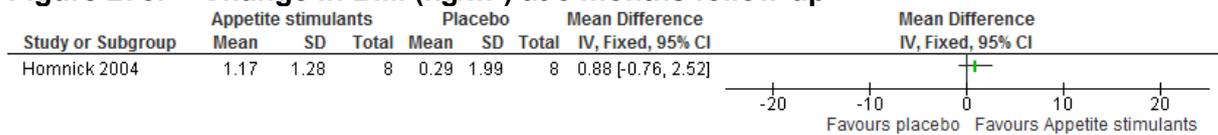
Abbreviations: CI: confidence interval; cm: centimetres; IV: inverse variance; SD: standard deviation

Figure 275: Change in FEV₁ % predicted at 3 and 6 months follow-up (range of scores: 0-100)



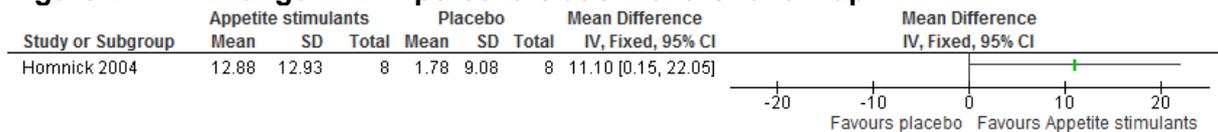
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 276: Change in BMI (kg/m²) at 3 months follow-up



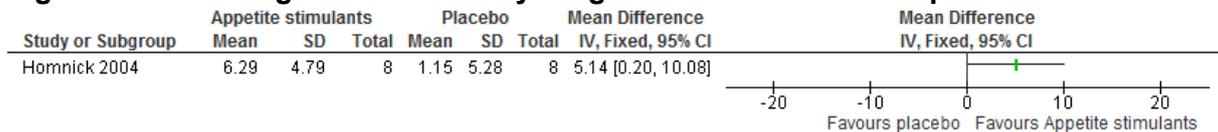
Abbreviations: BMI: body mass index; CI: confidence interval; kg: kilograms; IV: inverse variance; m²: square metres; SD: standard deviation

Figure 277: Change in BMI percentile at 3 months follow-up



Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 278: Change in % ideal body weight at 3 months follow-up



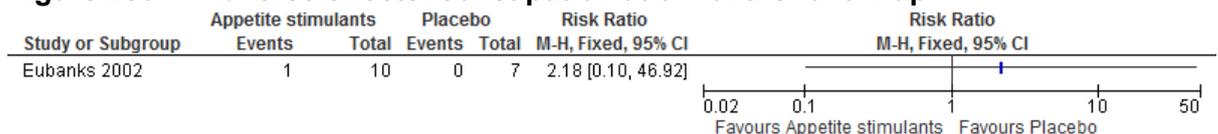
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 279: Number of pulmonary exacerbations at 3 months follow-up



Abbreviations: M-H: Mantel-Haenszel; CI: confidence interval

Figure 280: Adverse effects: constipation at 6 months follow-up



Abbreviations: M-H: Mantel-Haenszel; CI: confidence interval

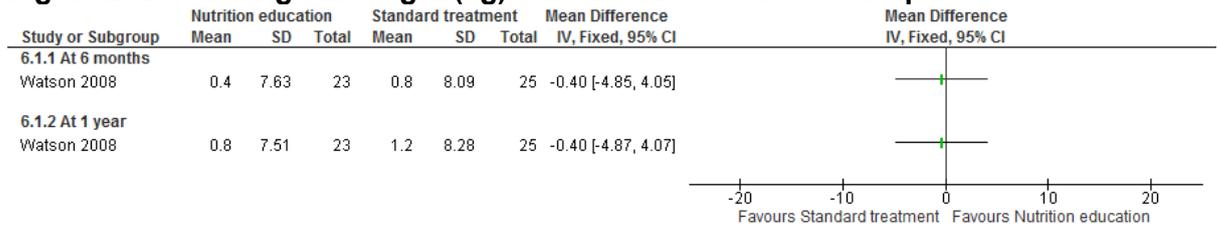
Figure 281: Adverse effects: decreased morning cortisol levels <30 nmol/L at 6 months follow-up



Abbreviations: M-H: Mantel-Haenszel; CI: confidence interval

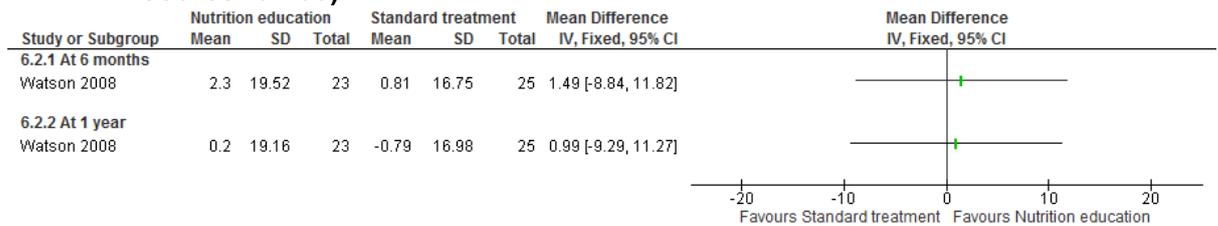
Comparison 4. Nutrition education versus usual care

Figure 282: Change in weight (kg) at 6 and 12 months follow-up



Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval

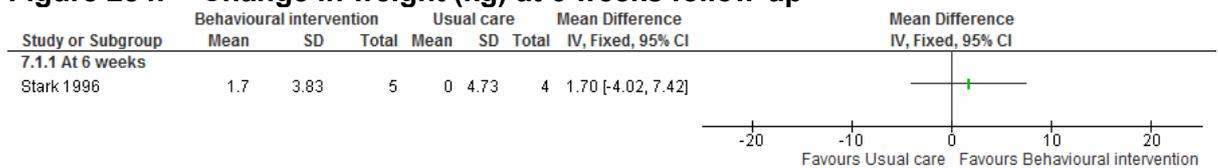
Figure 283: Change in FEV₁ % predicted at 6 and 12 months follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

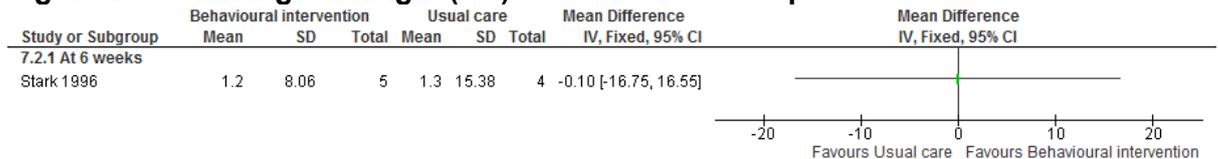
Comparison 5.1 Behavioural intervention versus usual care

Figure 284: Change in weight (kg) at 6 weeks follow-up



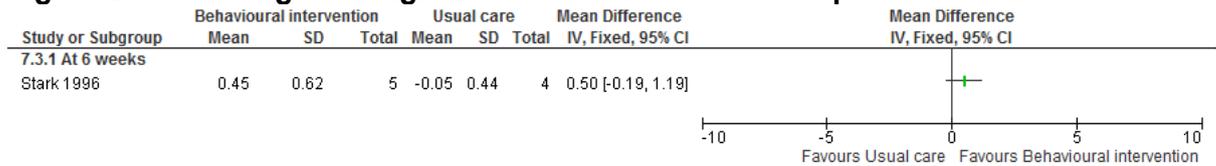
Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 285: Change in height (cm) at 6 weeks follow-up



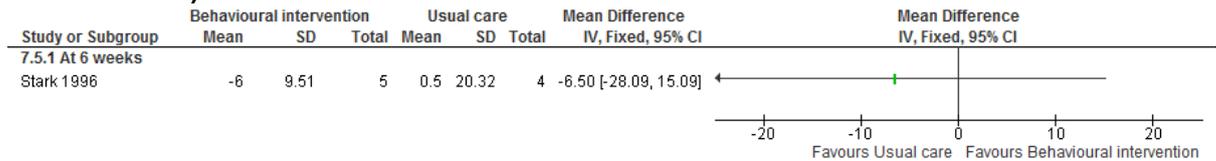
Abbreviations: CI: confidence interval; cm: centimetres; IV: inverse variance; SD: standard deviation

Figure 286: Change in weight z score at 6 weeks follow-up



Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

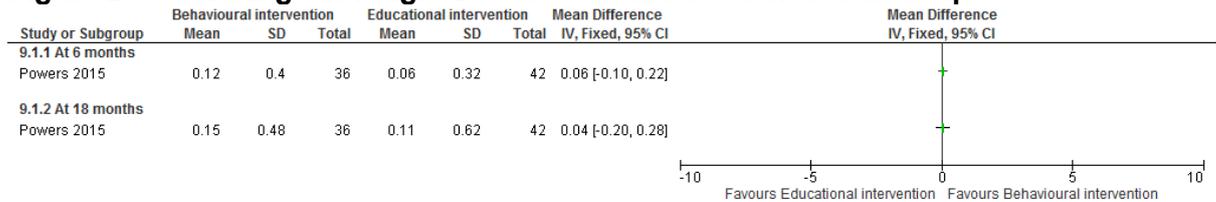
Figure 287: Change in FEV₁ % predicted at 6 weeks follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

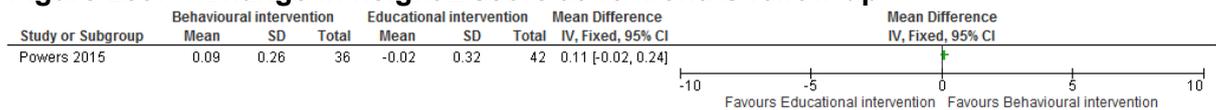
Comparison 5.2 Behavioural intervention versus education and attention control treatment

Figure 288: Change in weight z score at 6 and 18 months follow-up



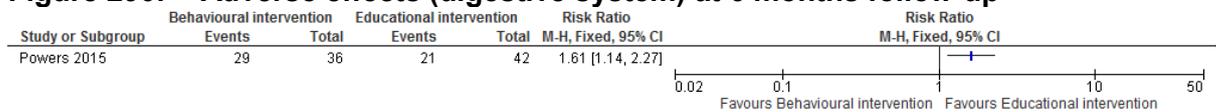
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 289: Change in height z score at 18 months follow-up



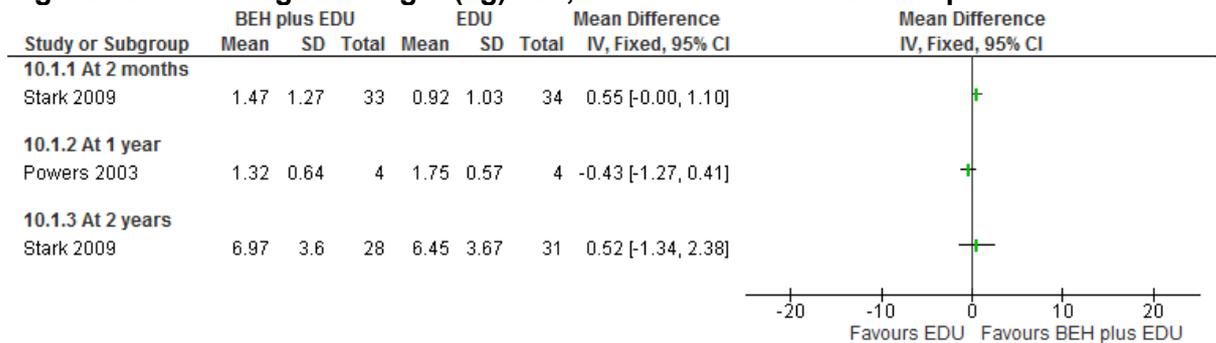
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 290: Adverse effects (digestive system) at 6 months follow-up



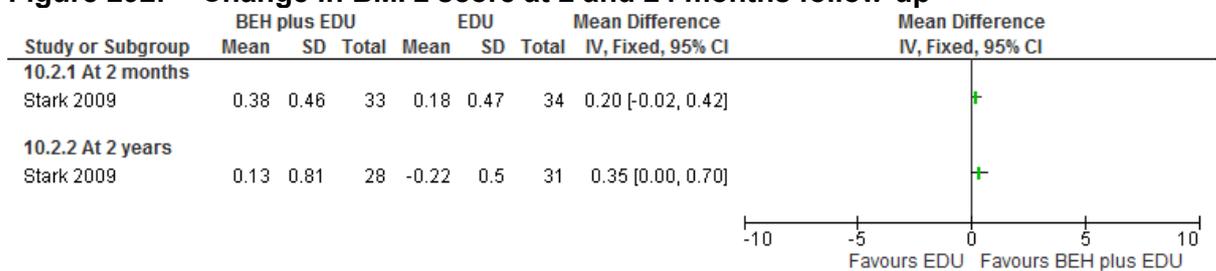
Comparison 5.3. Behavioural management training plus educational intervention versus educational intervention alone

Figure 291: Change in weight (kg) at 2,12 and 24 months follow-up



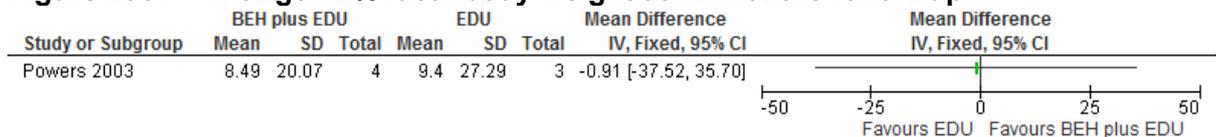
Abbreviations: kg: kilograms; BEH plus EDU: Behavioural management training plus educational intervention; EDU: educational intervention alone; SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 292: Change in BMI z score at 2 and 24 months follow-up



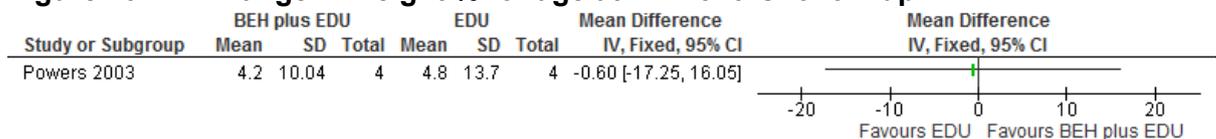
Abbreviations: BMI: body mass index; BEH plus EDU: Behavioural management training plus educational intervention; CI: confidence interval; EDU: educational intervention alone; IV: inverse variance; SD: standard deviation

Figure 293: Change in % ideal body weight at 12 months follow-up



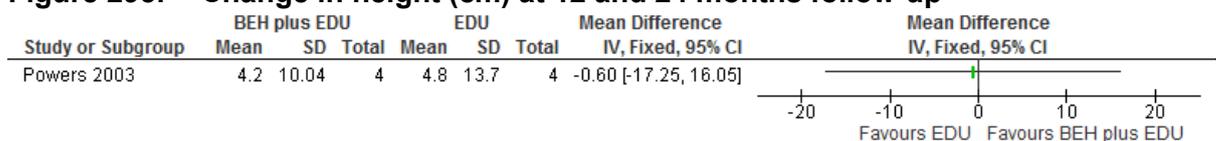
Abbreviations: BEH plus EDU: Behavioural management training plus educational intervention; EDU: educational intervention alone; SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 294: Change in weight % for age at 12 months follow-up



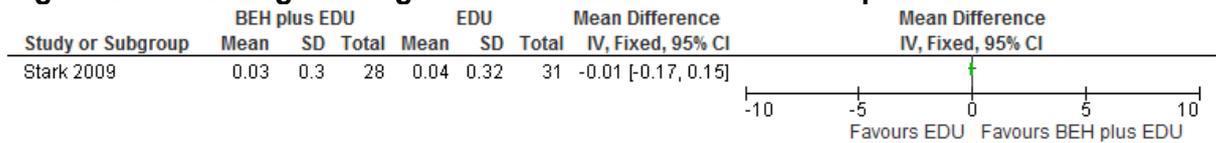
Abbreviations: BEH plus EDU: Behavioural management training plus educational intervention; EDU: educational intervention alone; SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 295: Change in height (cm) at 12 and 24 months follow-up



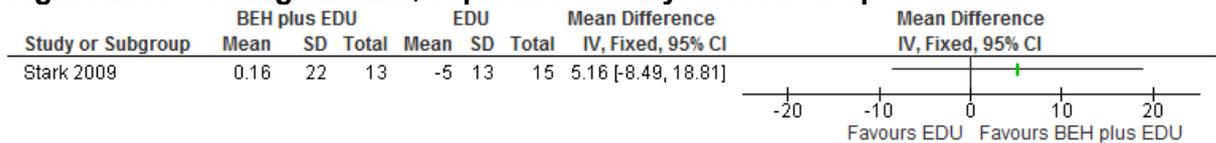
Abbreviations: BEH plus EDU: Behavioural management training plus educational intervention; CI: confidence interval; cm: centimetres; EDU: educational intervention alone; IV: inverse variance; SD: standard deviation

Figure 296: Change in height z score at 24 months follow-up



Abbreviations: BEH plus EDU: Behavioural management training plus educational intervention; CI: confidence interval; cm: centimetres; EDU: educational intervention alone; IV: inverse variance; SD: standard deviation

Figure 297: Change in FEV₁ % predicted at 2 years follow-up



Abbreviations: BEH plus EDU: Behavioural management training plus educational intervention; CI: confidence interval; EDU: educational intervention alone; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation.

Note: The study does not specify the unit of measurement for FEV₁.

I.14 Exocrine Pancreatic insufficiency

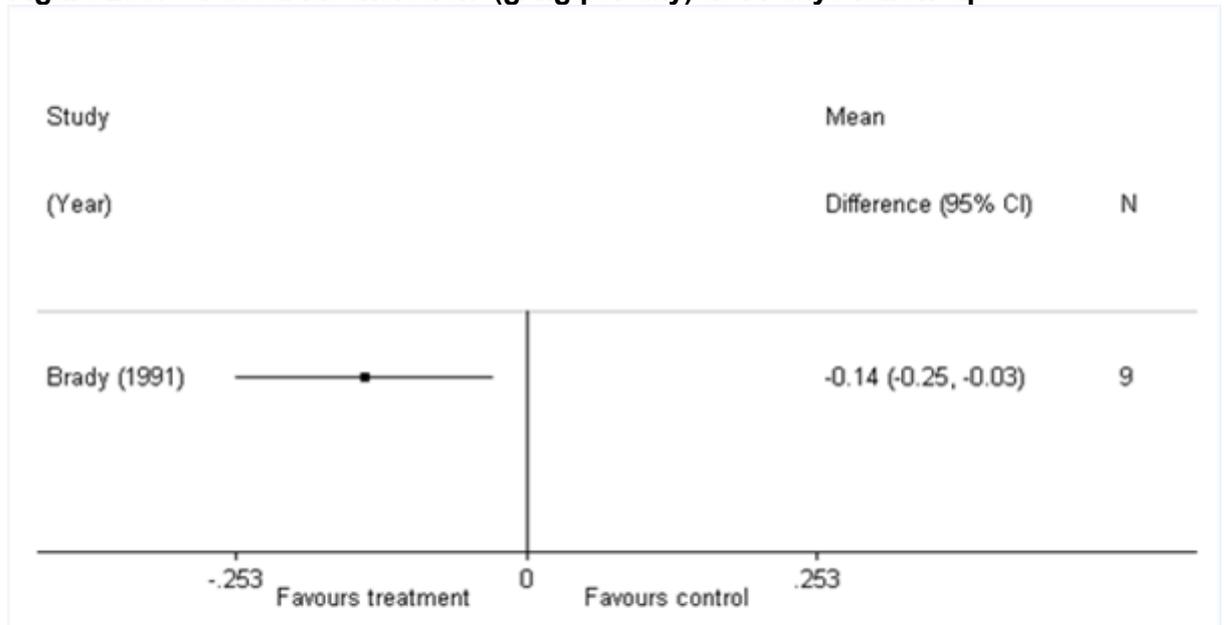
Comparison 1. Acid suppressing agents as adjuvant therapy to PERT

No forest plots available.

Comparison 2. High dose versus low dose PERT

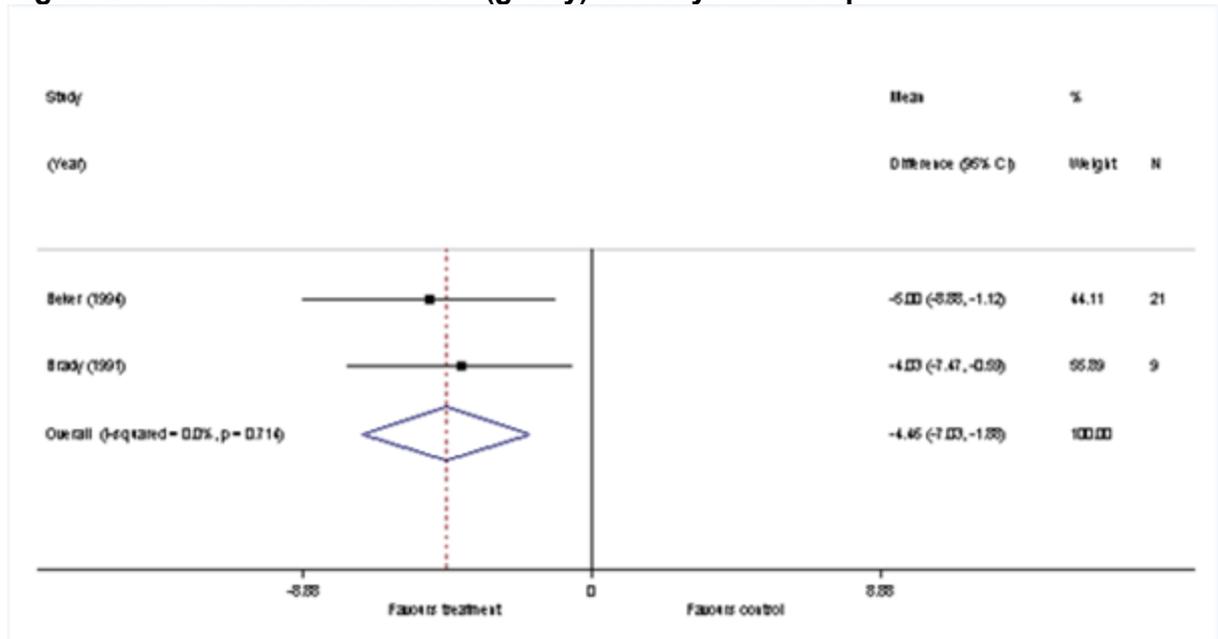
Comparison 2.1. High-dose PERT versus low dose PERT in children

Figure 298: Faecal fat excretion (g/ kg per day) at 14 days follow-up



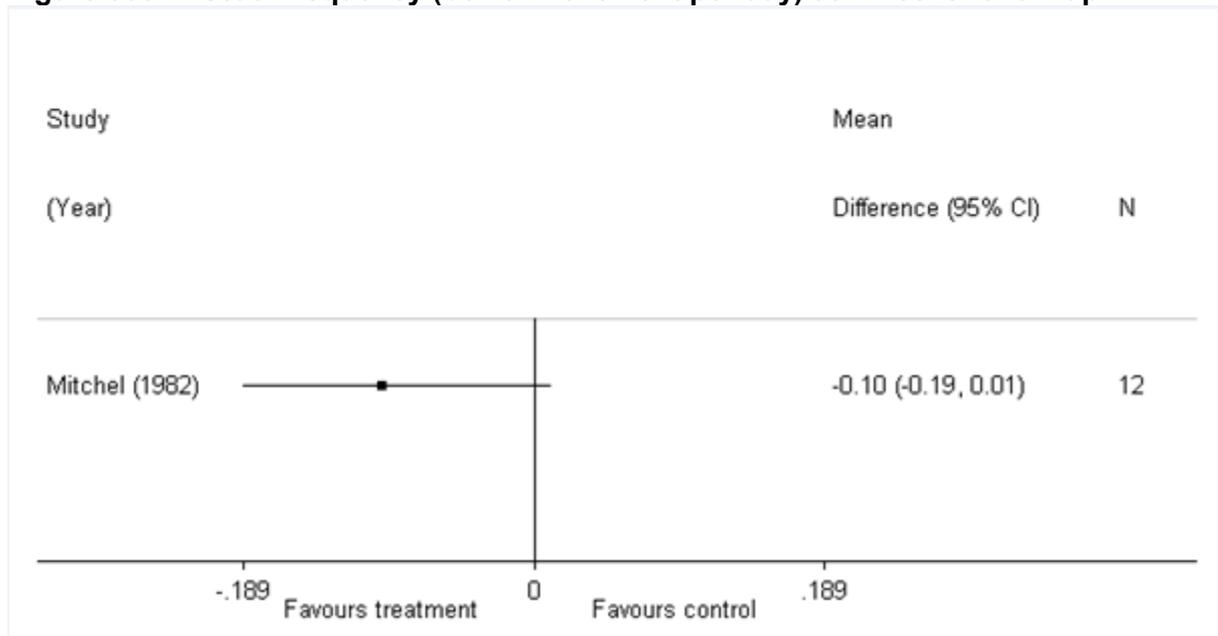
Abbreviations: g: grams; kg: kilograms; CI: confidence interval

Figure 299: Faecal fat excretion (g/ day) at 9 days follow-up



Abbreviations: g: grams; CI: confidence interval

Figure 300: Stool frequency (bowel movement per day) at 4 weeks follow-up



Abbreviations: CI: confidence interval

Comparison 2.1. High-dose PERT versus low dose PERT in children

No forest plots available.

I.15 Distal intestinal obstruction syndrome

Not applicable, as no studies were included in this review.

I.16 Monitoring liver disease

Not applicable to this review.

I.17 Ursodeoxycholic acid

Comparison 1. UDCA versus placebo or control

Figure 301: Lack of normalisation of hepatobiliary enzymes at 6 months follow-up

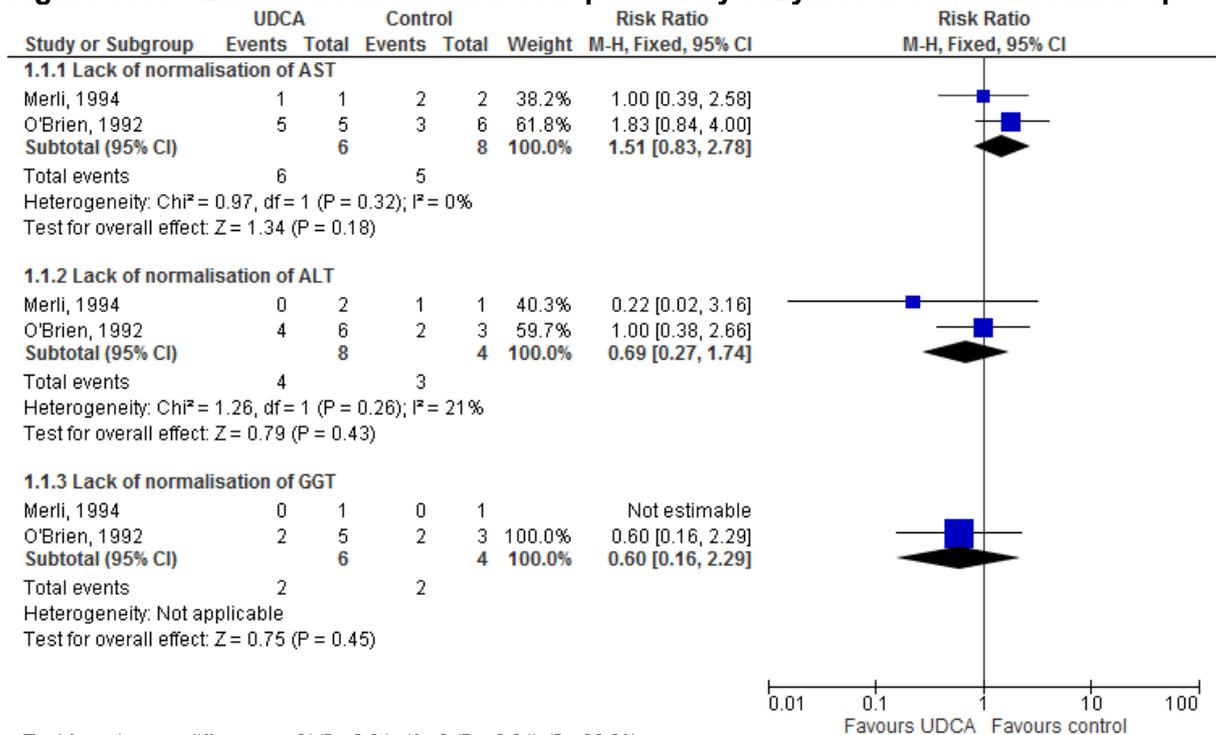


Figure 302: Final value of bilirubin value (umol/L) at 6 months follow-up

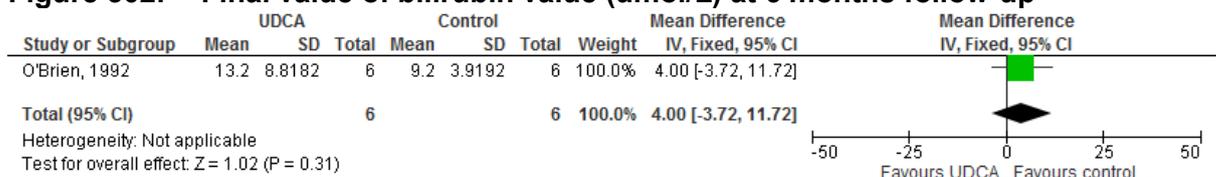
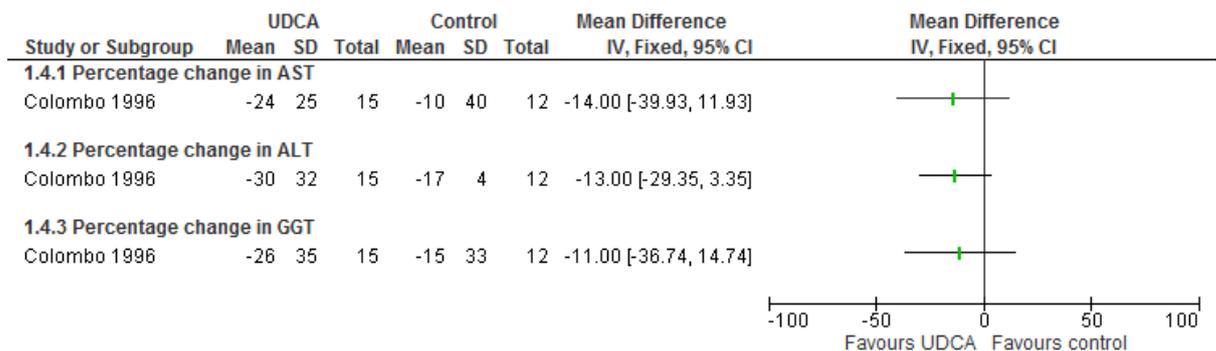


Figure 303: Percentage change in hepatobiliary enzymes at 12 months follow-up

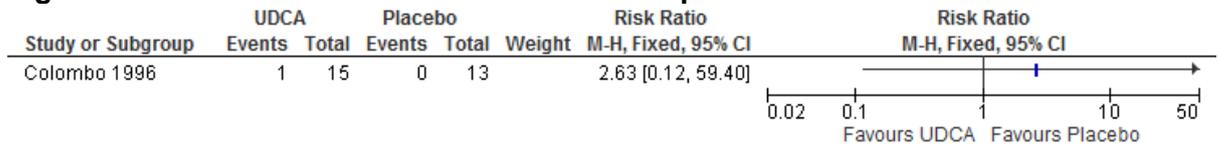


Abbreviations: UDCA: ursodeoxycholic acid; SD: standard deviation; IV: inverse variance; CI: confidence interval. Colombo: Data reported as multiples of the upper limit of normal reference values.

Figure 304: No development of liver disease at 6 months follow-up

Data cannot be plotted. None of the participants developed liver disease in either treatment arm.

Figure 305: Liver failure at 12 months follow-up



Abbreviations: UDCA: ursodeoxycholic acid; M-H: Mantel-Haenszel; CI: confidence interval

Figure 306: Liver transplantation at 12 months follow-up



Abbreviations: UDCA: ursodeoxycholic acid; M-H: Mantel-Haenszel; CI: confidence interval

I.18 Monitoring for CF related diabetes

Not applicable, as no studies were identified for this review.

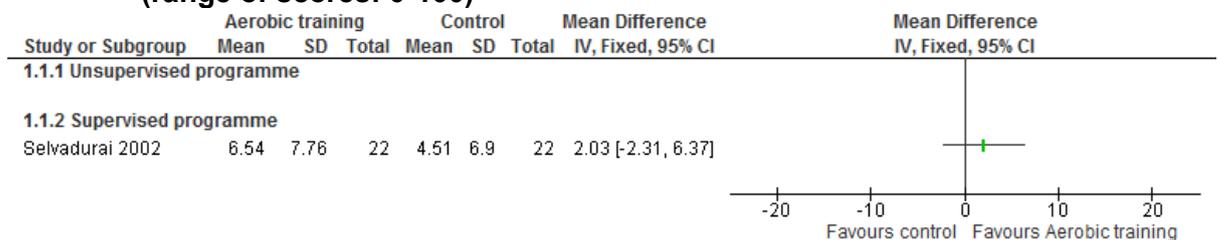
I.19 Bone mineral density

Not applicable to this review.

I.20 Exercise

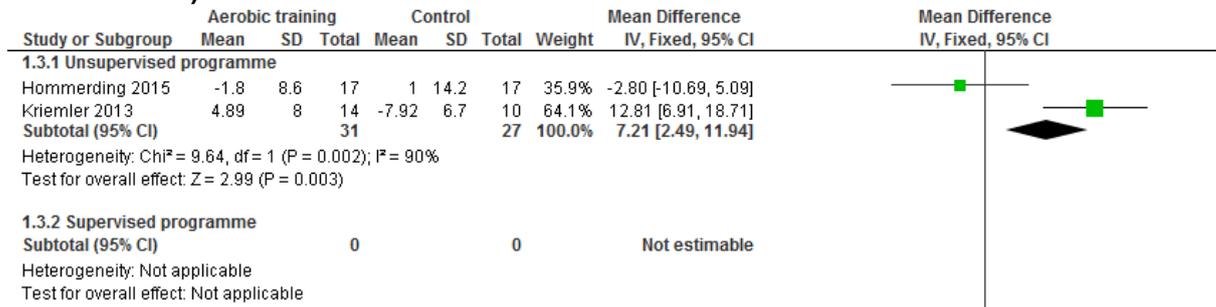
Comparison 1. Aerobic exercise training programme versus no exercise programme

**Figure 307: Change in FEV₁ % predicted at hospital discharge (mean ≈ 19 days)
(range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

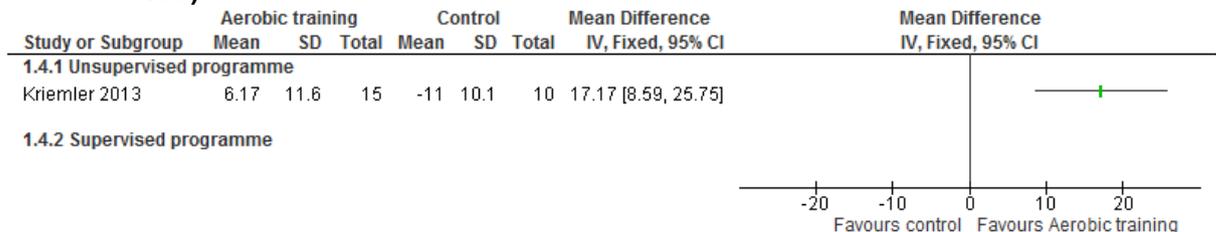
Figure 308: Change in FEV₁ % predicted at 3 months follow-up (range of scores: 0-100)



Test for subgroup differences: Not applicable

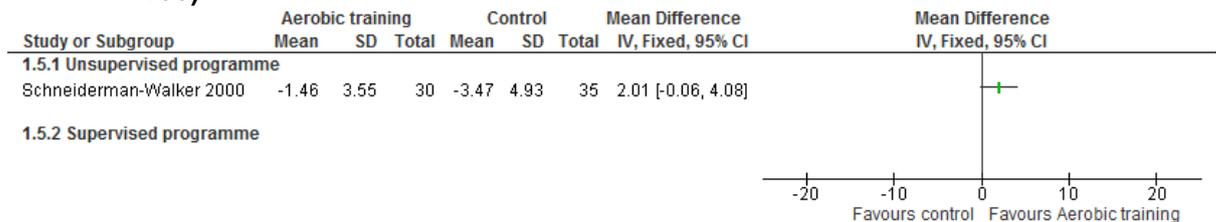
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 309: Change in FEV₁ % predicted at 6 months follow-up (range of scores: 0-100)



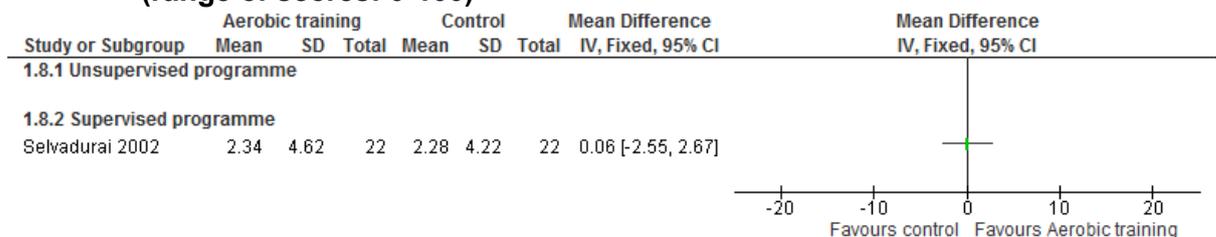
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 310: Change in FEV₁ % predicted at 3 years follow-up (range of scores: 0-100)



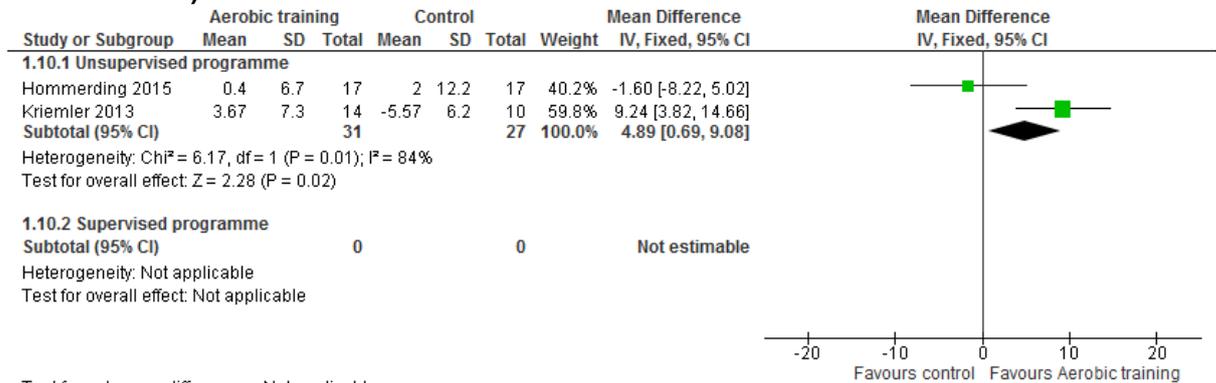
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 311: Change in FVC % predicted at hospital discharge (mean ≈ 19 days) (range of scores: 0-100)



Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

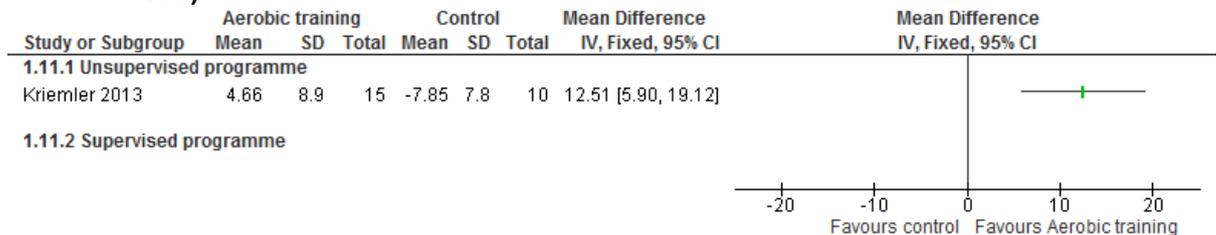
Figure 312: Change in FVC % predicted at 3 months follow-up (range of scores: 0-100)



Test for subgroup differences: Not applicable

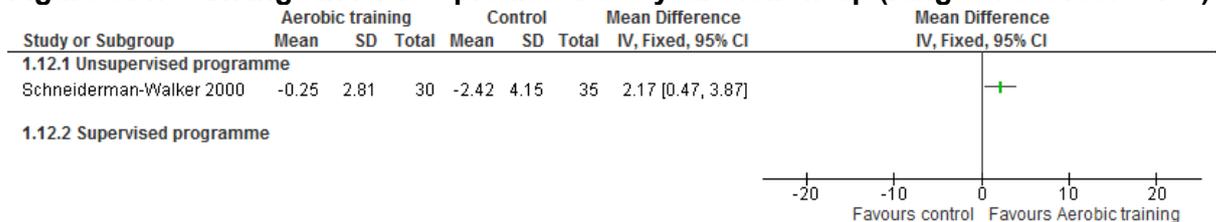
Abbreviations: CI: confidence interval; df: degrees of freedom; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation;

Figure 313: Change in FVC % predicted at 6 months follow-up (range of scores: 0-100)



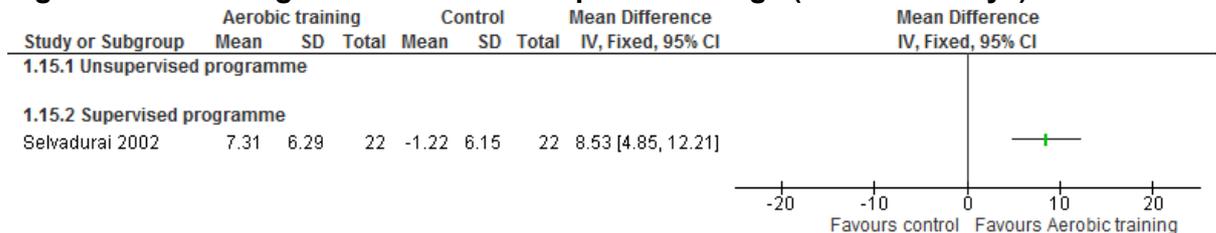
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

Figure 314: Change in FVC % predicted at 3 years follow-up (range of scores: 0-100)



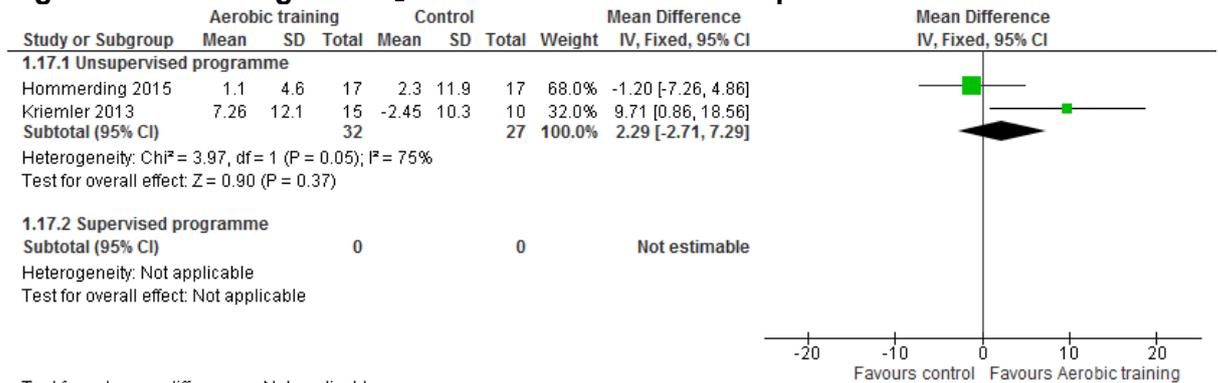
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

Figure 315: Change in VO₂ max. at hospital discharge (mean ≈ 19 days)



Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO₂ max: maximal oxygen consumption

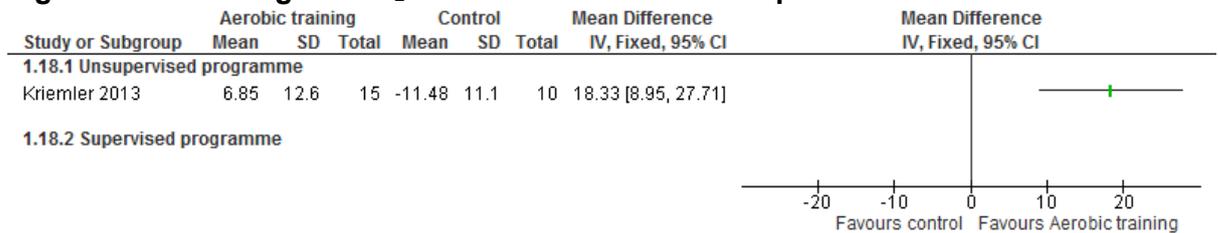
Figure 316: Change in VO₂ max. at 3 months follow-up



Test for subgroup differences: Not applicable

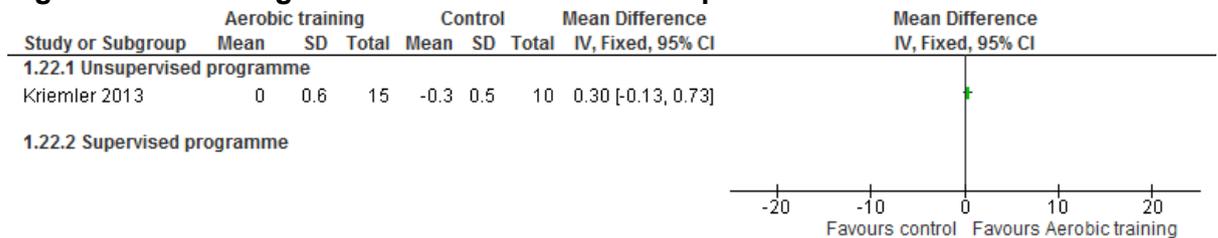
Abbreviations: CI: confidence interval; df: degrees of freedom; IV: inverse variance; SD: standard deviation; VO₂ max: maximal oxygen consumption

Figure 317: Change in VO₂ max. at 6 months follow-up



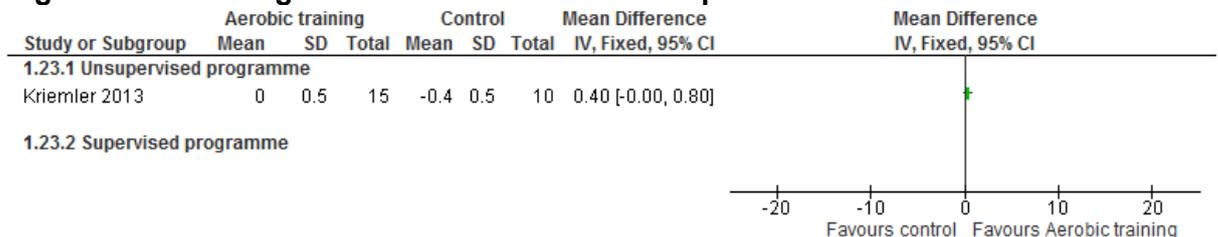
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO₂ max: maximal oxygen consumption

Figure 318: Change in BMI at 3 months follow-up



Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

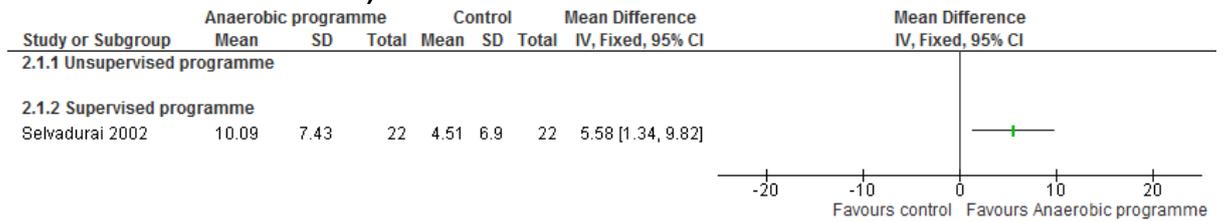
Figure 319: Change in BMI at 6 months follow-up



Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

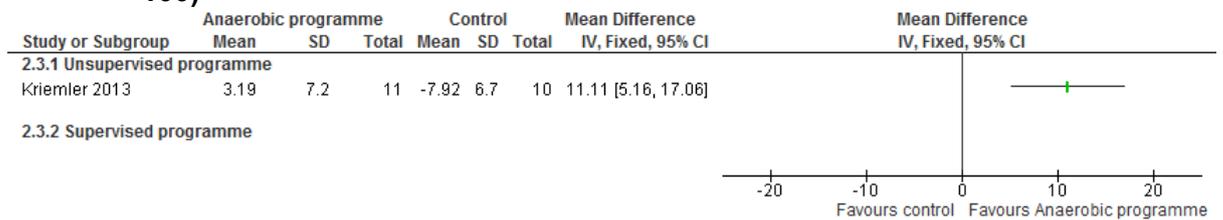
Comparison 2.1. Strength resistance/ anaerobic training programme versus no exercise programme

Figure 320: Change in FEV₁ % predicted at hospital discharge (mean ≈ 19 days) (range of scores: 0-100)



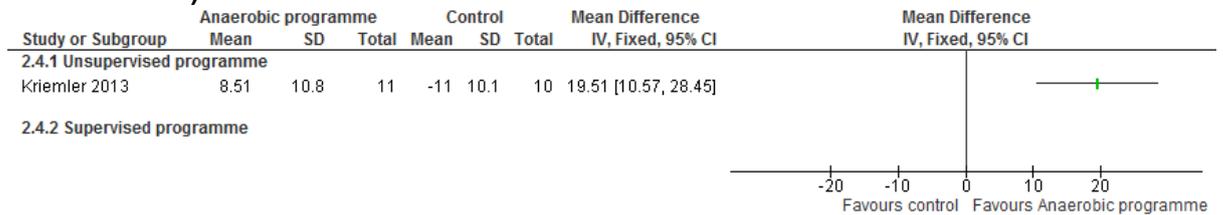
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 321: Change in FEV₁ % predicted at 3 months follow-up (range of scores: 0-100)



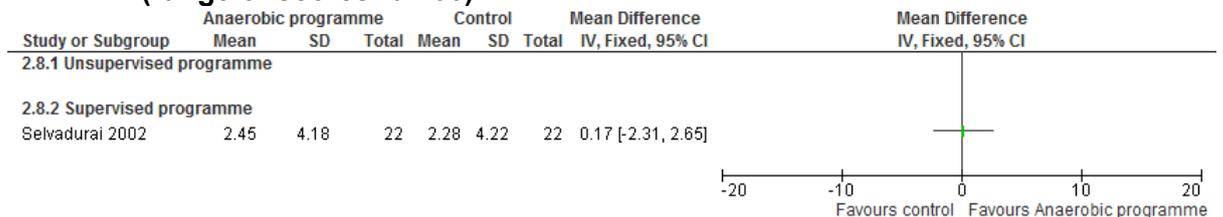
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 322: Change in FEV₁ % predicted at 6 months follow-up (range of scores: 0-100)



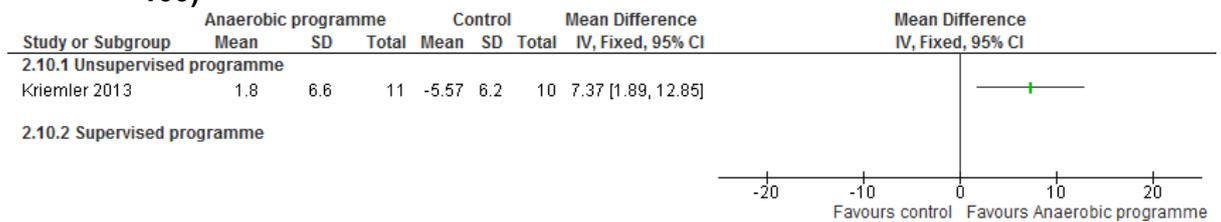
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 323: Change in FVC % predicted at hospital discharge (mean ≈ 19 days) (range of scores: 0-100)



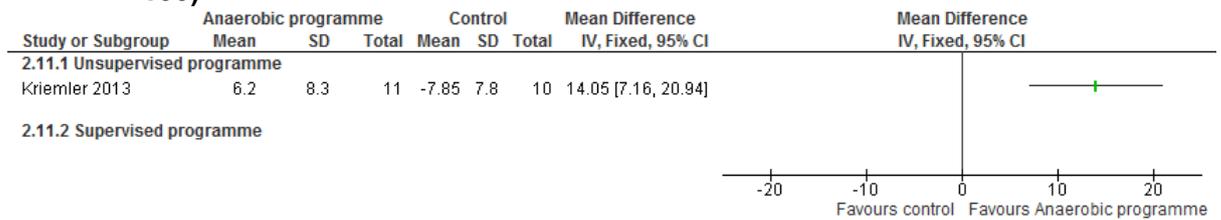
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

Figure 324: Change in FVC % predicted at 3 months follow-up (range of scores: 0-100)



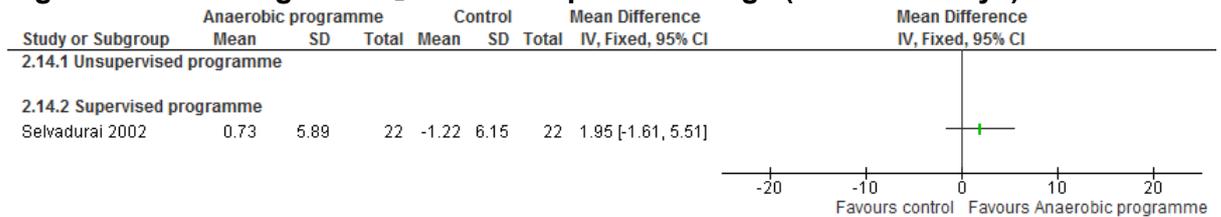
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

Figure 325: Change in FVC % predicted at 6 months follow-up (range of scores: 0-100)



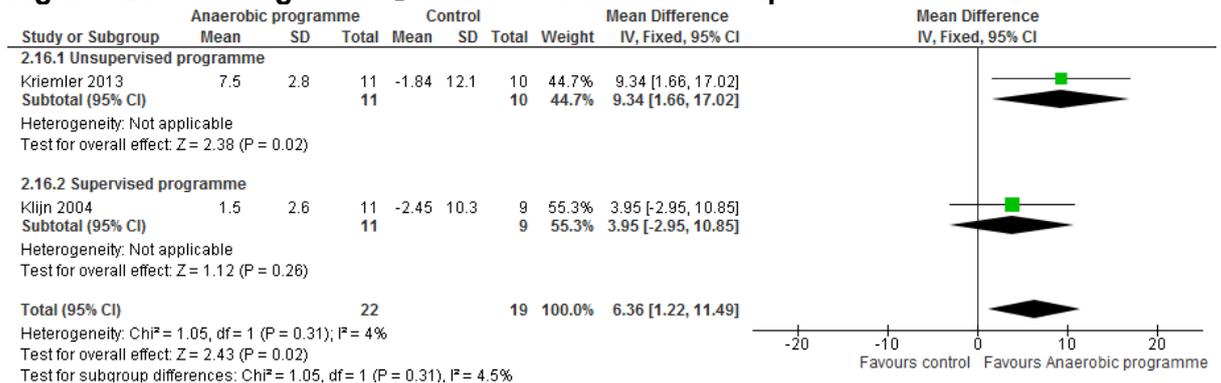
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

Figure 326: Change in VO₂ max at hospital discharge (mean ≈ 19 days)



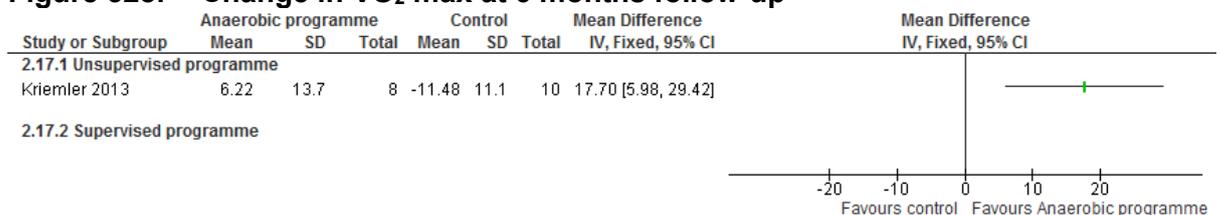
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO₂ max: maximal oxygen consumption

Figure 327: Change in VO₂ max at 3 months follow-up



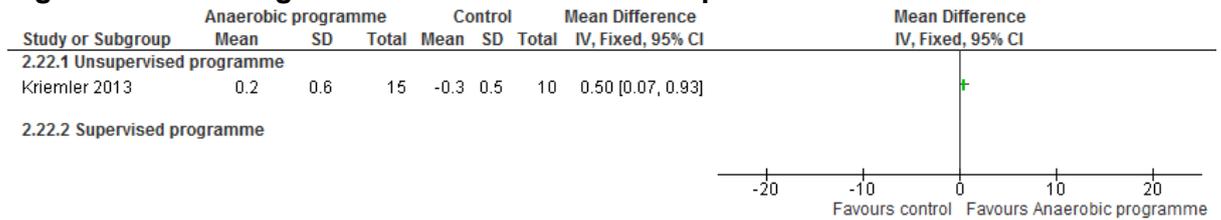
Abbreviations: CI: confidence interval; df: degrees of freedom; IV: inverse variance; SD: standard deviation; VO₂ max: maximal oxygen consumption

Figure 328: Change in VO₂ max at 6 months follow-up



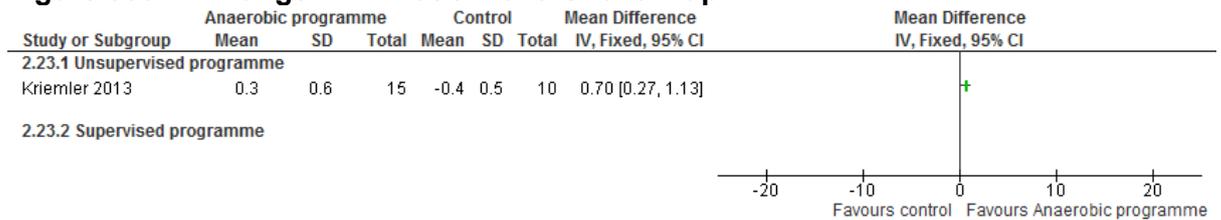
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO₂ max: maximal oxygen consumption

Figure 329: Change in BMI at 3 months follow-up



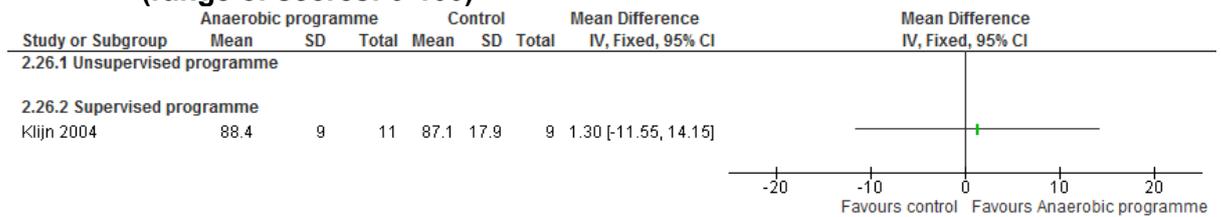
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 330: Change in BMI at 6 months follow-up



Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

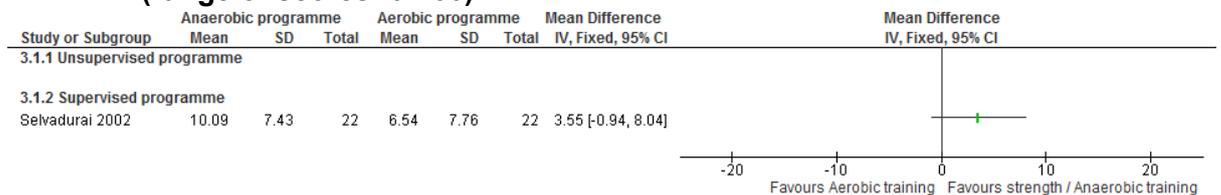
Figure 331: Change in quality of life (CFQ-R physical domain) at 3 months follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

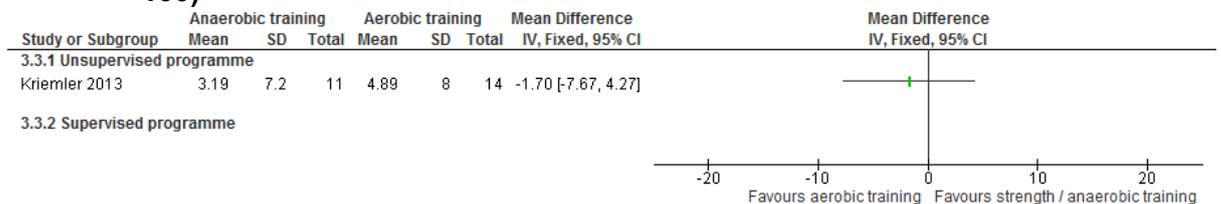
Comparison 2.2. Strength/ anaerobic training programme versus aerobic training programme

Figure 332: Change in FEV₁ % predicted at hospital discharge (mean ≈ 19 days) (range of scores: 0-100)



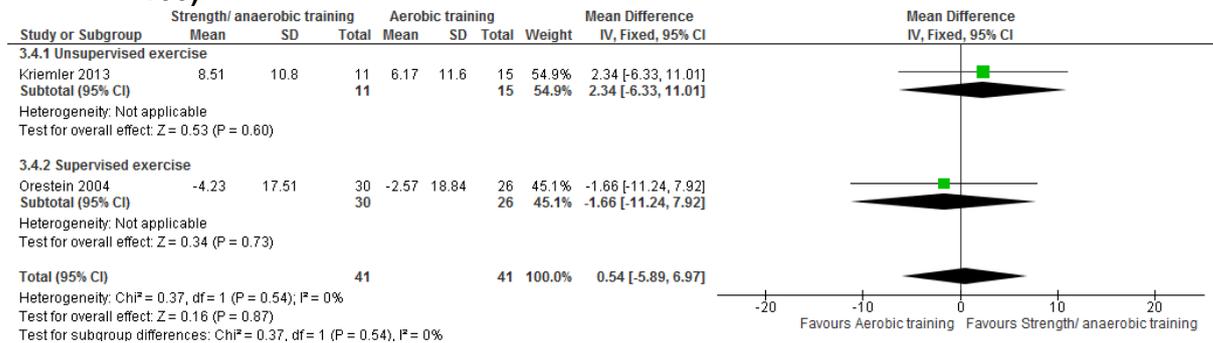
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 333: Change in FEV₁ % predicted at 3 months follow-up (range of scores: 0-100)



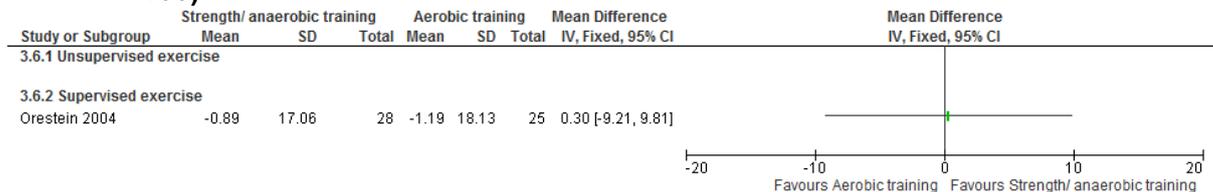
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 334: Change in FEV₁ % predicted at 6 months follow-up (range of scores: 0-100)



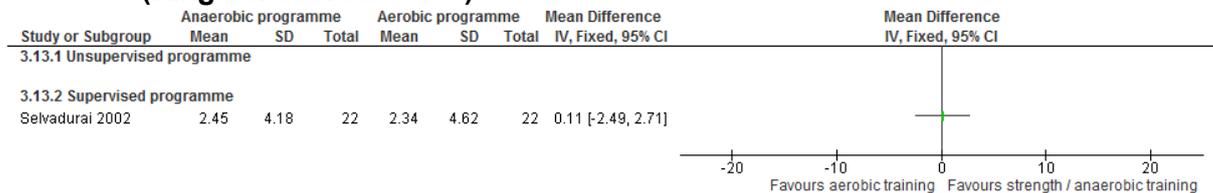
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 335: Change in FEV₁ % predicted at 12 months follow-up (range of scores: 0-100)



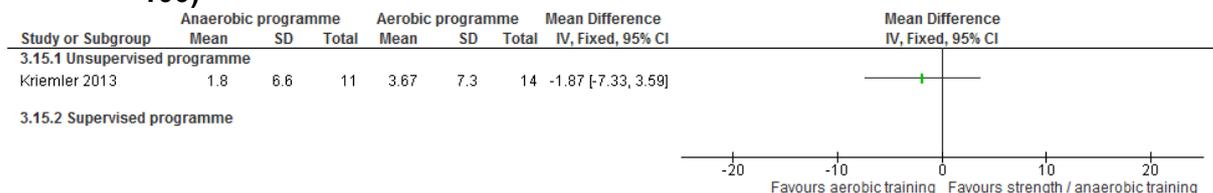
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 336: Change in FVC% predicted at hospital discharge (mean approx. 19 days) (range of scores: 0-100)



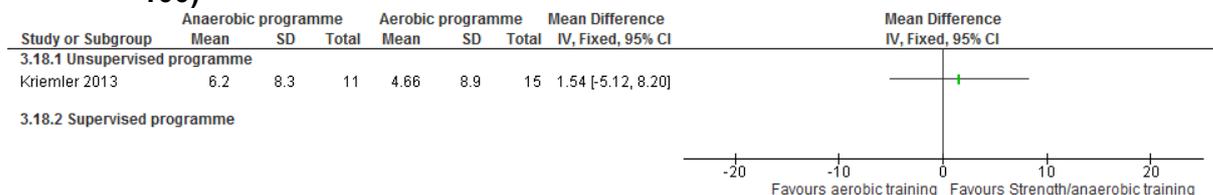
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

Figure 337: Change in FVC% predicted at 3 months follow-up (range of scores: 0-100)



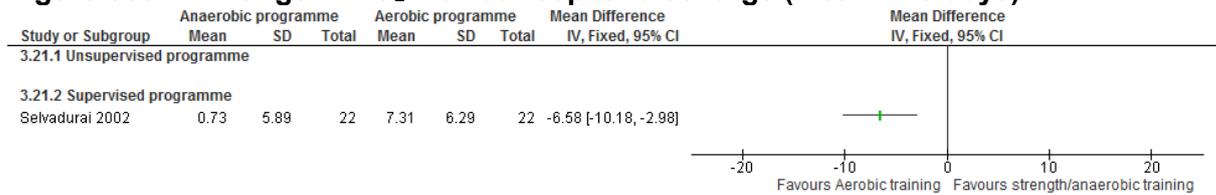
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

Figure 338: Change in FVC % predicted at 6 months follow-up (range of scores: 0-100)



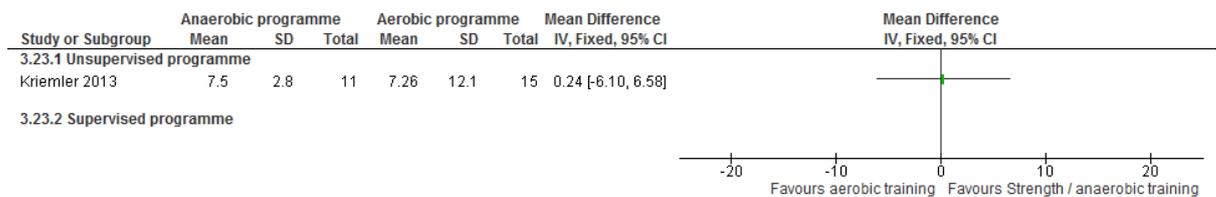
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

Figure 339: Change in VO₂ max at hospital discharge (mean ≈ 19 days)



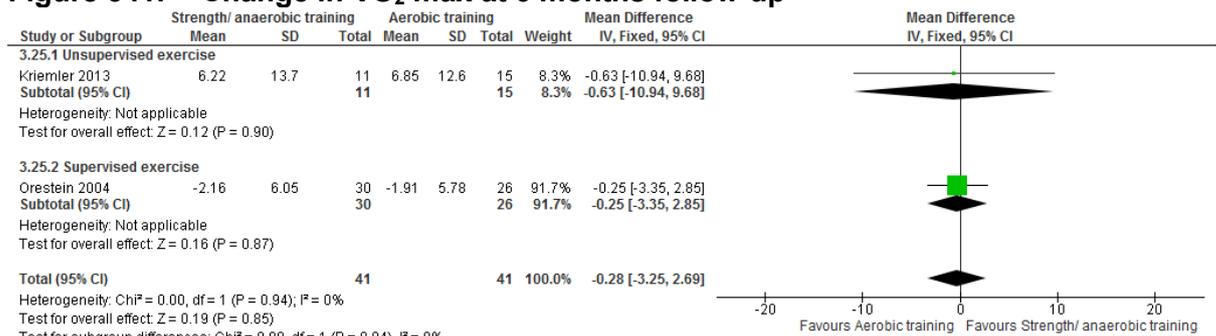
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO₂ max: maximal oxygen consumption

Figure 340: Change in VO₂ max at 3 months follow-up



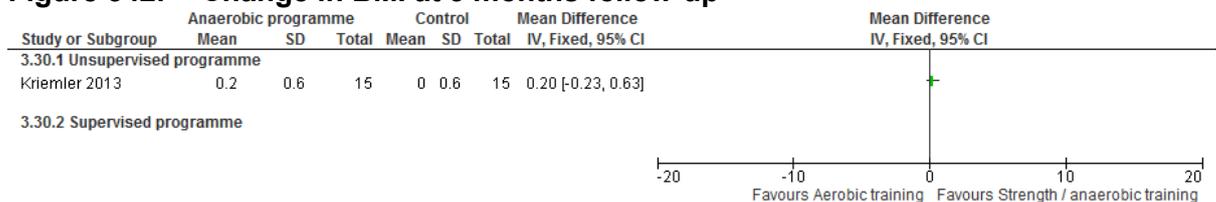
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO₂ max: maximal oxygen consumption

Figure 341: Change in VO₂ max at 6 months follow-up



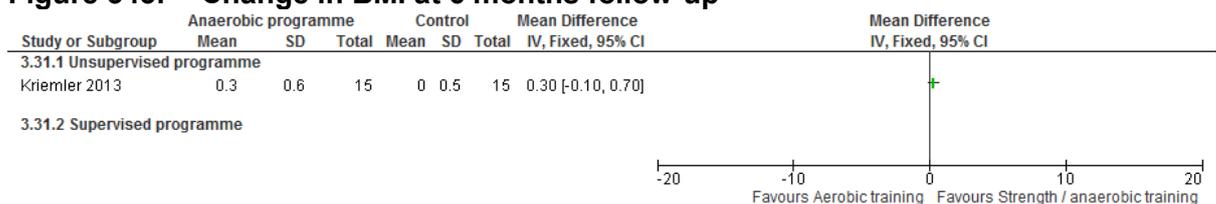
Abbreviations: CI: confidence interval; df: degrees of freedom; IV: inverse variance; SD: standard deviation; VO₂ max: maximal oxygen consumption

Figure 342: Change in BMI at 3 months follow-up



Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

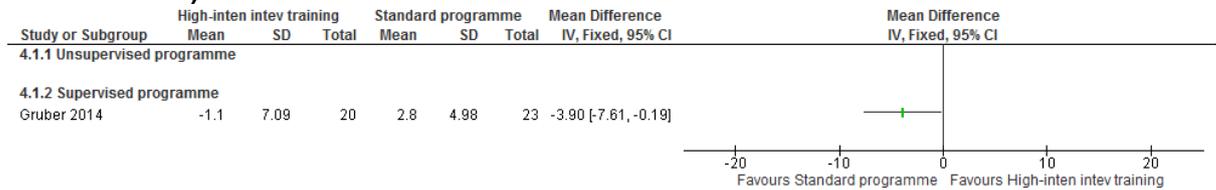
Figure 343: Change in BMI at 6 months follow-up



Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

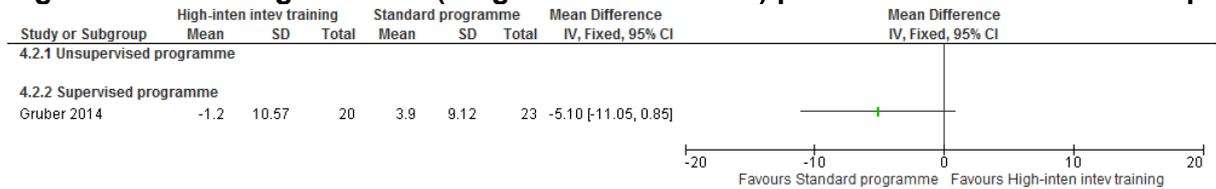
Comparison 3. High-intensity interval training *versus* standard aerobic and anaerobic exercise programme

Figure 344: Change in FEV₁ % predicted at 6 weeks follow-up (range of scores: 0-100)



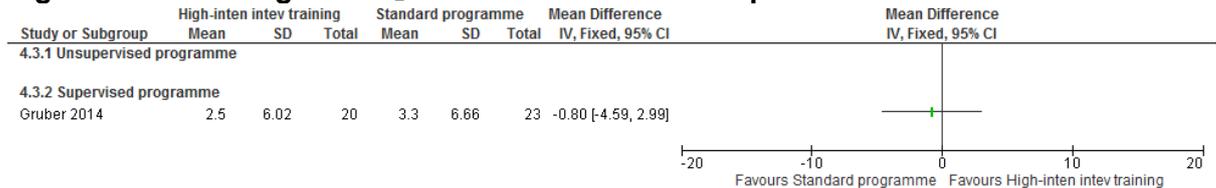
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 345: Change in VC % (range of scores: 0-100) predicted at 6 weeks follow-up



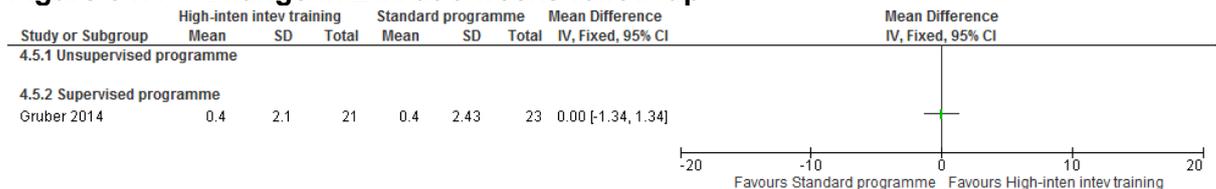
Abbreviations: VC: vital capacity; SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 346: Change in VO₂ max at 6 weeks follow-up



Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO₂ max: maximal oxygen consumption

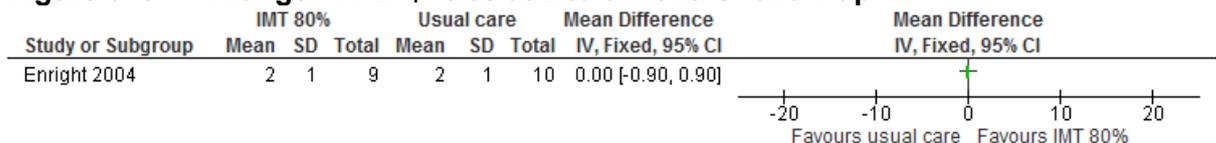
Figure 347: Change in BMI at 6 weeks follow-up



Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

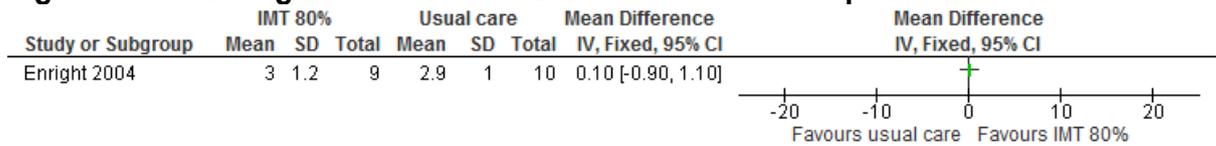
Comparison 4. Inspiratory muscle training (IMT) at 80% of maximal effort *versus* usual care

Figure 348: Change in FEV₁ litres at 2 to 6 months follow-up



Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IMT 80%: inspiratory muscle training at 80% of maximal effort; IV: inverse variance; SD: standard deviation

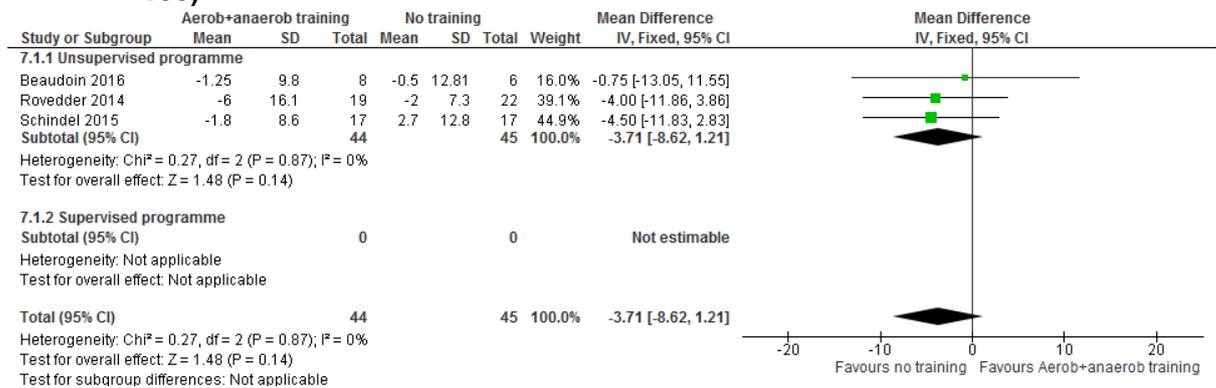
Figure 349: Change in FVC litres at 2 to 6 months follow-up



Abbreviations: CI: confidence interval; FVC: forced vital capacity; IMT 80%: inspiratory muscle training at 80% of maximal effort; IV: inverse variance; SD: standard deviation

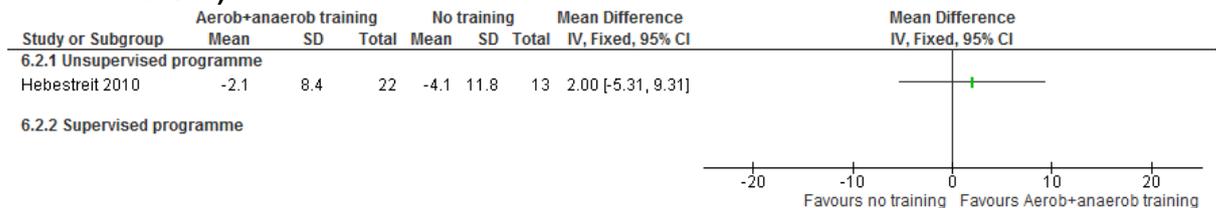
Comparison 5. Combined aerobic and anaerobic training programme versus no exercise programme

Figure 350: Change in FEV₁ % predicted at 3 months follow-up (range of scores: 0-100)



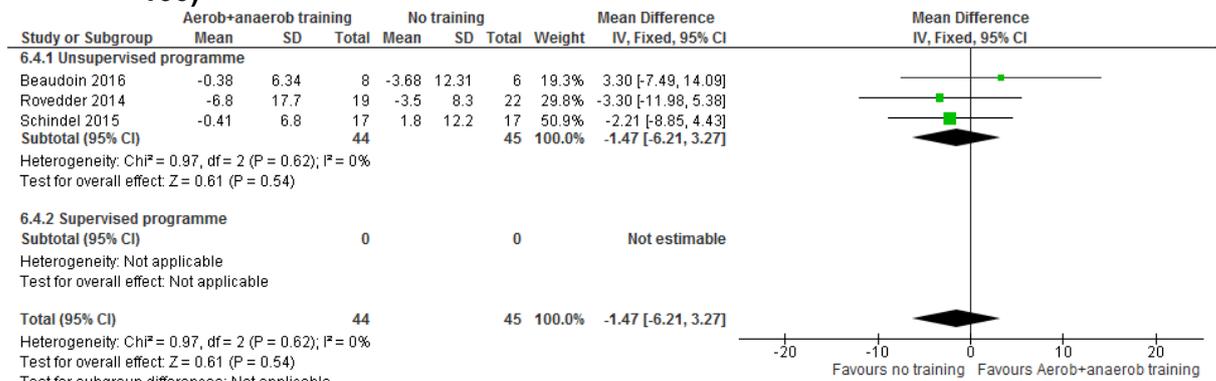
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 351: Change in FEV₁ % predicted at 3 to 6 months follow-up (range of scores: 0-100)



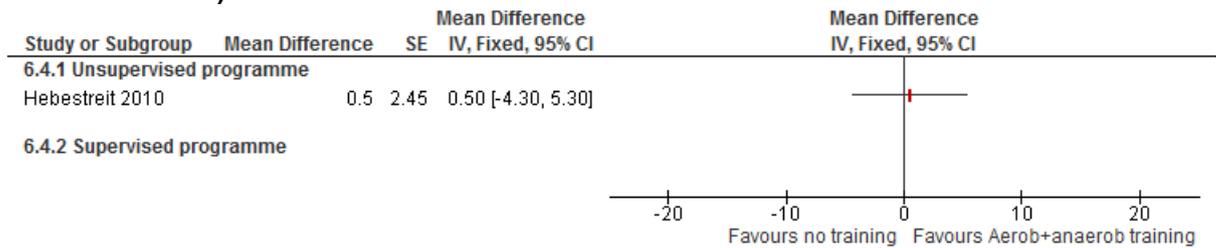
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 352: Change in FVC% predicted at 3 months follow-up (range of scores: 0-100)



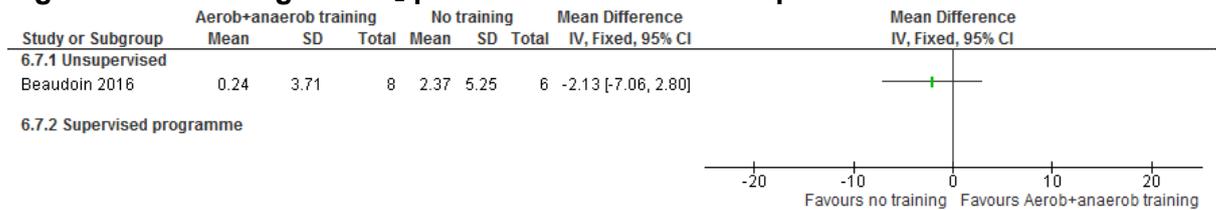
Abbreviations: CI: confidence interval; df: degrees of freedom; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

Figure 353: Change in FVC % predicted at 3 to 6 months follow-up (range of scores: 0-100)



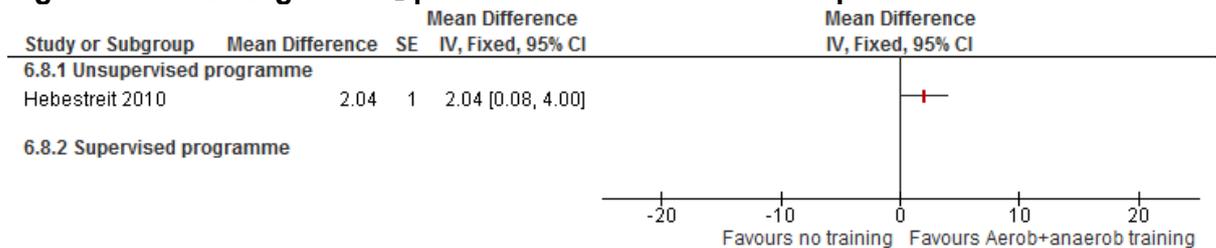
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

Figure 354: Change in VO₂ peak at 3 months follow-up



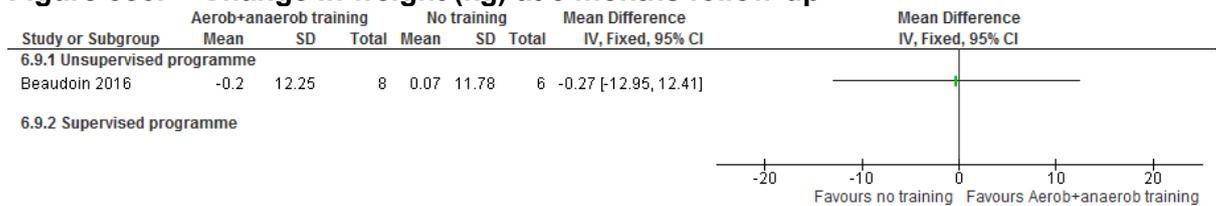
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO₂ max: maximal oxygen consumption

Figure 355: Change in VO₂ peak at 3 to 6 months follow-up



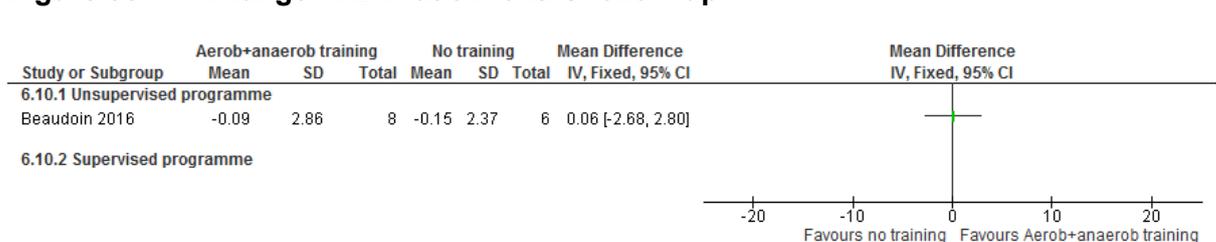
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO₂ max: maximal oxygen consumption

Figure 356: Change in weight (kg) at 3 months follow-up



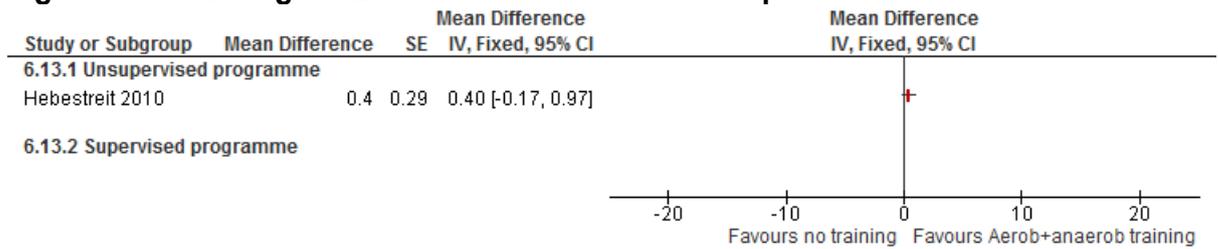
Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 357: Change in BMI at 3 months follow-up



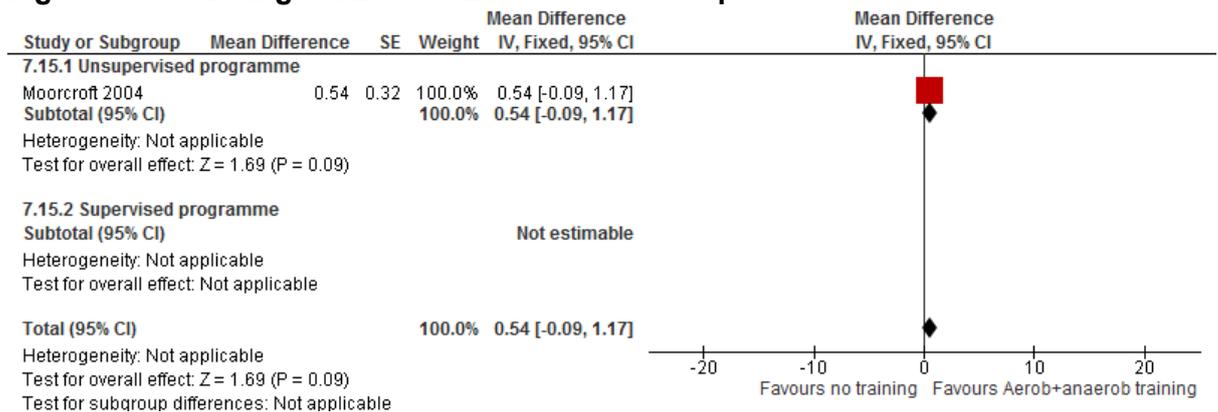
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 358: Change in BMI at 3 to 6 months follow-up



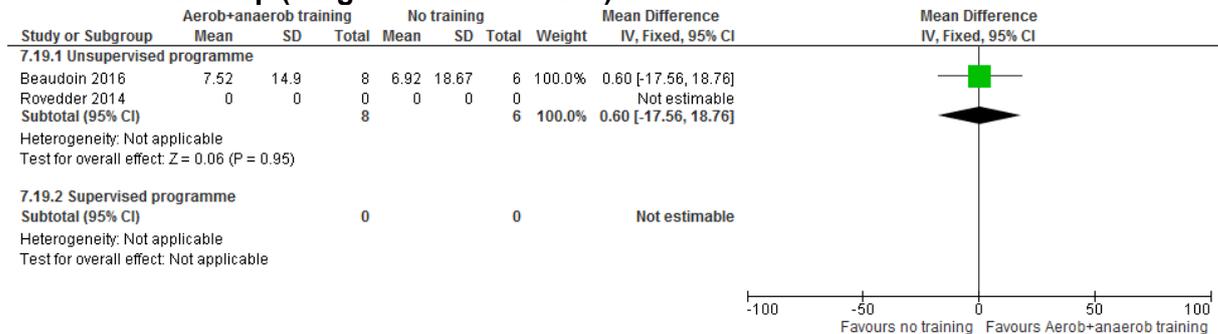
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 359: Change in BMI at 12 months follow-up



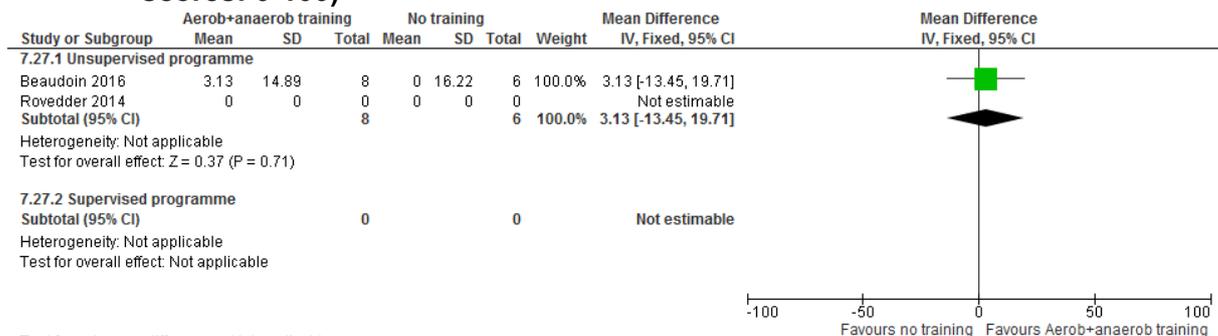
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

Figure 360: Change in quality of life – CFQ-R physical functioning at 3 months follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

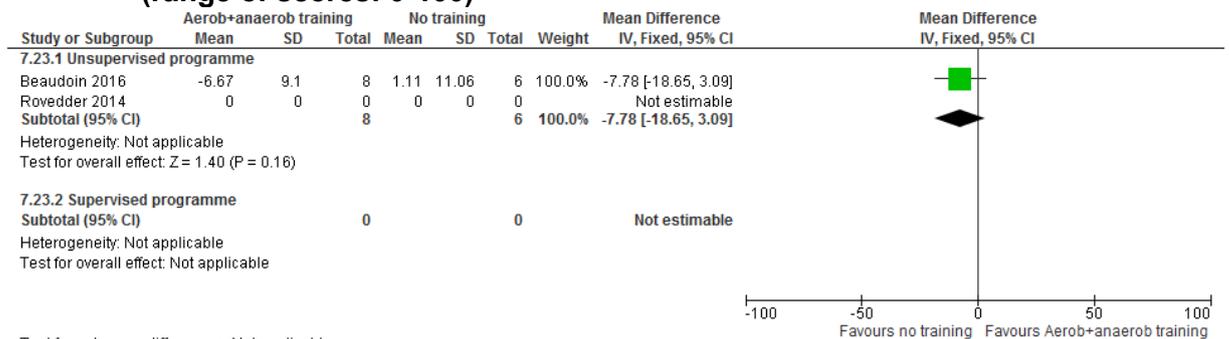
Figure 361: Change in quality of life – CFQ-R vitality at 3 months follow-up (range of scores: 0-100)



Test for subgroup differences: Not applicable

Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

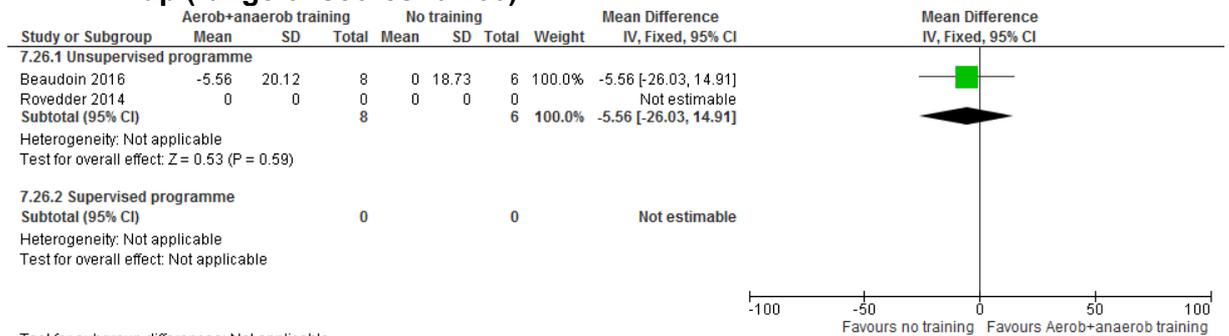
Figure 362: Change in quality of life – CFQ-R emotional state at 3 months follow-up (range of scores: 0-100)



Test for subgroup differences: Not applicable

Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

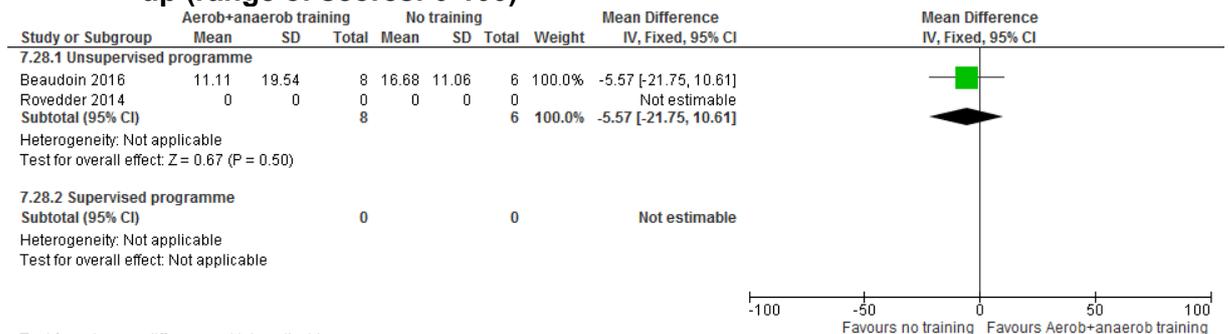
Figure 363: Change in quality of life – CFQ-R treatment burden at 3 months follow-up (range of scores: 0-100)



Test for subgroup differences: Not applicable

Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

Figure 364: Change in quality of life – CFQ-R health perception at 3 months follow-up (range of scores: 0-100)



Test for subgroup differences: Not applicable

Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

Figure 365: Change in quality of life – CFQ-R social limitations at 3 months follow-up (range of scores: 0-100)

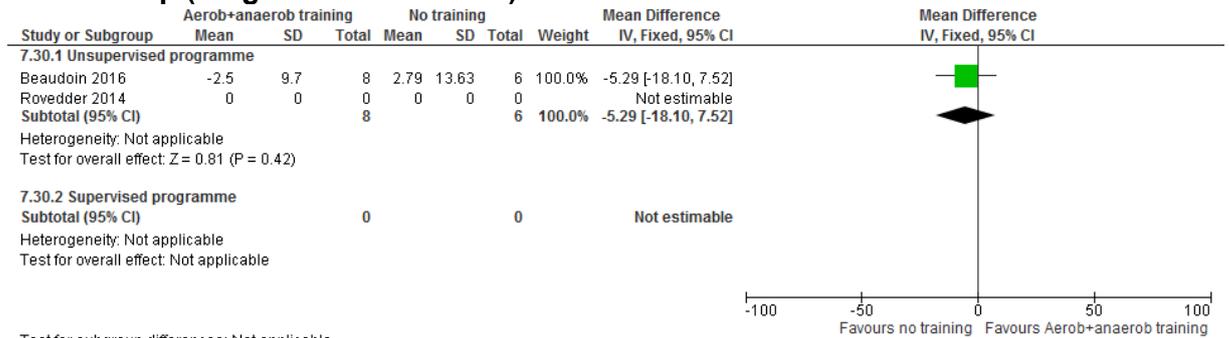


Figure 366: Change in quality of life – CFQ-R body image at 3 months follow-up (range of scores: 0-100)

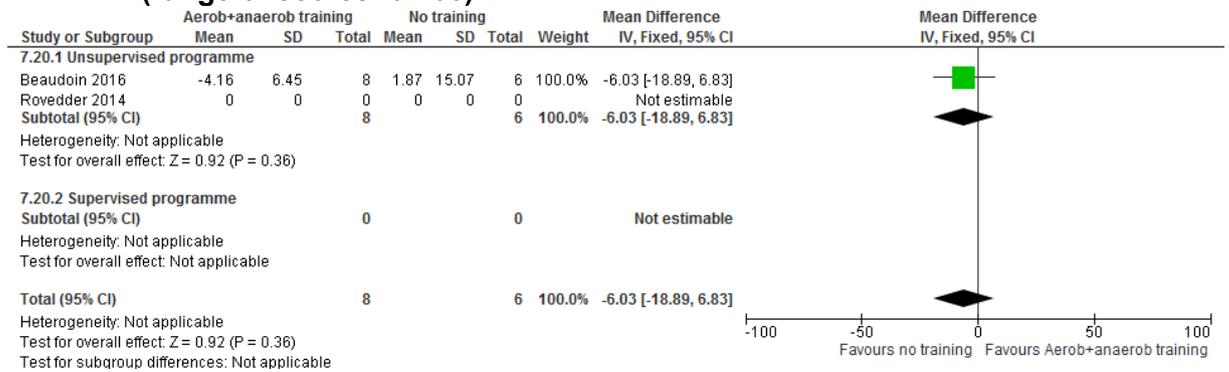


Figure 367: Change in quality of life – CFQ-R role limitations at 3 months follow-up (range of scores: 0-100)

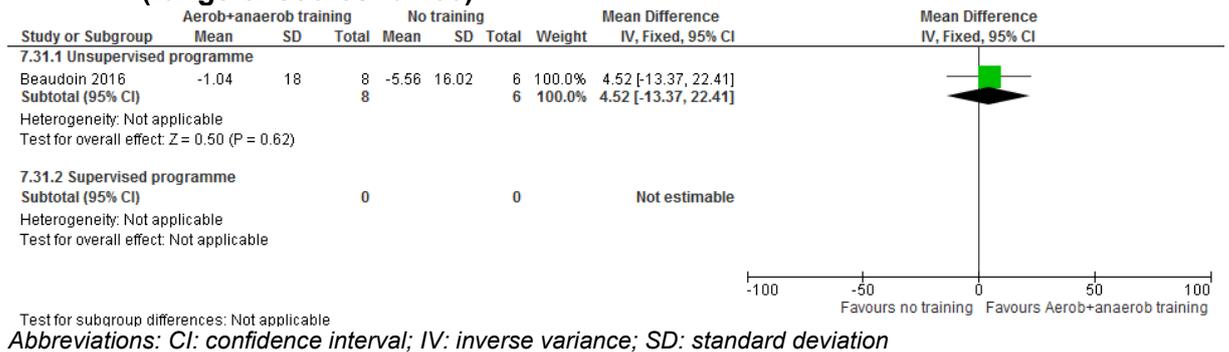
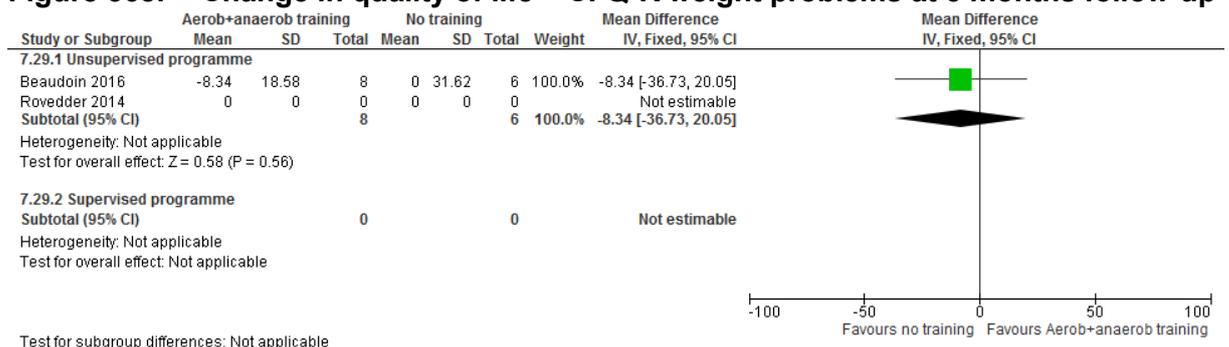
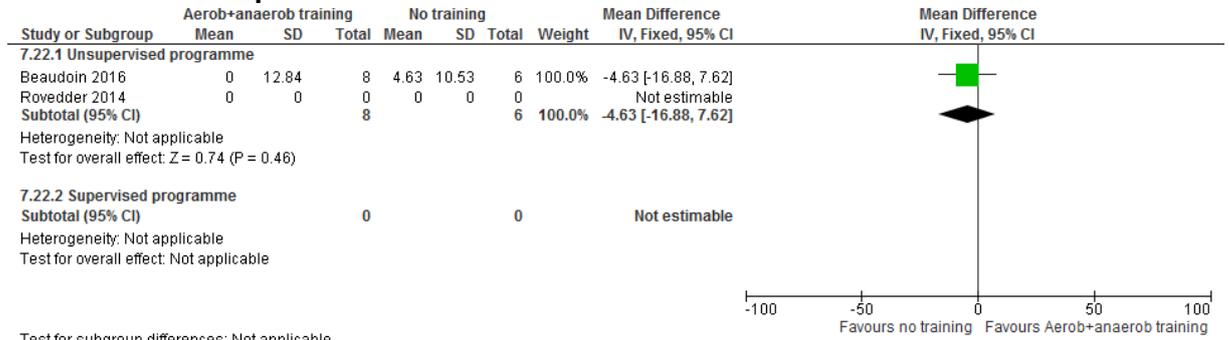


Figure 368: Change in quality of life – CFQ-R weight problems at 3 months follow-up



Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

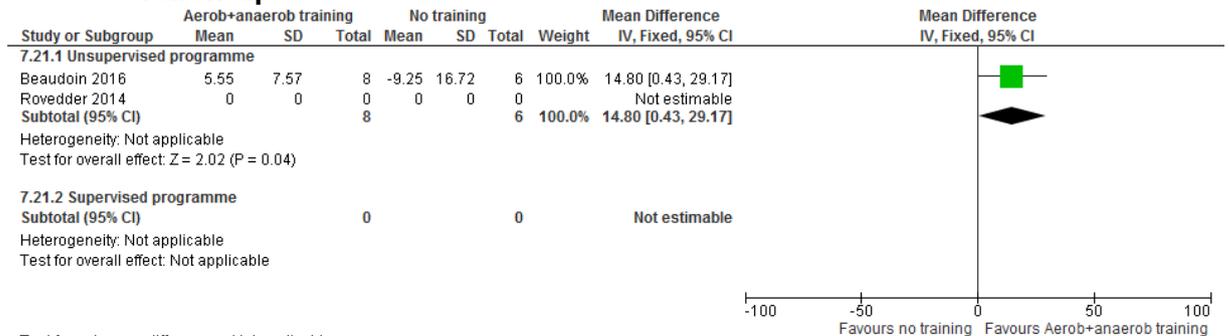
Figure 369: Change in quality of life – CFQ-R respiratory symptoms at 3 months follow-up



Test for subgroup differences: Not applicable

Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

Figure 370: Change in quality of life – CFQ-R digestion symptoms at 3 months follow-up

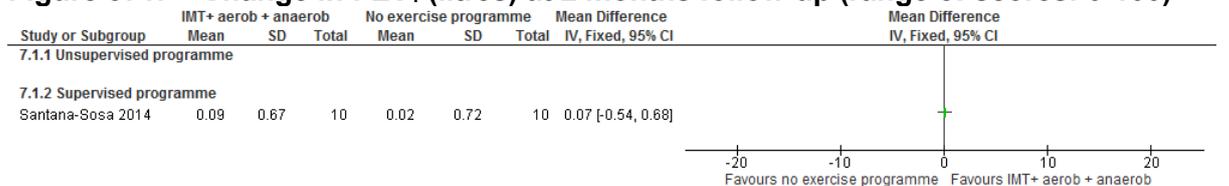


Test for subgroup differences: Not applicable

Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

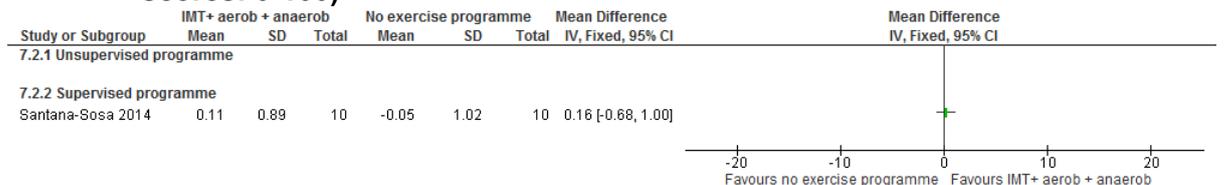
Comparison 6. Combined inspiratory muscle training (IMT), resistance and aerobic training versus no exercise programme

Figure 371: Change in FEV₁ (litres) at 2 months follow-up (range of scores: 0-100)



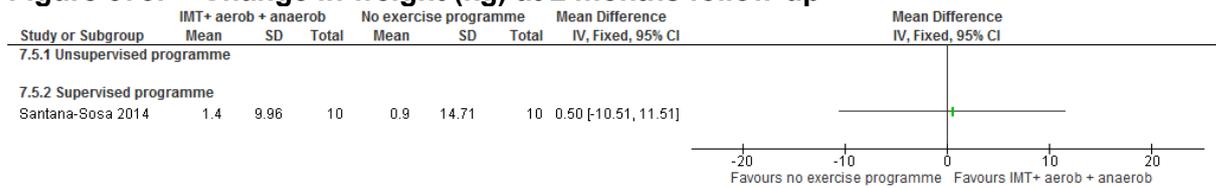
Abbreviations: CI: confidence interval; FEV₁: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

Figure 372: Change in forced vital capacity (litres) at 2 months follow-up (range of scores: 0-100)



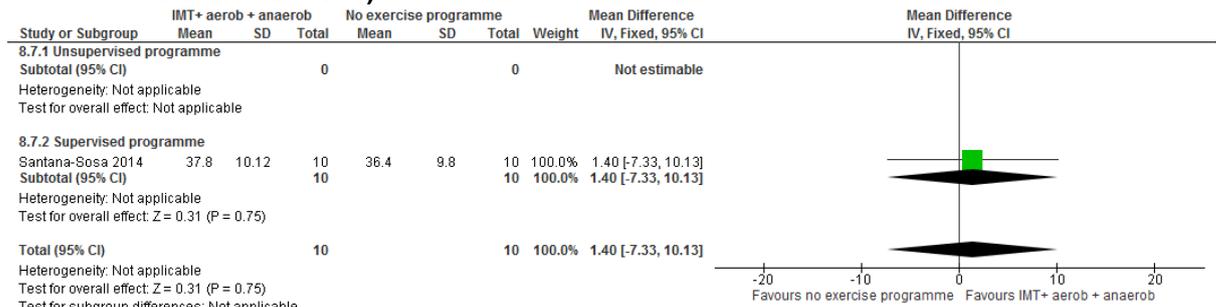
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

Figure 373: Change in weight (kg) at 2 months follow-up



Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval

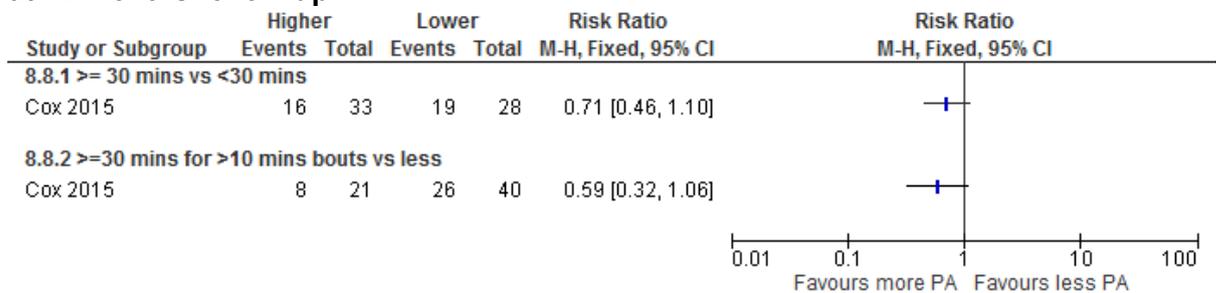
Figure 374: Change in quality of life (CFQ-R children's) at 2 months follow-up (range of scores: 0-100)



Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

Comparison 7. Physical activity: higher amount or longer duration versus lower amount or shorter duration

Figure 375: Need of hospitalization (proxy outcome for time to next exacerbation) at 12 months follow-up



Abbreviations: M-H: Mantel-Haenszel; CI: confidence interval; PA: physical activity

I.21 Psychological assessment

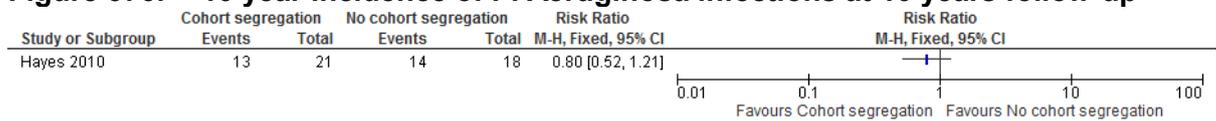
Not applicable to this review.

I.22 Cross-infection control

I.22.1 Outpatient care

Comparison 1. Cohort segregation by clinic times *versus* no cohort segregation

Figure 376: 10 year incidence of P. Aeruginosa infections at 10 years follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

4-year prevalence of MRSA at 4 years follow-up

Data could not be plotted

4-year prevalence of non-mucoid PA at 4 years follow-up

Data could not be plotted

4-year prevalence of mucoid PA at 4 years follow-up

Data could not be plotted

Staff compliance at 4 years follow-up

Data could not be plotted

Comparison 2. Cohort segregation by location *versus* no cohort segregation

Annual incidence of new growths of PA at 9 years follow-up

Data could not be plotted

Figure 377: Yearly prevalence of chronic P. Aeruginosa infections at 9 years follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 378: Yearly prevalence of intermittent P. Aeruginosa infections at 9 years follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Comparison 3. Combination of protective equipment + individual segregation *versus* incomplete protective equipment + incomplete individual segregation

4-month prevalence of PA infections at 5 years follow-up

Data could not be plotted

4-month prevalence of MRSA infections at 5 years follow-up

Data could not be plotted

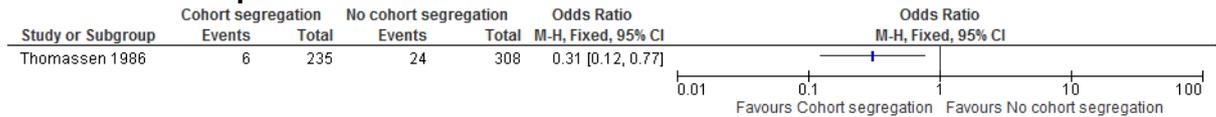
I.22.2 Inpatient care

Comparison 4. Cohort segregation by location *versus* no cohort segregation

Annual incidence of B. Cepacia Complex at 1 year follow-up

Data could not be plotted

Figure 379: 5-month incidence of hospital-associated colonization of P. Cepacia at 5 months follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Comparison 5. Individual segregation by location *versus* usual care

Patients' satisfaction

Data could not be plotted

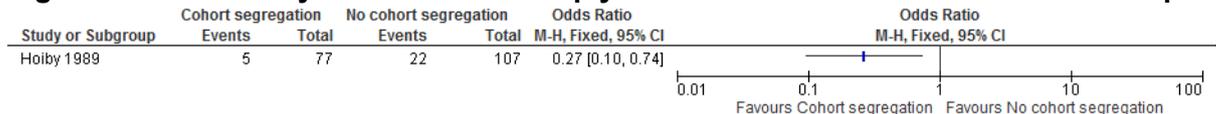
Parents' satisfaction

Data could not be plotted

I.22.3 Combined inpatient and outpatient care

Comparison 6. Cohort segregation *versus* no cohort segregation

Figure 380: Monthly incidence of multiply resistant PA strain at 1 month follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 381: Annual incidence of intermittent PA at 1 year follow-up



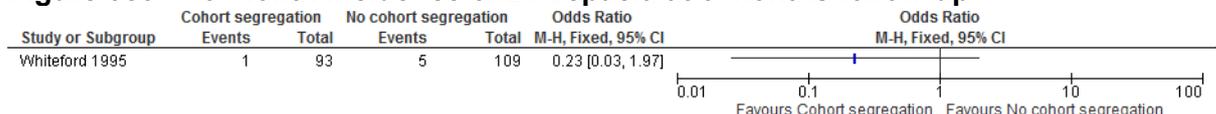
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Figure 382: Annual incidence of chronic PA at 1 year follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

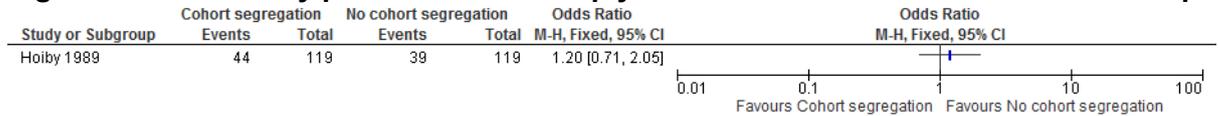
Figure 383: 6-month incidence of B. Cepacia at 6 months follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Annual incidence of Burkholderia species infection at 1 year follow-up
Data could not be plotted

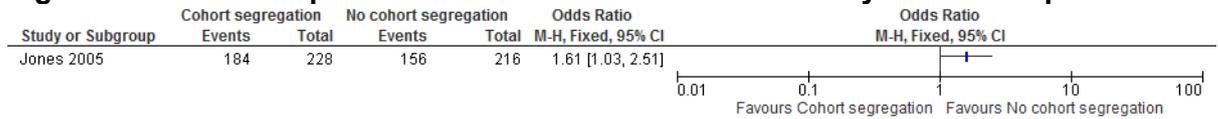
Figure 384: Monthly prevalence of multiply resistant PA strain at 1 month follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Prevalence of AES-1 (PA epidemic strain) at 2 years follow-up
Data could not be plotted

Figure 385: Annual prevalence of chronic PA infection at 1 year follow-up



Abbreviations: M-H: Mantel-Haenszel; CI: confidence interval

Figure 386: Annual prevalence of transmissible PA infection at 1 year follow-up



Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

Annual prevalence of chronic infection with transmissible PA strain at 1 year follow-up
Data could not be plotted

Comparison 7. Complete cohort segregation versus incomplete cohort segregation

Annual incidence of Burkholderia species at 1 year follow-up

Data could not be plotted

Comparison 8. Individual segregation versus usual care

Patient satisfaction

Data could not be plotted

Comparison 9. Cohort segregation + individual segregation versus cohort segregation

Yearly prevalence of B. Cepacia complex infection at 1 year follow-up

Data could not be plotted

Yearly prevalence of Burkholderia species at 5 years follow-up

Data could not be plotted

**Comparison 10. Cohort segregation + individual segregation + protective equipment
versus usual care**

Annual incidence of B. Cepacia complex infection at 1 year follow-up

Data could not be plotted

Comparison 11. Cohort segregation + individual segregation *versus* usual care

Patient satisfaction

Data could not be plotted