

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*



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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.

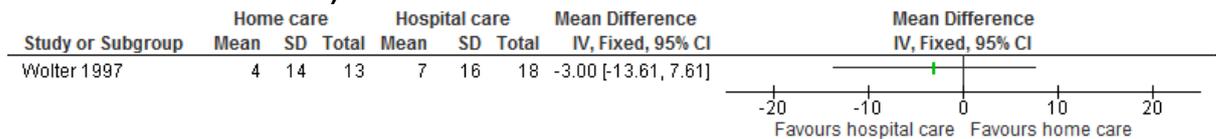
## I.3 Service delivery

### I.3.1 Service configuration

#### I.3.1.1 Home-based care

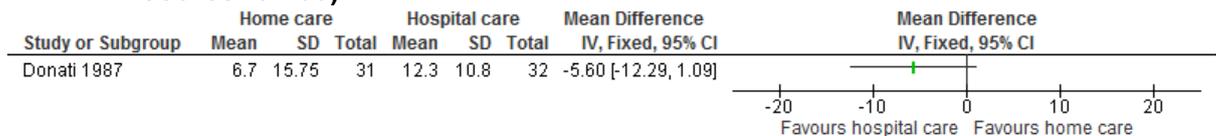
**Comparison 1.1: home versus hospital care for the administration of intravenous antibiotics (IV AB) in people with CF experiencing an acute pulmonary exacerbation**

**Figure 1: Lung function: Change in FEV<sub>1</sub> % predicted at 21 days follow-up (range of scores: 0-100)**



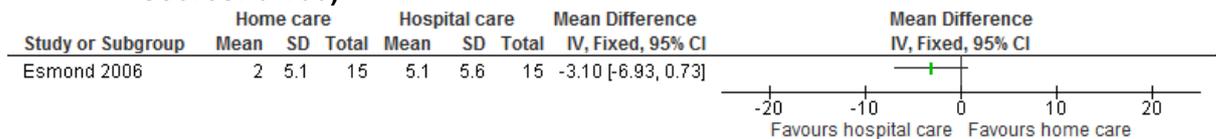
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 2: Lung function: Change in FEV<sub>1</sub> % predicted at 18 days follow-up (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 3: Lung function: Change in FEV<sub>1</sub> % predicted at 15 days follow-up (range of scores: 0-100)**



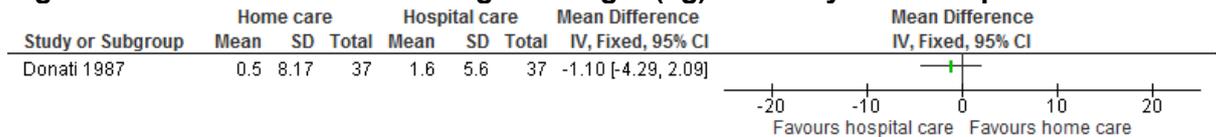
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**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**



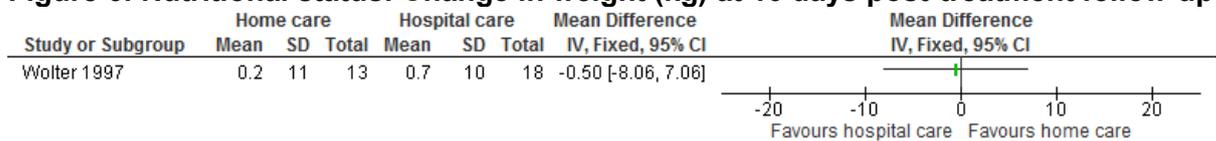
Abbreviations: AB: antibiotics; CI: confidence interval; M-H: Mantel Haenszel;

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



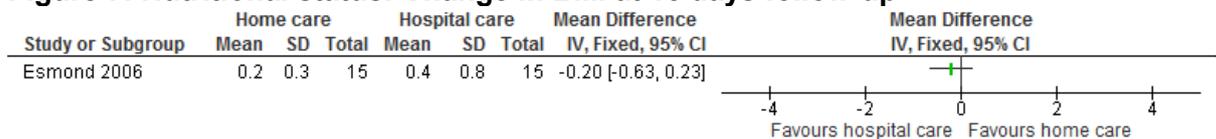
Abbreviations: CI: confidence interval; kg: kilograms; IV: inverse variance; SD: standard deviation;

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



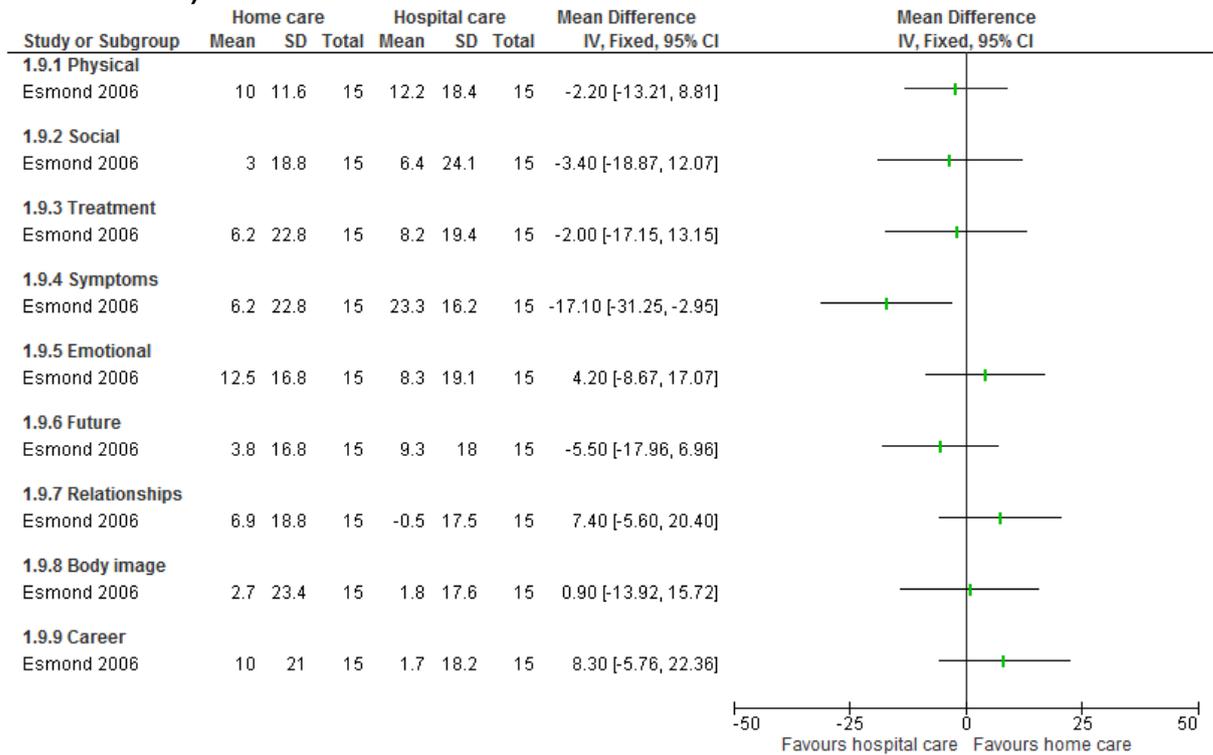
Abbreviations: CI: confidence interval; kg: kilograms; IV: inverse variance; SD: standard deviation;

**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;

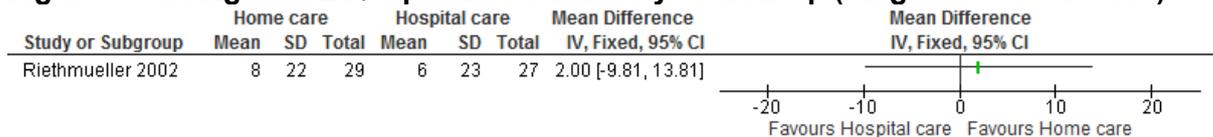
**Figure 8: Change in quality of life (CF-QOL) at 15 days follow-up (range of scores: 0-100)**



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

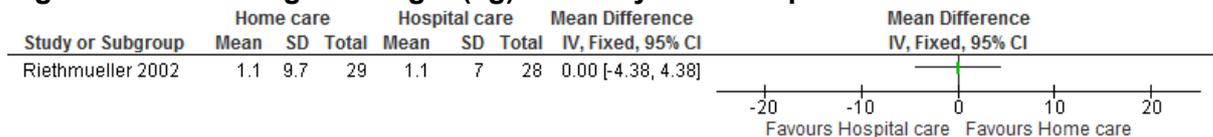
**Comparison 1.2. Home versus hospital care for the administration of intravenous antibiotics (IV AB) in people with CF and chronic pulmonary infection with P. Aeruginosa**

**Figure 9: Change in FEV<sub>1</sub>% predicted at 14 days follow-up (range of scores: 0-100)**



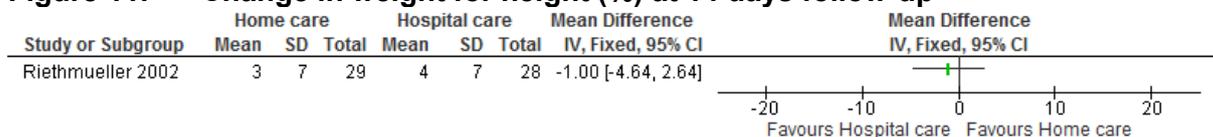
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**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**

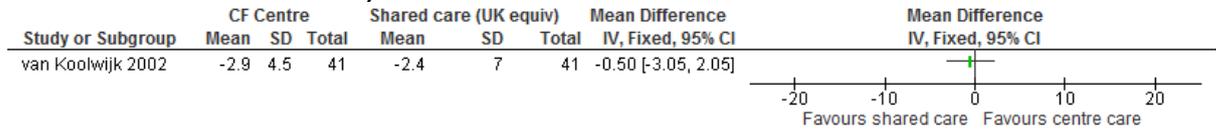


Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

### I.3.1.2 CF centre care

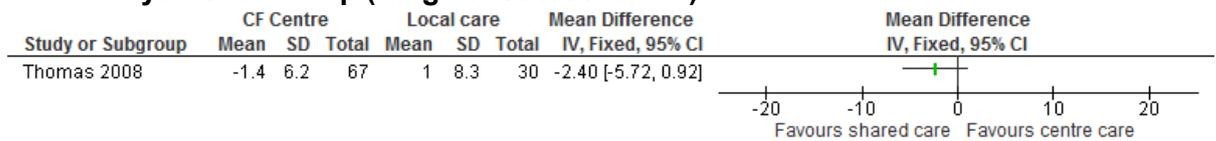
#### Comparison 2.1. CF centre care versus shared care

**Figure 12: Lung function: Change in FEV<sub>1</sub> % predicted at 1 year follow-up (range of scores: 0-100)**



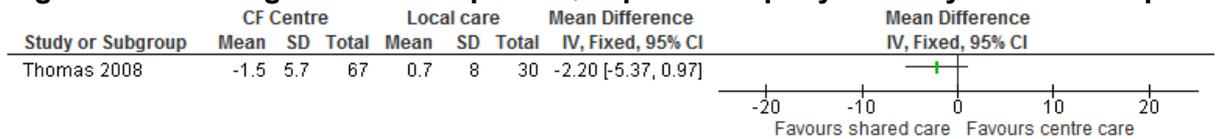
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 13: Lung function: Change from first to last FEV<sub>1</sub> % predicted per year at 3 years follow-up (range of scores: 0-100)**



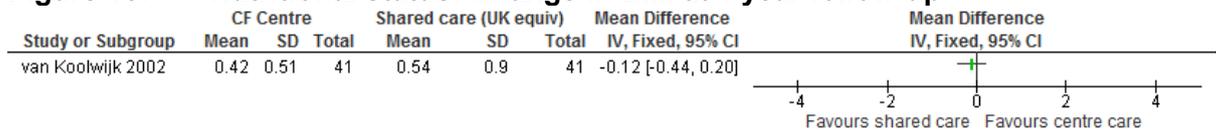
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 14: Lung function: Slope FEV<sub>1</sub> % predicted per year at 3 years follow-up**



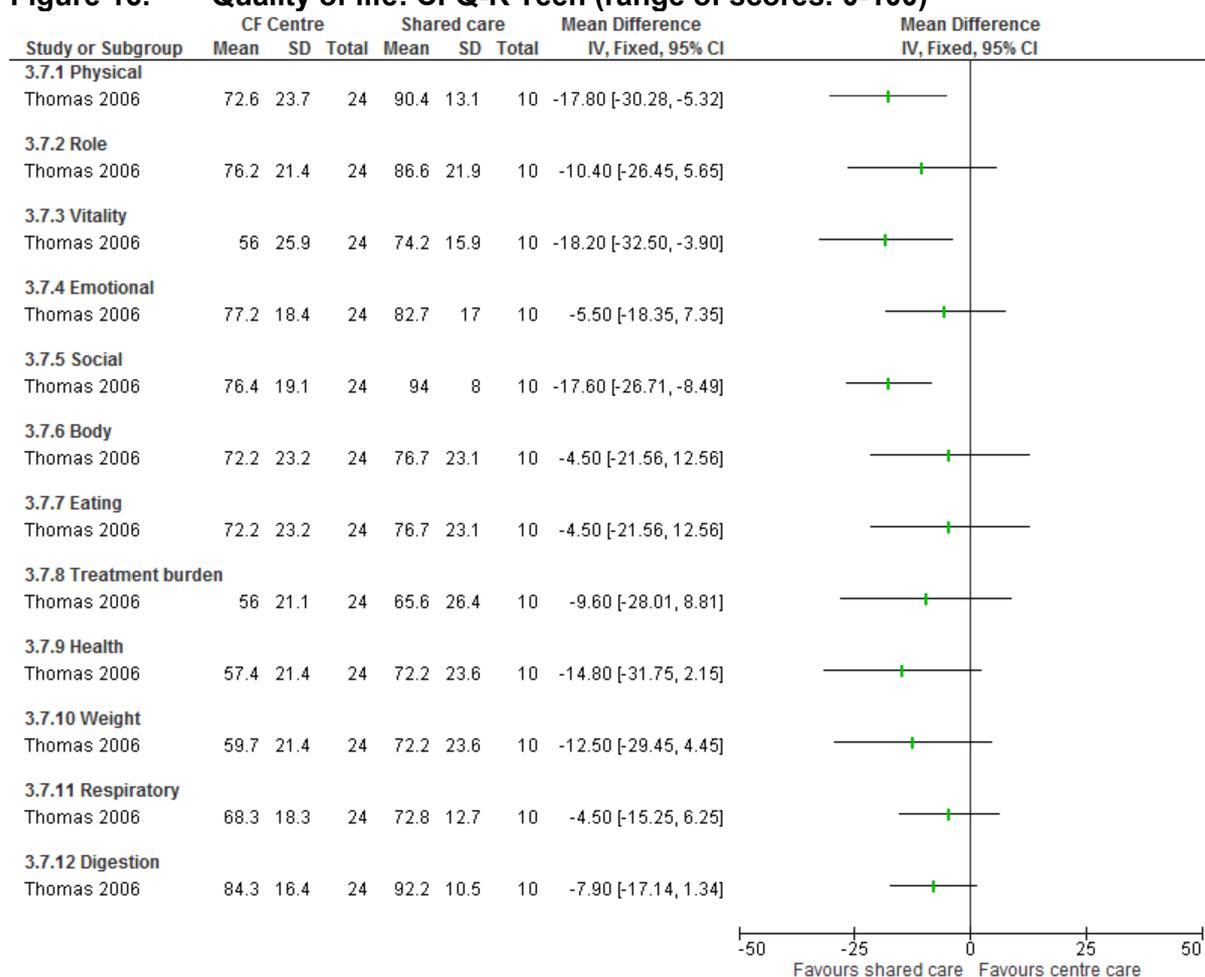
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**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

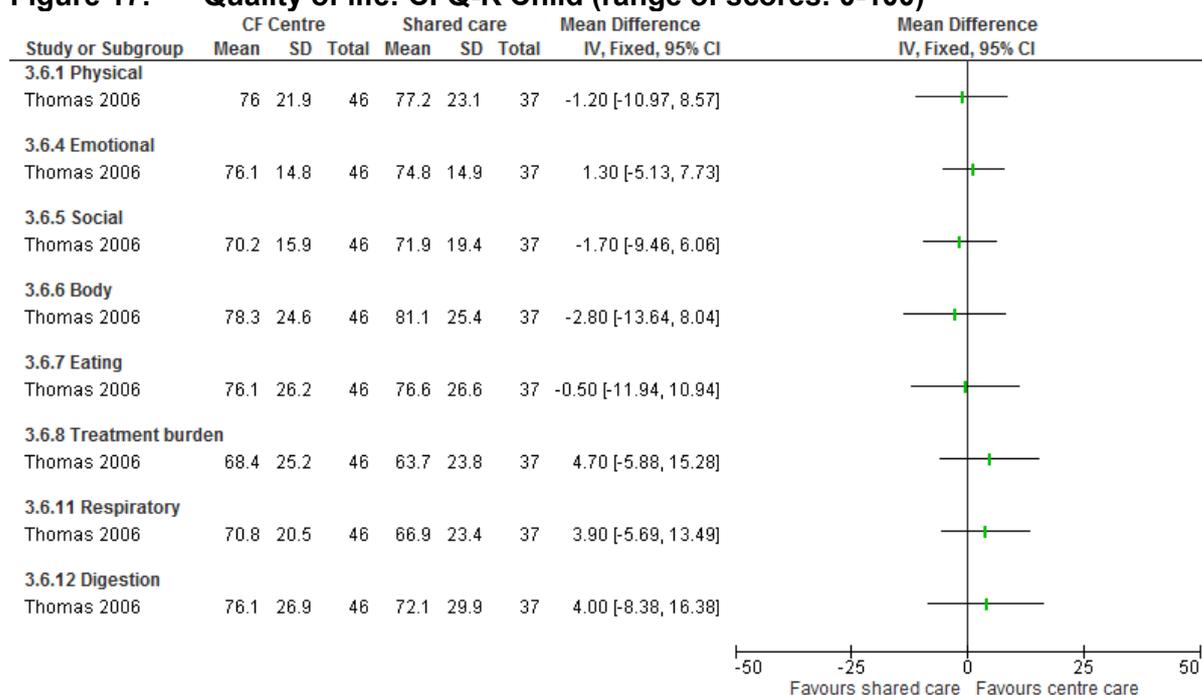
**Figure 16: Quality of life: CFQ-R Teen (range of scores: 0-100)**



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

Note: Cross-sectional study

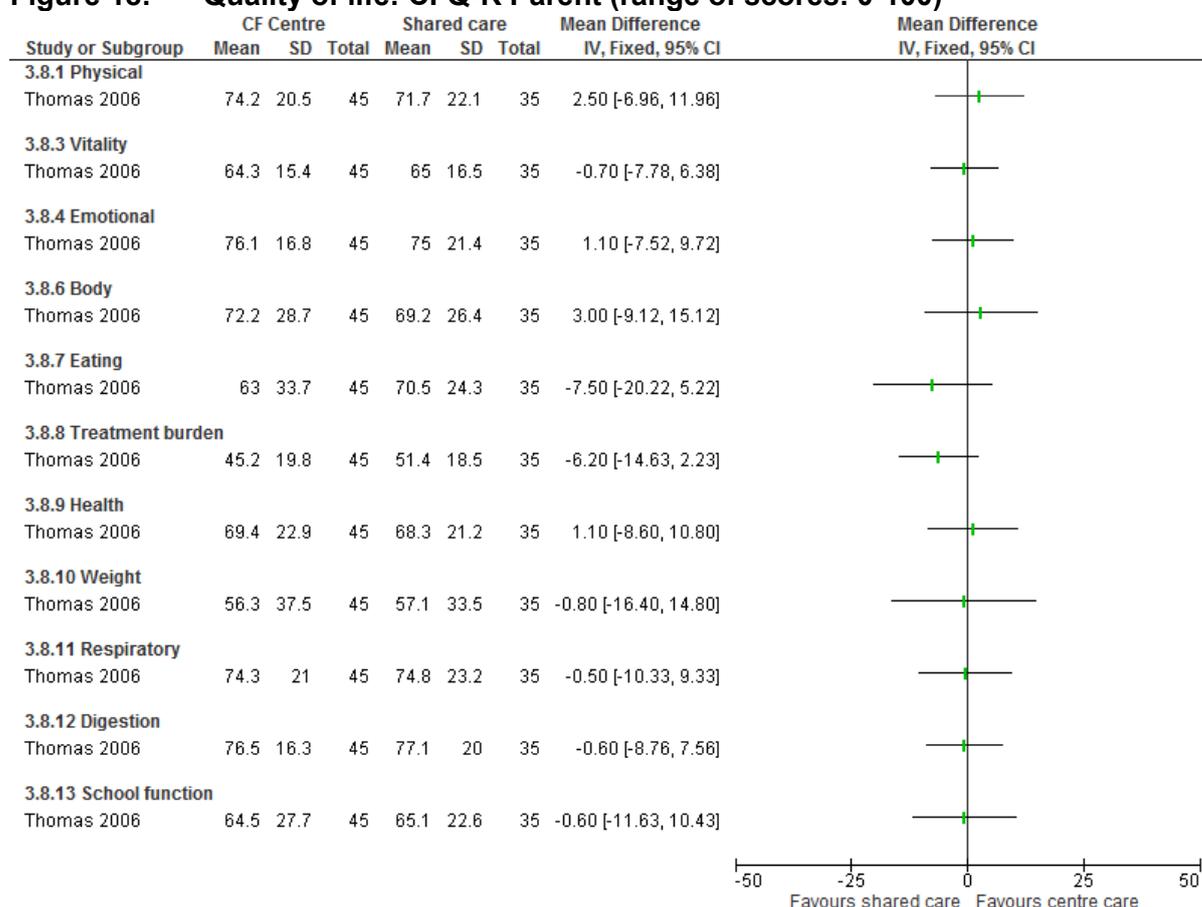
**Figure 17: Quality of life: CFQ-R Child (range of scores: 0-100)**



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)**

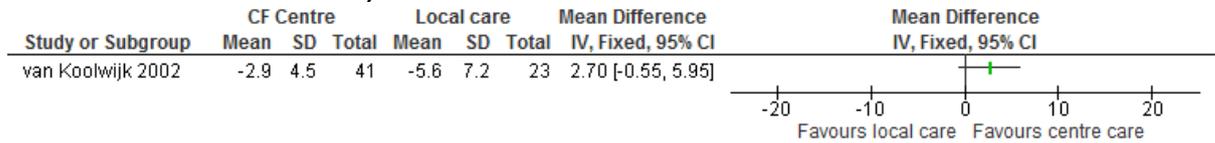


Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation.

Note: Cross-sectional study

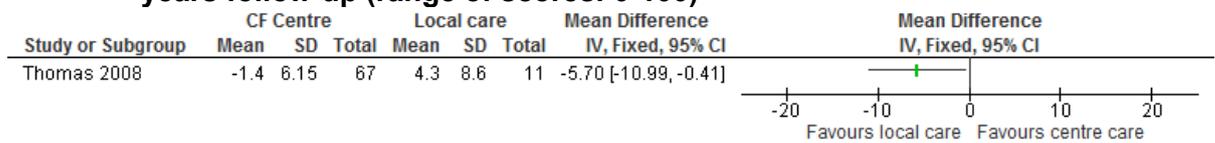
**Comparison 2.2. CF centre care versus local care (below CF Trust recommendations)**

**Figure 19: Lung function: Change in FEV<sub>1</sub> % predicted at 1 year follow-up (range of scores: 0-100)**



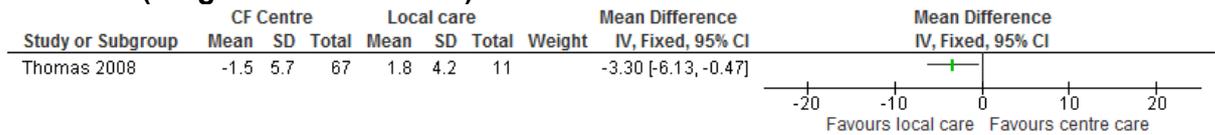
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 20: Lung function: Change from first to last FEV<sub>1</sub> % predicted per year at 3 years follow-up (range of scores: 0-100)**



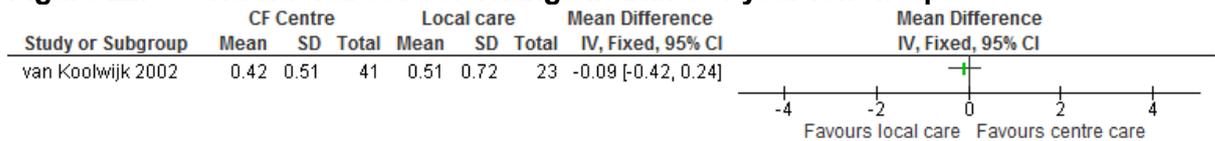
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 21: Lung function: Slope FEV<sub>1</sub> % predicted per year at 3 years follow-up (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: 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;

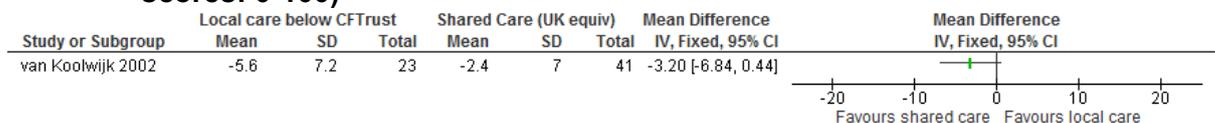
**Comparison 2.3. CF centre care versus general clinic (non-CF)**

Data could not be plotted.

**1.3.1.3 Shared care**

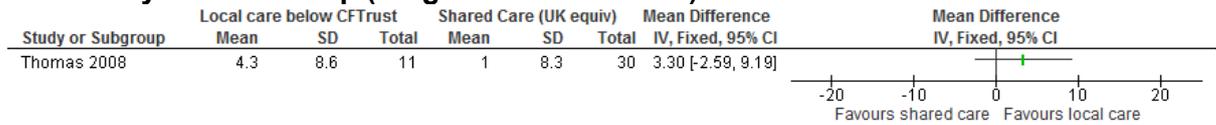
**Comparison 3.1. Local care (below CF Trust Standards) versus shared care (UK equivalent)**

**Figure 23: Lung function: Change in FEV<sub>1</sub> % predicted at 1 year follow-up (range of scores: 0-100)**



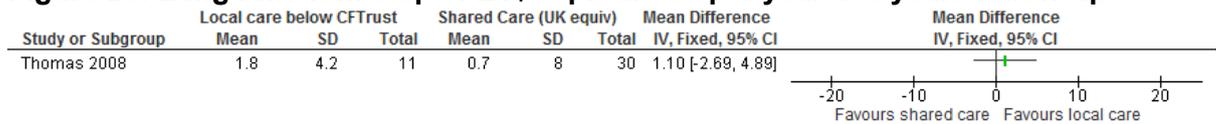
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 24: Lung function: Change from first to last FEV<sub>1</sub>% predicted per year at 3 years follow-up (range of scores: 0-100)**



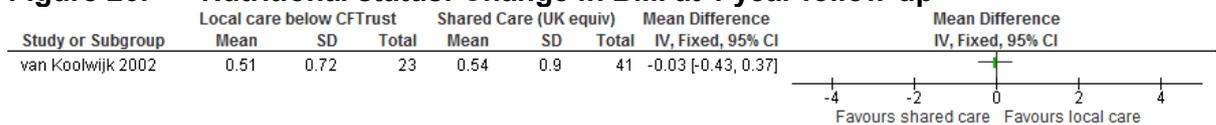
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 25: Lung function: slope FEV<sub>1</sub> % predicted per year at 3 years follow-up**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

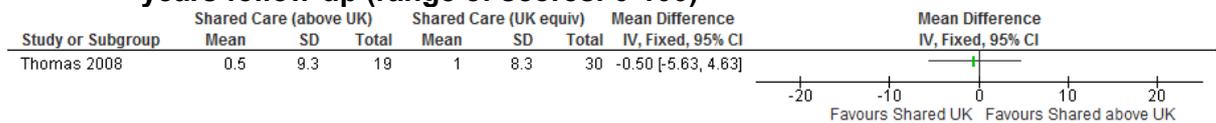
**Figure 26: Nutritional status: Change in BMI at 1 year follow-up**



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

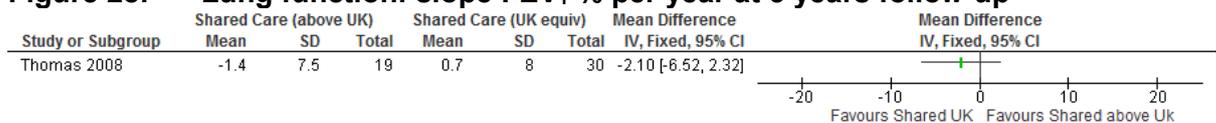
### Comparison 3.2 Shared care (above UK standards) versus shared care (UK equivalent)

**Figure 27: Lung function: Change from first to last FEV<sub>1</sub> % predicted per year at 3 years follow-up (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 28: Lung function: slope FEV<sub>1</sub> % per year at 3 years follow-up**

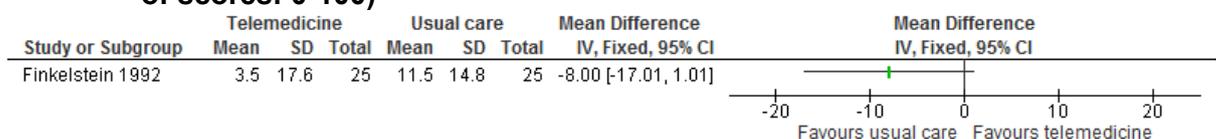


Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

#### 1.3.1.4 Telemedicine

### Comparison 4.1. Home monitoring + diary recording versus usual care

**Figure 29: Lung function: Change in FEV<sub>1</sub> % predicted at 4 years follow-up (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: 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.

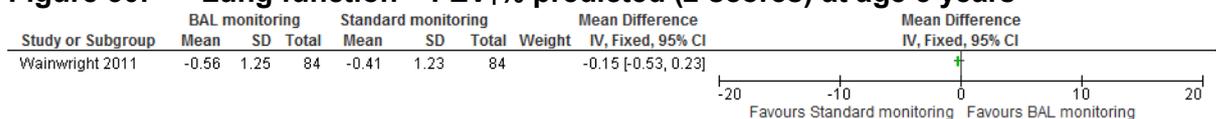
#### I.6.2 Review 2. Monitoring for evolving pulmonary disease in people with CF with established lung disease

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 – FEV<sub>1</sub>% predicted (z-scores) at age 5 years**



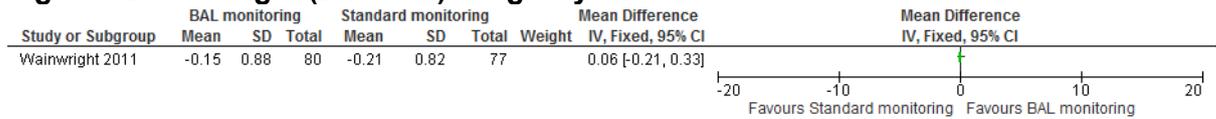
Abbreviations. BAL: bronchoalveolar lavage; CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation. Infants were recruited before age 6 months and followed until age 5 years.

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



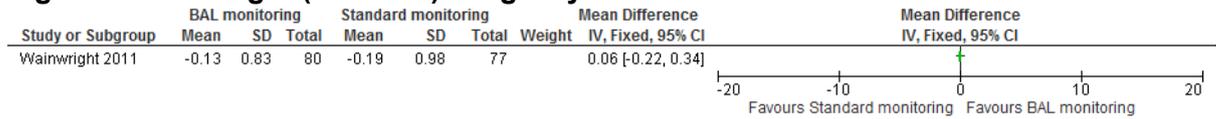
Abbreviations: BAL: bronchoalveolar lavage; M-H: Mantel-Haenszel; CI: confidence interval. Infants were recruited before age 6 months and followed until age 5 years

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



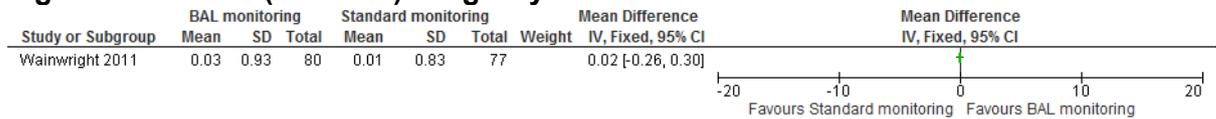
Abbreviations: BAL: bronchoalveolar lavage; SD: standard deviation; IV: inverse variance; CI: confidence interval. Infants were recruited before age 6 months and followed until age 5 years

**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

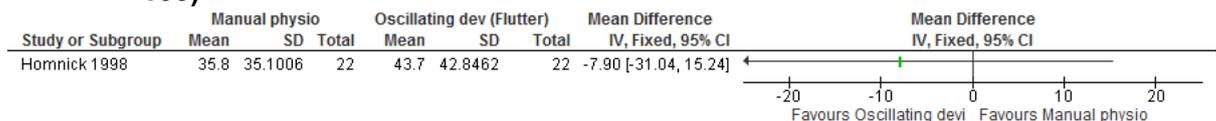
## I.7 Airway clearance techniques

### Comparison 1. Manual physiotherapy versus no airway clearance techniques

No evidence was found for this comparison.

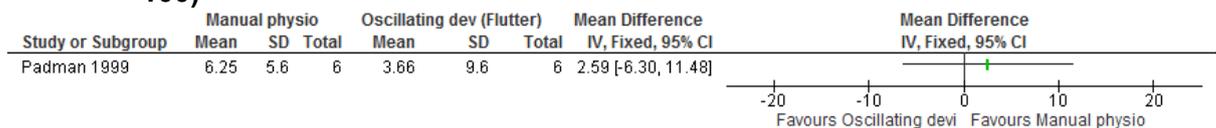
### Comparison 2. Manual physiotherapy techniques versus oscillating devices

**Figure 35: Change in FEV<sub>1</sub> % predicted after 8.8 days follow-up (range of scores: 0-100)**



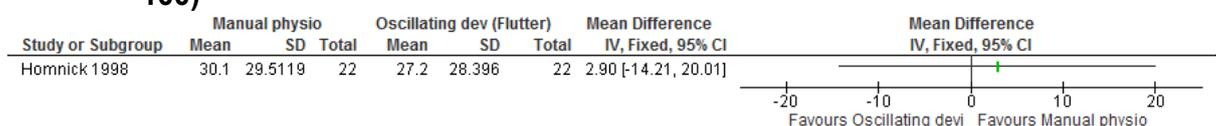
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 36: Change in FEV<sub>1</sub> % predicted at 1 month follow-up (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

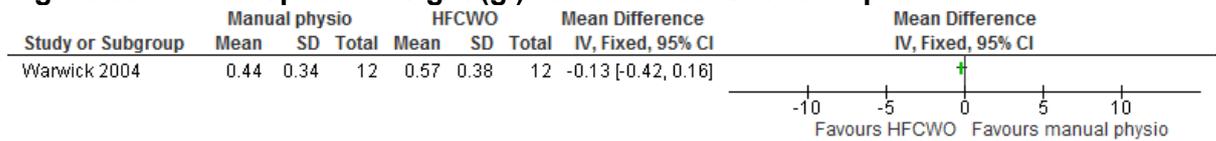
**Figure 37: Change in FVC % predicted at 2 weeks follow-up (range of scores: 0-100)**



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

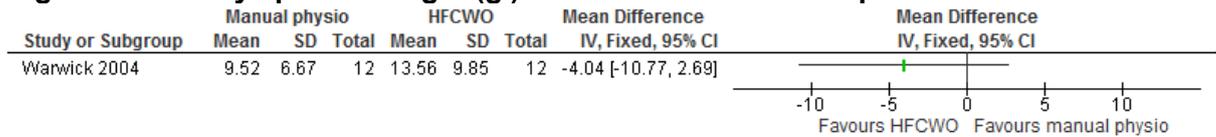
### Comparison 3. Manual physiotherapy versus high frequency chest wall oscillation (HFCWO)

**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

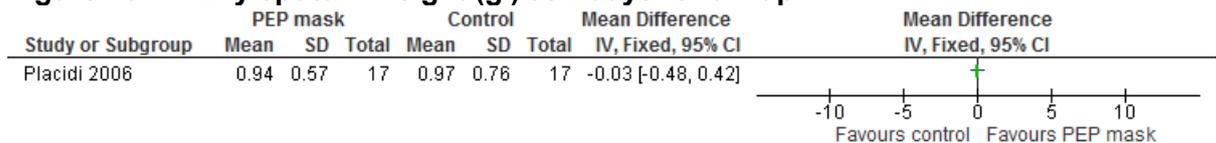
**Figure 39: Dry sputum weight (g.) at 1 to 2 weeks follow-up**



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

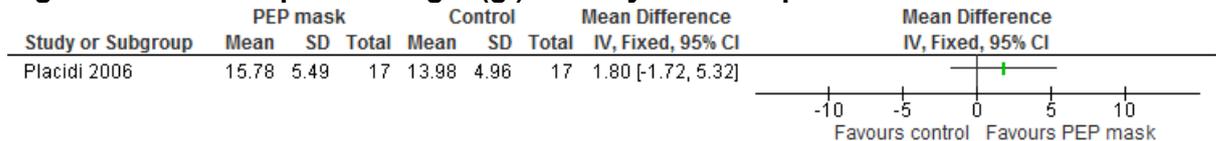
### Comparison 4. Positive expiratory pressure mask (PEP) versus no airway clearance technique

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



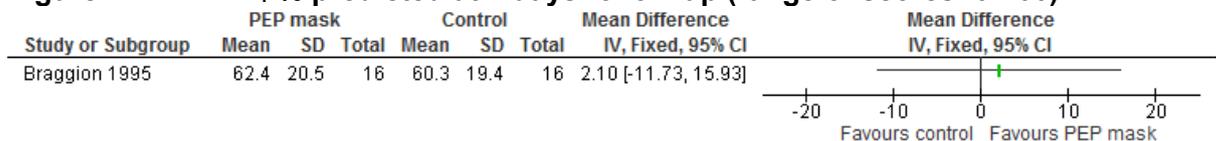
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

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



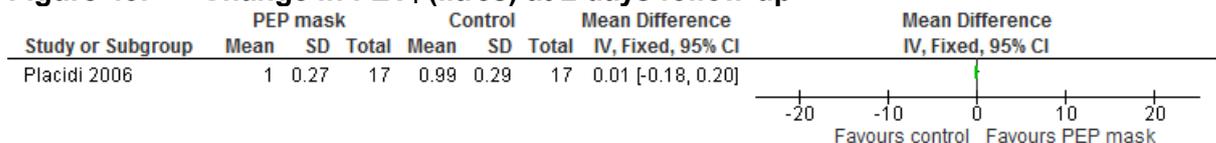
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

**Figure 42: FEV<sub>1</sub> % predicted at 2 days follow-up (range of scores: 0-100)**



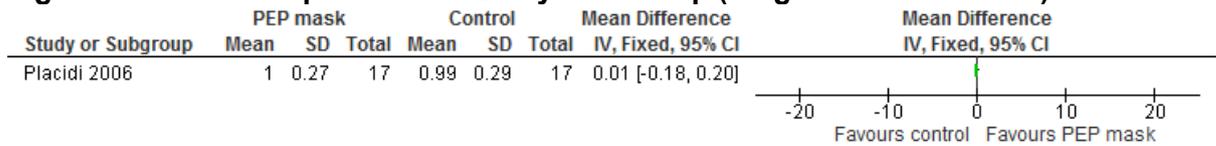
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 43: Change in FEV<sub>1</sub> (litres) at 2 days follow-up**



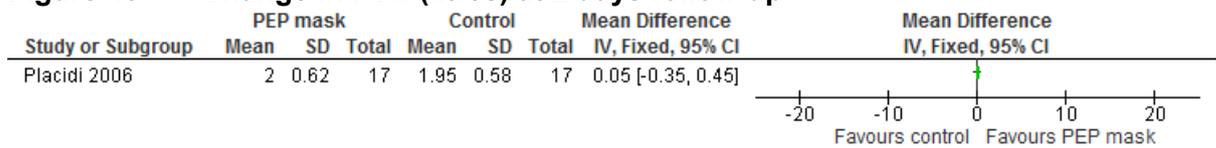
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

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



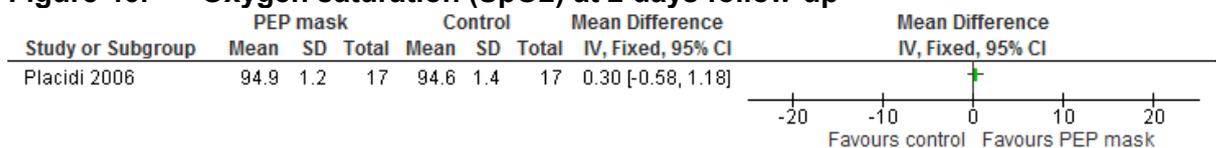
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

**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**



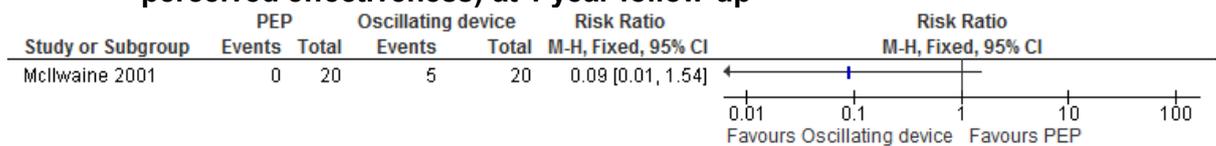
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

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

No evidence was found for this comparison.

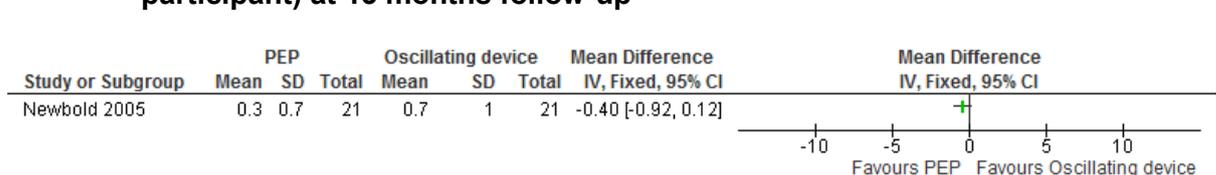
**Comparison 6. Positive expiratory pressure mask (PEP) versus oscillating devices**

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



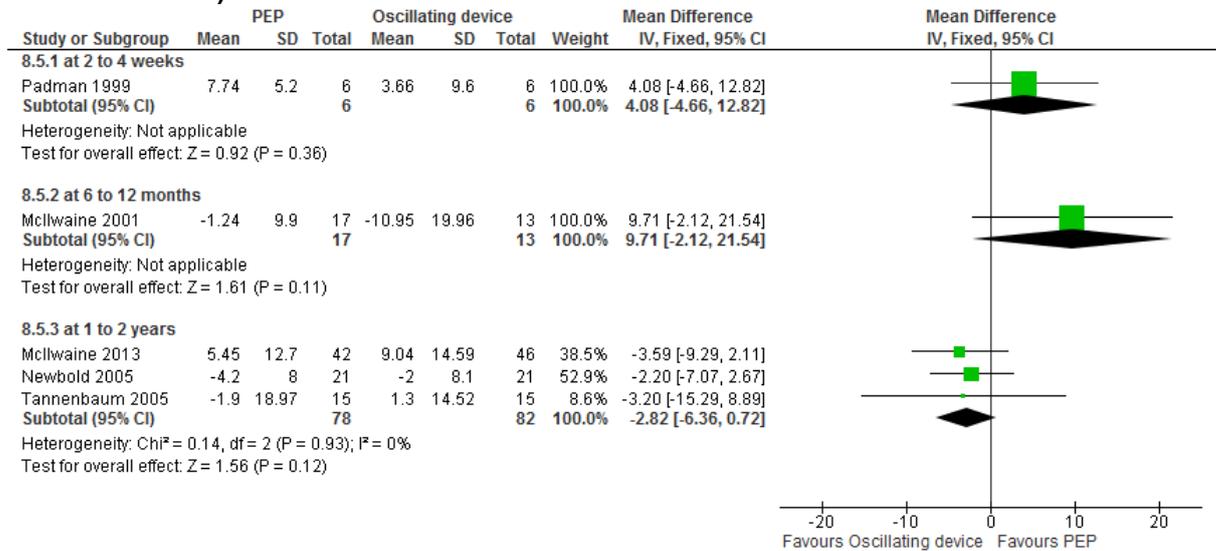
Abbreviations: PEP: positive expiratory pressure mask; M-H: Mantel-Haenszel; CI: confidence interval

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



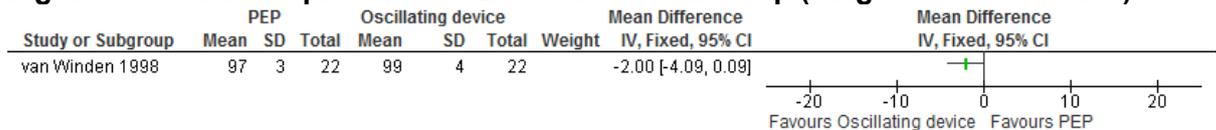
Abbreviations: PEP: positive expiratory pressure mask; SD: standard deviation; IV: inverse variance; CI: confidence interval

**Figure 49: Change in FEV<sub>1</sub> % predicted at up to 2 years follow-up (range of scores: 0-100)**



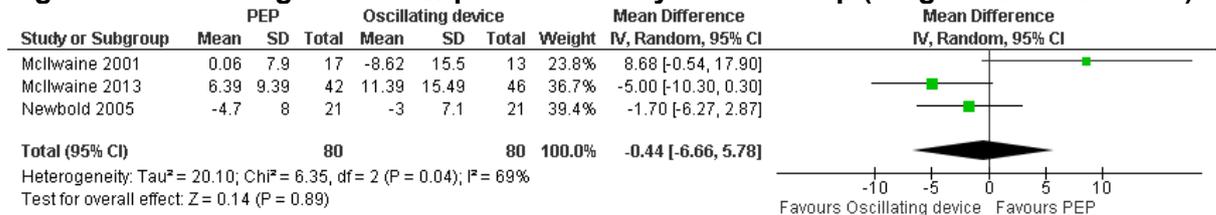
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

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



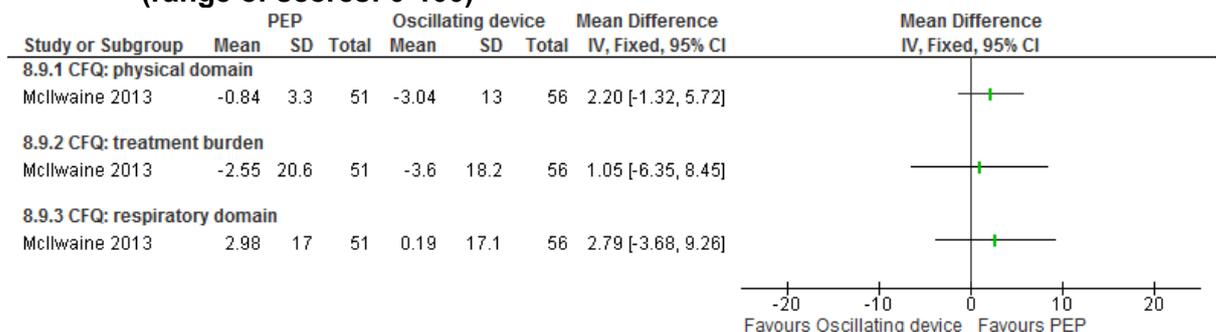
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

**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

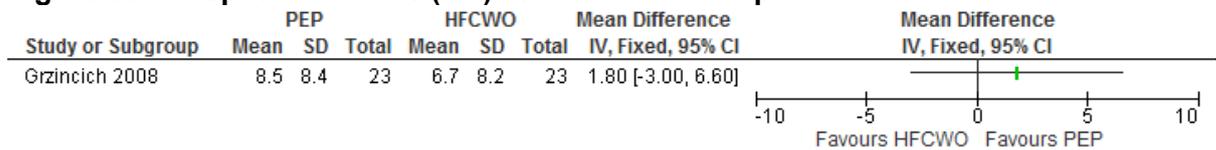
**Figure 52: Change in quality of life (measured with CF-QOL) at 1 year follow-up (range of scores: 0-100)**



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

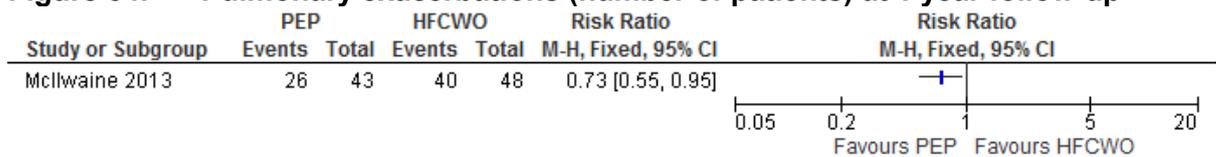
### Comparison 7. Positive expiratory pressure mask (PEP) versus high frequency chest wall oscillation (HFCWO)

**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**



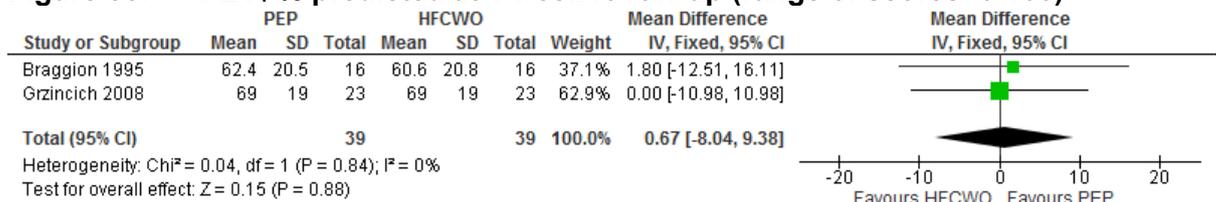
Abbreviations: PEP: positive expiratory pressure mask; HFCWO: high frequency chest wall oscillation; M-H: Mantel-Haenszel; CI: confidence interval

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



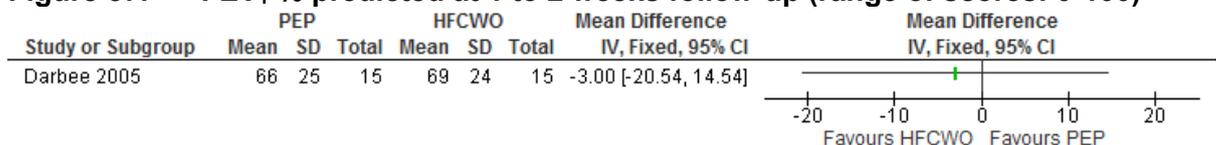
Abbreviations: PEP: positive expiratory pressure mask; HFCWO: high frequency chest wall oscillation; M-H: Mantel-Haenszel; CI: confidence interval

**Figure 56: FEV<sub>1</sub> % predicted at 1 week follow-up (range of scores: 0-100)**



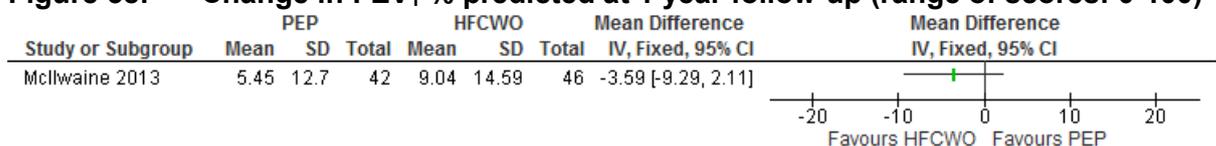
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV<sub>1</sub>: forced expiratory volume in 1 second; HFCWO: high frequency chest wall oscillation; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

**Figure 57: FEV<sub>1</sub> % predicted at 1 to 2 weeks follow-up (range of scores: 0-100)**



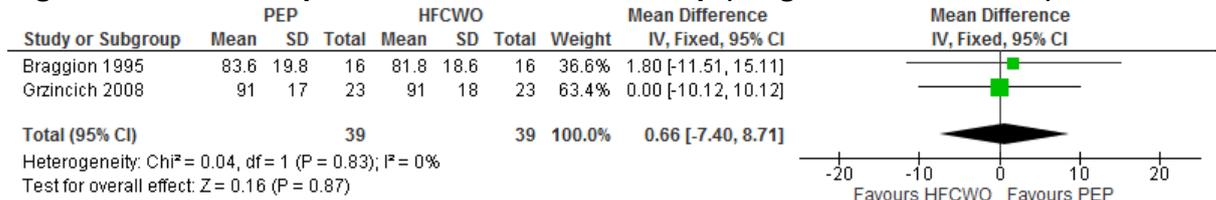
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; HFCWO: high frequency chest wall oscillation; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

**Figure 58: Change in FEV<sub>1</sub> % predicted at 1 year follow-up (range of scores: 0-100)**



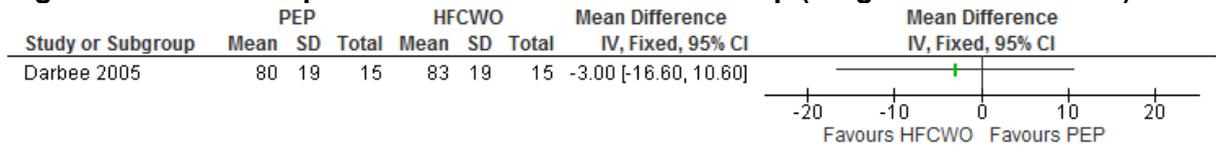
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; HFCWO: high frequency chest wall oscillation; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

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



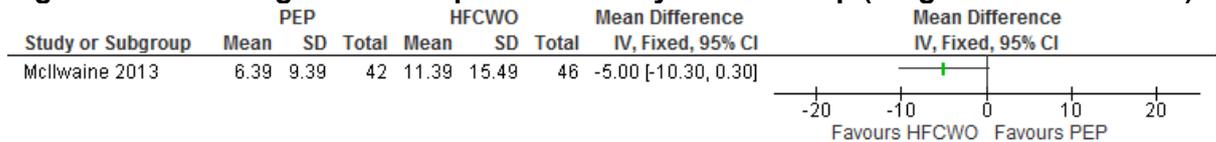
Abbreviations: CI: confidence interval; df: degrees of freedom; FVC: forced vital capacity; HFCWO: high frequency chest wall oscillation; IV: inverse variance; PEP: positive expiratory pressure mask; SD: standard deviation

**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**

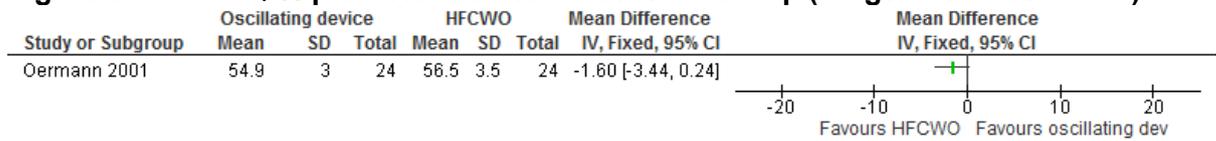
No evidence was retrieved for this comparison.

**Comparison 11. Oscillating device versus no airway clearance technique**

No evidence was retrieved for this comparison.

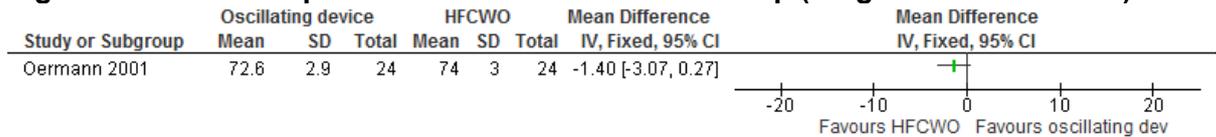
### Comparison 12. Oscillating device versus high frequency chest wall oscillation (HFCWO)

**Figure 62: FEV<sub>1</sub> % predicted at 2 to 4 weeks follow-up (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: 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)**



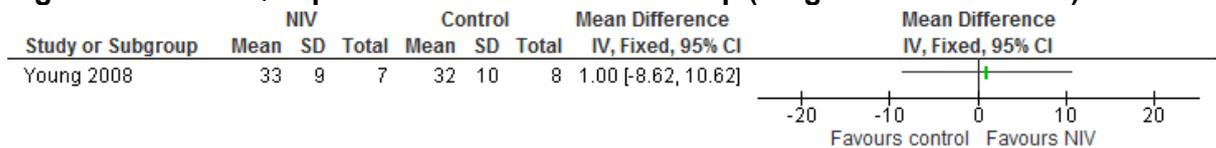
Abbreviations: CI: confidence interval; FVC: forced vital capacity; HFCWO: high frequency chest wall oscillation; IV: inverse variance; SD: standard deviation

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

No evidence was found for this comparison.

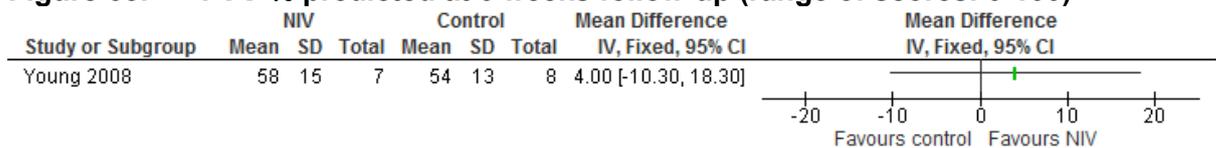
### Comparison 14. Non-invasive ventilation (NIV) versus no airway clearance technique

**Figure 64: FEV<sub>1</sub> % predicted at 6 weeks follow-up (range of scores: 0-100)**



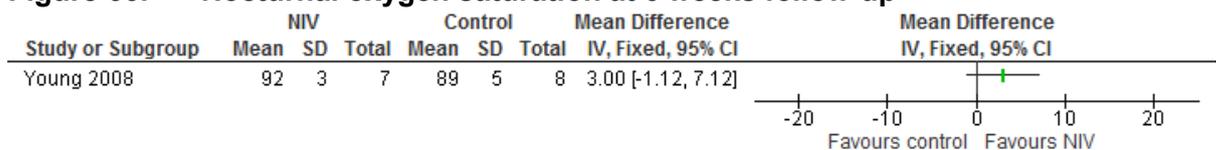
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; NIV: non-invasive ventilation; SD: standard deviation;

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



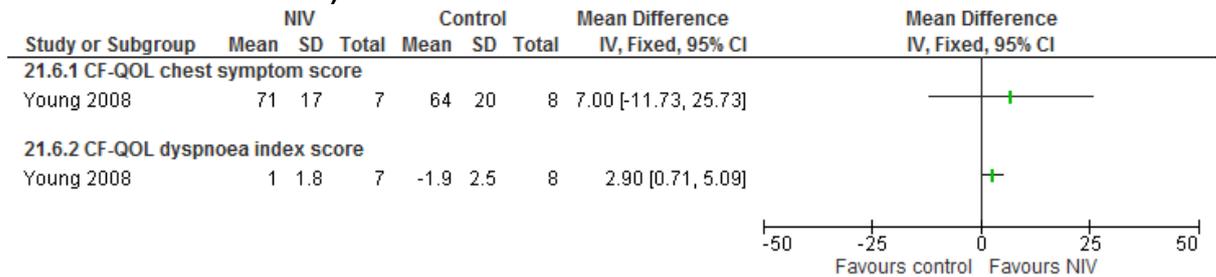
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; NIV: non-invasive ventilation; SD: standard deviation

**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)**



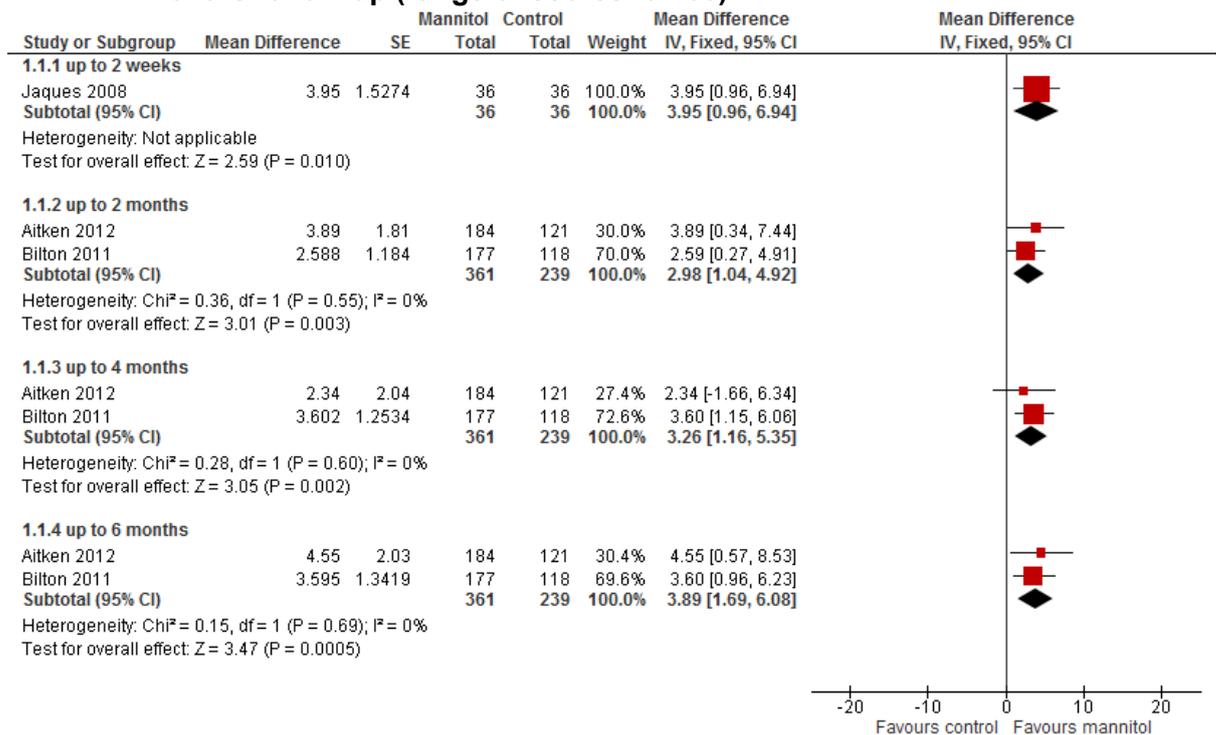
Abbreviations: CI: confidence interval; CF-QOL: cystic fibrosis quality of life questionnaire; IV: inverse variance; NIV: non-invasive ventilation; SD: standard deviation

## I.8 Mucoactive agents

### I.8.1 Mannitol

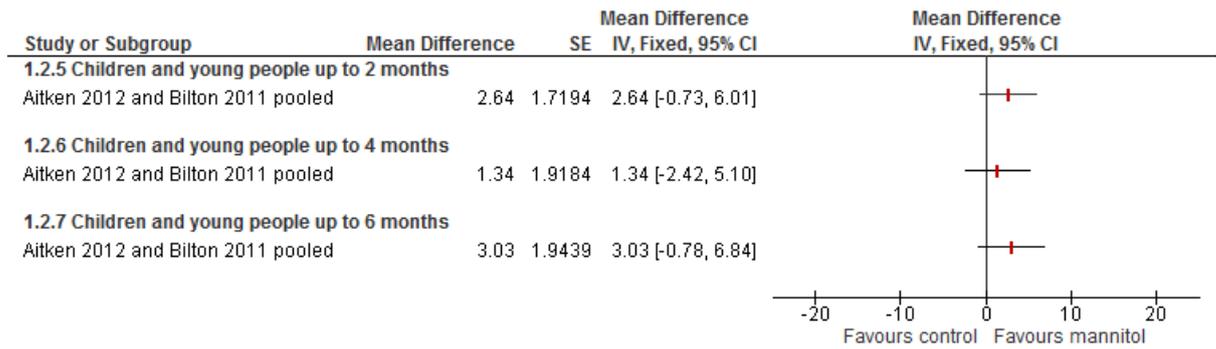
#### Comparison 1.1. Mannitol versus placebo

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



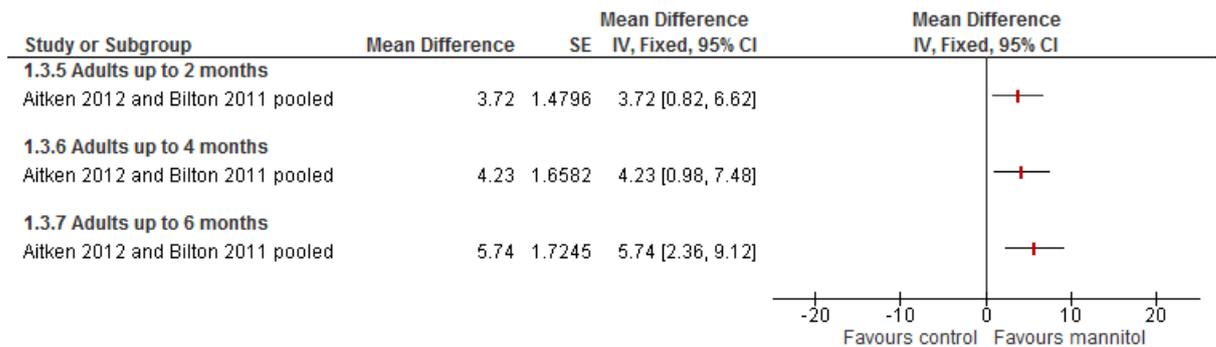
Abbreviations: CI: confidence interval; FEV1: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error

**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)**



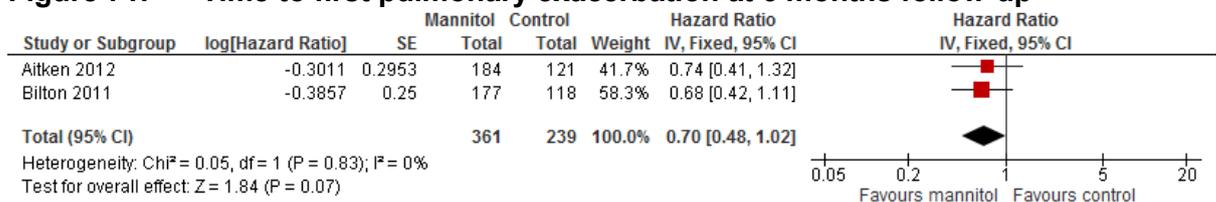
Abbreviations: CI: confidence interval; FEV1: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error  
Data was extracted from Cochrane SR Nolan 2015. Data was already pooled for Aitken 2012 and Bilton 2011 studies

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



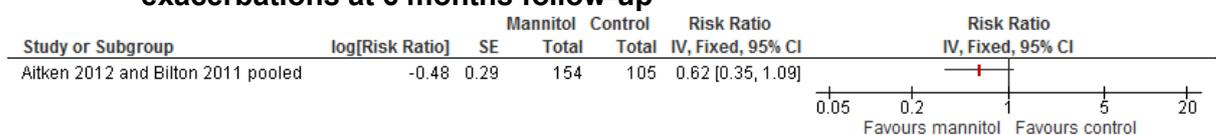
Abbreviations: CI: confidence interval; FEV1: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error  
Data was extracted from Cochrane SR Nolan 2015. Data was already pooled for Aitken 2012 and Bilton 2011 studies

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



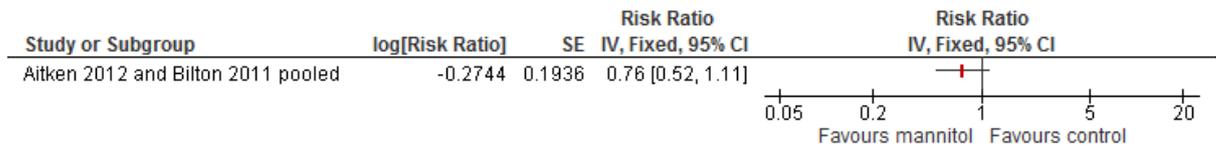
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

**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

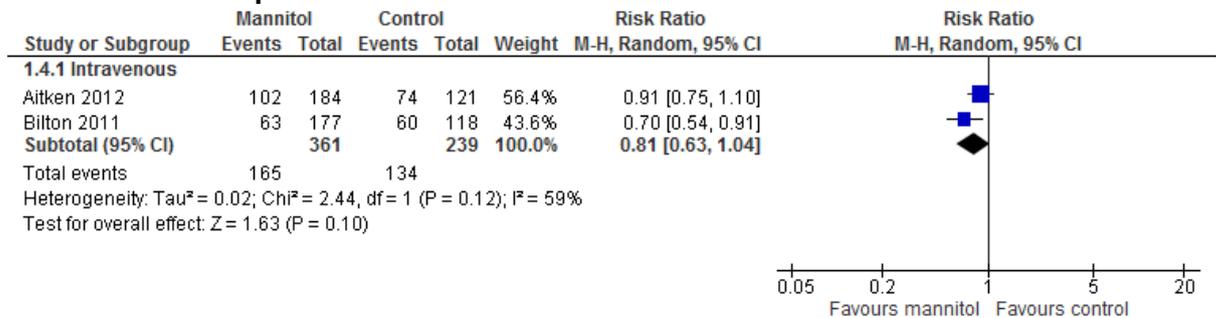
**Figure 73: Number of adults with protocol defined exacerbations at 6 months follow-up**



Abbreviations: IV: inverse variance; SE: standard error

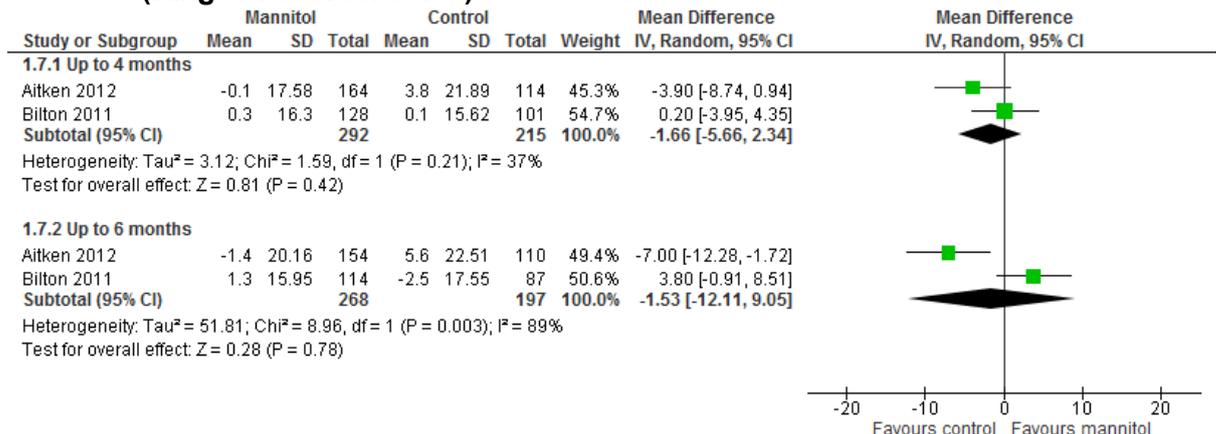
Data was extracted from Cochrane SR Nolan 2015. Data was already pooled for Aitken 2012 and Bilton 2011 studies

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



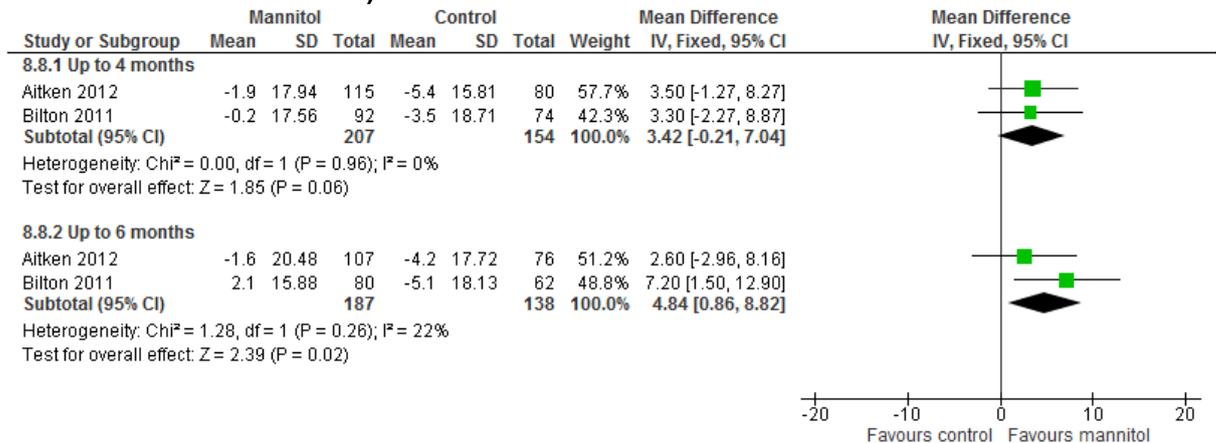
Abbreviations: CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel

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



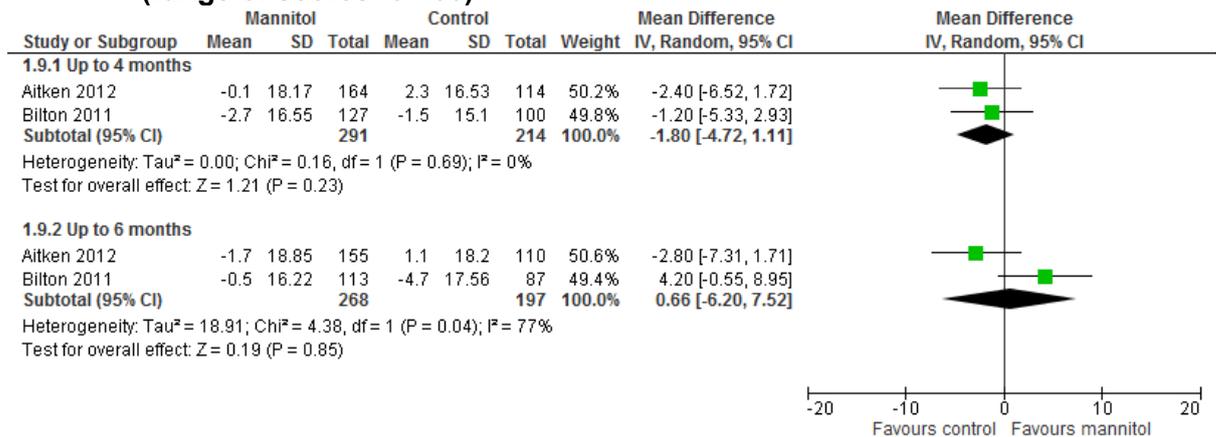
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

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



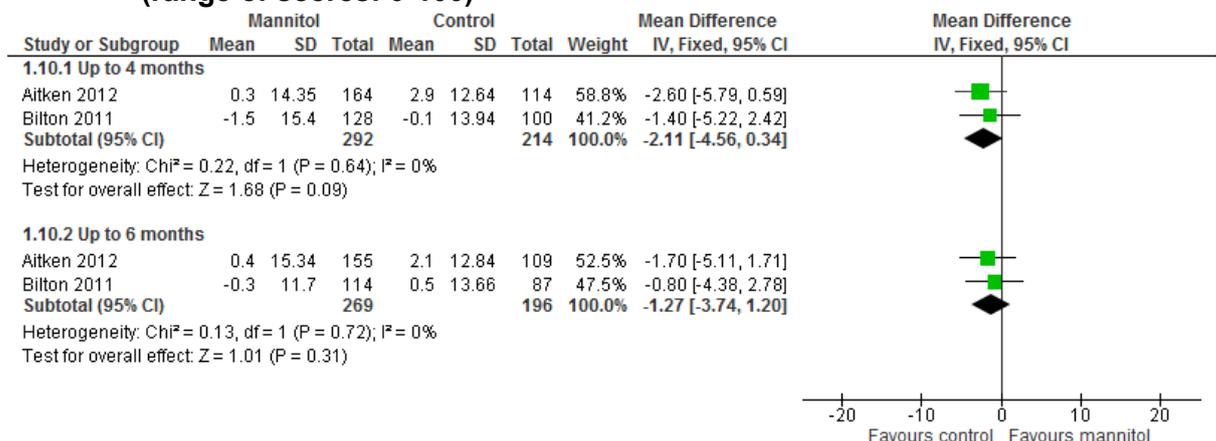
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

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



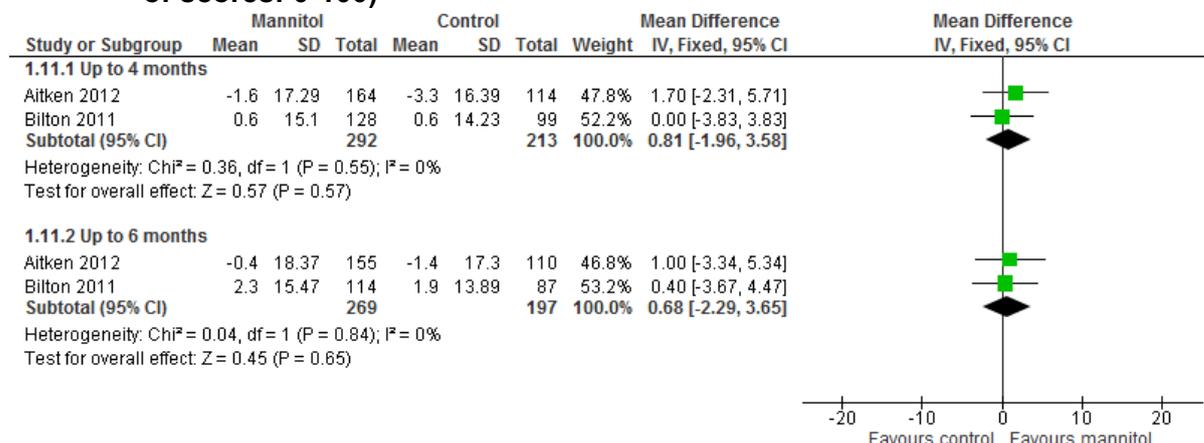
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

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



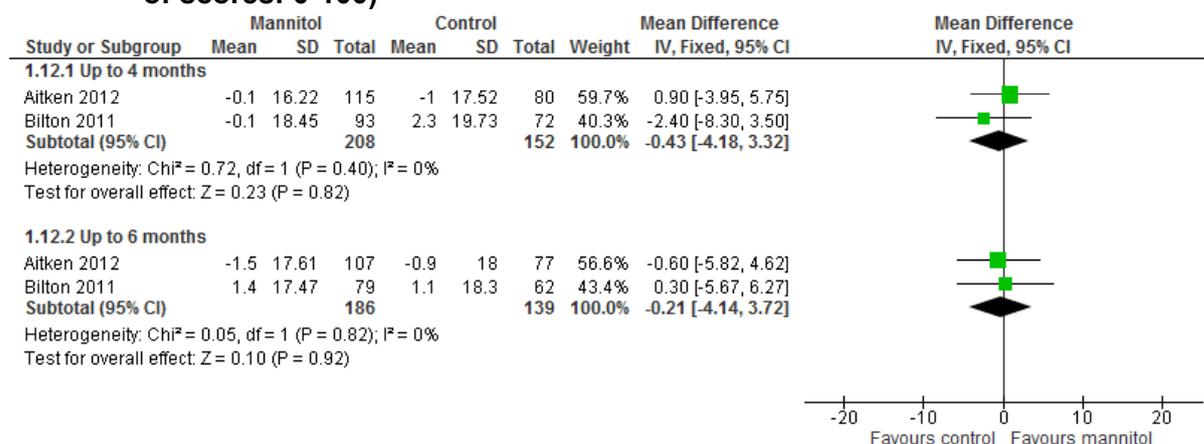
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

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



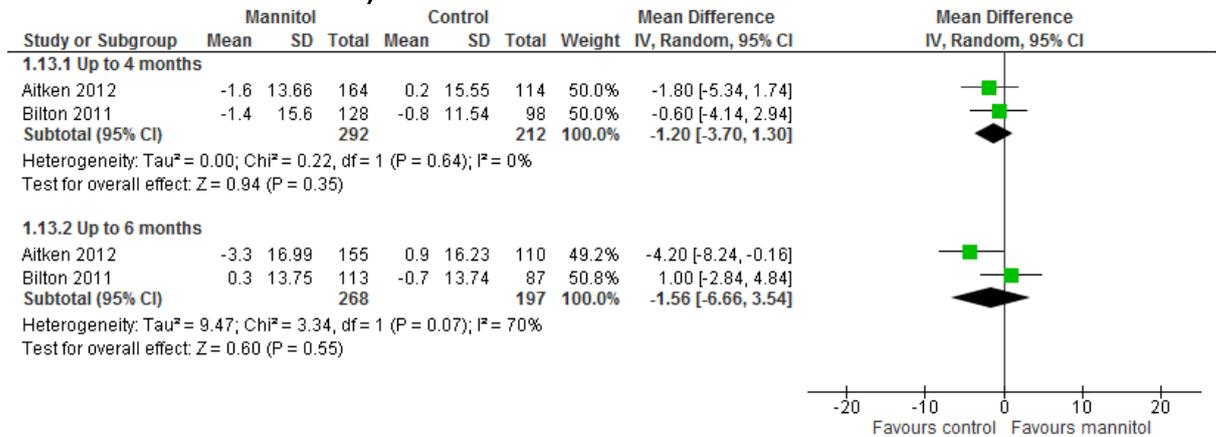
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

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



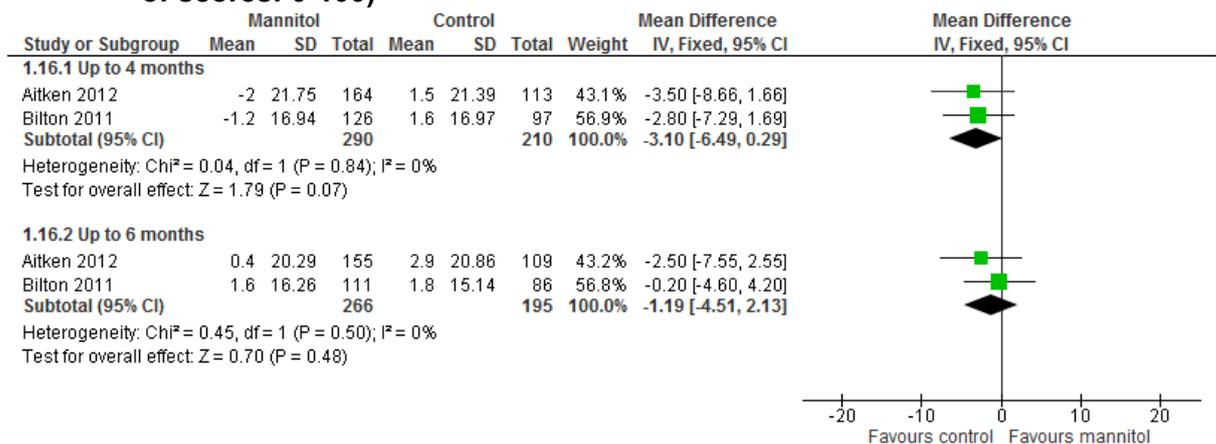
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

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



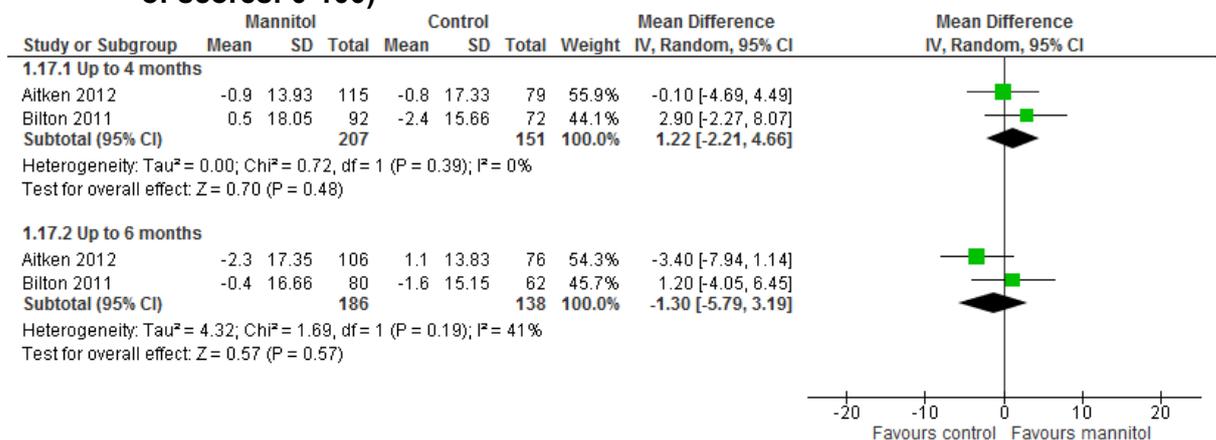
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

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



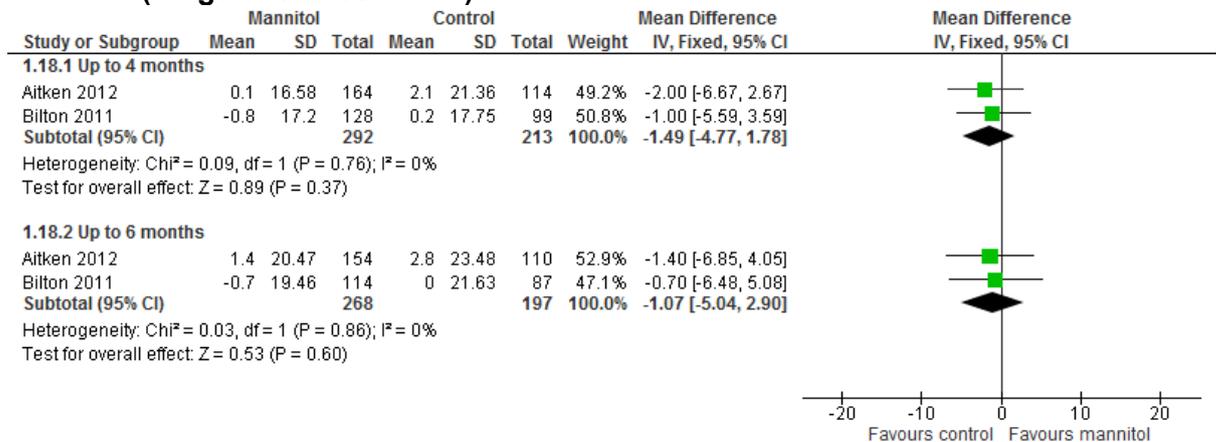
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

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



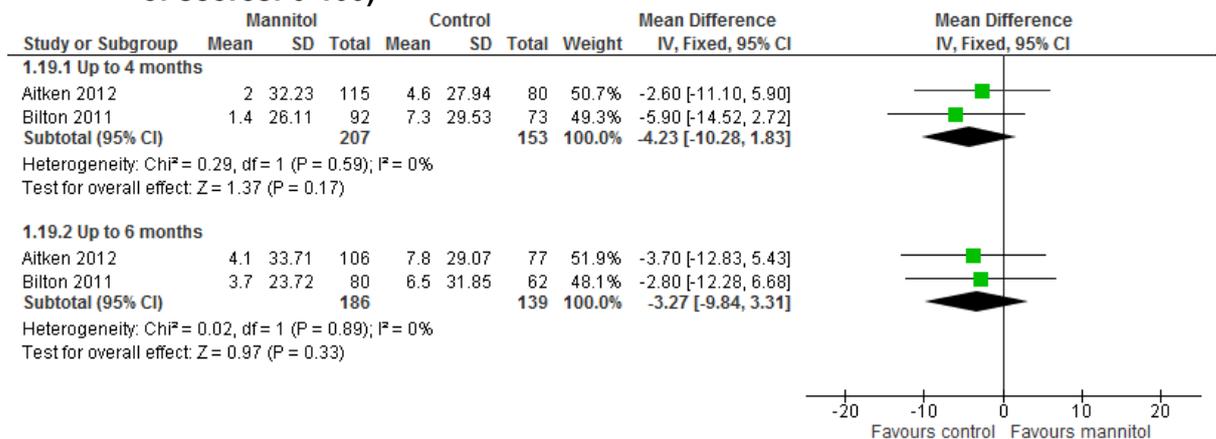
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

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



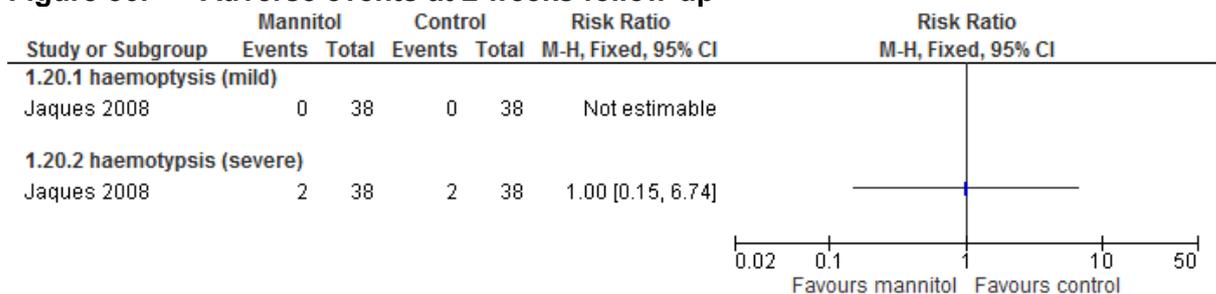
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

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



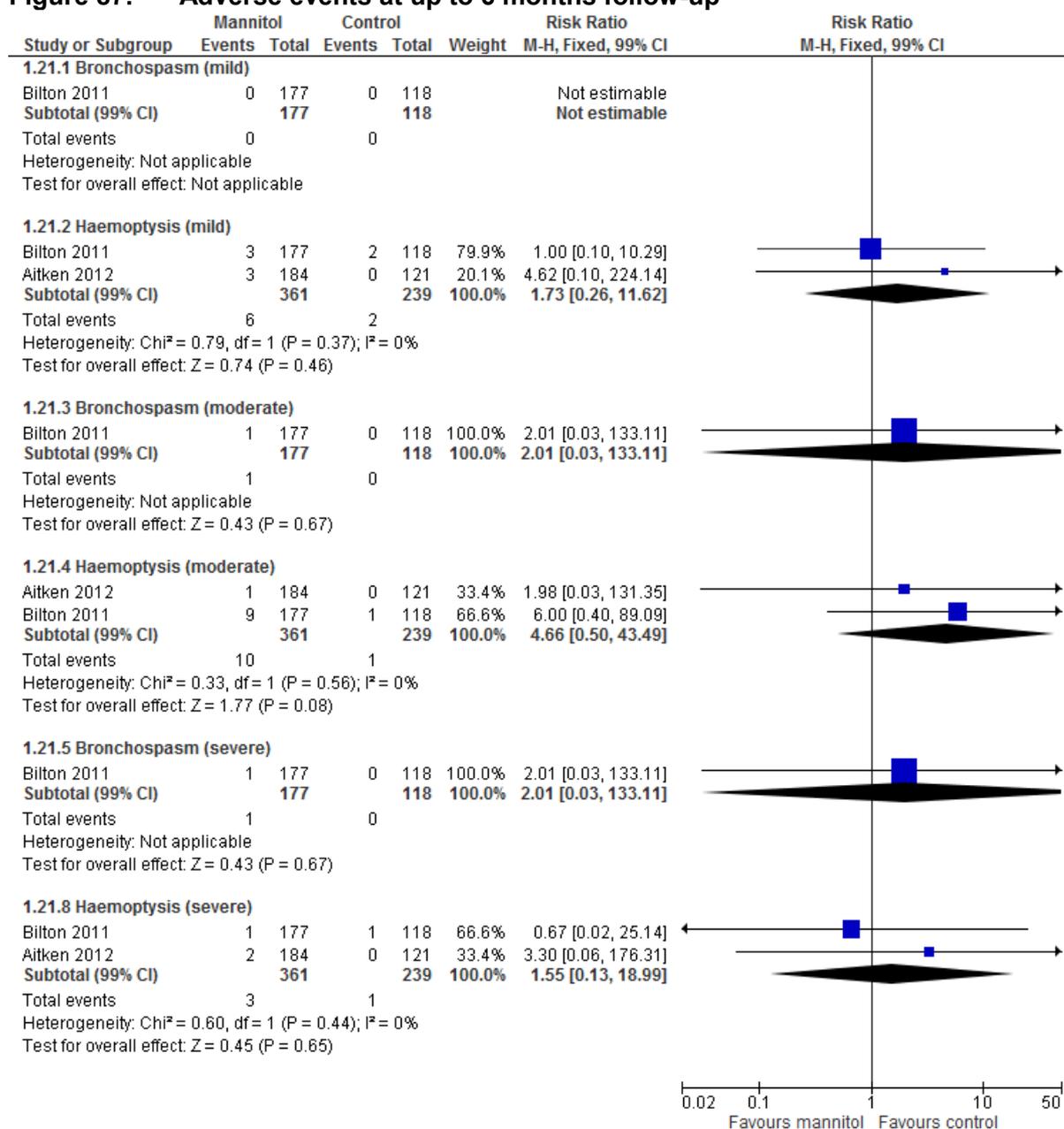
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

**Figure 86: Adverse events at 2 weeks follow-up**



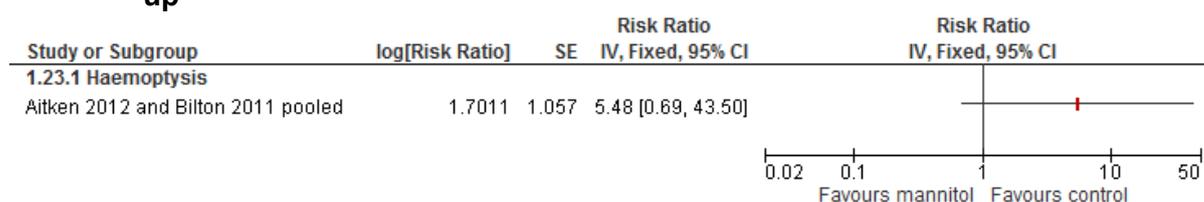
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

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



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

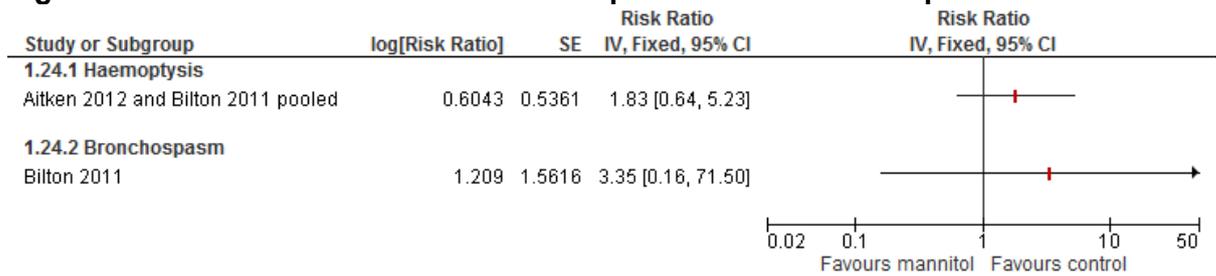
**Figure 88: Adverse events in children and young people at up to 6 months follow-up**



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**

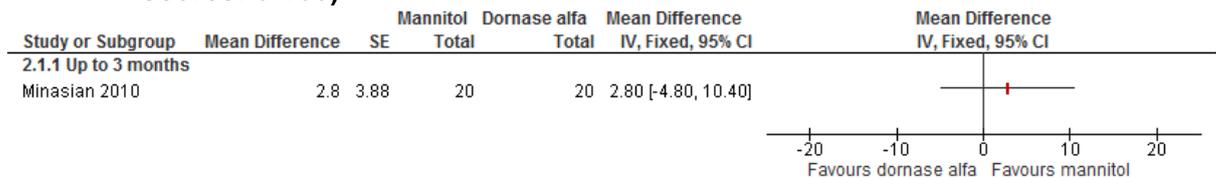


Abbreviations: IV: inverse variance; SE: standard error

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**

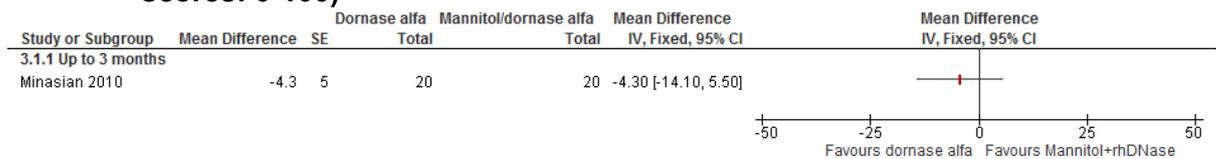
**Figure 90: Lung function – FEV<sub>1</sub> % change from baseline up to 3 months (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: 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 – FEV<sub>1</sub> % change from baseline up to 3 months (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: 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.

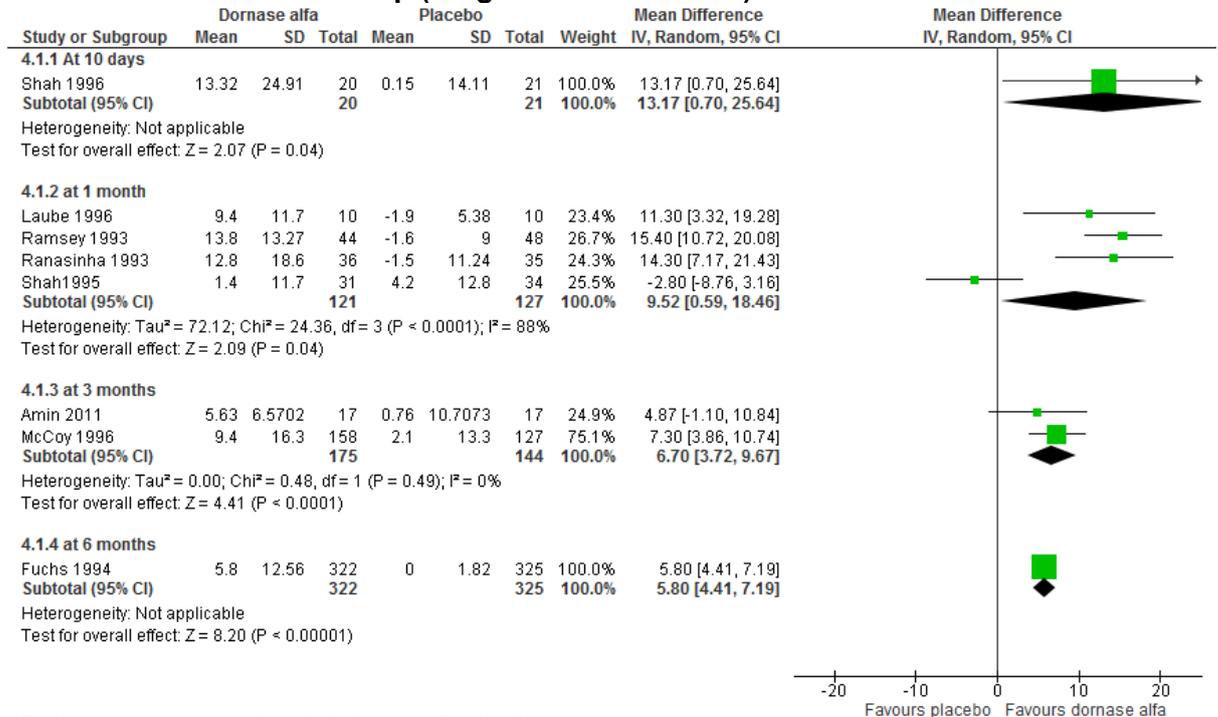
**Comparison 1.4. Mannitol versus acetylcysteine**

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 FEV<sub>1</sub> at 10 days; and at 1, 3 & 6 months follow-up (range of scores: 0-100)**

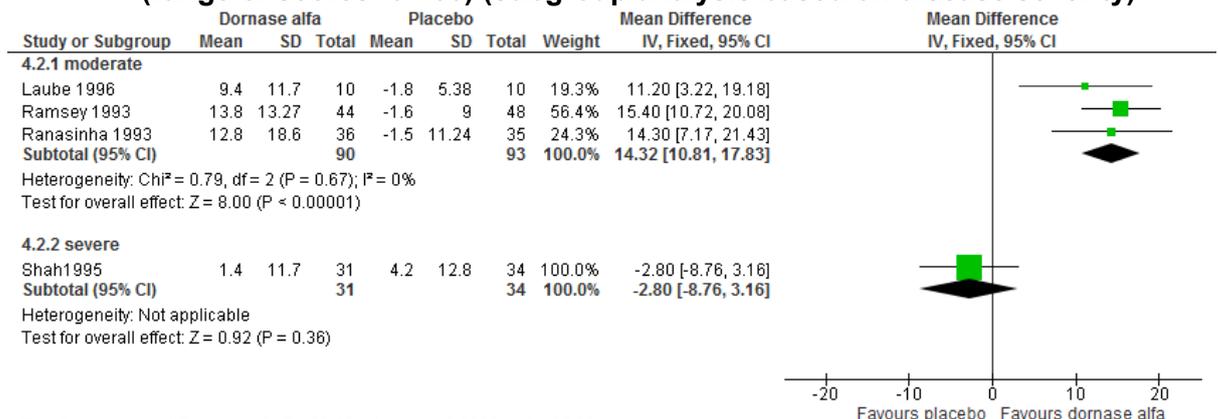


Test for subgroup differences: Chi<sup>2</sup> = 2.13, df = 3 (P = 0.55), I<sup>2</sup> = 0%

Abbreviations: CI: confidence interval; df: degrees of freedom; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation.

Note: See sensitivity analysis

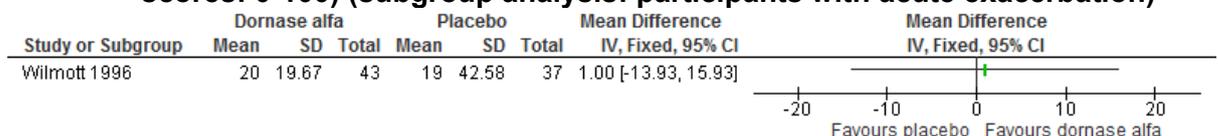
**Figure 93: Lung function: relative mean % change in FEV<sub>1</sub> at 1 month follow-up (range of scores: 0-100) (subgroup analysis based on disease severity)**



Test for subgroup differences: Chi<sup>2</sup> = 23.56, df = 1 (P < 0.00001), I<sup>2</sup> = 95.8%

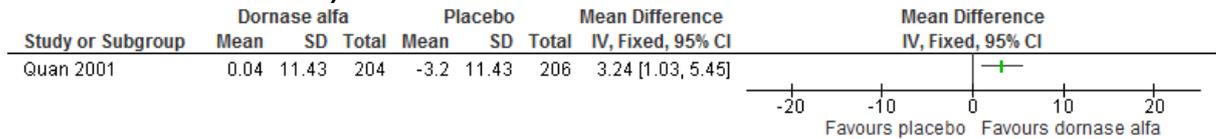
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

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



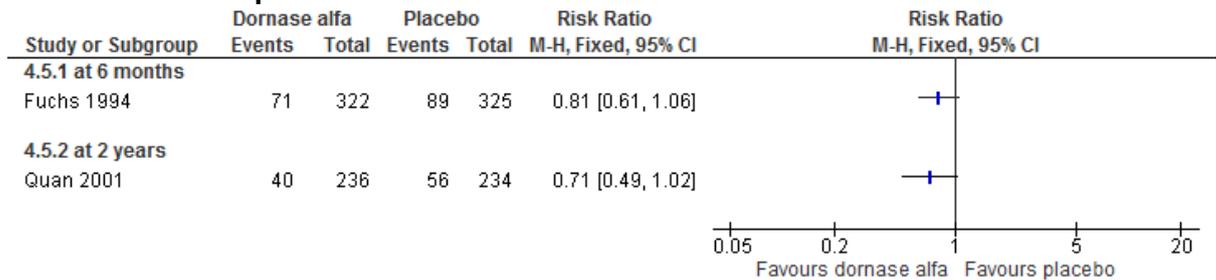
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 95: Lung function: absolute mean % change in FEV<sub>1</sub> at 2 years (range of scores: 0-100)**



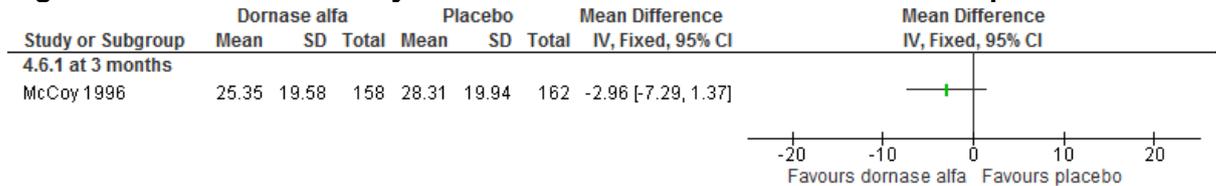
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

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



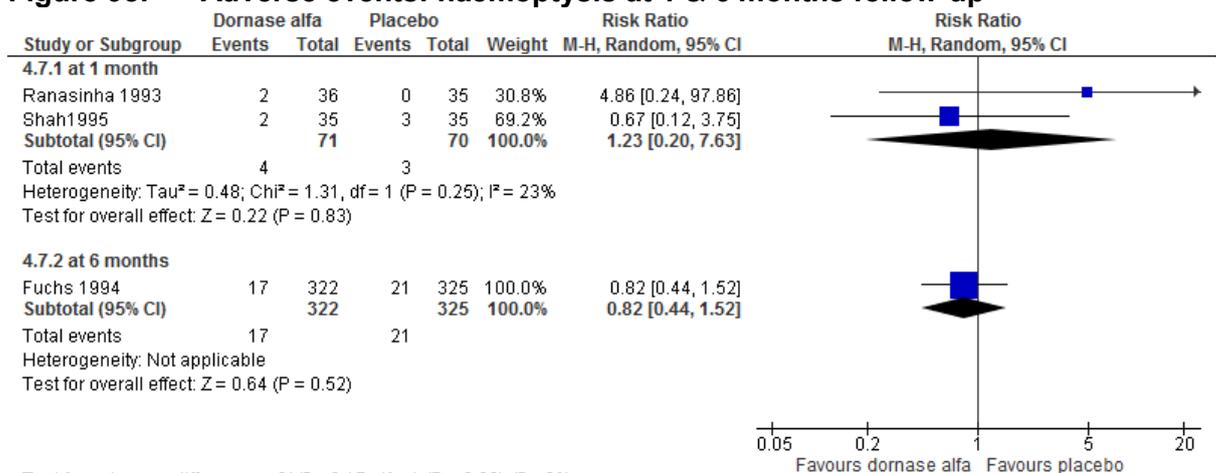
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

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



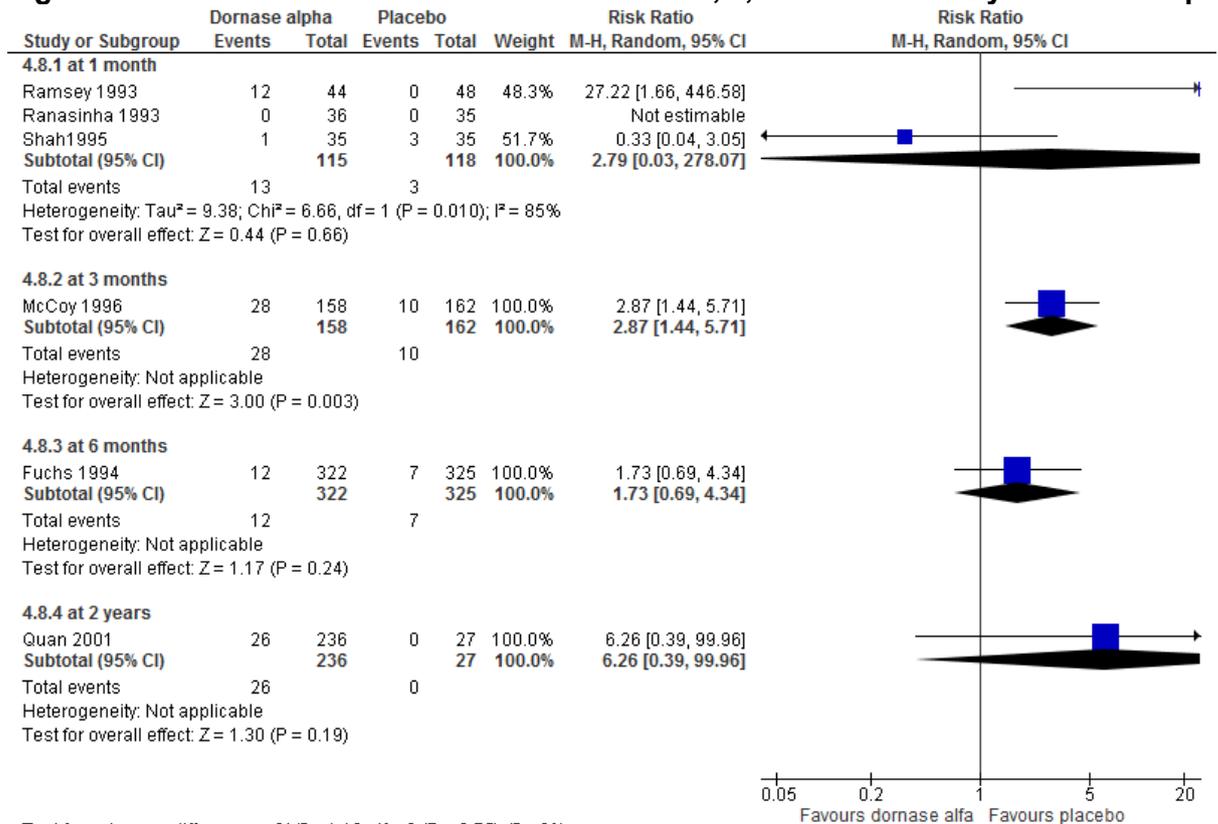
Abbreviations: CI: confidence interval; IV antibiotics: intravenous antibiotics; IV: inverse variance; SD: standard deviation

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

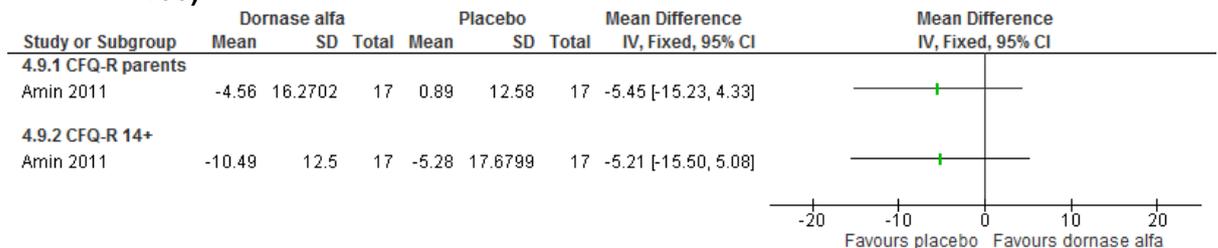


Test for subgroup differences: Chi<sup>2</sup> = 0.17, df = 1 (P = 0.68), I<sup>2</sup> = 0%  
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

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



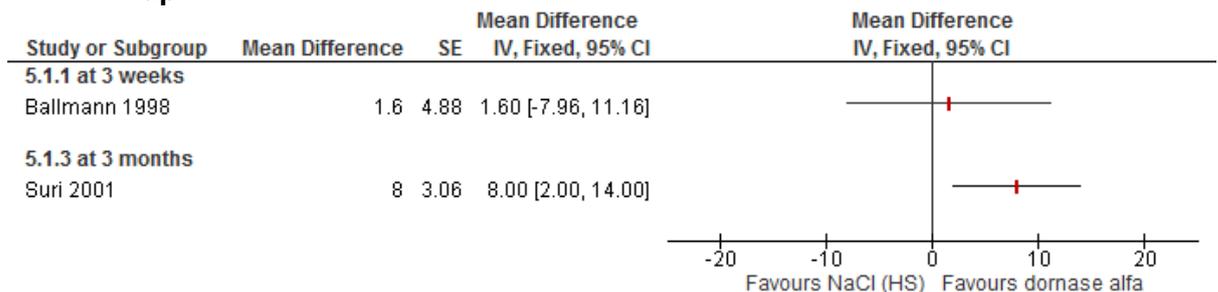
**Figure 100: Quality of life (measured with CFQ-R) at 3 months (range of scores: 0-100)**



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

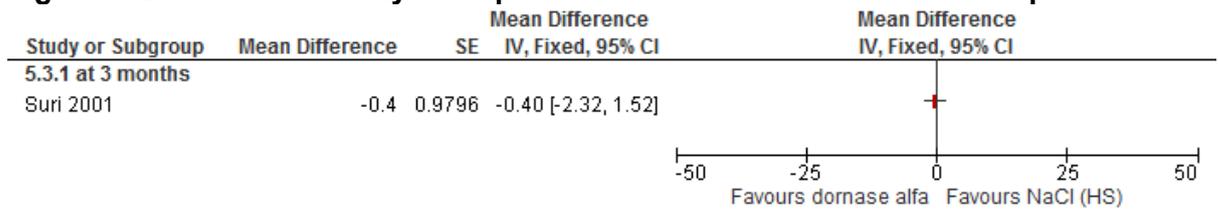
**Comparison 2.2. Dornase alfa versus nebulized sodium chloride**

**Figure 101: Lung function: mean % change in FEV<sub>1</sub> at 3 weeks and 3 months follow-up**



Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; NaCl (HS): sodium chloride (hypertonic saline); SE: standard error

**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

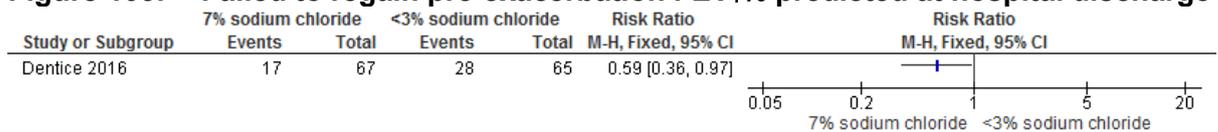
### Comparison 2.3. Dornase alfa versus acetylcysteine

No evidence was found for this comparison.

## I.8.3 Nebulised sodium chloride

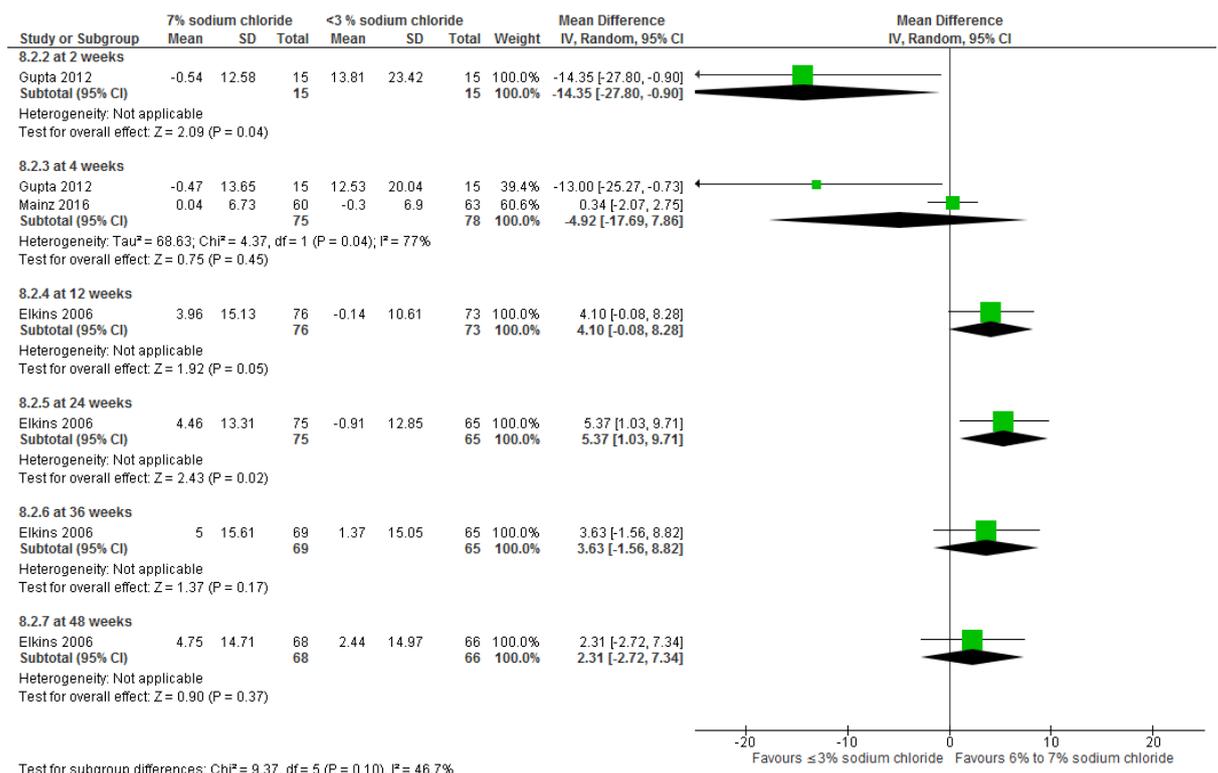
### Comparison 3.1. Nebulised sodium chloride (> 3% concentration) versus placebo (0.9% to 0.12%) or low-concentration (≤ 3%)

**Figure 103: Failed to regain pre-exacerbation FEV<sub>1</sub>% predicted at hospital discharge**



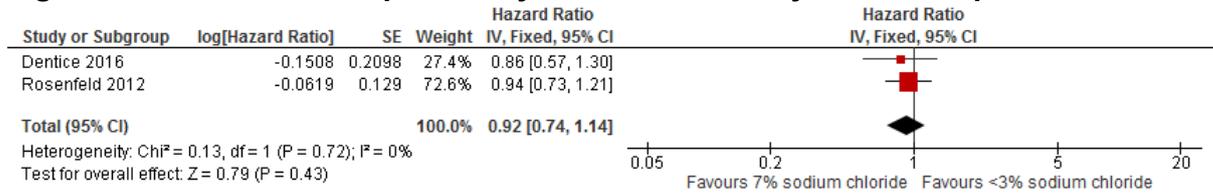
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel. Note: Length of hospital stay was 12 days for the intervention group, and 13 days for the control group. Pre-exacerbation FEV<sub>1</sub>% predicted was measured ≈ 6 months before.

**Figure 104: Lung function: % change in FEV<sub>1</sub> at 2, 4, 12, 24, 36 & 48 weeks follow-up (range of scores: 0-100)**



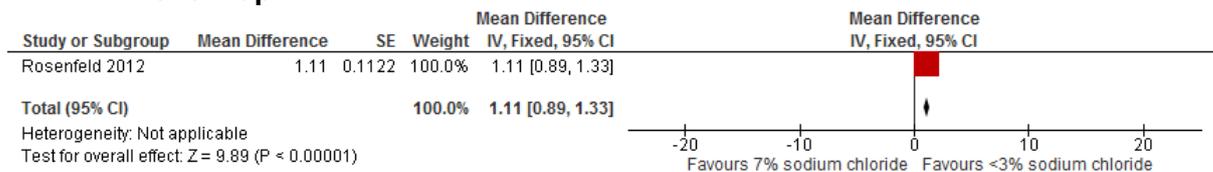
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

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



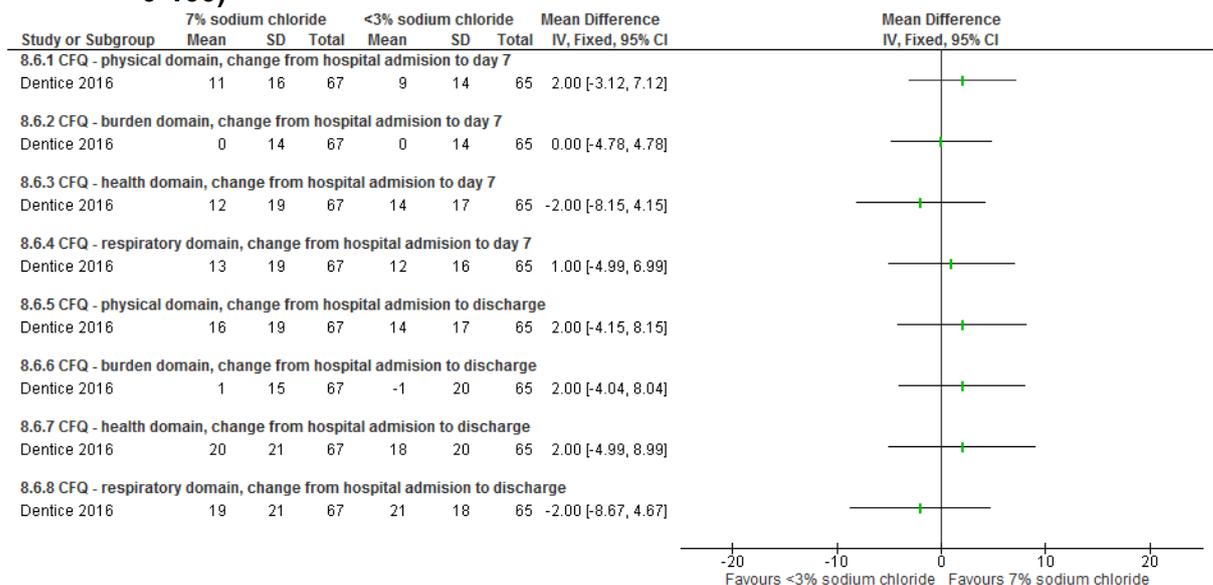
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

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



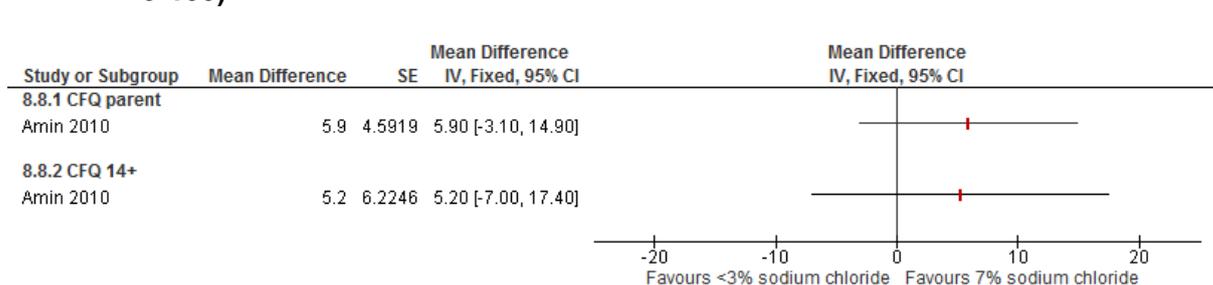
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

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



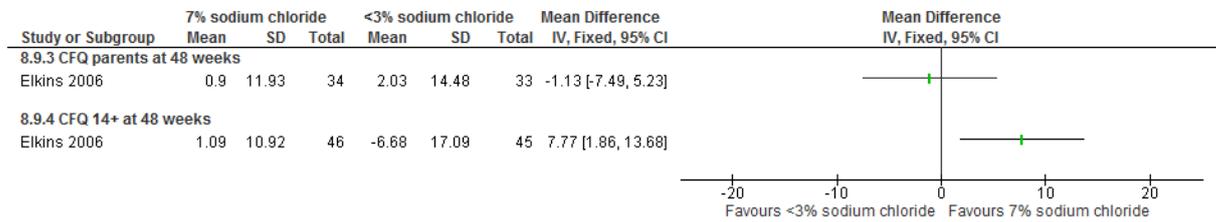
Abbreviations: CI: confidence interval; CF-QOL:: cystic fibrosis quality of life questionnaire; IV: inverse variance; SD: standard deviation

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



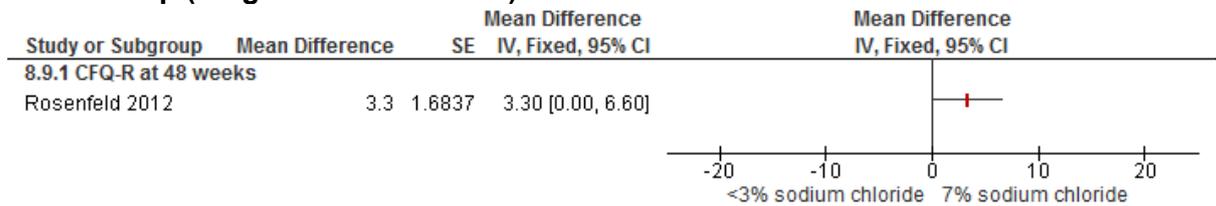
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SE: standard error

**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

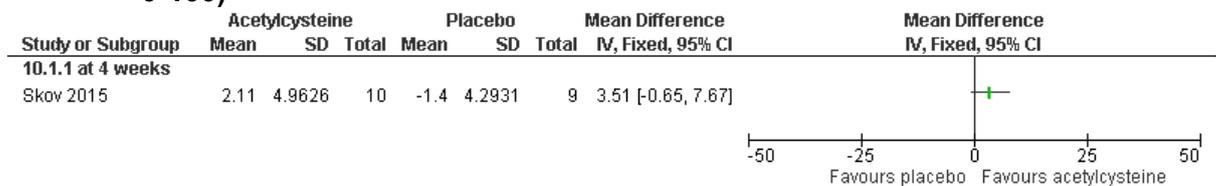
### Comparison 3.2. Nebulised sodium chloride versus acetylcysteine

No evidence was found for this comparison.

## I.8.4 Acetylcysteine

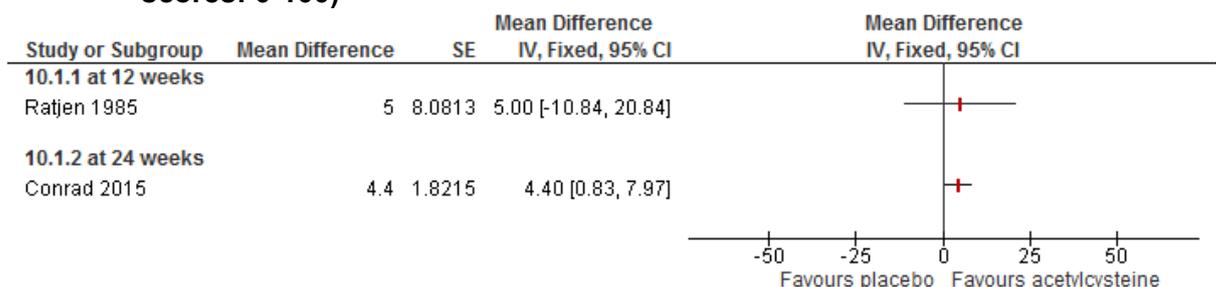
### Comparison 4. Acetylcysteine versus placebo

**Figure 111: Lung function: change in FEV<sub>1</sub> % predicted at 4 weeks (range of scores: 0-100)**



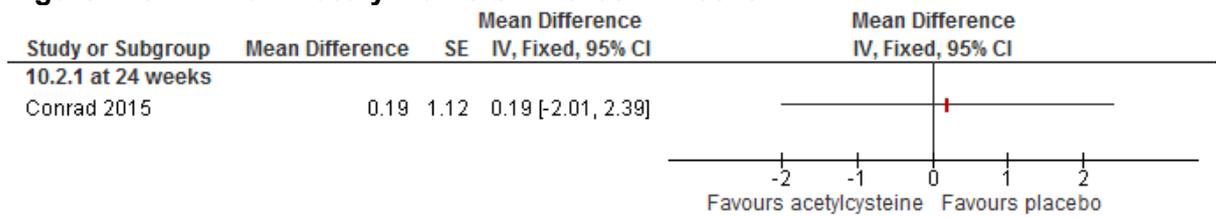
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

**Figure 112: Lung function: change in FEV<sub>1</sub> % predicted at 12 and 24 weeks (range of scores: 0-100)**



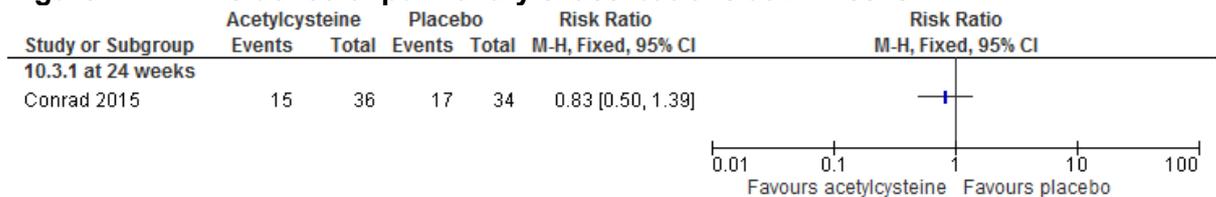
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

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



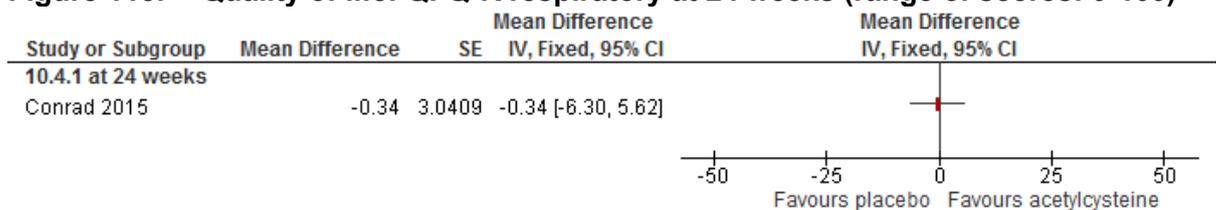
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

**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)**

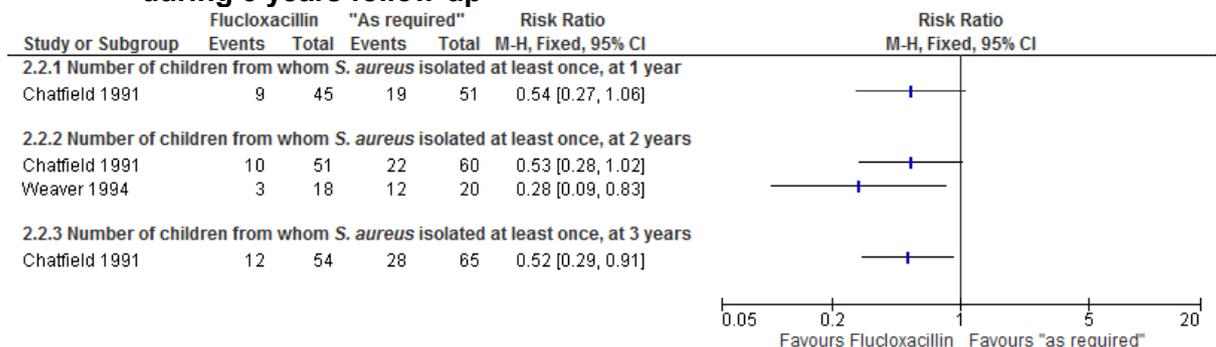


Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SE: standard error

## I.9 Pulmonary infection – prophylaxis

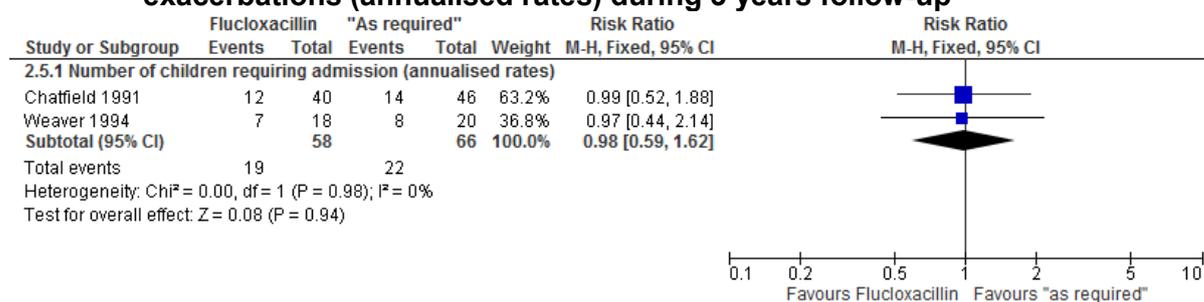
### Comparison 1. Continuous oral flucloxacillin versus antibiotics as required

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



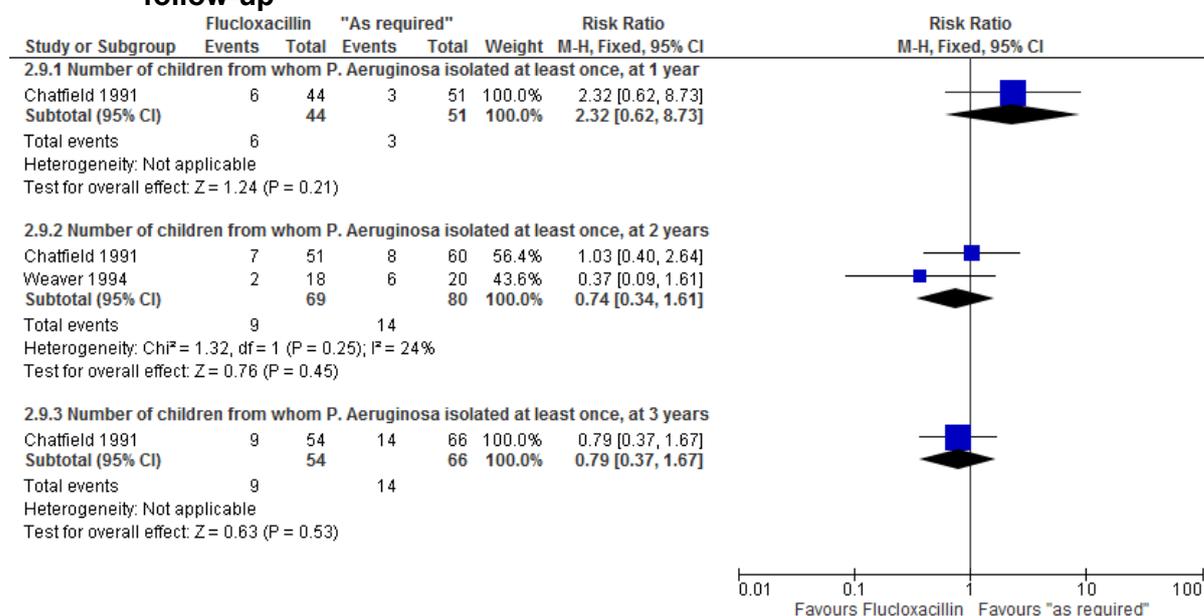
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

**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

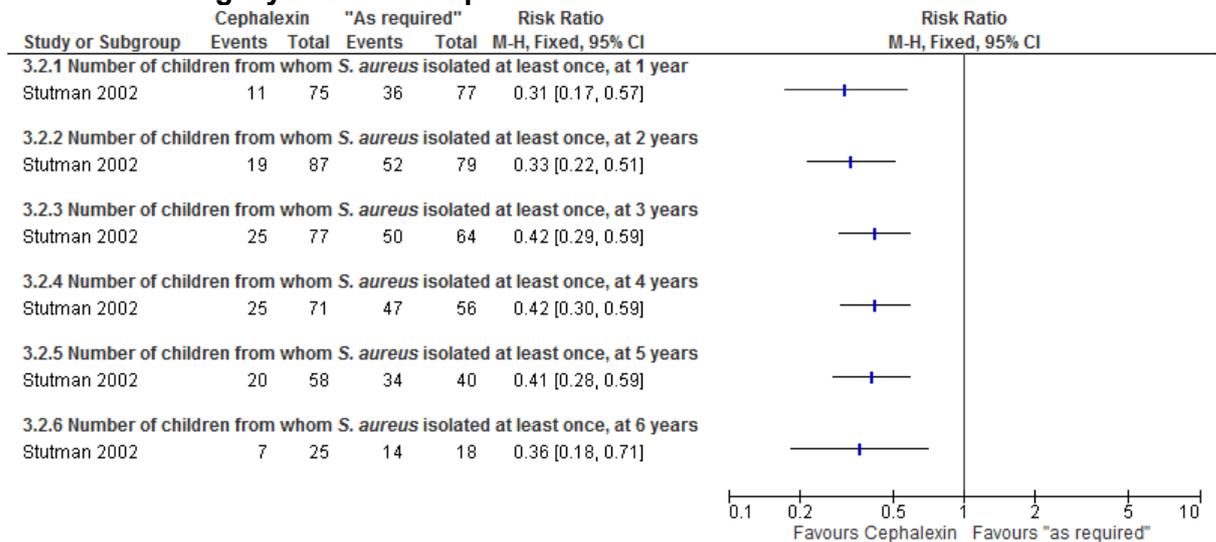
**Figure 118: Number of children in whom *P. aeruginosa* was identified during 3 years follow-up**



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

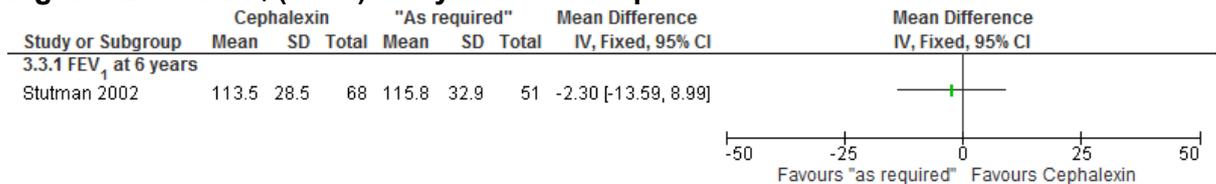
## Comparison 2. Continuous oral Cephalaxin *versus* antibiotics as required

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



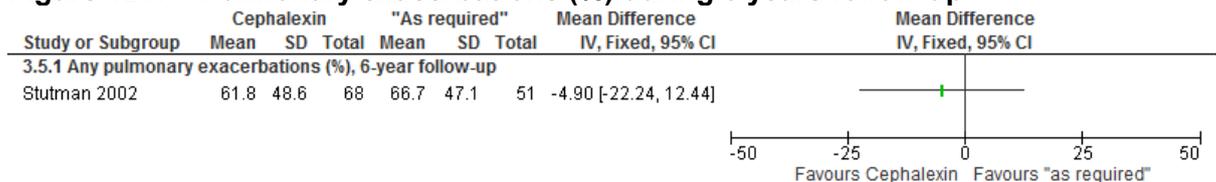
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

**Figure 120: FEV<sub>1</sub> (litres) at 6 years follow-up**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

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



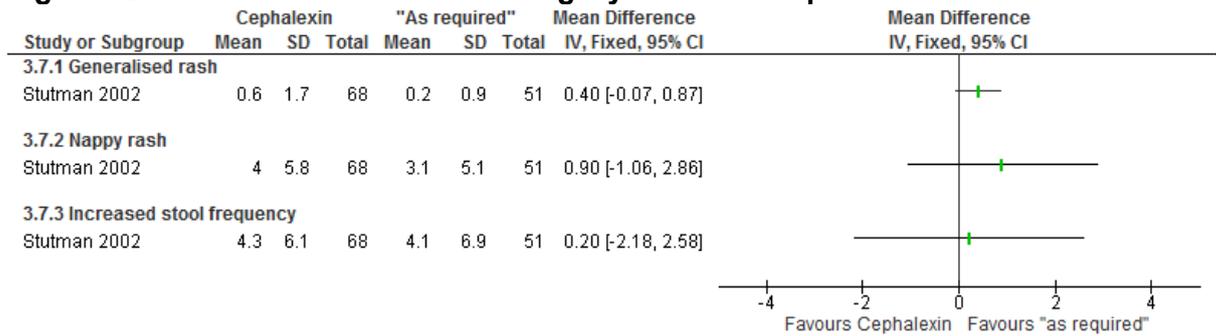
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation;

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



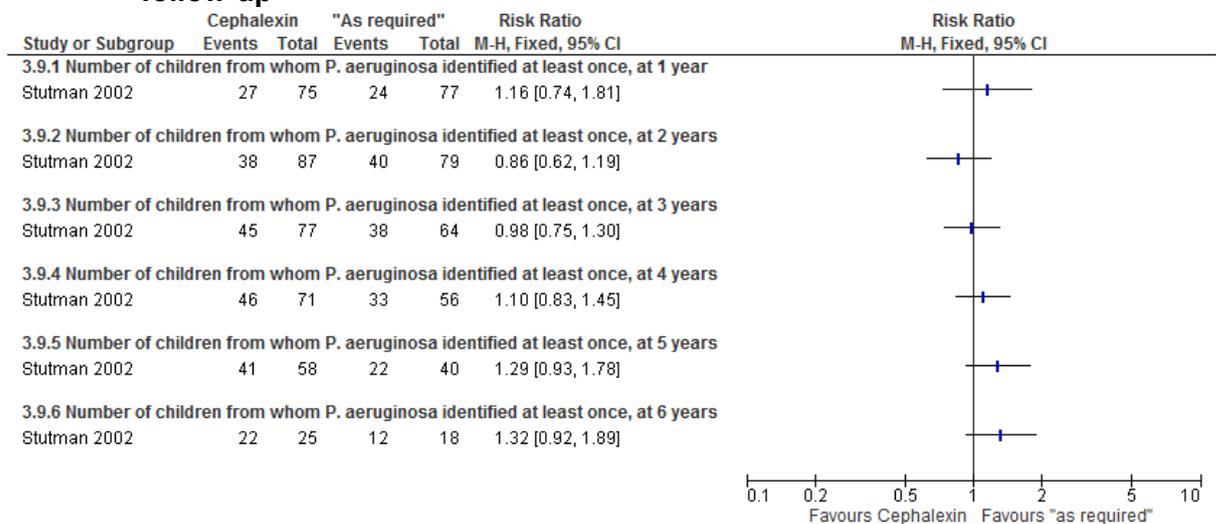
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

**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

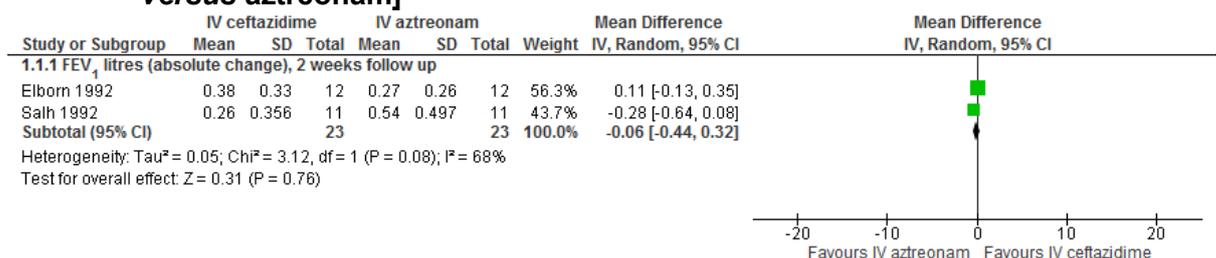
## I.10 Pulmonary infection – acute

### 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

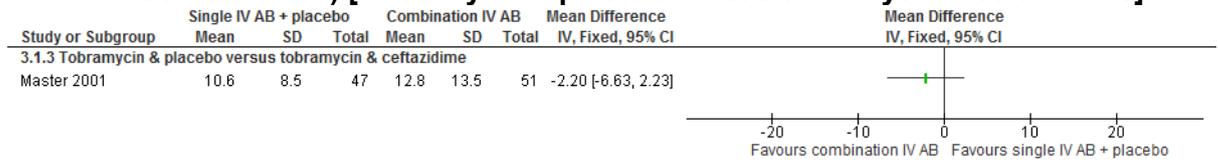
**Figure 125: FEV<sub>1</sub> litres (absolute change) at end of 2 week course [ceftazidime versus aztreonam]**



Abbreviations: CI: confidence interval; df: degrees of freedom; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

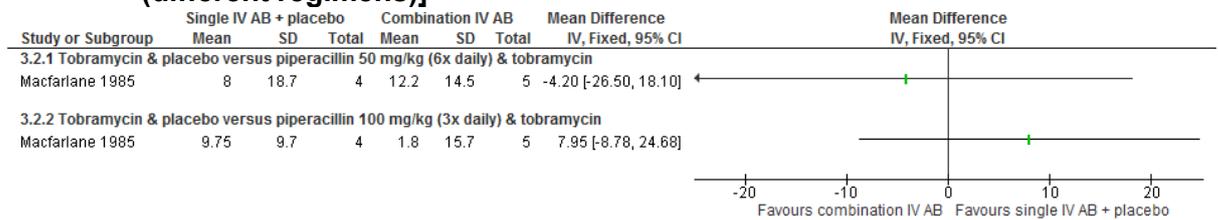
## Comparison 2. Single IV antibiotic (with placebo) versus combination IV

**Figure 126: FEV<sub>1</sub> % predicted (absolute change) at 10 days follow-up (range of scores: 0-100) [Tobramycin + placebo versus tobramycin + ceftazidime]**



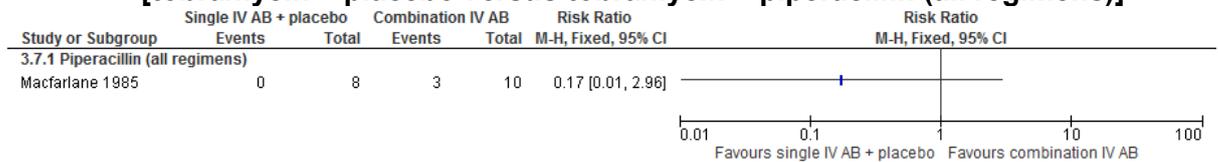
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance (at the top of the plot) or intravenous (at the bottom of the plot); SD: standard deviation

**Figure 127: FEV<sub>1</sub> % predicted (relative change) at end of 2 weeks course (range of scores: 0-100) [tobramycin + placebo versus tobramycin + piperacillin (different regimens)]**



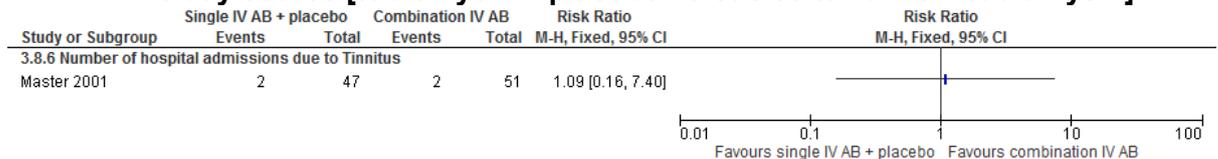
Abbreviations: AB: antibiotics; CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance (at the top of the plot) or intravenous (at the bottom of the plot); SD: standard deviation

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



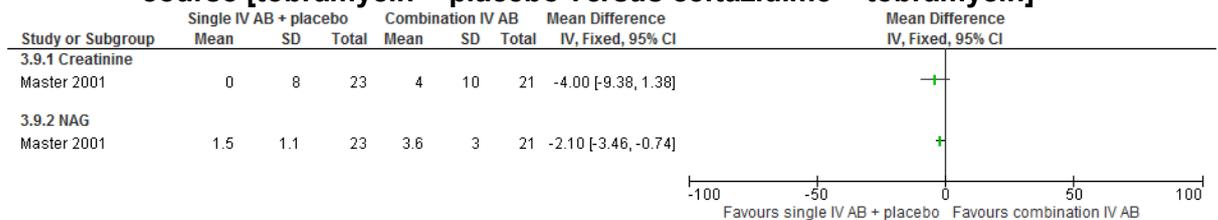
Abbreviations: AB: antibiotics; CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel

**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

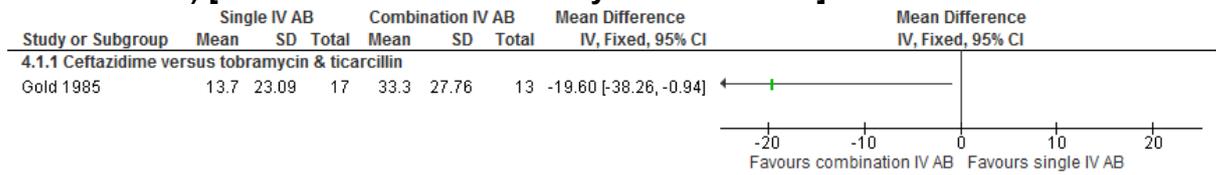
**Figure 130: Adverse effects: adverse effects (serum concentrations) during 10 day course [tobramycin + placebo versus ceftazidime + tobramycin]**



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

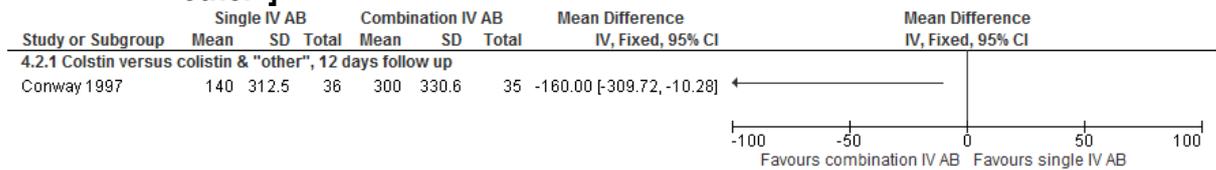
**Comparison 3. Single IV antibiotic versus combination IV antibiotic for pulmonary exacerbations with PA**

**Figure 131: FEV<sub>1</sub> (relative change) at 10 to 14 days follow-up (range of scores: 0-100) [ceftazidime versus tobramycin & ticarcillin]**



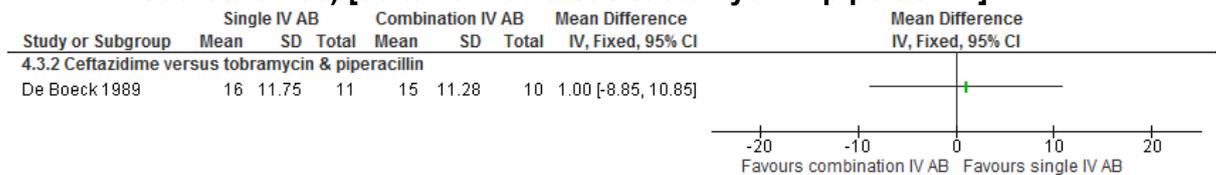
Abbreviations: AB: antibiotics; CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; IV AB: intravenous antibiotics; SD: standard deviation

**Figure 132: FEV<sub>1</sub> ml (absolute change) at 12 days follow-up [colistin versus colistin + "other"]**



Abbreviations: AB: antibiotics; CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; IV AB: intravenous antibiotics; SD: standard deviation

**Figure 133: FEV<sub>1</sub> % predicted (absolute change) at 14 days follow-up (range of scores: 0-100) [ceftazidime versus tobramycin + piperacillin]**



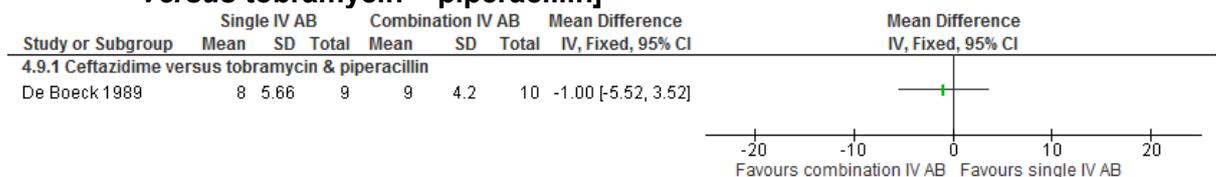
Abbreviations: AB: antibiotics; CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; IV AB: intravenous antibiotics; SD: standard deviation

**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]**



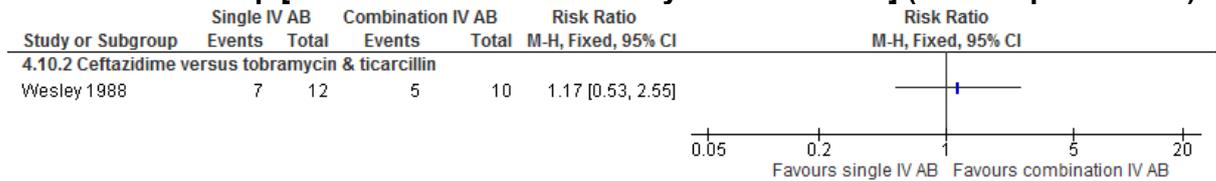
Abbreviations: AB: antibiotics; CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel;

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



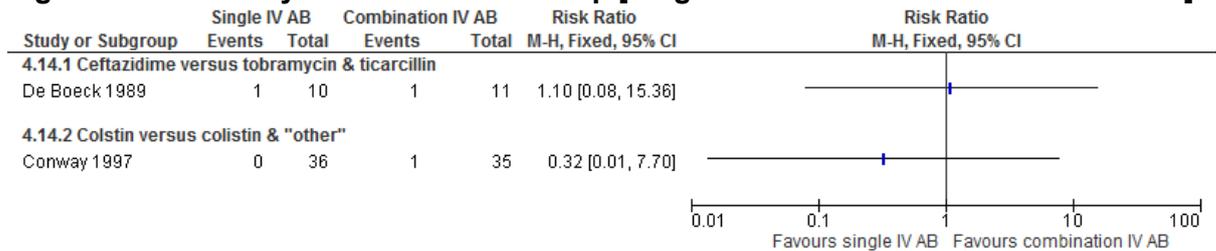
Abbreviations: AB: antibiotics; CI: confidence interval; IV: inverse variance; IV AB: intravenous antibiotics; SD: standard deviation

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



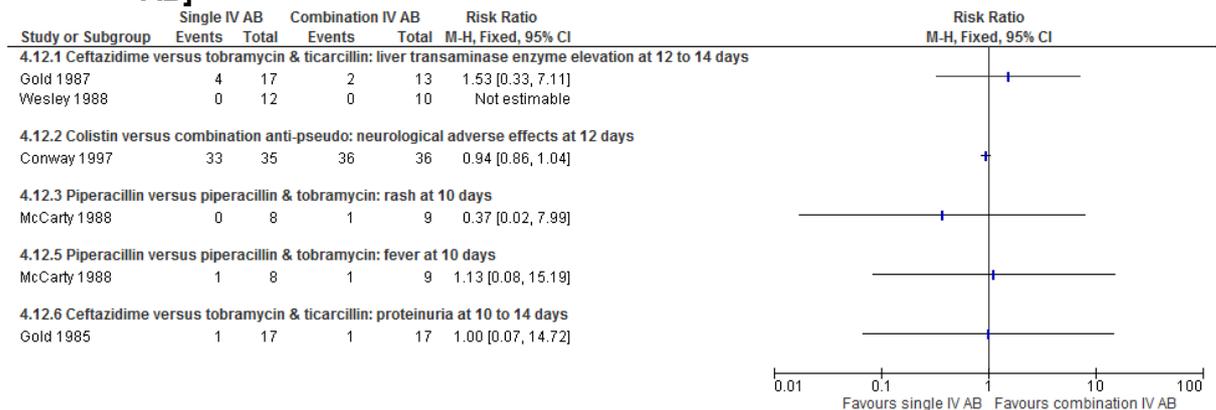
Abbreviations: AB: antibiotics; CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel

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



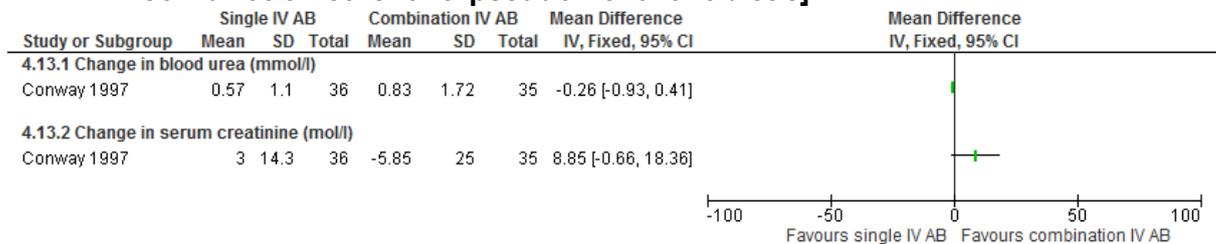
Abbreviations: AB: antibiotics; CI: confidence interval; IV: intravenous; M-H: Mantel-Haenszel;

**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

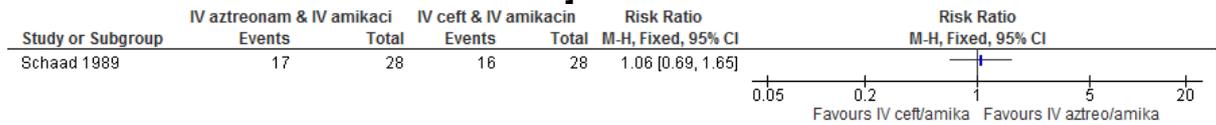
**Figure 139: Adverse events: renal toxicity at 12 days follow-up [colistin versus combination other anti-pseudomonal antibiotic]**



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

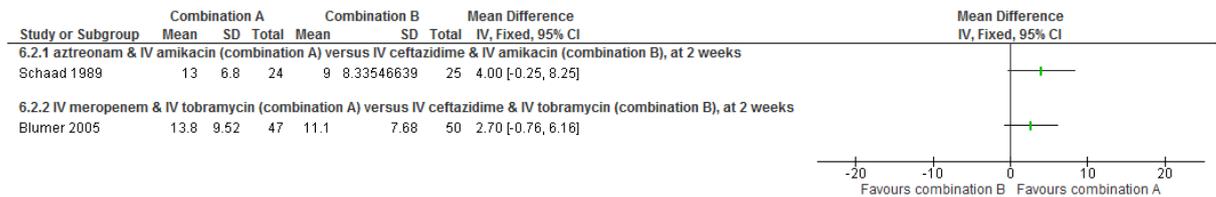
### Comparison 4. Combination IV antibiotics versus combination IV antibiotics for pulmonary exacerbations

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



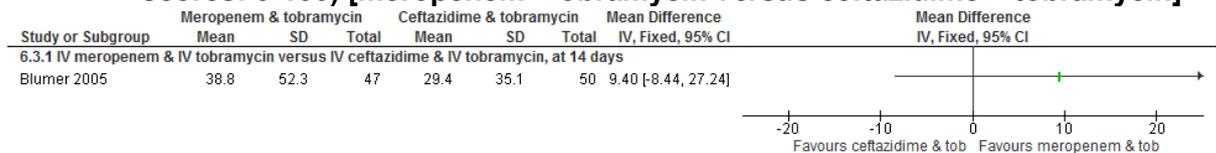
Abbreviations: *aztreo*: aztreonam; *amika*: amikacin; *M-H*: Mantel-Haenszel; *CI*: confidence interval

**Figure 141: FEV<sub>1</sub> % predicted (absolute change) at 2 weeks follow-up (range of scores: 0-100) [IV combination A vs IV combination B]**



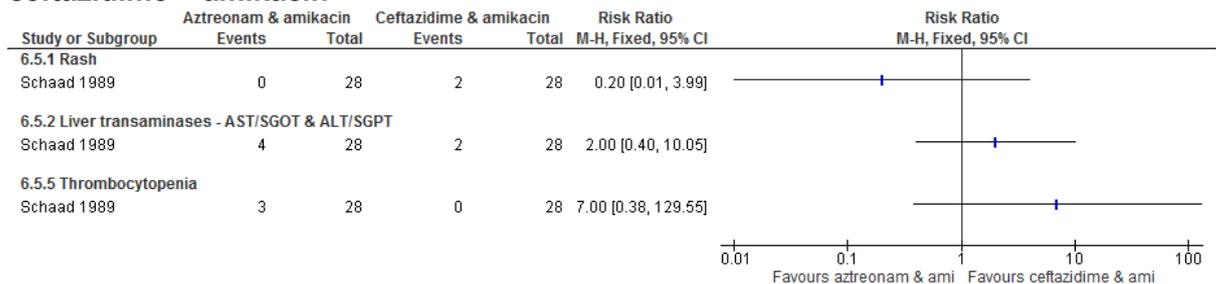
Abbreviations: *amika*: amikacin; *ceft*: ceftazidime; *CI*: confidence interval; *FEV<sub>1</sub>*: forced expiratory volume in 1 second; *IV*: inverse variance; *SD*: standard deviation

**Figure 142: FEV<sub>1</sub> % predicted (relative change) at 2 weeks follow-up (range of scores: 0-100) [meropenem + obramycin versus ceftazidime + tobramycin]**



Abbreviations: *CI*: confidence interval; *FEV<sub>1</sub>*: 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;

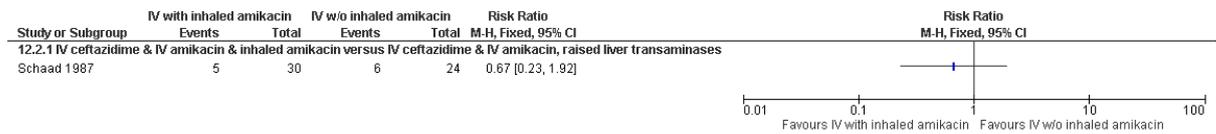
### Comparison 5. Two IV antibiotics + inhaled antibiotic versus 2 IV without inhaled antibiotic

**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

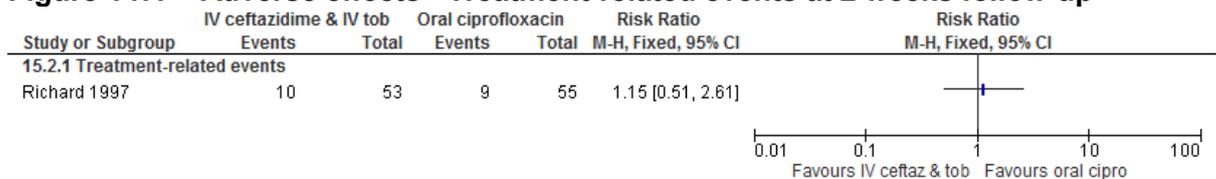
**Comparison 6. IV ceftazidime + IV tobramycin versus oral ciprofloxacin**

**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**

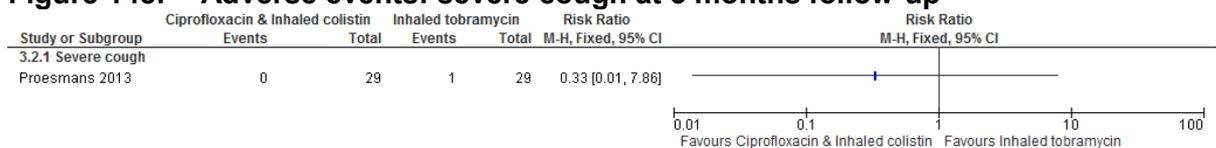


Abbreviations: ceft: ceftazidime; CI: confidence interval; cipro: ciprofloxacin; IV: intravenous; M-H: Mantel-Haenszel; tob: tobramycin

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

**Comparison 7. Oral ciprofloxacin + inhaled colistin versus inhaled tobramycin**

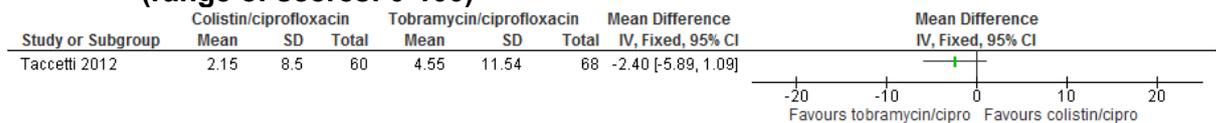
**Figure 148: Adverse events: severe cough at 3 months follow-up**



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

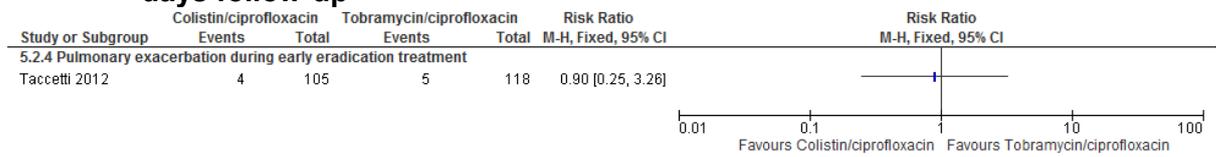
**Comparison 8. Inhaled colistin + oral ciprofloxacin versus inhaled tobramycin + oral ciprofloxacin**

**Figure 149: Relative change in % predicted FEV<sub>1</sub> from baseline at 54 days follow-up (range of scores: 0-100)**



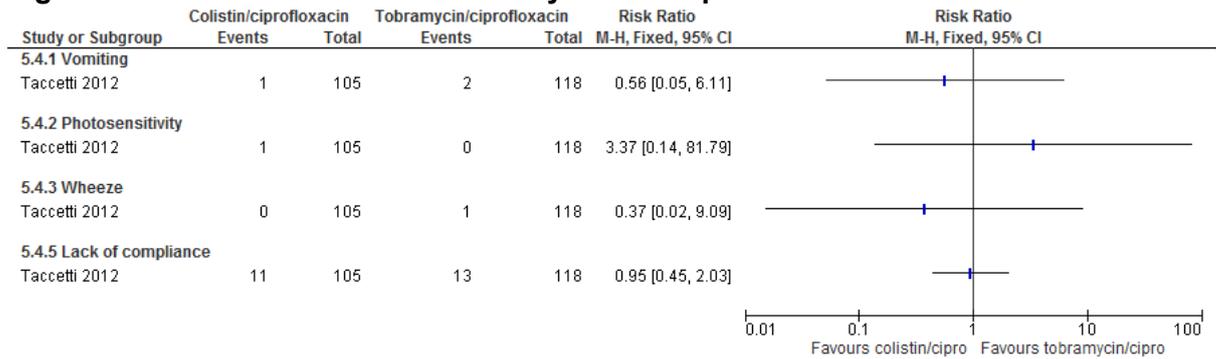
Abbreviations: CI: confidence interval; cipro: ciprofloxacin; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**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

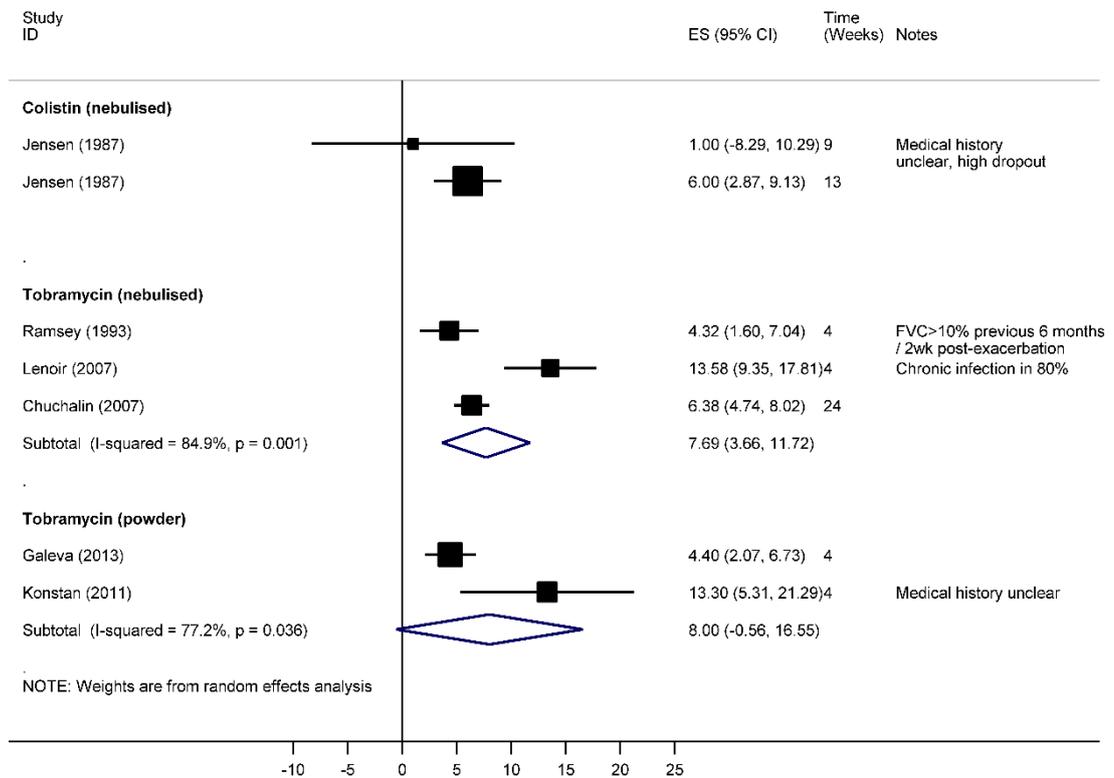
### I.11.1 Pseudomonas Aeruginosa

#### I.11.1.1 NMA outcomes

Outcome 1: NMA FEV<sub>1</sub> % predicted (range of scores: 0-100)

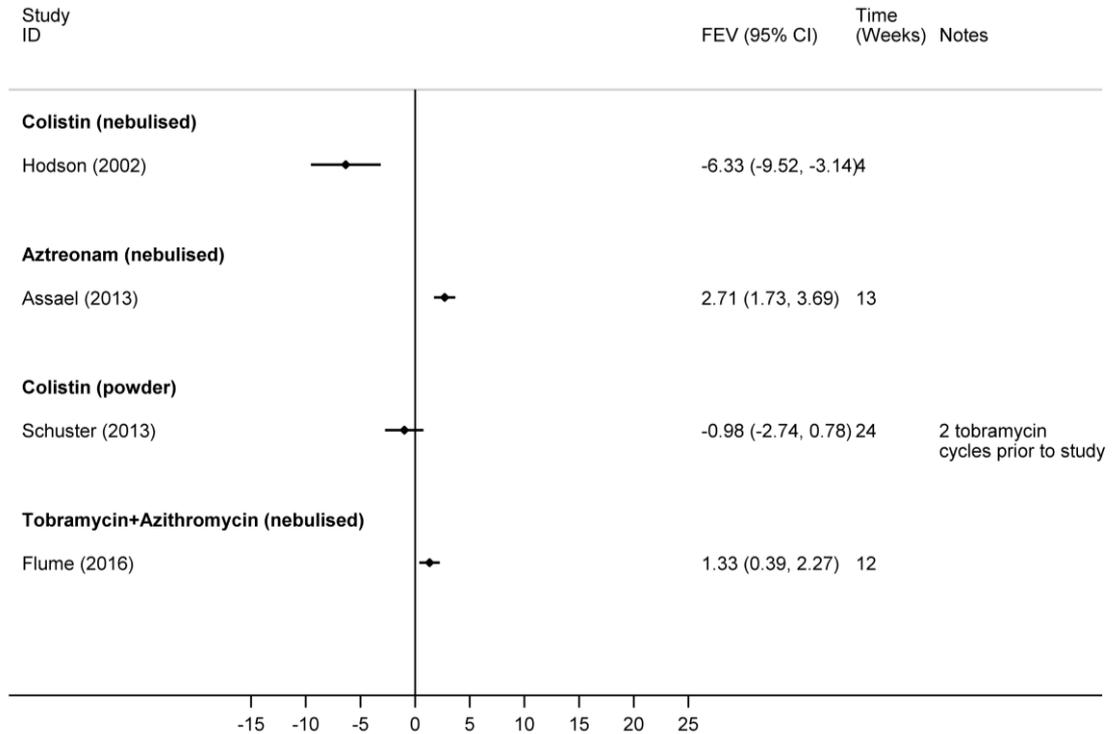
Figure 152: Forest plot showing mean differences (with their 95% CI) of study estimates for interventions *versus* placebo

### Treatments versus placebo



Abbreviations: CI: confidence interval; ES: effect size

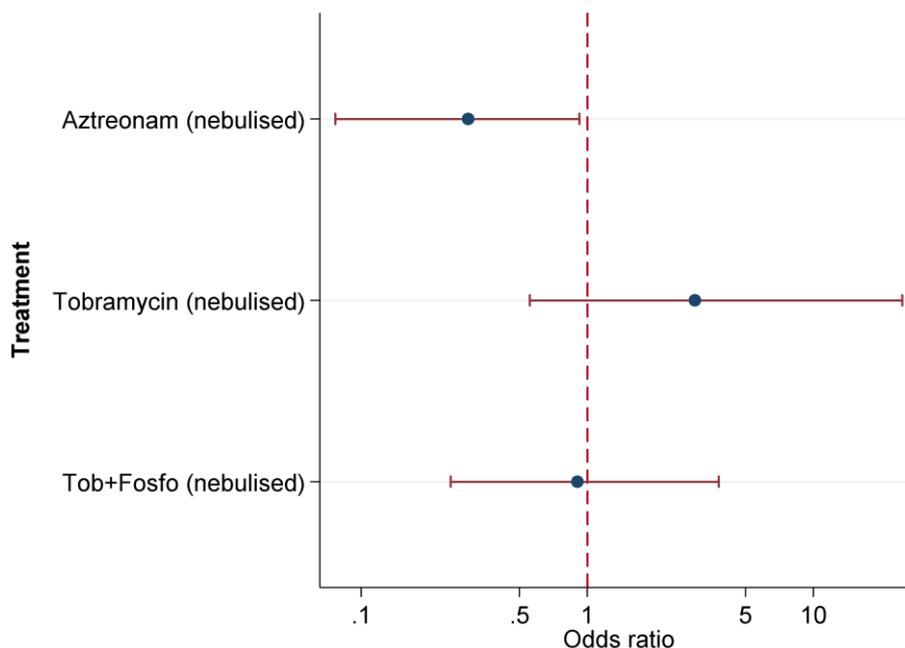
**Figure 153: Forest plot showing mean differences (with their 95% CI) of study estimates for interventions versus tobramycin (nebulised)**



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

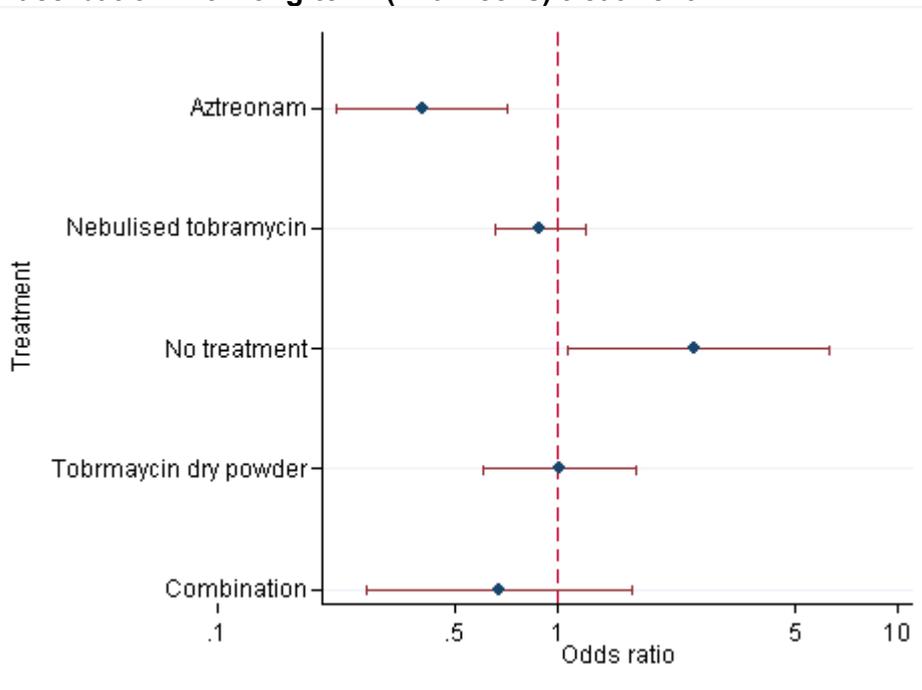
**Outcome 2: NMA number of patients experiencing at last one exacerbation**

**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**

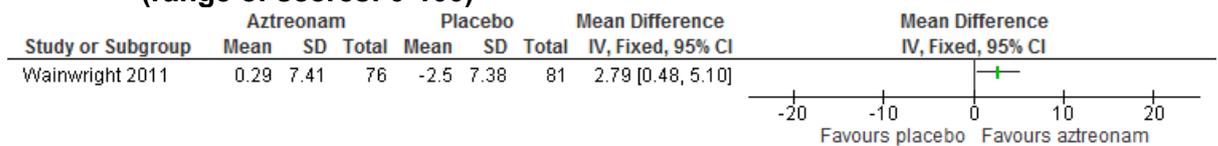


Combination: 28 days aztreonam lysine (nebulised) alternating with 28 days tobramycin (nebulised). Vertical dashed line shows the line of no effect

### I.11.1.2 Non-NMA outcomes (pairwise comparisons)

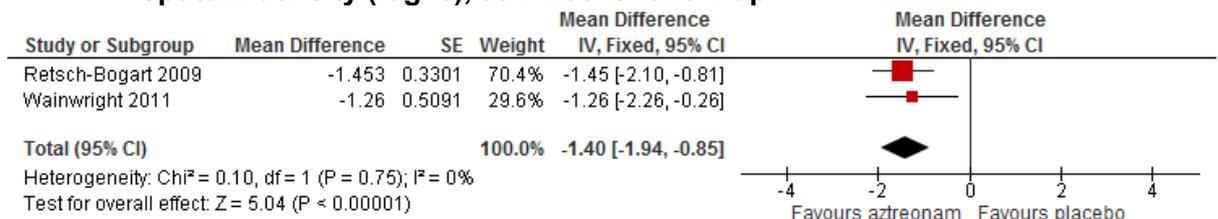
#### Pairwise comparison 1: Aztreonam lysine versus placebo

**Figure 156: Lung function: relative change in FEV<sub>1</sub>% predicted at 28 days follow-up (range of scores: 0-100)**



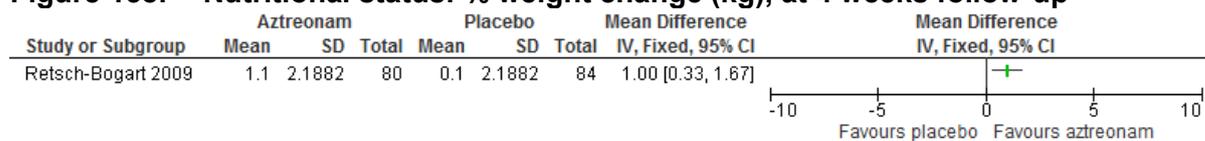
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 157: Suppression of the organism: adjusted mean change in P. aeruginosa sputum density (log<sub>10</sub>), at 4 weeks follow-up**



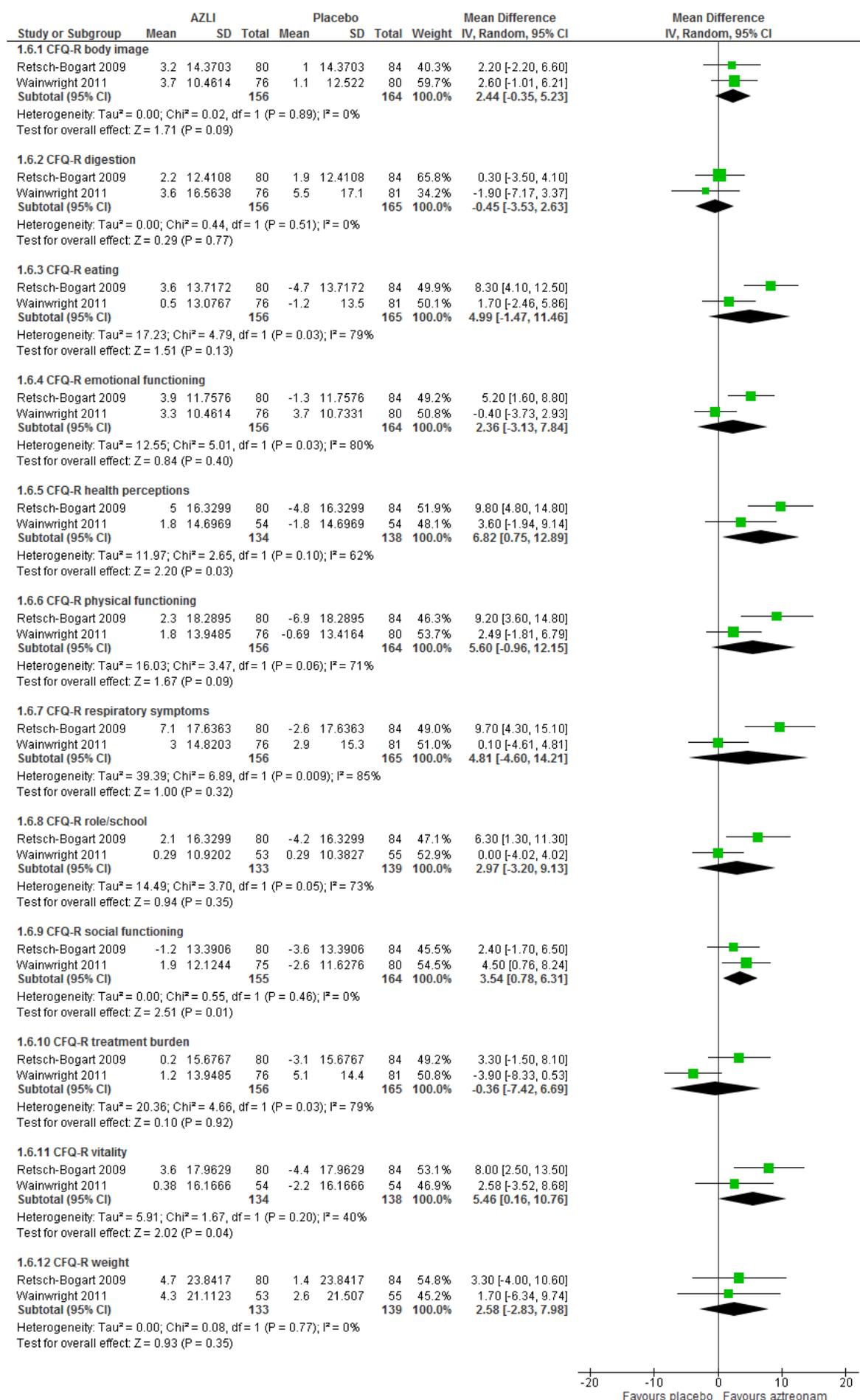
Abbreviations: CI: confidence interval; df: degrees of freedom; IV: inverse variance; SE: standard error

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



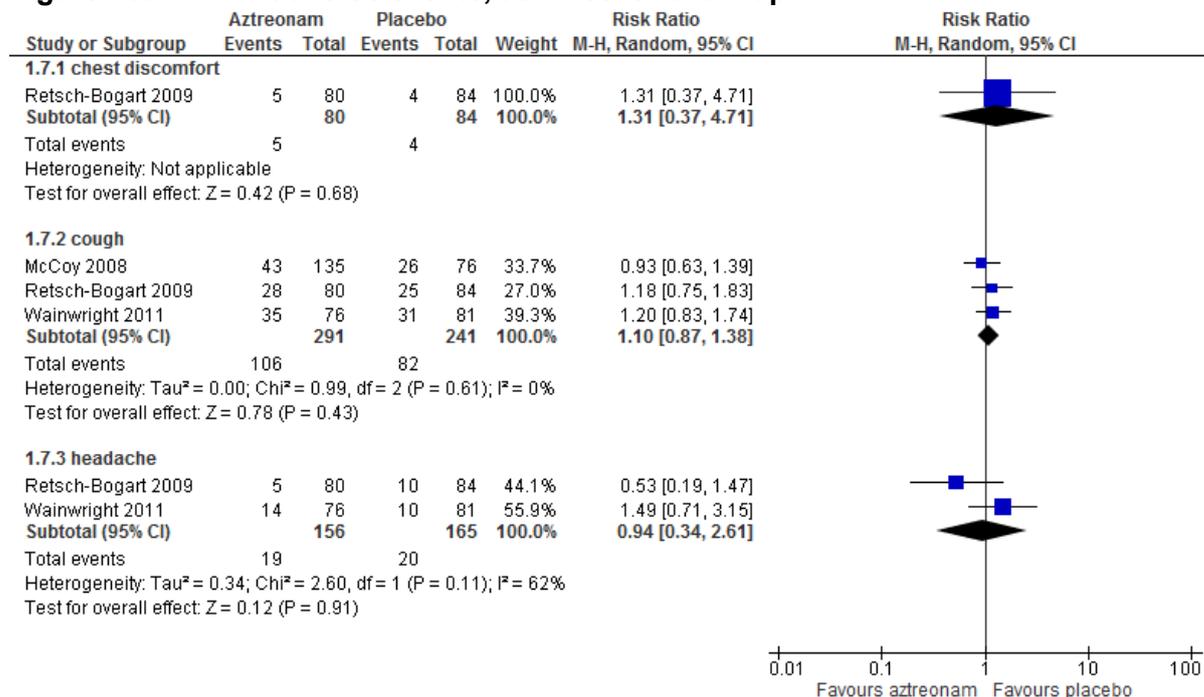
Abbreviations: CI: confidence interval; IV: inverse variance; kg: kilograms; SD: standard deviation

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



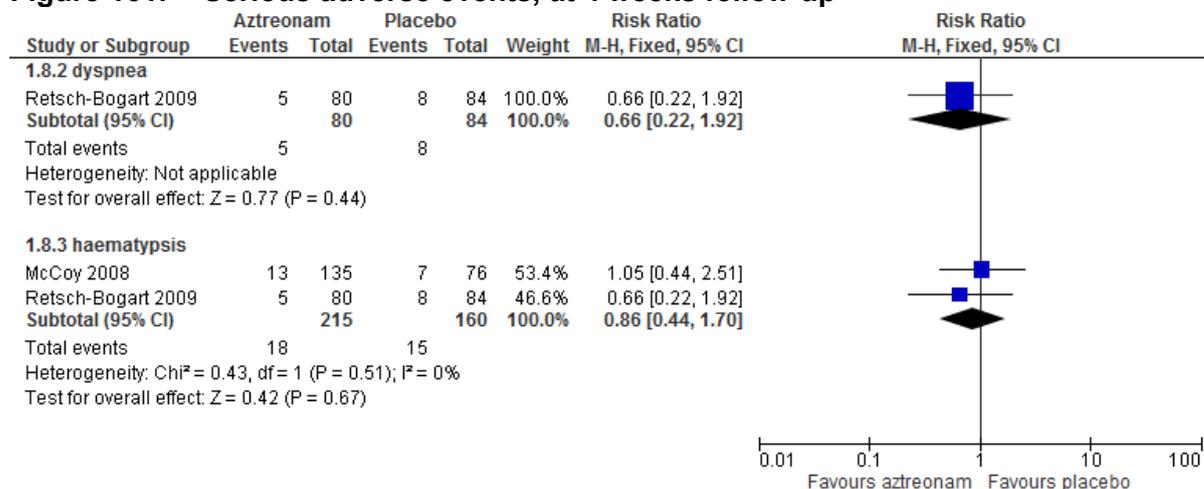
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; df: degrees of freedom; IV: inverse variance; SD: standard deviation

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



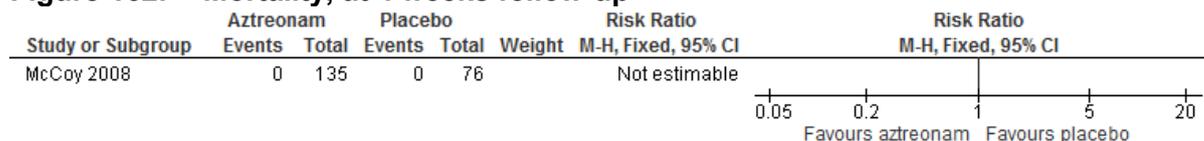
Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

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



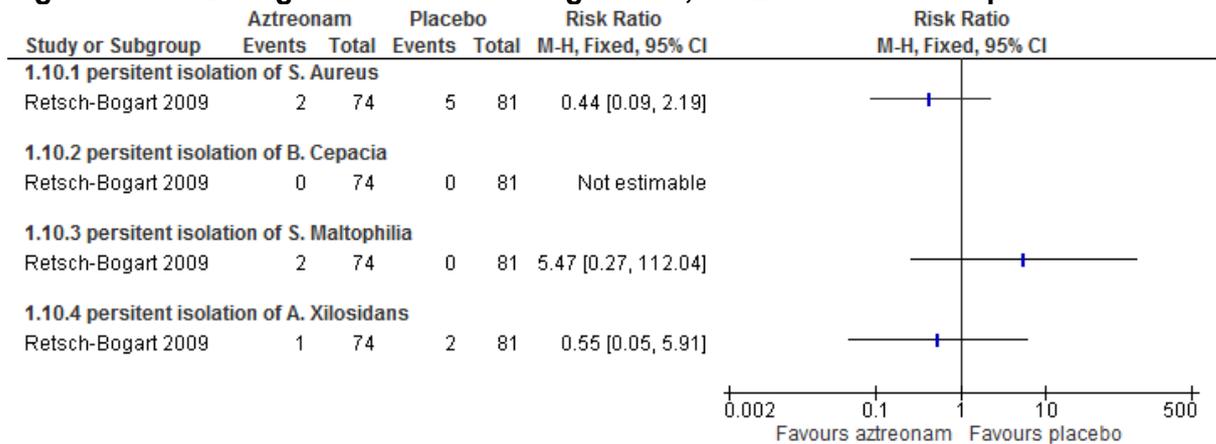
Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

**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.

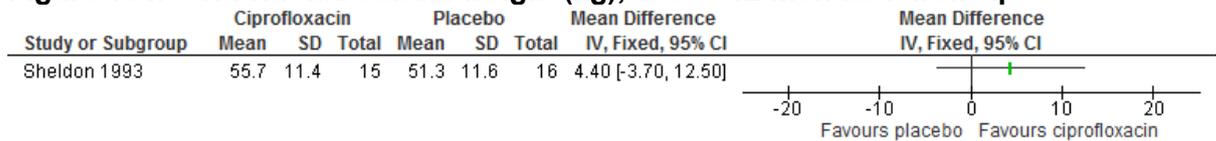
**Figure 163: Emergence of resistant organisms, at 42 weeks follow-up**



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

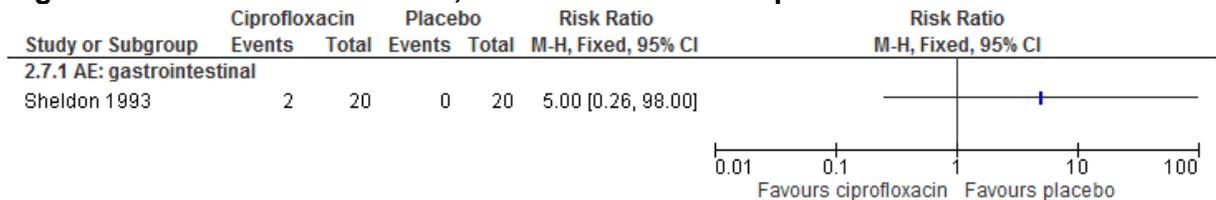
**Pairwise comparison 2: Ciprofloxacin versus placebo**

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



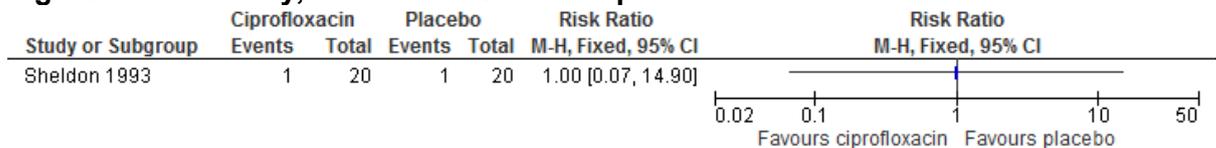
Abbreviations: CI: confidence interval; kg: kilograms; IV: inverse variance; SD: standard deviation

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



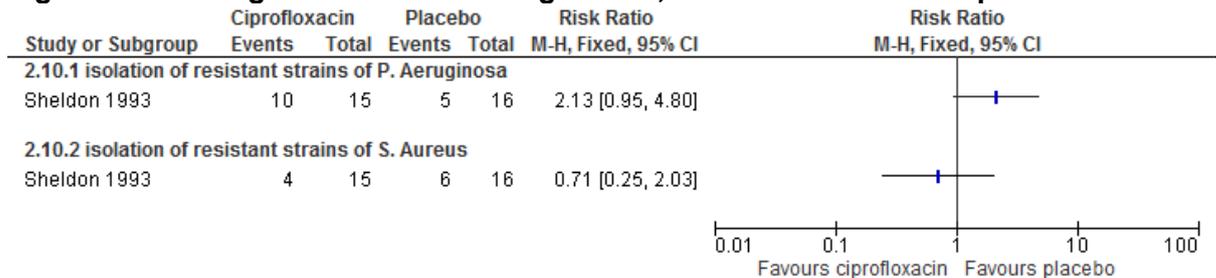
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel.

**Figure 166: Mortality, at 12 months follow-up**



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

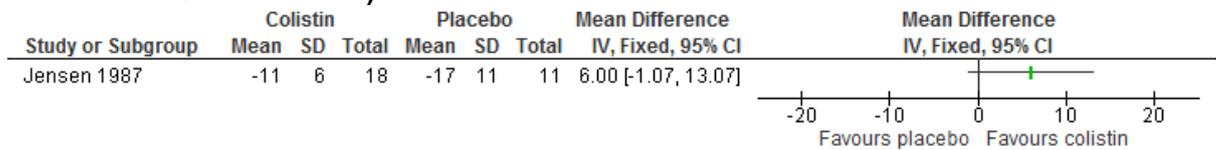
**Figure 167: Emergence of resistant organisms, at 12 months follow-up**



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

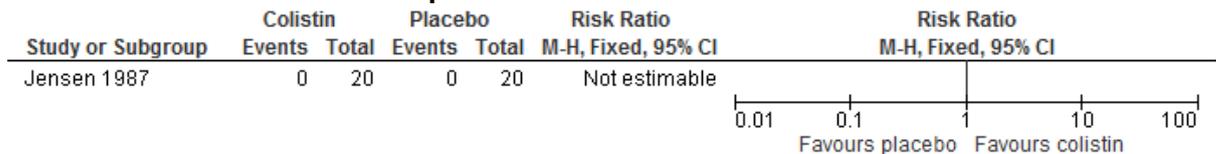
### Pairwise comparison 3.1. Colistin versus placebo

**Figure 168: Lung function: change in FEV<sub>1</sub> % predicted at 3 months follow-up (range of scores: 0-100)**



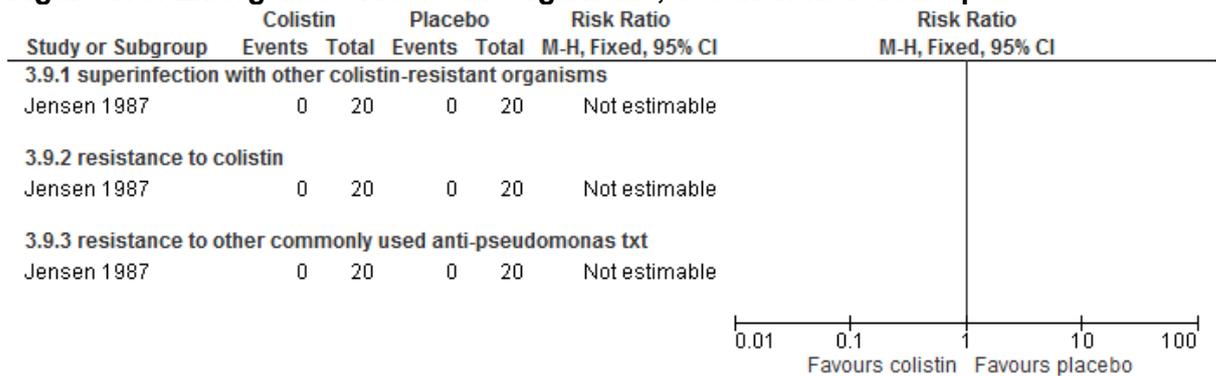
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**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.

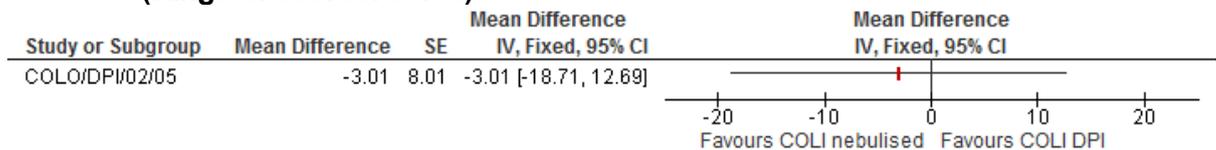
**Figure 170: Emergence of resistant organisms, at 3 months follow-up**



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

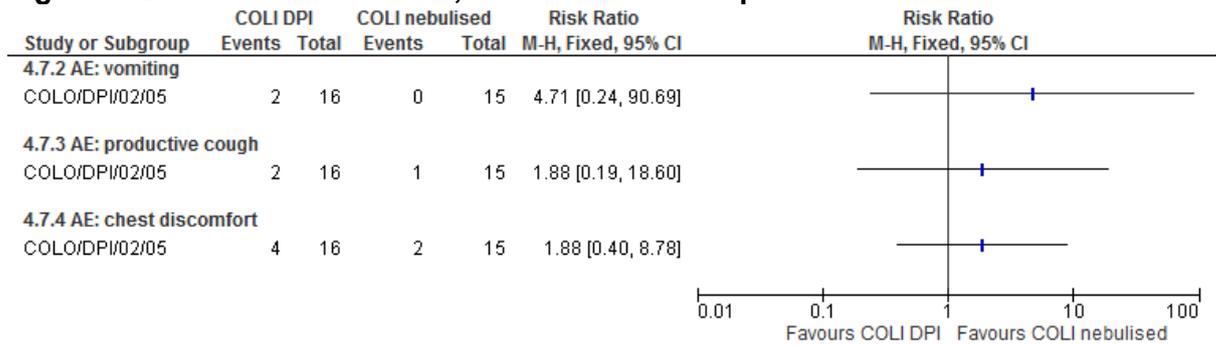
### Pairwise comparison 3.2. Colistin inhalation powder (COLO DPI) versus colistin inhalation solution (COLI nebulised)

**Figure 171: Lung function: % mean change in FEV<sub>1</sub>% predicted at 4 weeks follow-up (range of scores: 0-100)**



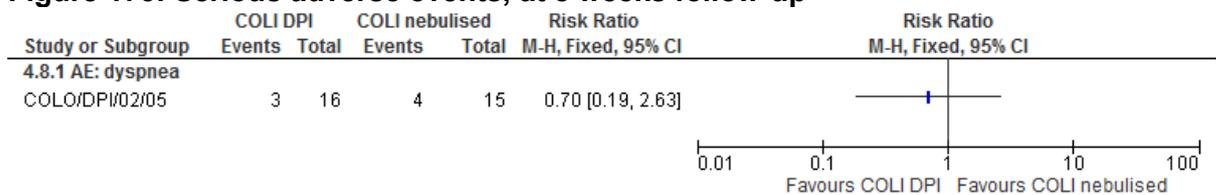
Abbreviations: CI: confidence interval; COLI: colistin; DPI: dry powder inhalation; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error

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



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

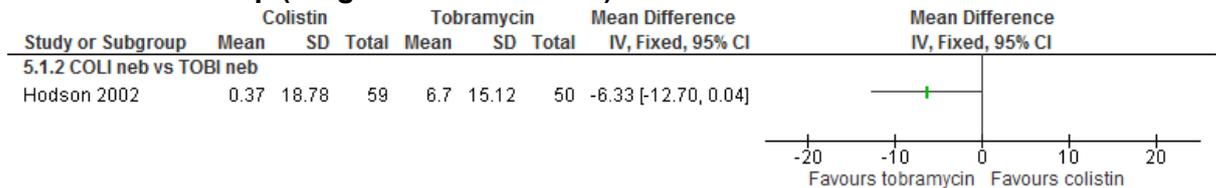
**Figure 173: Serious adverse events, at 8 weeks follow-up**



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

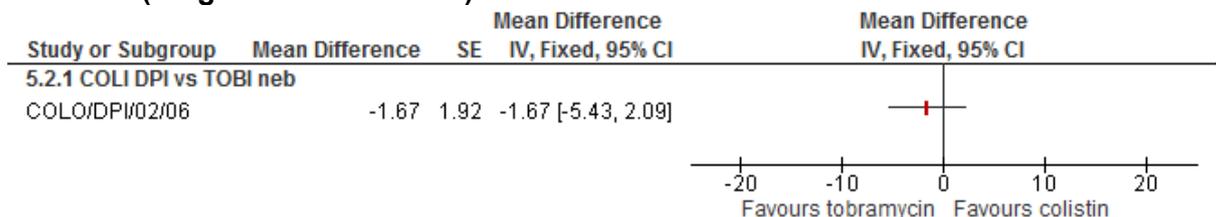
**Pairwise comparison 3.3. Colistin versus tobramycin**

**Figure 174: Lung function: mean % change in FEV<sub>1</sub>% predicted at 1 to 3 months follow-up (range of scores: 0-100)**



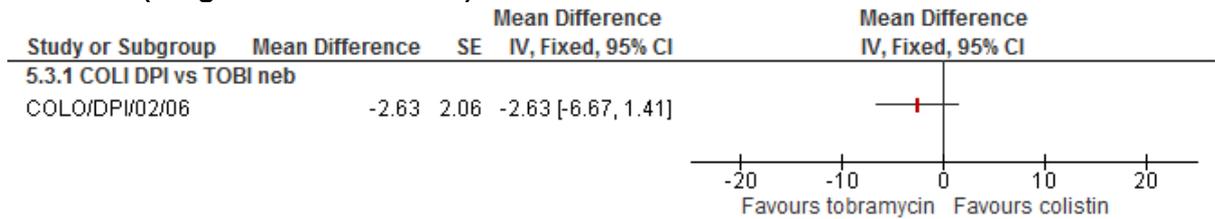
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; Neb: nebulised; SD: standard deviation

**Figure 175: Lung function: mean % change in FEV<sub>1</sub>% predicted at 4 weeks follow-up (range of scores: 0-100)**



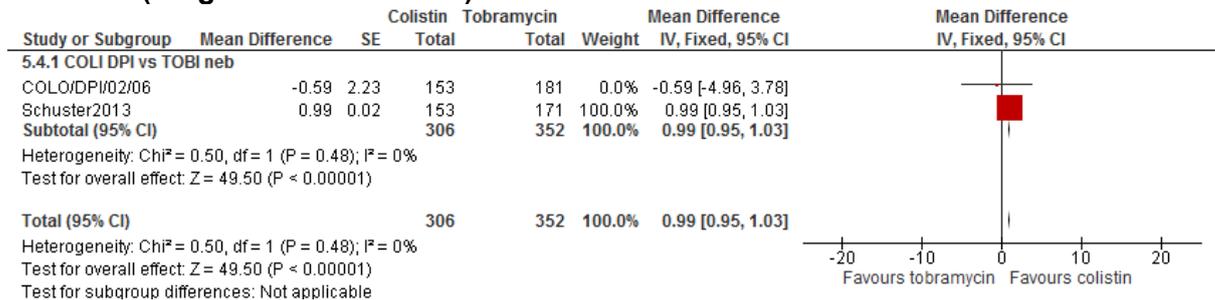
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; Neb: nebulised; SE: standard error

**Figure 176: Lung function: mean % change in FEV<sub>1</sub>% predicted at 12 weeks follow-up (range of scores: 0-100)**



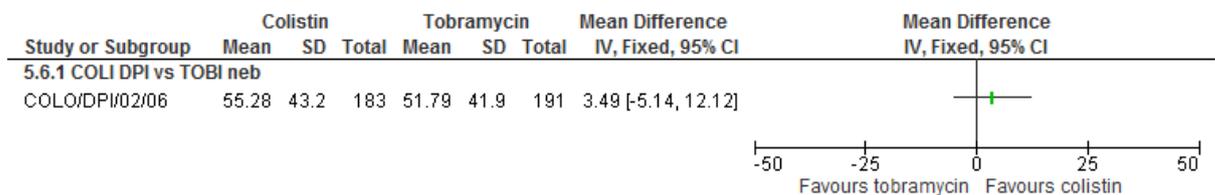
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; Neb: nebulised; SE: standard error

**Figure 177: Lung function: mean % change in FEV<sub>1</sub>% predicted at 24 weeks follow-up (range of scores: 0-100)**



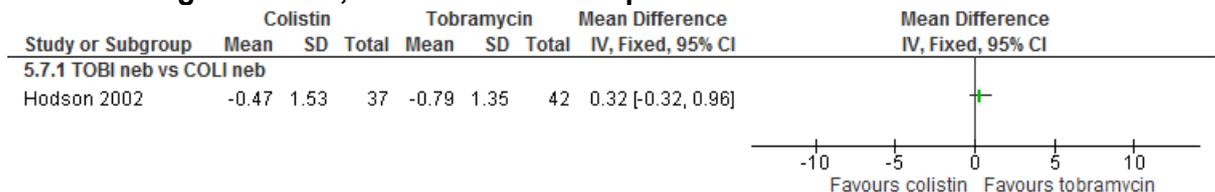
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; Neb: nebulised; SE: standard error

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



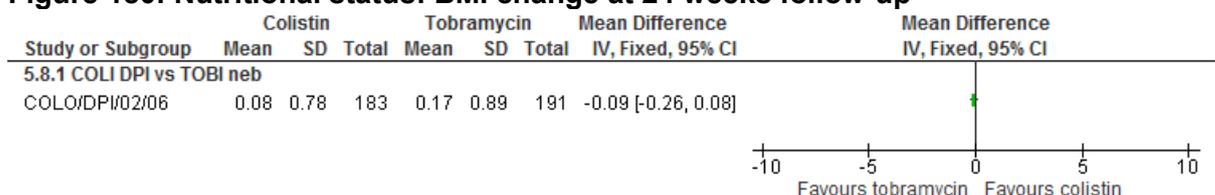
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

**Figure 179: Suppression of the organism: change in sputum P. aeruginosa density Log<sub>10</sub> 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**



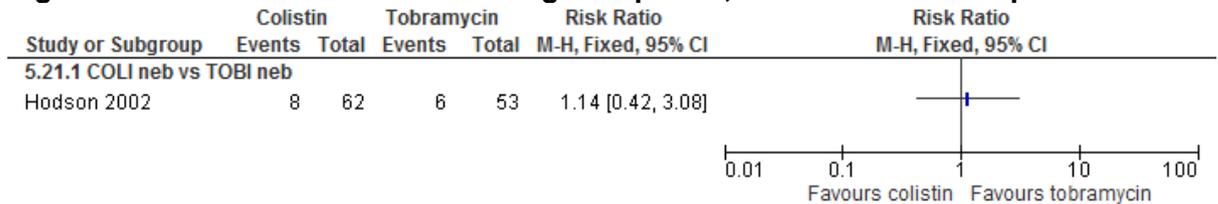
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

**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.

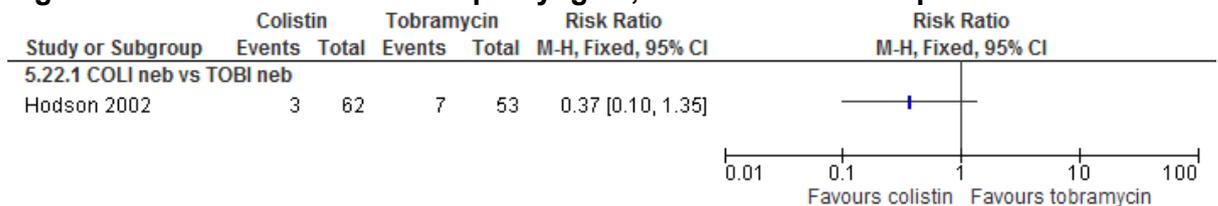
Abbreviations: CFQ-R: cystic fibrosis questionnaire revised

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



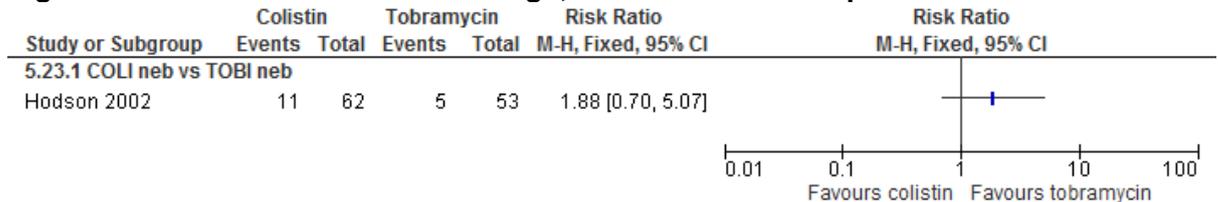
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

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



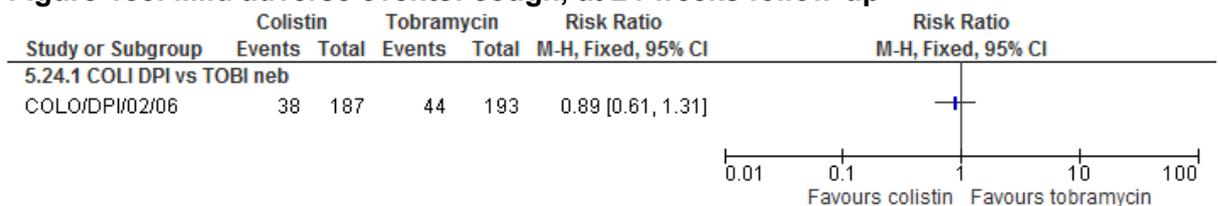
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

**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**



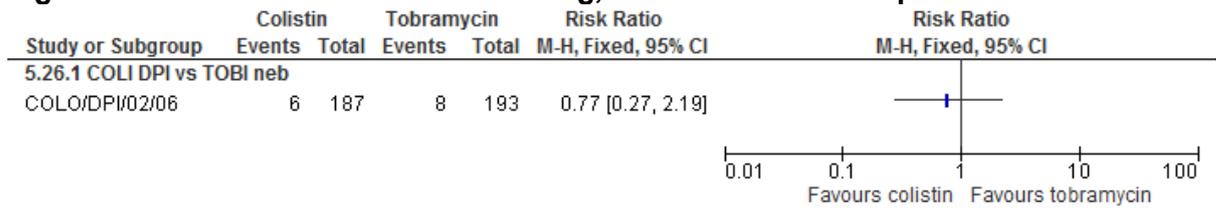
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

**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**



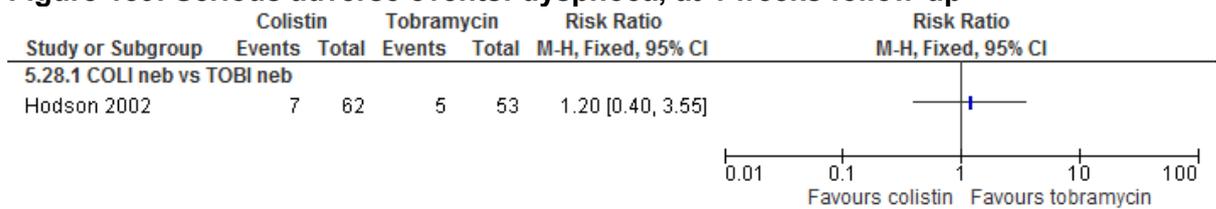
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

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



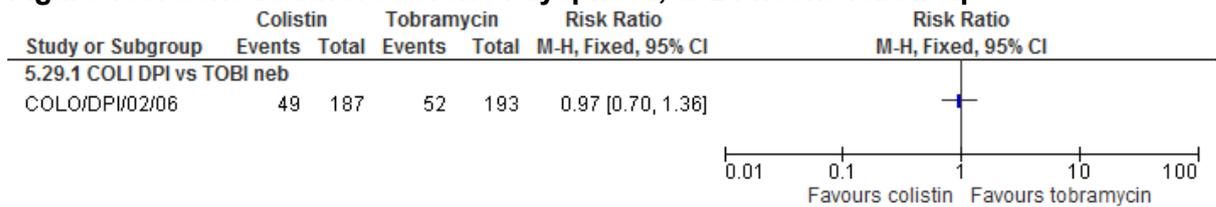
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

**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**



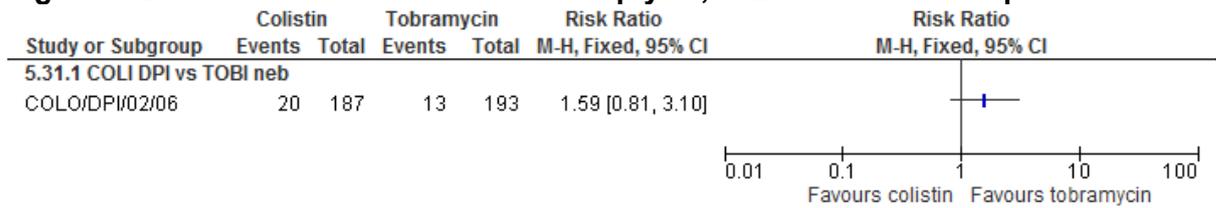
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

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



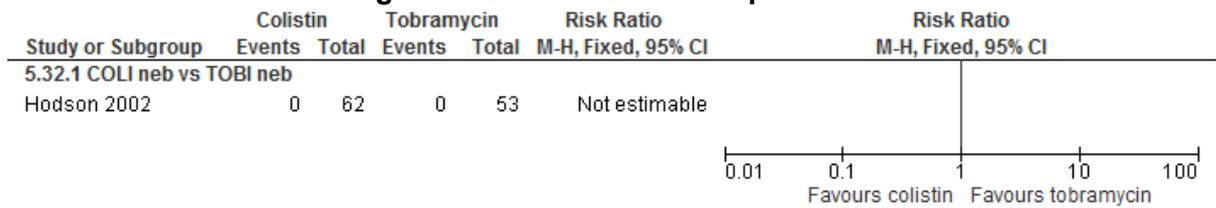
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

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



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

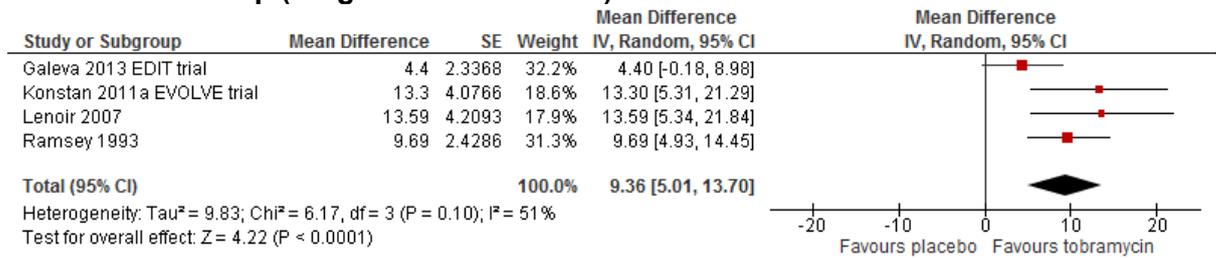
**Figure 193: Emergence of resistant organisms: emergence of highly tobramycin-resistant P. Aeruginosa at 4 weeks follow-up**



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

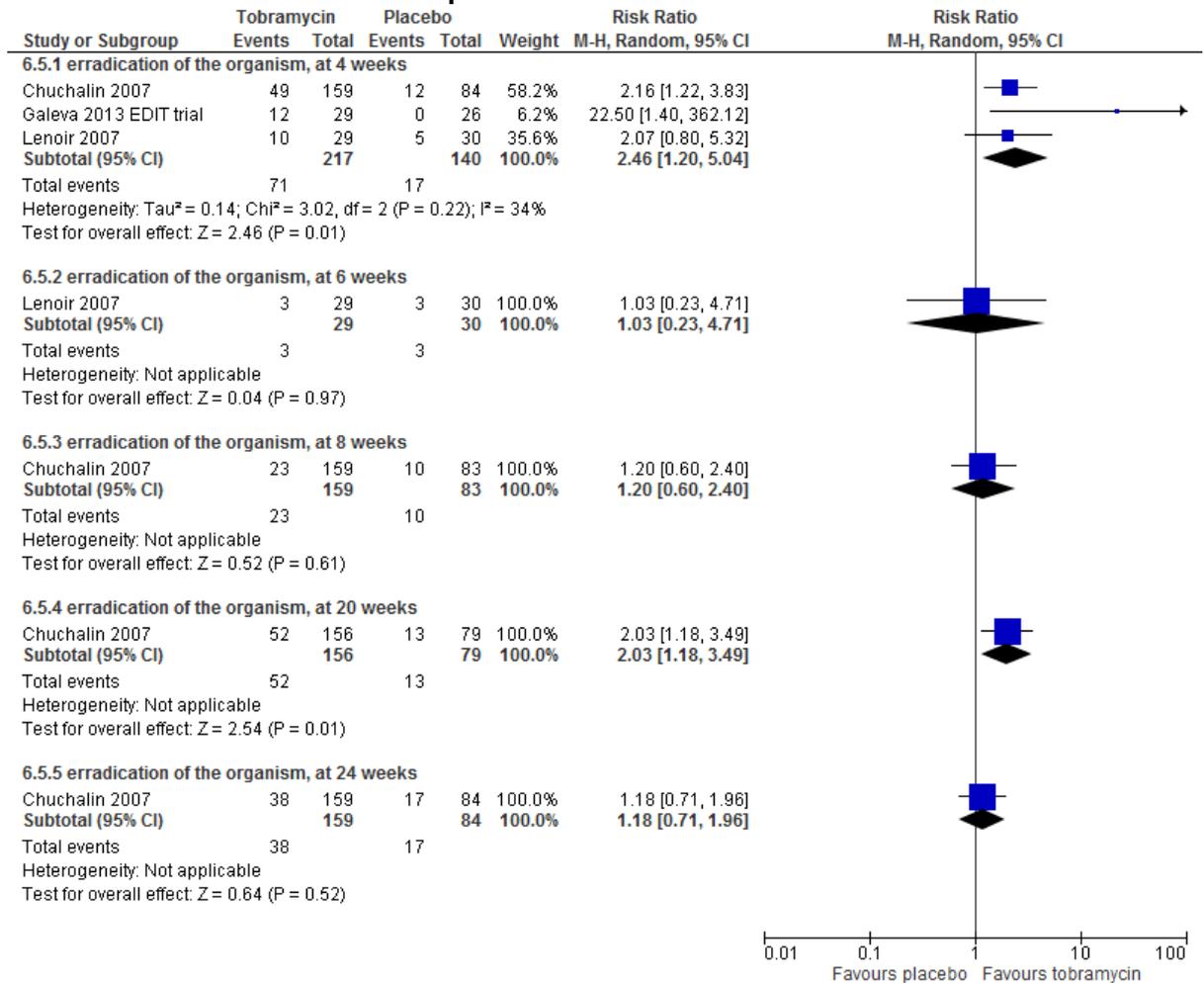
**Pairwise comparison 4.1. Tobramycin versus placebo**

**Figure 194: Lung function: mean % change in FEV<sub>1</sub>% predicted at 1 to 3 months follow-up (range of scores: 0-100)**



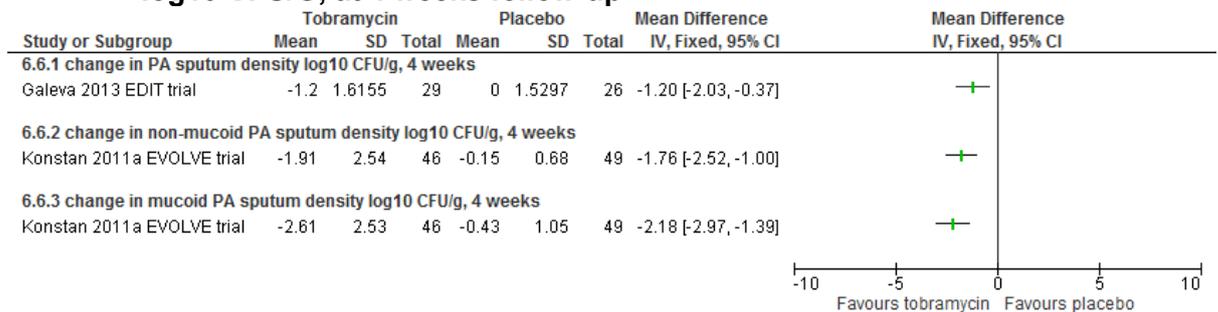
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error

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



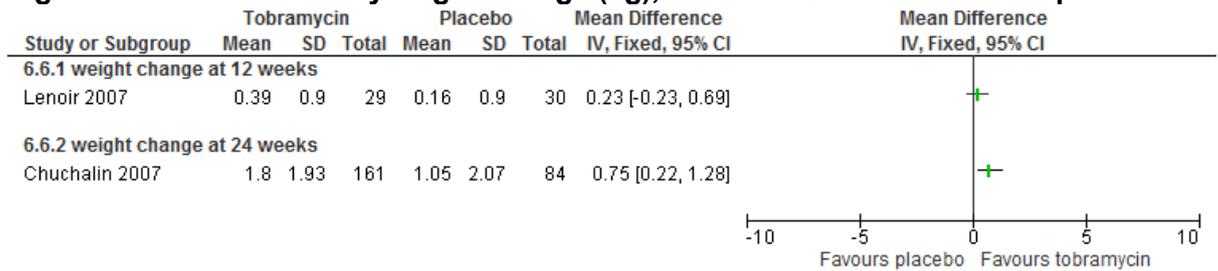
Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

**Figure 196: Suppression of the organism: change in P. aeruginosa sputum density log<sub>10</sub> CFU/G, at 4 weeks follow-up**



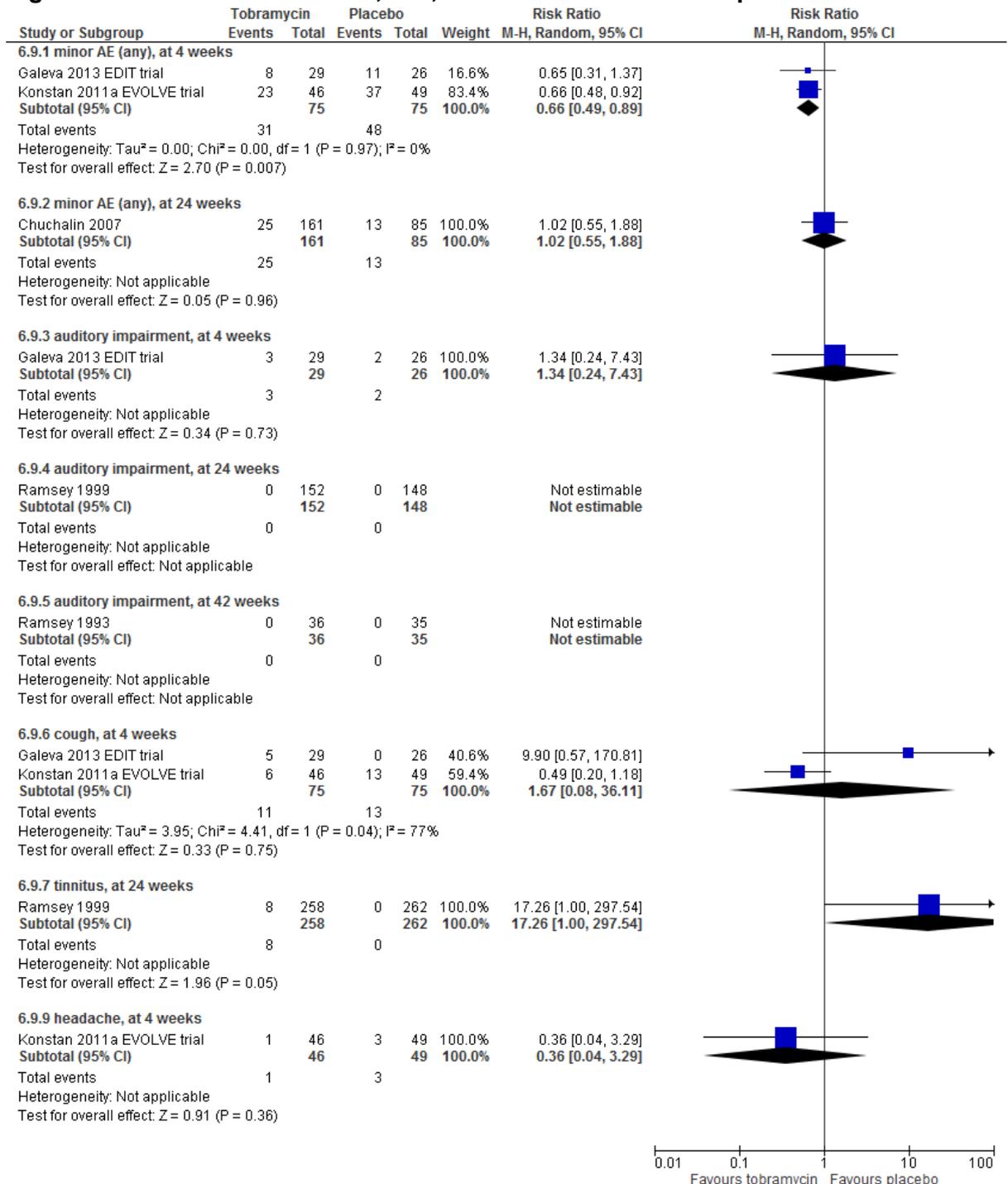
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

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



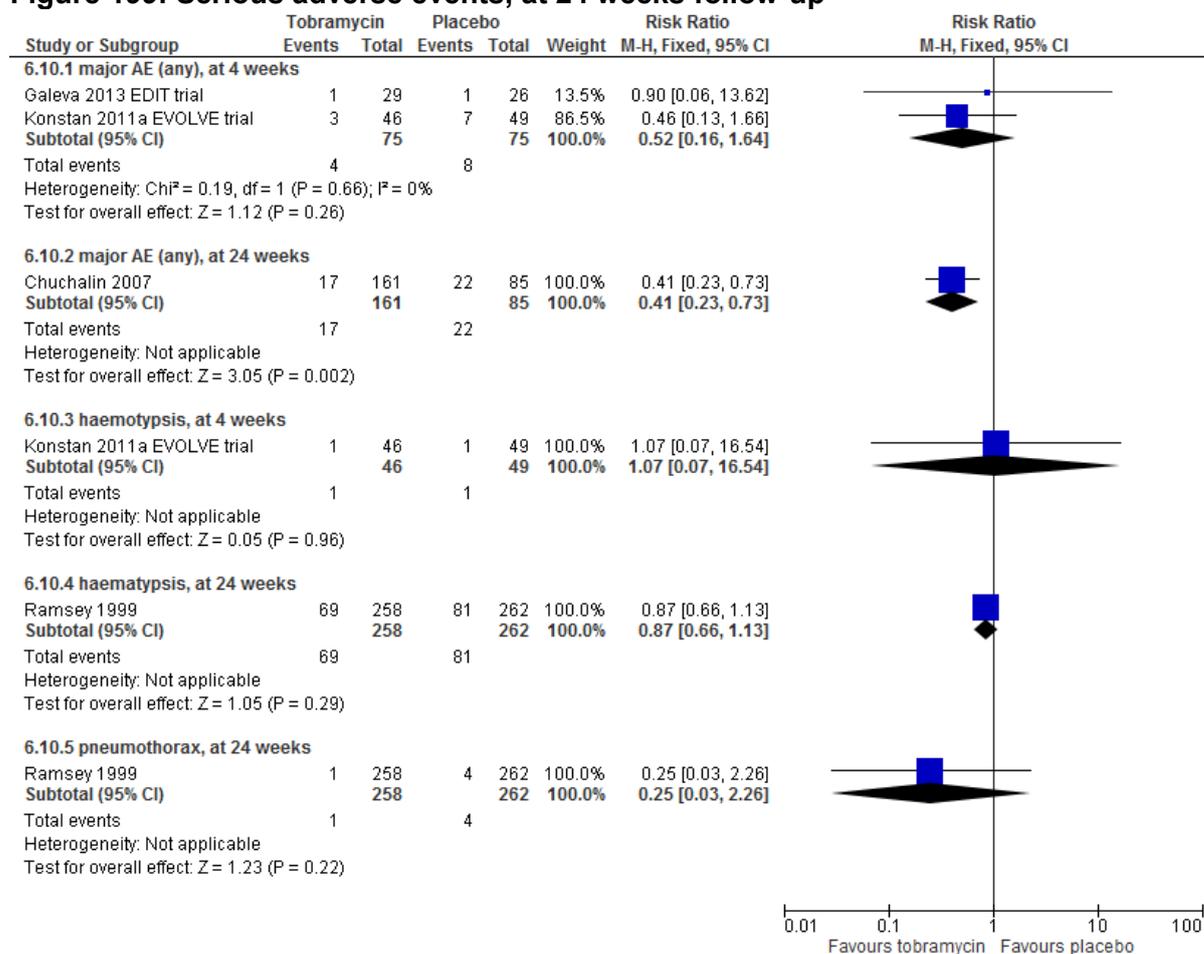
Abbreviations: CI: confidence interval; IV: inverse variance; kg: kilograms; SD: standard deviation

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



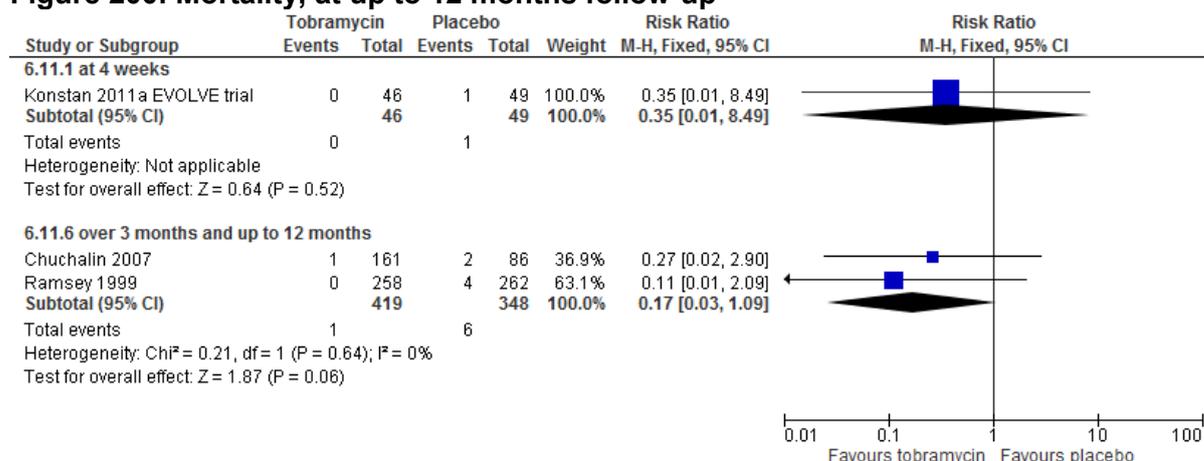
Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

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



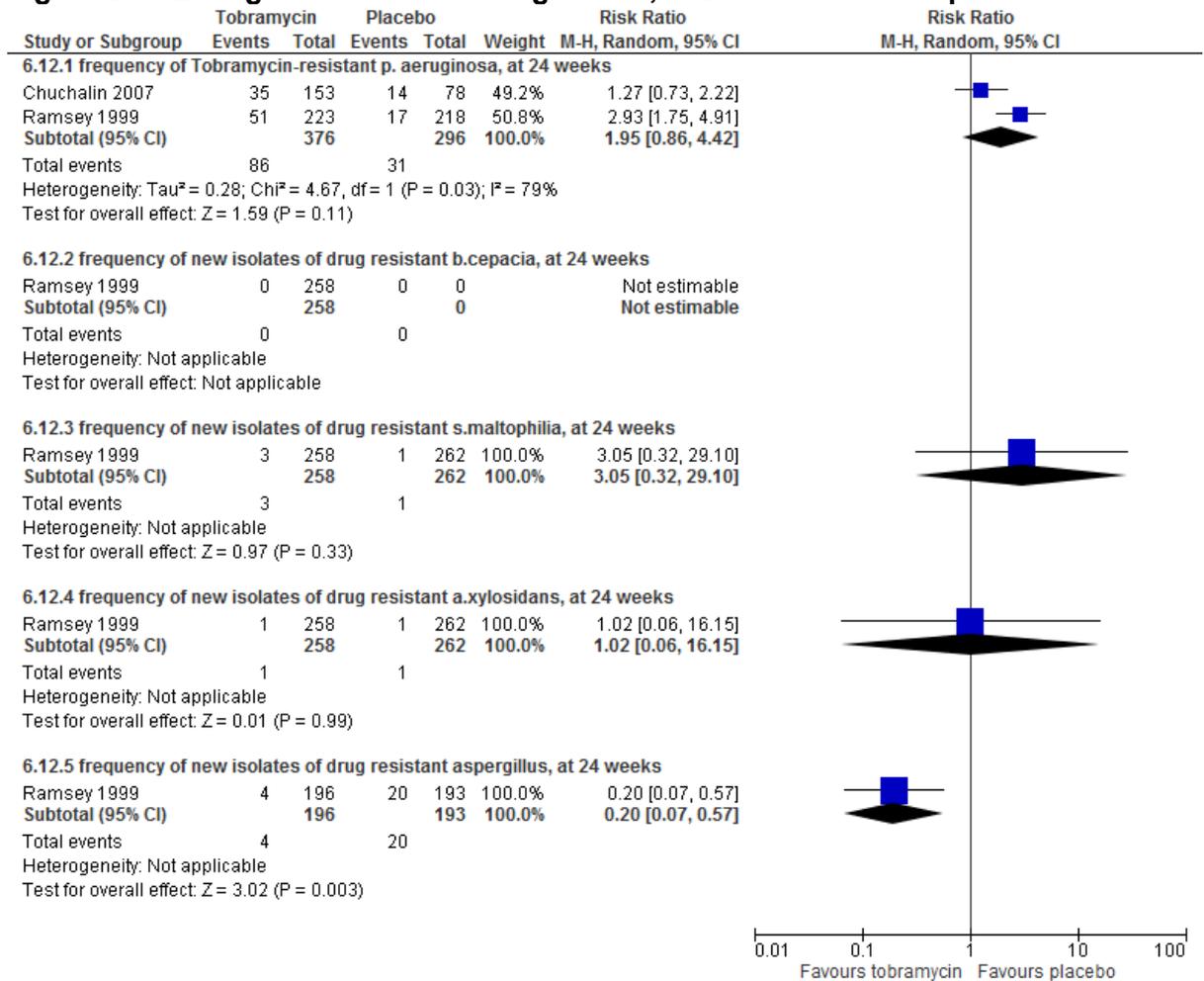
Abbreviations: CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel

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



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

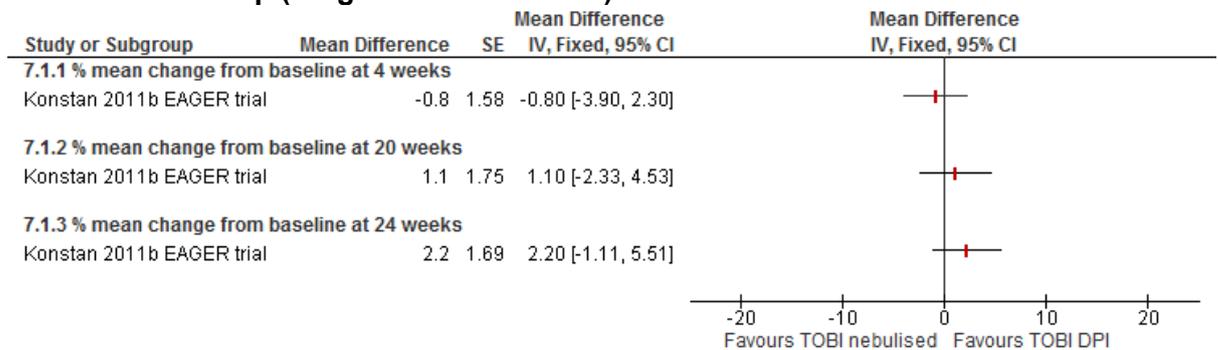
**Figure 201: Emergence of resistant organisms, at 24 weeks follow-up**



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

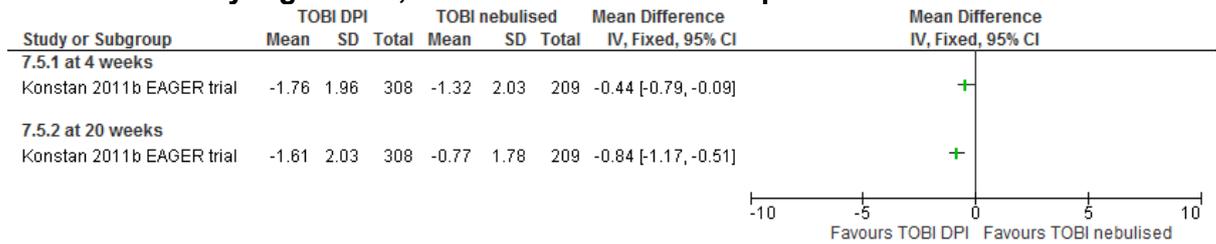
**Pairwise comparison 4.2. Tobramycin inhalation powder (TOBI DPI) versus tobramycin inhalation solution (TOBI nebulised)**

**Figure 202: Lung function: mean change in FEV<sub>1</sub>% predicted at 4, 20 and 24 weeks follow-up (range of scores: 0-100)**



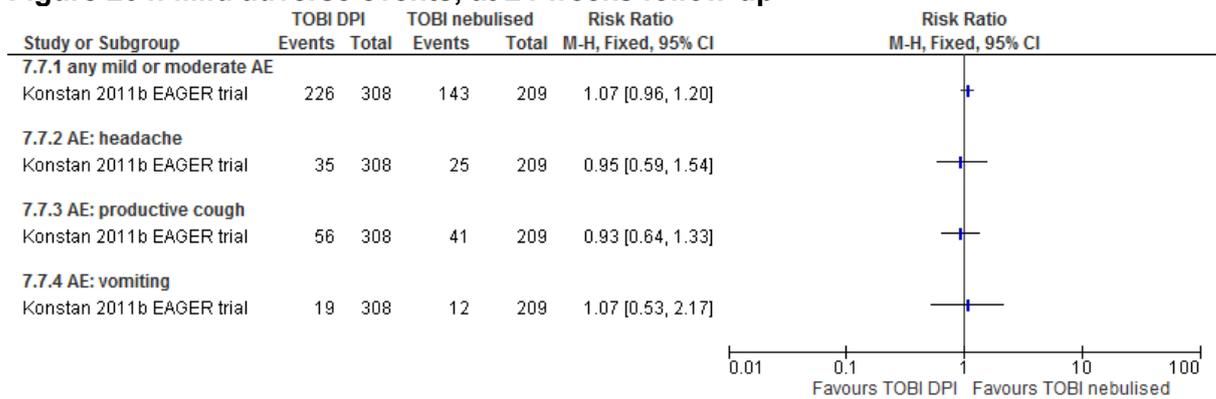
Abbreviations: CI: confidence interval; DPI: dry powder inhalation; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SE: standard error; TOBI: tobramycin

**Figure 203: Suppression of the organism: mean change in *P. aeruginosa* sputum density log<sub>10</sub> CFU, at 4 to 20 weeks follow-up**



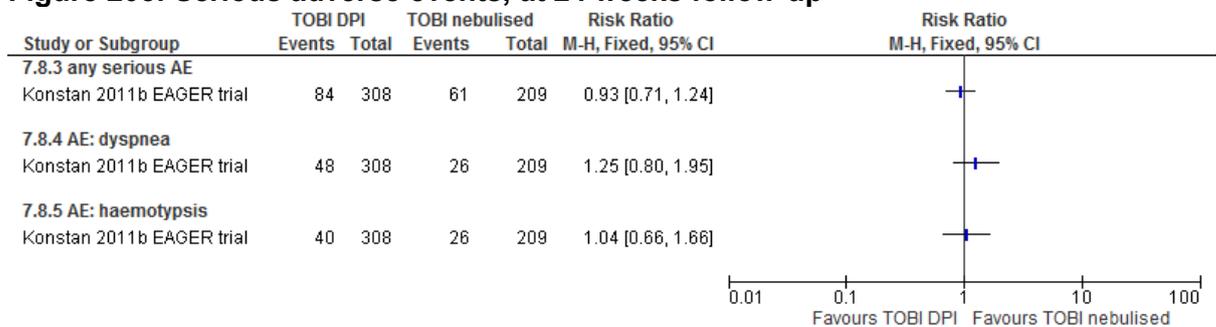
Abbreviations: CI: confidence interval; DPI: dry powder inhalation; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; PA: *Pseudomonas aeruginosa*; SD: standard deviation; TOBI: tobramycin

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



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

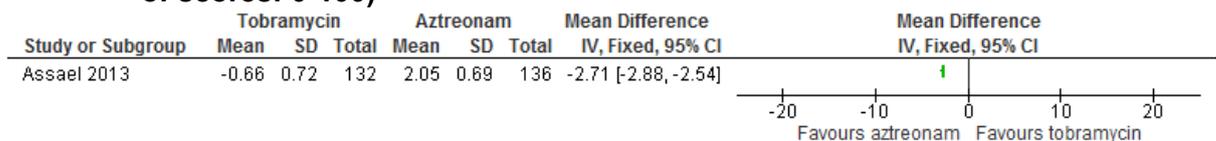
**Figure 205: Serious adverse events, at 24 weeks follow-up**



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

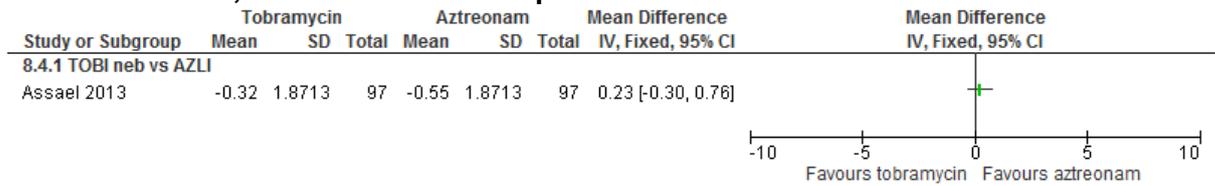
### Pairwise comparison 4.3. Tobramycin versus Aztreonam lysine

**Figure 206: Lung function: % change in FEV<sub>1</sub>% predicted at 3 months follow-up (range of scores: 0-100)**



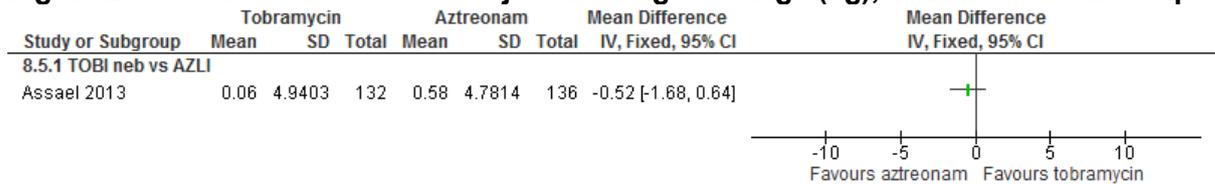
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation. Calculated across 3x28-day treatment courses

**Figure 207: Suppression of the organism: adj mean change sputum density log<sub>10</sub> PA CFU/G, at 20 weeks follow-up**



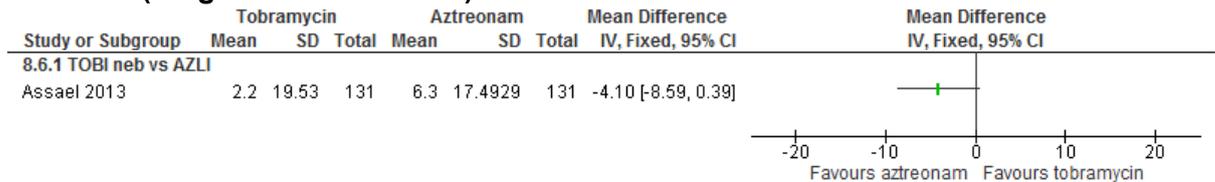
Abbreviations: CI: confidence interval; CFU: colony forming unit; IV: inverse variance; PA: *Pseudomonas aeruginosa*; SD: standard deviation

**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)**



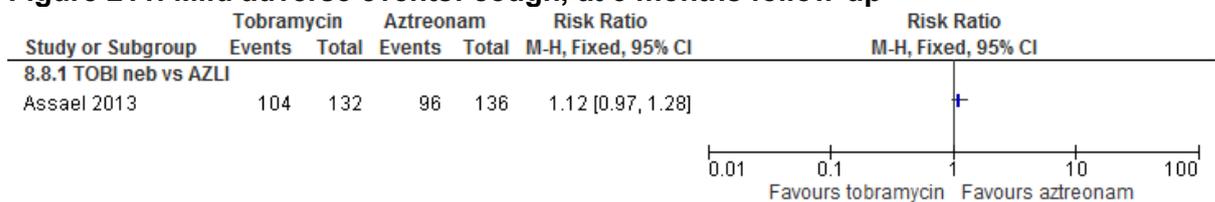
Abbreviations: CI: confidence interval; CFQ-R: cystic fibrosis questionnaire revised; IV: inverse variance; SD: standard deviation

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



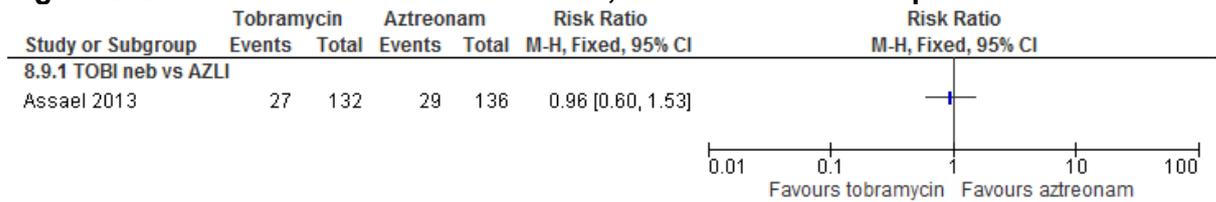
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

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



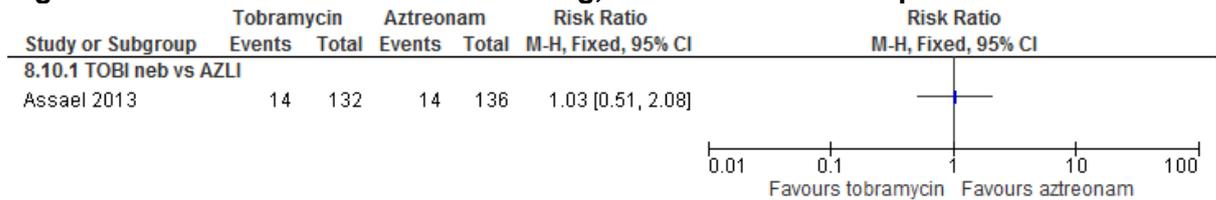
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

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



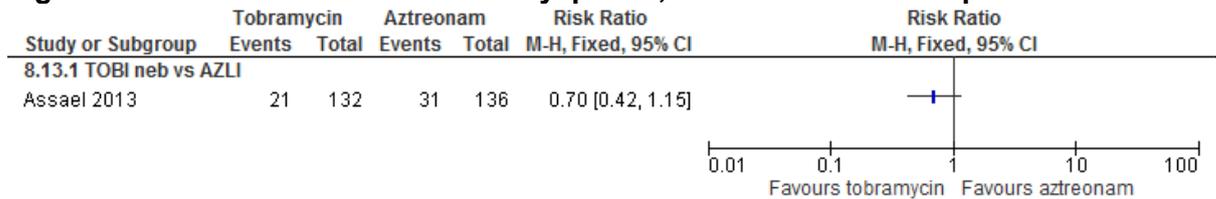
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

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



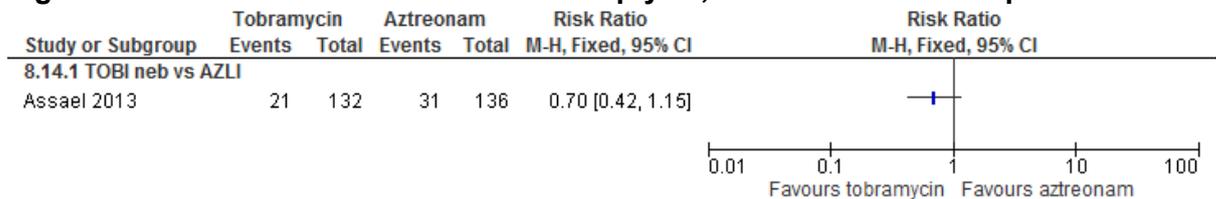
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

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



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

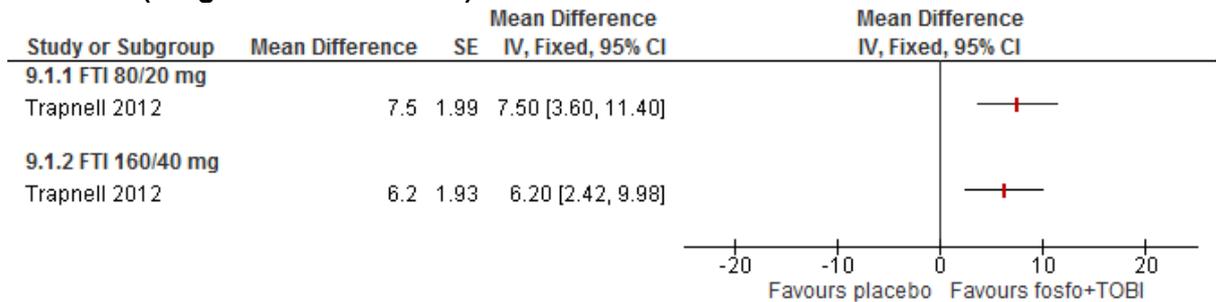
**Figure 215: Serious adverse events: haemoptysis, at 3 months follow-up**



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

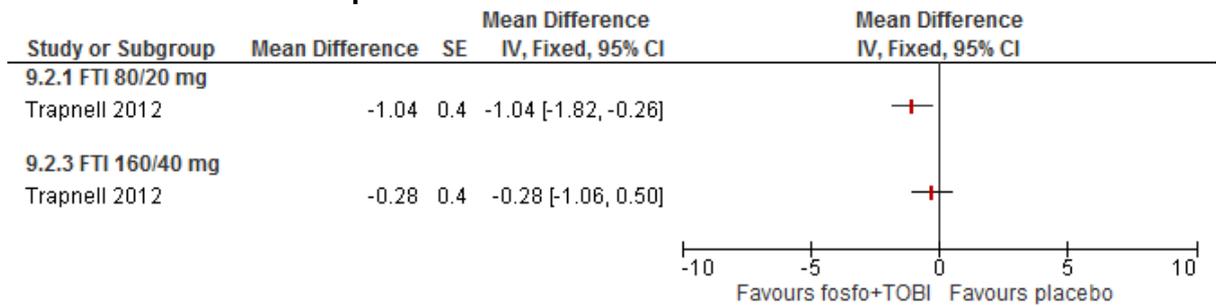
**Pairwise comparison 5. Combination of fosfomycin + tobramycin versus placebo**

**Figure 216: Lung function: relative change in FEV<sub>1</sub>% predicted, at 4 weeks follow-up (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; fosfo+TOBI: fosfomycin + tobramycin; IV: inverse variance; SE: standard error

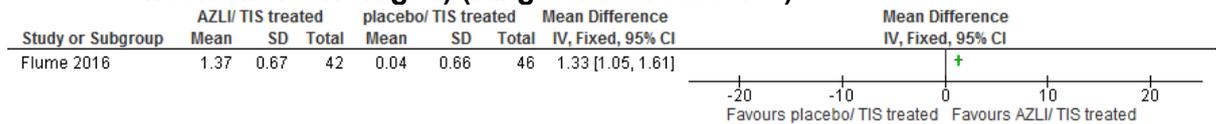
**Figure 217: Suppression of the organism: sputum PA density, log 10 CFU/g at 4 weeks follow-up**



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

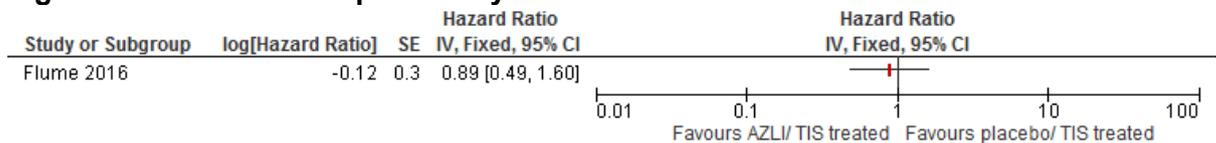
**Pairwise comparison 6. Continuous alternating therapy versus intermittent treatment: aztreonam lysine + tobramycin or placebo + tobramycin**

**Figure 218: Lung function: % change in FEV<sub>1</sub>% predicted (values at 4, 12 and 20 weeks were averaged) (range of scores: 0-100)**



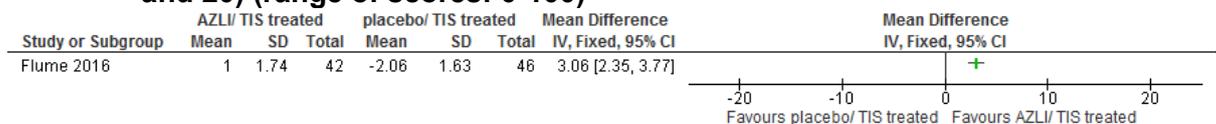
Abbreviations: AZLI: aztreonam lysine; CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation; TIS: tobramycin inhaled solution

**Figure 219: Time to next pulmonary exacerbation**



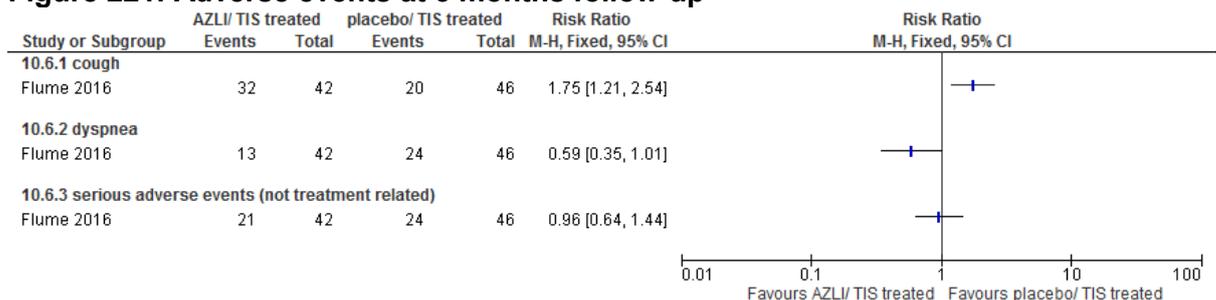
Abbreviations: AZLI: aztreonam lysine; CI: confidence interval; IV: inverse variance; SE: standard error; TIS: tobramycin inhaled solution

**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.

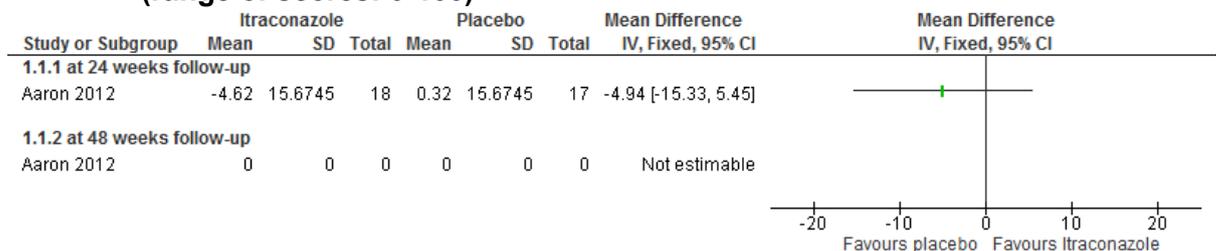
### I.11.3 Burkholderia Cepacia Complex

Not applicable, as no relevant studies were identified.

### I.11.4 Aspergillus Fumigatus

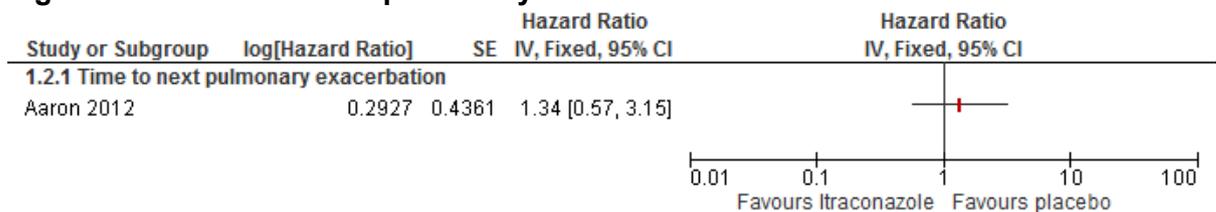
#### Pairwise comparison 7: Itraconazole versus placebo

**Figure 222: Percentage change in FEV<sub>1</sub> from baseline at 24 and 48 weeks follow-up (range of scores: 0-100)**



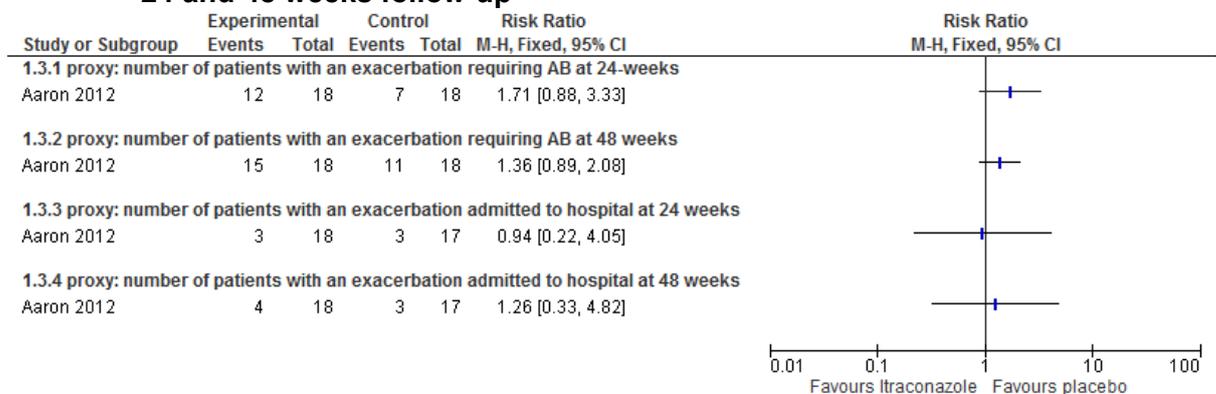
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation. Mean difference (95% CI) at 48-weeks follow-up: -3.71% (-13.26 to 20.28). Not enough data was provided for RevMan.

**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**

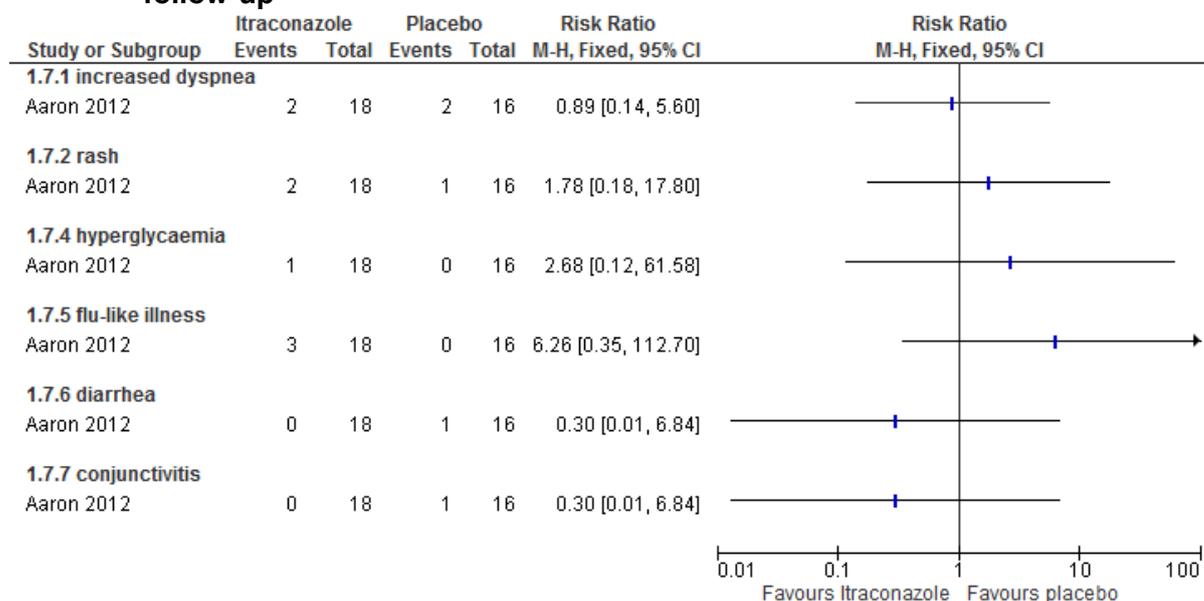


Abbreviations: AB: antibiotics; CI: confidence interval; M-H: Mantel-Haenszel. Proxy outcome.

**Figure 225: Quality of life**

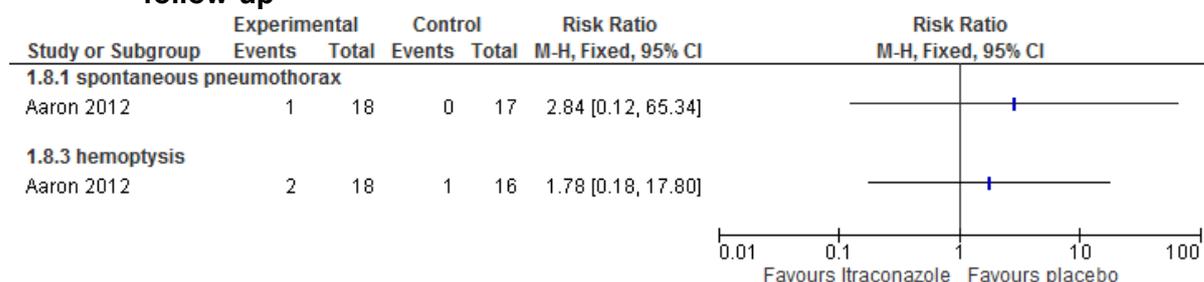
Data could not be plotted.

**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**



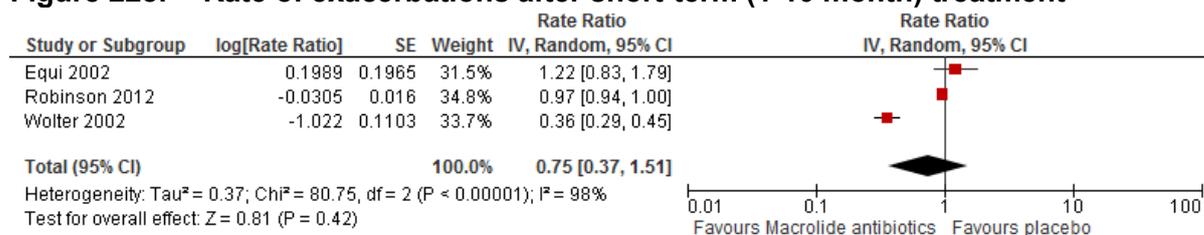
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

## 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**

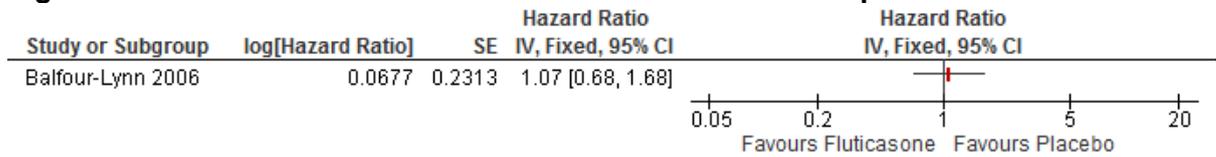


Abbreviations: CI: confidence interval; df: degrees of freedom; IV: inverse variance; SE: standard error

## I.12.2 Non-NMA outcomes (pairwise comparisons)

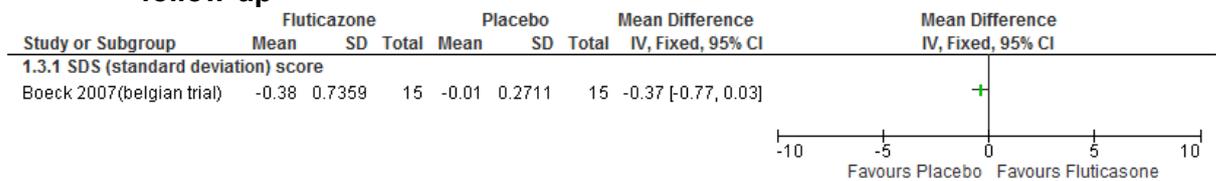
### Pairwise comparison 1. Fluticasone versus placebo

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



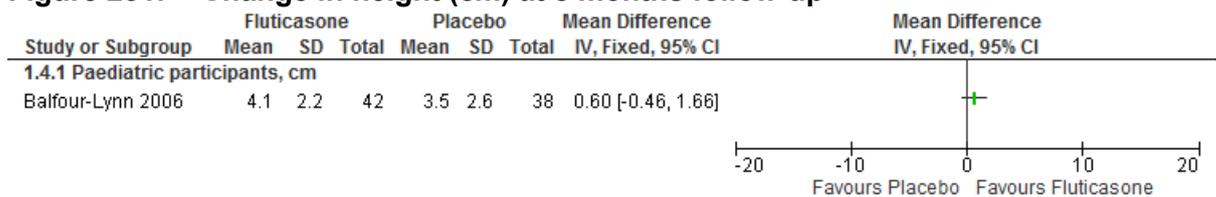
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

**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

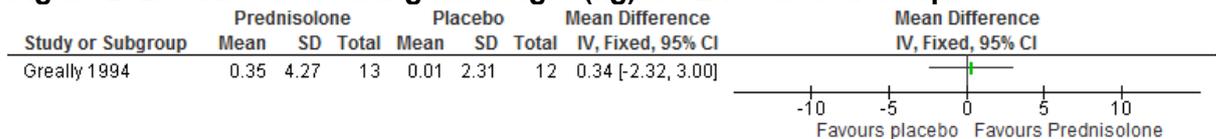
**Figure 231: Change in height (cm) at 8 months follow-up**



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

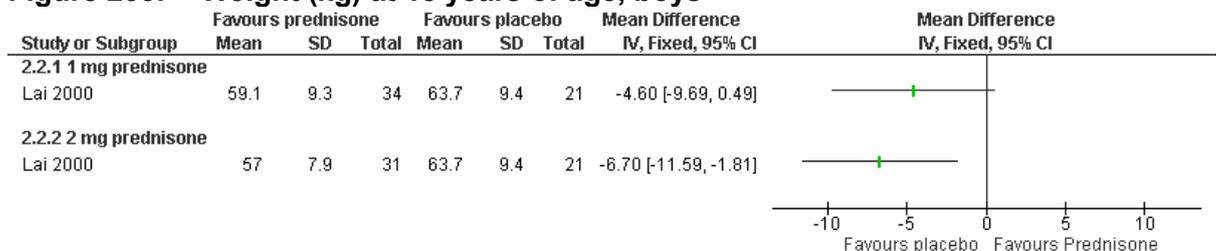
### Pairwise comparison 2. Prednisone/ Prednisolone versus placebo

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



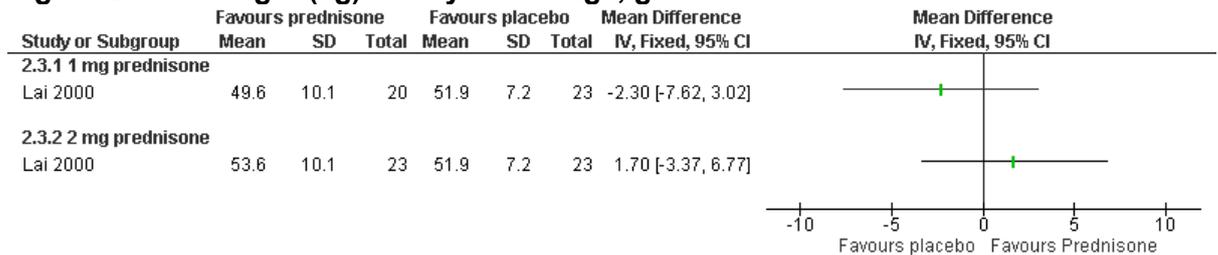
Abbreviations: CI: confidence interval; IV: inverse variance; kg: kilograms; SD: standard deviation. Intervention: 2mg/kg Prednisolone;

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



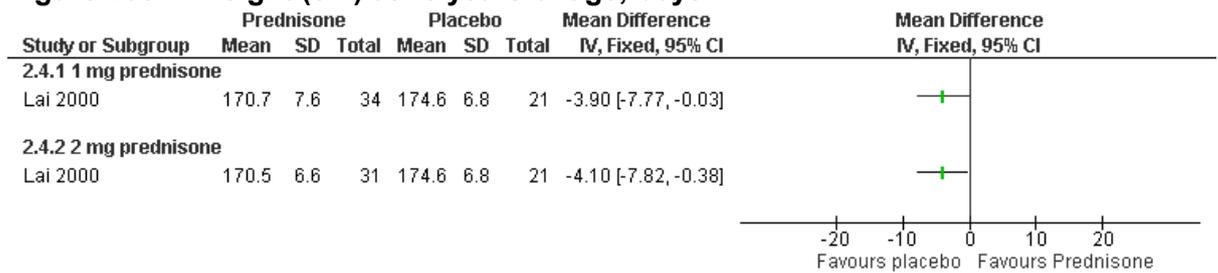
Abbreviations: CI: confidence interval; IV: inverse variance; kg: kilograms; SD: standard deviation

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



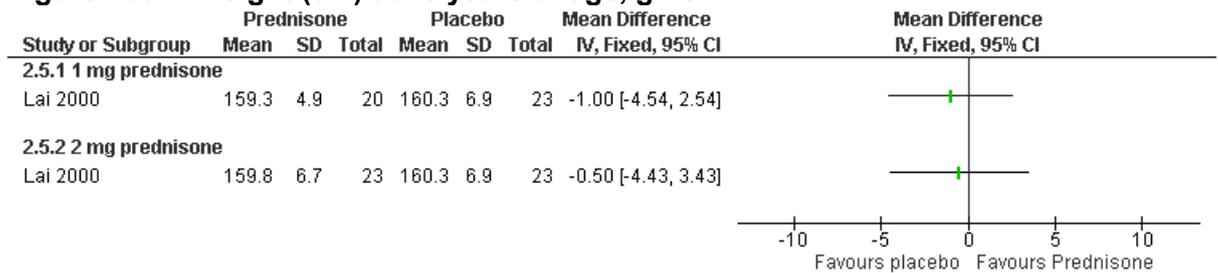
Abbreviations: CI: confidence interval; IV: inverse variance; kg: kilograms; SD: standard deviation

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



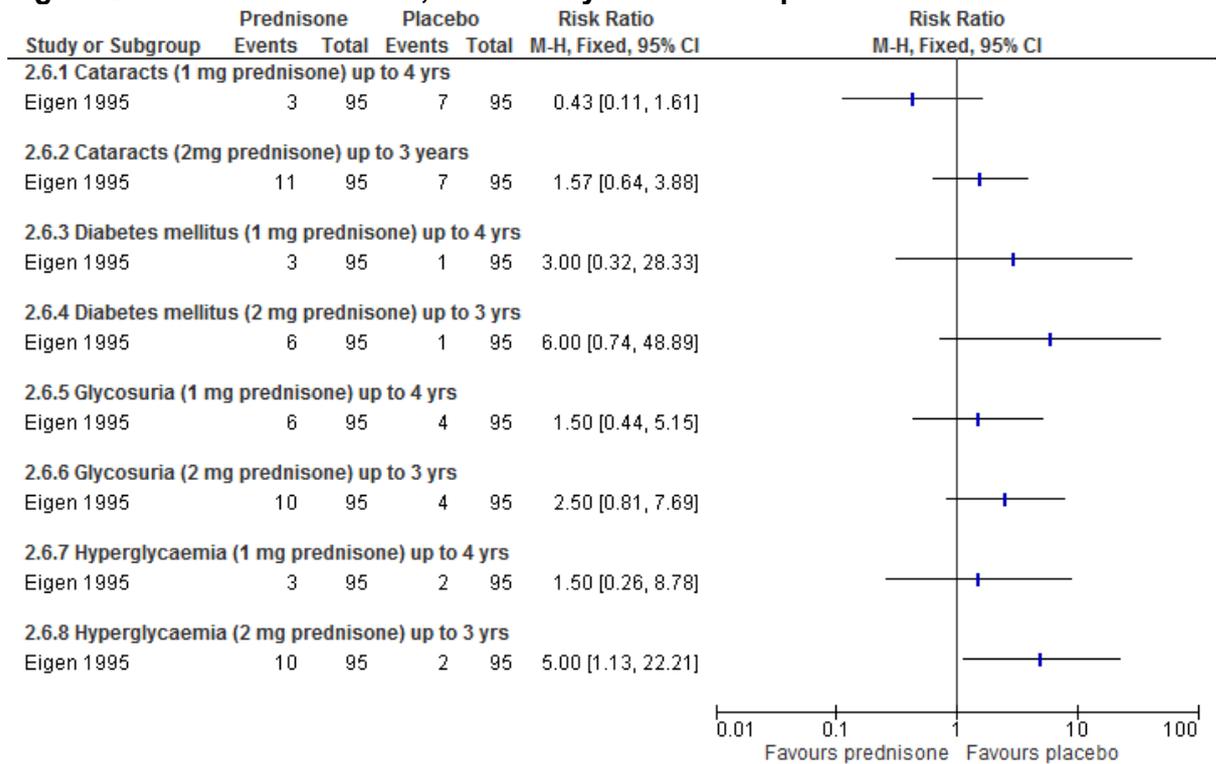
Abbreviations: CI: confidence interval; cm: centimetres; IV: inverse variance; SD: standard deviation

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



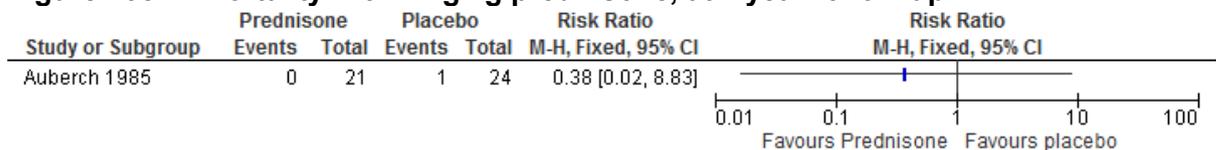
Abbreviations: CI: confidence interval; cm: centimetres; IV: inverse variance; SD: standard deviation

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



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

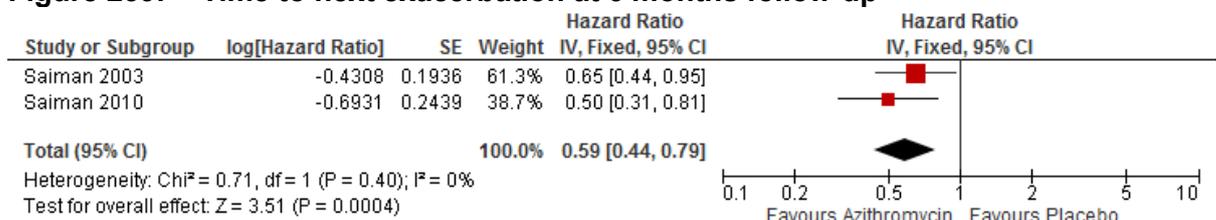
**Figure 238: Mortality with 2mg/kg prednisone, at 4 year follow-up**



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

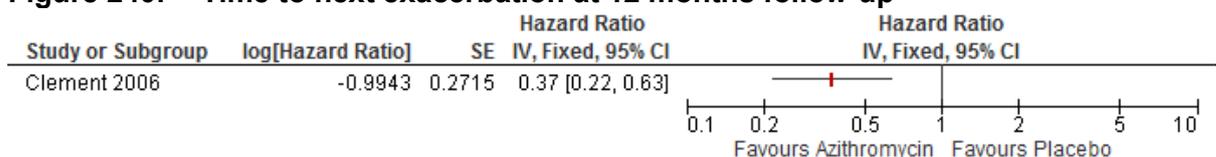
### Pairwise comparison 3. Azithromycin versus placebo

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



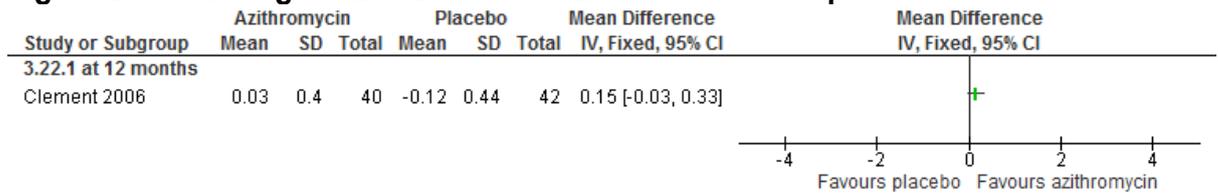
Abbreviations: CI: confidence interval; df: degrees of freedom; IV: inverse variance; SE: standard error

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



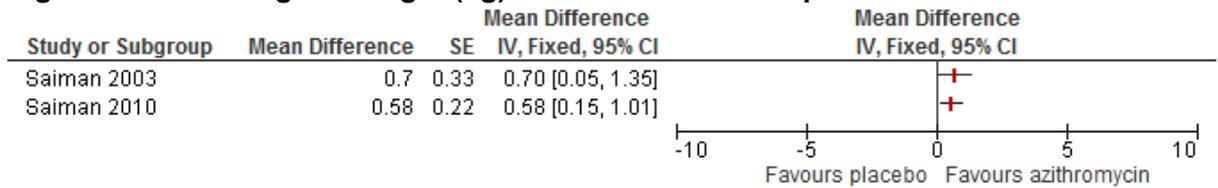
Abbreviations: CI: confidence interval; IV: inverse variance; SE: standard error

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



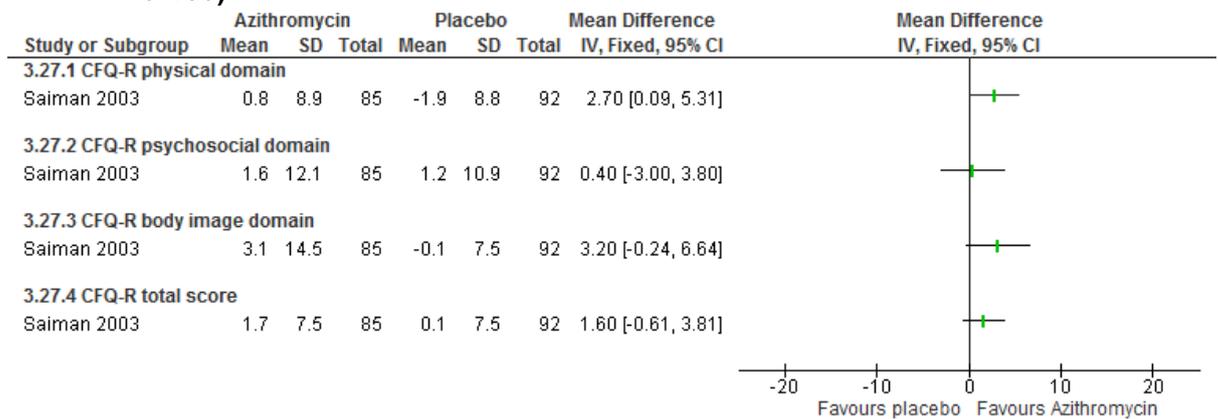
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

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



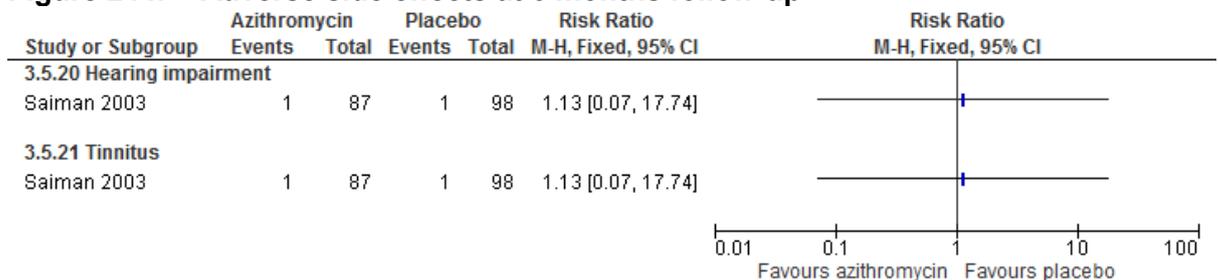
Abbreviations: CI: confidence interval; IV: inverse variance; kg: kilograms; SE: standard error

**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

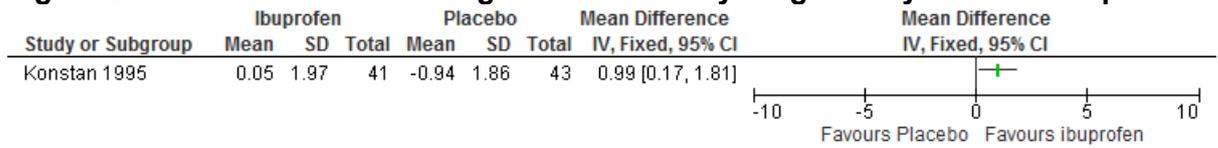
**Figure 244: Adverse side effects at 6 months follow-up**



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

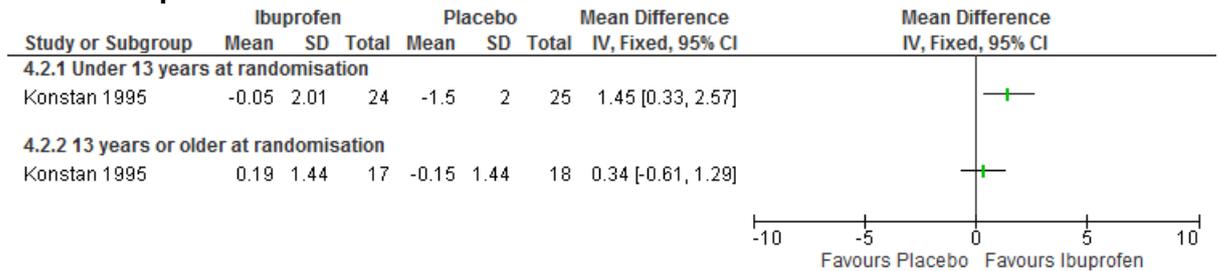
**Pairwise comparison 4. Ibuprofen versus placebo**

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



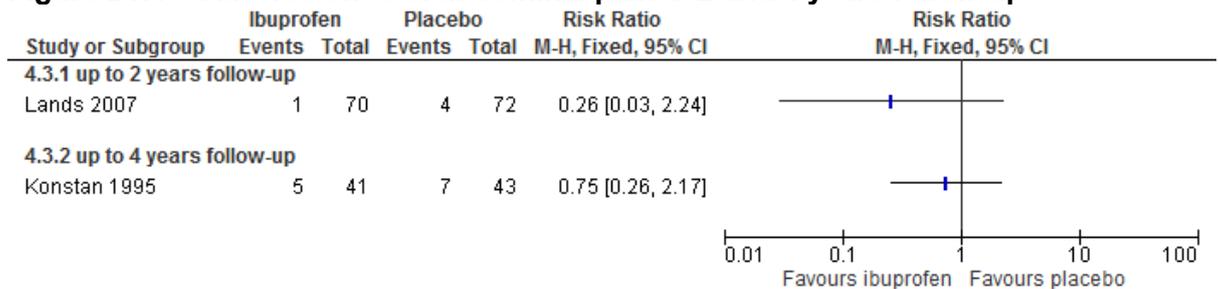
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

**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**

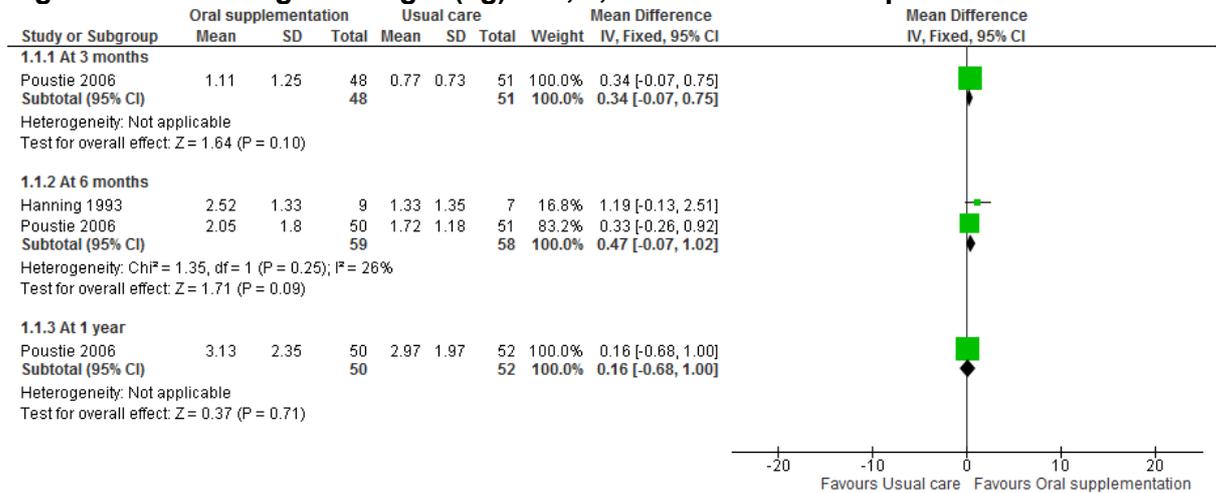


Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

## I.13 Nutritional interventions

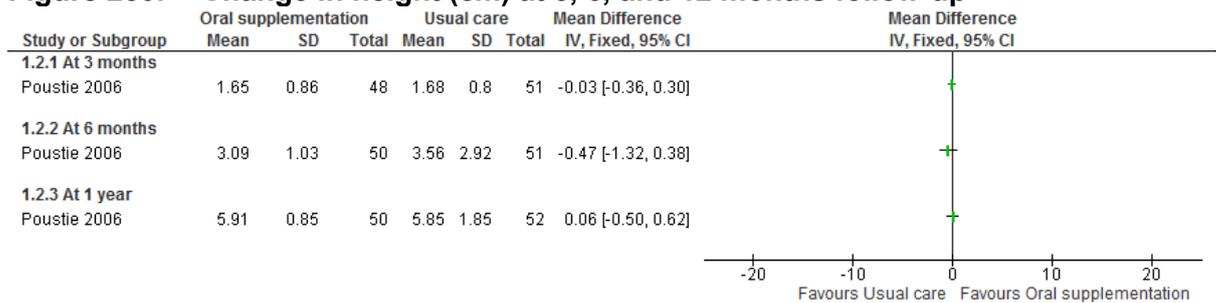
### Comparison 1. Oral supplements versus usual care

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



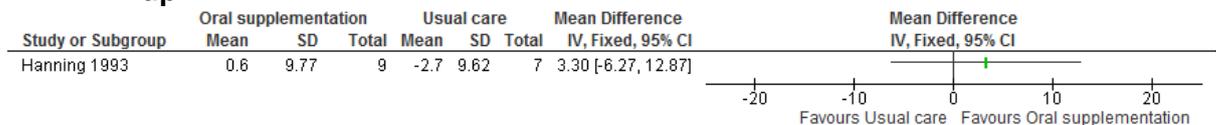
Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval

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



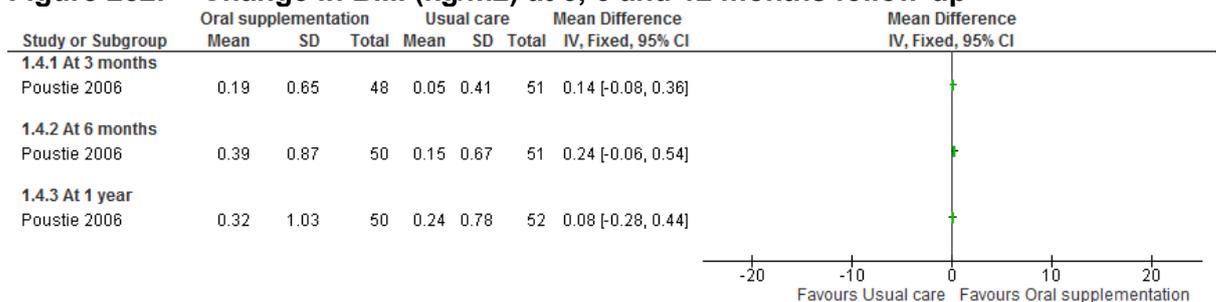
Abbreviations: CI: confidence interval; cm: centimetres; IV: inverse variance; SD: standard deviation;

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



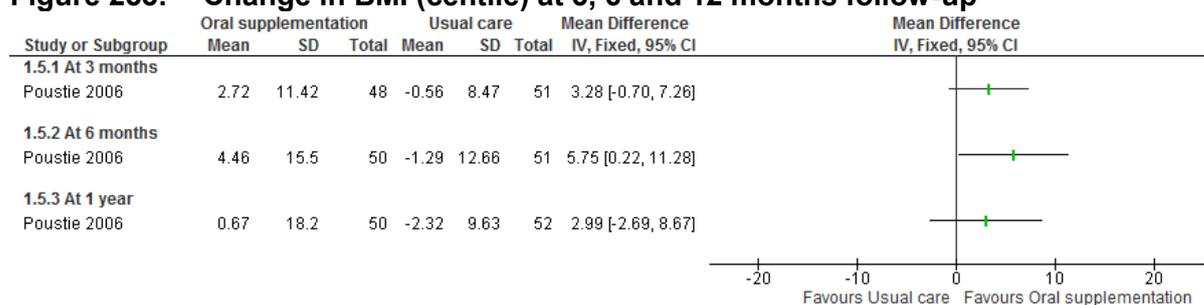
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation;

**Figure 252: Change in BMI (kg/m<sup>2</sup>) at 3, 6 and 12 months follow-up**



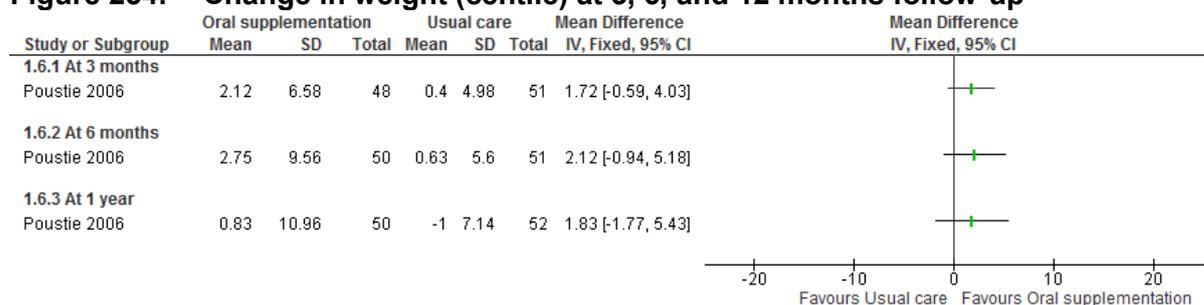
Abbreviations: BMI: body mass index; CI: confidence interval; kg: kilograms; IV: inverse variance; m<sup>2</sup>: square metres; SD: standard deviation

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



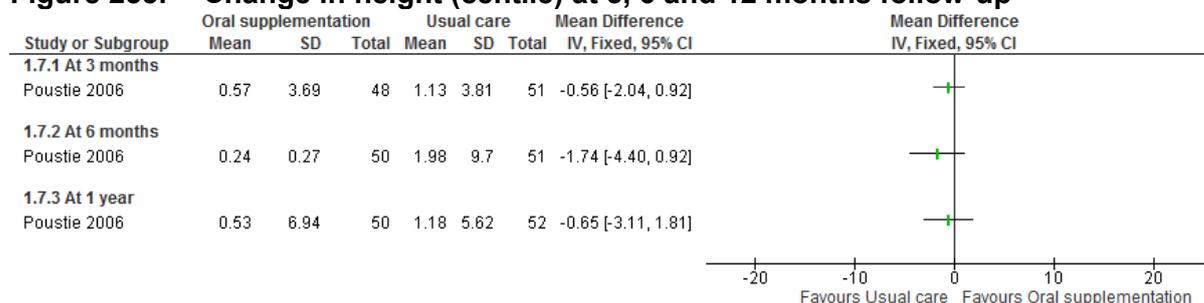
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

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



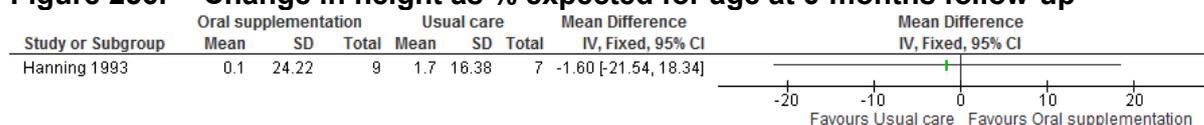
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

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



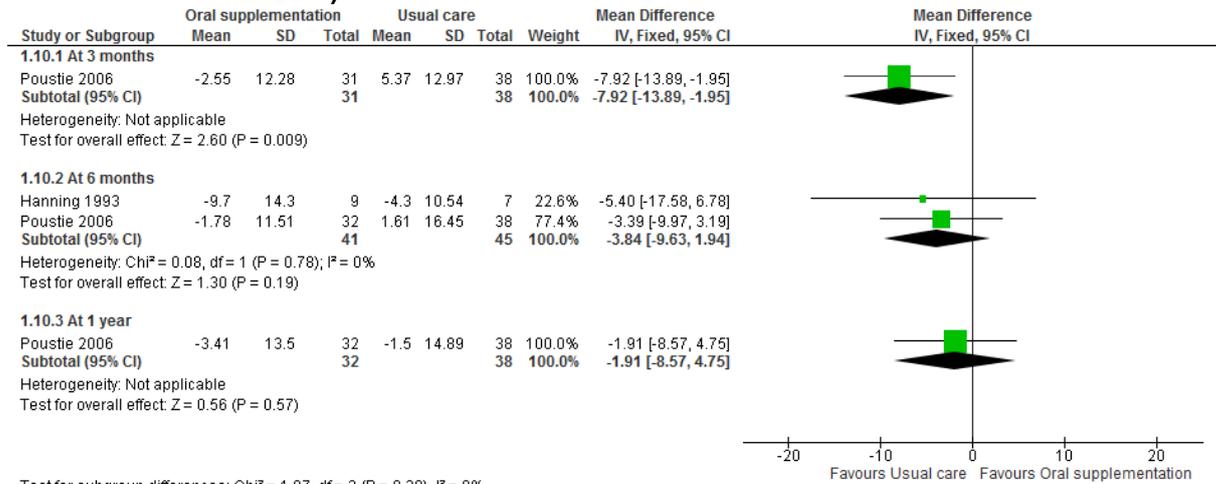
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

**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 FEV<sub>1</sub> % predicted at 3, 6 and 12 months follow-up (range of scores: 0-100)**

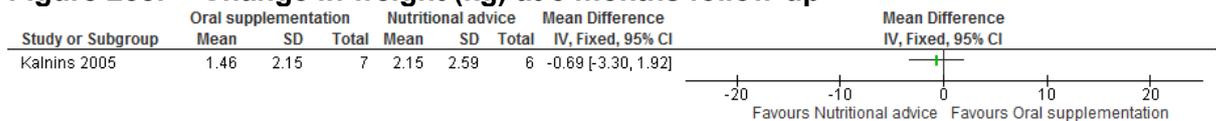


Test for subgroup differences: Chi<sup>2</sup> = 1.87, df = 2 (P = 0.39), I<sup>2</sup> = 0%

Abbreviations: CI: confidence interval; df: degrees of freedom; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

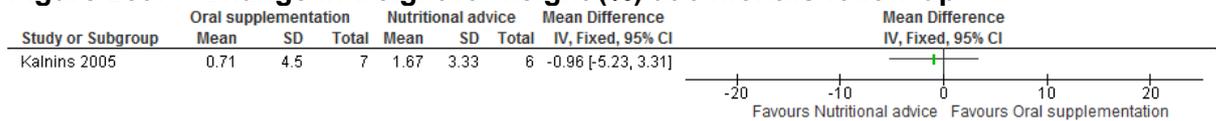
**Comparison 1.2 Oral calorie supplementation versus nutritional advice**

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



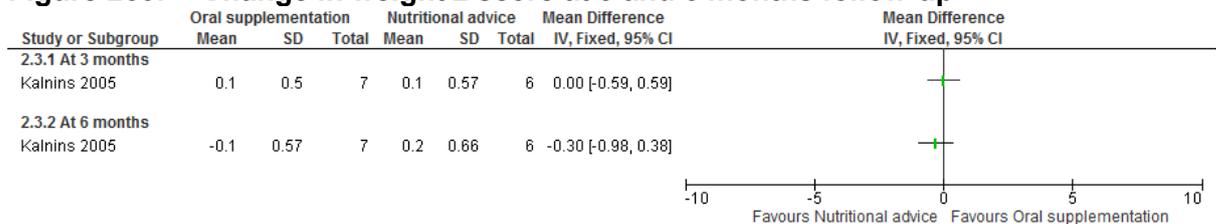
Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval

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



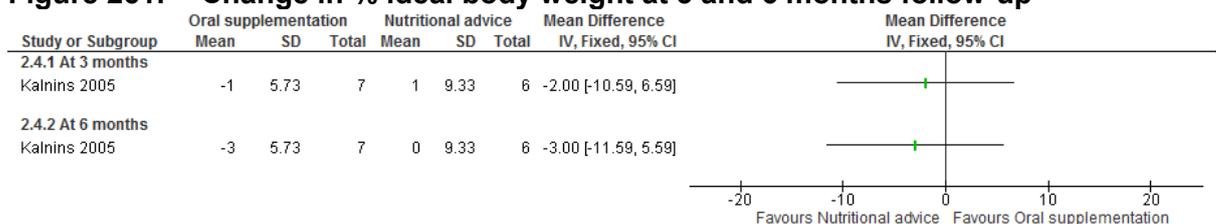
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

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



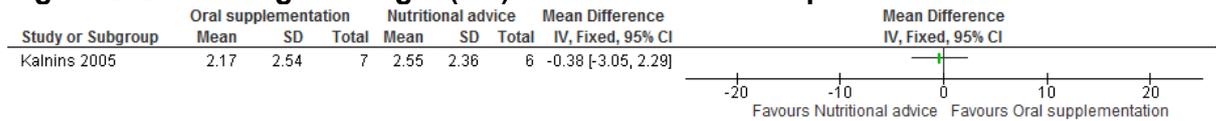
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

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



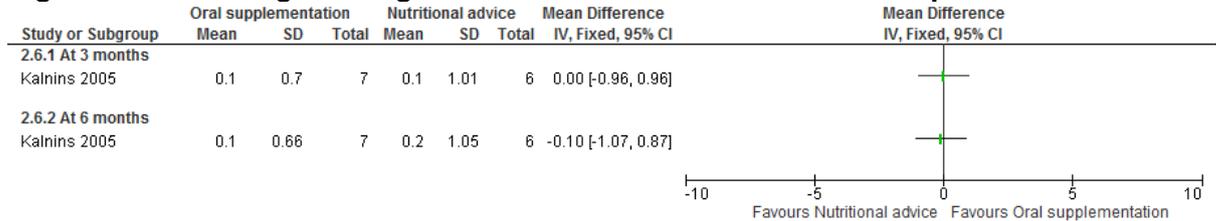
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

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



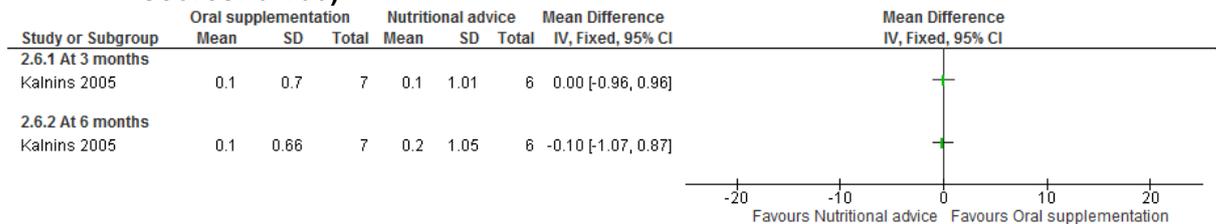
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

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



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

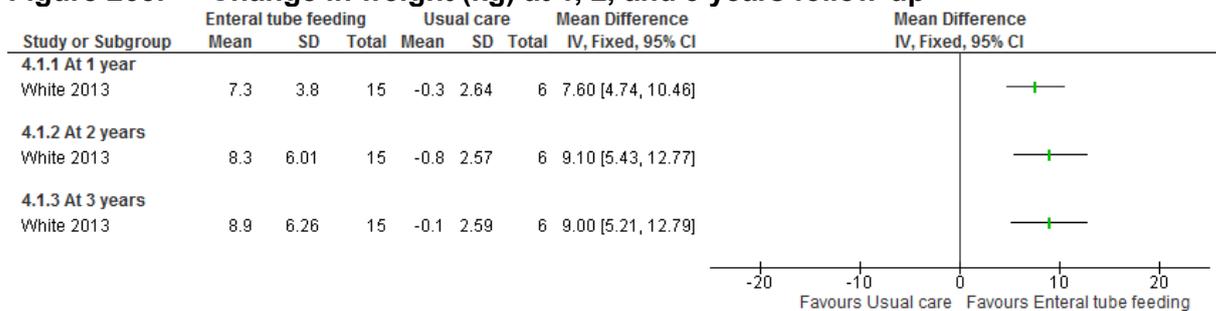
**Figure 264: Change in FEV<sub>1</sub> % predicted at 3 and 6 months follow-up (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

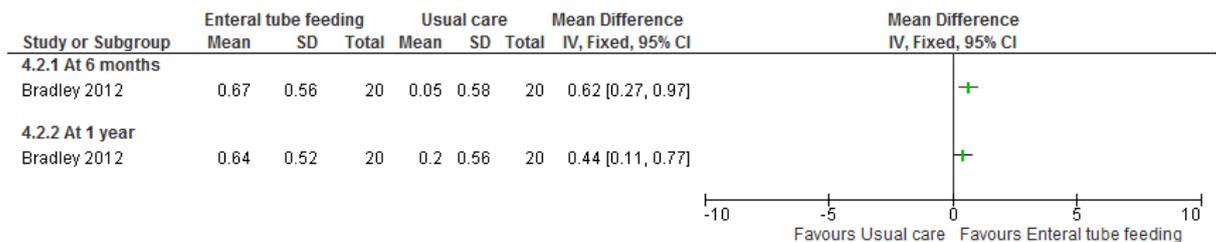
**Comparison 2. Enteral tube feeding versus nutritional advice**

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



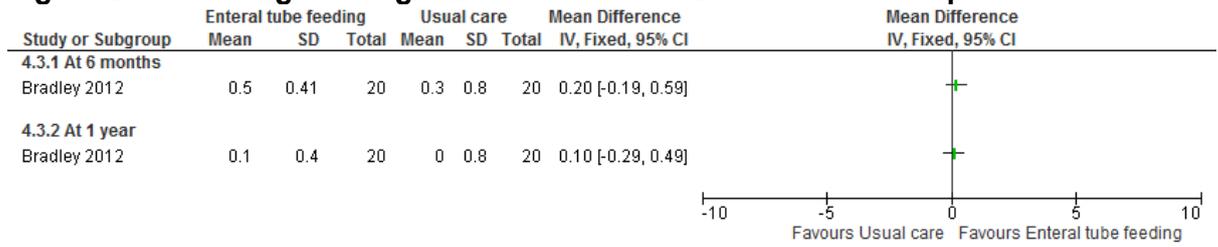
Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval

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



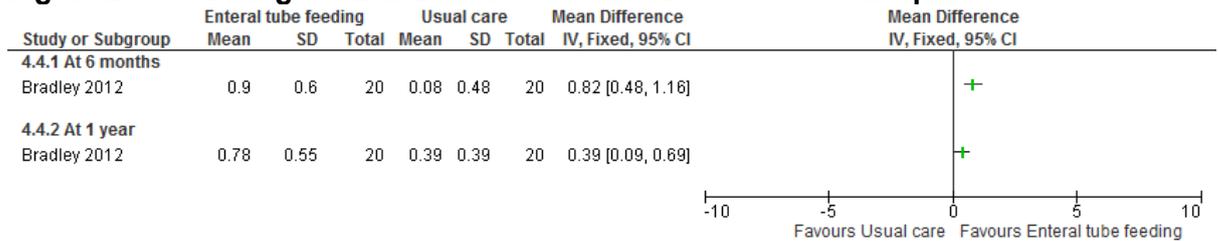
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

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



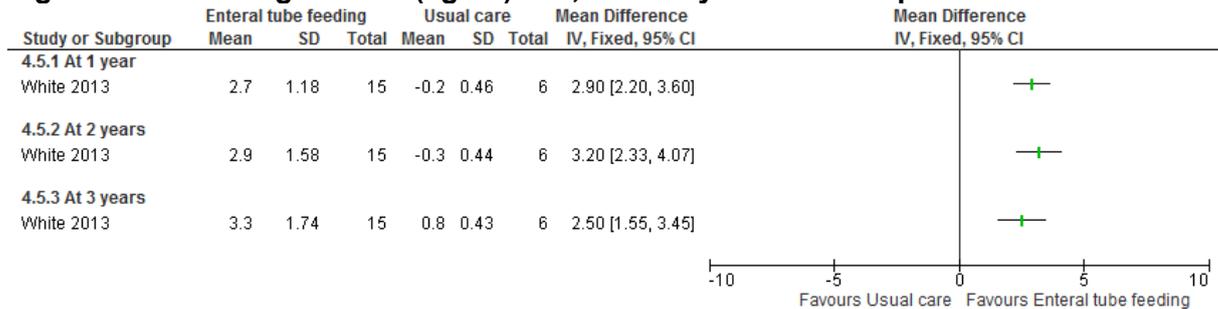
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

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



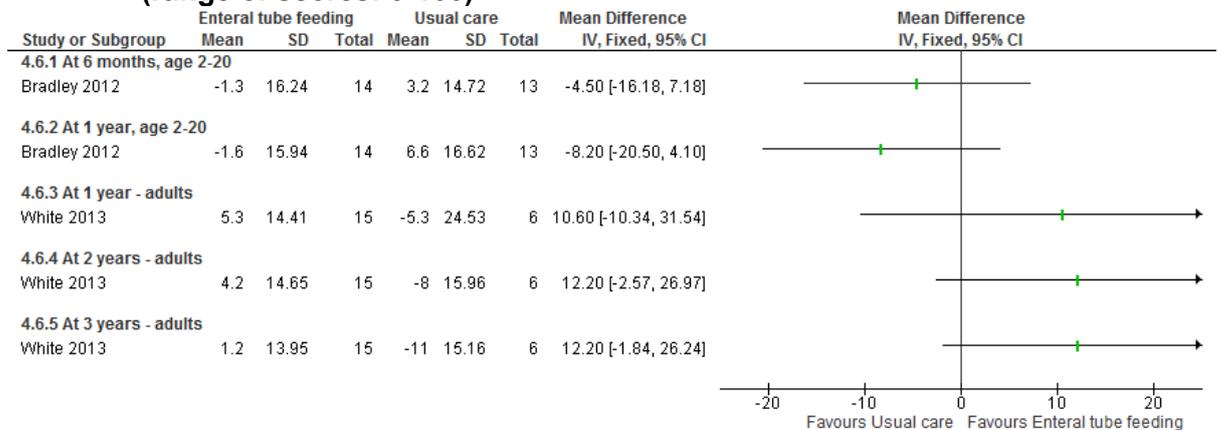
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

**Figure 269: Change in BMI (kg/m<sup>2</sup>) at 1, 2 and 3 years follow-up**



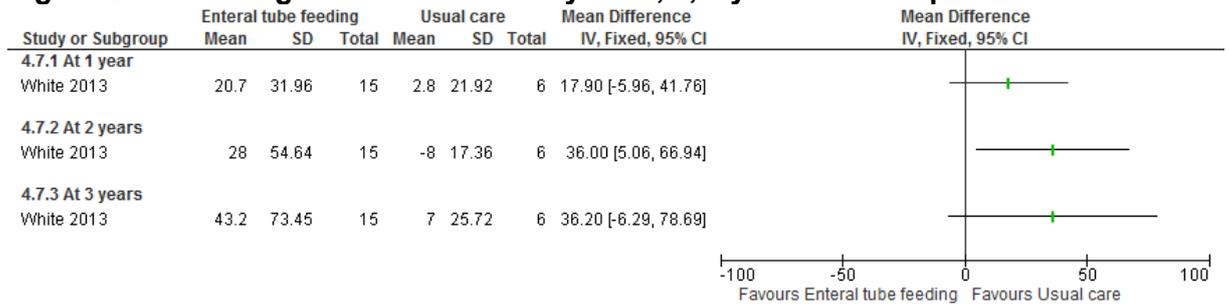
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; kg: kilograms; m<sup>2</sup>: square metres; SD: standard deviation

**Figure 270: Change in FEV<sub>1</sub> % predicted at 6 months and at 1, 2, 3 years follow-up (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

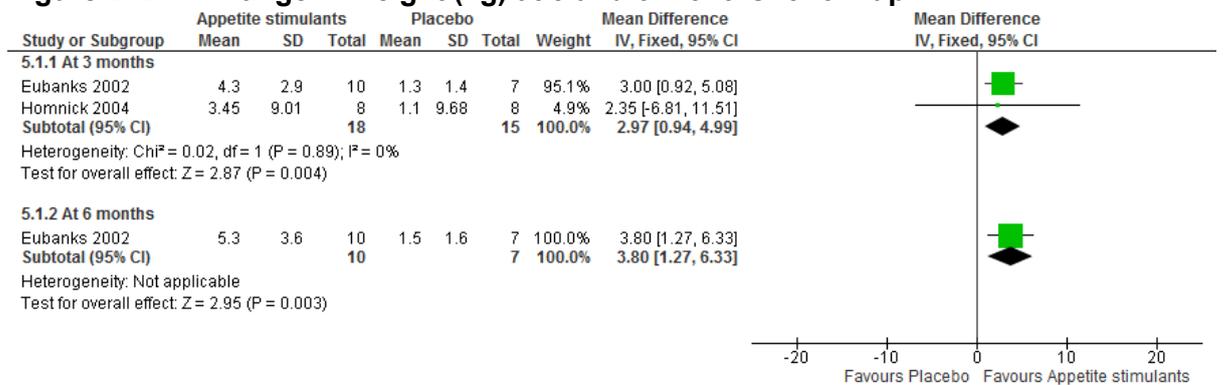
**Figure 271: Change in IV treatment days at 1, 2, 3 years follow-up**



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

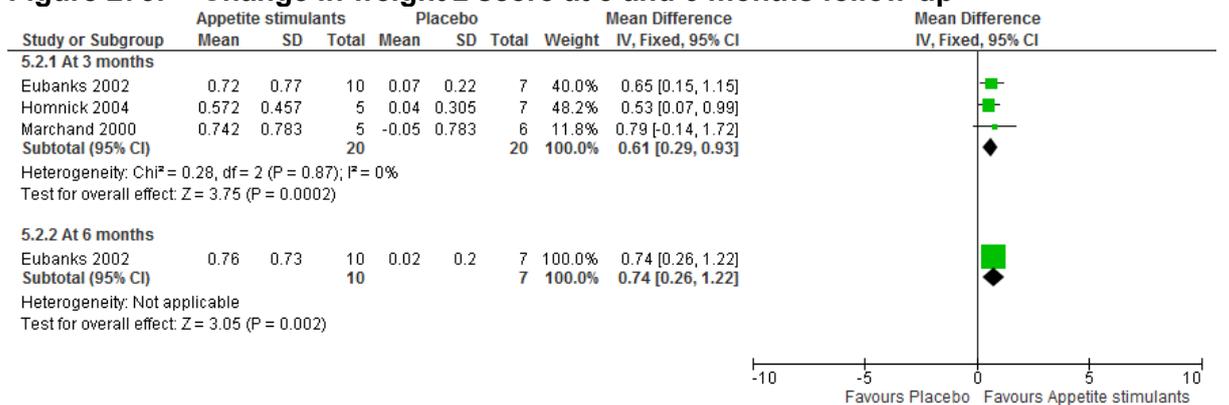
**Comparison 3. Appetite stimulants versus placebo**

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



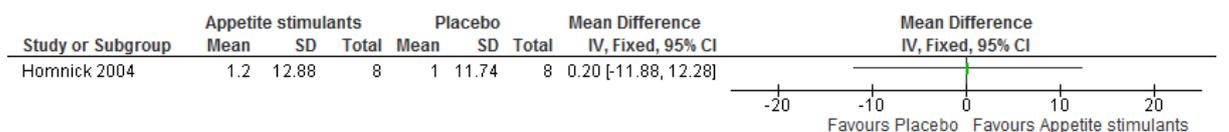
Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval; df: degrees of freedom

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



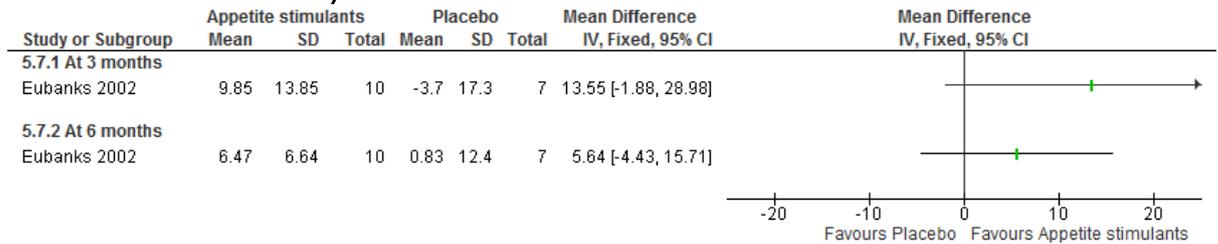
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval; df: degrees of freedom

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



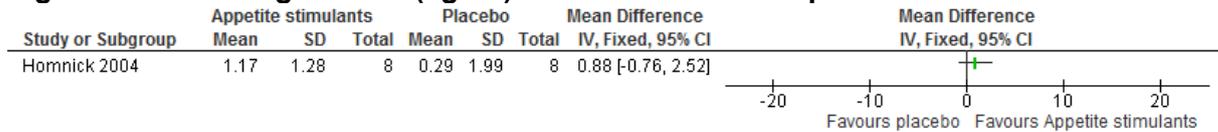
Abbreviations: CI: confidence interval; cm: centimetres; IV: inverse variance; SD: standard deviation

**Figure 275: Change in FEV<sub>1</sub> % predicted at 3 and 6 months follow-up (range of scores: 0-100)**



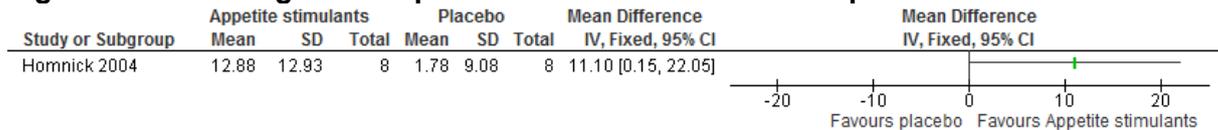
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 276: Change in BMI (kg/m<sup>2</sup>) at 3 months follow-up**



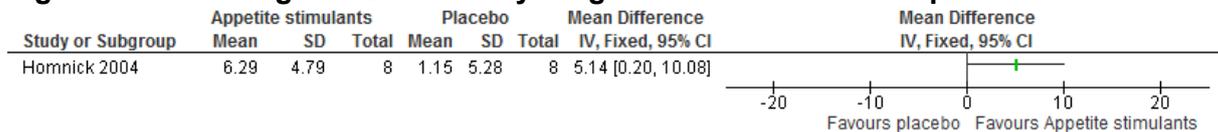
Abbreviations: BMI: body mass index; CI: confidence interval; kg: kilograms; IV: inverse variance; m<sup>2</sup>: square metres; SD: standard deviation

**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**



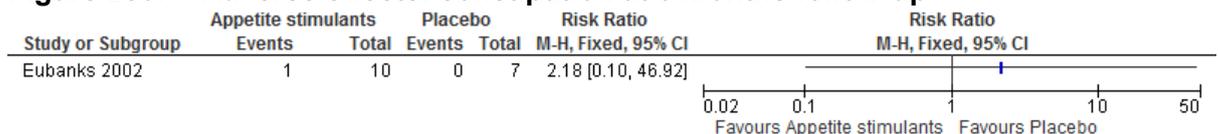
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

**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

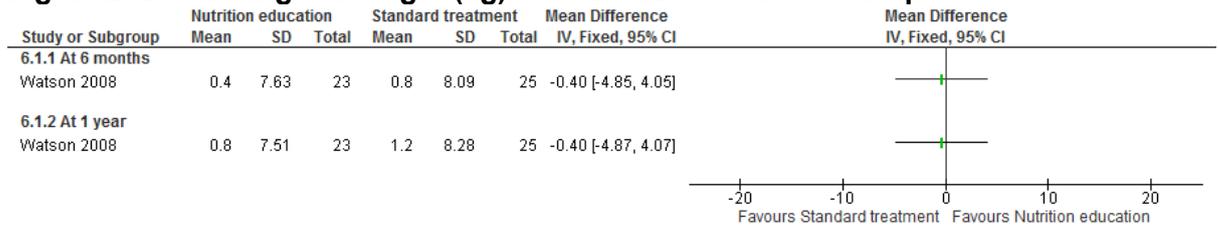
**Figure 281: Adverse effects: decreased morning cortisol levels <30 nmol/L at 6 months follow-up**



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

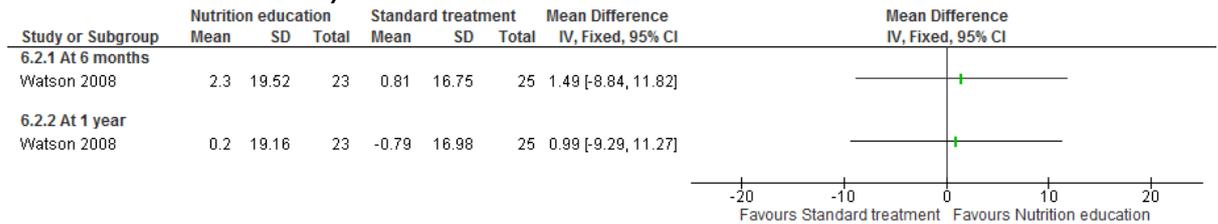
**Comparison 4. Nutrition education versus usual care**

**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

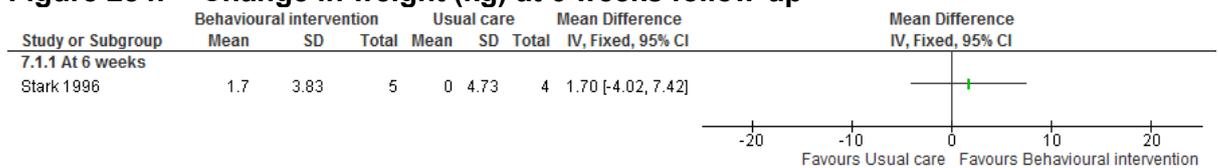
**Figure 283: Change in FEV<sub>1</sub> % predicted at 6 and 12 months follow-up (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

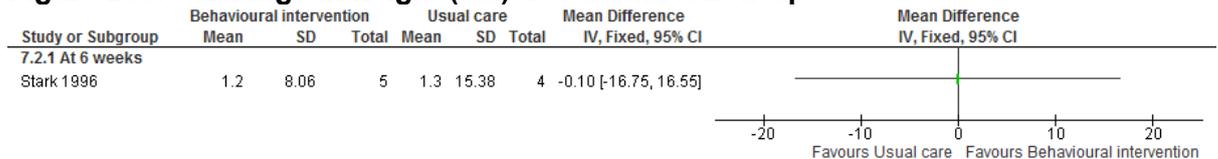
**Comparison 5.1 Behavioural intervention versus usual care**

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



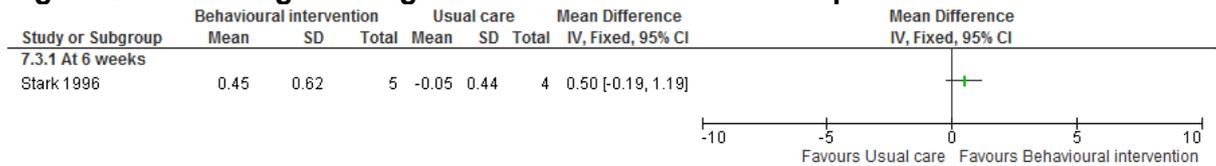
Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval

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



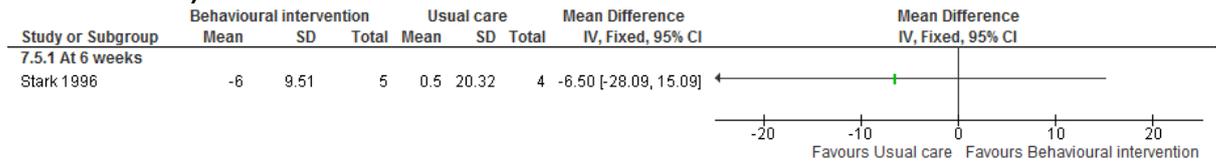
Abbreviations: CI: confidence interval; cm: centimetres; IV: inverse variance; SD: standard deviation

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



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

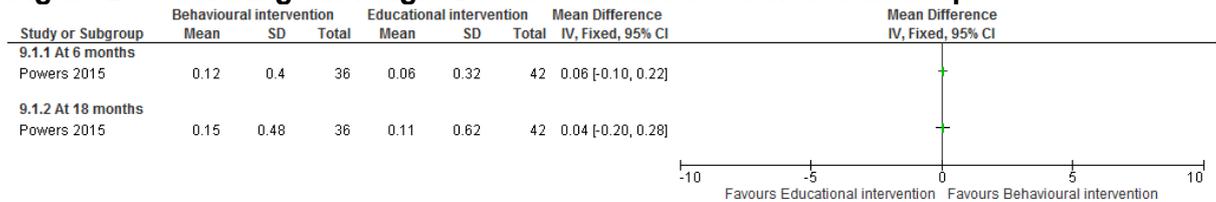
**Figure 287: Change in FEV<sub>1</sub> % predicted at 6 weeks follow-up (range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

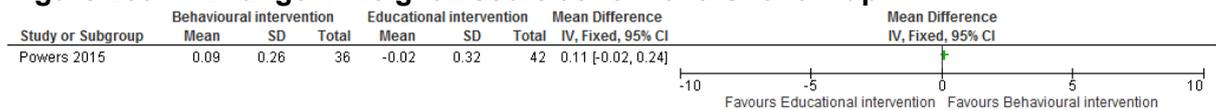
**Comparison 5.2 Behavioural intervention versus education and attention control treatment**

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



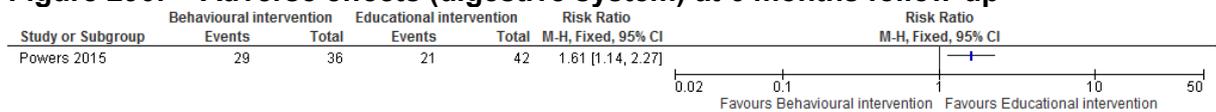
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

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



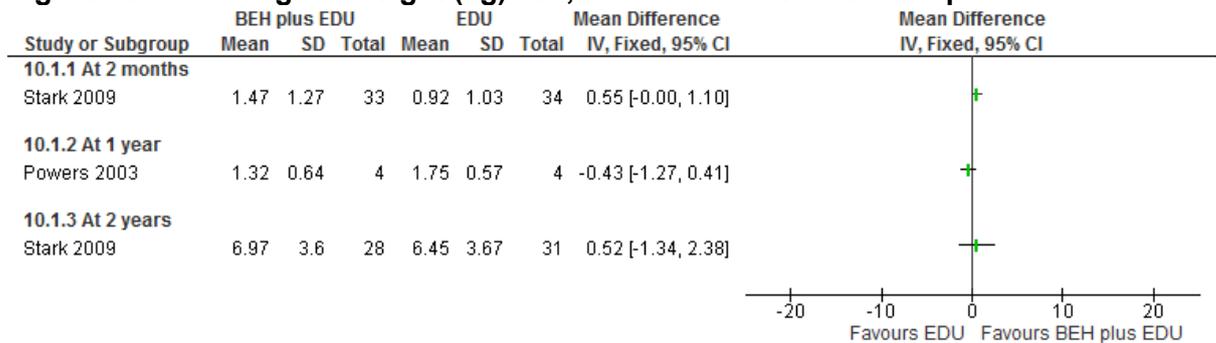
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation

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



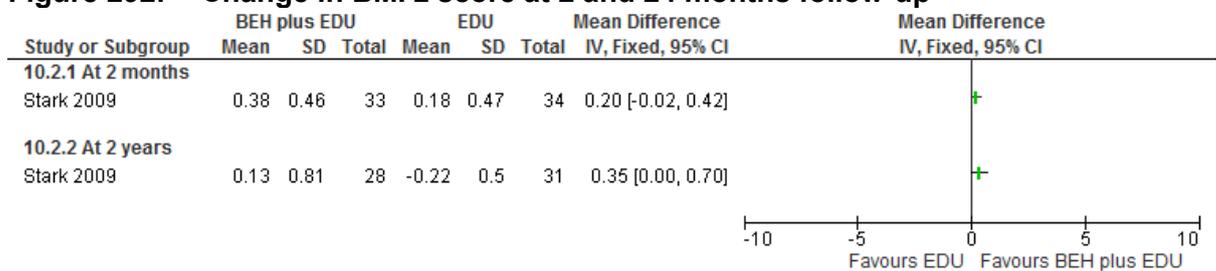
### Comparison 5.3. Behavioural management training plus educational intervention versus educational intervention alone

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



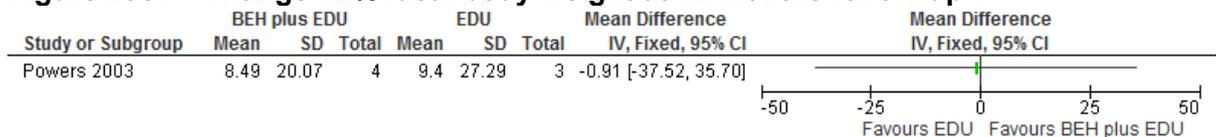
Abbreviations: kg: kilograms; BEH plus EDU: Behavioural management training plus educational intervention; EDU: educational intervention alone; SD: standard deviation; IV: inverse variance; CI: confidence interval

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



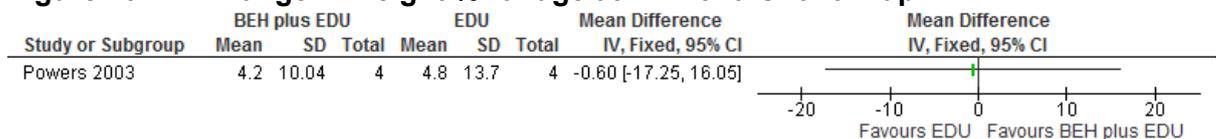
Abbreviations: BMI: body mass index; BEH plus EDU: Behavioural management training plus educational intervention; CI: confidence interval; EDU: educational intervention alone; IV: inverse variance; SD: standard deviation

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



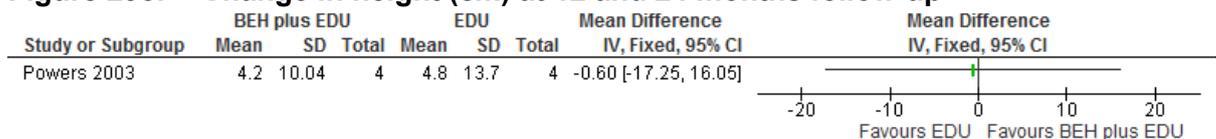
Abbreviations: BEH plus EDU: Behavioural management training plus educational intervention; EDU: educational intervention alone; SD: standard deviation; IV: inverse variance; CI: confidence interval

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



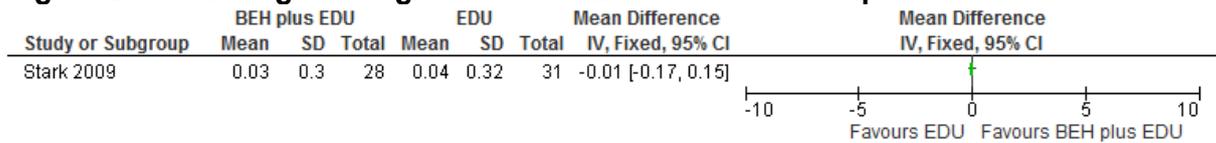
Abbreviations: BEH plus EDU: Behavioural management training plus educational intervention; EDU: educational intervention alone; SD: standard deviation; IV: inverse variance; CI: confidence interval

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



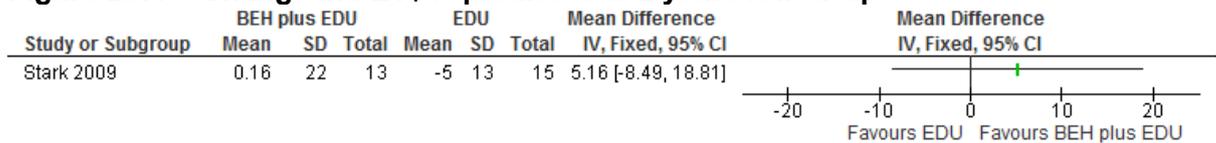
Abbreviations: BEH plus EDU: Behavioural management training plus educational intervention; CI: confidence interval; cm: centimetres; EDU: educational intervention alone; IV: inverse variance; SD: standard deviation

**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 FEV<sub>1</sub> % predicted at 2 years follow-up**



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

Note: The study does not specify the unit of measurement for FEV<sub>1</sub>.

## I.14 Exocrine Pancreatic insufficiency

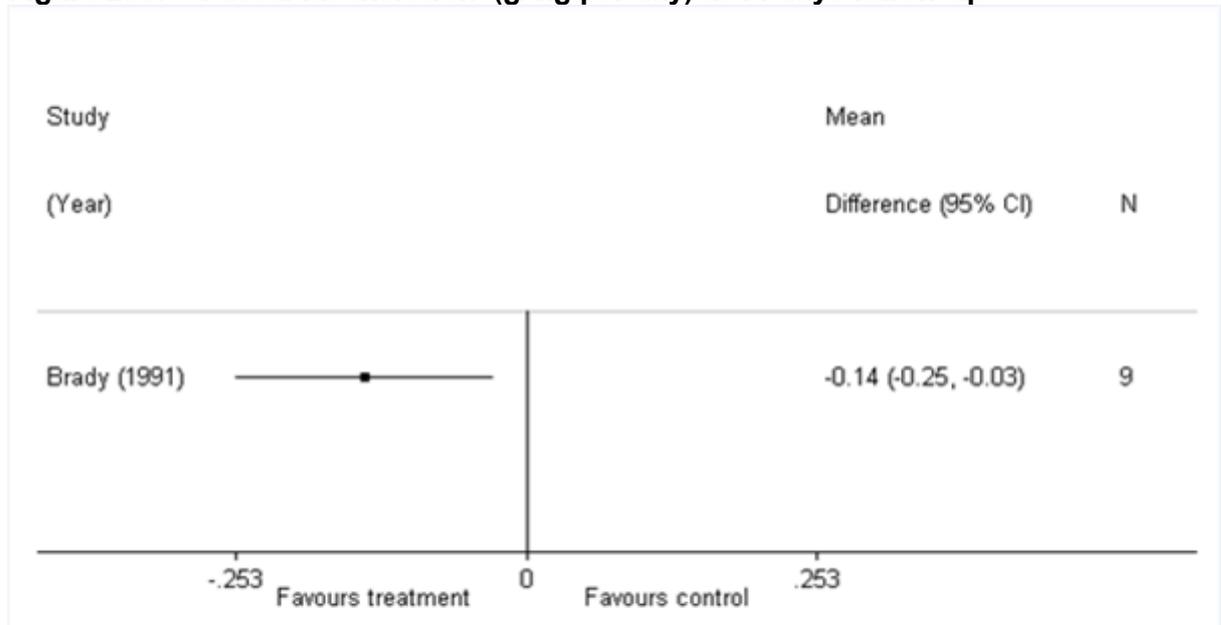
### Comparison 1. Acid suppressing agents as adjuvant therapy to PERT

No forest plots available.

### Comparison 2. High dose versus low dose PERT

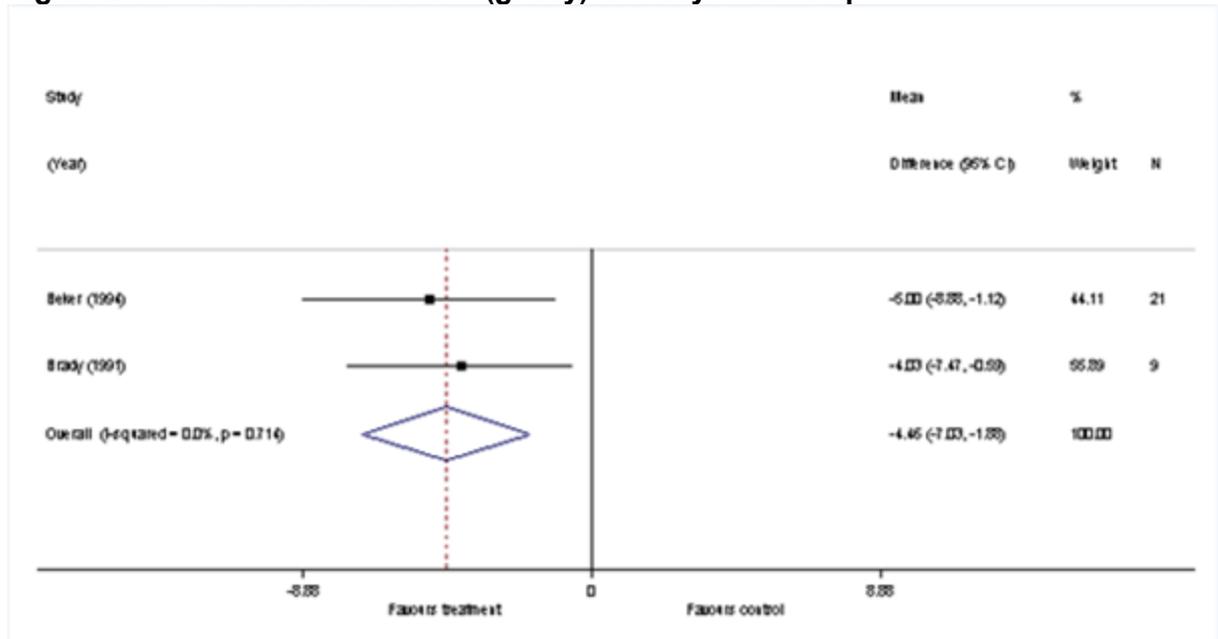
#### Comparison 2.1. High-dose PERT versus low dose PERT in children

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



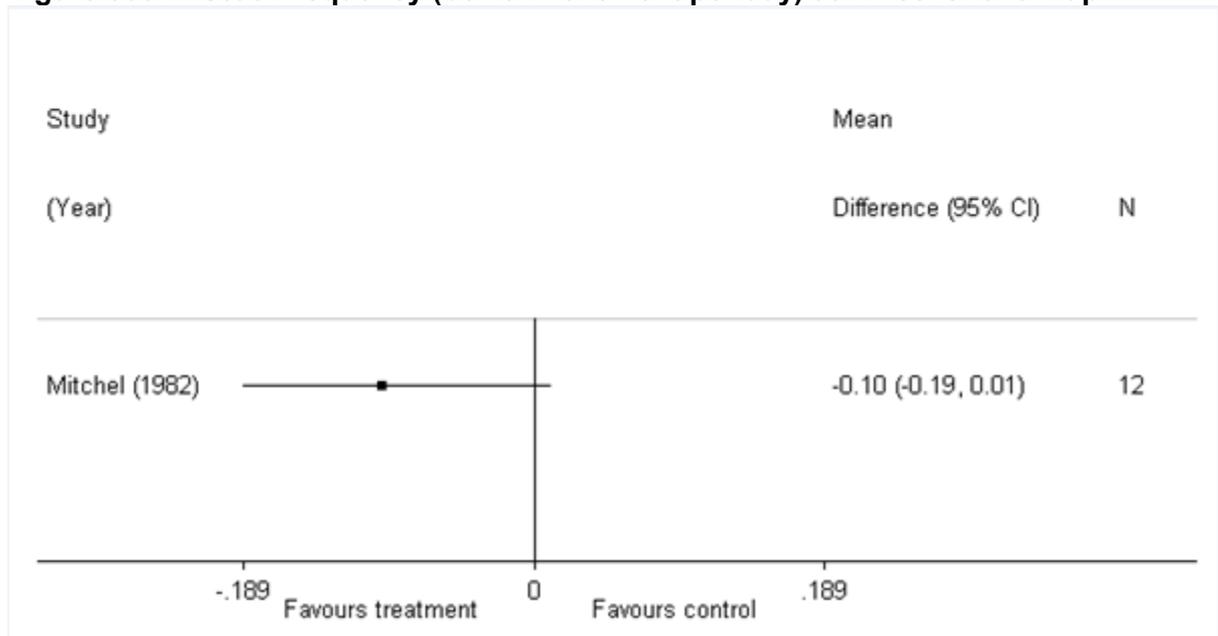
Abbreviations: g: grams; kg: kilograms; CI: confidence interval

**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.

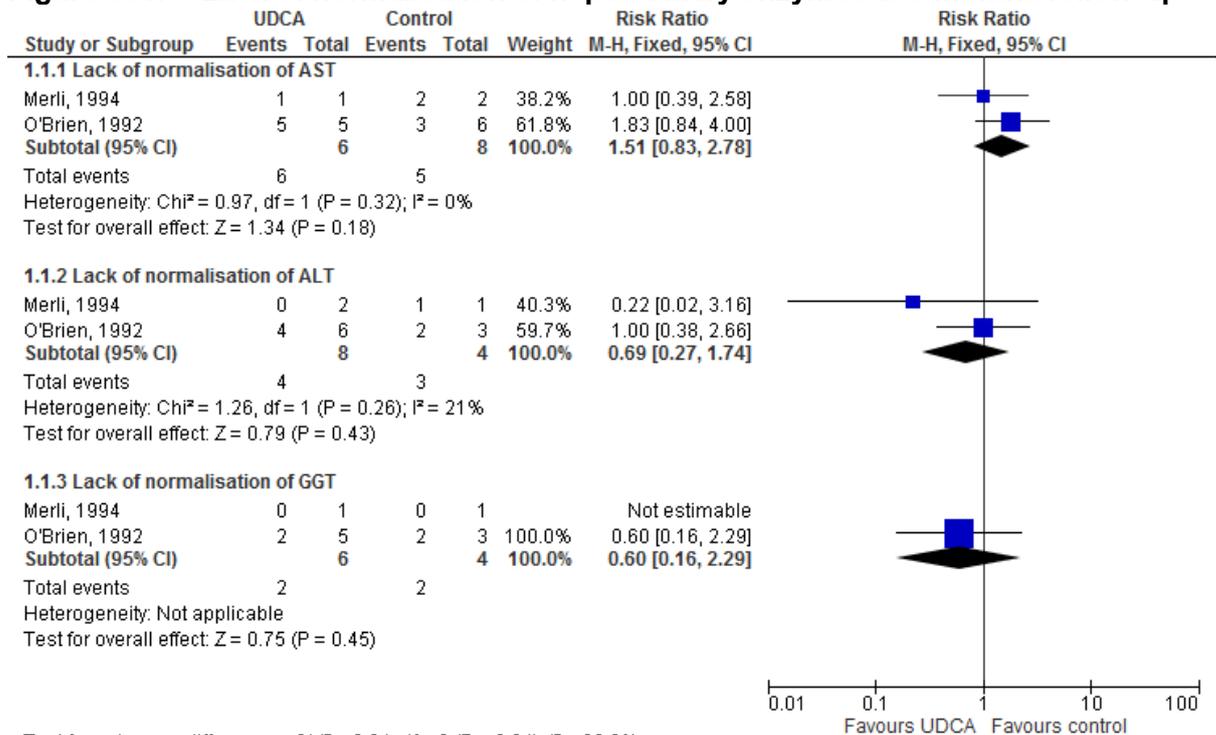
## I.16 Monitoring liver disease

Not applicable to this review.

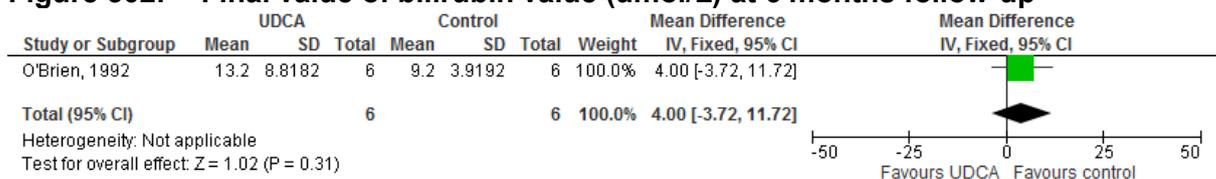
## I.17 Ursodeoxycholic acid

### Comparison 1. UDCA versus placebo or control

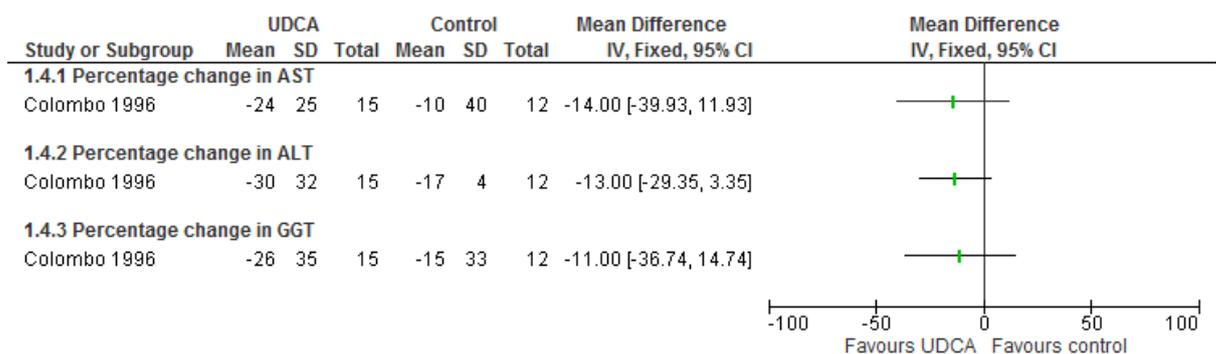
**Figure 301: Lack of normalisation of hepatobiliary enzymes at 6 months follow-up**



**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**

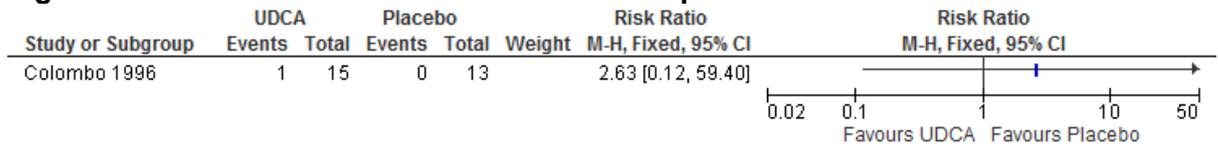


Abbreviations: UDCA: ursodeoxycholic acid; SD: standard deviation; IV: inverse variance; CI: confidence interval. Colombo: Data reported as multiples of the upper limit of normal reference values.

**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.

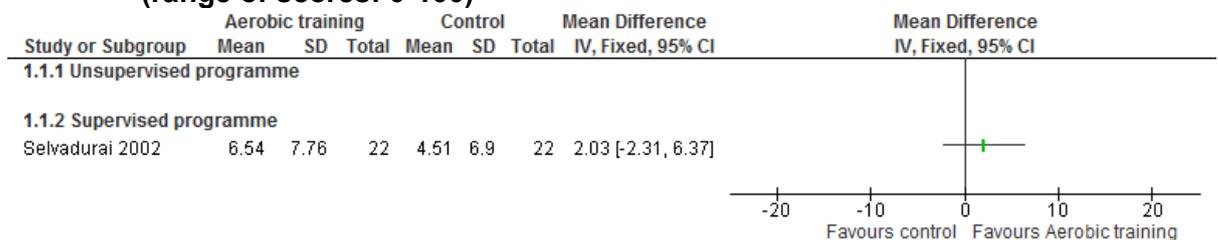
## I.19 Bone mineral density

Not applicable to this review.

## I.20 Exercise

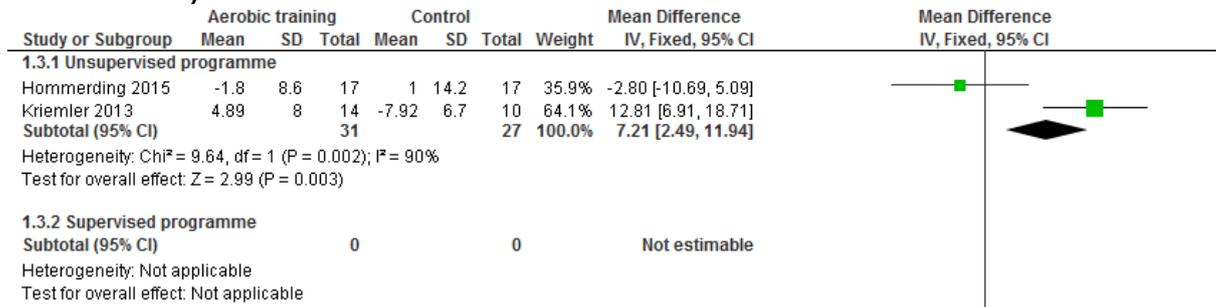
### Comparison 1. Aerobic exercise training programme versus no exercise programme

**Figure 307: Change in FEV<sub>1</sub> % predicted at hospital discharge (mean ≈ 19 days)  
(range of scores: 0-100)**



Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

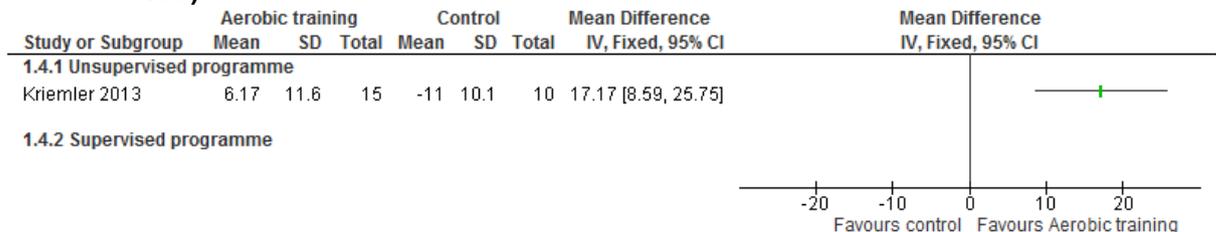
**Figure 308: Change in FEV<sub>1</sub> % predicted at 3 months follow-up (range of scores: 0-100)**



Test for subgroup differences: Not applicable

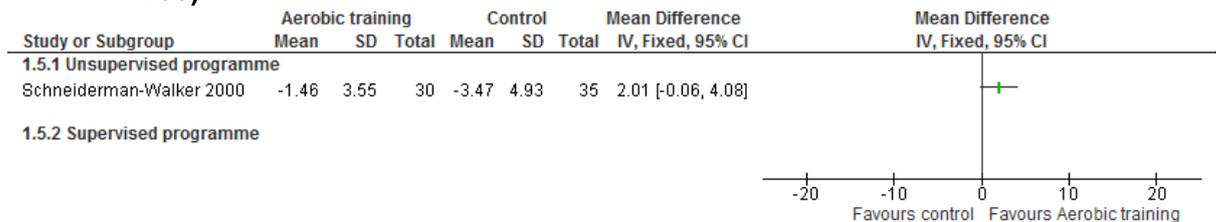
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 309: Change in FEV<sub>1</sub> % predicted at 6 months follow-up (range of scores: 0-100)**



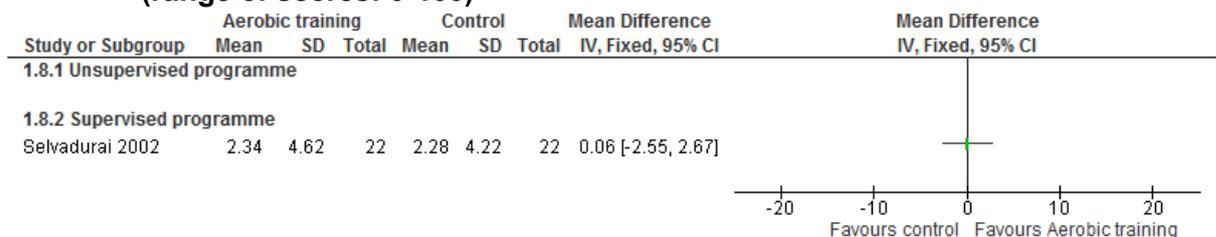
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 310: Change in FEV<sub>1</sub> % predicted at 3 years follow-up (range of scores: 0-100)**



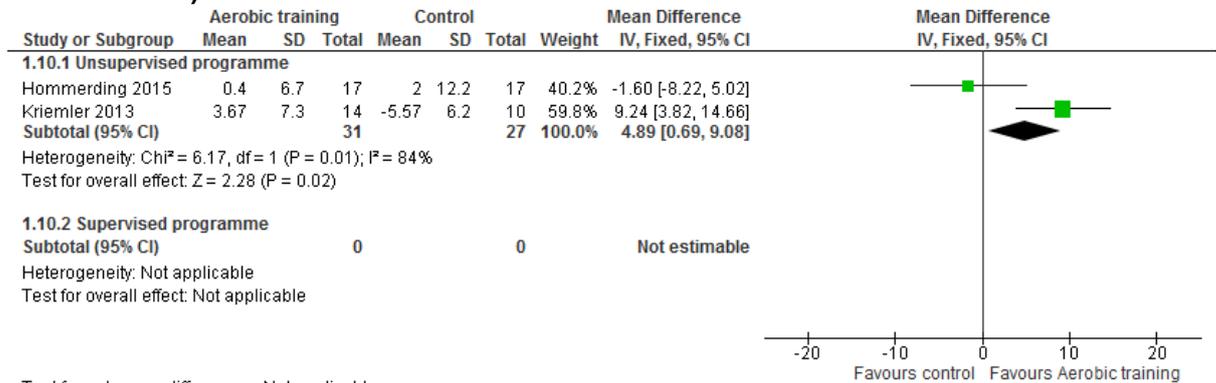
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**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

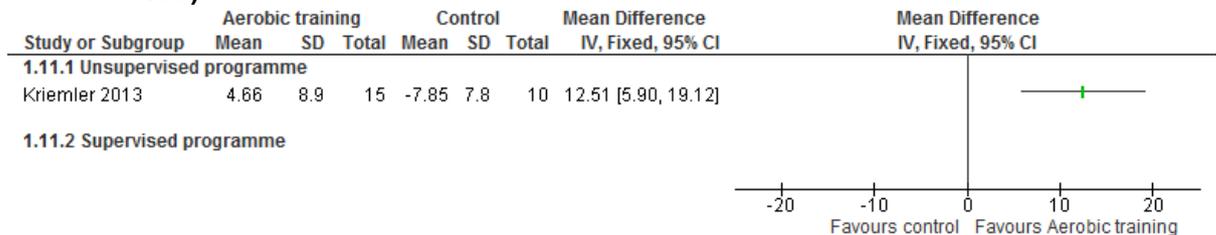
**Figure 312: Change in FVC % predicted at 3 months follow-up (range of scores: 0-100)**



Test for subgroup differences: Not applicable

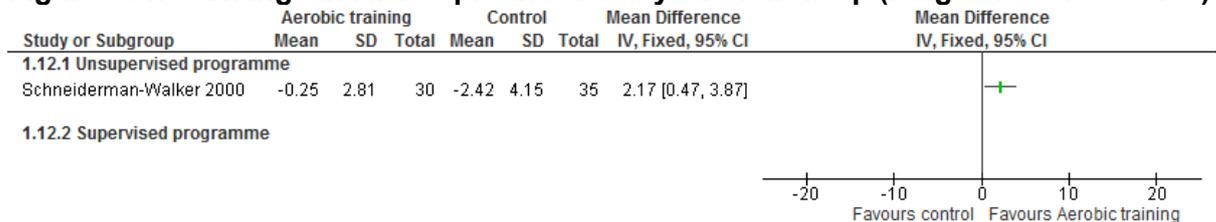
Abbreviations: CI: confidence interval; df: degrees of freedom; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation;

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



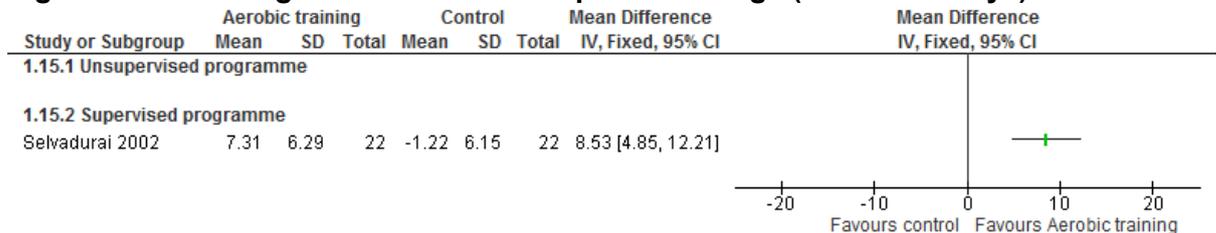
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

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



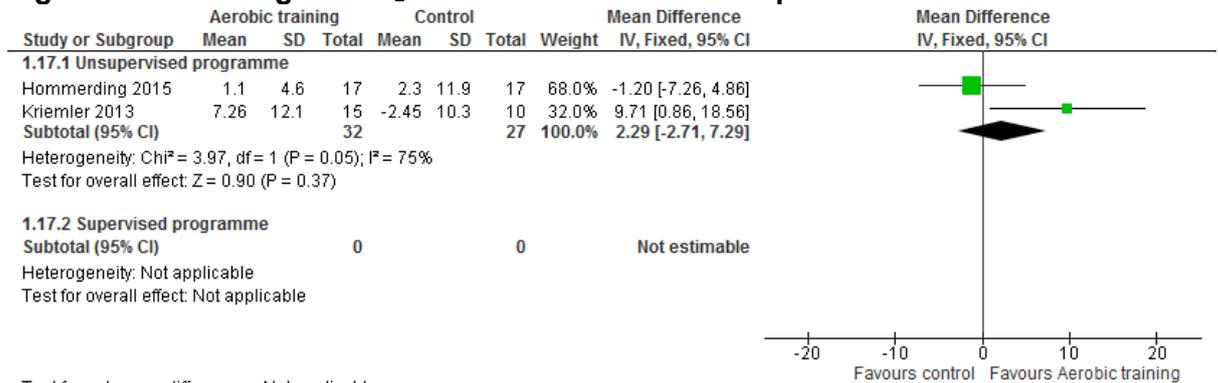
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

**Figure 315: Change in VO<sub>2</sub> max. at hospital discharge (mean ≈ 19 days)**



Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO<sub>2</sub> max: maximal oxygen consumption

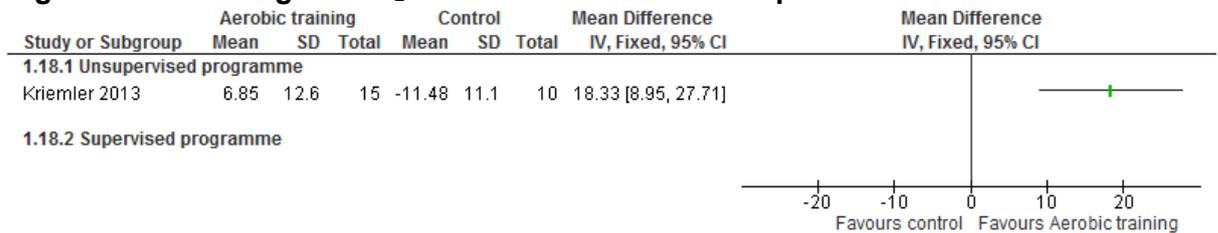
**Figure 316: Change in VO<sub>2</sub> max. at 3 months follow-up**



Test for subgroup differences: Not applicable

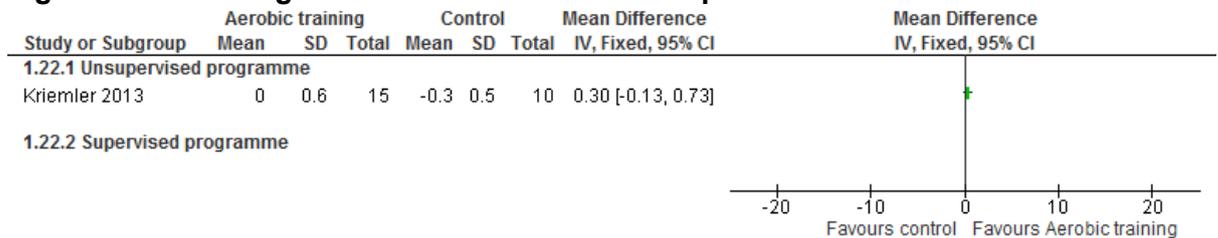
Abbreviations: CI: confidence interval; df: degrees of freedom; IV: inverse variance; SD: standard deviation; VO<sub>2</sub> max: maximal oxygen consumption

**Figure 317: Change in VO<sub>2</sub> max. at 6 months follow-up**



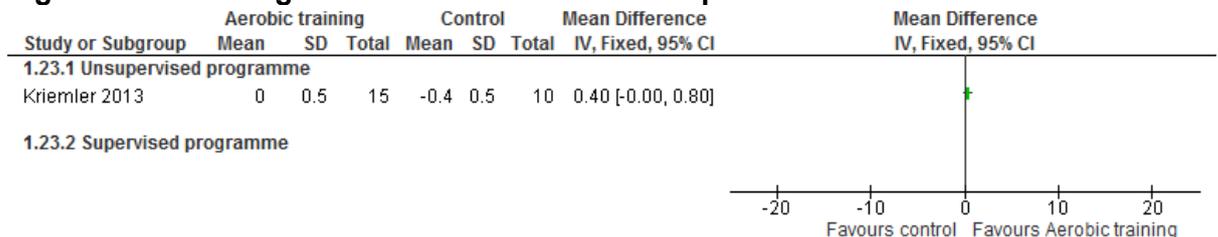
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO<sub>2</sub> max: maximal oxygen consumption

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



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

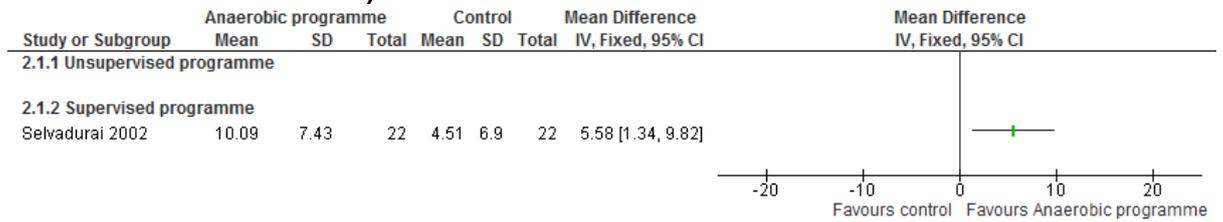
**Figure 319: Change in BMI at 6 months follow-up**



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

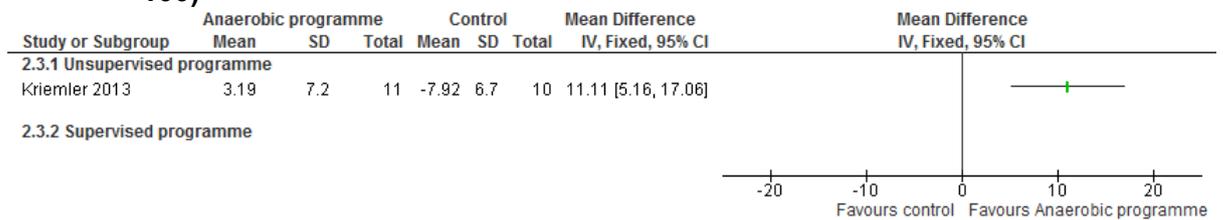
**Comparison 2.1. Strength resistance/ anaerobic training programme versus no exercise programme**

**Figure 320: Change in FEV<sub>1</sub> % predicted at hospital discharge (mean ≈ 19 days) (range of scores: 0-100)**



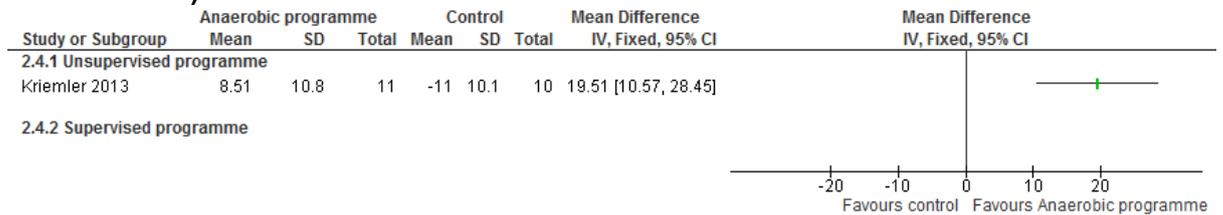
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 321: Change in FEV<sub>1</sub> % predicted at 3 months follow-up (range of scores: 0-100)**



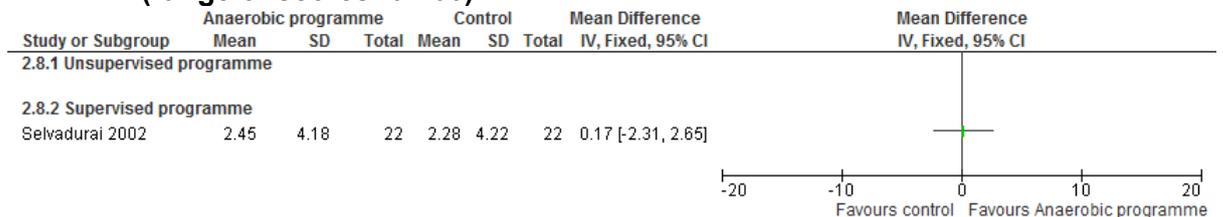
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 322: Change in FEV<sub>1</sub> % predicted at 6 months follow-up (range of scores: 0-100)**



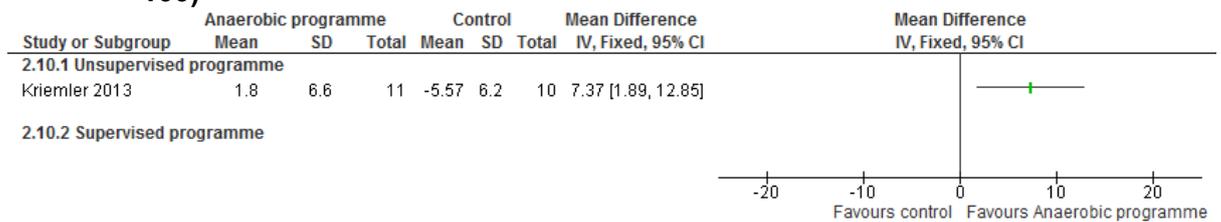
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

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



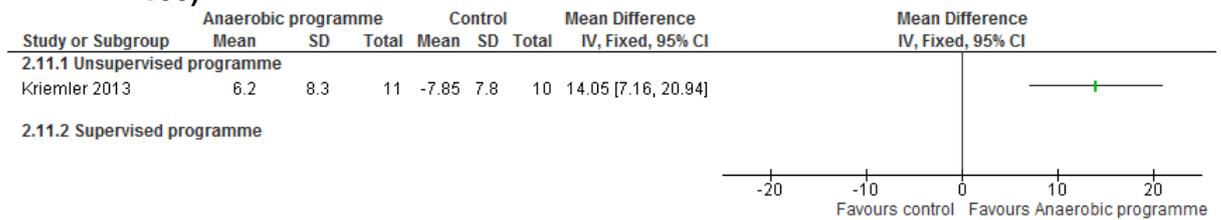
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

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



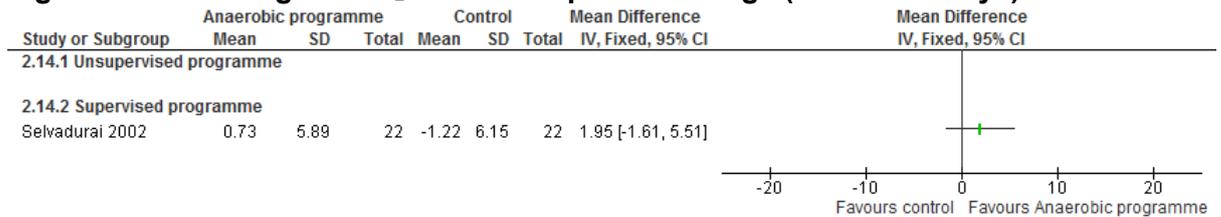
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

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



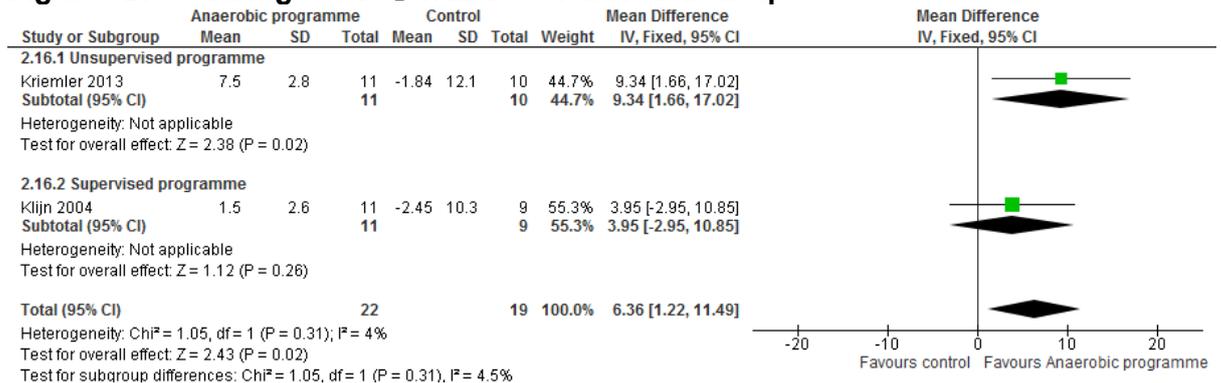
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

**Figure 326: Change in VO<sub>2</sub> max at hospital discharge (mean ≈ 19 days)**



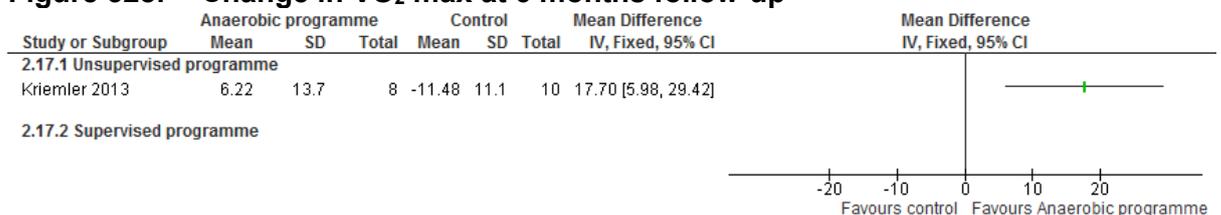
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO<sub>2</sub> max: maximal oxygen consumption

**Figure 327: Change in VO<sub>2</sub> max at 3 months follow-up**



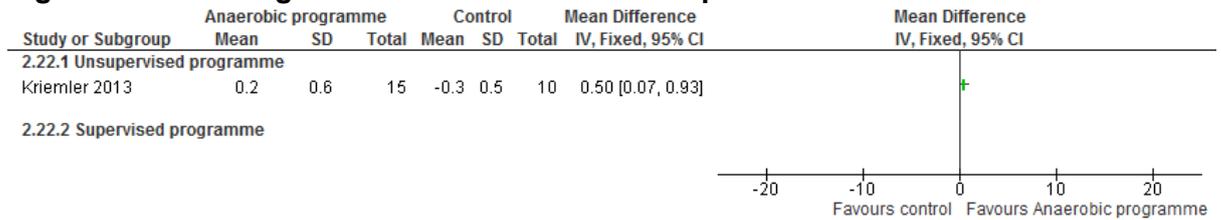
Abbreviations: CI: confidence interval; df: degrees of freedom; IV: inverse variance; SD: standard deviation; VO<sub>2</sub> max: maximal oxygen consumption

**Figure 328: Change in VO<sub>2</sub> max at 6 months follow-up**



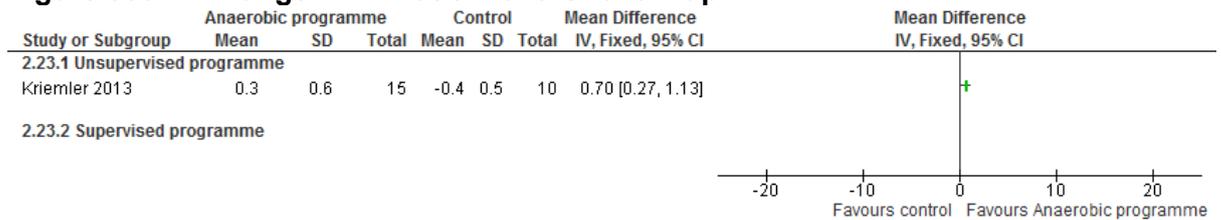
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO<sub>2</sub> max: maximal oxygen consumption

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



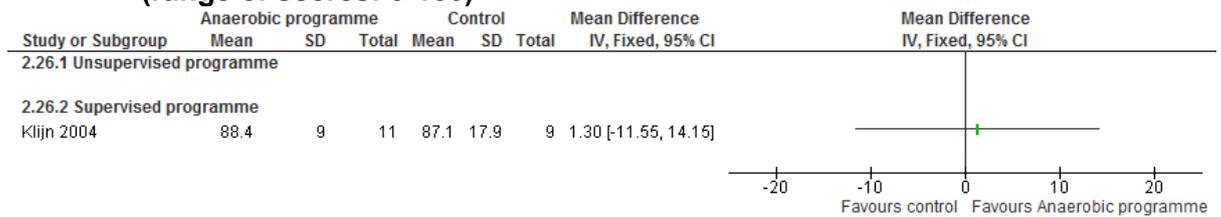
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

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



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

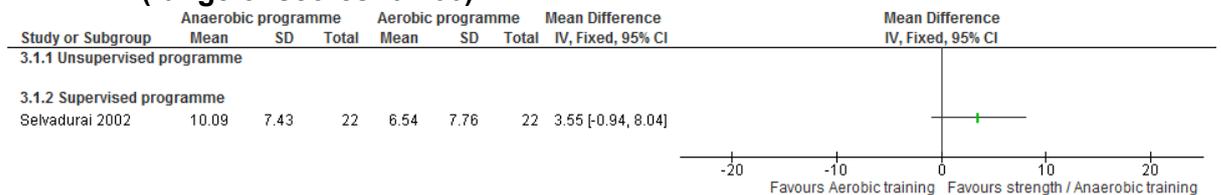
**Figure 331: Change in quality of life (CFQ-R physical domain) at 3 months follow-up (range of scores: 0-100)**



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

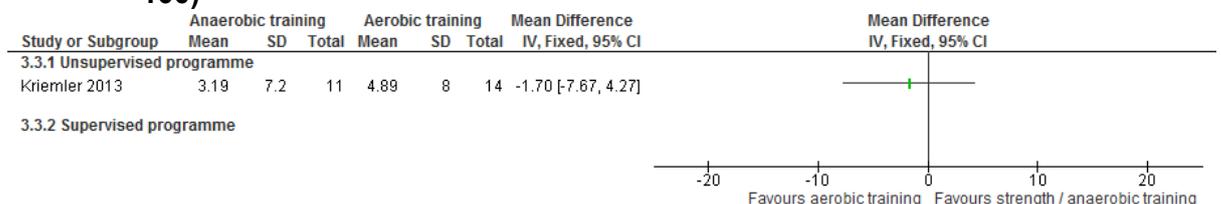
**Comparison 2.2. Strength/ anaerobic training programme versus aerobic training programme**

**Figure 332: Change in FEV<sub>1</sub> % predicted at hospital discharge (mean ≈ 19 days) (range of scores: 0-100)**



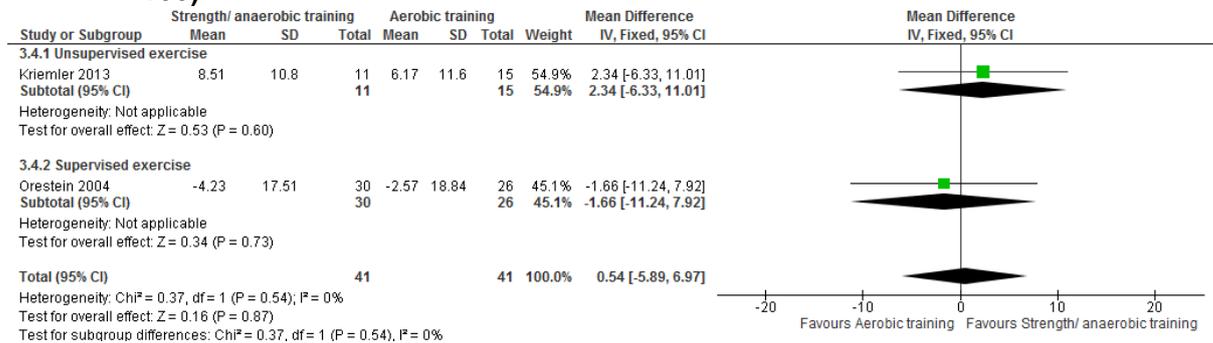
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 333: Change in FEV<sub>1</sub> % predicted at 3 months follow-up (range of scores: 0-100)**



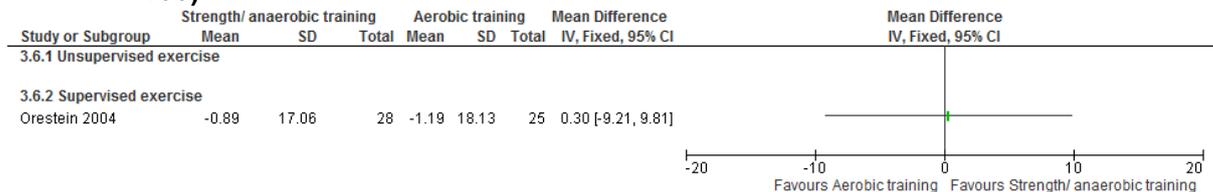
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 334: Change in FEV<sub>1</sub> % predicted at 6 months follow-up (range of scores: 0-100)**



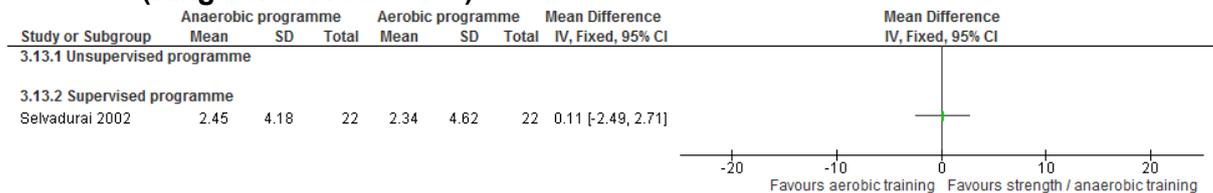
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 335: Change in FEV<sub>1</sub> % predicted at 12 months follow-up (range of scores: 0-100)**



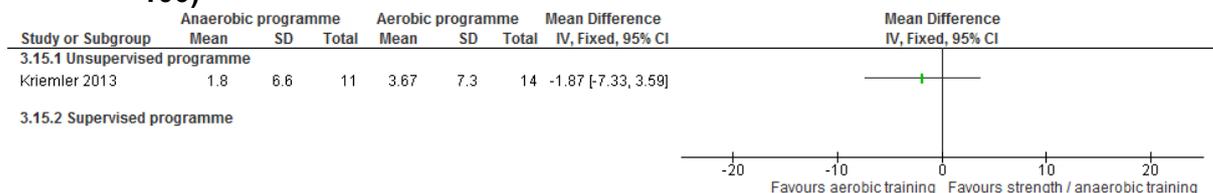
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

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



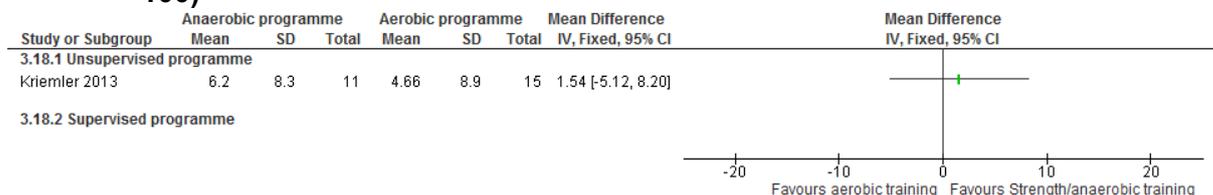
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

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



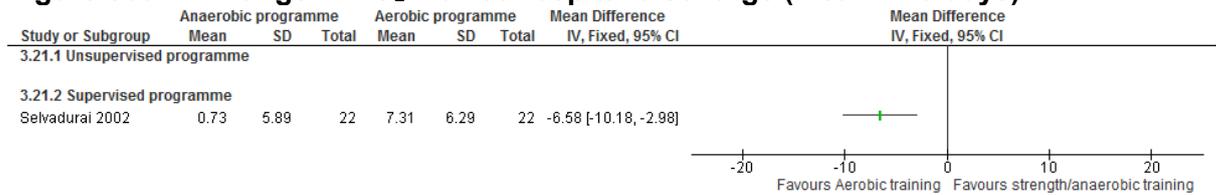
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

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



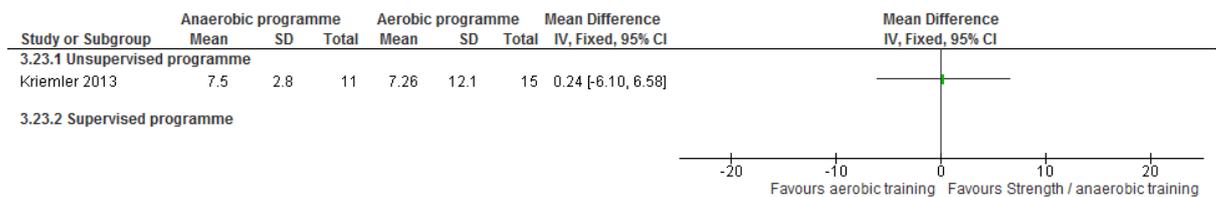
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

**Figure 339: Change in VO<sub>2</sub> max at hospital discharge (mean ≈ 19 days)**



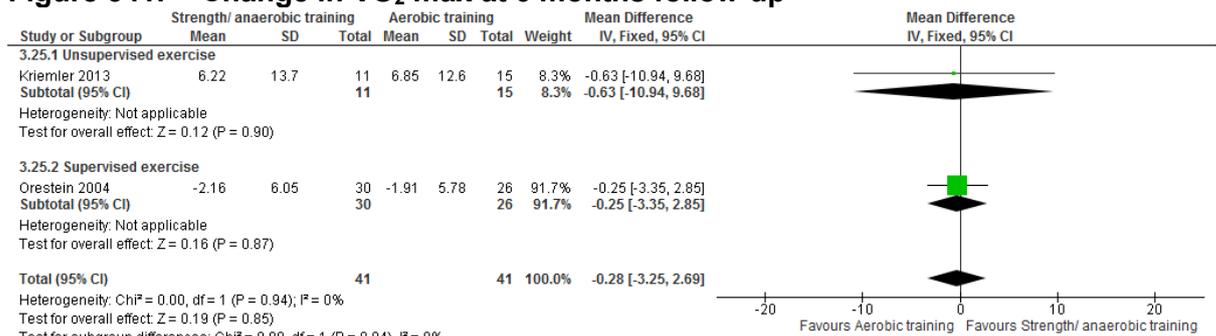
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO<sub>2</sub> max: maximal oxygen consumption

**Figure 340: Change in VO<sub>2</sub> max at 3 months follow-up**



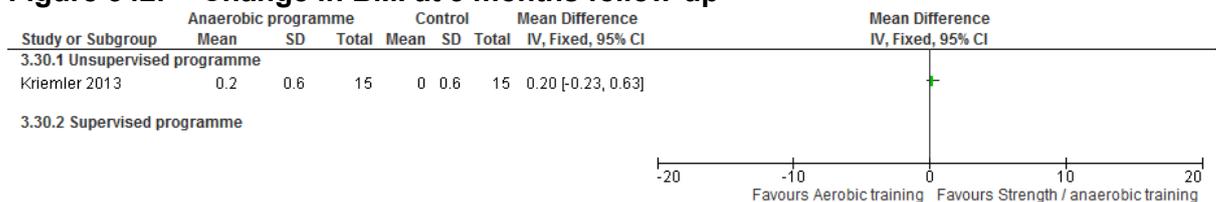
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO<sub>2</sub> max: maximal oxygen consumption

**Figure 341: Change in VO<sub>2</sub> max at 6 months follow-up**



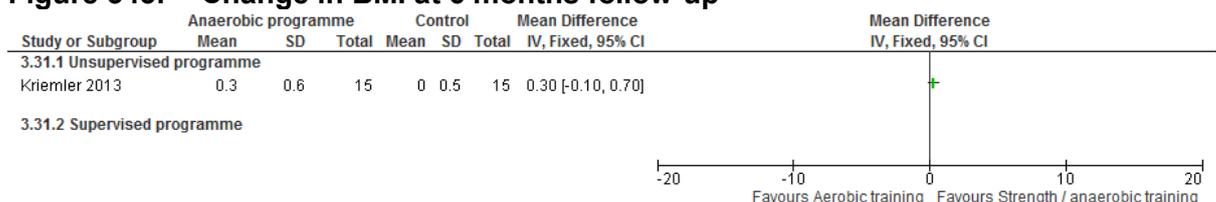
Abbreviations: CI: confidence interval; df: degrees of freedom; IV: inverse variance; SD: standard deviation; VO<sub>2</sub> max: maximal oxygen consumption

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



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

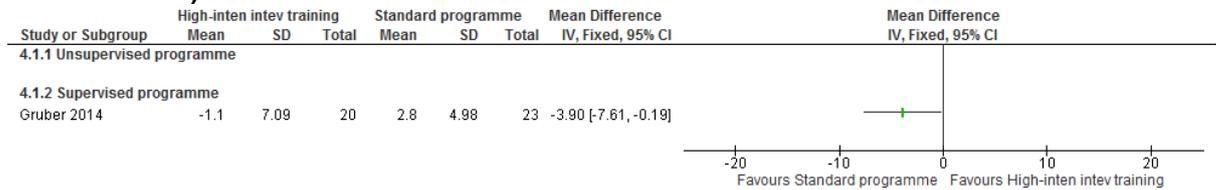
**Figure 343: Change in BMI at 6 months follow-up**



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

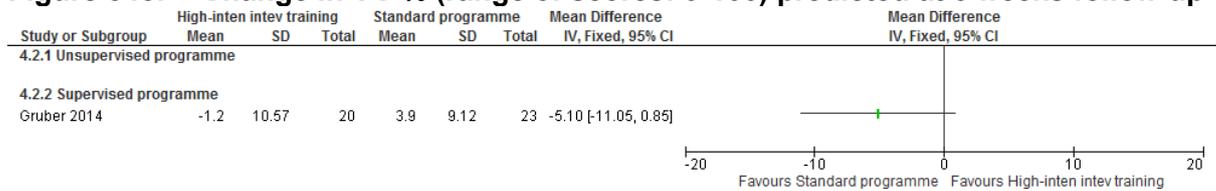
### Comparison 3. High-intensity interval training *versus* standard aerobic and anaerobic exercise programme

**Figure 344: Change in FEV<sub>1</sub> % predicted at 6 weeks follow-up (range of scores: 0-100)**



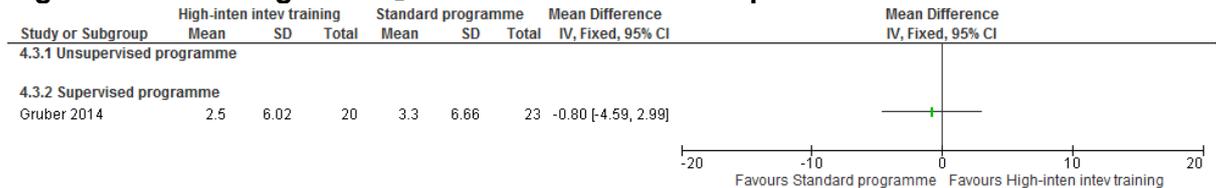
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

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



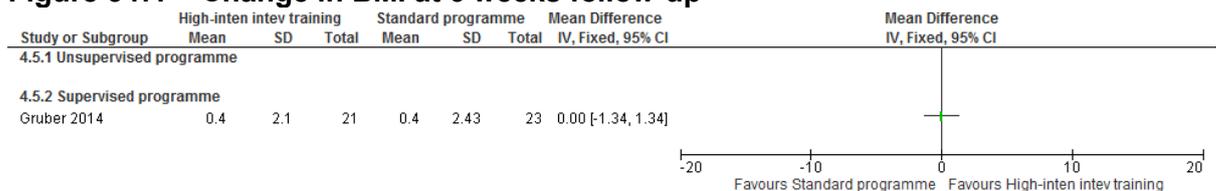
Abbreviations: VC: vital capacity; SD: standard deviation; IV: inverse variance; CI: confidence interval

**Figure 346: Change in VO<sub>2</sub> max at 6 weeks follow-up**



Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO<sub>2</sub> max: maximal oxygen consumption

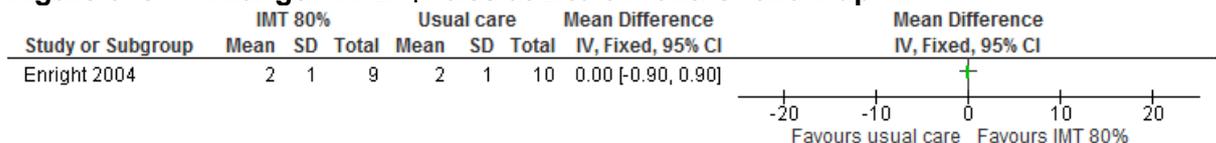
**Figure 347: Change in BMI at 6 weeks follow-up**



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

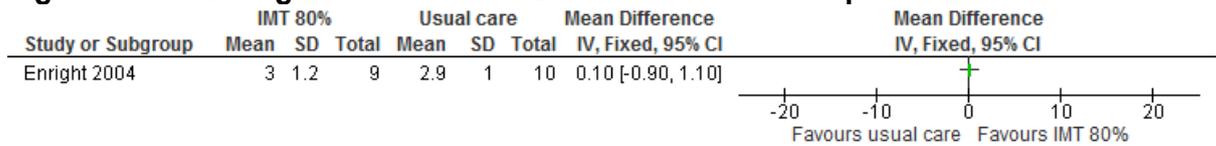
### Comparison 4. Inspiratory muscle training (IMT) at 80% of maximal effort *versus* usual care

**Figure 348: Change in FEV<sub>1</sub> litres at 2 to 6 months follow-up**



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

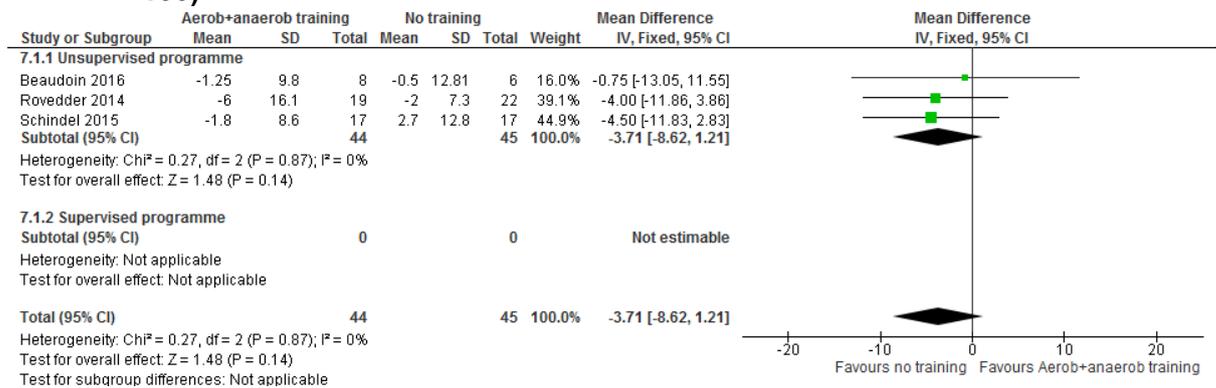
**Figure 349: Change in FVC litres at 2 to 6 months follow-up**



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

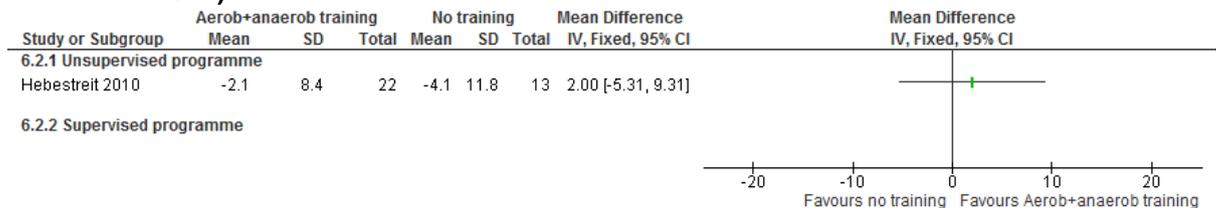
**Comparison 5. Combined aerobic and anaerobic training programme versus no exercise programme**

**Figure 350: Change in FEV<sub>1</sub> % predicted at 3 months follow-up (range of scores: 0-100)**



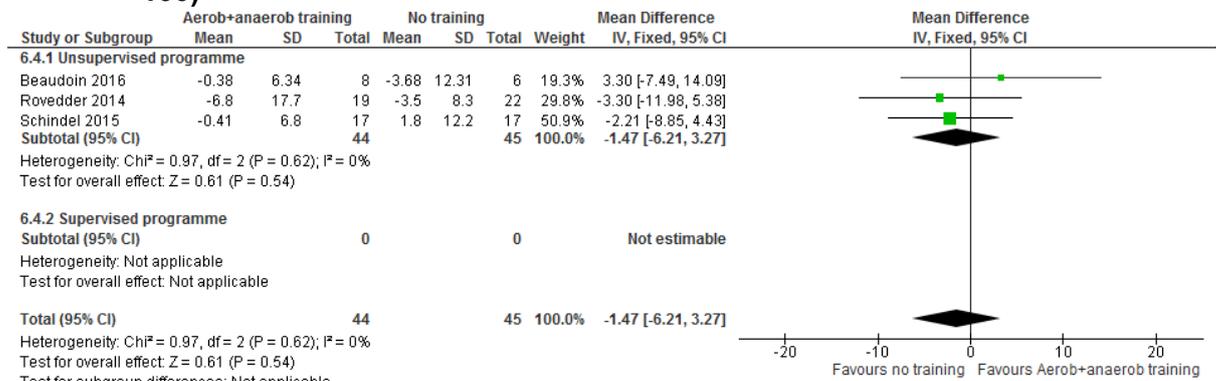
Abbreviations: CI: confidence interval; df: degrees of freedom; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

**Figure 351: Change in FEV<sub>1</sub> % predicted at 3 to 6 months follow-up (range of scores: 0-100)**



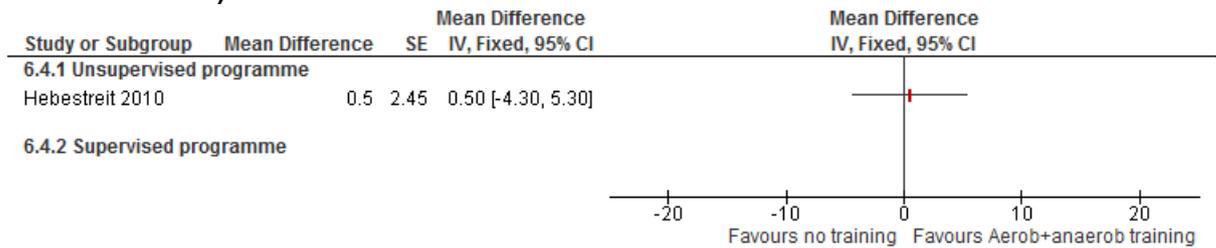
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

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



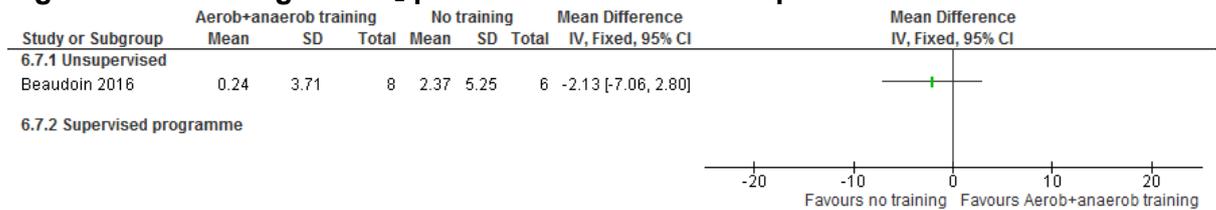
Abbreviations: CI: confidence interval; df: degrees of freedom; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

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



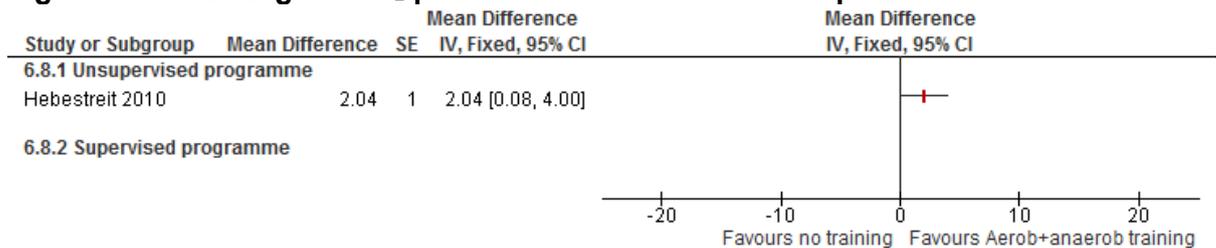
Abbreviations: CI: confidence interval; FVC: forced vital capacity; IV: inverse variance; SD: standard deviation

**Figure 354: Change in VO<sub>2</sub> peak at 3 months follow-up**



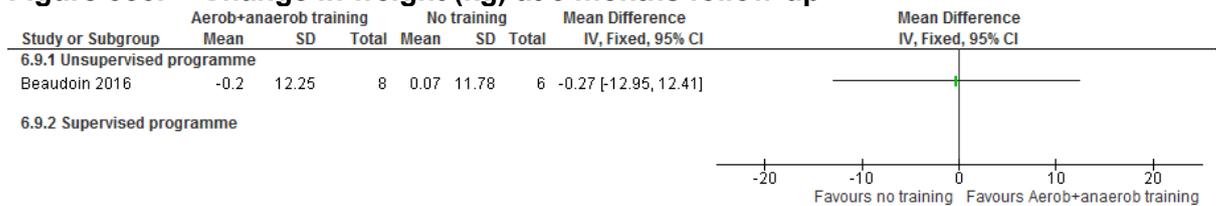
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO<sub>2</sub> max: maximal oxygen consumption

**Figure 355: Change in VO<sub>2</sub> peak at 3 to 6 months follow-up**



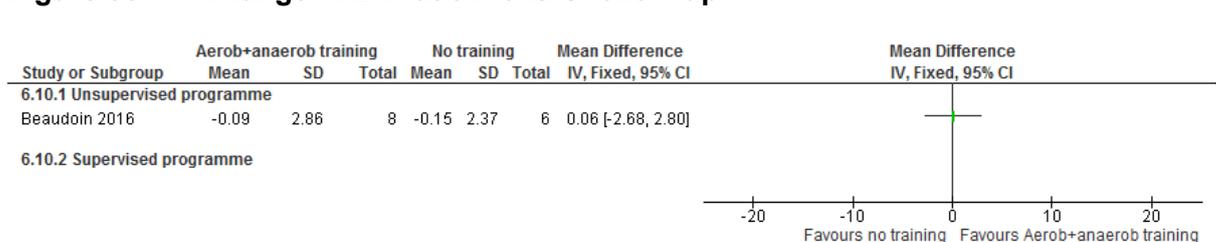
Abbreviations: CI: confidence interval; IV: inverse variance; SD: standard deviation; VO<sub>2</sub> max: maximal oxygen consumption

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



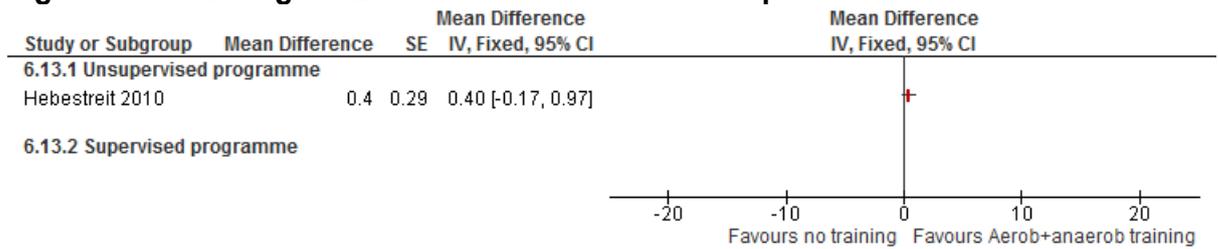
Abbreviations: kg: kilograms; SD: standard deviation; IV: inverse variance; CI: confidence interval

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



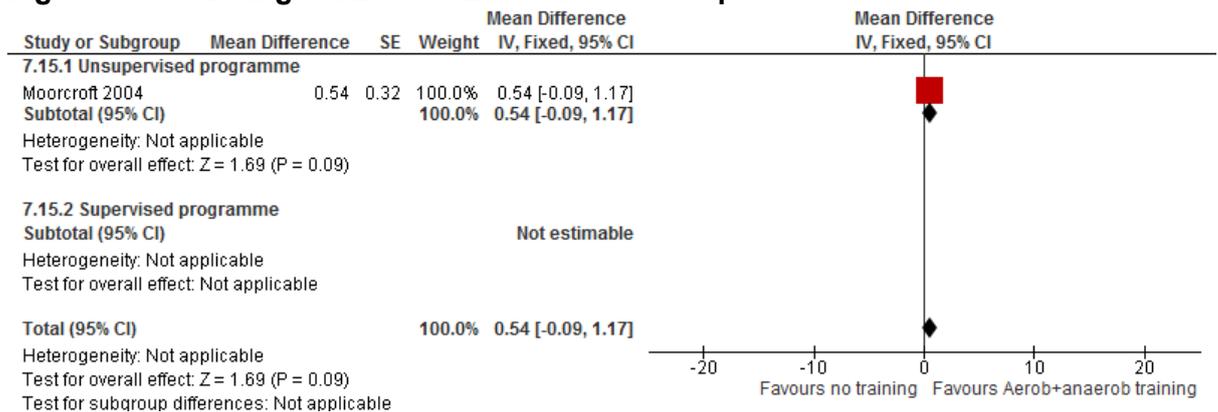
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

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



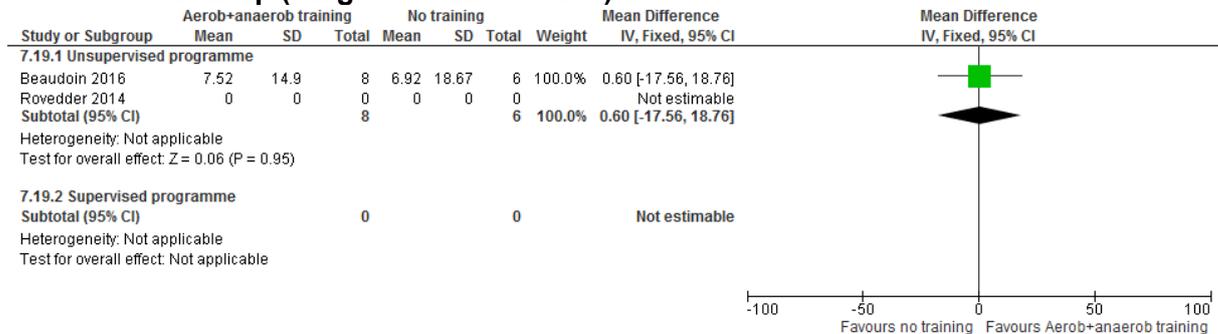
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

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



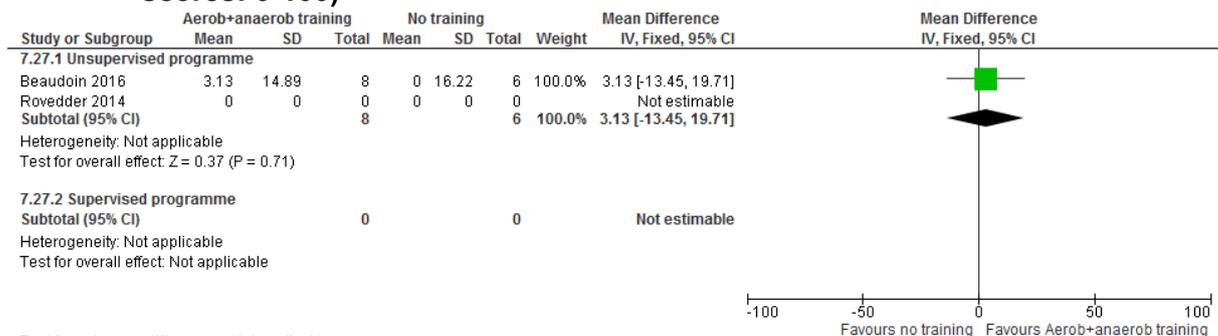
Abbreviations: BMI: body mass index; CI: confidence interval; IV: inverse variance; SD: standard deviation

**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

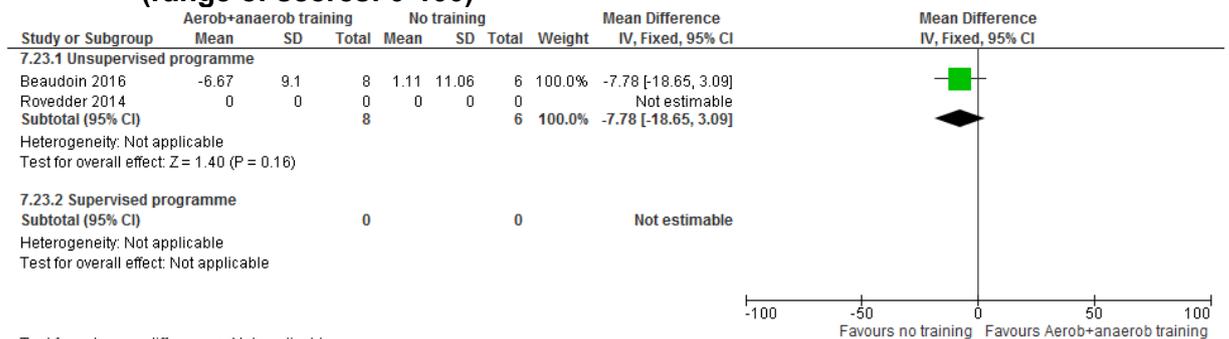
**Figure 361: Change in quality of life – CFQ-R vitality at 3 months follow-up (range of scores: 0-100)**



Test for subgroup differences: Not applicable

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

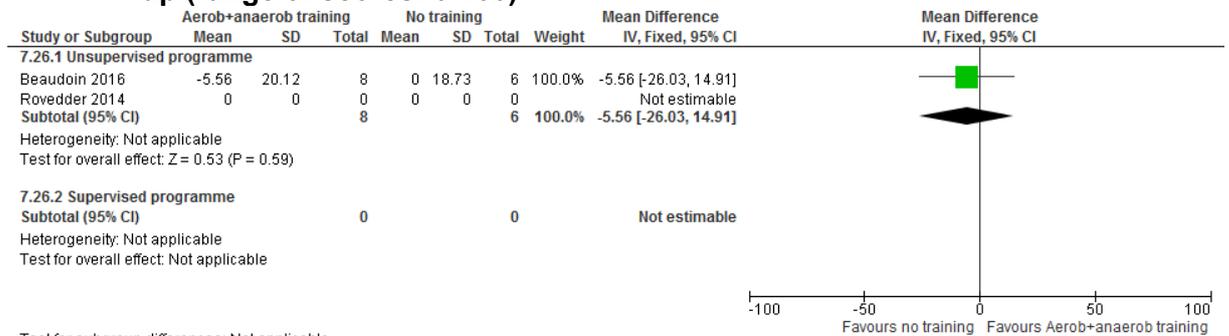
**Figure 362: Change in quality of life – CFQ-R emotional state at 3 months follow-up (range of scores: 0-100)**



Test for subgroup differences: Not applicable

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

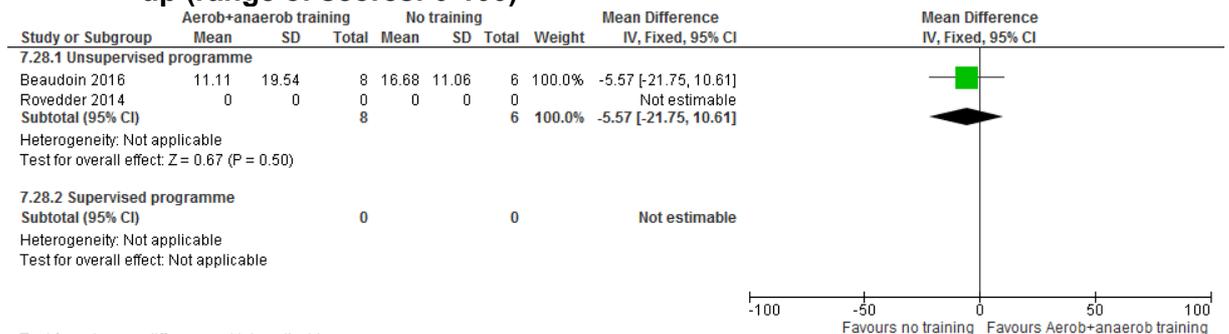
**Figure 363: Change in quality of life – CFQ-R treatment burden at 3 months follow-up (range of scores: 0-100)**



Test for subgroup differences: Not applicable

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

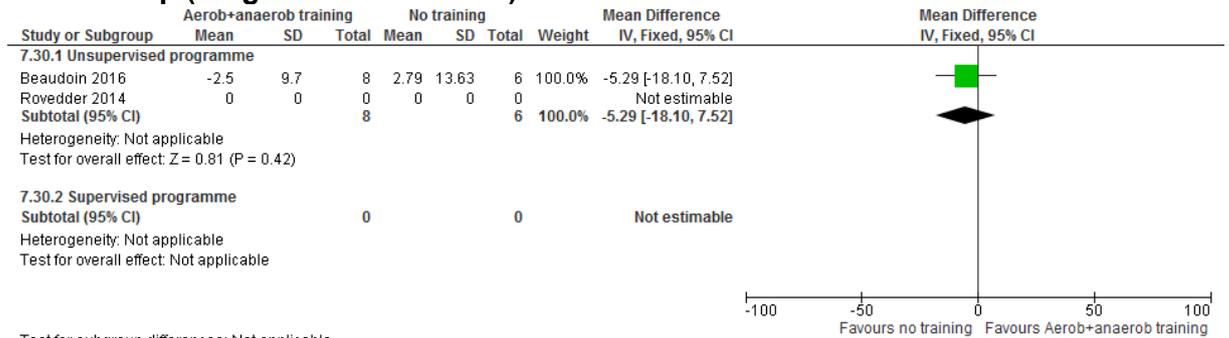
**Figure 364: Change in quality of life – CFQ-R health perception at 3 months follow-up (range of scores: 0-100)**



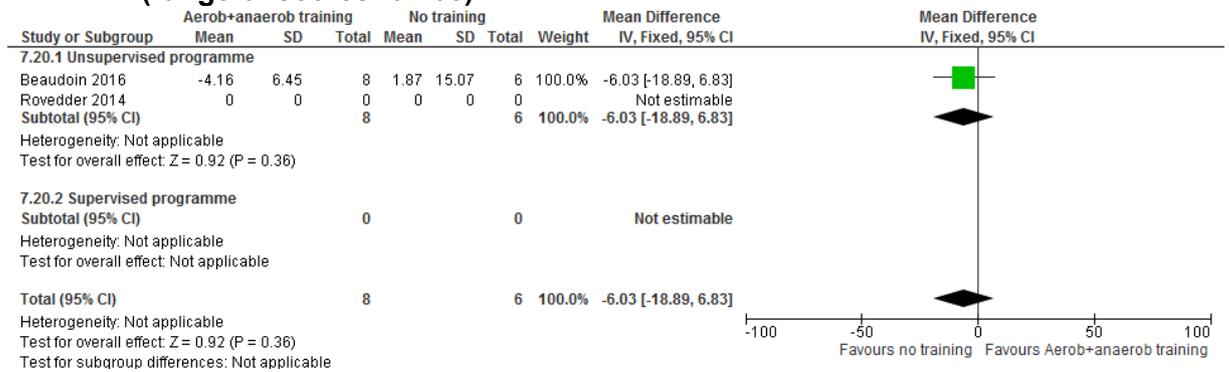
Test for subgroup differences: Not applicable

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

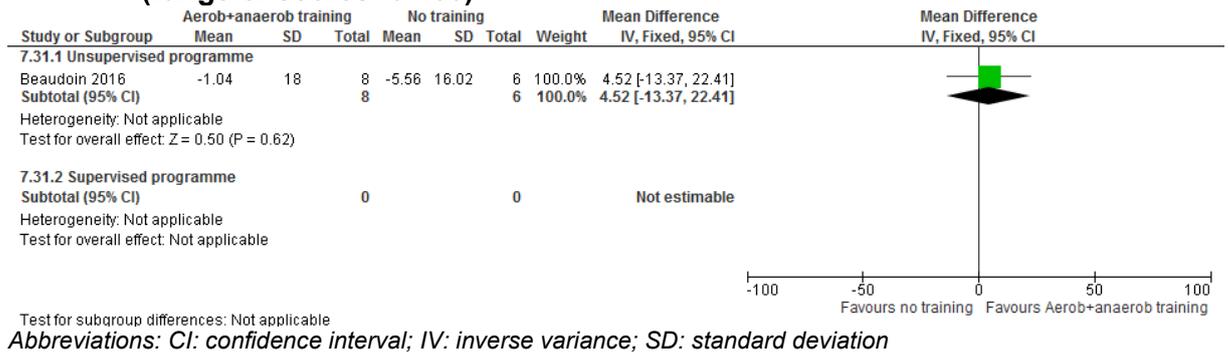
**Figure 365: Change in quality of life – CFQ-R social limitations at 3 months follow-up (range of scores: 0-100)**



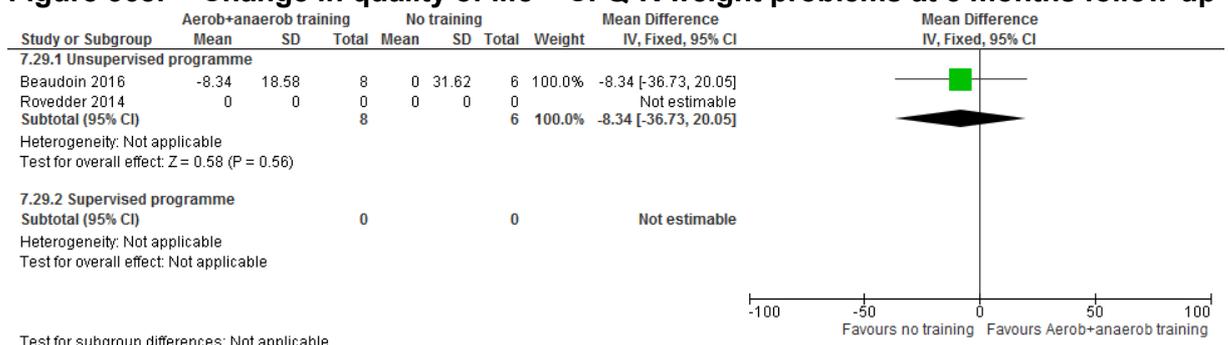
**Figure 366: Change in quality of life – CFQ-R body image at 3 months follow-up (range of scores: 0-100)**



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

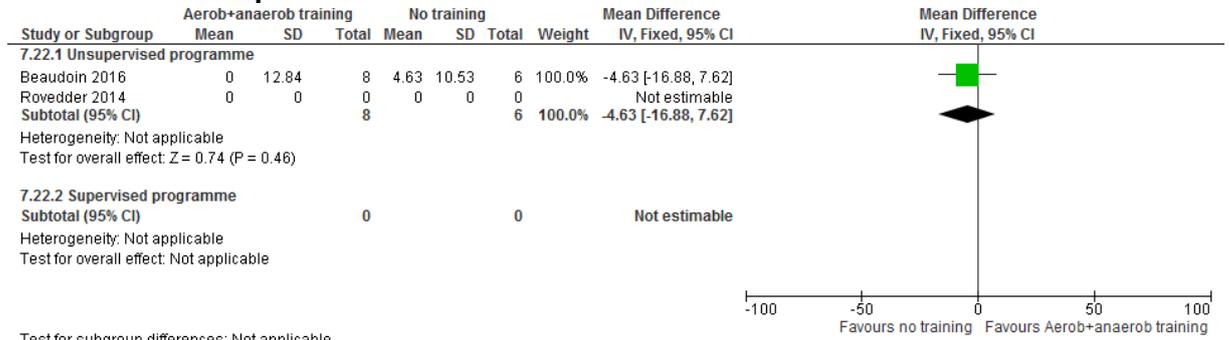


**Figure 368: Change in quality of life – CFQ-R weight problems at 3 months follow-up**



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

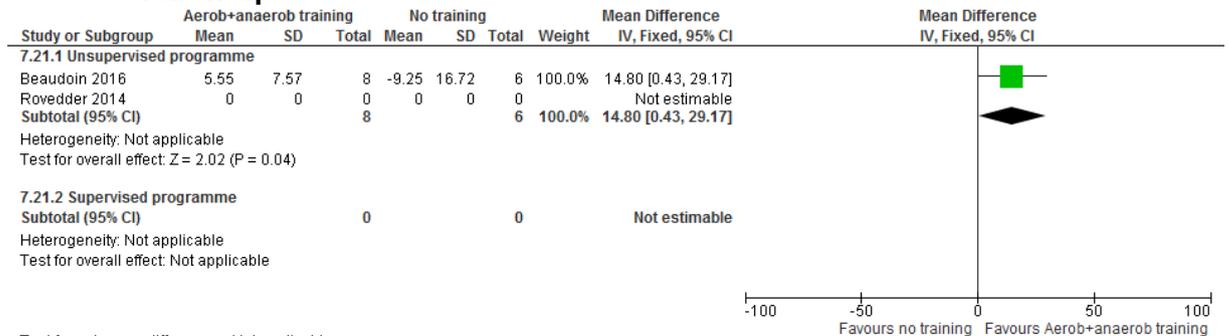
**Figure 369: Change in quality of life – CFQ-R respiratory symptoms at 3 months follow-up**



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**

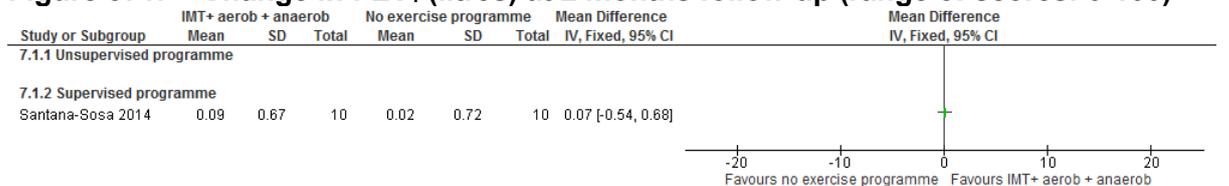


Test for subgroup differences: Not applicable

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

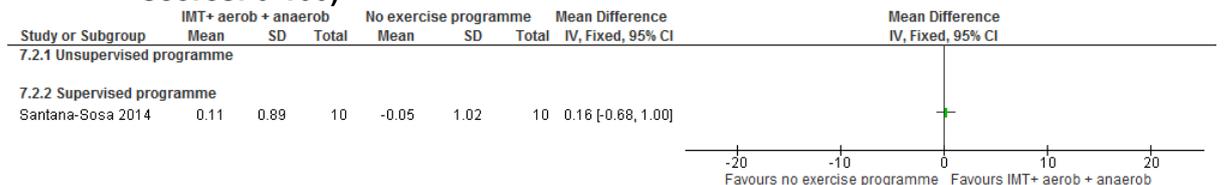
**Comparison 6. Combined inspiratory muscle training (IMT), resistance and aerobic training versus no exercise programme**

**Figure 371: Change in FEV<sub>1</sub> (litres) at 2 months follow-up (range of scores: 0-100)**



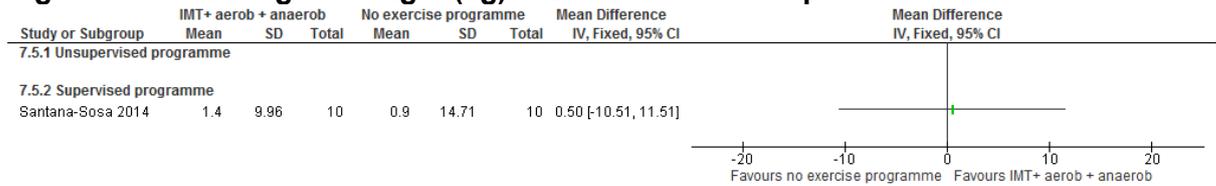
Abbreviations: CI: confidence interval; FEV<sub>1</sub>: forced expiratory volume in 1 second; IV: inverse variance; SD: standard deviation

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



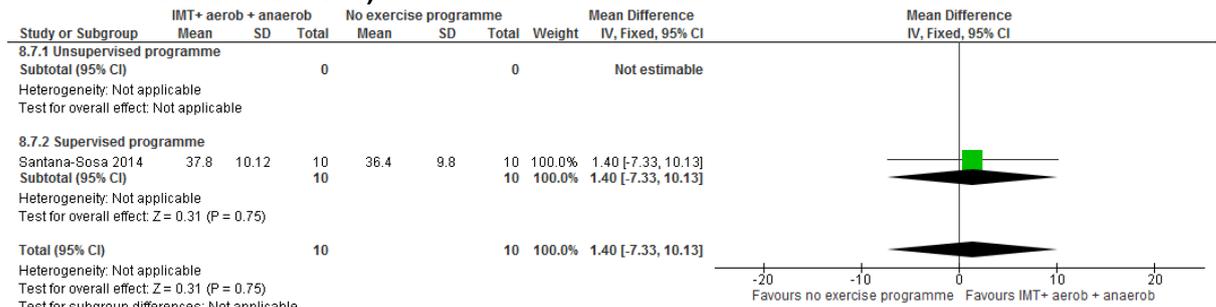
Abbreviations: SD: standard deviation; IV: inverse variance; CI: confidence interval

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



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

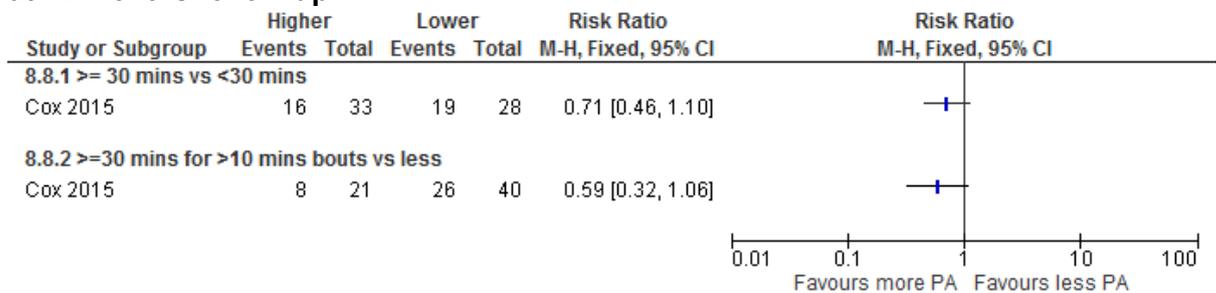
**Figure 374: Change in quality of life (CFQ-R children's) at 2 months follow-up (range of scores: 0-100)**



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

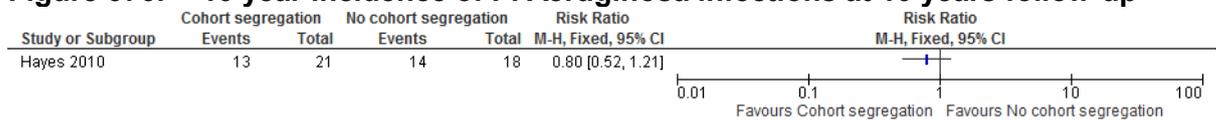
Not applicable to this review.

## 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

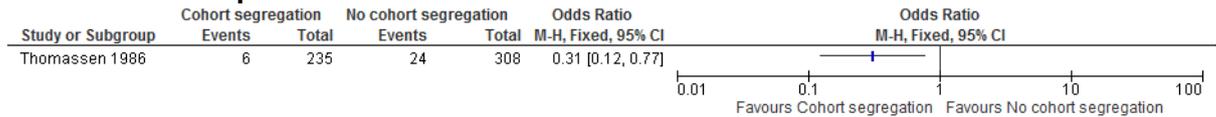
## I.22.2 Inpatient care

### 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

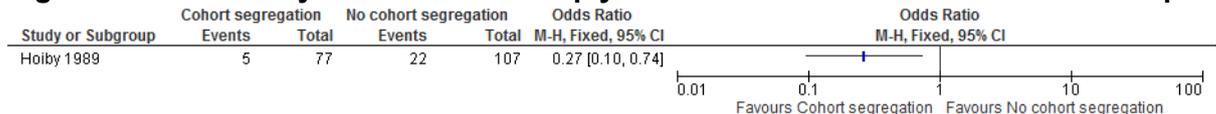
#### Parents' satisfaction

Data could not be plotted

## I.22.3 Combined inpatient and outpatient care

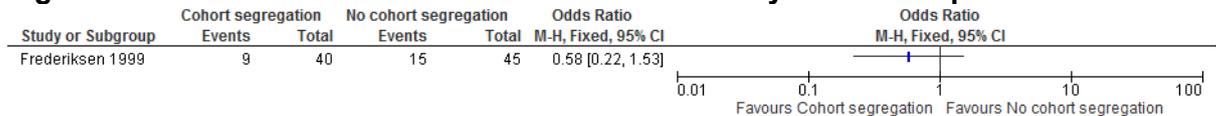
### Comparison 6. Cohort segregation versus no cohort segregation

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



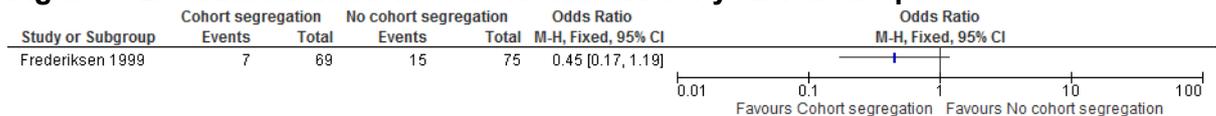
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

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



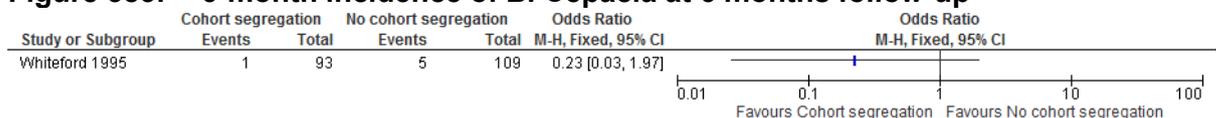
Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel

**Figure 382: Annual incidence of chronic PA at 1 year follow-up**



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

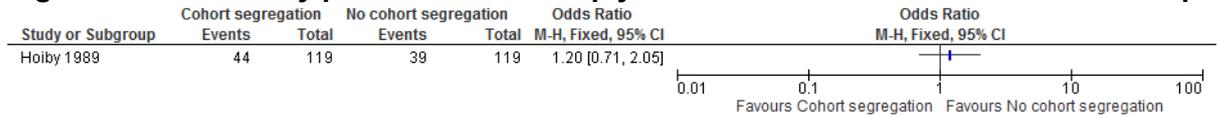
**Figure 383: 6-month incidence of B. Cepacia at 6 months follow-up**



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

**Annual incidence of Burkholderia species infection at 1 year follow-up**  
Data could not be plotted

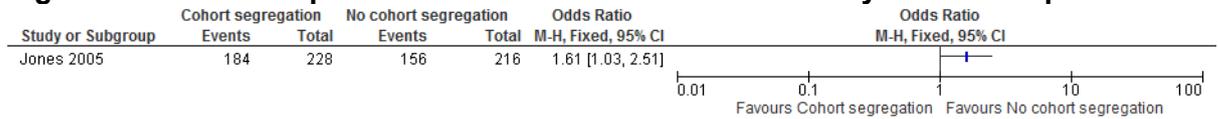
**Figure 384: Monthly prevalence of multiply resistant PA strain at 1 month follow-up**



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