

Symptomatic treatment of the cough in whooping cough (Review)

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Disease Description

- Pertussis, a cough illness commonly known as whooping cough (100 Day Cough), is caused by the bacterium *Bordetella pertussis*.
- Prolonged paroxysmal cough often accompanied by an inspiratory whoop.
- Around 16 million cases of whooping cough (pertussis) occur worldwide each year, mostly in low-income countries.
- Much of the morbidity of whooping cough in children and adults is due to the effects of the paroxysmal cough

Pertussis Complications

- Syncope
- Sleep disturbance
- Incontinence
- Rib fractures
- Complications among infants
 - Pneumonia (22%)
 - Seizures (2%)
 - Encephalopathy (<0.5%)
- Death
 - Infants, particularly those who have not received a primary vaccination series, are at risk for complications and mortality.



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Symptomatic treatment of the cough in whooping cough (Review)

Wang K, Bettiol S, Thompson MJ, Roberts NW, Perera R, Heneghan CJ, Harnden A

Cough treatments proposed include

- corticosteroids,**
- beta2-adrenergic agonists,**
- pertussis-specific immunoglobulin,**
- antihistamines**
- leukotriene receptor antagonists (LTRAs).**

Objectives

To assess the effectiveness and safety of interventions to reduce the severity of paroxysmal cough in whooping cough in children and adults.

Outcome

- Paroxysms of cough per 24 hours
- Mean paroxysmal cough per hour
- Mean number of whoops per day (first week)
- Mean whoops per hour

Secondary outcomes

- Frequency of vomiting
- Frequency of whoop
- Frequency of cyanosis (turning blue) during cough
- Development of a serious complication, for example cerebral haemorrhage or convulsions; or presence of subcutaneous emphysema or pneumothorax
- Mortality from any cause
- Side effects of medication
- Admission to hospital
- Duration of hospital stay

- Twelve trials from our literature search between 1950 and 2014 met our inclusion criteria.
- Most of the trials were generally old and poorly reported while the majority of randomised controlled trials (RCTs) were performed in the 1980s.
- There were two exceptions (Halperin 2007; Wang 2014), which were well designed and well executed.

Beta2-adrenergic agonists

Pavesio 1977	Salbutamol 0.5 mg/kg/day orally in 3 doses for 15 days	
Krantz 1985	Salbutamol 0.6 mg/kg/day orally in 4 doses for 2 days	
Mertsola 1986	Salbutamol orally 0.1 mg/kg orally 3 times a day for 10 days	

Beta2-adrenergic agonists

- (Krantz 1985). The dosage of salbutamol was 0.6 mg/kg/day in four divided doses for two days. (N = 17)
- There was no statistically significant difference in coughing paroxysms, with a mean increase of 0.3 coughs per 24 hours in the salbutamol group (95%CI - 5.3 to 6).
- In the second study (Mertsola 1986) (N = 27) treatment was administered orally at 0.1 mg/kg three times a day for 10 days
- There was no statistically significant difference in coughing paroxysms: MD -0.7 coughs per day in the salbutamol group (95% CI -6.2 to 4.7).

Beta2-adrenergic agonists

- In both trials, data were reported for each 24-hour period.
- There was no evidence of heterogeneity in paroxysmal cough per 24 hours (P value = 0.79).
- There was no statistically significant difference in coughing paroxysms: MD -0.22 coughs per 24 hours in groups treated with salbutamol (95% CI -4.1 to 3.7; P value = 0.91)

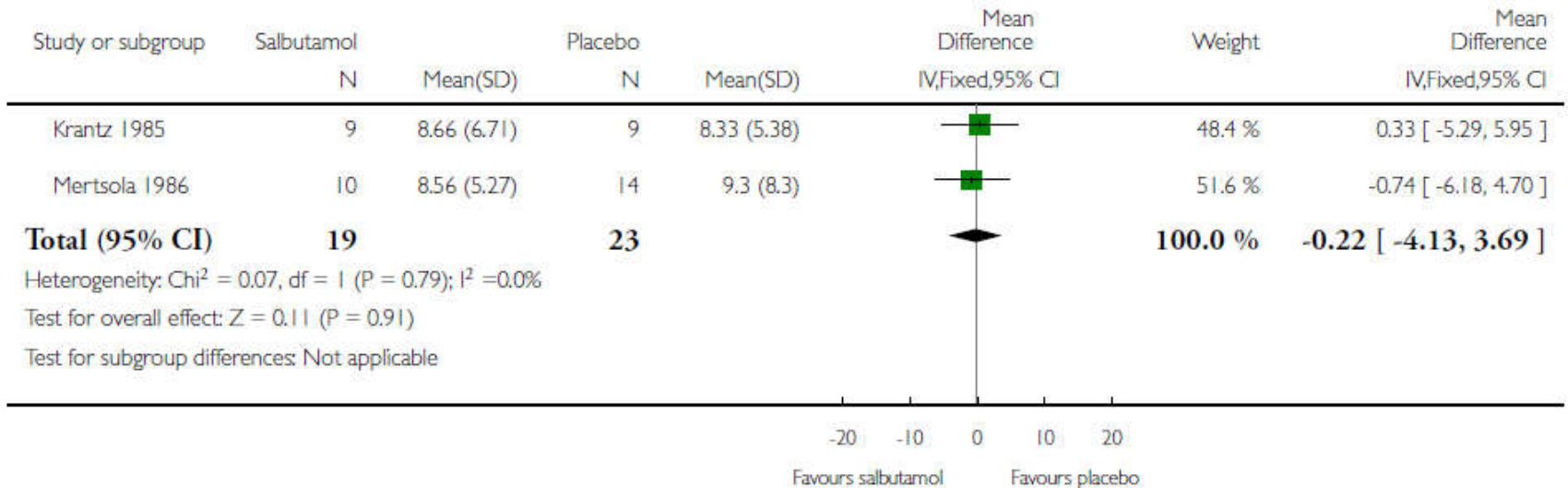
Beta2-adrenergic agonists

Analysis 3.1. Comparison 3 Salbutamol versus placebo, Outcome 1 Paroxysms of cough per day.

Review: Symptomatic treatment of the cough in whooping cough

Comparison: 3 Salbutamol versus placebo

Outcome: 1 Paroxysms of cough per day



Antihistamines

Miraglia 1984	Chlophedianol 1.62 mg/kg/day orally plus sobrerol 3.6 mg/kg/day orally	
Danzon 1988	Diphenhydramine 5 mg/kg/day orally in 3 doses	
Ghaffari 2011	Intervention group: azithromycin +, cetirizine 10 ml + tramadol 50 mg Control group: azithromycin + cetirizine 10 ml daily from days 1 to 5	

Antihistamine versus placebo

- There was no statistically significant difference between the numbers of paroxysms of cough in 24 hours
- diphenhydramine group (mean 22.6, standard deviation (SD) 13.1)
- placebo group (mean 20.7, SD 10.2; mean difference (MD) 1.90; 95% CI -4.7 to 8.5; P value = 0.66)

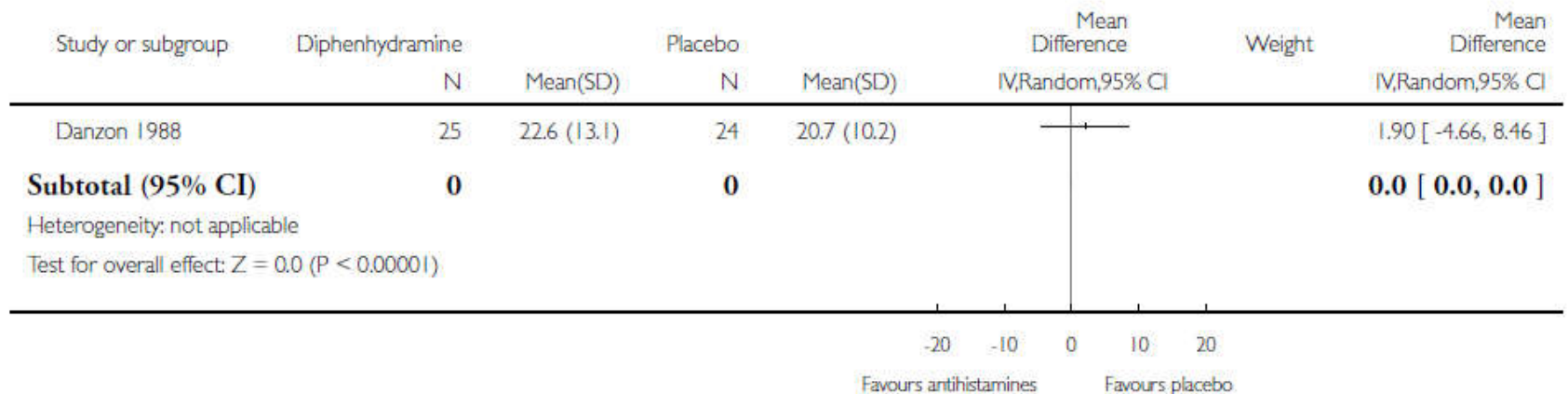
Antihistamines

Analysis 1.1. Comparison 1 Antihistamines versus placebo, Outcome 1 Paroxysms of cough per 24 hours.

Review: Symptomatic treatment of the cough in whooping cough

Comparison: 1 Antihistamines versus placebo

Outcome: 1 Paroxysms of cough per 24 hours



Pertussis-specific immunoglobulin

Lucchesi 1949	Pertussis immune serum, 50 to 100 ml IV by 50 ml/ day until improvement, or 5 doses	
Granstrom 1991	Specific immunoglobulin treatment, 8 ml IM into the buttocks, 2 ml either side on the second day	
Halperin 2007	P-IGIV (750mg/kg) or placebo was administered as a single infusion over 3 hours; initial infusion was 1.5 ml/kg/hr increasing gradually to 6.0 ml/kg/hr	

Pertussis-specific immunoglobulin

- **Granstrom 1991** reported a possible mean reduction of -3.1 whoops per 24 hours (95% CI -6.2 to 0.02, N = 47 participants) but no change in hospital stay (MD -0.7 days; 95% CI -3.8 to 2.4, N = 46 participants).
- (Halperin 2007, N = 25) assessing the effect of intravenous pertussis immunoglobulin (P-IGIV) There was no statistically significant difference in paroxysmal cough in the treatment group compared to the placebo group: MD-0.07 coughs per hour (95% CI -0.42 to 0.27; P value = 0.65)

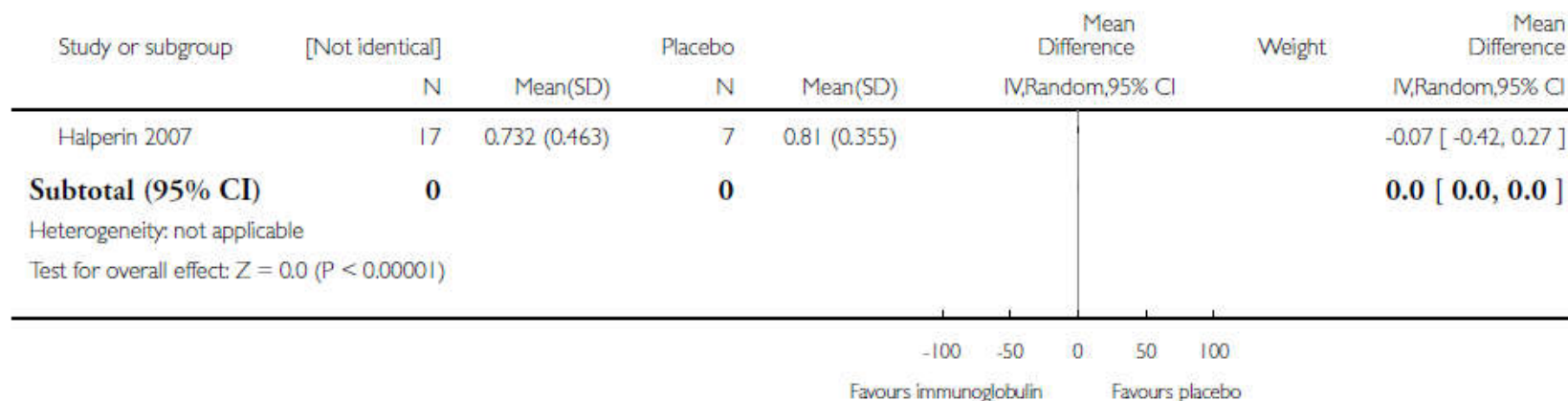
Pertussis-specific immunoglobulin

Analysis 2.1. Comparison 2 Pertussis immunoglobulin versus placebo, Outcome 1 Mean paroxysmal cough per hour.

Review: Symptomatic treatment of the cough in whooping cough

Comparison: 2 Pertussis immunoglobulin versus placebo

Outcome: 1 Mean paroxysmal cough per hour

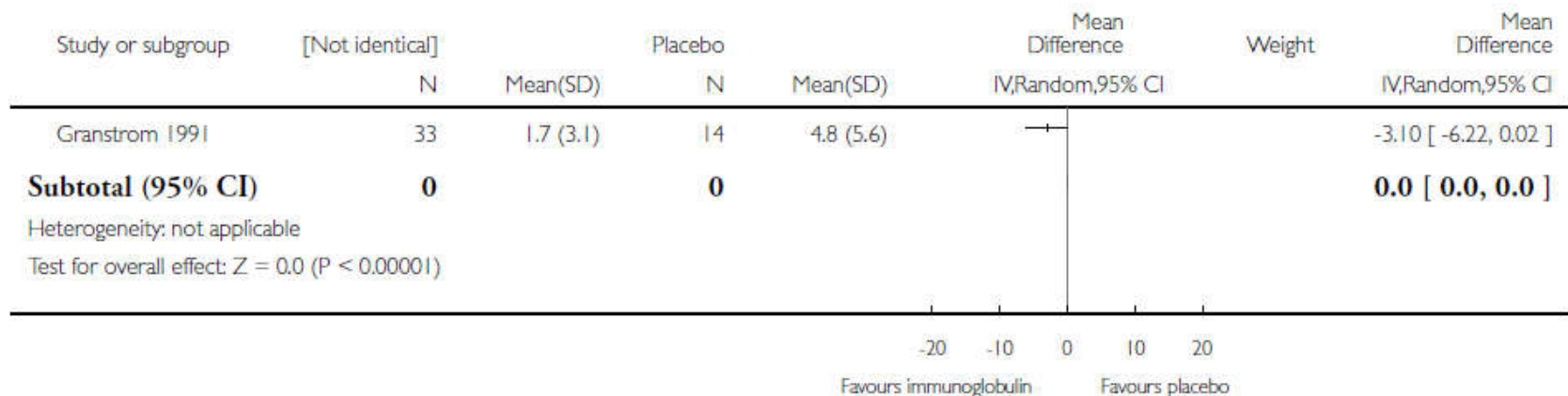


Analysis 2.2. Comparison 2 Pertussis immunoglobulin versus placebo, Outcome 2 Mean number of whoops per day (first week).

Review: Symptomatic treatment of the cough in whooping cough

Comparison: 2 Pertussis immunoglobulin versus placebo

Outcome: 2 Mean number of whoops per day (first week)

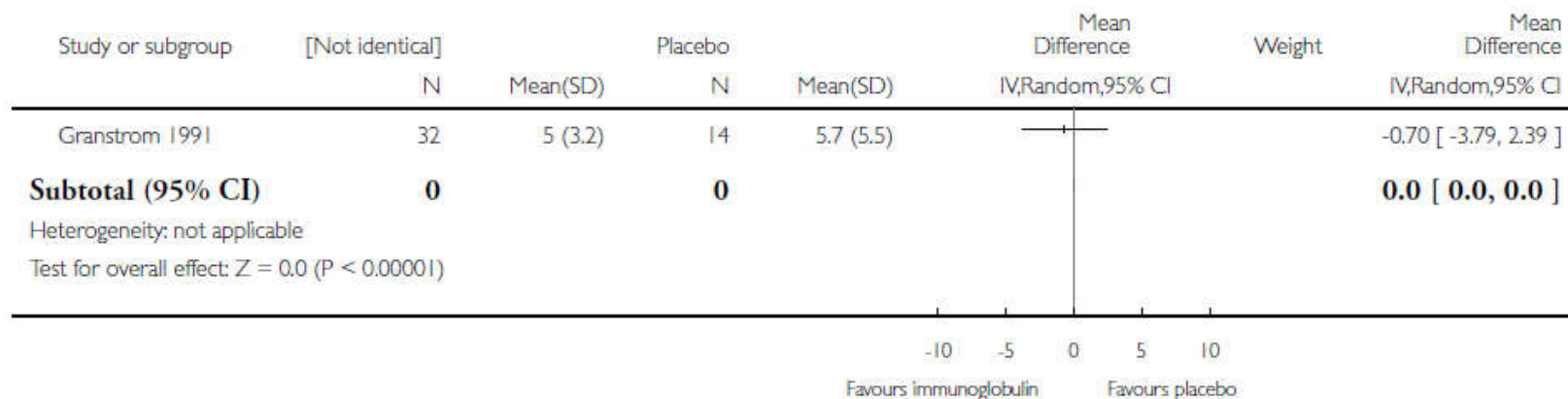


Analysis 2.4. Comparison 2 Pertussis immunoglobulin versus placebo, Outcome 4 Duration of hospital stay (days).

Review: Symptomatic treatment of the cough in whooping cough

Comparison: 2 Pertussis immunoglobulin versus placebo

Outcome: 4 Duration of hospital stay (days)



Corticosteroids

Zoumboulakis 1973	Hydrocortisone 30 mg/kg/day intramuscularly for 2 days followed by a reduced dosage over 6 days	
Roberts 1992	Dexamethasone 0.3 mg/kg/day for 4 days.	

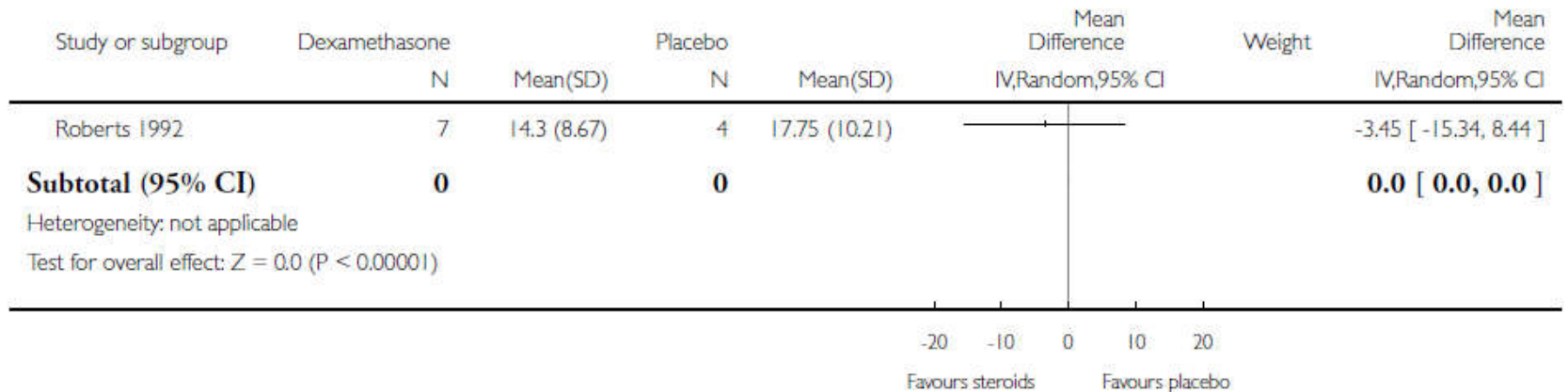
Corticosteroids

Analysis 4.1. Comparison 4 Steroids versus placebo, Outcome 1 Duration of hospital stay (days).

Review: Symptomatic treatment of the cough in whooping cough

Comparison: 4 Steroids versus placebo

Outcome: 1 Duration of hospital stay (days)



leukotriene receptor antagonists (LTRAs)

Wang 2014	Montelukast sodium 10 mg tablets or image-matched placebo tablets (main excipient lactose monohydrate) for 14 days. Participants chose whether to continue taking study medication after 2 weeks	

Outcomes	Mean (standard deviation)		Mean difference (95% CI)	No. of participants (studies)
	Treatment	Placebo		
Paroxysms of cough per 24 hours (diphenhydramine)	22.6 (13.1)	20.7(10.2)	1.90 (-4.66 to 8.46)	49 (1)
Paroxysms of cough per day (salbutamol)	*	*	-0.22 (-4.13 to 3.69)	42 (2)
Mean paroxysmal cough per hour (pertussis immunoglobulin)	0.73 (0.46)	0.81 (0.36)	-0.07 (-0.42 to 0.27)	24 (1)
Mean whoops per hour (pertussis immunoglobulin)	0.39 (0.38)	0.46 (0.28)	-0.06 (-0.34 to 0.21)	24 (1)
Duration of hospital stay, days (pertussis immunoglobulin)	5 (3.2)	5.7 (5.5)	-0.70 (-3.79 to 2.39)	46 (1)
Duration of hospital stay, days (dexamethasone)	14.3 (8.7)	17.8 (10.2)	-3.45 (-15.34 to 8.44)	11 (1)

Summary of main results

- This systematic review has found that there is insufficient evidence to support the use of current interventions.
- Only one trial indicated some benefit in the use of **pertussis immunoglobulin** but more research is required to substantiate this finding.

SUMMARY AND RECOMMENDATIONS

- Supportive care is the mainstay of treatment for pertussis in infants and children (child's fluid and nutritional status)
- Indications for hospitalization include increased work of breathing, inability to feed, cyanosis, apnea, seizures, or concerns for rapid deterioration, or infants <3 months
- Adjunctive treatments including bronchodilators, corticosteroids, and antitussive agents have not been proven.

- thank for attention!