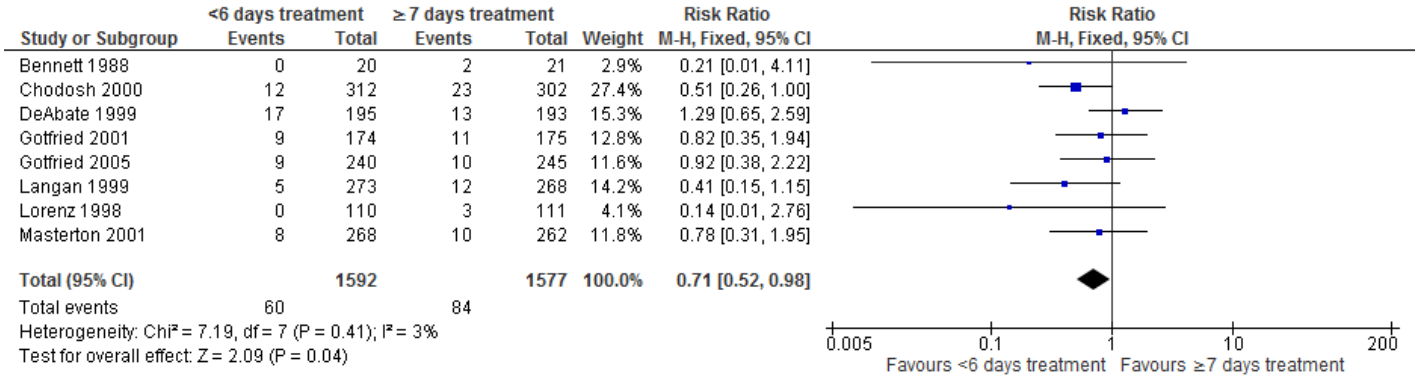
Does antibiotic treatment duration affect the outcomes of exacerbations of asthma and COPD? A Systematic Review

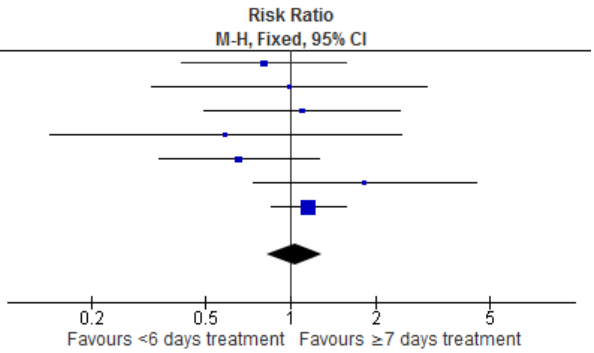
Supplementary data



Study or Subgroup	<6 days treatment Events	Total	≥7 days treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bennett 1988	0	20	2	21	2.9%	0.21 [0.01, 4.11]
Chodosh 2000	12	312	23	302	27.4%	0.51 [0.26, 1.00]
DeAbate 1999	17	195	13	193	15.3%	1.29 [0.65, 2.59]
Gotfried 2001	9	174	11	175	12.8%	0.82 [0.35, 1.94]
Gotfried 2005	9	240	10	245	11.6%	0.92 [0.38, 2.22]
Langan 1999	5	273	12	268	14.2%	0.41 [0.15, 1.15]
Lorenz 1998	0	110	3	111	4.1%	0.14 [0.01, 2.76]
Masterton 2001	8	268	10	262	11.8%	0.78 [0.31, 1.95]
Total (95% CI)		**1592**		**1577**	**100.0%**	**0.71 [0.52, 0.98]**
Total events	60		84			

Heterogeneity: Chi² = 7.19, df = 7 (P = 0.41); I² = 3%
Test for overall effect: Z = 2.09 (P = 0.04)

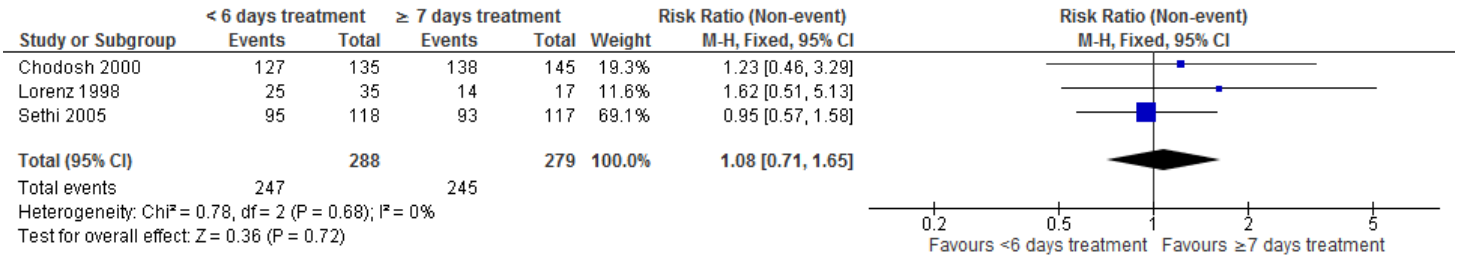
Supplementary Figure 1 – Forest plot of nausea (adverse outcome), < 6 versus ≥ 7 days antibiotic duration



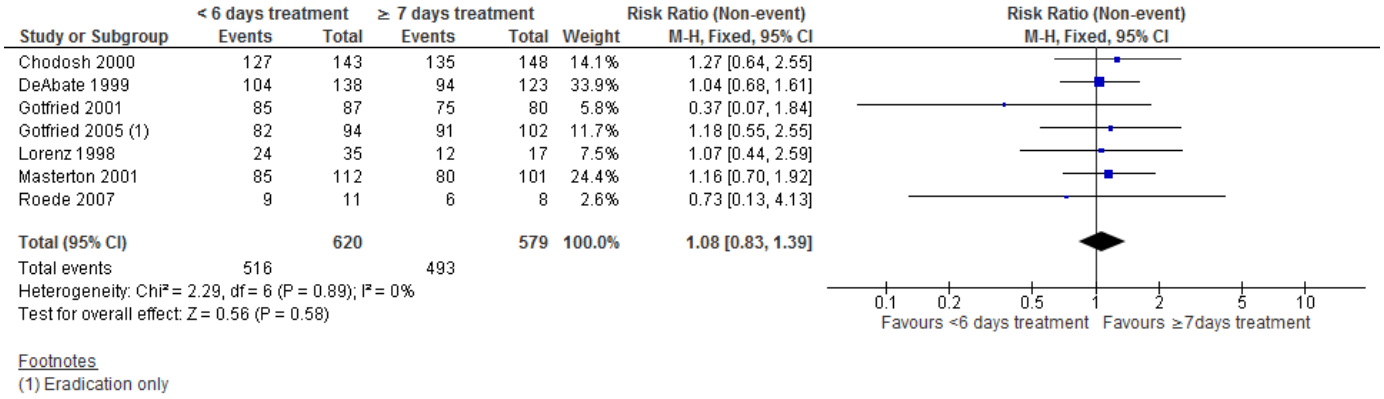
Study or Subgroup	<6 days treatment Events	Total	≥7 days treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chodosh 2000	15	312	18	302	13.9%	0.81 [0.41, 1.57]
DeAbate 1999	6	195	6	193	4.6%	0.99 [0.32, 3.02]
Gotfried 2001	12	174	11	175	8.3%	1.10 [0.50, 2.42]
Langan 1999	3	273	5	268	3.8%	0.59 [0.14, 2.44]
Lorenz 1998	13	110	20	111	15.1%	0.66 [0.34, 1.25]
Masterton 2001	13	268	7	262	5.4%	1.82 [0.74, 4.48]
Sethi 2005	74	443	65	450	48.9%	1.16 [0.85, 1.57]
Total (95% CI)		**1775**		**1761**	**100.0%**	**1.03 [0.82, 1.29]**
Total events	136		132			

Heterogeneity: Chi² = 5.07, df = 6 (P = 0.53); I² = 0%
Test for overall effect: Z = 0.29 (P = 0.77)

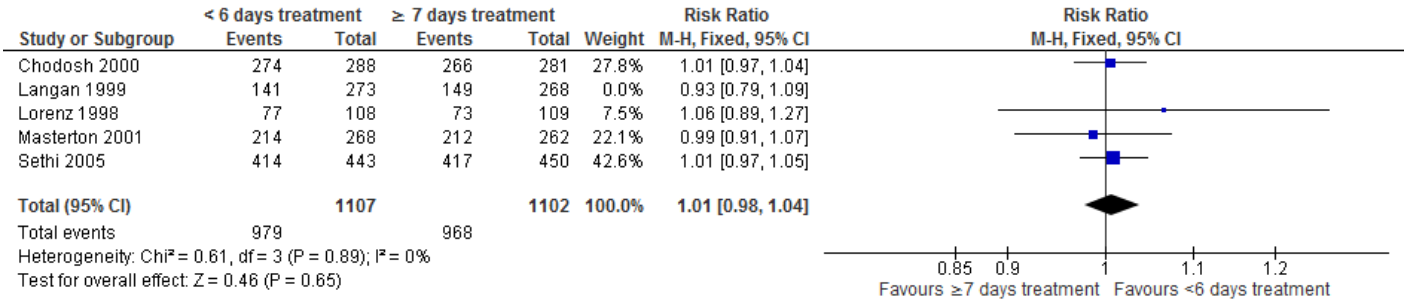
Supplementary Figure 2 – Forest plot of diarrhea (adverse outcome), < 6 versus ≥ 7 days antibiotic duration



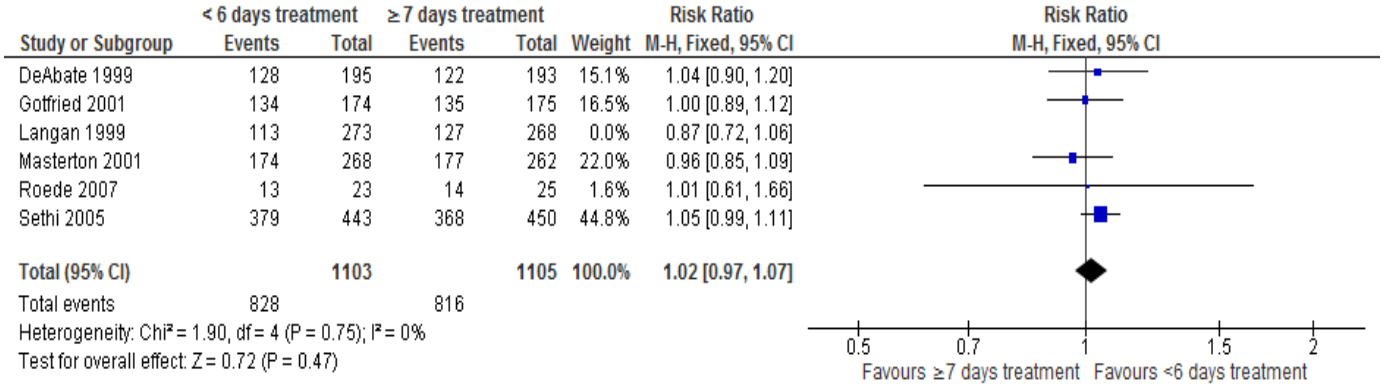
Supplementary Figure 3 – Eradication or presumed eradication of bacteria from sputum within 6 days of treatment completion, < 6 versus ≥ 7 days antibiotic duration



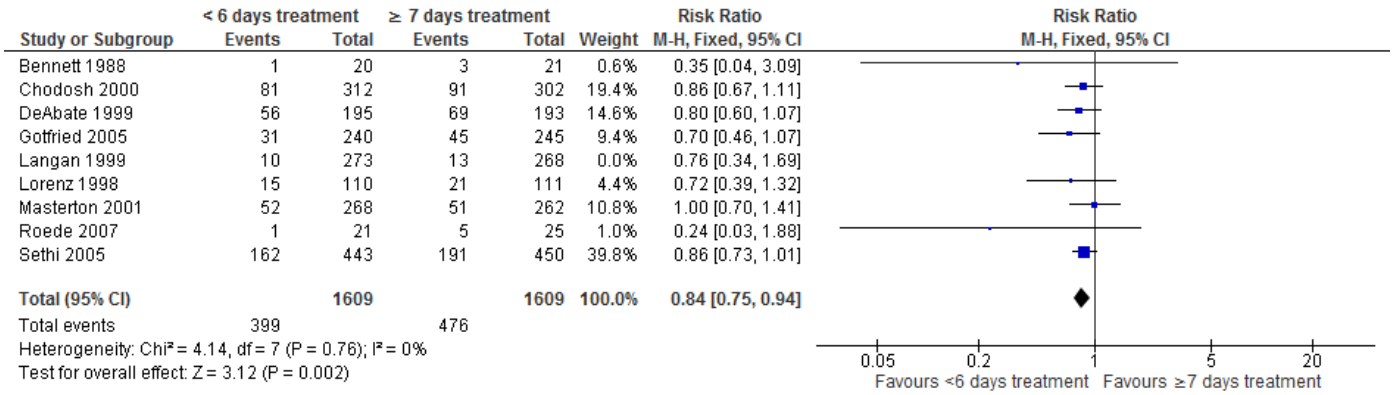
Supplementary Figure 4 - Eradication or presumed eradication of bacteria from sputum within 7-23 days of treatment completion, < 6 versus ≥ 7 days antibiotic duration



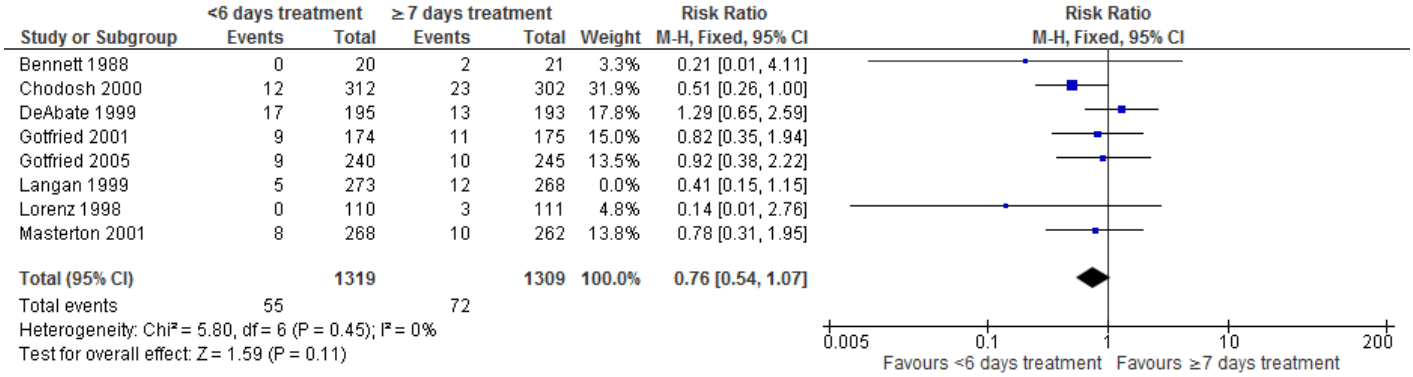
Supplementary Figure 5 - Forest plot of clinical success within 6 days of treatment completion, < 6 versus ≥ 7 days antibiotic duration, sensitivity analysis excluding Langan et al.



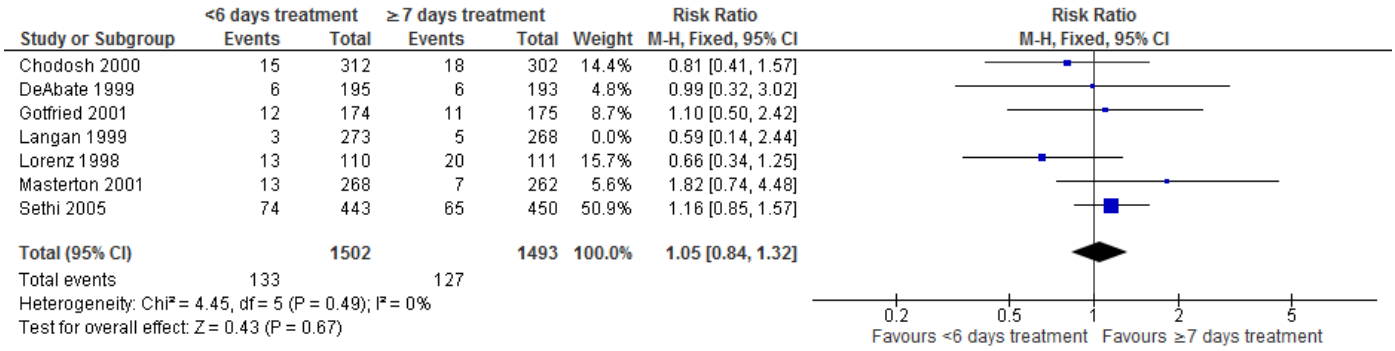
Supplementary Figure 6 - Forest plot of clinical success > 20 days after treatment completion, < 6 versus ≥ 7 days antibiotic duration, sensitivity analysis excluding Langan et al.



Supplementary Figure 7 - Forest plot of overall adverse events, < 6 versus ≥ 7 days antibiotic duration, sensitivity analysis excluding Langan et al.



Supplementary Figure 8 - Forest plot of nausea (adverse event), < 6 versus ≥ 7 days antibiotic duration, sensitivity analysis excluding Langan et al.



Supplementary Figure 9 - Forest plot of diarrhea (adverse event), < 6 versus ≥ 7 days antibiotic duration, sensitivity analysis excluding Langan et al.

Supplementary Table 1 - Overview of clinical outcome assessment by study

Study	Early follow up	Medium / Late follow up	Outcomes
Bennett 1988 [28]	0 days after treatment completion	12 months	Absence of mucoid sputum At 12 months: number of exacerbations; time to first exacerbation
Chodosh 2000 [29]	0-6 days after treatment completion	7-17 days after treatment completion	Clinical success: resolution of acute signs / symptoms related to infection or sufficient improvement so that additional / alternative antibiotics were not required
DeAbate 1999 [36]		21-24 days after treatment completion	Clinical cure or improvement
Gotfried 2001 [37]		7-14 days after treatment completion Extended follow up (21-28 days after treatment completion)	Clinical cure: resolution of all signs & symptoms of acute exacerbation of chronic bronchitis which were present at study entry, without need for further antibiotics
Gotfried 2005 [25]		Days 10-14 after treatment completion	Clinical cure: resolution of signs / symptoms of acute exacerbation of chronic bronchitis
Langan 1999 [27]	1-3 days after treatment completion	21-28 days after treatment completion	Satisfactory clinical response: cure or signs / symptoms of acute exacerbation of chronic bronchitis have improved / resolved at post-

			treatment visit (day 1-3) and absent at follow up visit or incomplete resolution at follow up visit
Lorenz 1998 [30]	0-3 days after treatment completion	17-23 days after treatment completion	Clinical success: cure or improvement of acute bacterial exacerbation based on volume and nature of sputum and symptoms of breathlessness
Masterton 2001[23]	1-3 days after treatment completion	7-10 days after treatment completion (primary outcome) 4-5 weeks after treatment completion	Clinical success: resolution of all infection related signs / symptoms or return to pre-infection state or improvement with no subsequent antibacterial treatment indicated
Roede 2007 [26]		11 days after treatment completion 3 months (minus 10 days) after treatment completion	Cure: resolution of acute signs / symptoms of acute exacerbation of chronic bronchitis back to baseline
Sethi 2005 [24]	2-4 days after treatment completion	7-14 days after treatment completion (primary outcome) 21-28 days after treatment completion	Clinical success: sufficient improvement or resolution of the signs and symptoms of acute exacerbation of chronic bronchitis recorded at the screening such that no additional antibacterial therapy was prescribed for the episode of acute exacerbation of chronic bronchitis