National Clinical Guideline Centre

Forest plots

Pneumonia

Diagnosis and management of community- and hospital-acquired pneumonia in adults

Clinical guideline 191

Appendix I

3 December 2014

Final version

Commissioned by the National Institute for Health and Care Excellence

Funding
National Institute for Health and Care Excellence

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1 Community-acquired pneumonia

1.1 Diagnostic tests

1.1.1.1 CRP compared with standard care

Figure 1: Antibiotic treatment

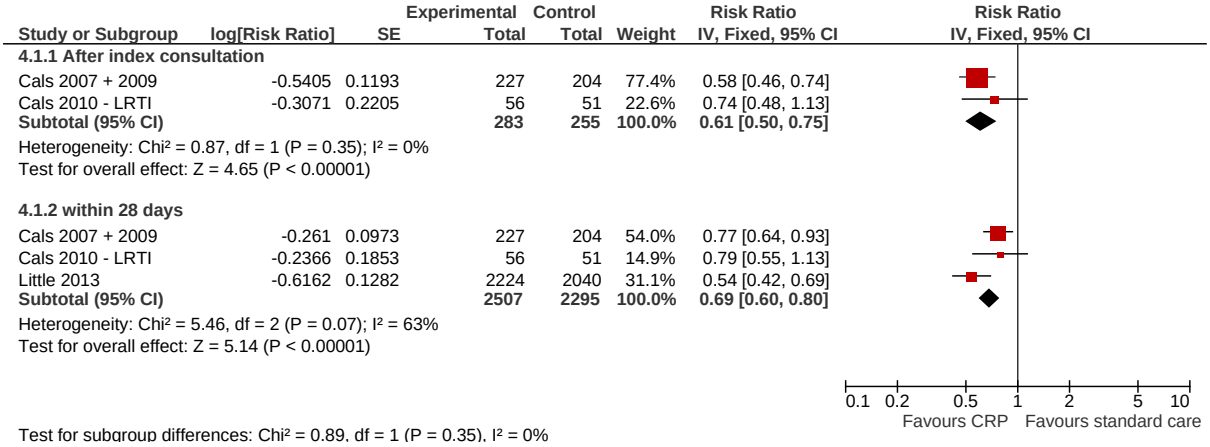


Figure 2: Mortality

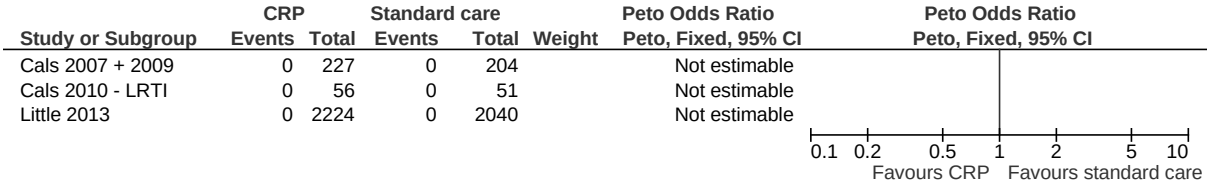


Figure 3: Hospital admission

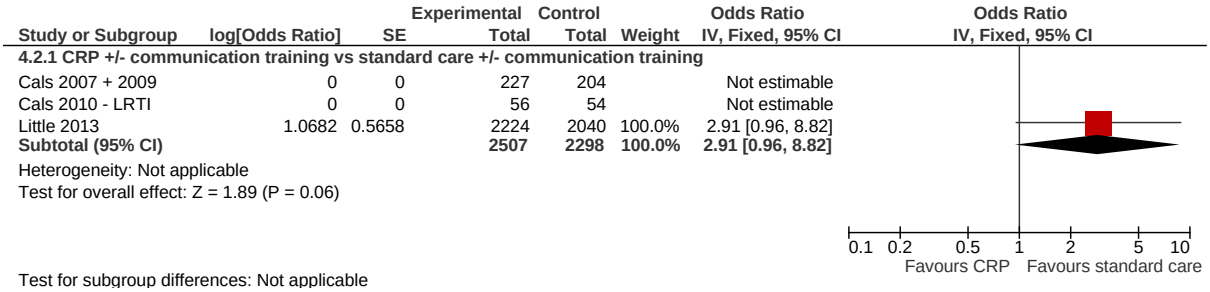


Figure 4: Resolution of symptoms

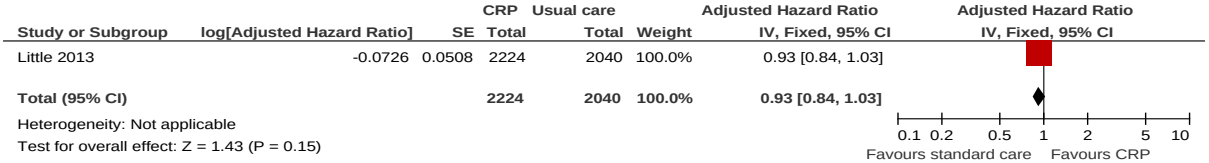


Figure 5: Resolution of symptoms (Feeling recovered as a surrogate at 7 days)

Study or Subgroup	CRP Events	CRP Total	Standard care Events	Standard care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cals 2010 - LRTI	12	51	9	49	100.0%	1.28 [0.59, 2.77]
Total (95% CI)		**51**		**49**	**100.0%**	**1.28 [0.59, 2.77]**
Total events	12		9			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.63 (P = 0.53)

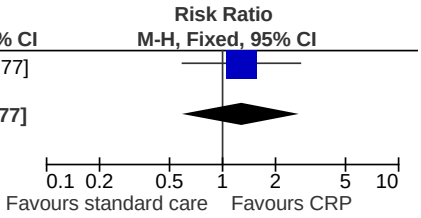


Figure 6: Quality-of-life (patient enablement score)

Study or Subgroup	CRP Mean	CRP SD	CRP Total	Standard care Mean	Standard care SD	Standard care Total	Weight	Mean Difference IV, Random, 95% CI
Cals 2007 + 2009	2.97	2.59	227	3.4	2.48	204	54.7%	-0.43 [-0.91, 0.05]
Cals 2010 - LRTI or URTI	2.5	2.6	129	2.3	2.4	129	45.3%	0.20 [-0.41, 0.81]
Total (95% CI)			**356**			**333**	**100.0%**	**-0.14 [-0.76, 0.47]**

Heterogeneity: Tau² = 0.12; Chi² = 2.53, df = 1 (P = 0.11); I² = 61%
Test for overall effect: Z = 0.46 (P = 0.64)

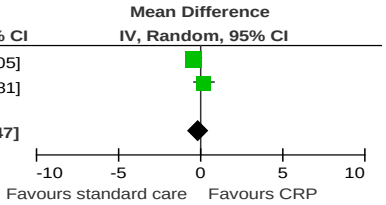
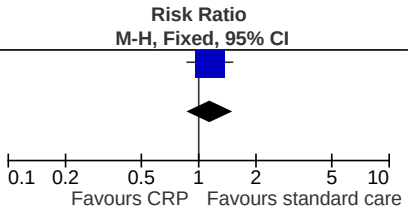


Figure 7: Re-consultation (follow-up 28 days)

Study or Subgroup	CRP Events	CRP Total	Standard care Events	Standard care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cals 2007 + 2009	79	227	62	204	100.0%	1.15 [0.87, 1.51]
Total (95% CI)		**227**		**204**	**100.0%**	**1.15 [0.87, 1.51]**
Total events	79		62			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.97 (P = 0.33)



1.1.1.2 PCT compared with standard care

Figure 8: Antibiotic treatment (initiation of antibiotics-overall)

Study or Subgroup	log[Adjusted Odds Ratio]	SE	PCT Total	Standard care Total	Weight	Adjusted Odds Ratio IV, Fixed, 95% CI
Schuetz 2012	-1.4271	0.093	2085	2126	100.0%	0.24 [0.20, 0.29]
Total (95% CI)			**2085**	**2126**	**100.0%**	**0.24 [0.20, 0.29]**

Heterogeneity: Not applicable
Test for overall effect: Z = 15.35 (P < 0.00001)

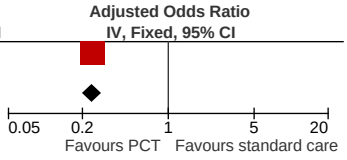


Figure 9: Antibiotic treatment (initiation of antibiotics- primary and ED settings)

Study or Subgroup	log[Adjusted Odds Ratio]	SE	PCT Total	Standard care Total	Weight	Adjusted Odds Ratio IV, Fixed, 95% CI
2.2.2 Primary care						
Schuetz 2012	-2.3026	0.182	507	501	100.0%	0.10 [0.07, 0.14]
Subtotal (95% CI)			**507**	**501**	**100.0%**	**0.10 [0.07, 0.14]**

Heterogeneity: Not applicable
Test for overall effect: Z = 12.65 (P < 0.00001)

2.2.3 ED						
Schuetz 2012	-1.0788	0.0991	1291	1314	100.0%	0.34 [0.28, 0.41]
Subtotal (95% CI)			**1291**	**1314**	**100.0%**	**0.34 [0.28, 0.41]**

Heterogeneity: Not applicable
Test for overall effect: Z = 10.89 (P < 0.00001)

Test for subgroup differences: Chi² = 34.87, df = 1 (P < 0.00001), I² = 97.1%

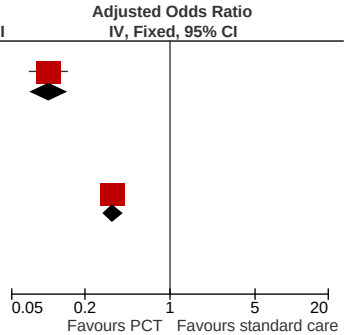


Figure 10: Mortality (all settings)

Study or Subgroup	log[Adjusted Odds Ratio]	SE	Favours PCT Total	Standard care Total	Weight	Adjusted Odds Ratio IV, Fixed, 95% CI
Schuetz 2012	-0.0619	0.1432	2085	2126	100.0%	0.94 [0.71, 1.24]
Total (95% CI)			**2085**	**2126**	**100.0%**	**0.94 [0.71, 1.24]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.43 (P = 0.67)

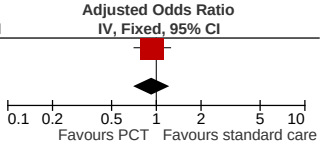


Figure 11: Mortality (Primary and ED settings)

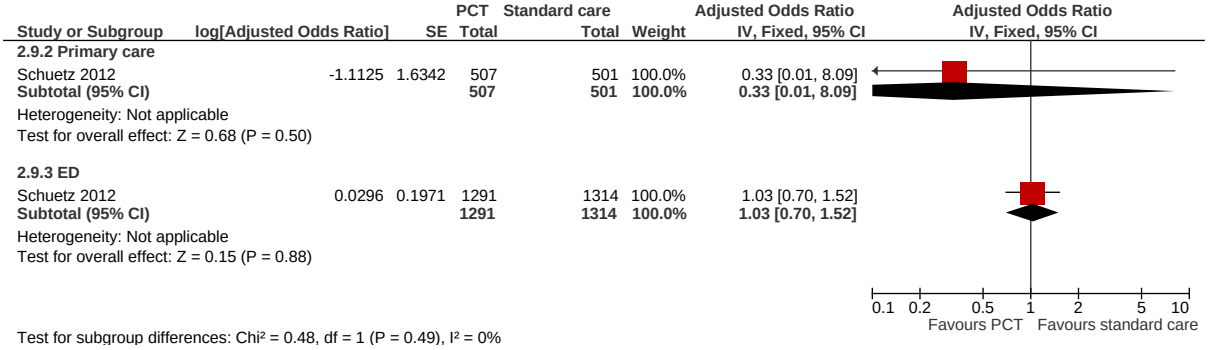


Figure 12: Hospital admission (ED)

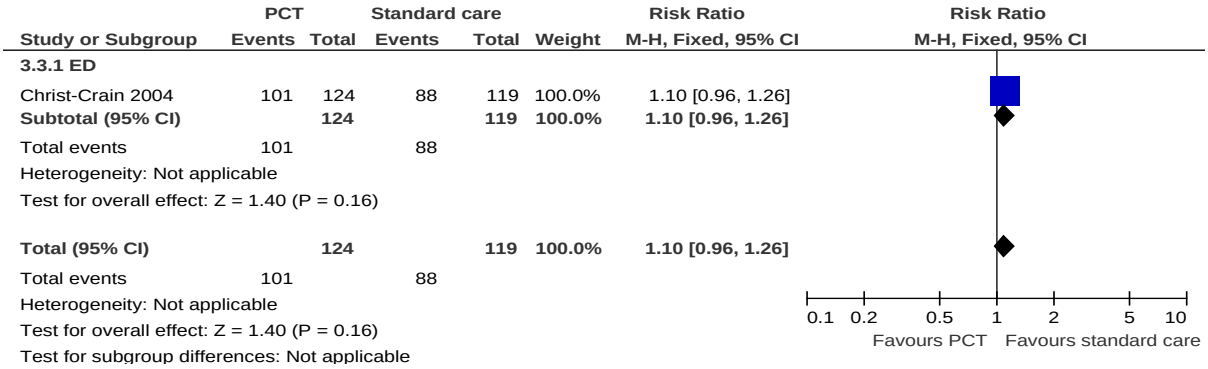


Figure 13: Resolution of symptoms (days with restricted activities for primary care setting)

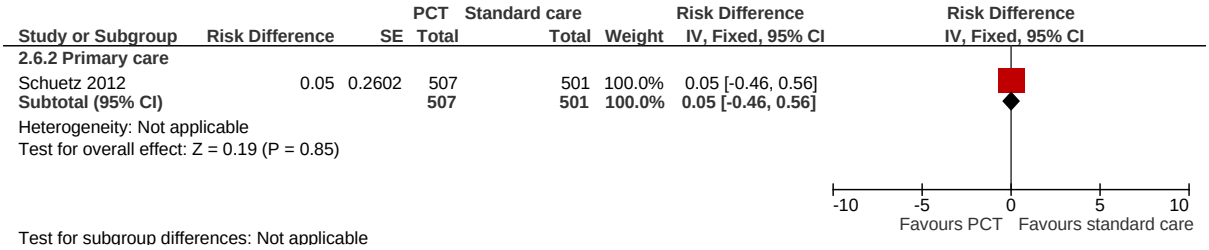


Figure 14: Resolution of symptoms (treatment failure - all settings)

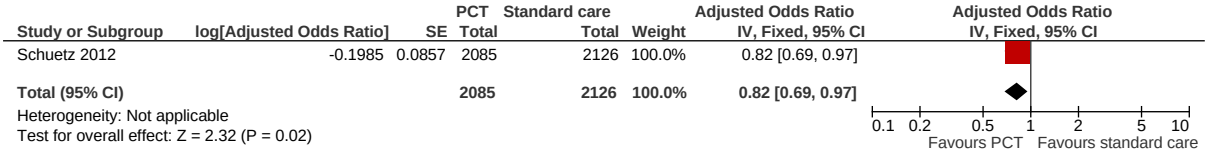


Figure 15: Resolution of symptoms (treatment failure - primary care and ED settings)

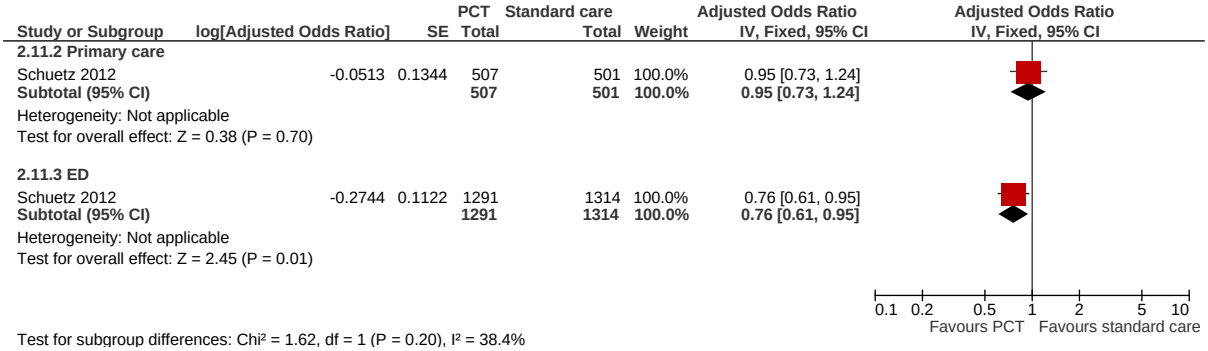
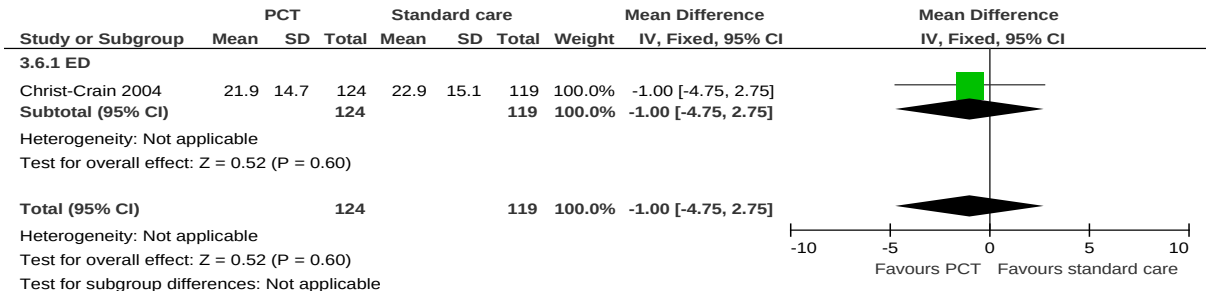
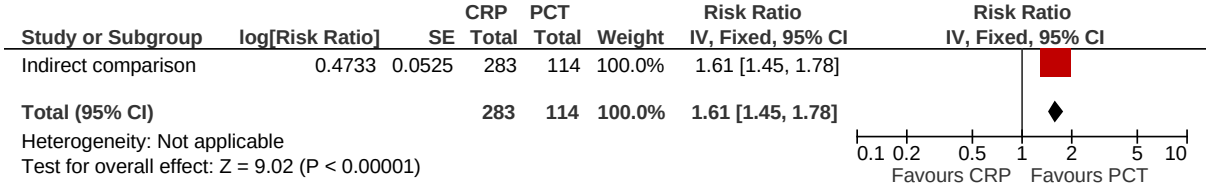


Figure 16: Quality-of-life (final score, scale not known- ED setting)



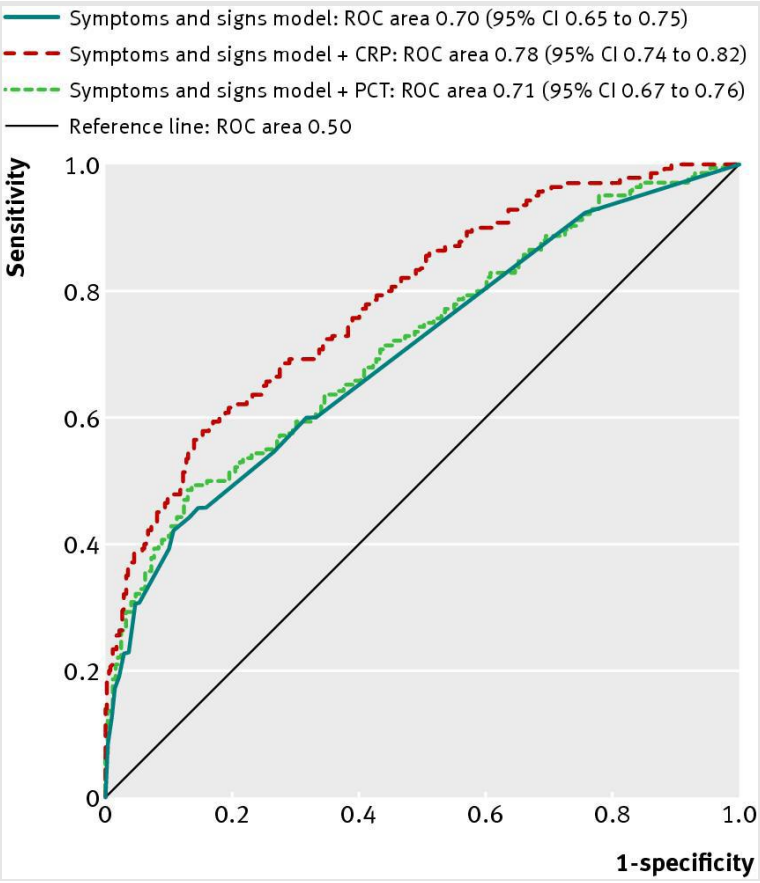
1.1.1.3 CRP compared with PCT (indirect comparison)

Figure 17: Antibiotic treatment (at index consultation)



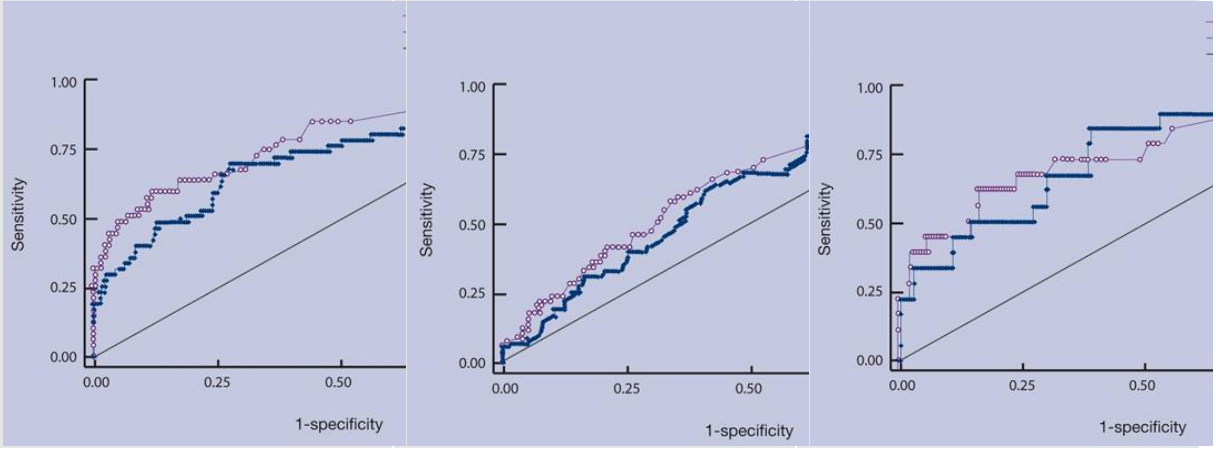
1.1.2 Receiver operating characteristic curves

Figure 18: ROC curves of symptoms and signs and added value of CRP and procalcitonin to determine diagnosis of pneumonia (continuous results)



Source/Note:van Vugt SF, Broekhuizen BD, Lammens C, Zuithoff NP, de Jong PA, Coenen S et al. Use of serum C reactive protein and procalcitonin concentrations in addition to symptoms and signs to predict pneumonia in patients presenting to primary care with acute cough

Figure 19:ROC curves of PCT and CRP predicting radiographic pneumonia	Figure 20:ROC curves of PCT and CRP predicting bacterial aetiology	Figure 21:ROC curves of PCT and CRP predicting hospitalisation



Source/Note:Holm A, Pedersen SS, Nexoe J, Obel N, Nielsen LP, Koldkjaer O et al. Procalcitonin versus C-reactive protein for predicting pneumonia in adults with lower respiratory tract infection in primary care. British Journal of General Practice. 2007; 57(540):555-560. (Guideline Ref ID HOLM2007)

1.2 Severity assessment

1.2.1 PSI compared with CURB65, CRB65 or CURB

1.2.1.1 Prediction of mortality - range of point estimates of AUCs for PSI, CURB65 and CRB65

Figure 22: AUCs for PSI

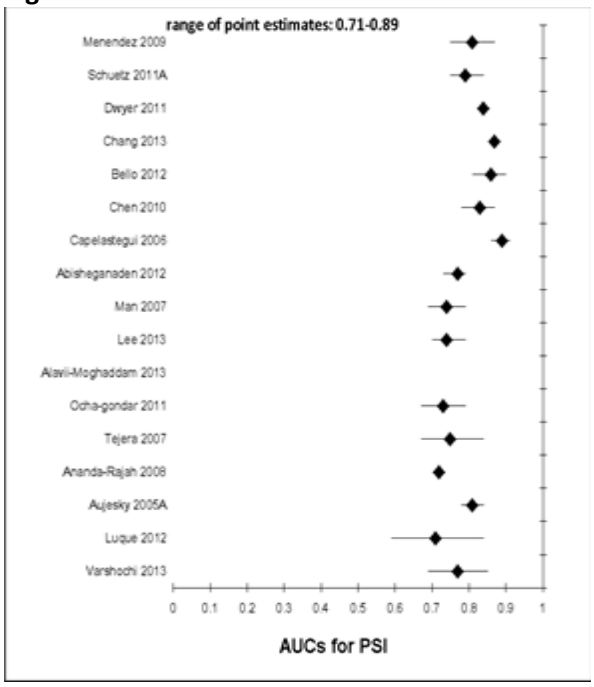


Figure 23: AUCs for CURB65

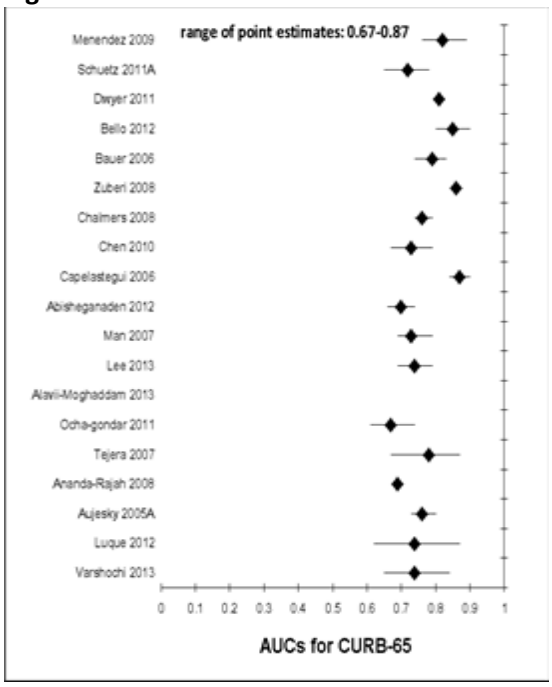


Figure 24: AUCs for CURB

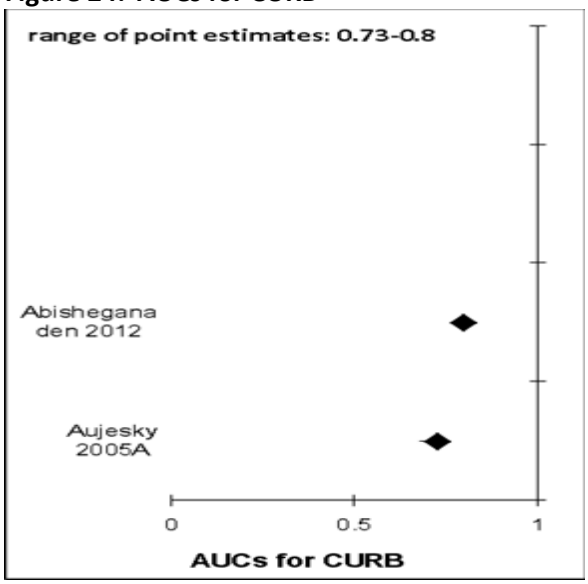


Figure 25: AUCs forCRB65

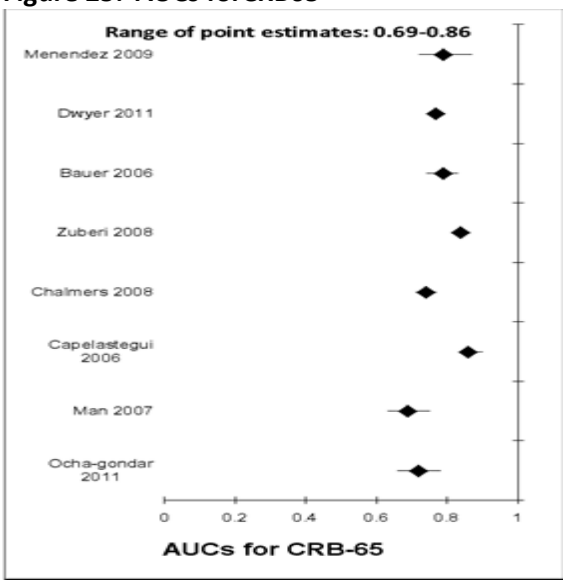


Figure 26: High-risk PSI (≥ IV) compared with low-risk PSI (< IV) to predict mortality

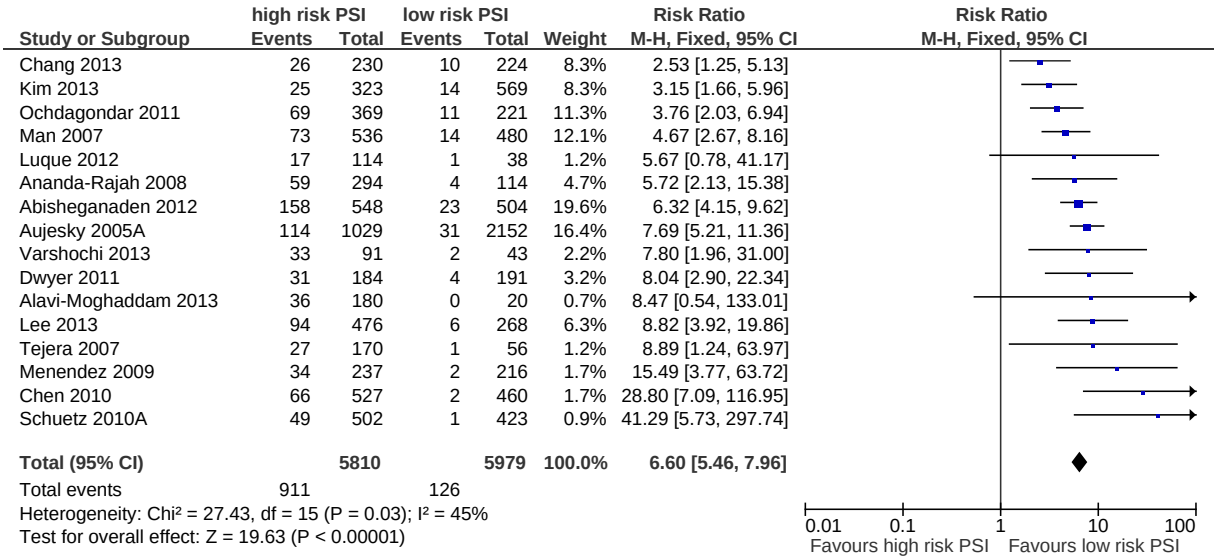


Figure 27: Intermediate-risk PSI (=III) compared with low-risk PSI (< III) to predict mortality

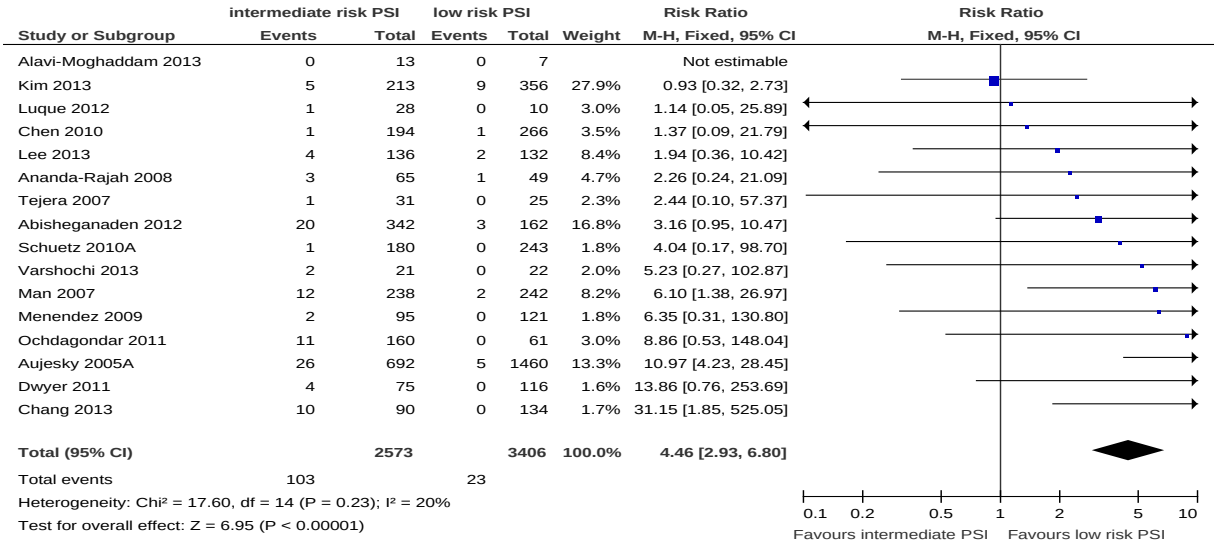


Figure 28: High-risk PSI (≥ IV) compared with intermediate-risk PSI (= III) to predict mortality

Study or Subgroup	high risk PSI Events	Total	intermediate risk PSI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chang 2013	26	230	10	90	10.4%	1.02 [0.51, 2.02]
Man 2007	73	536	12	238	12.0%	2.70 [1.50, 4.88]
Ochdagondar 2011	69	369	11	160	11.1%	2.72 [1.48, 5.00]
Aujesky 2005A	114	1029	26	692	22.5%	2.95 [1.95, 4.46]
Dwyer 2011	31	184	4	75	4.1%	3.16 [1.16, 8.64]
Kim 2013	25	314	5	213	4.3%	3.39 [1.32, 8.72]
Varshochi 2013	33	91	2	21	2.4%	3.81 [0.99, 14.63]
Luque 2012	17	114	1	28	1.2%	4.18 [0.58, 30.06]
Ananda-Rajah 2008	59	294	3	65	3.6%	4.35 [1.41, 13.44]
Tejera 2007	27	170	1	31	1.2%	4.92 [0.69, 34.91]
Abisheganaden 2012	158	548	20	342	17.8%	4.93 [3.16, 7.69]
Alavi-Moghaddam 2013	36	180	0	13	0.7%	5.65 [0.37, 87.21]
Lee 2013	94	476	4	136	4.5%	6.71 [2.51, 17.93]
Menendez 2009	34	237	2	95	2.1%	6.81 [1.67, 27.80]
Schuetz 2010A	49	502	1	180	1.1%	17.57 [2.44, 126.31]
Chen 2010	66	527	1	194	1.1%	24.30 [3.40, 173.85]
Total (95% CI)		**5801**		**2573**	**100.0%**	**3.83 [3.14, 4.68]**
Total events	911		103			

Heterogeneity: Chi² = 27.59, df = 15 (P = 0.02); I² = 46%
Test for overall effect: Z = 13.13 (P < 0.00001)

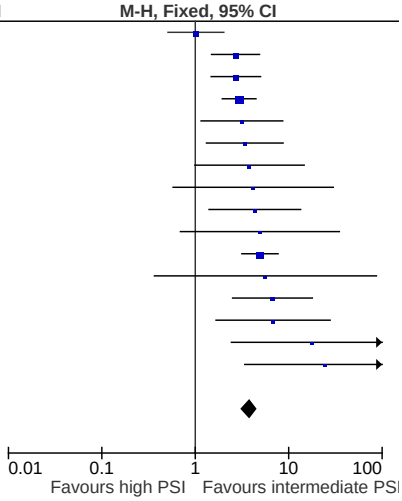


Figure 29: High-risk PSI (≥ IV) compared with low-risk PSI (< IV) to predict ITU admission

Study or Subgroup	high risk PSI Events	Total	low risk PSI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Man 2007	28	536	13	480	35.4%	1.93 [1.01, 3.68]
Ananda-Rajah 2008	37	294	6	114	22.3%	2.39 [1.04, 5.51]
Kim 2013	57	314	23	569	42.2%	4.49 [2.82, 7.14]
Total (95% CI)		**1144**		**1163**	**100.0%**	**3.11 [2.22, 4.37]**
Total events	122		42			

Heterogeneity: Chi² = 4.89, df = 2 (P = 0.09); I² = 59%
Test for overall effect: Z = 6.58 (P < 0.00001)

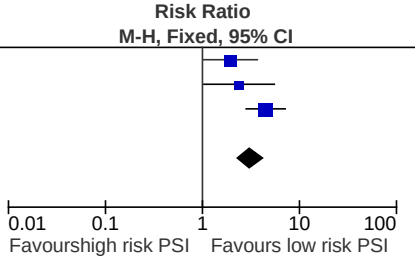


Figure 30: High-risk CURB65 (≥ 3) compared with low-risk CURB65 (< 3) to predict mortality

Study or Subgroup	high risk CURB-65 Events	Total	low risk CURB-65 Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Kim 2013	9	107	31	776	3.7%	2.11 [1.03, 4.30]
Schuetz 2010A	21	202	29	723	6.2%	2.59 [1.51, 4.45]
Ananda-Rajah 2008	39	155	24	253	9.0%	2.65 [1.66, 4.23]
Abisheganaden 2012	46	108	135	944	13.7%	2.98 [2.28, 3.90]
Alavi-Moghaddam 2013	36	193	0	7	0.5%	3.01 [0.20, 44.78]
Ochdagondar 2011	26	77	54	513	7.0%	3.21 [2.15, 4.79]
Lee 2013	51	181	49	563	11.8%	3.24 [2.27, 4.61]
Chen 2010	33	199	35	788	7.0%	3.73 [2.38, 5.85]
Man 2007	51	261	36	755	9.1%	4.10 [2.74, 6.13]
Luque 2012	13	59	5	93	1.9%	4.10 [1.54, 10.90]
Chang 2013	14	98	10	315	2.3%	4.50 [2.06, 9.81]
Aujesky 2005A	65	454	80	2727	11.3%	4.88 [3.57, 6.67]
Varshochi 2013	29	60	6	74	2.7%	5.96 [2.65, 13.41]
Tejera 2007	24	104	4	122	1.8%	7.04 [2.52, 19.63]
Dwyer 2011	23	77	12	298	2.4%	7.42 [3.87, 14.23]
Menendez 2009	27	118	9	335	2.3%	8.52 [4.13, 17.58]
Zuberi 2008	14	36	4	101	1.0%	9.82 [3.46, 27.89]
Capelastegui 2006	79	296	40	1550	6.3%	10.34 [7.22, 14.82]
Total (95% CI)		**2785**		**10937**	**100.0%**	**4.29 [3.83, 4.81]**
Total events	600		563			

Heterogeneity: Chi² = 57.02, df = 17 (P < 0.00001); I² = 70%
Test for overall effect: Z = 25.02 (P < 0.00001)

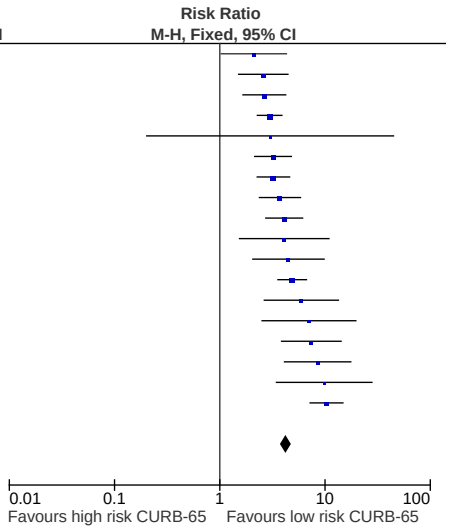


Figure 31: Intermediate-risk CURB65 (= 2) compared with low-risk CURB65 (< 2) to predict mortality

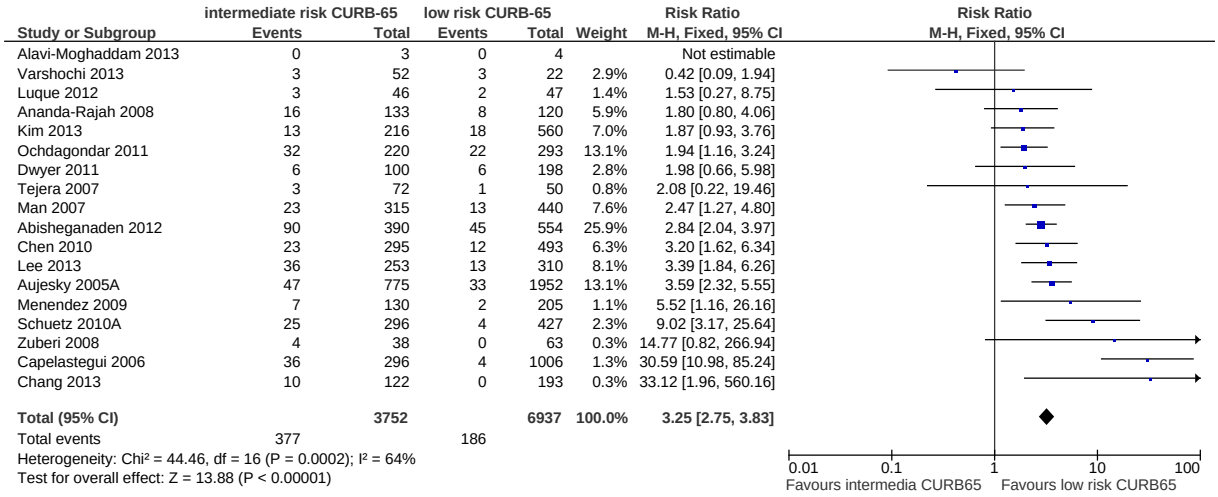


Figure 32: High-risk CURB65 (≥ 3) compared with intermediate-risk CURB65 (= 2) to predict mortality

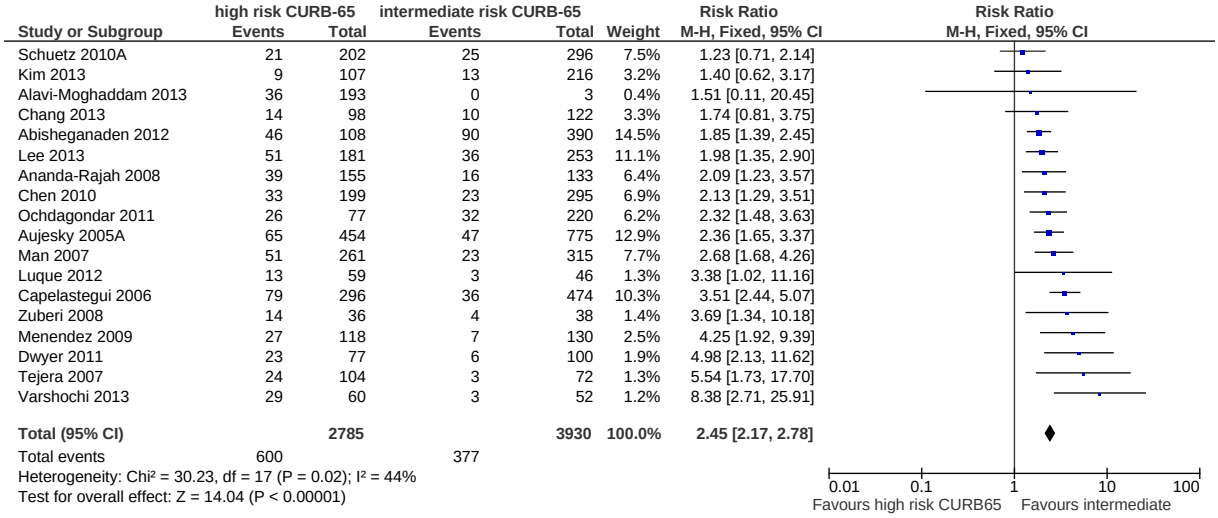


Figure 33: High-risk CURB65 (≥ 3) compared with low-risk CURB65 (< 3) to predict ITU admission

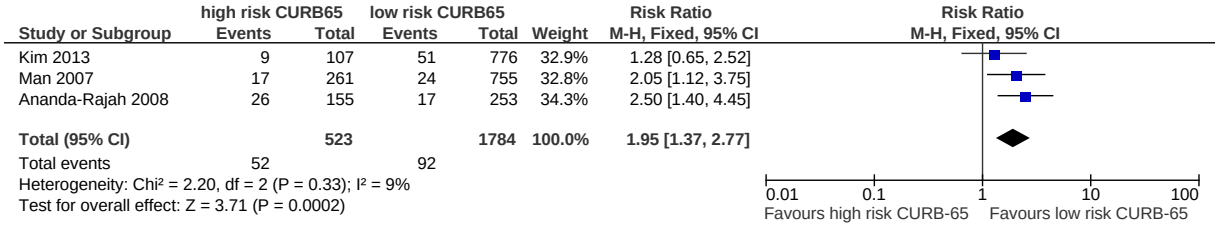


Figure 34: High-risk CURB (≥ 2) compared with low-risk CURB (< 2) to predict mortality

Study or Subgroup	high risk CURB Events	Total	low risk CURB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Aujesky 2005A	68	511	77	2670	70.0%	4.61 [3.38, 6.30]
Bauer 2006	43	297	24	1046	30.0%	6.31 [3.89, 10.22]
Total (95% CI)		**808**		**3716**	**100.0%**	**5.12 [3.94, 6.66]**
Total events	111		101			

Heterogeneity: Chi² = 1.15, df = 1 (P = 0.28); I² = 13%
Test for overall effect: Z = 12.21 (P < 0.00001)

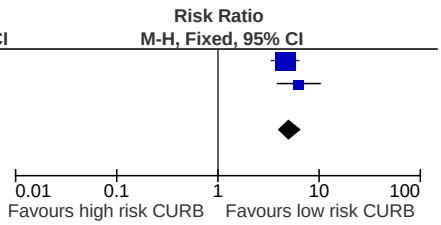


Figure 35: High-risk CRB65 (≥ 3) compared with low-risk CRB65 (< 3) to predict mortality

Study or Subgroup	high risk CRB-65 Events	Total	low risk CRB-65 Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ochdagondar 2011	17	41	63	549	19.6%	3.61 [2.35, 5.56]
Man 2007	26	105	61	901	28.6%	3.66 [2.42, 5.52]
Zuberi 2008	5	9	13	128	3.8%	5.47 [2.51, 11.92]
Dwyer 2011	16	38	19	247	11.4%	5.47 [3.09, 9.69]
Bauer 2006	15	63	53	1370	10.5%	6.15 [3.68, 10.30]
Menendez 2009	17	49	19	398	9.3%	7.27 [4.06, 13.02]
Capelastegui 2006	36	80	83	1696	16.8%	9.20 [6.67, 12.67]
Total (95% CI)		**385**		**5289**	**100.0%**	**5.45 [4.57, 6.51]**
Total events	132		311			

Heterogeneity: Chi² = 18.46, df = 6 (P = 0.005); I² = 67%
Test for overall effect: Z = 18.79 (P < 0.00001)

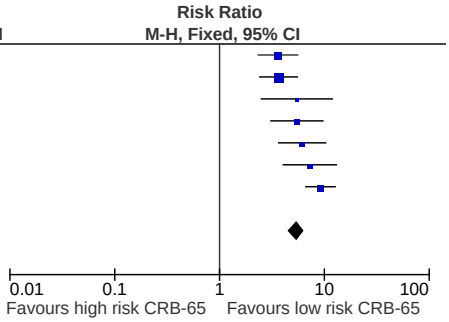


Figure 36: Intermediate-risk CRB65 (= 1 or 2) compared with low-risk CRB65 (= 0) to predict mortality

Study or Subgroup	Intermediate risk CRB-65 Events	Total	low risk CRB-65 Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ochdagondar 2011	63	549	0	0		Not estimable
Dwyer 2011	16	240	3	97	32.7%	2.16 [0.64, 7.23]
Man 2007	58	783	3	128	39.5%	3.16 [1.01, 9.94]
Menendez 2009	18	319	1	79	12.3%	4.46 [0.60, 32.89]
Zuberi 2008	13	94	0	34	5.6%	9.95 [0.61, 162.92]
Bauer 2006	53	987	0	383	5.5%	41.59 [2.57, 671.84]
Capelastegui 2006	83	980	0	716	4.4%	122.06 [7.58, 1964.36]
Total (95% CI)		**3952**		**1437**	**100.0%**	**10.75 [5.70, 20.26]**
Total events	304		7			

Heterogeneity: Chi² = 15.75, df = 5 (P = 0.008); I² = 68%
Test for overall effect: Z = 7.34 (P < 0.00001)

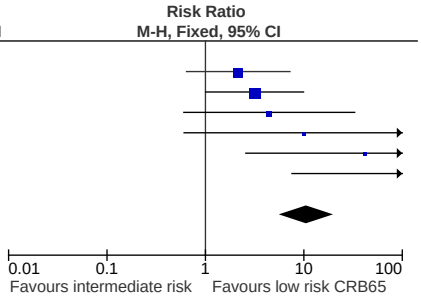
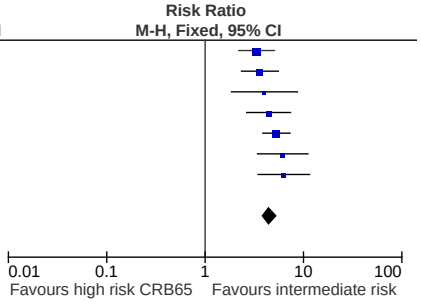


Figure 37: High-risk CRB65 (≥ 3) compared with intermediate-risk CRB65 (= 1 or 2) to predict mortality

Study or Subgroup	high risk CRB-65 Events	Total	intermediate risk CRB-65 Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Man 2007	26	105	58	783	26.0%	3.34 [2.21, 5.06]
Ochdagondar 2011	17	41	63	549	16.6%	3.61 [2.35, 5.56]
Zuberi 2008	5	9	13	94	4.3%	4.02 [1.86, 8.69]
Bauer 2006	15	63	53	987	12.0%	4.43 [2.65, 7.41]
Capelastegui 2006	36	80	83	980	23.7%	5.31 [3.87, 7.30]
Menendez 2009	17	49	18	319	9.1%	6.15 [3.41, 11.10]
Dwyer 2011	16	38	16	240	8.3%	6.32 [3.46, 11.54]
Total (95% CI)		**385**		**3952**	**100.0%**	**4.52 [3.78, 5.39]**
Total events	132		304			

Heterogeneity: Chi² = 6.38, df = 6 (P = 0.38); I² = 6%
Test for overall effect: Z = 16.64 (P < 0.00001)



1.2.2 PSI, CURB65 compared with modified American Thoracic Society 2001 criteria (mATS)

1.2.2.1 Summary of discriminatory analysis (AUCs) for PSI and CURB65 compared with mATS in prediction of mortality

Figure 38: AUCs for PSI

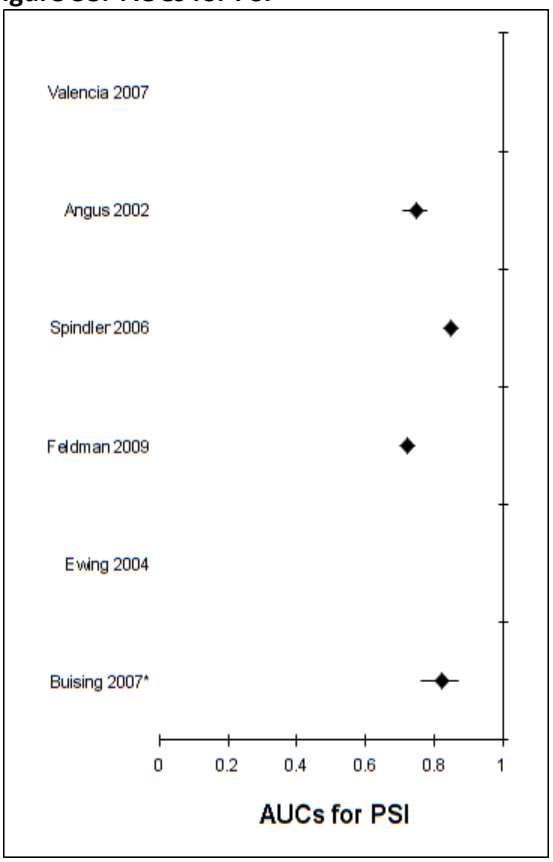


Figure 39: AUCs for CURB65

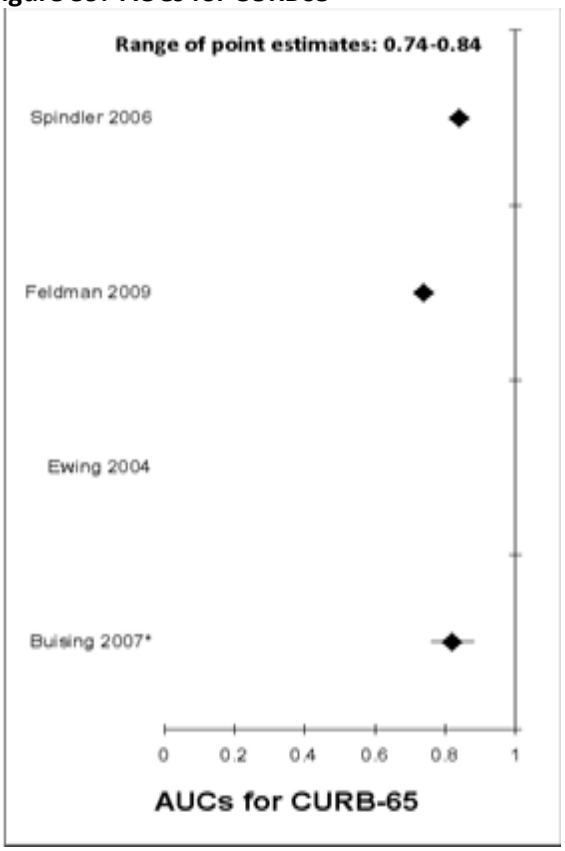
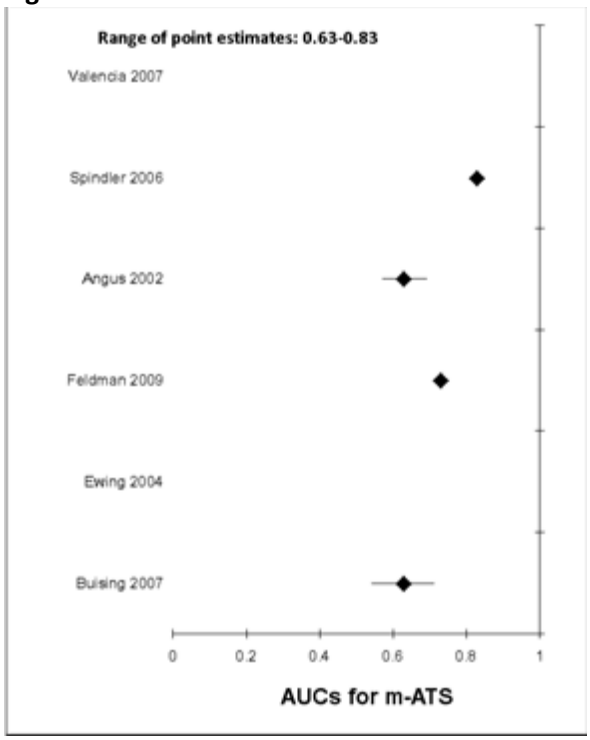


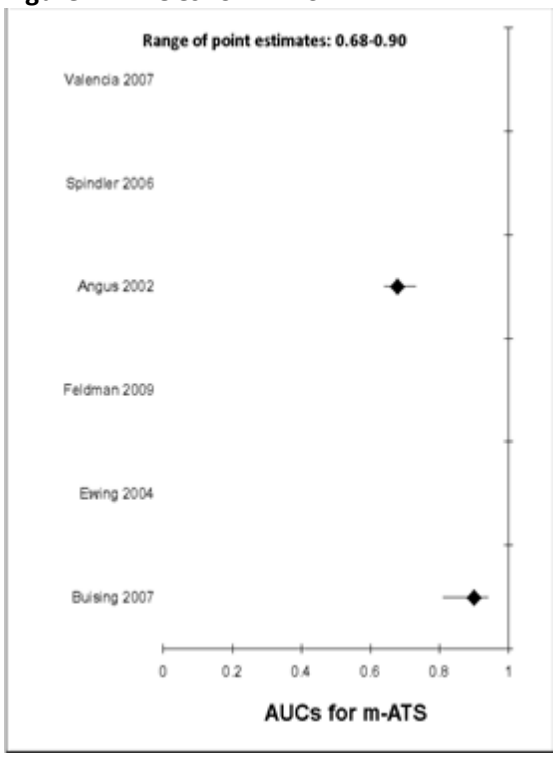
Figure 40: AUC for mATS



1.2.2.2 Summary of discriminatory analysis (AUCs) for PSI and CURB65 compared with mATS in prediction of ITU admission

Figure 41: AUCs for PSI

Figure 42: AUCs for mATS



1.2.3 PSI, CURB65 compared with IDSA/ATS

1.2.3.1 Prediction of mortality

Figure 43: High-risk CURB65 (≥ 3) compared with low-risk CURB65 (< 3) groups to predict mortality

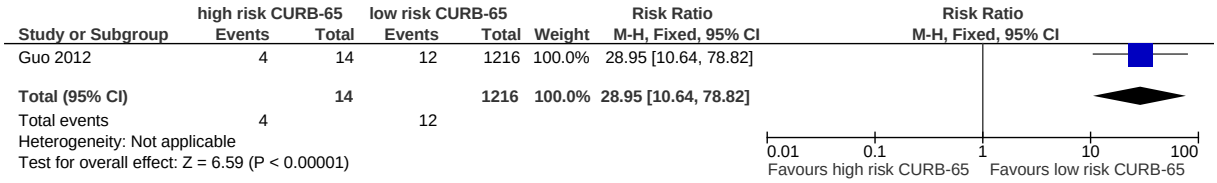
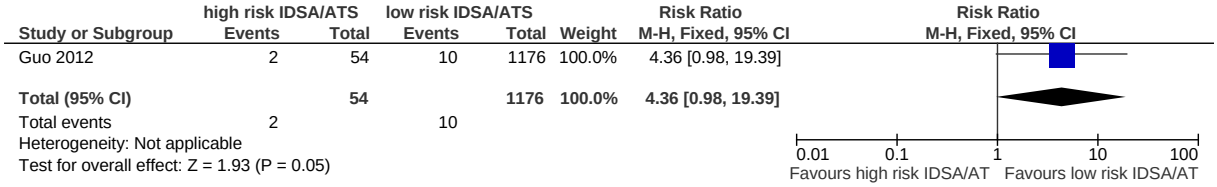


Figure 44: High-risk (≥ 3) groups compared with low-risk IDSA/ATS minor criteria (< 3) to predict mortality



1.3 Microbiological tests

1.3.1.1 Targeted compared with empirical treatment using a combination of tests

Figure 45: Mortality

Test for subgroup differences: Chi² = 0.89, df = 1 (P = 0.34), I² = 0%

Figure 46: Clinical failure

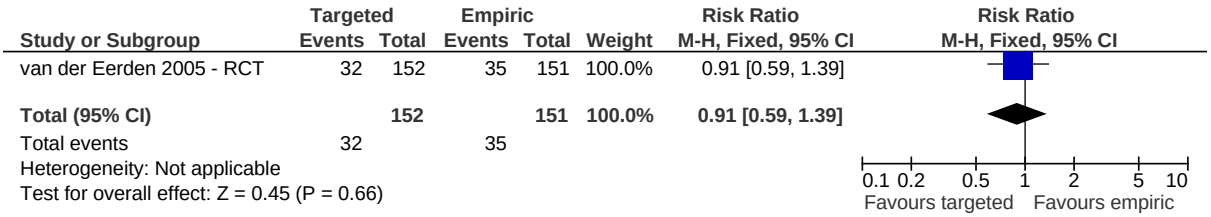


Figure 47: Length of hospital stay

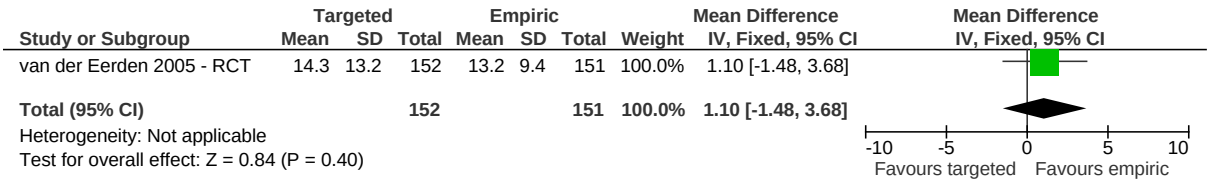


Figure 48: Quality-of-life (SF-36)

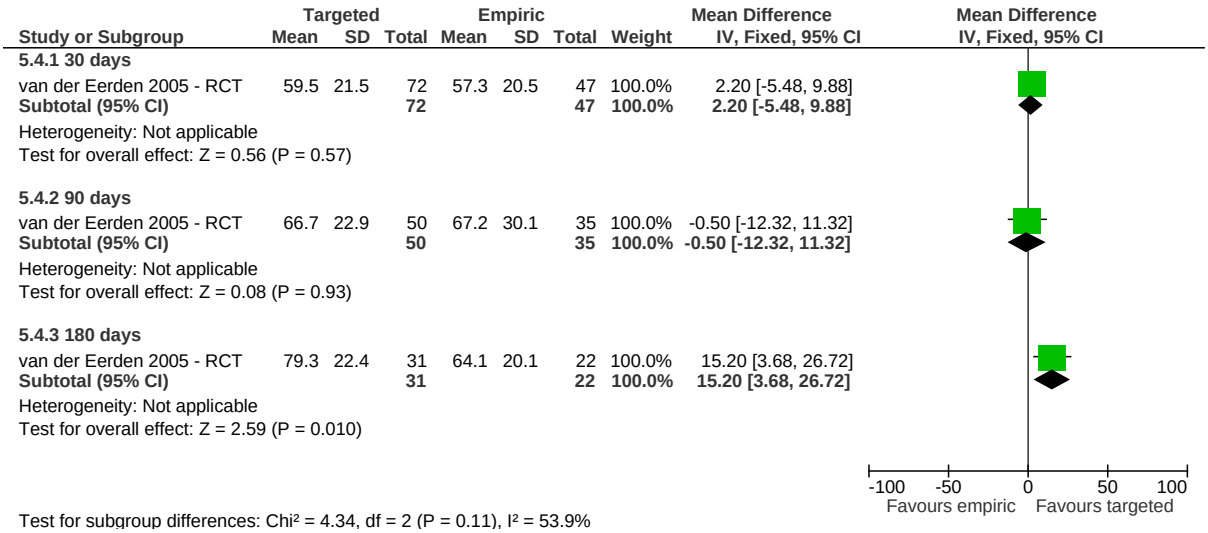
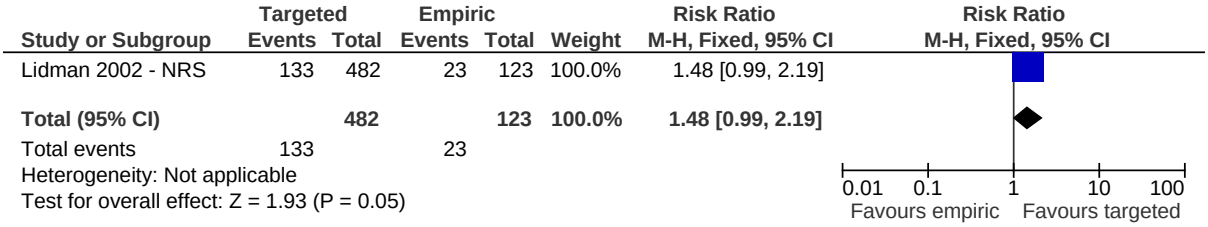
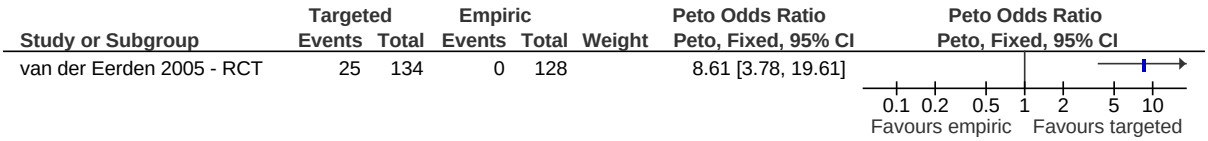


Figure 49: Change in prescription based on test results or clinical judgement





1.3.1.2 Targeted compared with empirical treatment using urinary antigen tests

Figure 50: Mortality

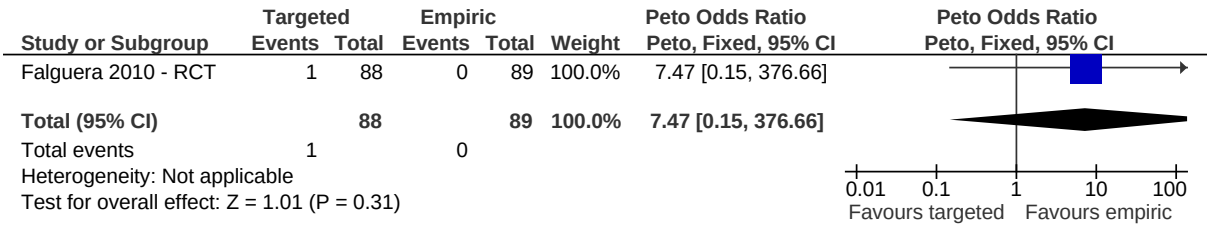


Figure 51: Clinical relapse

Study or Subgroup	Targeted Events	Total	Empiric Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Falguera 2010 - RCT	4	88	2	89	100.0%	2.02 [0.38, 10.76]
Total (95% CI)		**88**		**89**	**100.0%**	**2.02 [0.38, 10.76]**
Total events	4		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)

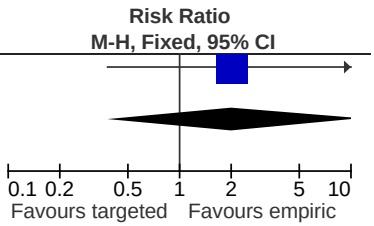


Figure 52: Re-admission

Study or Subgroup	Targeted Events	Total	Empiric Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Falguera 2010 - RCT	4	88	2	89	100.0%	2.02 [0.38, 10.76]
Total (95% CI)		**88**		**89**	**100.0%**	**2.02 [0.38, 10.76]**
Total events	4		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)

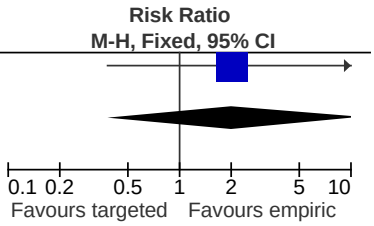


Figure 53: Treatment withdrawal due to adverse events

Study or Subgroup	Targeted Events	Total	Empiric Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Falguera 2010 - RCT	1	88	1	89	100.0%	1.01 [0.06, 15.92]
Total (95% CI)		**88**		**89**	**100.0%**	**1.01 [0.06, 15.92]**
Total events	1		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.01 (P = 0.99)

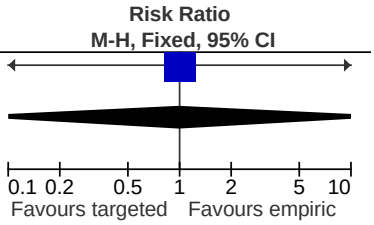
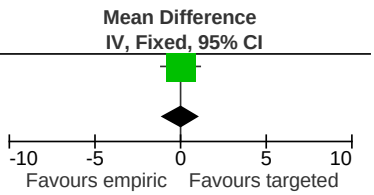


Figure 54: Length of hospital stay

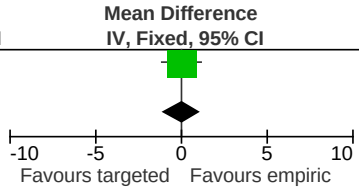
Study or Subgroup	Targeted Mean	SD	Total	Empiric Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Falguera 2010 - RCT	7.1	4	88	7.1	3.8	89	100.0%	0.00 [-1.15, 1.15]
Total (95% CI)			**88**			**89**	**100.0%**	**0.00 [-1.15, 1.15]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



Study or Subgroup	Empiric Mean	SD	Total	Targeted Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Falguera 2010 - RCT	7.1	3.8	89	7.1	4	88	100.0%	0.00 [-1.15, 1.15]
Total (95% CI)			**89**			**88**	**100.0%**	**0.00 [-1.15, 1.15]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



1.3.1.3 Targeted compared with empirical treatment using blood culture

Figure 55: Mortality

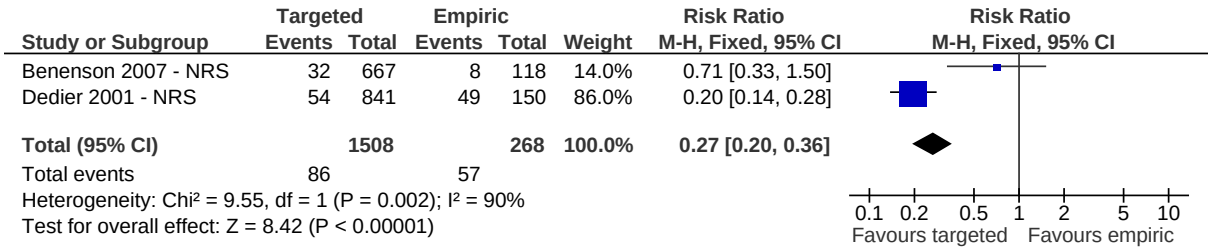


Figure 56: Mortality

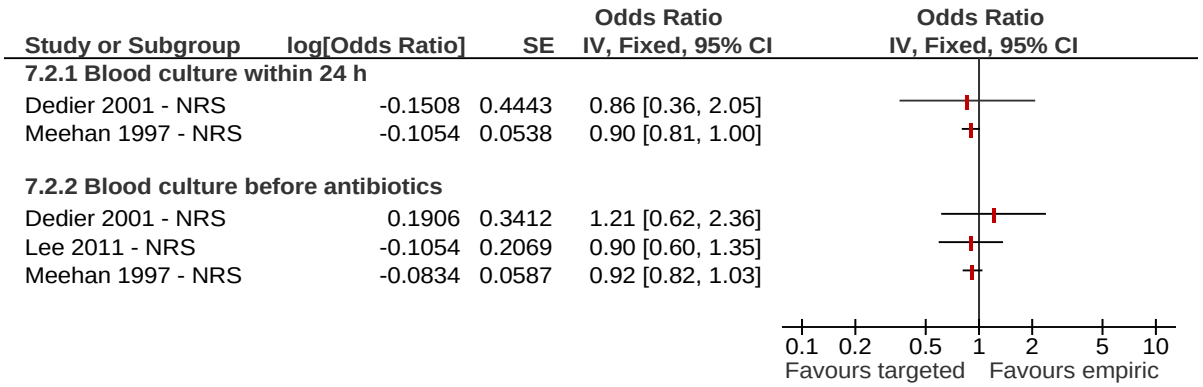


Figure 57: Clinical instability at 48 hours

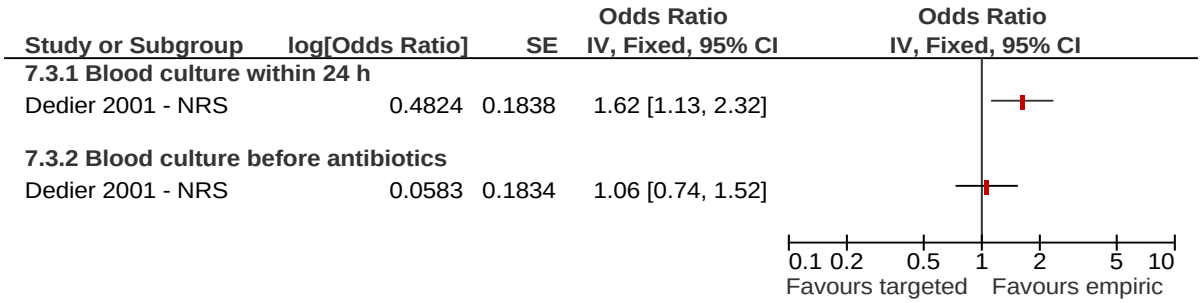


Figure 58: Length of hospital stay

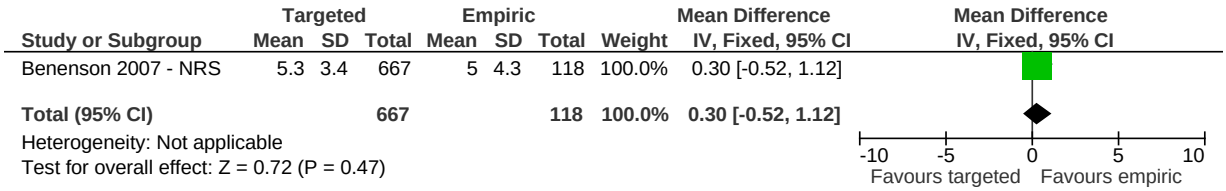


Figure 59: Length of hospital stay

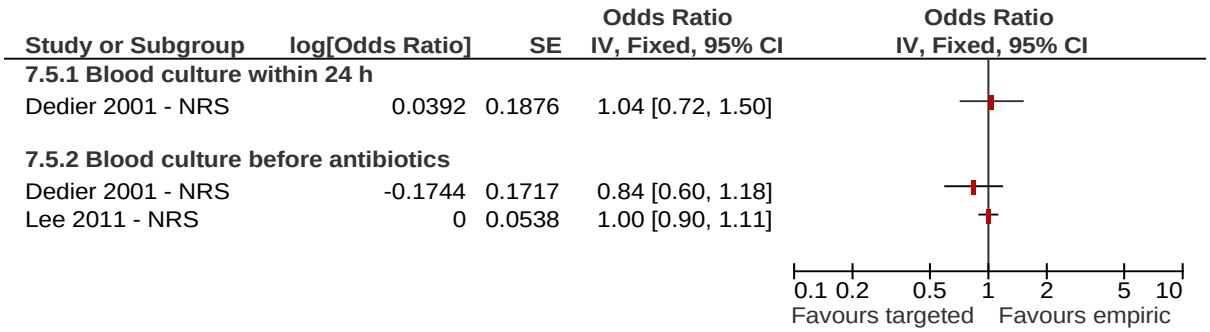
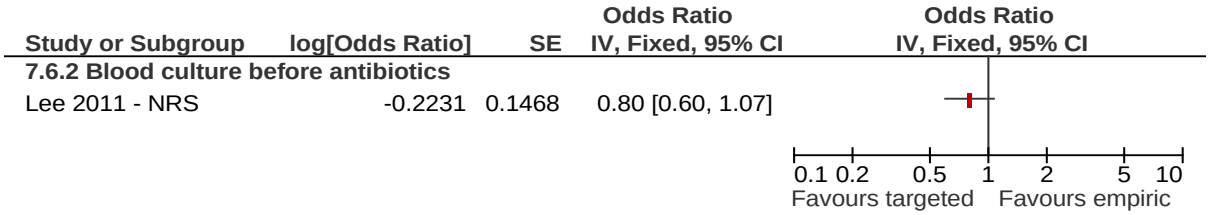
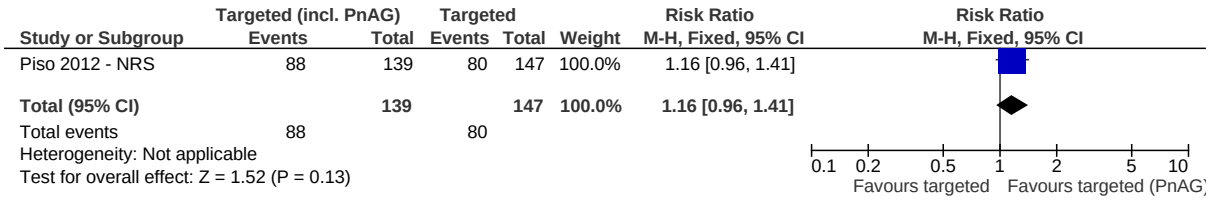


Figure 60: Hospital re-admission



1.3.1.4 Targeted treatment following pneumococcal antigen compared with targeted treatment not using pneumococcal antigen

Figure 61: Change in prescription (within 48 to 72 hours)



1.4 Antibiotic therapy

1.4.1 Timing of antibiotic therapy

1.4.1.1 Early compared with late antibiotic therapy (multivariable analysis)

Figure 62: Mortality

Study or Subgroup	log[Odds Ratio]	SE	Early antibiotics Total	Later antibiotics Total	Odds Ratio IV, Fixed, 95% CI
1.1.1 Less than or equal to 4 hours versus more than 4 hours					
Houck 2004	-0.16251893	0.057	8388	5383	0.85 [0.76, 0.95]
Houck 2004 PSI II-III	-0.478	0.1987	2424	1561	0.62 [0.42, 0.92]
Houck 2004 PSI IV-V	-0.1393	0.0557	5964	3822	0.87 [0.78, 0.97]
Lee 2011	-0.35667494	0.2	1632	444	0.70 [0.47, 1.04]
Simonetti 2012 - CAP	0.11332868	0.55	477	797	1.12 [0.38, 3.29]
Waterer 2006	-0.61618614	0.403	222	229	0.54 [0.25, 1.19]
Wilson 2005	-1.23787436	0.59	70	17	0.29 [0.09, 0.92]
1.1.2 Less than or equal to 8 hours versus more than 8 hours					
Bader 2011	-1.38629436	0.61	155	51	0.25 [0.08, 0.83]
Dedier 2001	0.52472853	0.394	809	253	1.69 [0.78, 3.66]
Houck 2004	-0.16251893	0.078	11814	1957	0.85 [0.73, 0.99]
Meehan 1997	-0.16251893	0.064	0	0	0.85 [0.75, 0.96]
Mortensen 2008	0.18232155	0.279	364	56	1.20 [0.69, 2.07]
Simonetti 2012 - CAP	0.45742485	0.459	0	0	1.58 [0.64, 3.88]
1.1.3 Less than or equal to 12 hours versus more than 12 hours					
Houck 2004	-0.03045921	0.105	8388	5383	0.97 [0.79, 1.19]
1.1.4 Timing as a continuous variable					
Jo 2012	0	0.001	0	0	1.00 [1.00, 1.00]

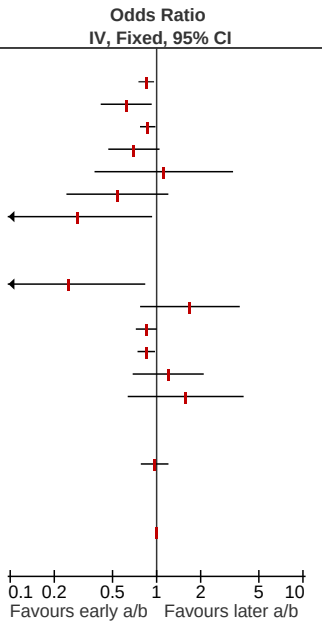


Figure 63: Mortality - full time series

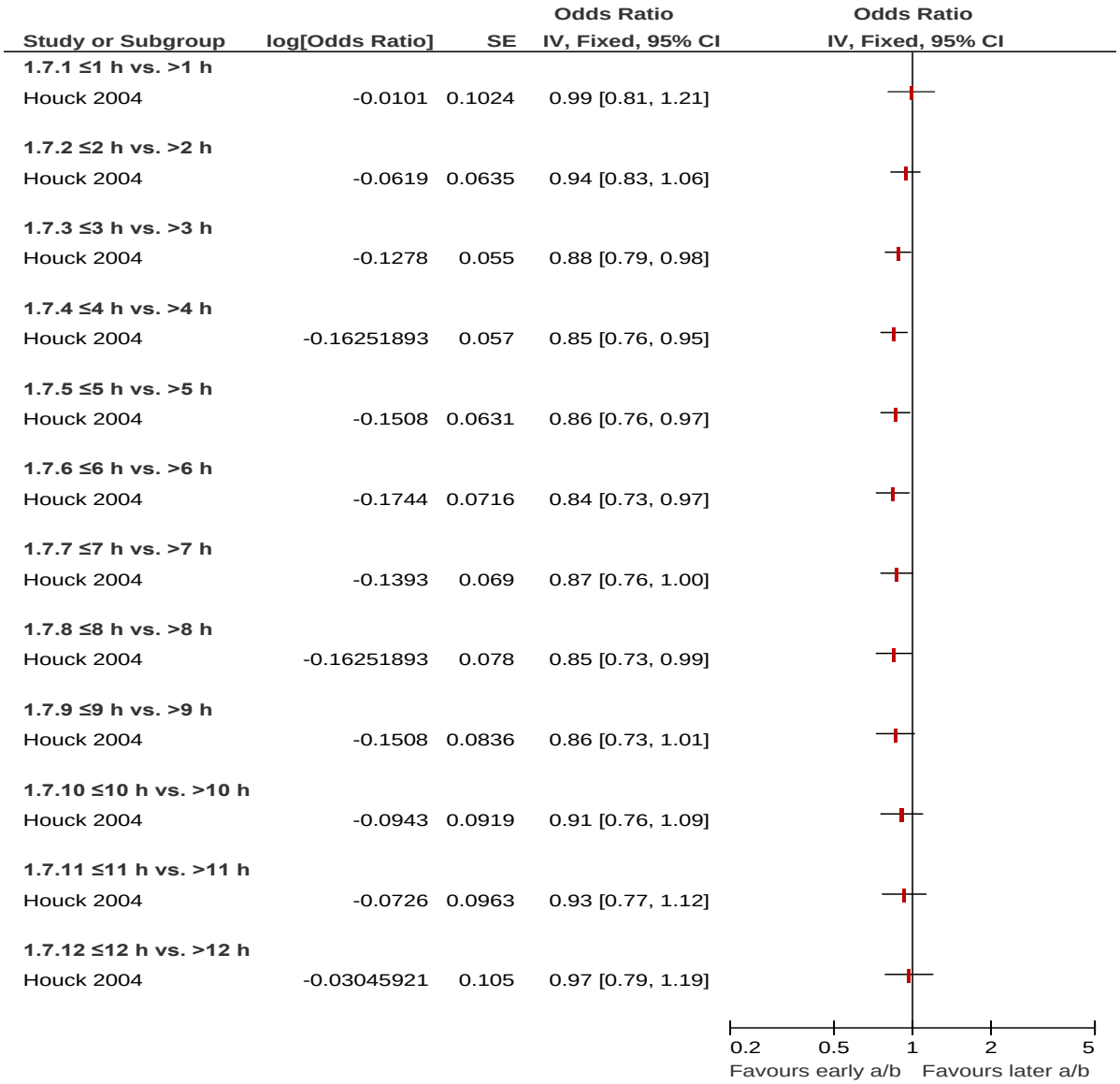


Figure 64: Prolonged length of stay (above median)

Study or Subgroup	log[Odds Ratio]	SE	Early antibiotics Total	Later antibiotics Total	Odds Ratio IV, Fixed, 95% CI
1.3.1 Less than or equal to 4 hours versus more than 4 hours					
Houck 2004	-0.10536052	0.036	8388	5383	0.90 [0.84, 0.97]
Houck 2004 PSI II-III	-0.1508	0.0698	2424	1561	0.86 [0.75, 0.99]
Houck 2004 PSI IV-V	-0.0834	0.0464	5964	3822	0.92 [0.84, 1.01]
Lee 2011	0.1823	0.0464	1632	444	1.20 [1.10, 1.31]
1.3.2 Less than or equal to 8 hours versus more than 8 hours					
Dedier 2001	-0.11653382	0.16	809	253	0.89 [0.65, 1.22]
1.3.3 Less than or equal to 4 hours versus 4-8 hours					
Huang 2006	0.01980263	0.105	0	0	1.02 [0.83, 1.25]
1.3.4 Less than or equal to 4 hours versus more than 8 hours					
Huang 2006	-0.24846136	0.11	0	0	0.78 [0.63, 0.97]

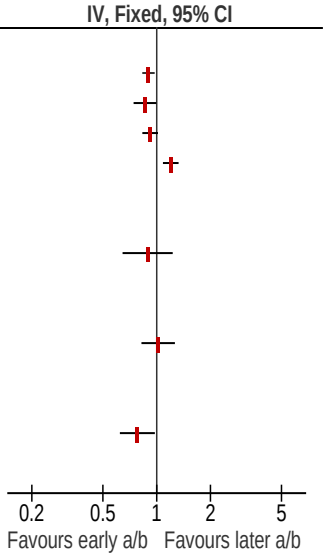


Figure 65: Prolonged length of stay (above 75th percentile)

Study or Subgroup	log[Odds Ratio]	SE	Early antibiotics Total	Later antibiotics Total	Odds Ratio IV, Fixed, 95% CI
1.3.1 Less than or equal to 8 hours versus more than 8 hours					
Battleman 2002	-0.56211892	0.13	0	0	0.57 [0.44, 0.74]

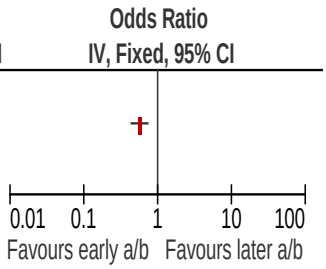


Figure 66: Re-admission after discharge

Study or Subgroup	log[Odds Ratio]	SE	Early a/b Total	Later antibiotics Total	Odds Ratio IV, Fixed, 95% CI
1.4.1 Less than or equal to 4 hours versus more than 4 hours					
Houck 2004	-0.05129329	0.055	8388	5383	0.95 [0.85, 1.06]
Houck 2004 PSI II-III	-0.1393	0.1109	2424	1561	0.87 [0.70, 1.08]
Houck 2004 PSI IV-V	-0.0101	0.0601	5964	3822	0.99 [0.88, 1.11]
Lee 2011	0.3365	0.2254	1545	416	1.40 [0.90, 2.18]

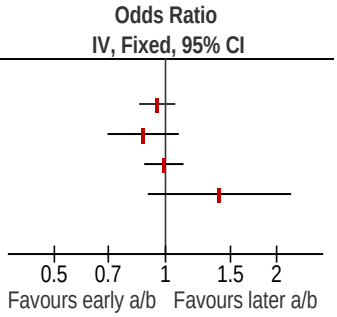
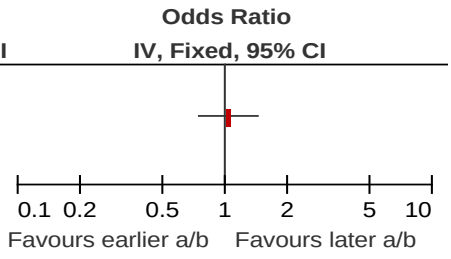


Figure 67: Clinical instability at 48 hours

Study or Subgroup	log[Odds Ratio]	SE	Odds Ratio IV, Fixed, 95% CI
1.6.2 Less than or equal to 8 hours versus more than 8 hours			
Dedier 2001	0.0392	0.1668	1.04 [0.75, 1.44]



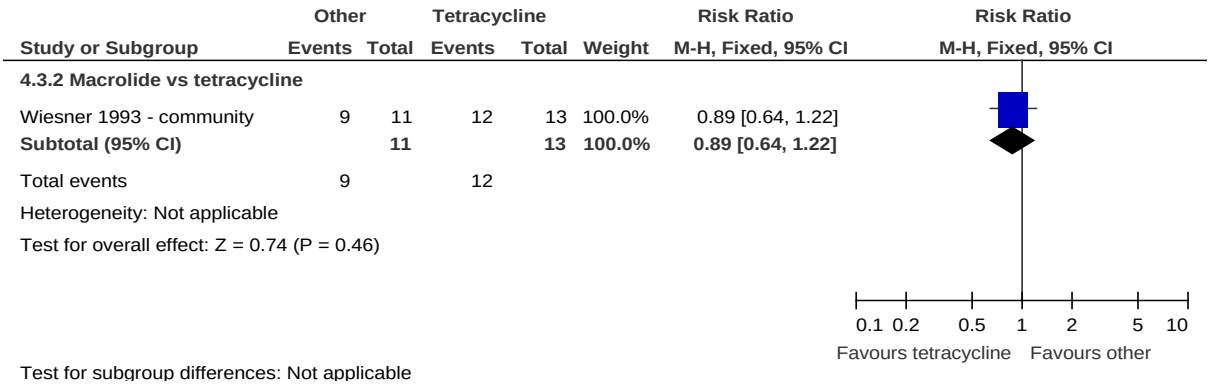
1.4.2 In adults with community-acquired pneumonia what is the most clinically- and cost-effective empirical antibiotic choice?

1.4.3 Low-severity community-acquired pneumonia

1.4.3.1 Single- compared with other single-antibiotic therapy for low-severity community-acquired pneumonia managed in the community

1.4.3.1.1 Macrolide compared with tetracycline

Figure 68: Clinical cure (end of treatment)



1.4.3.1.2 Cephalosporin compared with tetracycline

Figure 69: Clinical cure at end of treatment

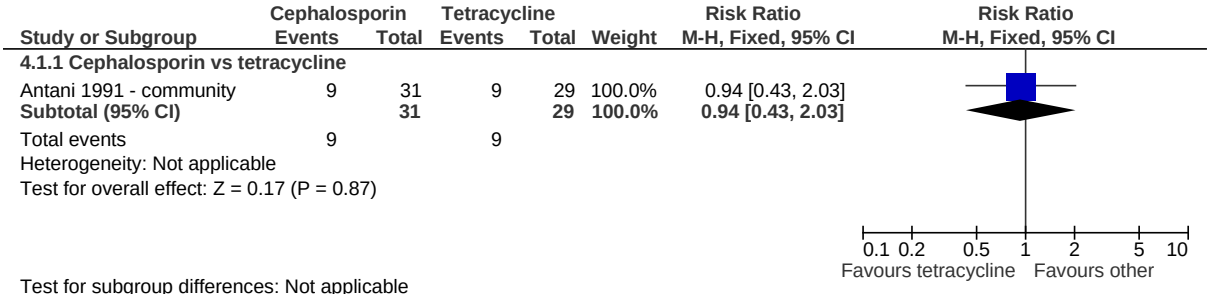
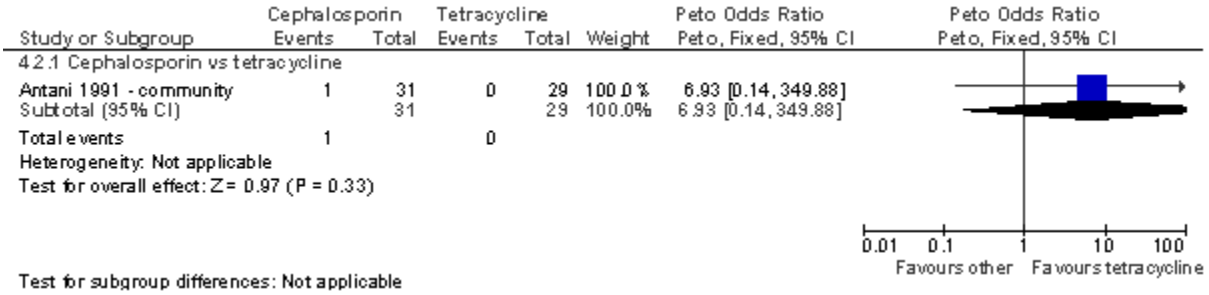
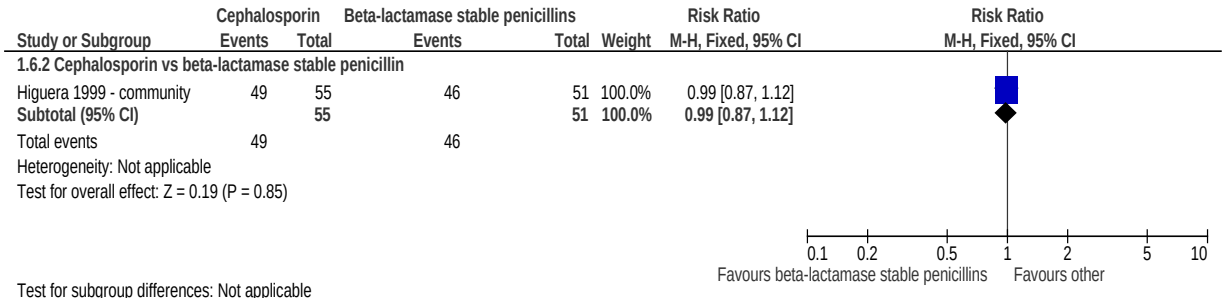


Figure 70: Withdrawals due to adverse events



1.4.3.1.3 Cephalosporin compared with beta-lactamase-stable penicillin

Figure 71: Clinical cure at the end of follow up



1.4.3.1.4 Macrolide compared with beta-lactam stable penicillin

Figure 72: Mortality

Figure 1: Mortality

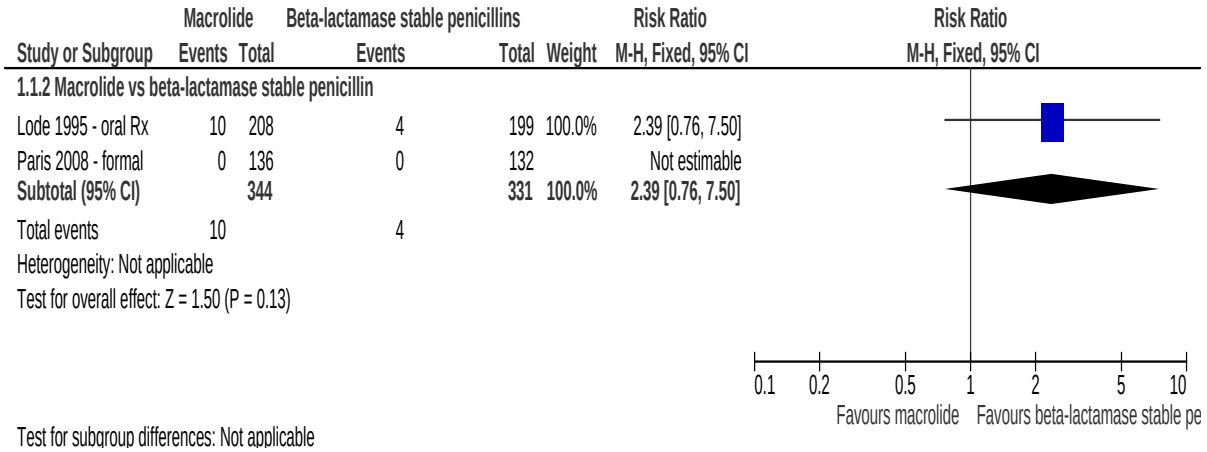


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Figure 73: Clinical cure at end of treatment

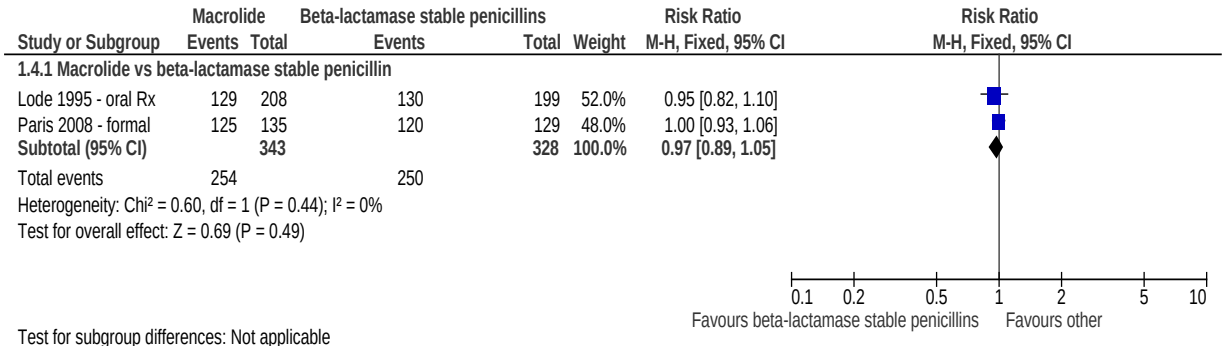


Figure 74: Clinical cure at end of follow-up

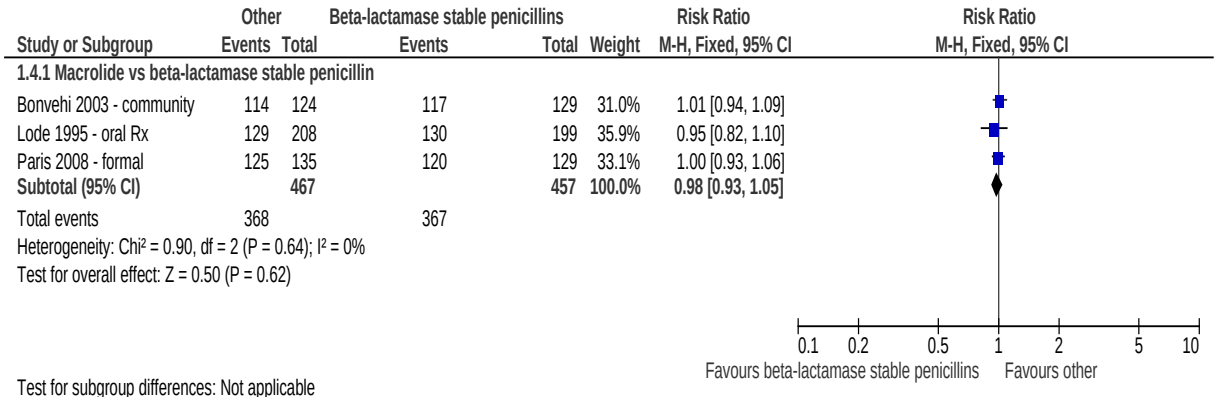
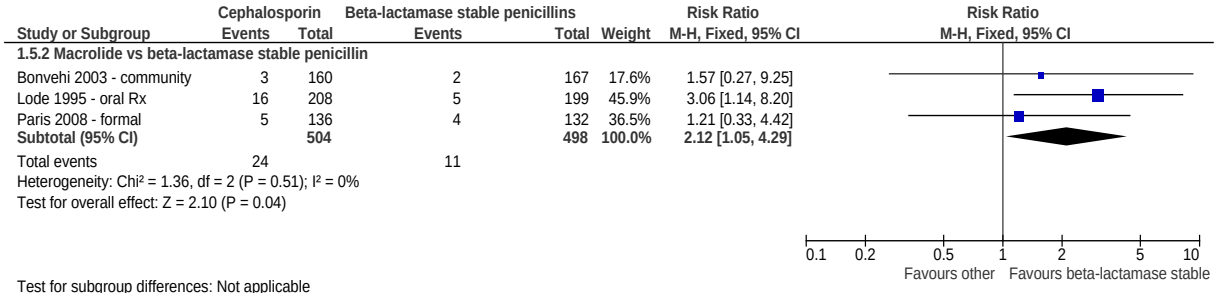


Figure 75: Withdrawal due to adverse events



1.4.3.1.5 Respiratory fluoroquinolone compared with narrow spectrum beta-lactam (class 2)

Figure 76: Mortality

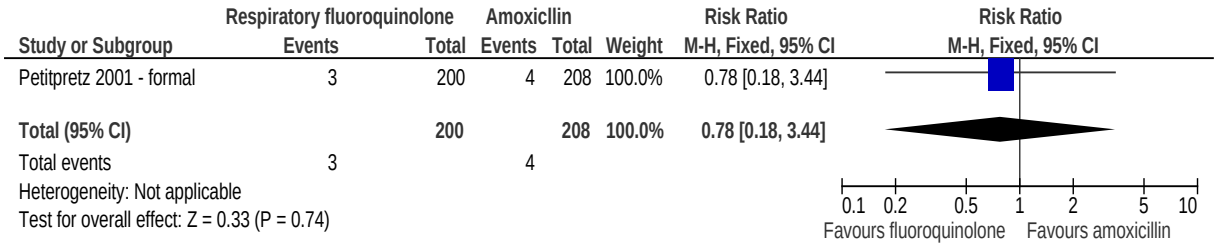


Figure 77: Clinical cure at end of treatment

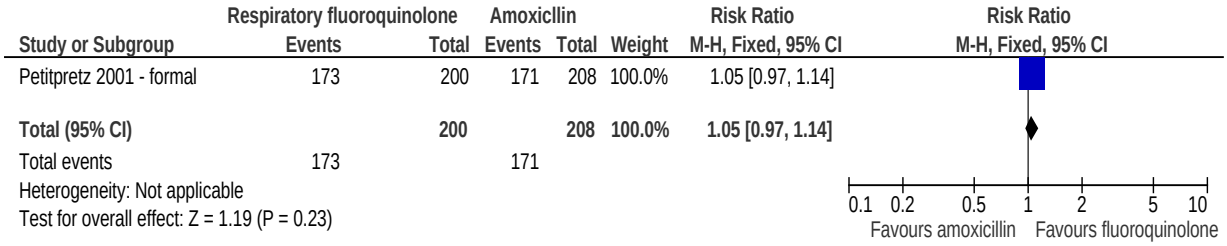


Figure 78: Clinical cure at end of follow-up

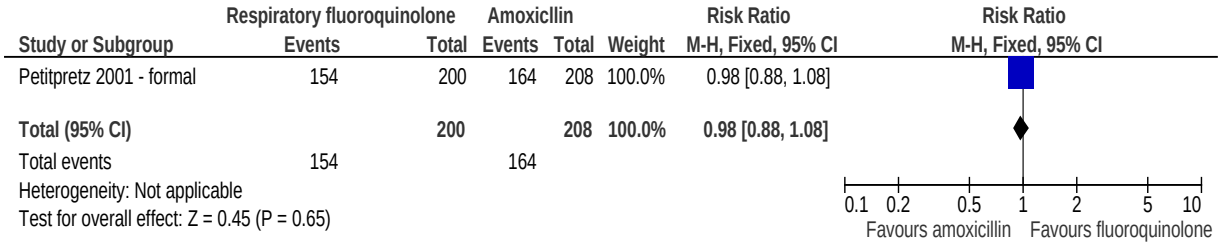


Figure 79: Complications

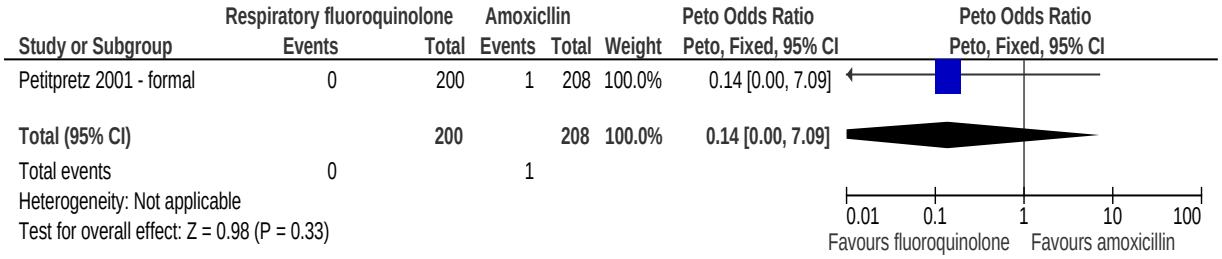
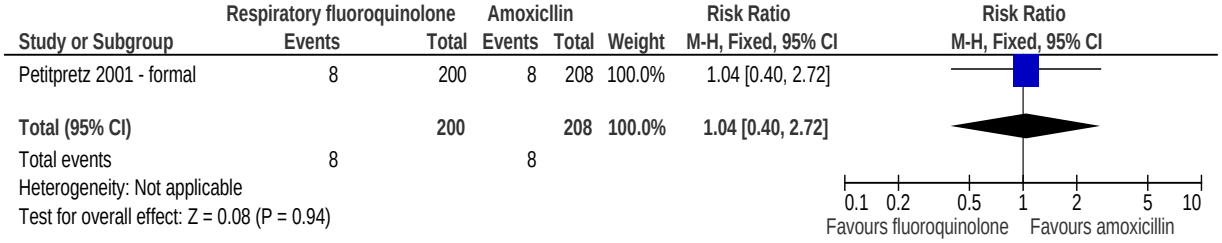
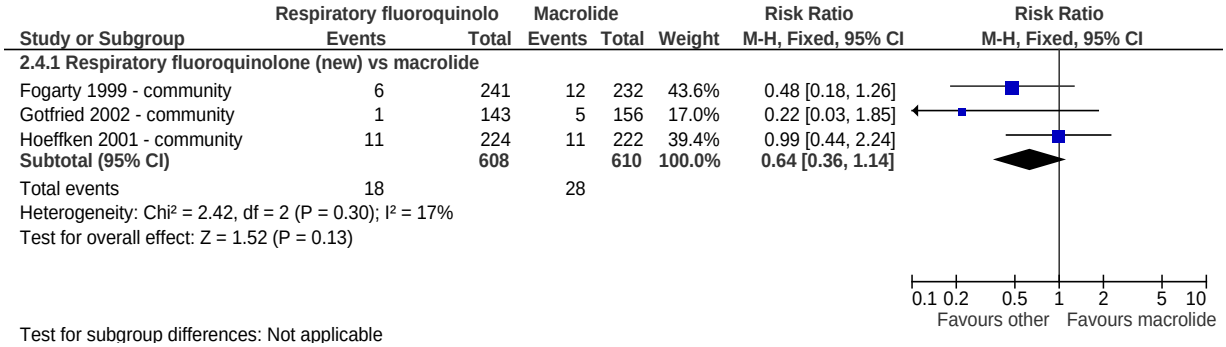


Figure 80: Withdrawal or treatment discontinuation due to adverse events



1.4.3.1.6 Respiratory fluoroquinolone compared with beta-lactam stable penicillin

Figure 81: Withdrawal due to adverse events (respiratory fluoroquinolone compared with macrolide)



1.4.3.1.7 Non-respiratory fluoroquinolone compared with macrolide

Figure 82: Clinical cure at end of treatment

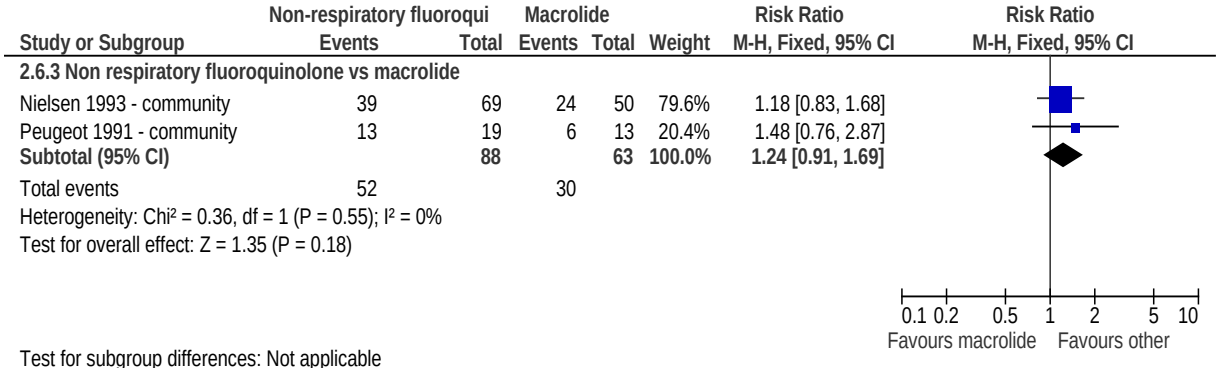
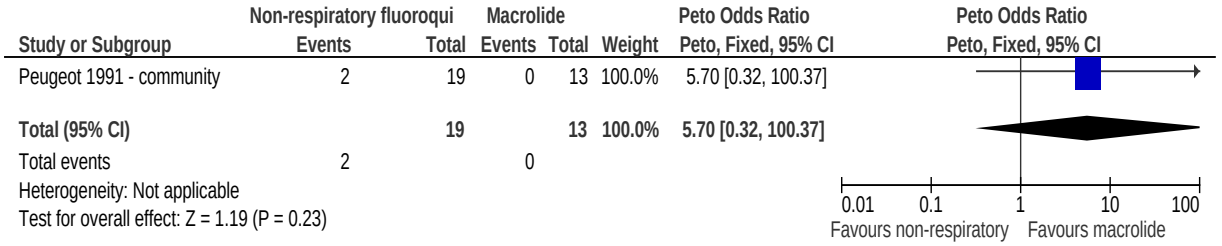


Figure 83: Withdrawal due to adverse events



1.4.3.1.8 Azithromycin compared with other macrolides

Figure 84: Clinical cure at end of treatment (azithromycin compared with clarithromycin)

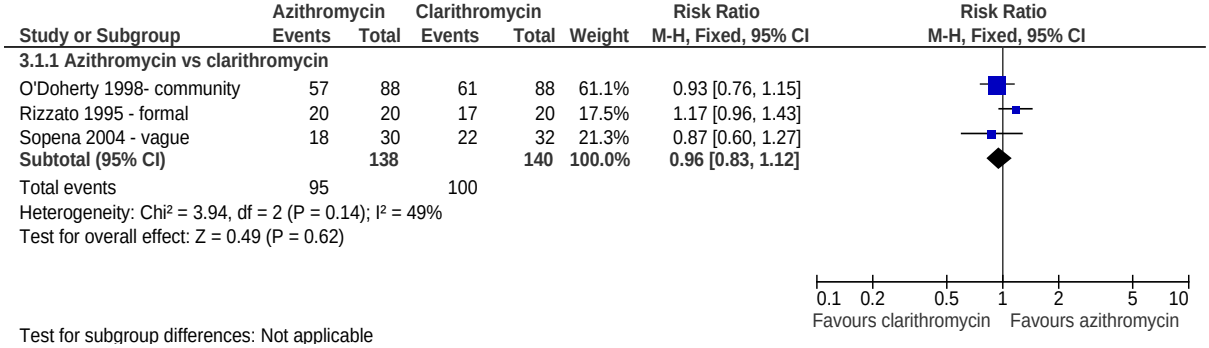


Figure 85: Clinical cure at end of follow-up (azithromycin compared with clarithromycin)

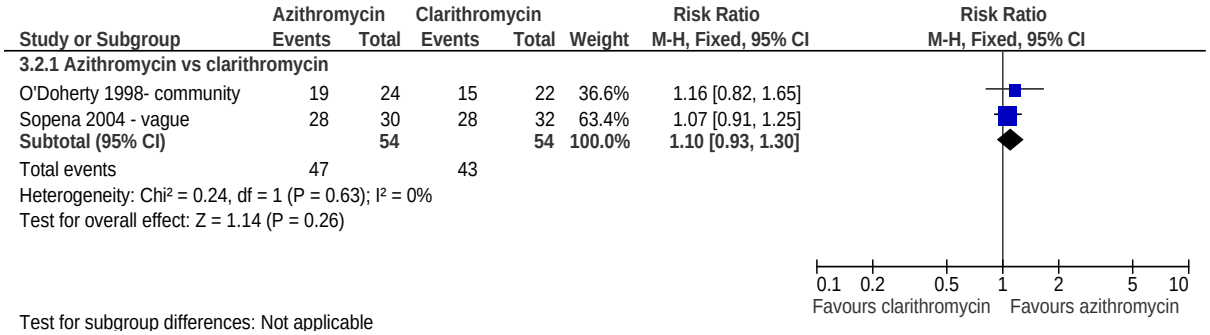


Figure 86: Withdrawal due to adverse events (azithromycin compared with clarithromycin)

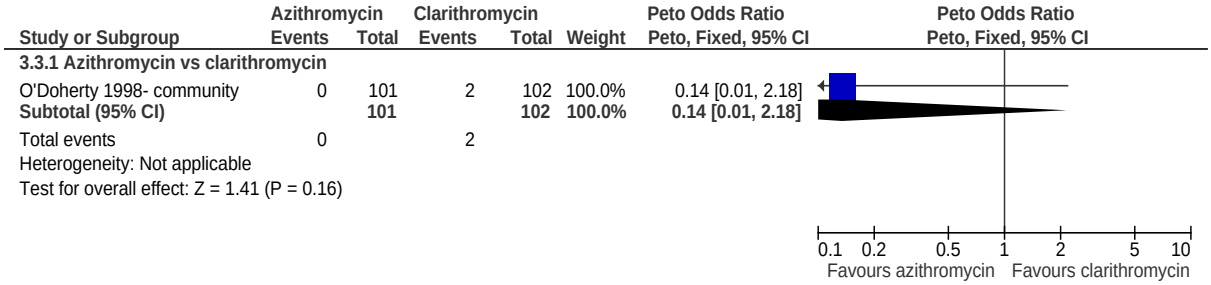
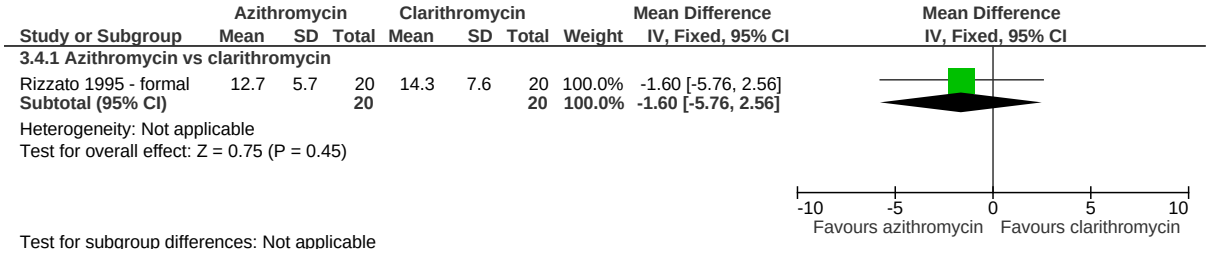


Figure 87: Length of hospital stay (azithromycin compared with clarithromycin)



1.4.3.1.9 Clarithromycin compared with amoxicillin (indirect comparison)

Figure 88: Mortality

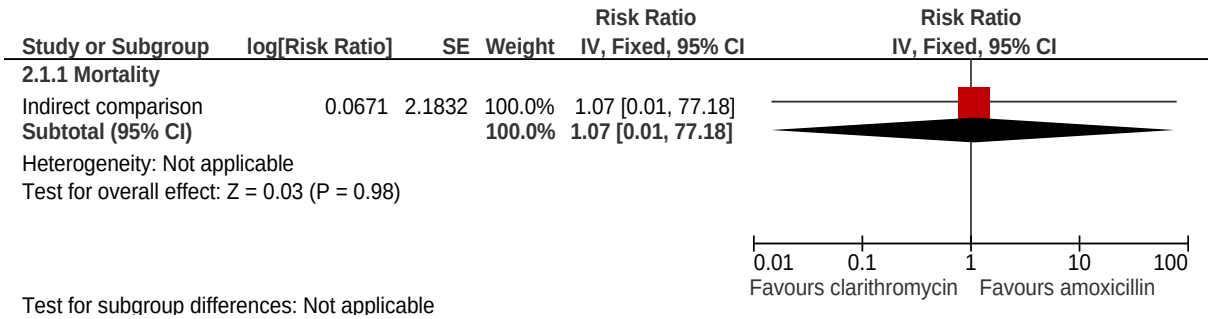


Figure 89: Cure at end of follow up

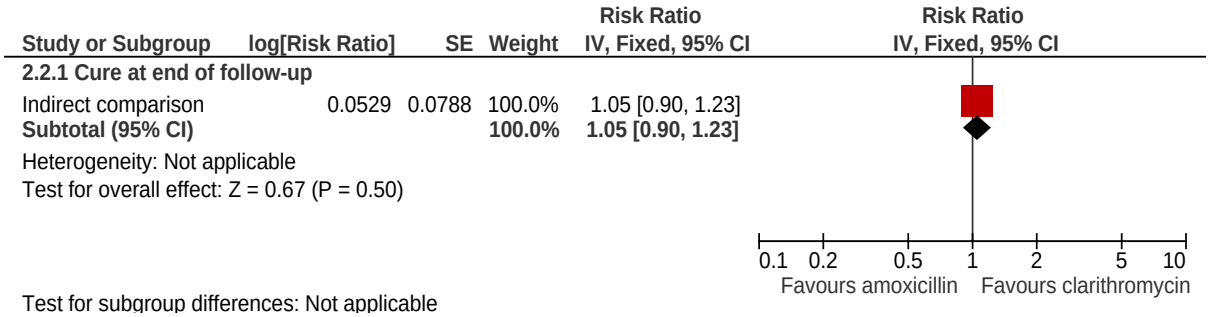
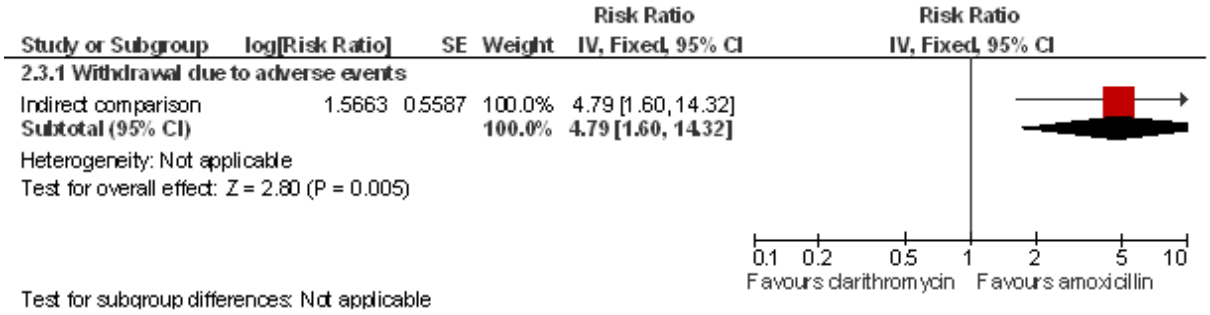


Figure 90: Withdrawal due to adverse events



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1.4.4 Low-severity community-acquired pneumonia managed in hospital

1.4.4.1.1 Macrolide compared with narrow-spectrum beta-lactam (class 1)

Figure 91: Clinical cure

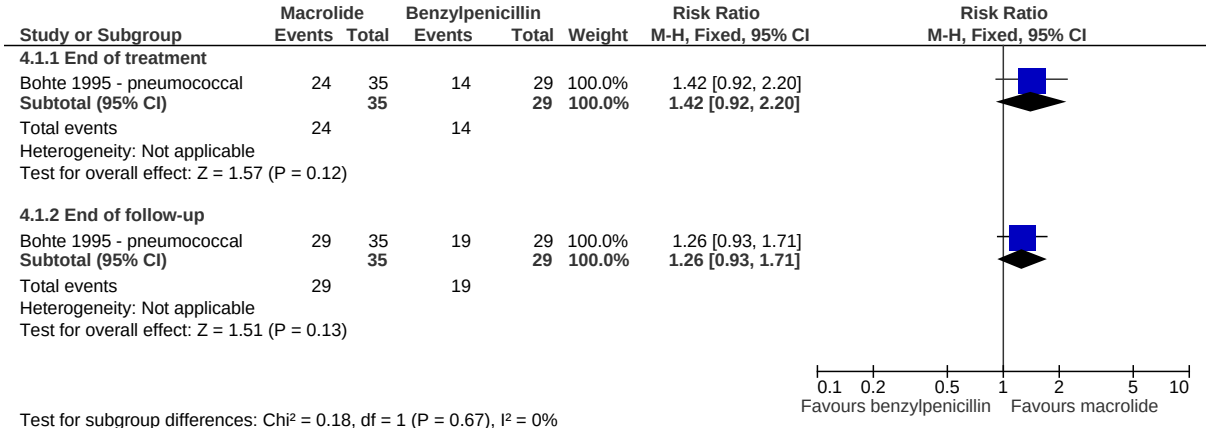
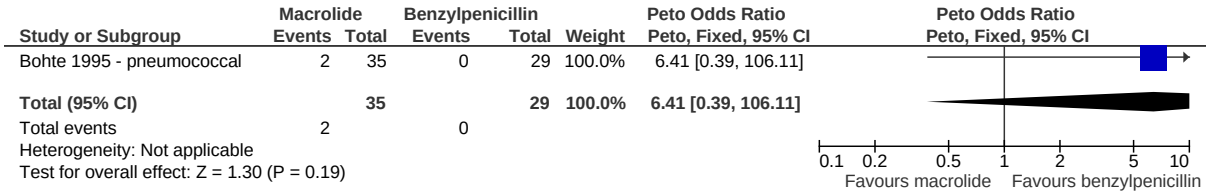


Figure 92: Withdrawal/switching of treatment due to adverse events



1.4.4.1.2 Macrolide compared with beta-lactamase stable penicillin

Figure 93: Mortality

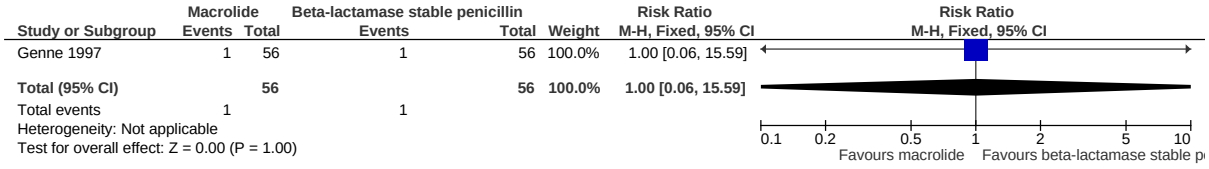


Figure 94: Clinical cure at end of treatment

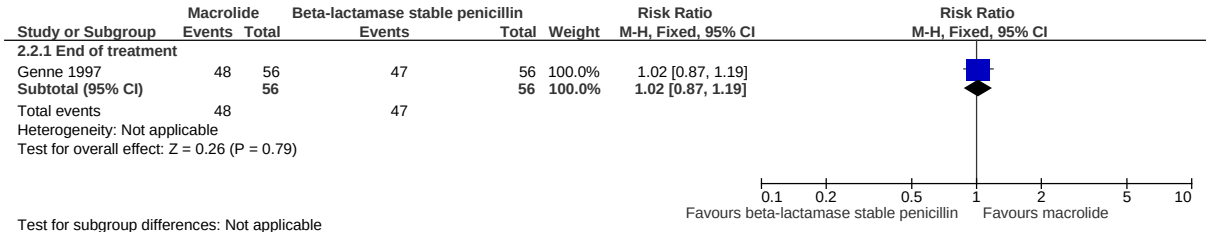


Figure 95: Withdrawal due to adverse events

1.4.4.1.3 Azithromycin compared with other macrolide

Figure 96: Mortality (during treatment)

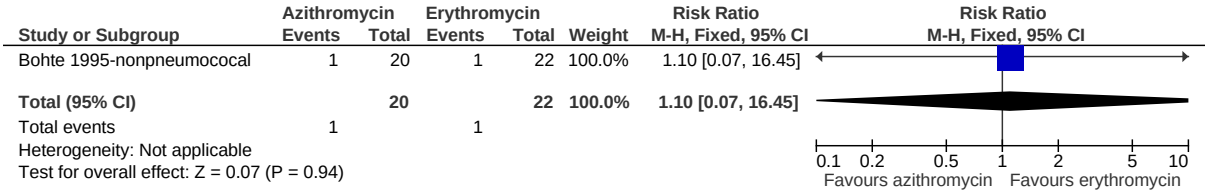


Figure 97: Clinical cure

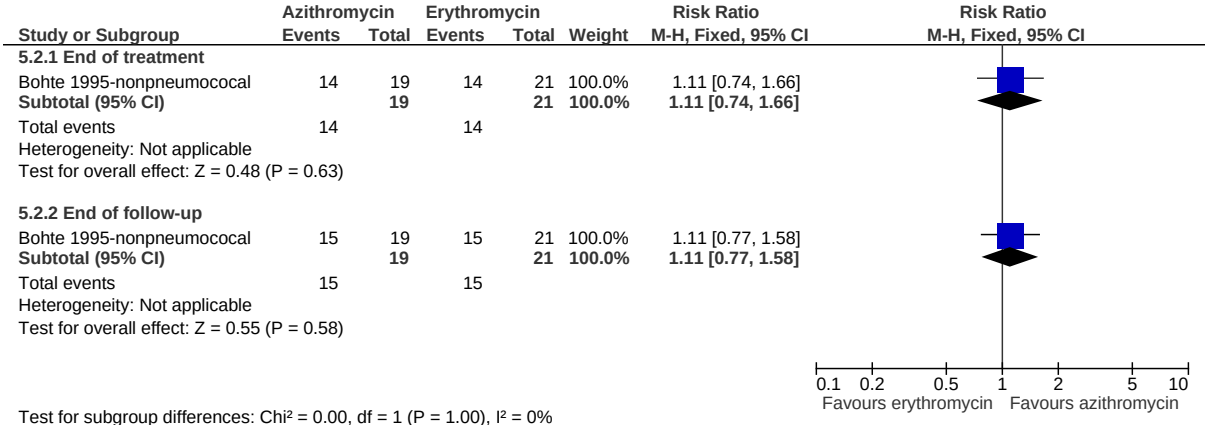
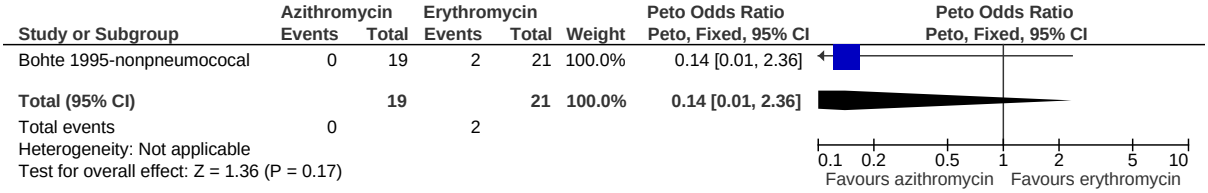


Figure 98: Withdrawal/switching of treatment due to adverse events



1.4.4.1.4 Cephalosporin compared with beta-lactamase stable penicillin

Figure 99: Clinical cure

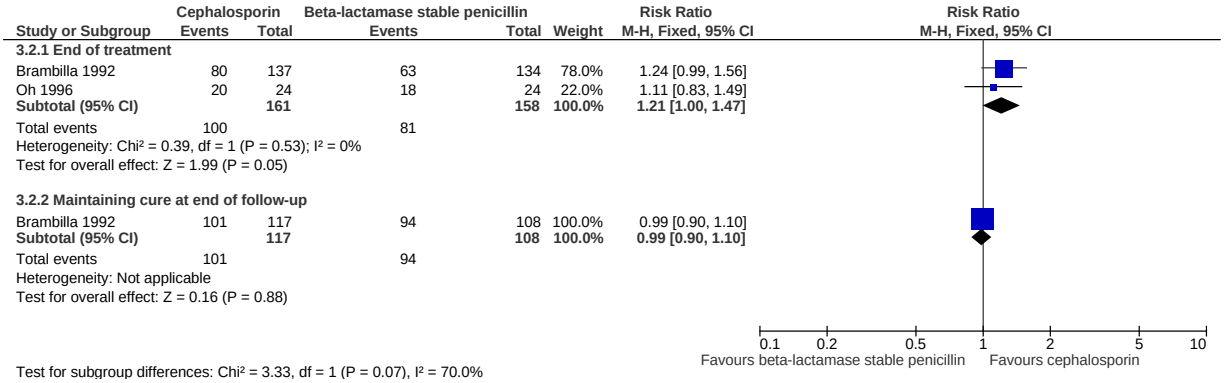
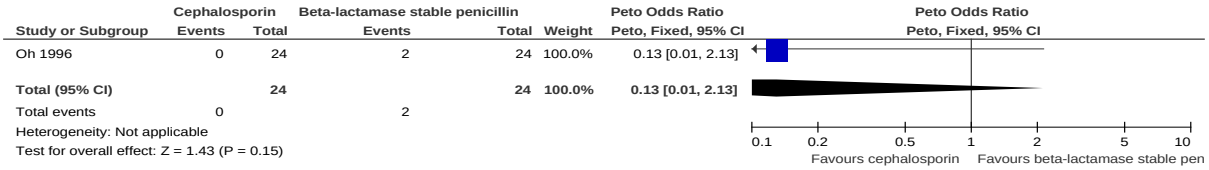
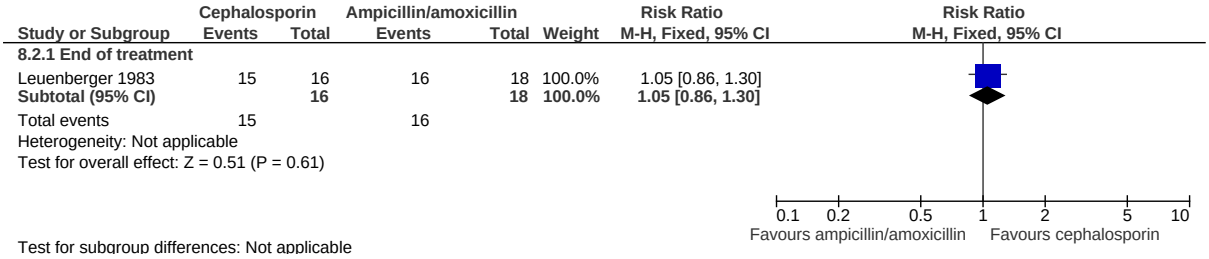


Figure 100: Treatment discontinuation due to adverse events



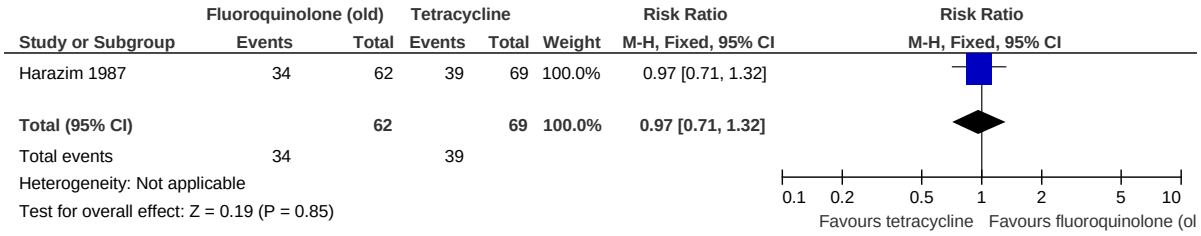
1.4.4.1.5 Cephalosporin compared with narrow-spectrum beta-lactam (class 2)

Figure 101: Clinical cure



1.4.4.1.6 Non-respiratory fluoroquinolone (FQ) compared with tetracycline

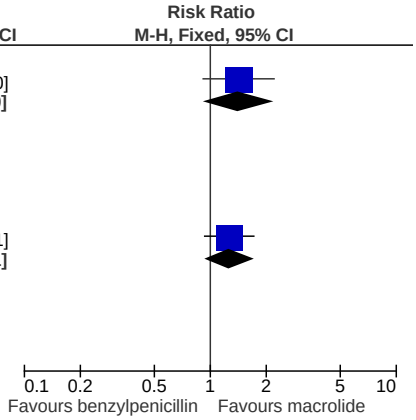
Figure 102: Clinical cure at end of treatment



1.4.4.1.7 Macrolide compared with narrow-spectrum beta-lactam (class 1)

Figure 103: Clinical cure

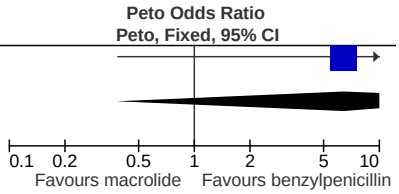
Study or Subgroup	Macrolide Events	Total	Benzylpenicillin Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.1.1 End of treatment						
Bohte 1995 - pneumococcal	24	35	14	29	100.0%	1.42 [0.92, 2.20]
Subtotal (95% CI)		**35**		**29**	**100.0%**	**1.42 [0.92, 2.20]**
Total events	24		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.57 (P = 0.12)						
4.1.2 End of follow-up						
Bohte 1995 - pneumococcal	29	35	19	29	100.0%	1.26 [0.93, 1.71]
Subtotal (95% CI)		**35**		**29**	**100.0%**	**1.26 [0.93, 1.71]**
Total events	29		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.51 (P = 0.13)						



Test for subgroup differences: Chi² = 0.18, df = 1 (P = 0.67), I² = 0%

Figure 104: Withdrawal/switching of treatment due to adverse events

Study or Subgroup	Macrolide Events	Total	Benzylpenicillin Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Bohte 1995 - pneumococcal	2	35	0	29	100.0%	6.41 [0.39, 106.11]
Total (95% CI)		**35**		**29**	**100.0%**	**6.41 [0.39, 106.11]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.30 (P = 0.19)						



1.4.4.2 Single- compared with dual-antibiotic therapy

1.4.4.2.1 Macrolide compared with macrolide plus cephalosporin

Figure 105: CAP-related mortality

No forest plot available

Figure 106: Treatment failure

Study or Subgroup	Single antibiotic therapy Events	Total	Dual antibiotic therapy Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
7.2.3 Macrolide vs macrolide + cephalosporin						
Rovira 1999 - formal	0	45	2	45	100.0%	0.13 [0.01, 2.15]
Subtotal (95% CI)		**45**		**45**	**100.0%**	**0.13 [0.01, 2.15]**
Total events	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.42 (P = 0.15)						

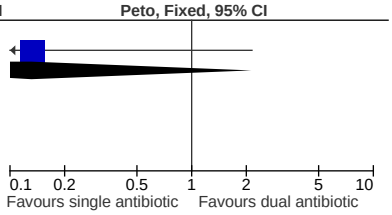
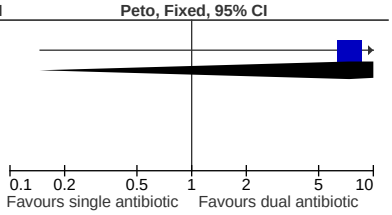


Figure 107: Complications (pleural effusion)

Study or Subgroup	Single antibiotic therapy Events	Total	Dual antibiotic therapy Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
7.4.3 Macrolide vs macrolide + cephalosporin						
Rovira 1999 - formal	1	45	0	45	100.0%	7.39 [0.15, 372.38]
Subtotal (95% CI)		**45**		**45**	**100.0%**	**7.39 [0.15, 372.38]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.00 (P = 0.32)						



1.4.4.2.2 Respiratory fluoroquinolone compared with cephalosporin plus macrolide (azithromycin)

Figure 108: Clinical cure or improvement at end of treatment

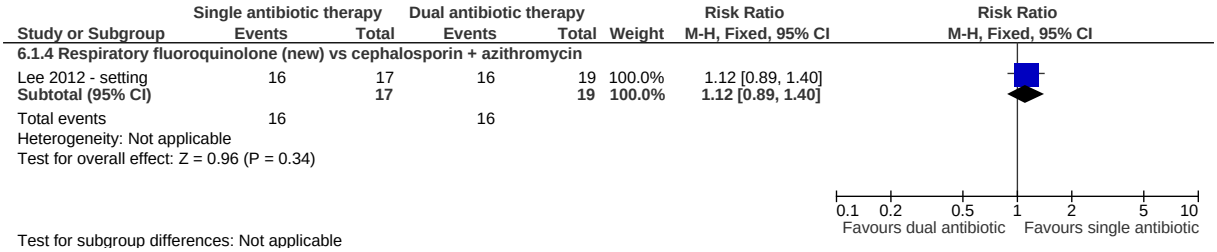


Figure 109: Withdrawal due to adverse events

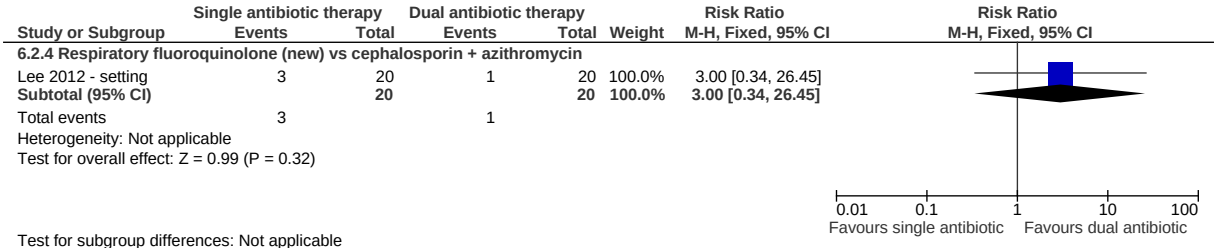
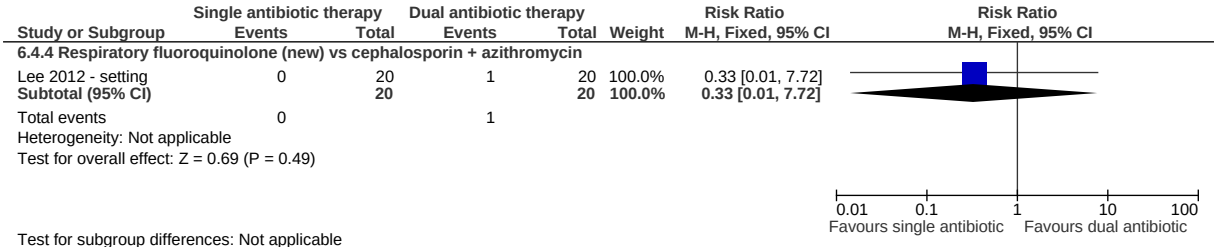


Figure 110: Complications (pleural effusion)



1.4.5 Moderate- to high-severity community-acquired pneumonia

1.4.5.1 Single- compared with other single-antibiotic therapy

1.4.5.1.1 Cephalosporin compared with beta-lactamase stable penicillin

Figure 111: All-cause mortality

Figure 112: Clinical cure

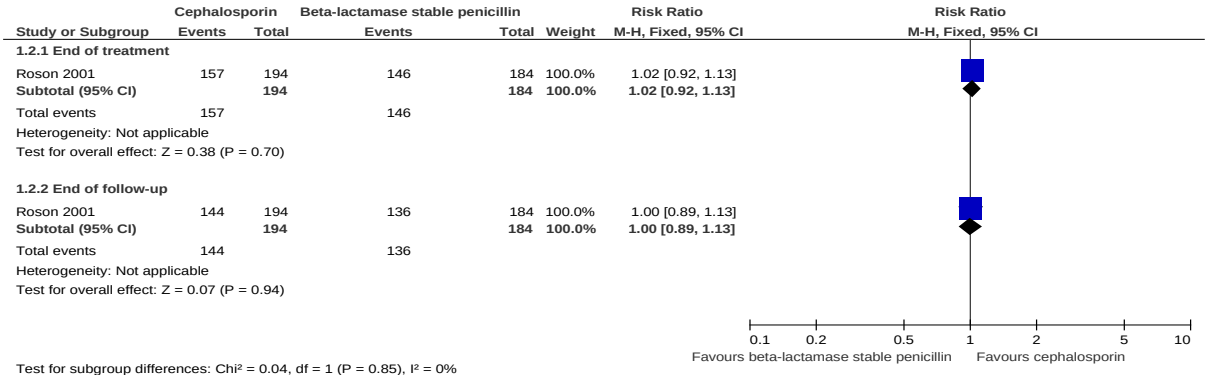


Figure 113: ITU admission

Figure 114: Length of hospital stay

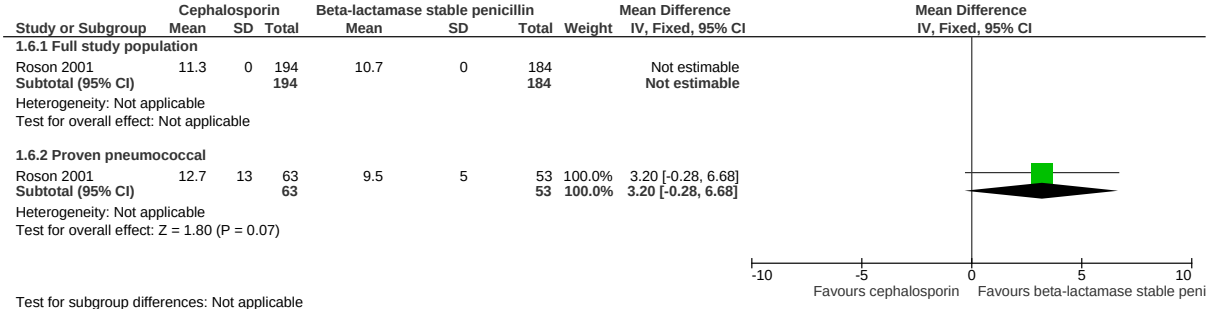
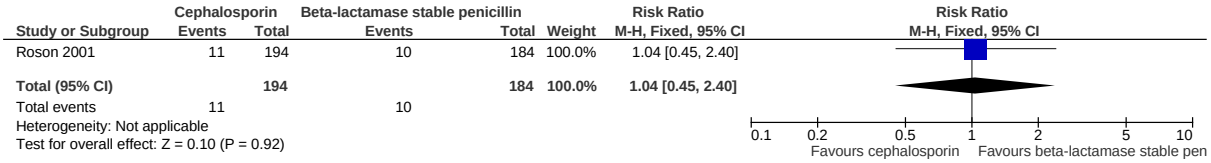


Figure 115: Complications (empyema)



1.4.5.1.2 Cephalosporin compared with narrow-spectrum beta-lactam (class 2)

Figure 116: Mortality

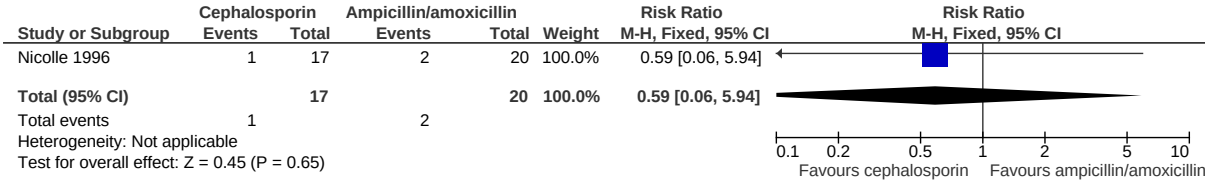


Figure 117: Clinical cure

Study or Subgroup	Cephalosporin Events	Total	Ampicillin/amoxicillin Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.2 End of follow-up						
Nicolle 1996	16	17	14	20	100.0%	1.34 [0.99, 1.83]
Subtotal (95% CI)		**17**		**20**	**100.0%**	**1.34 [0.99, 1.83]**
Total events	16		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.87 (P = 0.06)						

Test for subgroup differences: Not applicable

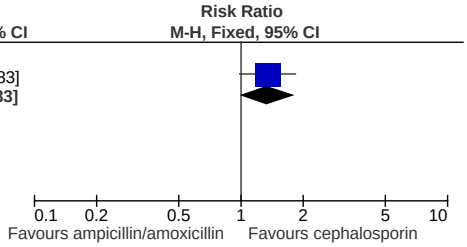
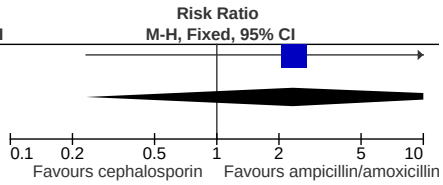


Figure 118: C. difficile-associated diarrhoea

Study or Subgroup	Cephalosporin Events	Total	Ampicillin/amoxicillin Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Nicolle 1996	2	17	1	20	100.0%	2.35 [0.23, 23.75]
Total (95% CI)		**17**		**20**	**100.0%**	**2.35 [0.23, 23.75]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.73 (P = 0.47)						



1.4.5.2 Single- compared with dual-antibiotic therapy

1.4.5.2.1 Macrolide compare with macrolide plus cephalosporin

Figure 119: All-cause mortality

Study or Subgroup	Single antibiotic therapy Events	Total	Dual antibiotic therapy Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 Macrolide vs macrolide + cephalosporin						
Vergis 2000 - setting	3	83	1	86	19.6%	3.11 [0.33, 29.29]
Vetter 1997 - setting	5	118	4	117	80.4%	1.24 [0.34, 4.50]
Subtotal (95% CI)		**201**		**203**	**100.0%**	**1.61 [0.54, 4.81]**
Total events	8		5			
Heterogeneity: Chi² = 0.49, df = 1 (P = 0.48); I² = 0%						
Test for overall effect: Z = 0.85 (P = 0.40)						
Total (95% CI)		**201**		**203**	**100.0%**	**1.61 [0.54, 4.81]**
Total events	8		5			
Heterogeneity: Chi² = 0.49, df = 1 (P = 0.48); I² = 0%						
Test for overall effect: Z = 0.85 (P = 0.40)						

Test for subgroup differences: Not applicable

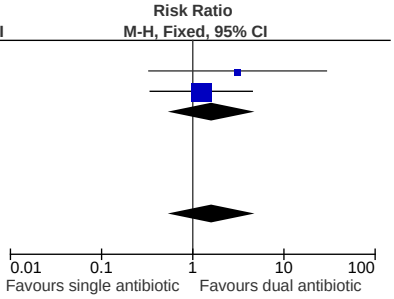


Figure 120: Clinical cure at end of treatment

Study or Subgroup	Single antibiotic therapy Events	Total	Dual antibiotic therapy Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.2.1 Macrolide vs macrolide + cephalosporin						
Vergis 2000 - setting	62	83	71	86	57.8%	0.90 [0.77, 1.06]
Vetter 1997 - setting	66	118	58	117	42.2%	1.13 [0.88, 1.44]
Subtotal (95% CI)		**201**		**203**	**100.0%**	**0.99 [0.79, 1.25]**
Total events	128		129			
Heterogeneity: Tau² = 0.02; Chi² = 2.58, df = 1 (P = 0.11); I² = 61%						
Test for overall effect: Z = 0.06 (P = 0.95)						

Test for subgroup differences: Not applicable

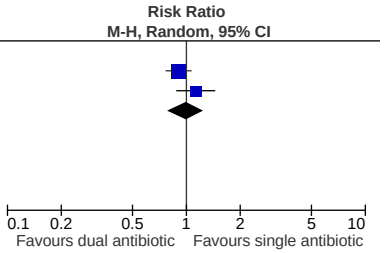


Figure 121: Clinical cure at end of follow-up

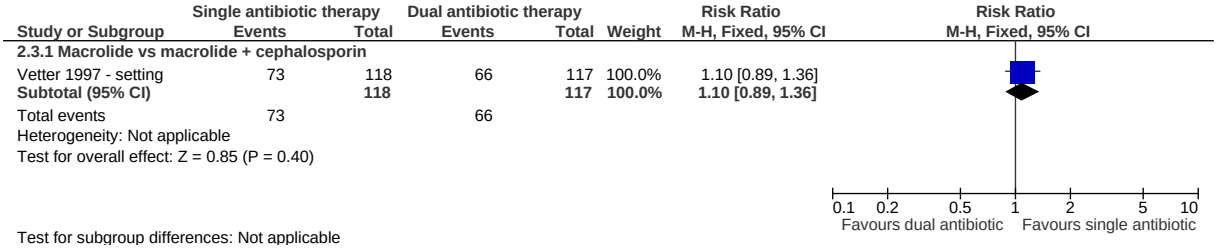


Figure 122: Withdrawal due to adverse events

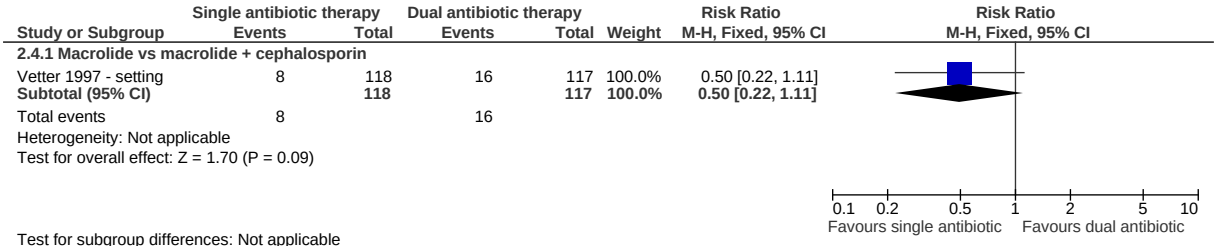
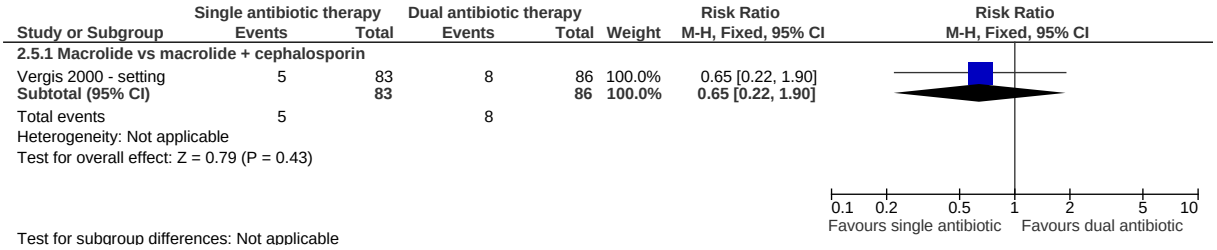


Figure 123: ITU admission



1.4.5.2.2 Respiratory fluoroquinolone compare with cephalosporin plus macrolide

Figure 124: All-cause mortality

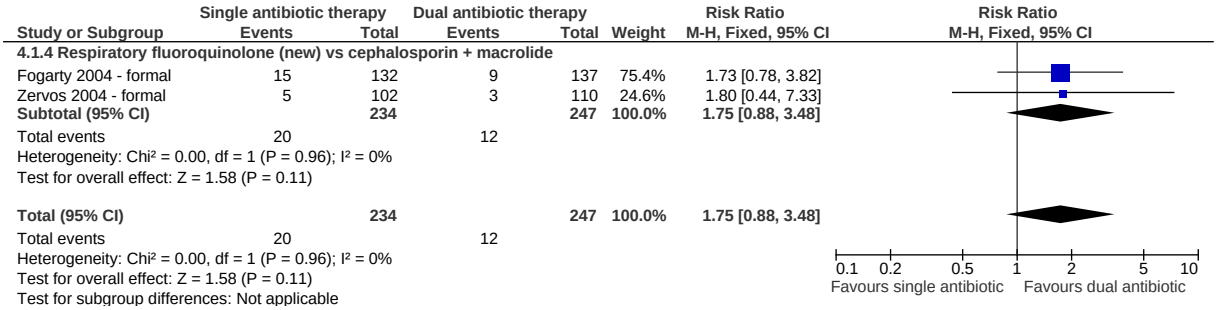


Figure 125: Clinical cure or improvement at end of treatment

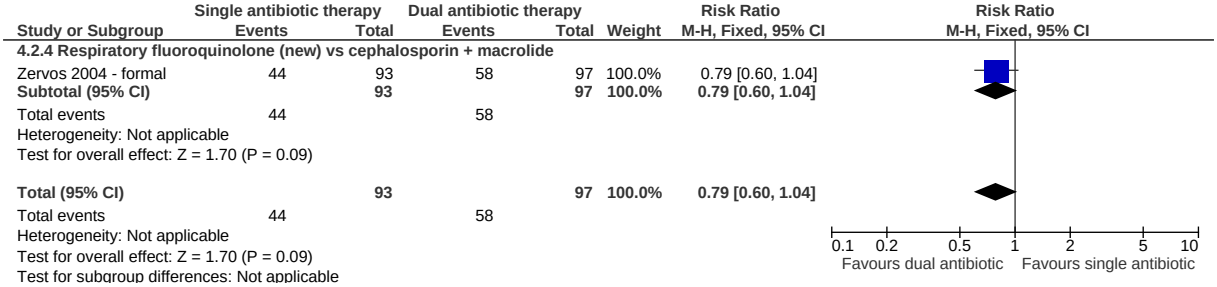


Figure 126: Clinical cure or improvement at end of follow up

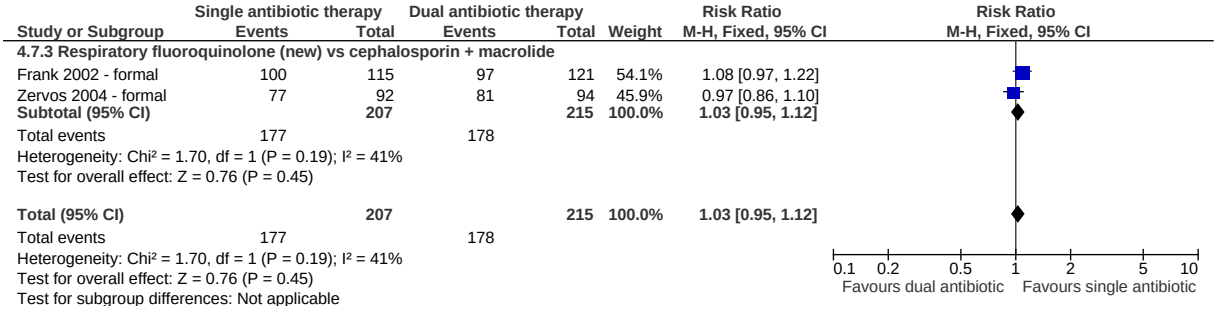


Figure 127: Withdrawal due to adverse events

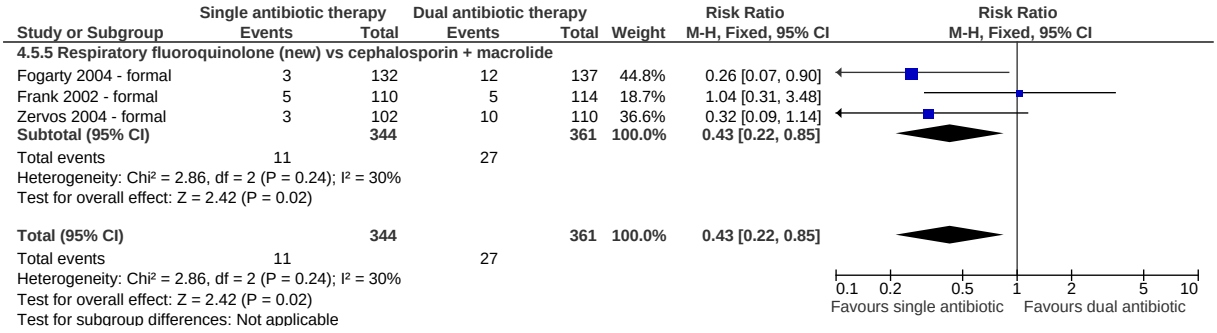
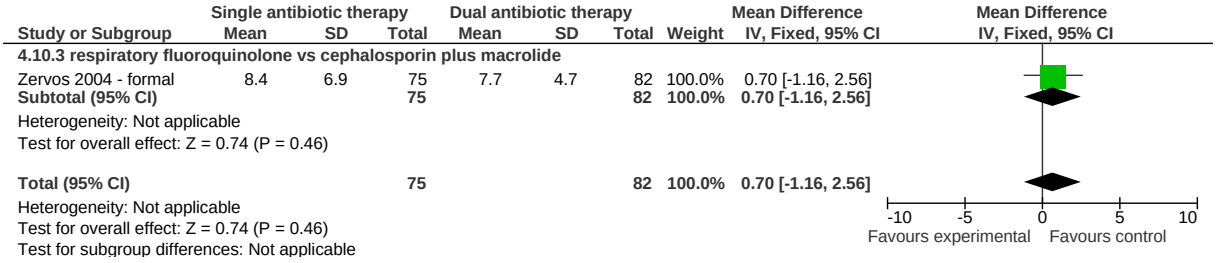


Figure 128: Length of hospital stay



1.4.5.2.3 Respiratory fluoroquinolone compare with beta-lactamase stable penicillin plus macrolide

Figure 129: Clinical cure at end of treatment

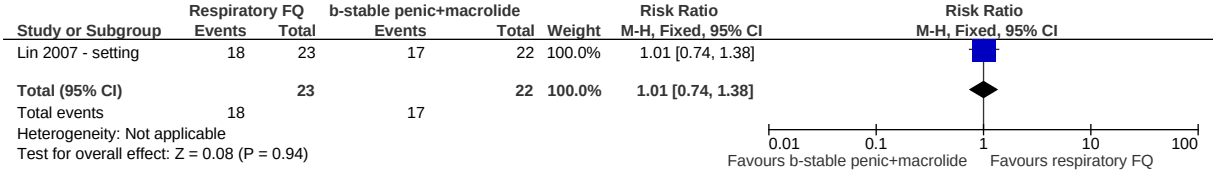


Figure 130: Clinical cure at end of follow-up

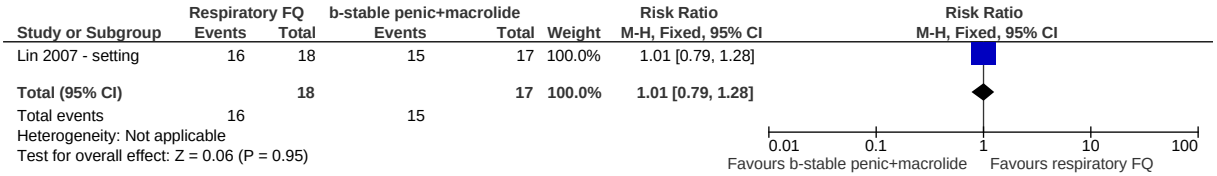
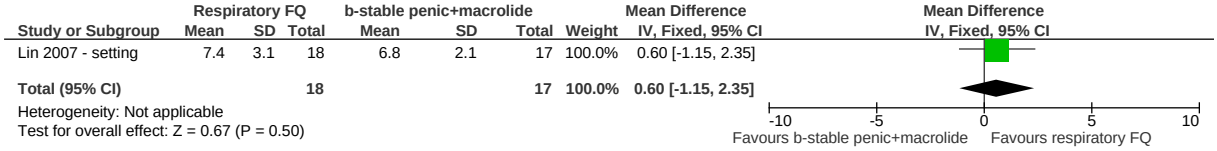


Figure 131: Length of hospital stay



1.4.5.2.4 Respiratory fluoroquinolone compare with cephalosporin plus respiratory fluoroquinolone

Figure 132: All-cause mortality

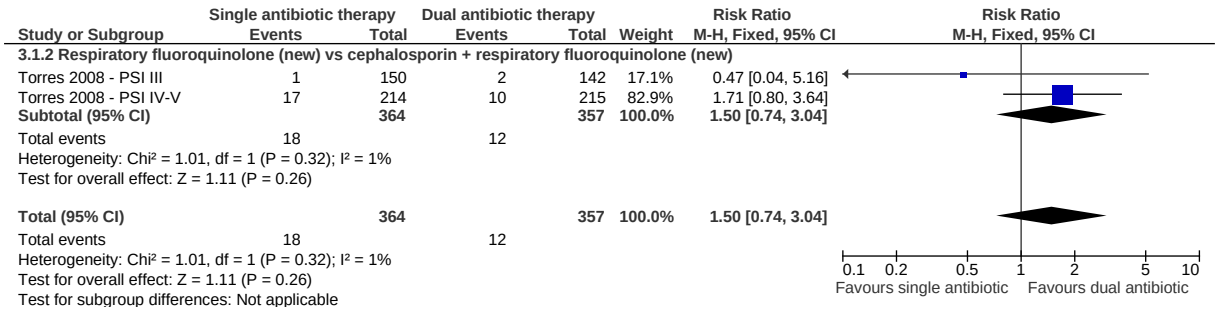


Figure 133: Clinical cure or improvement at end of treatment

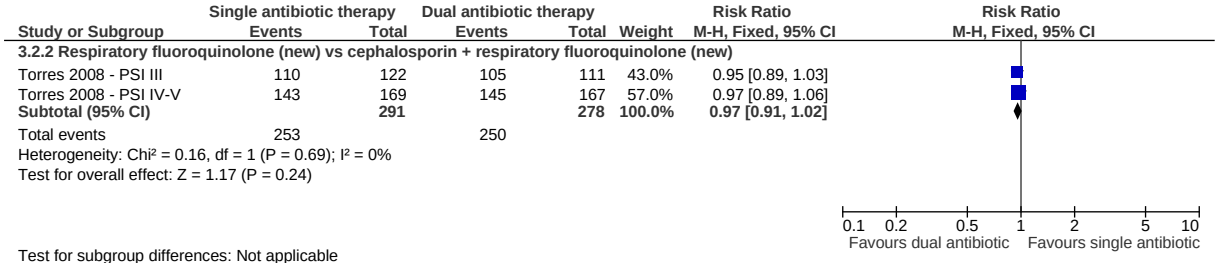


Figure 134: Maintaining clinical cure at end of follow-up

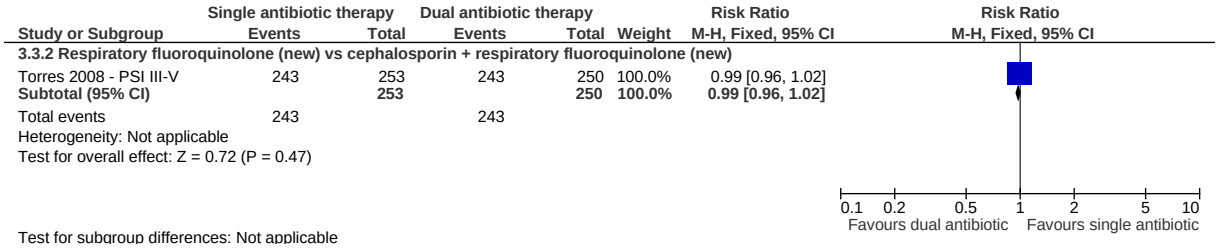
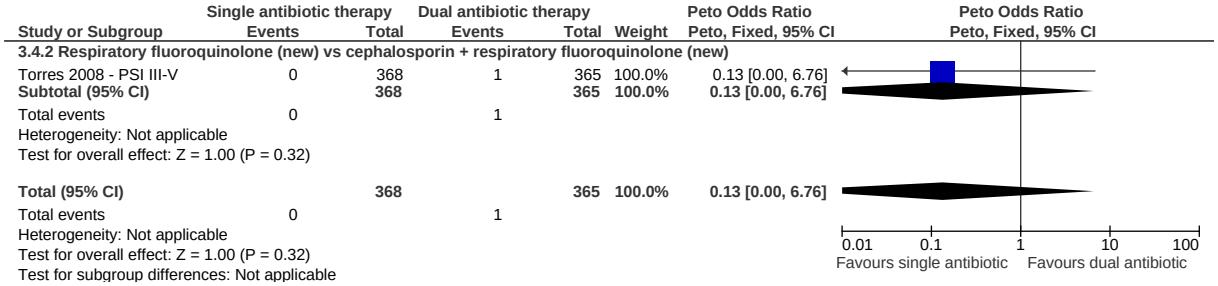


Figure 135: *C. difficile*-associated diarrhoea



1.4.5.2.5 Respiratory fluoroquinolone compare with cephalosporin plus non-respiratory fluoroquinolone

Figure 136: All-cause mortality

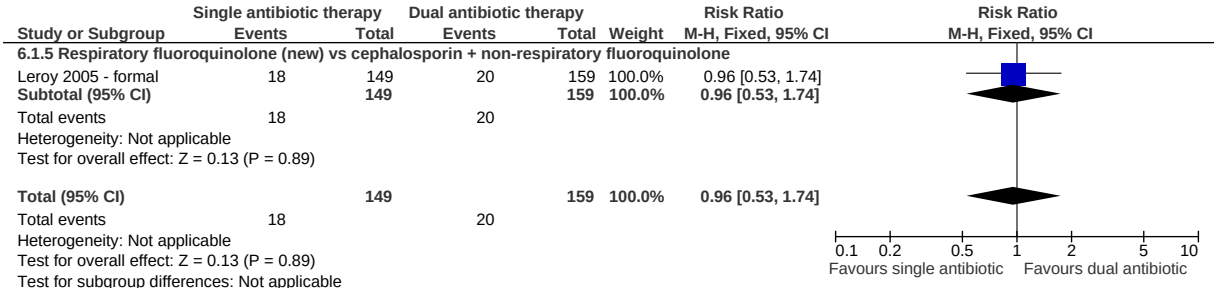


Figure 137: Clinical cure at end of treatment

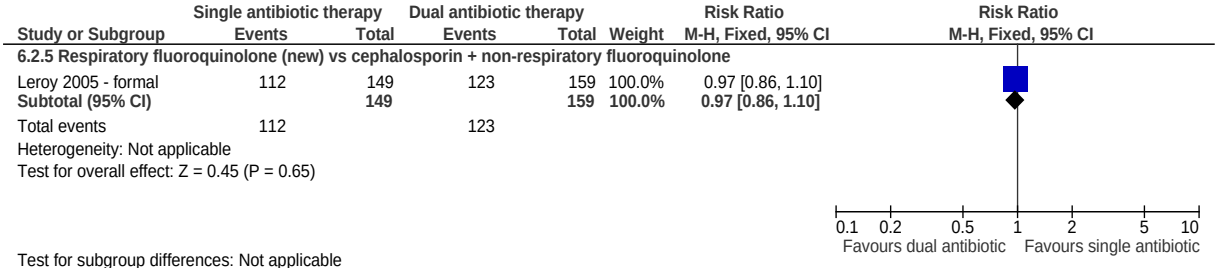


Figure 138: Clinical cure at follow-up

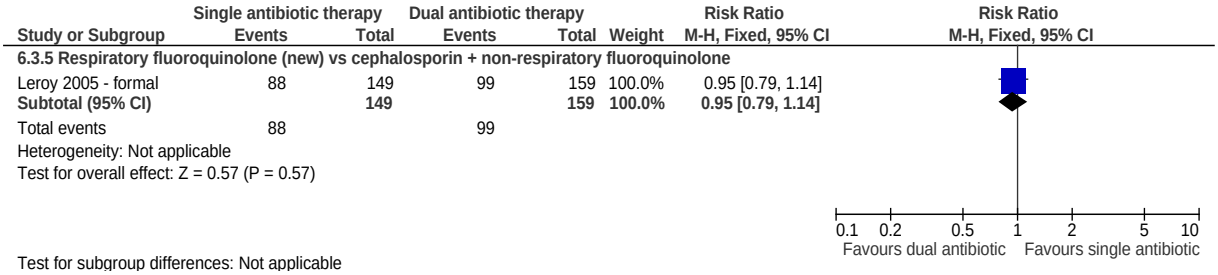


Figure 139: Withdrawal due to adverse events

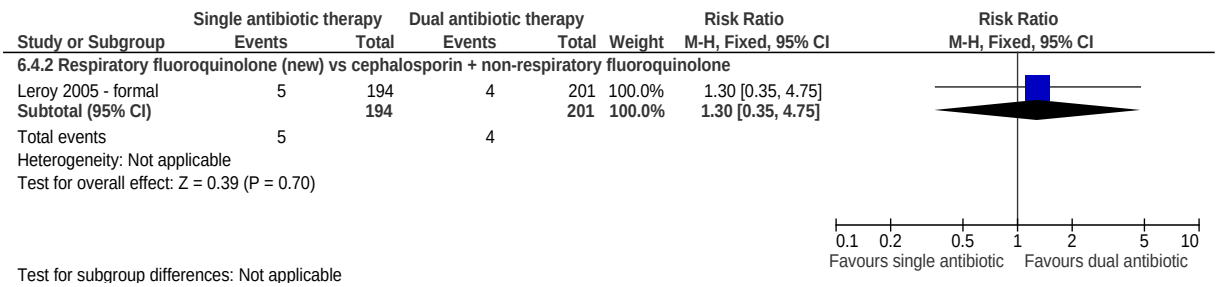
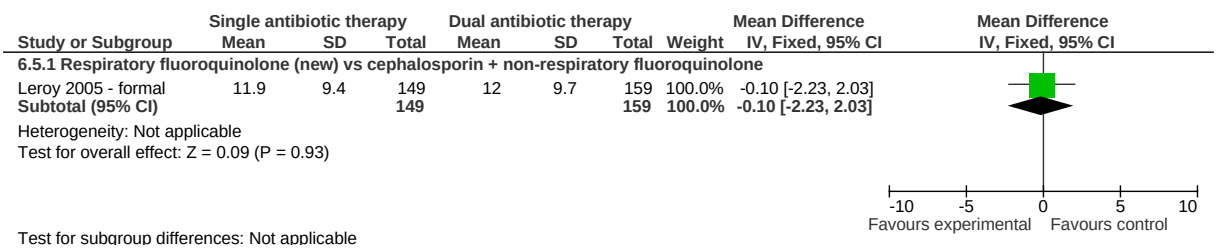


Figure 140: Length of hospital stay



1.4.5.3 Dual-compared with dual-antibiotic therapy

1.4.5.3.1 Non-respiratory fluoroquinolone (FQ) plus narrow spectrum beta-lactam (class 1) compared with macrolide plus beta-lactamase stable penicillin

Figure 141: All-cause mortality

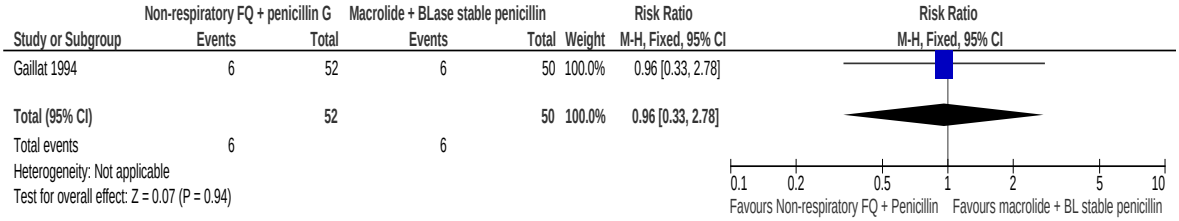


Figure 142: Clinical cure at end of treatment

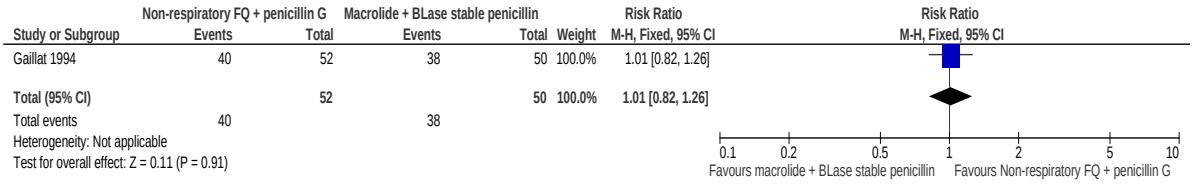
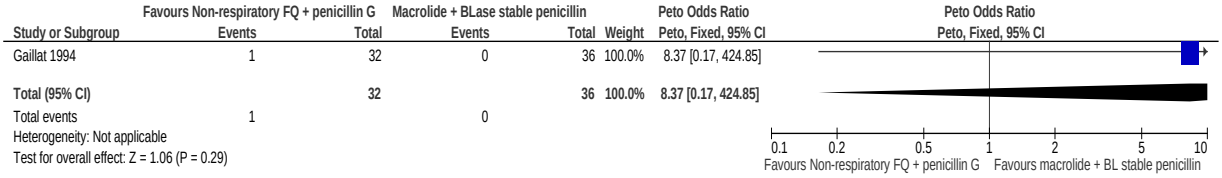


Figure 143: Complications - superinfection



1.4.5.3.2 Azithromycin plus cephalosporin compared with other macrolide plus cephalosporin

Figure 144: Mortality

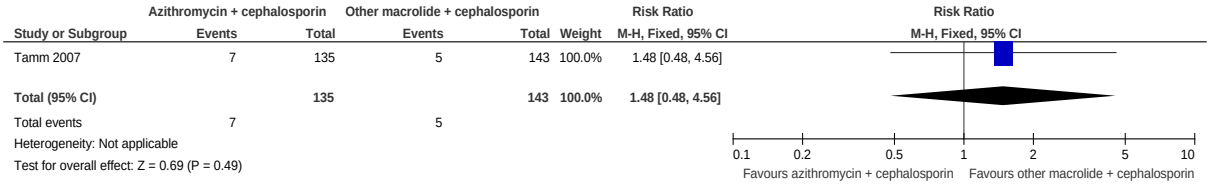


Figure 145: Clinial cure at end of treatment

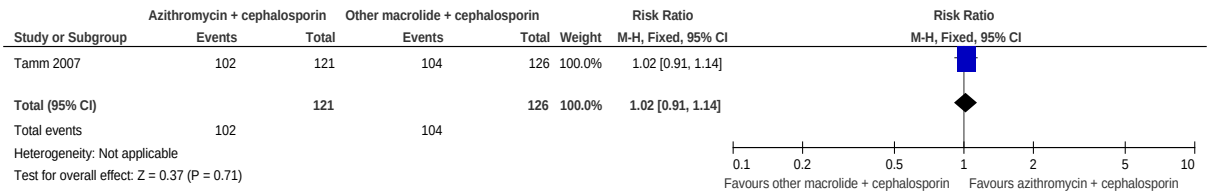


Figure 146: Withdrawal due to adverse events

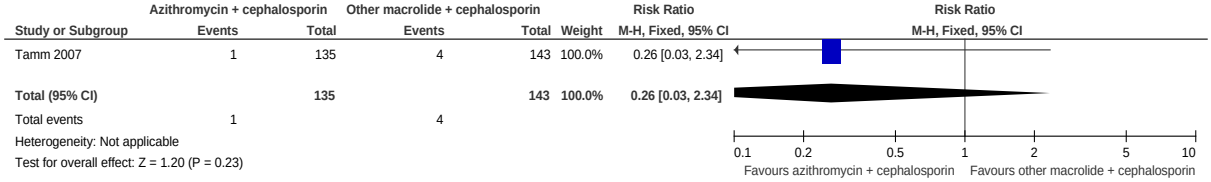
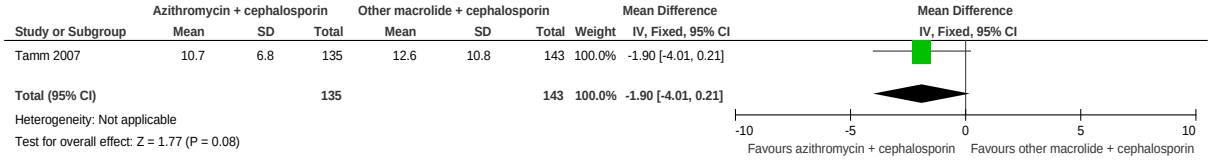


Figure 147: Length of hospital stay



1.4.6 Duration of antibiotic therapy

1.4.6.1 Higher dose of antibiotic therapy with shorter duration compared with lower dose and longer duration of antibiotic therapy

Figure 148: All-cause mortality

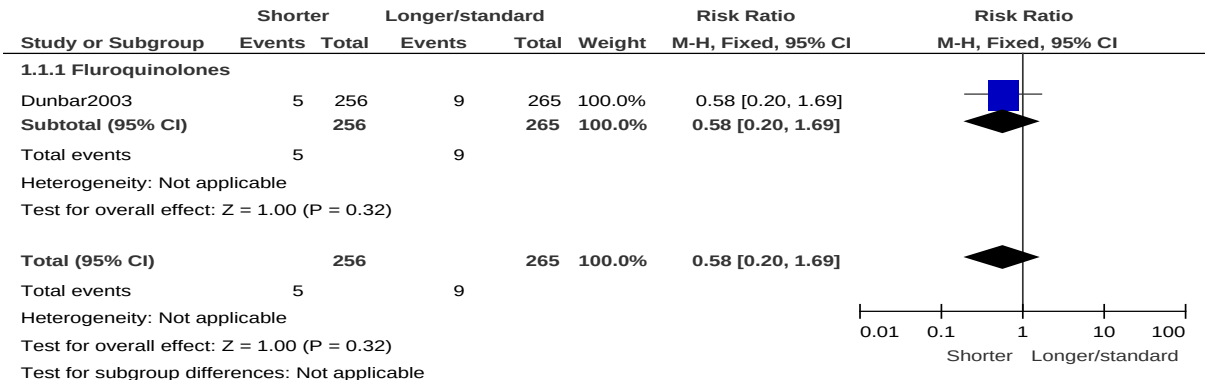


Figure 149: Clinical cure (7 to 14 days after therapy)

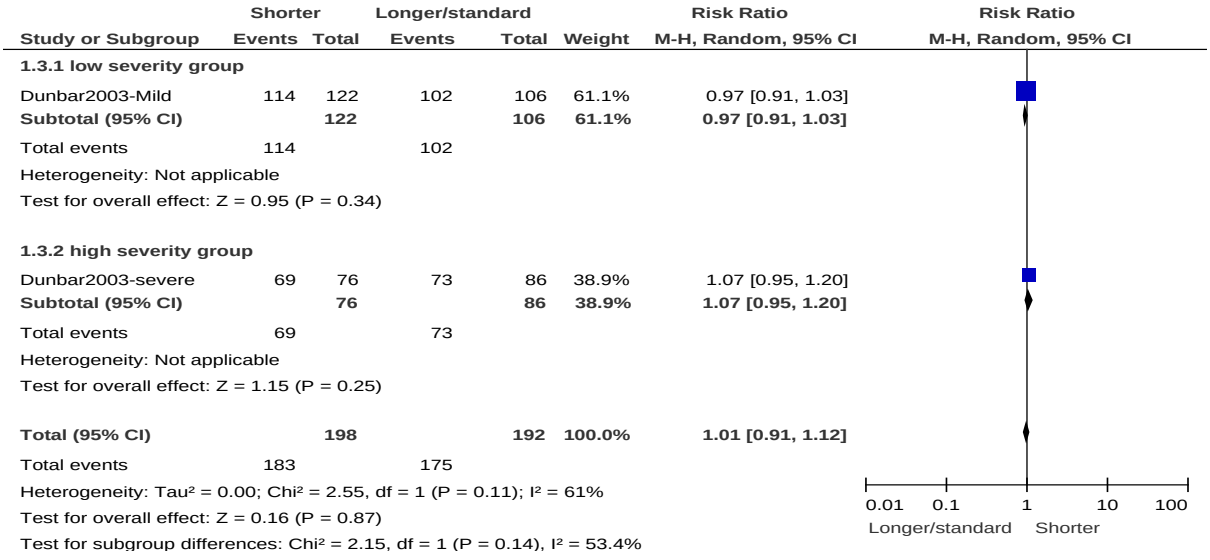
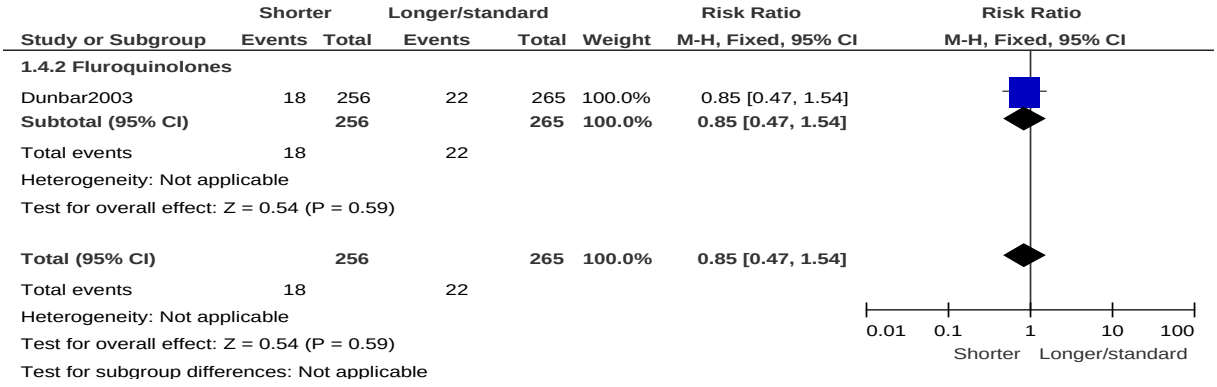


Figure 150: Withdrawal due to treatment-related adverse events



1.4.6.2 Shorter duration compared with longer duration of antibiotic therapy

Figure 151: All-cause 30-day mortality

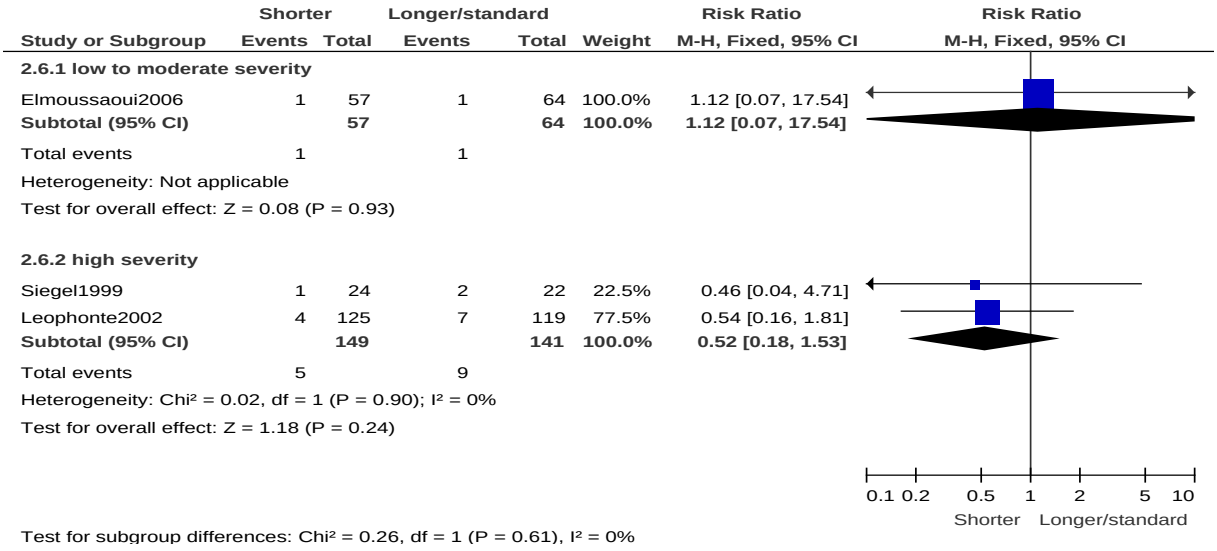


Figure 152: Clinical cure

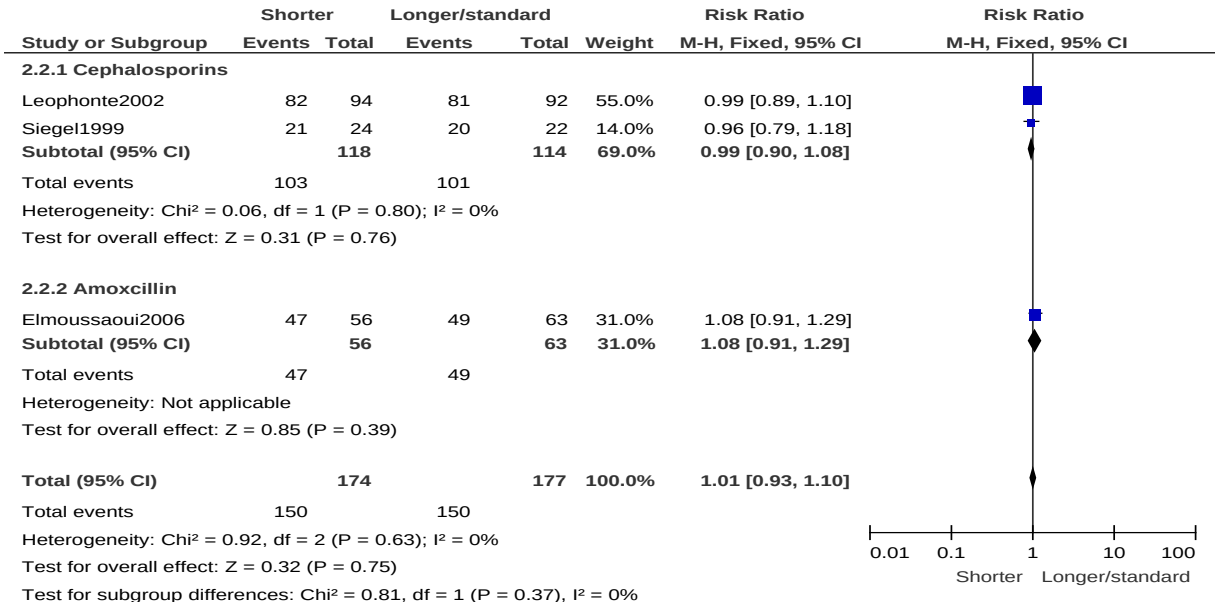


Figure 153: Withdrawal due to adverse events

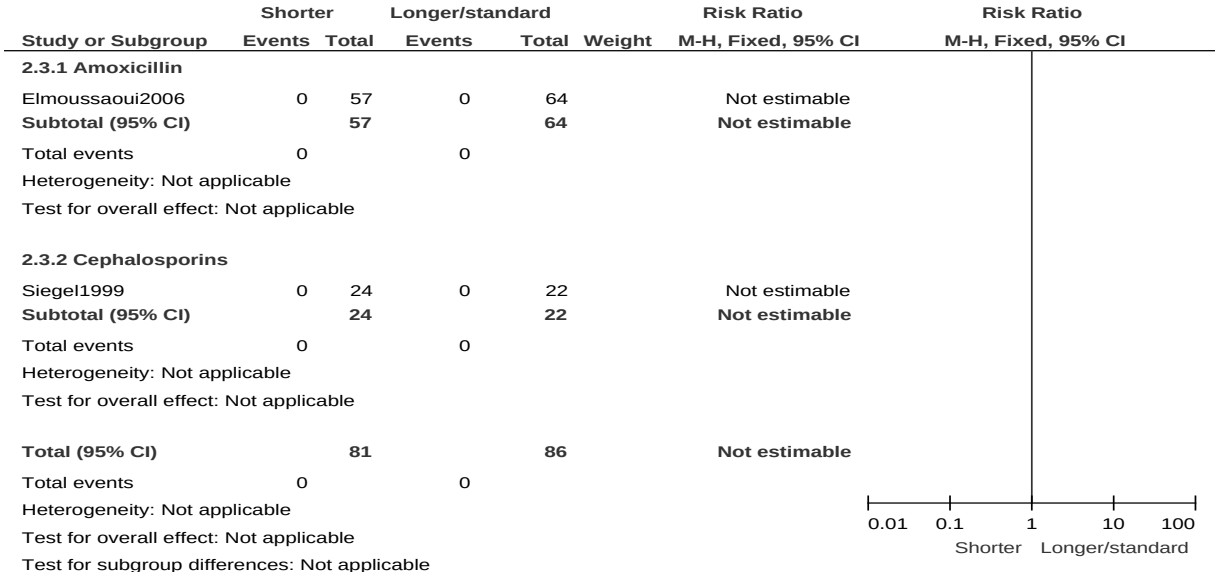


Figure 154: Complications (worsening infection, abscess, metastatic infection, MODS)

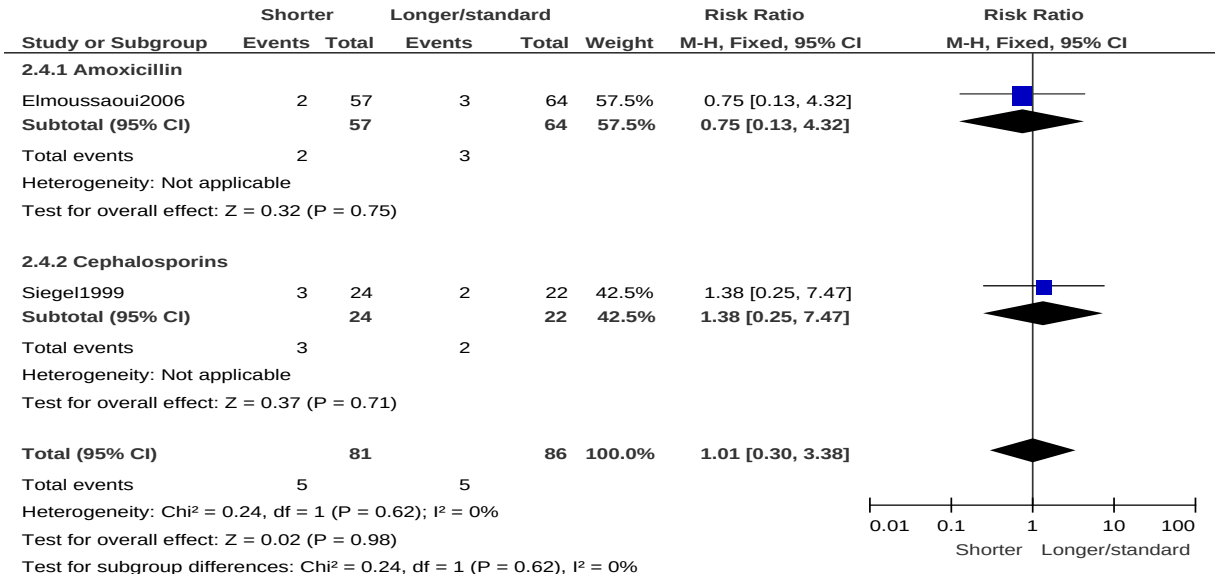
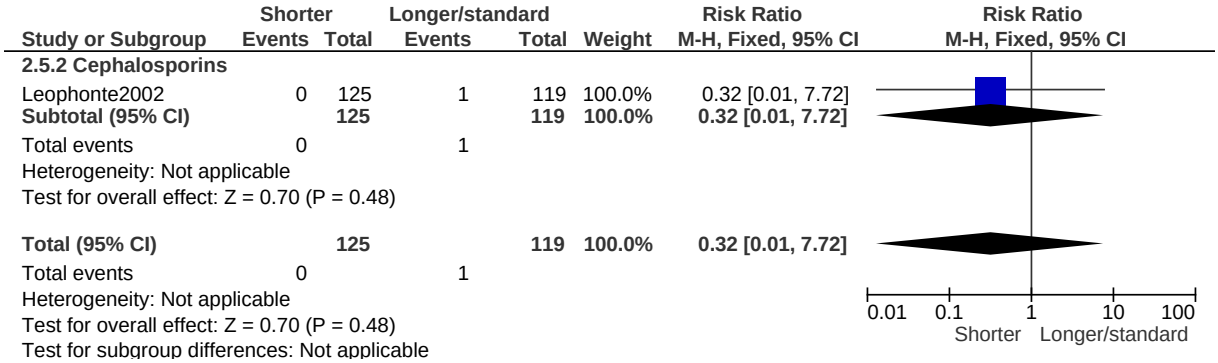
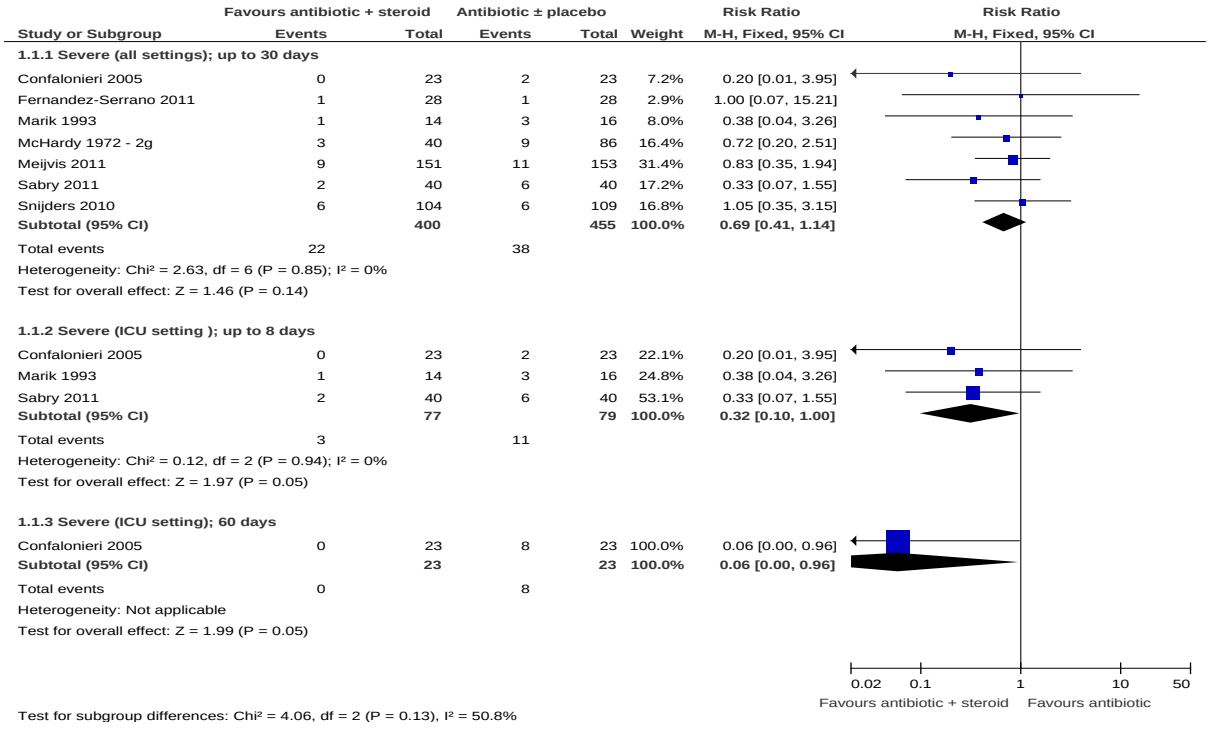


Figure 155: *C. difficile*-associated diarrhoea



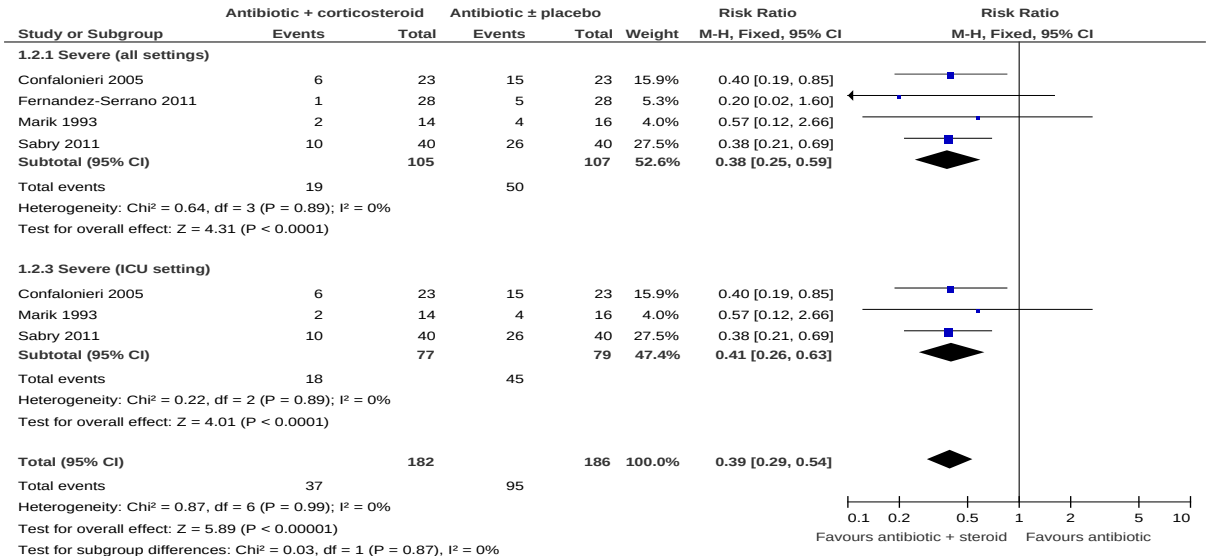
1.5 Glucocorticosteroid treatment

Figure 156: Mortality



Test for subgroup differences: Chi² = 4.06, df = 2 (P = 0.13), I² = 50.8%

Figure 157: Mechanical ventilation



Test for subgroup differences: Chi² = 0.03, df = 1 (P = 0.87), I² = 0%

Figure 158: Clinical cure (time to clinical stability)

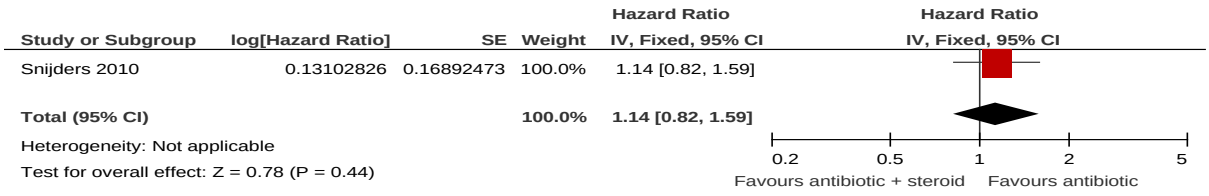


Figure 159: Length of hospital stay

Study or Subgroup	Antibiotic+Steroid Mean	SD	Total	Antibiotic Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Mikami 2007	11.3	5.5	15	15.5	10.7	16	100.0%	-4.20 [-10.14, 1.74]
Total (95% CI)			**15**			**16**	**100.0%**	**-4.20 [-10.14, 1.74]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.39 (P = 0.17)

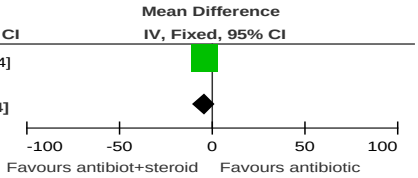


Figure 160: Hyperglycaemia

Study or Subgroup	Antibiotic + corticosteroid Events	Total	Antibiotic ± placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Meijvis 2011	67	151	35	153	94.7%	1.94 [1.38, 2.73]
Snijders 2010	5	104	2	109	5.3%	2.62 [0.52, 13.21]
Total (95% CI)		**255**		**262**	**100.0%**	**1.98 [1.41, 2.76]**
Total events	72		37			

Heterogeneity: Chi² = 0.13, df = 1 (P = 0.72); I² = 0%
Test for overall effect: Z = 3.98 (P < 0.0001)

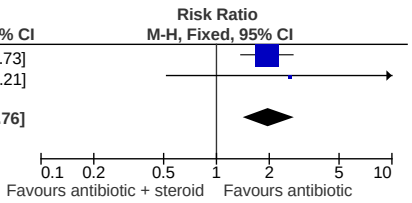
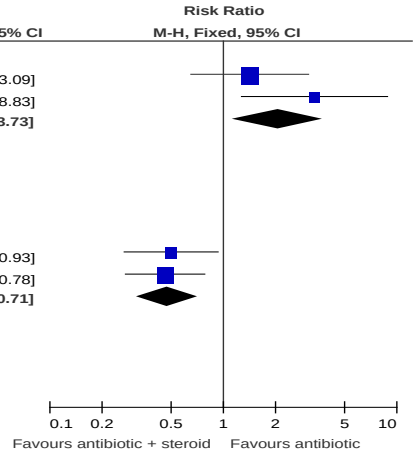


Figure 161: Complications

Study or Subgroup	Antibiotic + corticosteroid Events	Total	Antibiotic ± placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.7.1 In hospital: Superinfection, empyema or pleural effusion (upto 30 days)						
Meijvis 2011	14	151	10	153	67.0%	1.42 [0.65, 3.09]
Snijders 2010	16	104	5	109	33.0%	3.35 [1.27, 8.83]
Subtotal (95% CI)		**255**		**262**	**100.0%**	**2.06 [1.13, 3.73]**
Total events	30		15			
Heterogeneity: Chi² = 1.85, df = 1 (P = 0.17); I² = 46%						
Test for overall effect: Z = 2.37 (P = 0.02)						
1.7.2 In ICU: MODS (8 days)						
Confalonieri 2005	8	23	16	23	38.1%	0.50 [0.27, 0.93]
Sabry 2011	12	40	26	40	61.9%	0.46 [0.27, 0.78]
Subtotal (95% CI)		**63**		**63**	**100.0%**	**0.48 [0.32, 0.71]**
Total events	20		42			
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.85); I² = 0%						
Test for overall effect: Z = 3.62 (P = 0.0003)						

Test for subgroup differences: Chi² = 15.94, df = 1 (P < 0.0001), I² = 93.7%



1.6 Gas exchange

1.6.1 CPAP compared with usual care

Figure 162: Hospital mortality

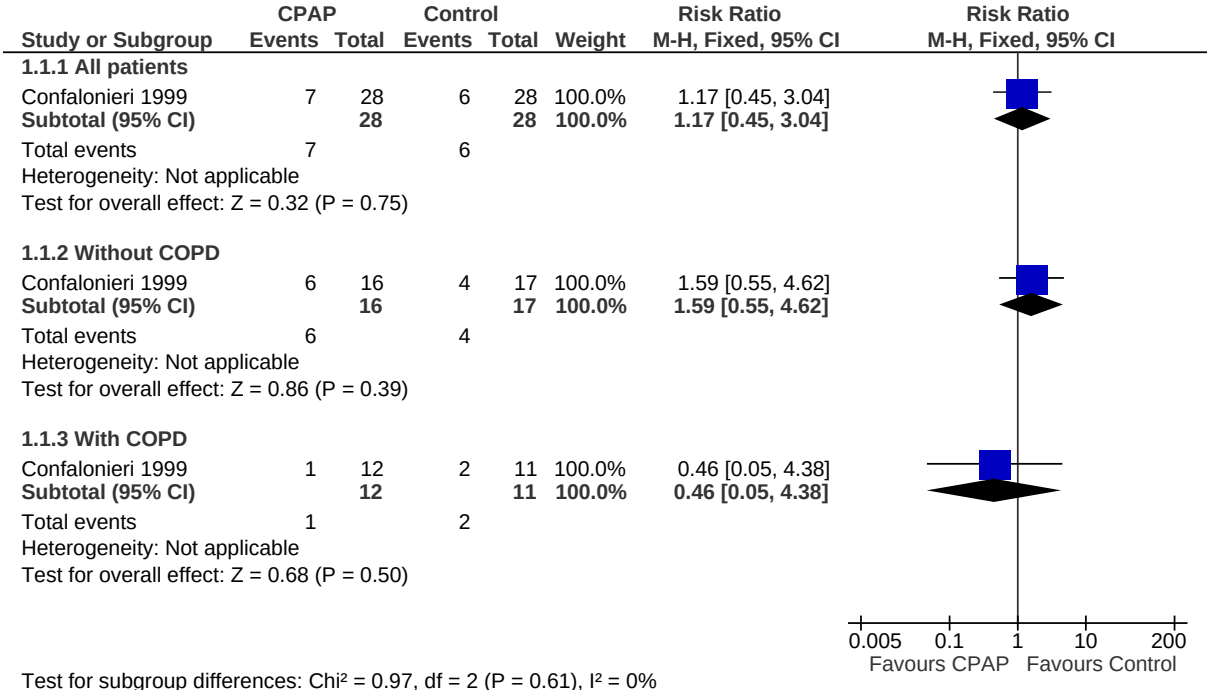


Figure 163: Need for intubation

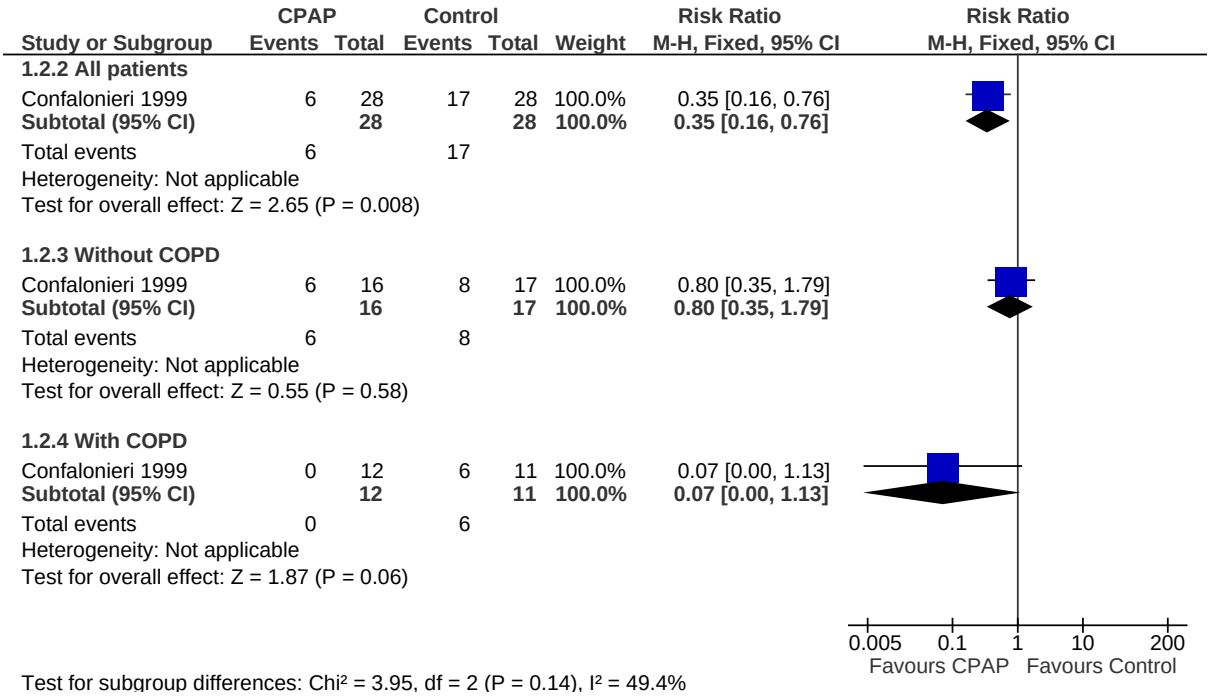
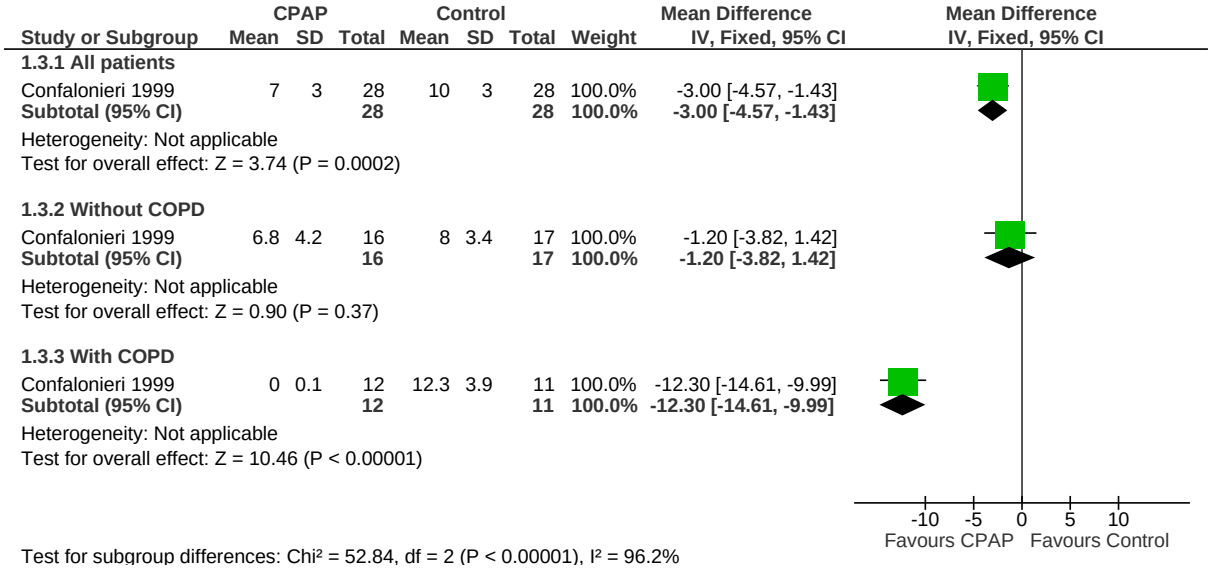
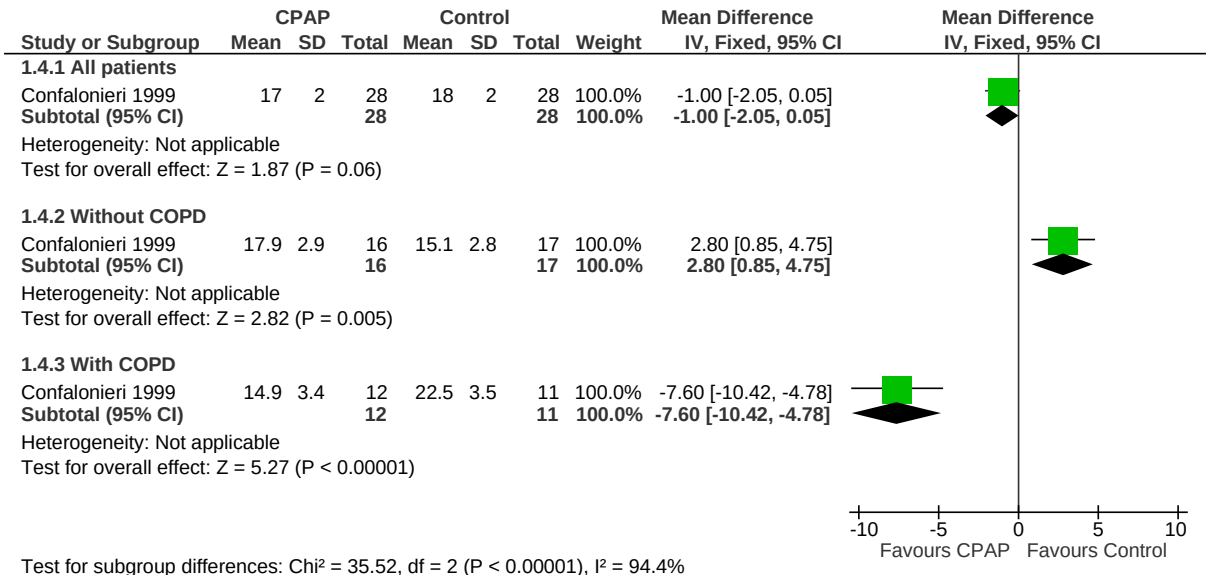


Figure 164: Duration of intubation



Test for subgroup differences: Chi² = 52.84, df = 2 (P < 0.00001), I² = 96.2%

Figure 165: Duration of hospital stay



Test for subgroup differences: Chi² = 35.52, df = 2 (P < 0.00001), I² = 94.4%

Figure 166: Duration of ITU stay

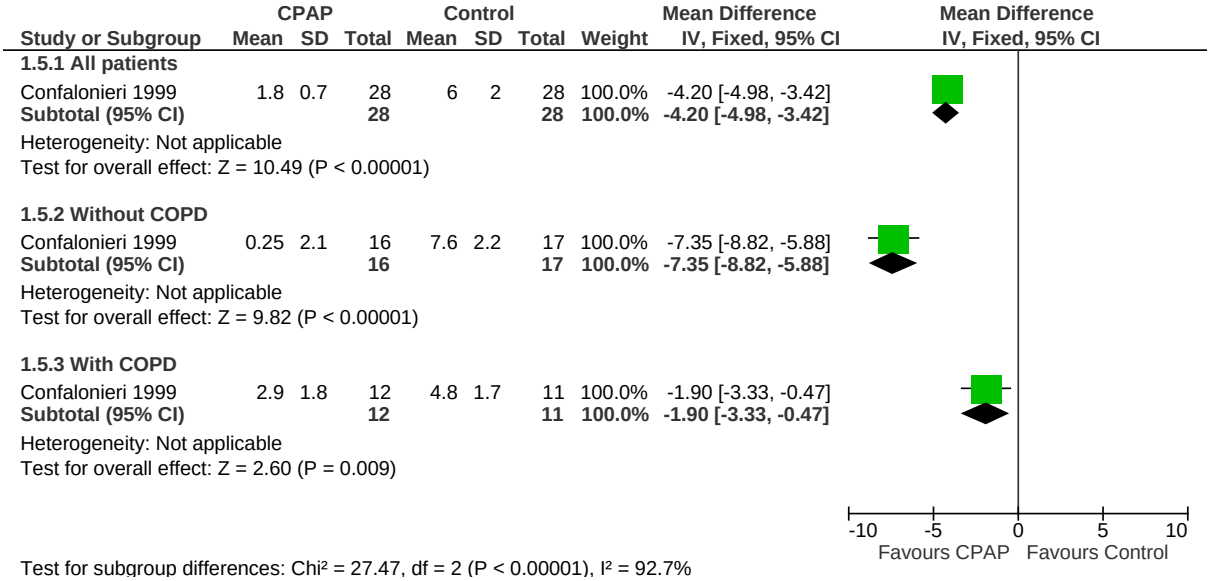
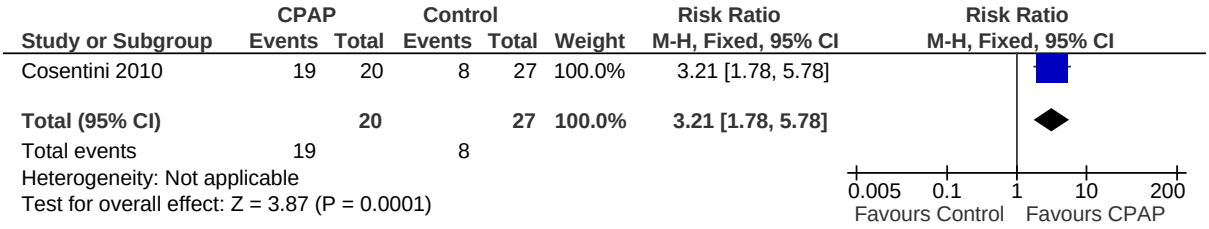


Figure 167: Patients who reached $PaO_2/FiO_2 \geq 315$



1.7 Monitoring

1.7.1 PCT to guide antibiotic administration and monitoring decisions compared with standard care (randomised data)

Figure 168: Mortality

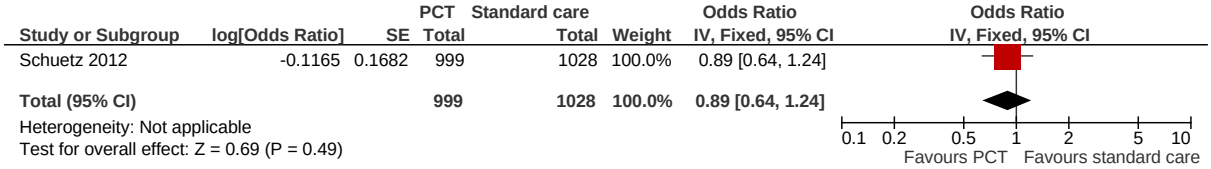


Figure 169: Treatment failure

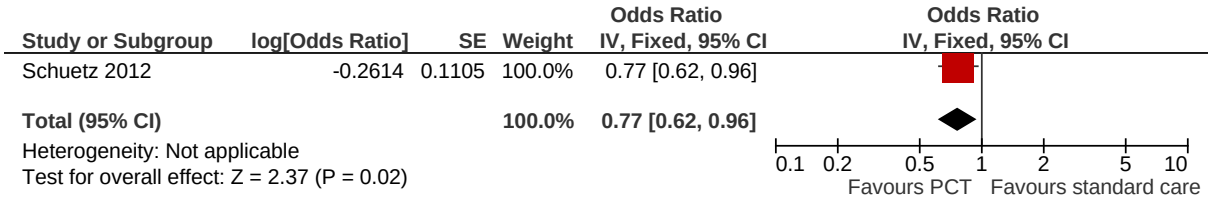


Figure 170: Median duration of antibiotic therapy

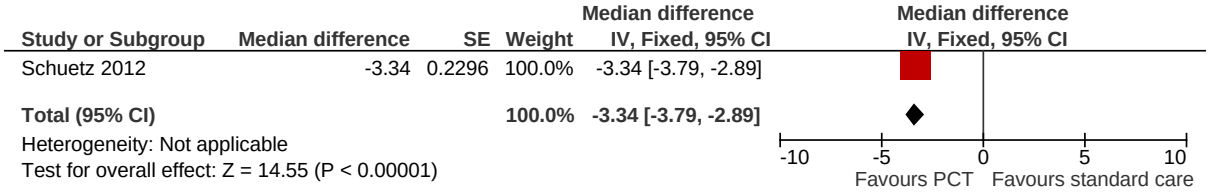
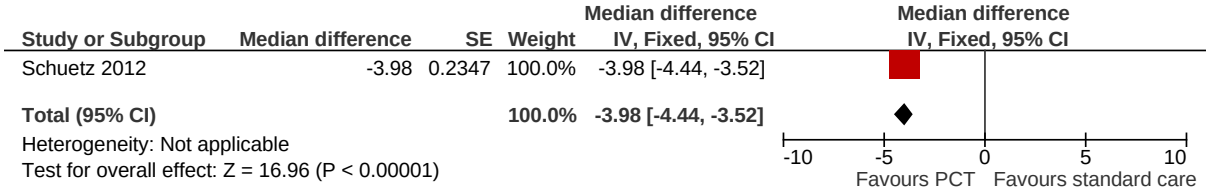


Figure 171: Total exposure to antibiotics



1.7.2 PCT to guide antibiotic administration and monitoring decisions compared with standard care for the subgroup of patients with community-acquired pneumonia who received antibiotic therapy (unpublished data)

Figure 172: Mortality

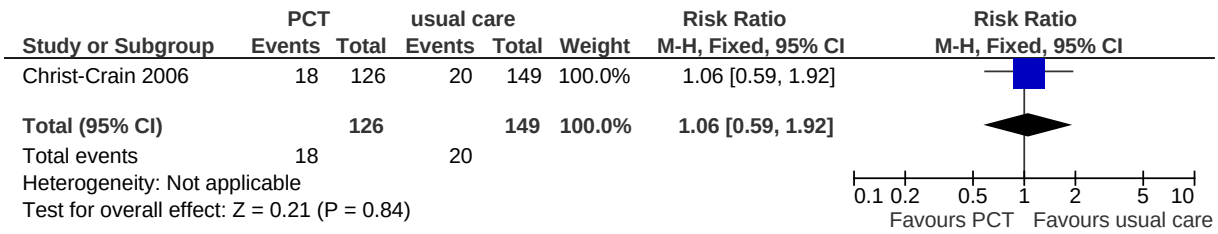


Figure 173: Length of hospital stay

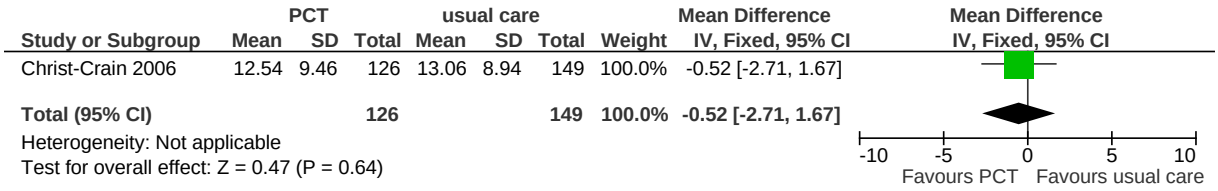


Figure 174: Treatment failure

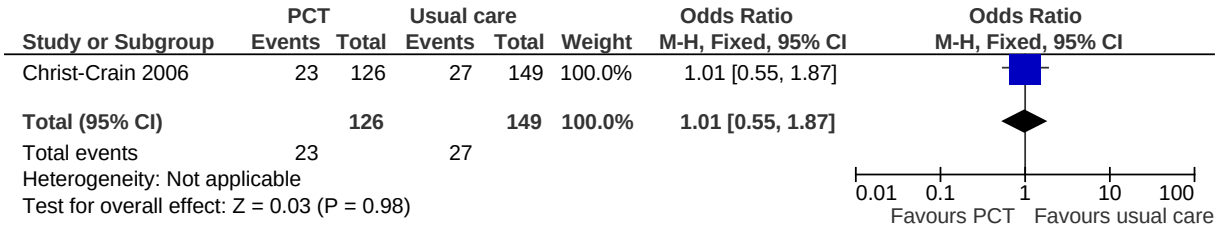


Figure 175: Duration of antibiotics

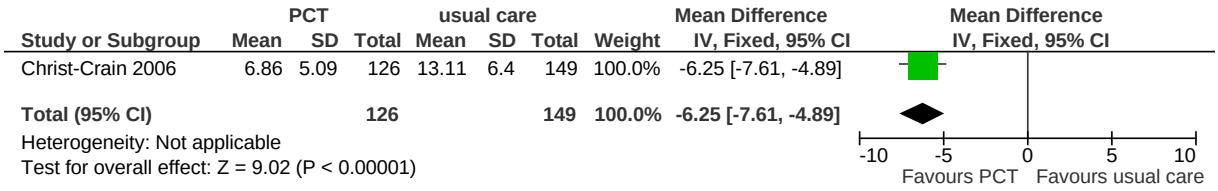
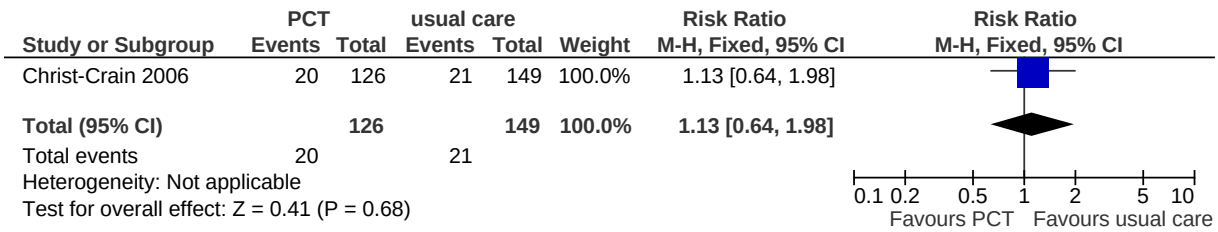


Figure 176: ITU admission



1.7.3 CRP or PCT to guide monitoring decisions (non-randomised data)

Figure 177: Mortality

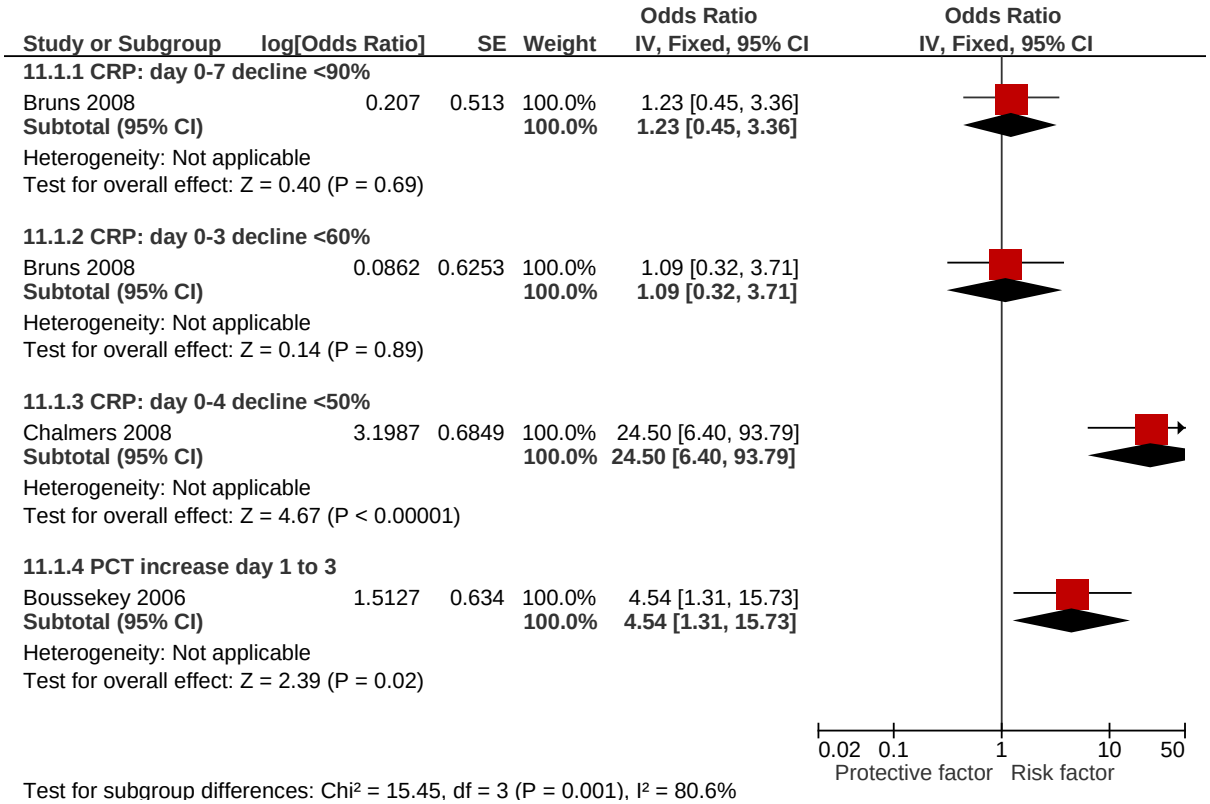


Figure 178: ITU mortality

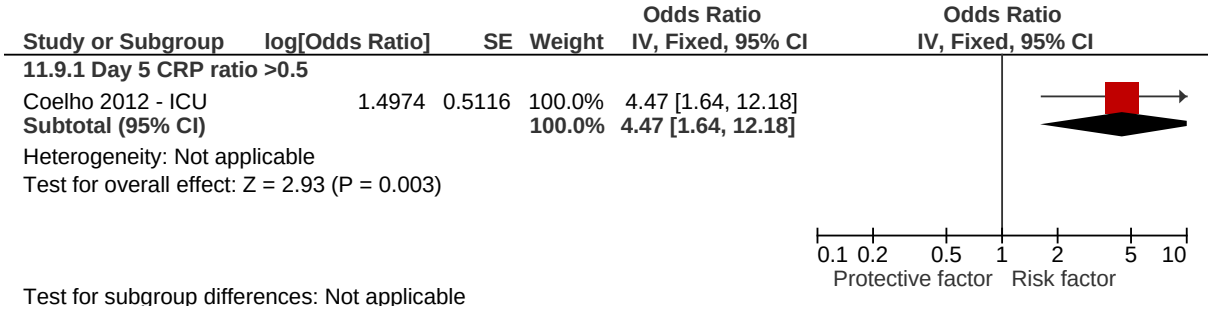


Figure 179: Inappropriate antibiotic therapy

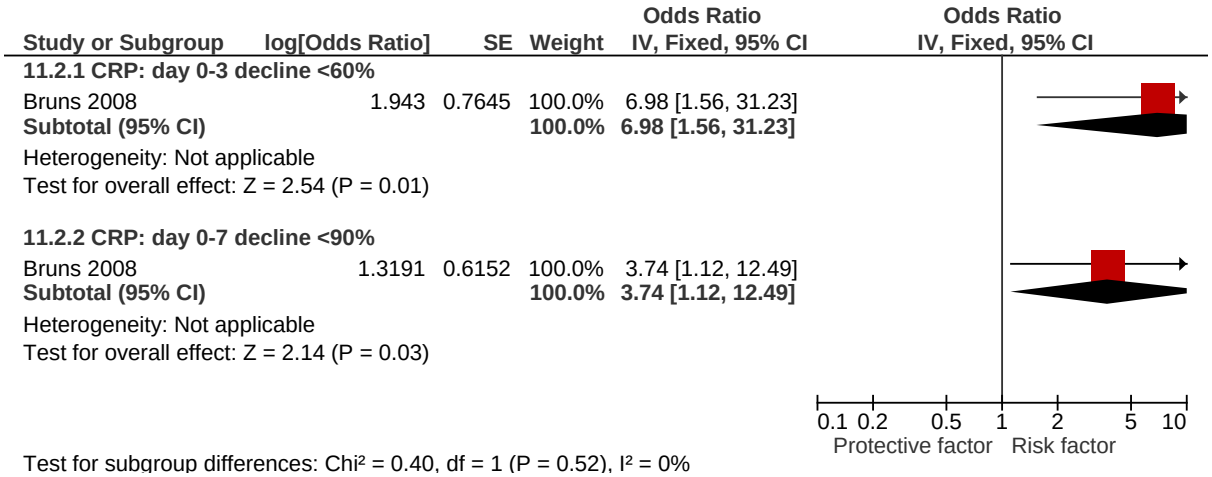


Figure 180: Overall treatment failure

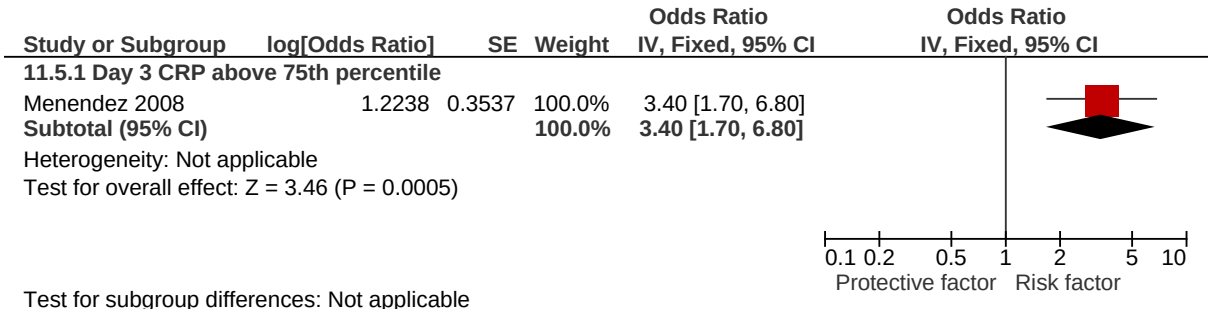


Figure 181: Early treatment failure

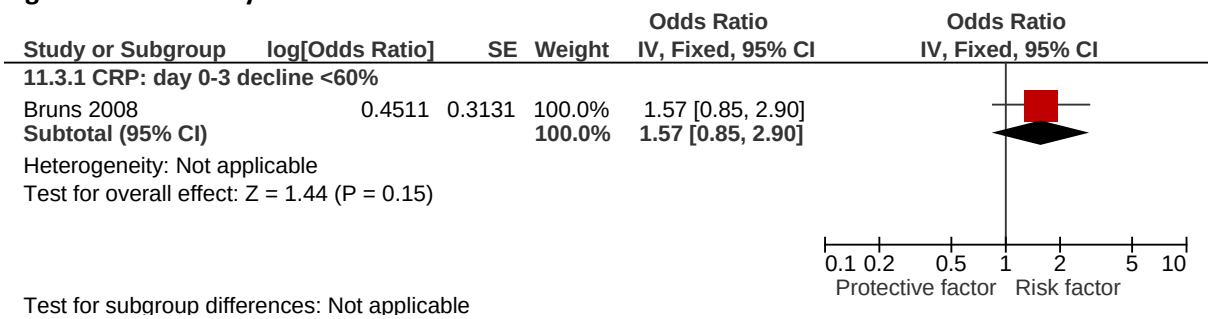


Figure 182: Late treatment failure

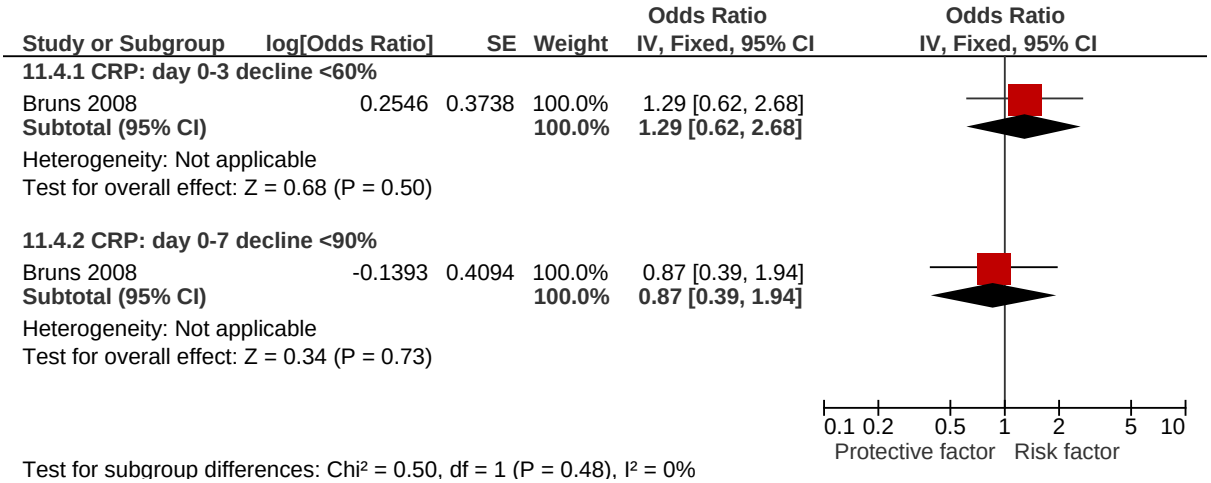


Figure 183: Late treatment failure (after 72 hours)

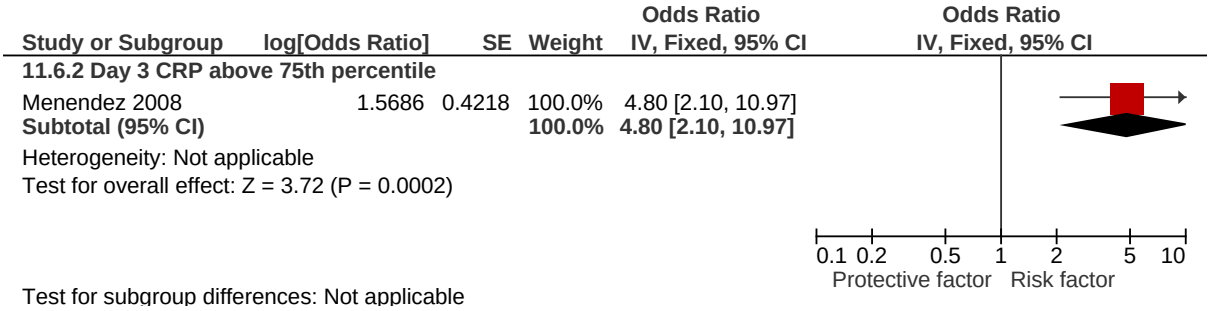


Figure 184: Severe complications after 72 hours

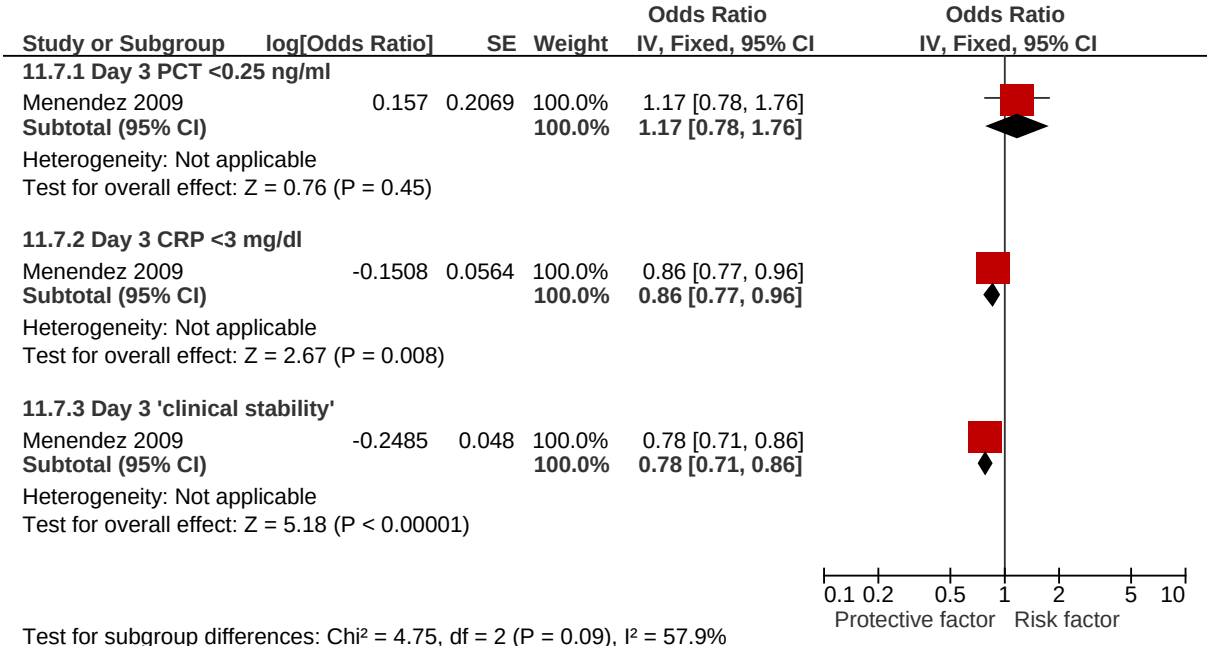


Figure 185: Hospital re-admission within 7 days

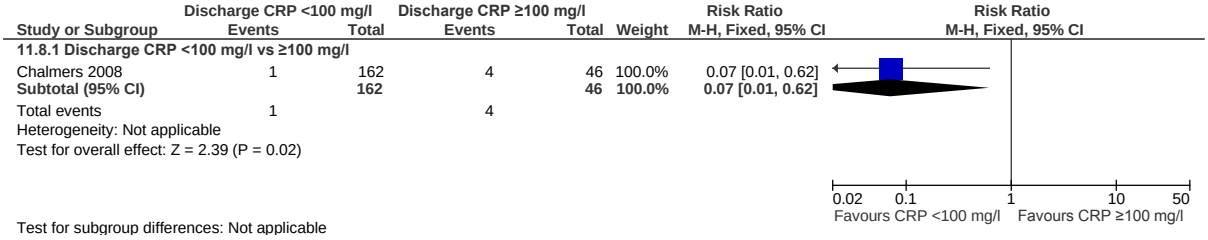


Figure 186: Need for invasive ventilation or ionotropic support

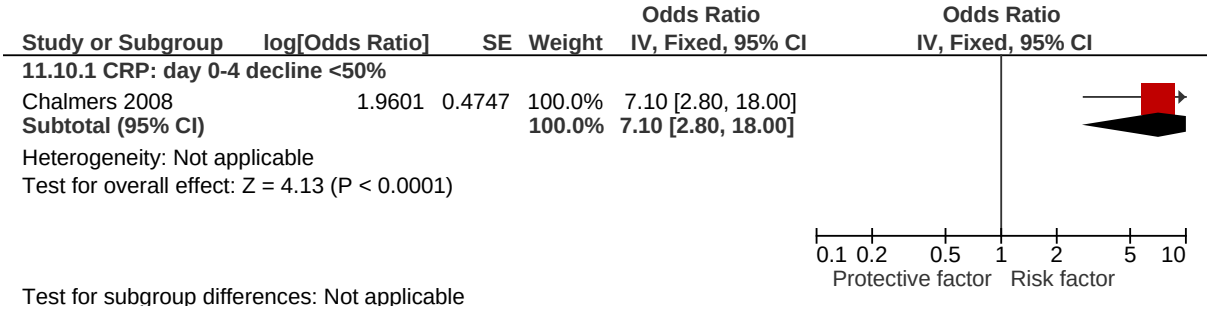
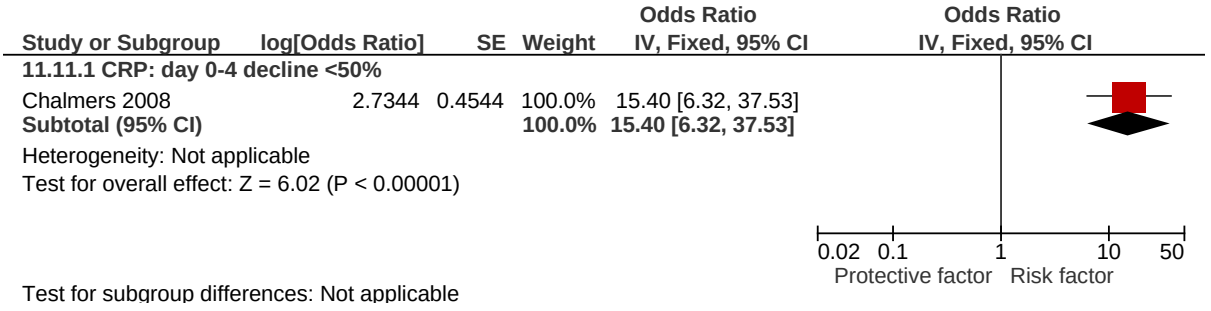


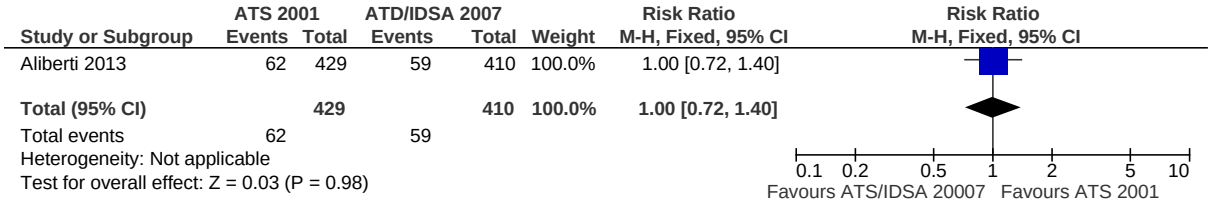
Figure 187: Complicated pneumonia



1.8 Safe discharge

1.8.1 Clinical outcomes of patients who reached clinical stability according to ATS 2001 and ATS/IDSA 2007 criteria of clinical stability or number of instabilities

Figure 188: Hospital re-admission 30 days after discharge



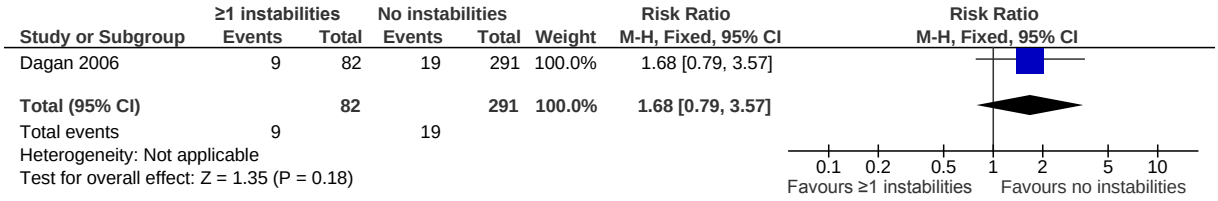
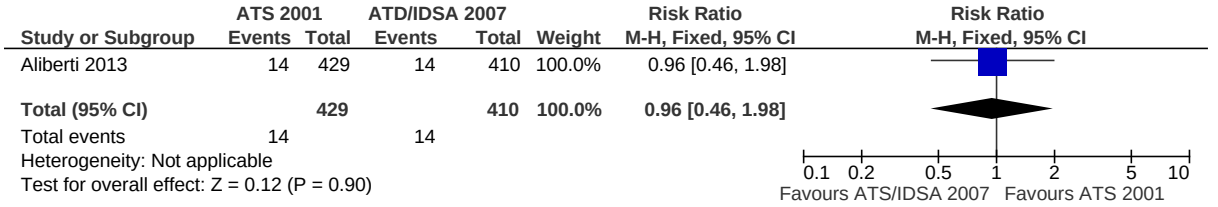
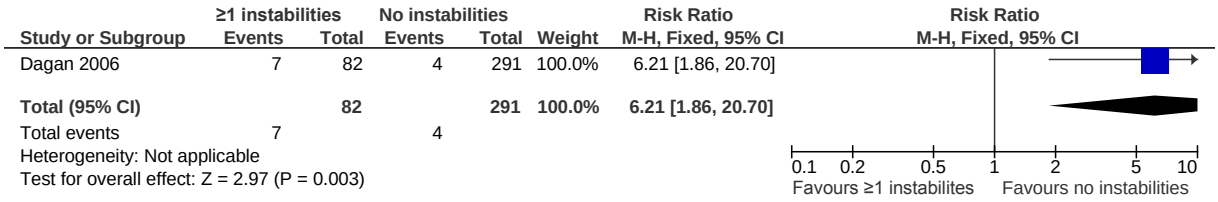


Figure 189: Mortality 30 days after discharge





1.9 Patient information

No forest plots were generated for this question.

2 HAP

2.1 Diagnostic tests

No data available.

2.2 Severity assessment

No data available.

2.3 Microbiological tests

No data available.

2.4 Antibiotic therapy

2.4.1 Single- compared with other single-antibiotic therapy

2.4.1.1 Respiratory fluoroquinolone compared with cephalosporin

Figure 190: All-cause mortality

Study or Subgroup	Moxifloxacin Events	Total	Ceftriaxone Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hoffken 2007	8	77	11	82	100.0%	0.77 [0.33, 1.82]
Total (95% CI)		**77**		**82**	**100.0%**	**0.77 [0.33, 1.82]**
Total events	8		11			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.56)

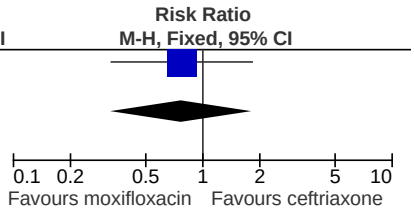


Figure 191: Clinical cure or improvement at end of follow-up

Study or Subgroup	Moxifloxacin Events	Total	Ceftriaxone Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hoffken 2007	56	77	56	82	100.0%	1.06 [0.87, 1.30]
Total (95% CI)		**77**		**82**	**100.0%**	**1.06 [0.87, 1.30]**
Total events	56		56			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.61 (P = 0.54)

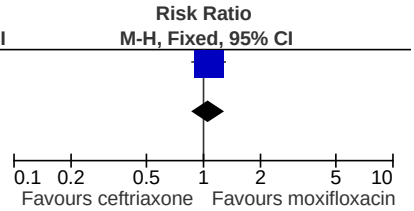
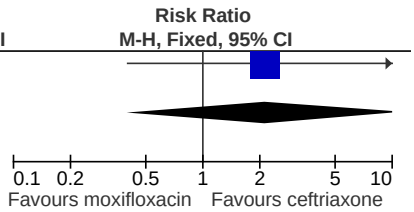


Figure 192: Withdrawal due to adverse events

Study or Subgroup	Moxifloxacin Events	Total	Ceftriaxone Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hoffken 2007	4	78	2	83	100.0%	2.13 [0.40, 11.29]
Total (95% CI)		**78**		**83**	**100.0%**	**2.13 [0.40, 11.29]**
Total events	4		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.89 (P = 0.38)



2.4.1.2 Beta-lactamase-stable penicillin compared with carbapenem

Figure 193: All cause mortality

Study or Subgroup	Favours piperacillin-tazobactam Events	Total	Imipenem-cilastatin Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Schmitt 2006	17	110	11	111	100.0%	1.56 [0.77, 3.18]
Total (95% CI)		**110**		**111**	**100.0%**	**1.56 [0.77, 3.18]**
Total events	17		11			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.22 (P = 0.22)

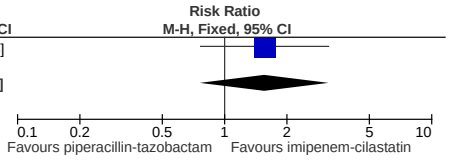


Figure 194: Clinical cure at end of treatment

Study or Subgroup	Piperacillin-tazobactam Events	Total	Imipenem-cilastatin Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Schmitt 2006	76	107	85	110	100.0%	0.92 [0.78, 1.08]
Total (95% CI)		**107**		**110**	**100.0%**	**0.92 [0.78, 1.08]**
Total events	76		85			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.05 (P = 0.30)

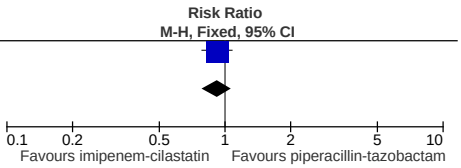


Figure 195: Clinical cure at end of follow-up

Study or Subgroup	Piperacillin-tazobactam Events	Total	Imipenem-cilastatin Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Schmitt 2006	64	107	73	110	100.0%	0.90 [0.73, 1.11]
Total (95% CI)		**107**		**110**	**100.0%**	**0.90 [0.73, 1.11]**
Total events	64		73			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.00 (P = 0.32)

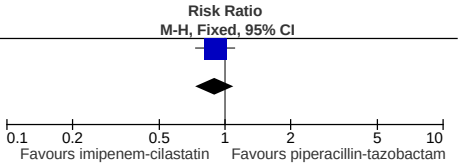
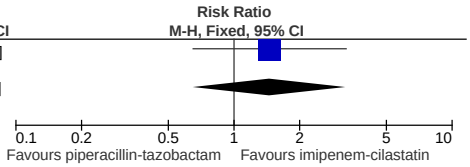


Figure 196: Withdrawal due to adverse events

Study or Subgroup	Piperacillin-tazobactam Events	Total	Imipenem-cilastatin Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Schmitt 2006	13	110	9	111	100.0%	1.46 [0.65, 3.27]
Total (95% CI)		**110**		**111**	**100.0%**	**1.46 [0.65, 3.27]**
Total events	13		9			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.91 (P = 0.36)



2.4.2 Single- compared with dual-antibiotic therapy

2.4.2.1 Cephalosporin compared with cephalosporin plus aminoglycoside

Table 1: All-cause mortality

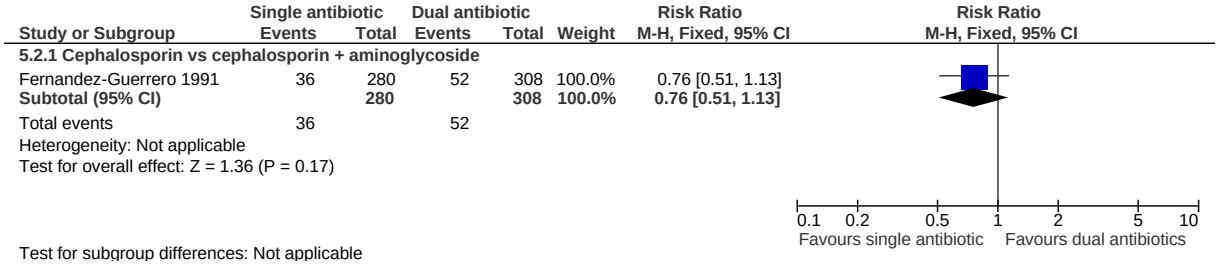
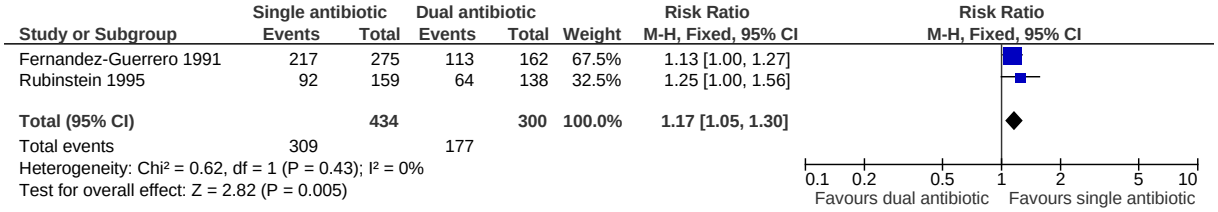


Table 2: Clincal cure at end of treatment



2.4.2.2 Carbapenem versus cephalosporin plus aminoglycoside

Figure 197: Clinical cure at end of treatment

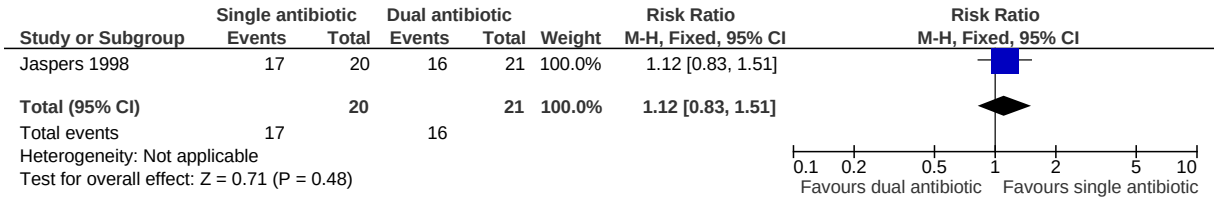
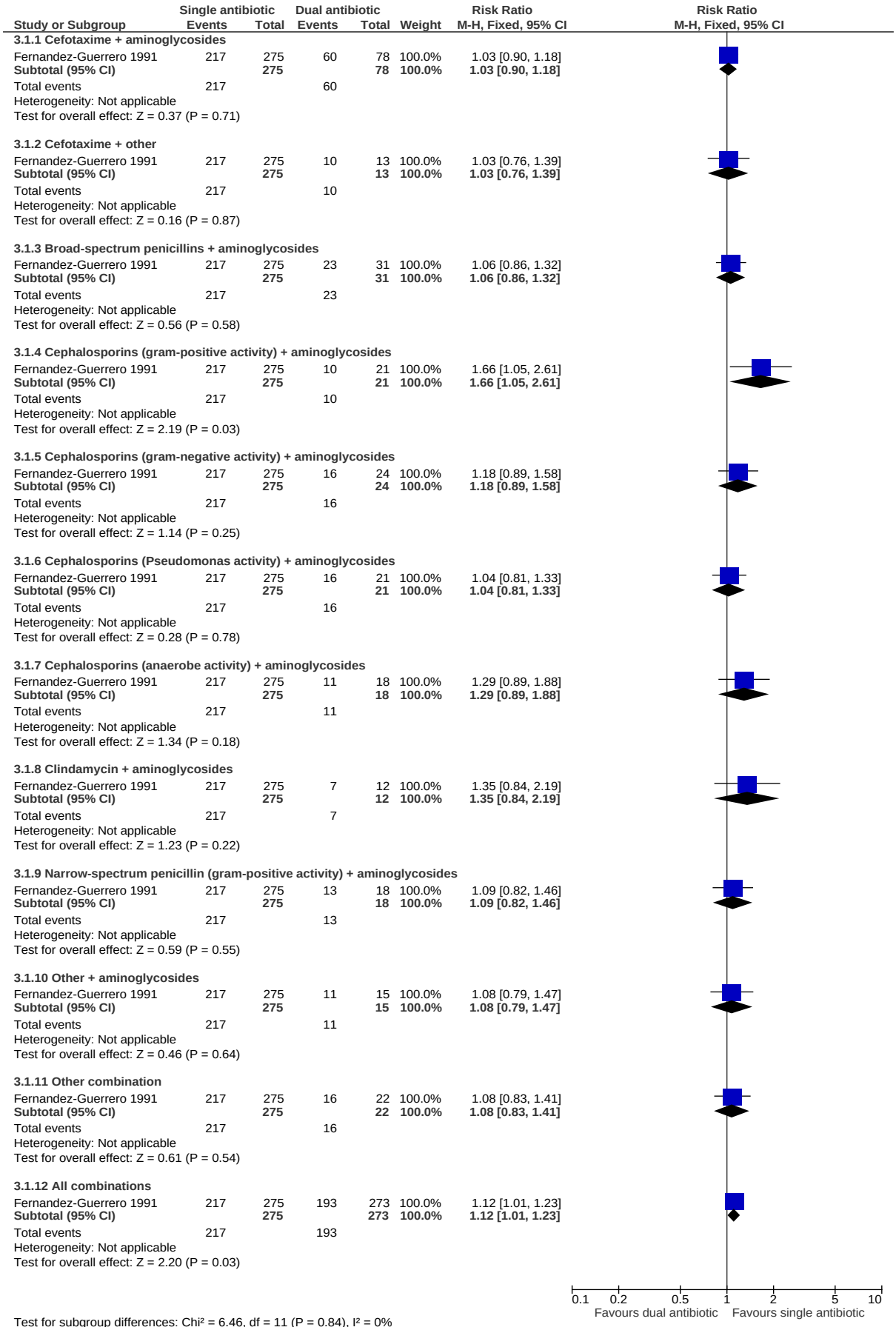


Table 3: Clinical cure at end of treatment (comparison subgroups from Fernandez-Guerrero 1991)



2.4.3 Dual- compared with other dual-antibiotic therapy

2.4.3.1 Beta-lactamase stable penicillin plus aminoglycoside compared with cephalosporin plus aminoglycoside

Figure 198: All-cause mortality

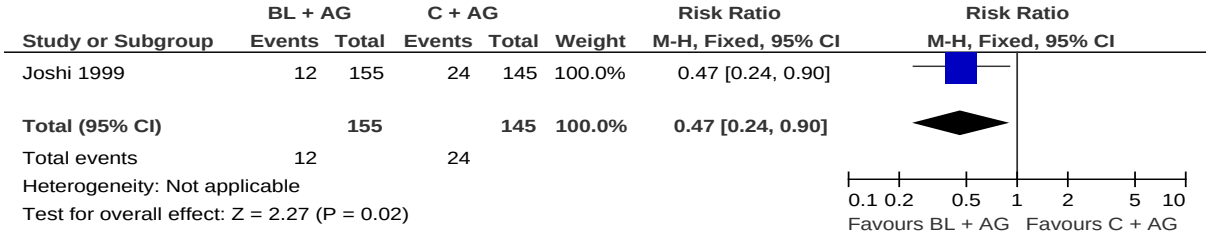


Figure 199: Clinical cure or improvement at end of follow-up

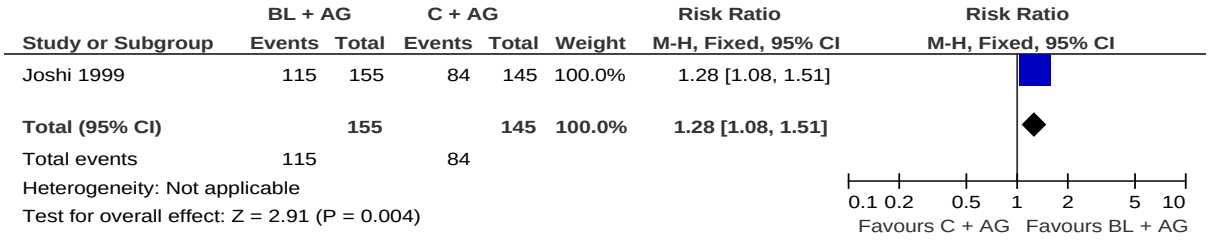


Figure 200: Withdrawal due to adverse events

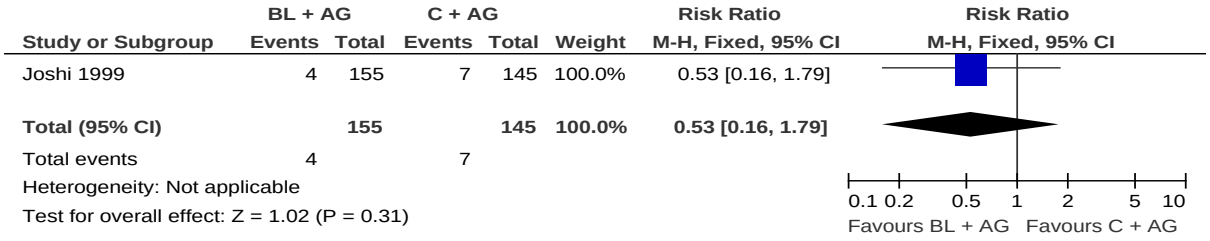
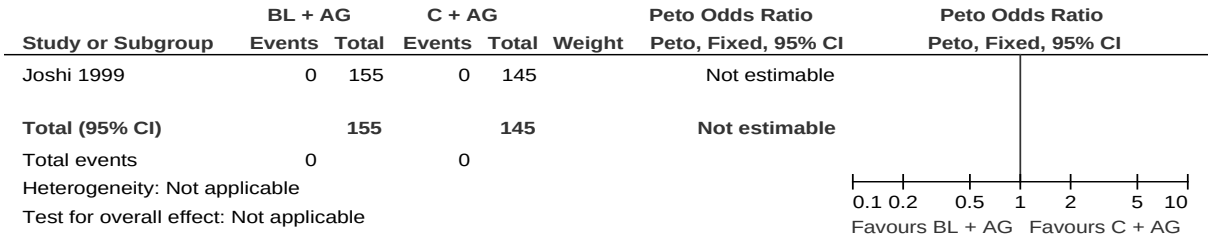


Figure 201: C. diffiile-associated diarrhoea



2.4.4 Duration of antibiotic therapy

No data available.

2.4.5 Timing of antibiotic therapy

No data available.

2.5 Glucocorticosteroid treatment

No data available.

2.6 Gas exchange

No data available.

2.7 Monitoring

No data available.

2.8 Safe discharge

No data available.

2.9 Patient information

No data available.