

Procalcitonin to Guide Antibiotic Therapy for Respiratory Infections:



A Systematic Review of Systematic Reviews

Joshua A York, Maithili Varadarajan, Joseph Yates, Gavin Barlow



Introduction

Antimicrobial resistance is of major international concern and closely linked to antibiotic use. Safely reducing antibiotic course length and overall use are imperative. Procalcitonin (PCT) is a biomarker expressed in serum in response to bacterial infection¹. Systematic reviews (SRs) evaluating PCT as an adjunct to guide antibiotic therapy have been performed, but its use remains contentious. The aim of this SR of SRs was to evaluate the extent to which PCT impacts the likelihood of antibiotic initiation and antibiotic duration in respiratory infections.

Methods

A systematic search of databases using an *a priori* strategy was conducted. SRs which reported an outcome related to antibiotic initiation and/or duration in the context of respiratory infection were included. Data extraction was performed by the first author and checked independently by a second author. The quality of SRs was assessed by three authors independently using ROBIS criteria³. Disagreements were resolved by consensus, or if necessary, a fourth author. Results are presented narratively and in tabular format (Table 1 and Table 2).

Table 1: Summary of odds ratios/ risk ratios for antibiotic initiation with use of procalcitonin

Year	First author	Population	Type	Number of studies	Number of participants	Antibiotic initiation OR/RR in PCT group versus control (<i>a</i> = OR, <i>b</i> = RR)	P-value
2011	Li H	General respiratory Infections	SR and Meta-analysis (MA)	7	3431	0.69 (0.55 to 0.88) <i>b</i>	p=0.03
2015	Westwood M	Respiratory infections in ED	SR and MA	9	3637	0.77 (0.68 to 0.87) (adults) <i>b</i>	Not given
2017	Ibrahim WH	Adults with acute asthma	SR and MA	4	457	0.58 (0.50-0.67) <i>b</i>	p<0.00001
2017	Mathioudakis AG	Acute exacerbations of COPD	SR and MA	7	974	0.56 (0.43 to 0.73) <i>b</i>	p<0.0001
2017	Schuetz P	Respiratory infections in ED/Primary Care	SR and MA	26	6708	0.27 (0.24 to 0.32) <i>a</i>	p<0.001
2017	Odermatt J	Respiratory infections in Primary Care	SR and MA	2	644	0.2 (0.1 to 0.3) <i>a</i>	p<0.001
2018	Lin C	Acute exacerbations of COPD	SR and MA	4	679	0.26 (0.14 to 0.50) <i>a</i>	p<0.0001
2018	Hey J	Adults with lower respiratory infections	SR and MA	10	3912	0.26 (0.13 to 0.52) <i>a</i>	p<0.001

Results

13 SRs were included (see PRISMA diagram). The number of respiratory patients included in these SRs ranged from 308 to 6708 (median = 3457). There was a consistent finding of a statistically significant reduction in antibiotic initiation in the PCT study group compared to the control group (Table 1). SRs that meta-analysed antibiotic duration (n = 9) as a difference in days showed a median reduction of 2.35 days (reduction range 1.27 to 4.49 days) with PCT use. 10 SRs examined mortality with procalcitonin versus standard of care. 9 found no significant difference, whilst 1 found that in a patient level data analysis, there was a significant reduction in mortality with procalcitonin use. This effect was not observed in the non patient level analysis carried out in the same SR. 4 of the 13 SRs were found to have an area with a high risk of bias, whilst 1 paper had an unclear risk of bias.

Figure 1: PRISMA Flow Diagram of Search⁴

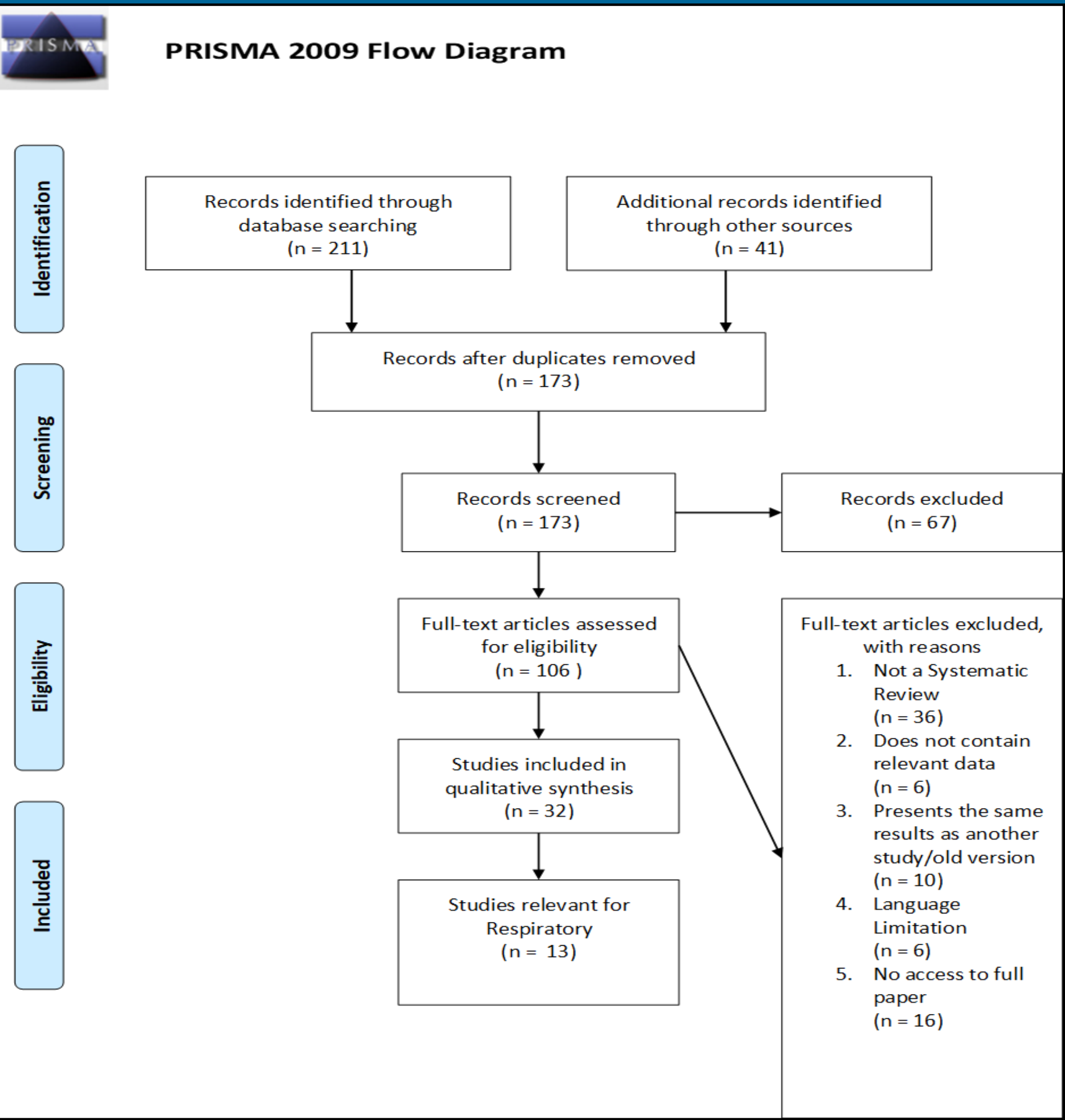


Figure 2: Antibiotic Initiation OR/RR against Year of SR.

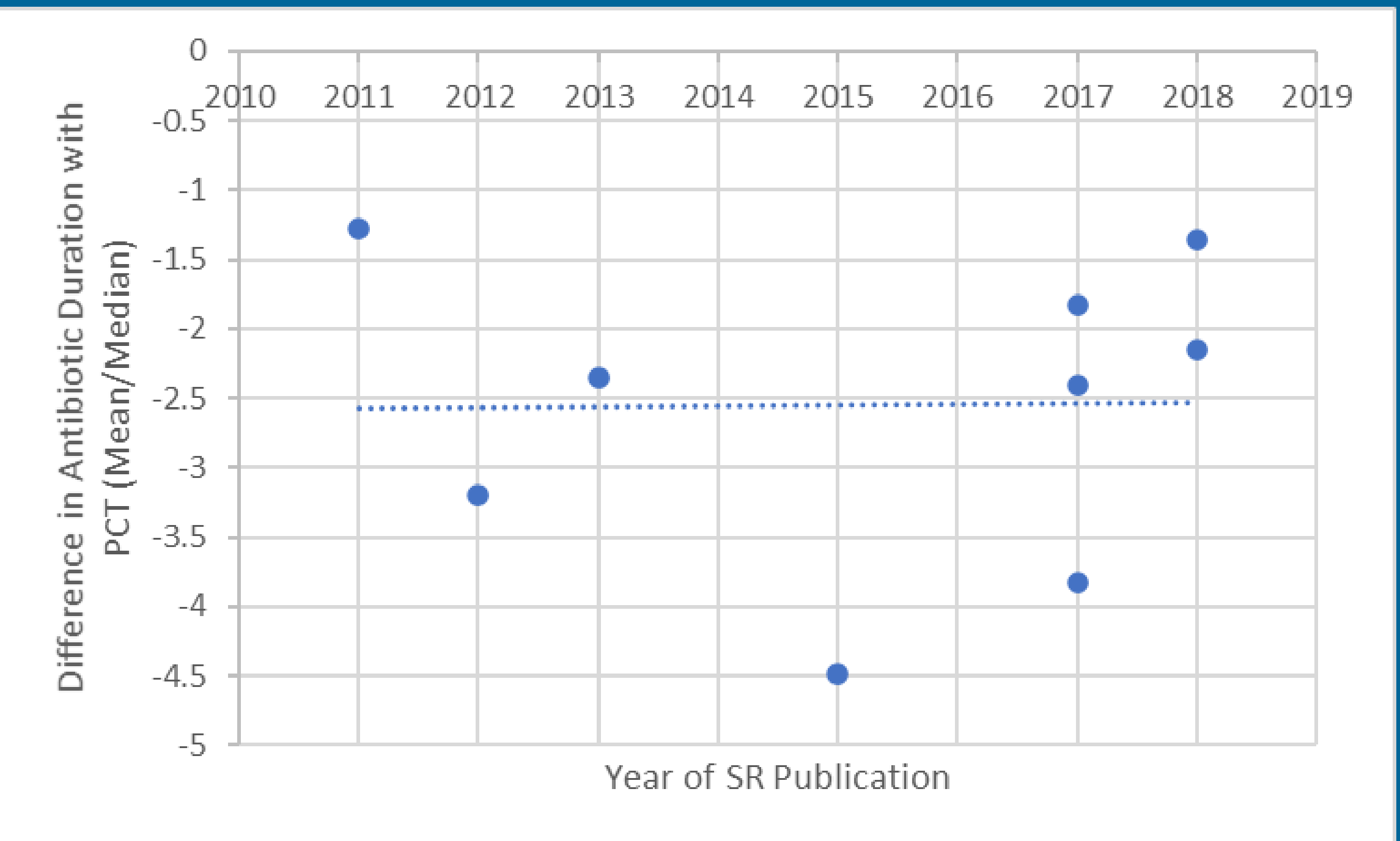


Table 2: Summary of antibiotic duration differences with use of procalcitonin

Year	First author	Population	Type	Number of studies	Number of participants	Duration reduction (Mean/median days)	P-value
2011	Li H	General respiratory infections	SR and MA	7	3223	-1.27	p<0.001
2012	Pugh R	HAP or VAP in ICU	SR and MA	3	308	-3.20	p<0.00001
2013	Soni NJ	General respiratory infections	SR and MA	7	3284	-2.35	p=0.02
2015	Westwood M	Lower respiratory tract infections	SR and MA	2	545	-4.49	Not given
2017	Mathioudakis AG	Acute exacerbation of COPD	SR and MA	6	776	-3.83	Not given
2017	Schuetz P	Respiratory infections in ED/Primary Care	SR and patient data MA	26	6708	-1.83	p<0.001
2017	Odermatt J	Respiratory infections in Primary Care	SR and patient data MA	2	644	-2.4	p<0.001
2018	Hey J	Adults with lower respiratory infections	SR and MA	9	3704	-2.15	p<0.001
2018	Wirz Y	Respiratory infections in ICU	SR and patient data MA	11	2203	-1.36	p=0.582

Conclusion

In SRs to date, PCT use has consistently resulted in a reduction in antibiotic initiation in respiratory infections. Additionally, when antibiotics were commenced, PCT was shown to significantly reduce antibiotic duration in most systematic reviews (by at least 1 day in 8 of 9 studies; by at least 2 days in 6 of 9 studies). Use of procalcitonin in this context appears to be safe with no evidence of increased mortality. There is a lack of data on the impact of procalcitonin use on antimicrobial resistance. Some of these data may be affected by a risk of bias in the systematic reviews.

References

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