

Appendix 1 Details of the literature search strategy

(1) PubMed (1977 to January 16, 2021)

Search	Query	Items found
#1	"Anti-Bacterial Agents"[Mesh]	385232
#2	(((((((((((((Anti Bacterial Agents[Title/Abstract]) OR Agents, Antibacterial[Title/Abstract]) OR Bacteriocidal Agents[Title/Abstract]) OR Bacteriocides[Title/Abstract]) OR Antimycobacterial Agent*[Title/Abstract]) OR antibiotic*[Title/Abstract]) OR antibacterial[Title/Abstract]) OR anti-acterial[Title/Abstract]) OR amoxicillin[Title/Abstract]) OR amoxycillin[Title/Abstract]) OR penicillin[Title/Abstract]) OR ampicillin[Title/Abstract]) OR cotrimoxazole[Title/Abstract]) OR chloramphenicol[Title/Abstract]) OR trimethoprim[Title/Abstract]) OR sulphamethoxazole[Title/Abstract]) OR tmp smx[Title/Abstract]) OR tmp- mx[Title/Abstract]	506080
#3	#1OR#2	687035
#4	"C-Reactive Protein"[Mesh]	47029
#5	((c reactive protein[Title/Abstract]) OR c-reactive protein[Title/Abstract]) OR CRP[Title/Abstract]	87077
#6	#4 OR #5	95790
#7	#3 AND #6	5215
#8	#7 AND ("Randomized Controlled Trial" [Publication Type] OR "Controlled Clinical Trial" [Publication Type] OR "Clinical Trials as Topic"[Mesh:NoExp] OR randomized[Title/Abstract] OR placebo [Title/Abstract] OR randomly[Title/Abstract] OR trial[Title/Abstract]) NOT ("Animals"[Mesh] NOT "Humans"[Mesh])	341

(2) Embase (1974 to January 16, 2021)

Search	Query	Items found
#1	'anti bacterial agents':ab,ti OR 'agents, antibacterial':ab,ti OR 'bacteriocidal agents':ab,ti OR bacteriocides:ab,ti OR 'antimycobacterial agent*':ab,ti OR antibiotic*:ab,ti OR antibacterial:ab,ti OR 'anti-bacterial':ab,ti OR amoxicillin:ab,ti OR amoxycillin:ab,ti OR penicillin:ab,ti OR ampicillin:ab,ti OR cotrimoxazole:ab,ti OR chloramphenicol:ab,ti OR trimethoprim:ab,ti OR sulphamethoxazole:ab,ti OR 'tmp smx':ab,ti OR 'tmp-smx':ab,ti	645998
#2	'c reactive protein'/exp	187951
#3	'c reactive protein':ab,ti OR 'c-reactive protein':ab,ti OR crp:ab,ti	151134
#4	#2 OR #3	230851
#5	#1 AND #4	13894
#6	random*:ab,ti	1615319
#7	#5 AND #6	805

(3) Cochrane Library (January 16, 2021)

Search	Query	Items found
#1	MeSH descriptor: [Anti-Bacterial Agents] explode all trees	12180
#2	("Anti Bacterial Agents"):ti,ab,kw OR ("Agents, Antibacterial"):ti,ab,kw OR (Bacteriocidal Agents):ti,ab,kw OR ("Bacteriocides"):ti,ab,kw OR ("Antimycobacterial Agent*"):ti,ab,kw	12986
#3	("antibiotic*"):ti,ab,kw OR ("antibacterial"):ti,ab,kw OR ("anti-bacterial"):ti,ab,kw OR ("amoxicillin"):ti,ab,kw OR ("amoxicillin") ti,ab,kw	40350
#4	("penicillin"):ti,ab,kw OR ("ampicillin"):ti,ab,kw OR (cotrimoxazole):ti,ab,kw OR ("chloramphenicol"):ti,ab,kw OR ("trimethoprim"):ti,ab,kw	6942
#5	("sulphamethoxazole"):ti,ab,kw OR ("tmp smx"):ti,ab,kw OR (tmp-smx):ti,ab,kw	416
#6	#1 OR #2 OR #3 OR #4 OR #5	45850
#7	MeSH descriptor: [C-Reactive Protein] explode all trees	4637
#8	("c reactive protein"):ti,ab,kw OR (c-reactive protein):ti,ab,kw OR (CRP):ti,ab,kw	25632
#9	#7 OR #8	25632
#10	#6 AND #9	1194
#11	("antibiotic*"):ti,ab,kw	1037710
#12	#10 AND #11	885

Table S1 Results of sensitivity analysis

Outcomes	Deletion	Result	
Antibiotic prescribing rate at the index consultation	Prins 2019	$\chi^2=16.25$; $P=0.006$; $I^2=69\%$	RR: 0.75; 95% CI: 0.71–0.80
	Butler 2019	$\chi^2=16.41$; $P=0.006$; $I^2=70\%$	RR: 0.75; 95% CI: 0.71–0.81
	Diederichsen 2000	$\chi^2=5.96$; $P=0.31$; $I^2=16\%$	RR: 0.71; 95% CI: 0.66–0.76
	Do 2016	$\chi^2=13.20$; $P=0.02$; $I^2=62\%$	RR: 0.78; 95% CI: 0.73–0.84
	Cals 2010	$\chi^2=16.37$; $P=0.006$; $I^2=69\%$	RR: 0.75; 95% CI: 0.70–0.80
	Gonzales 2011	$\chi^2=12.85$; $P=0.02$; $I^2=61\%$	RR: 0.74; 95% CI: 0.70–0.79
	Francis 2020	$\chi^2=14.63$; $P=0.01$; $I^2=66\%$	RR: 0.77; 95% CI: 0.71–0.82

RR, risk ratio; CI, confidence interval.

Table S2 Adverse events

Study	Adverse events	The number of events	
		CRP testing	Routine care
Prins 2019 (29)	Hyperglycaemia	1	5
	Steroid induced myopathy		
	Oral candidiasis		
	Urinary retention bladder		
Butler 2019 (30)	Pneumonia	9	12
Do 2016 (32)	Hospital admissions	6	8
Cals 2010 (33)	Death or hospitalization	These serious adverse events were not related to the intervention or to trial participation	
Francis 2020 (35)	Died	These serious adverse events were not related to the intervention or to trial participation	

CRP, C-reactive protein.

Table S3 Summary of subgroup analyses about antibiotic prescribing rate at the index consultation

Basis of subgroup	Subgroup	No. of trials	No. of participants	Mean difference (95% CI)	Heterogeneity (I^2)
Type of ARI	Low ARI	3	1,405	0.71 (0.65–0.78); P<0.00001	0%
	Upper ARI	4	2,209	0.83 (0.66–1.03); P=0.09	78%
CRP level as recommended	40 mg/L	2	1,185	0.71 (0.65–0.78); P<0.00001	0%
	50 mg/L	2	1,032	0.83 (0.62–1.12); P=0.23	62%
	100 mg/L	3	1,397	0.77 (0.61–0.98); P=0.03	62%

CI, confidence interval; ARI, acute respiratory tract infections; CRP, C-reactive protein.