Appendix 3 Sensitivity analyses for the comparison between antibiotics versus placebo/standard care

Table A Sensitivity analyses using alternative effect measures

Outcomes	No. of trials	Events/total		RR(95%CI)	P value	I^2	Tau^2
		Antibiotics	Placebo/ standard care	M-H, Random			
Treatment failure within 1 month							
Antibiotics vs Placebo	8	110/1396	165/1121	0.62(0.42,0.91)	0.02	48%	0.12
Recurrence within 1 month							
Antibiotics vs Placebo	6	93/1213	134/921	0.53(0.35,0.80)	0.003	45%	0.11
Late recurrence 1 to 3 months							
Antibiotics vs Placebo	2	96/550	140/561	0.72(0.54,0.97)	0.03	18%	0.01
Hospitalization							
Antibiotics vs Placebo	2	19/597	35/609	0.56(0.33,0.96)	0.04	0%	0.00
Gastrointestinal side effects							
TMP-SMX vs Placebo	4	303/1064	252/1072	1.18(1.03,1.34)	0.02	0%	0.00
Clindamycin vs Placebo	1	49/265	23/255	2.05(1.29,3.26)	0.002	-	-
Nausea							

TMP-SMX vs Placebo	3	149/987	108/988	1.44(0.91,2.28)	0.12	19%	0.06
Clindamycin vs Placebo	1	6/265	6/255	0.96(0.31,2.94)	0.95	-	-
Diarrhoea							
TMP-SMX vs Placebo	3	111/964	117/948	0.93(0.73,1.19)	0.57	0%	0.00
Clindamycin vs Placebo	1	43/265	17/255	2.43(1.43,4.15)	0.001	-	-
Anaphylaxis							
TMP-SMX vs Placebo	3	7/434	3/455	1.78(0.49,6.42)	0.38	0%	0.00
Clindamycin vs Placebo	1	7/265	3/255	2.25(0.59,8.59)	0.24	-	-
Death							
TMP-SMX vs Placebo	2	1/891	1/872	0.98(0.06,15.62)	0.99	-	-
Clindamycin vs Placebo	1	0/265	0/255	-	-	-	-
Sepsis							
TMP-SMX vs Placebo	1	1/630	0/617	2.94(0.12,71.99)	0.51	-	-

Table B Sensitivity analyses using alternative statistical model

Outcomes	No. of trials	Events/total		OR(95%CI)	P value	I^2
		Antibiotics	Placebo/ standard care	M-H, Fixed		
Late reccurence						
Antibiotics vs Placebo	2	96/550	140/561	0.64(0.48.0.85)	0.003	0%
Hospitalization						
Antibiotics vs Placebo	2	19/597	35/609	0.54(0.31,0.96)	0.03	0%
Gastrointestinal side effects						
TMP-SMX vs Placebo	4	303/1064	252/1072	1.30(1.05,1.60)	0.01	0%
Clindamycin vs Placebo	1	49/265	23/255	2.29(1.35,3.88)	0.002	-
Nausea						
TMP-SMX vs Placebo	3	149/987	108/988	1.44(1.10,1.90)	0.008	11%
Clindamycin vs Placebo	1	6/265	6/255	0.96(0.31,3.32)	0.95	-
Diarrhoea						
TMP-SMX vs Placebo	3	111/964	117/948	0.92(0.70,1.22)	0.56	0%
Clindamycin vs Placebo	1	43/265	17/255	2.71(1.50,4.89)	0.0009	-

Anaphylaxis	3	14/699	3/455	2.41(0.80,7.22)	0.12	0%
TMP-SMX vs Placebo	3	7/434	3/455	2.10(0.63,6.96)	0.23	0%
Clindamycin vs Placebo	1	7/265	3/255	2.28(0.58,8.91)	0.24	-

Table C Sensitivity analyses using alternative pooling method

Outcomes	No. of trials	Events/total		OR(95%CI)	P value	I^2	Tau^2
		Antibiotics	Placebo/ standard care	M-H, Random			
Hospitalization							
Antibiotics vs Placebo	2	19/597	35/609	0.54(0.31,0.96)	0.04	0%	0.00
Infections in family members							
TMP-SMX vs Placebo	1	20/504	34/509	0.58(0.33,1.02)	0.06	-	-
Invasive infections (1 month)							
TMP-SMX vs Placebo	1	2/524	2/533	1.02(0.14,7.25)	0.99	-	-
Invasive infections (3 month)							
TMP-SMX vs Placebo	1	1/504	0/509	3.04(0.12,74.70)	0.50	-	-
Anaphylactic reaction							
TMP-SMX vs Placebo	3	7/434	3/455	1.80(0.49,6.58)	0.38	0%	0.00
Clindamycin vs Placebo	1	7/265	3/255	2.28(0.58, 8.91)	0.24	-	-
Sepsis							
TMP-SMX vs Placebo	1	1/630	0/617	2.94(0.12,72.38)	0.51	-	-

Death							
TMP-SMX vs Placebo	2	1/891	1/872	0.98(0.06,15.69)	0.99	-	-

Table D Sensitivity analyses using different inclusion criteria and different definition of treatment failure

Outcomes	No. of trials	Events/total		OR(95%CI)	P value	I^2	Tau^2
		Antibiotics	Placebo/ standard care	M-H, Random			
Sensitivity analyses by omiting trials exclusively reporting recurrence							
Treatment failure within 1 month	6	101/1262	157/1036	0.56 (0.35,0.90)	0.02	53%	0.16
Sensitivity analyses by omiting trials with patients treated by primary suture							
Treatment failure within 1 month	7	101/1319	160/1077	0.54 (0.34,0.86)	0.010	49%	0.16
Recurrence within 1 month	5	84/1136	129/877	0.43 (0.27,0.71)	0.0008	45%	0.13
Sensitivity analyses by omiting trials published before 1990							
Treatment failure within 1 month	5	100/1235	156/1013	0.56 (0.34,0.93)	0.03	62%	0.19
Recurrence within 1 month	4	84/1079	126/836	0.45 (0.27,0.74)	0.002	51%	0.13

Table E Sensitivity analyses using alternative methods of random effects meta-analysis

Outcomes	No. of trials	Events/total		OR (95%CI)	P value
		Antibiotics	Placebo/ standard care	HKSJ	
Treatment failure within 1 month					
Antibiotics vs Placebo	8	110/1396	165/1121	0.58 (0.33,1.01)	0.05
Recurrence within 1 month					
Antibiotics vs Placebo	6	93/1213	134/921	0.48 (0.26,0.88)	0.03
Late recurrence 1 to 3 month					
Antibiotics vs Placebo	2	96/550	140/561	0.64 (0.10,4.08)	0.20
Hospitalization					
Antibiotics vs Placebo	2	19/597	35/609	0.54 (0.19,1.56)	0.09
Gastrointestinal side effects					
TMP-SMX vs Placebo	4	303/1064	252/1072	1.28 (0.92,1.78)	0.10
Nausea					
TMP-SMX vs Placebo	3	149/987	108/988	1.49 (0.58,3.82)	0.21
Diarrhoea					
TMP-SMX vs Placebo	3	111/964	117/948	0.92 (0.74,1.15)	0.25

Anaphylaxis					
TMP-SMX vs Placebo	3	7/434	3/455	1.80(0.13,24.56)	0.44

HKSJ=Hartung-Knapp-Sidik-Jonkman

Table F Sensitivity analyses using different assumptions about missing data

Assumptions	No. of trials	Events/total		OR(95%CI)	P value	I^2	Tau^2
		Antibiotics	Placebo/ standard care				
Treatment failure within 1 month							
None has event*	8	110/1597	165/1293	0.59 (0.38,0.91)	0.02	46%	0.15
All had event†	8	311/1597	337/1293	0.71 (0.51,0.97)	0.03	46%	0.08
Best case scenario††	8	110/1597	337/1293	0.28 (0.15,0.53)	<0.0001	78%	0.52
Worst case scenario‡	8	311/1597	165/1293	1.59 (0.97,2.60)	0.07	68%	0.26
Worst plausible analysis #	8	183/1597	191/1293	0.82 (0.56,1.19)	0.30	44%	0.29
Recurrence within 1 month							
None has event*	6	93/1472	134/1171	0.52 (0.30,0.89)	0.02	57%	0.22
All had event†	6	352/1472	384/1171	0.62 (0.48,0.79)	0.0002	27%	0.02
Best case scenario††	6	93/1472	384/1171	0.15 (0.07,0.31)	<0.00001	82%	0.58
Worst case scenario‡	6	352/1472	134/1171	2.02 (0.96,4.24)	0.06	86%	0.62
Worst plausible analysis	6	193/1472	177/1171	0.83 (0.53,1.29)	0.4	61%	0.16
Later recurrence 1 to 3 month							
Worst plausible analysis #	2	187/713	178/713	1.48 (0.55,3.96)	0.44	87%	0.45

***Hospitalizations*§**							
Worst plausible analysis #	2	39/713	41/713	0.94 (0.60,1.47)	0.78	0%	0.00
Pain (tenderness) (3 to 4 days)							
Worst plausible analysis #	1	337/636	352/629	0.89 (0.71,1.11)	0.29	-	-
Pain (tenderness) (8 to 10 days)							
Worst plausible analysis #	1	63/636	64/629	0.97 (0.67,1.40)	0.87	-	-
Additional surgical procedures							
Worst plausible analysis #	1	97/636	85/629	1.15 (0.84,1.58)	0.38	-	-

***** All the participants lost to follow up did not have the event;

†All the participants lost to follow up had the event;

†† None of those lost to follow-up in the treatment group had the event and all those lost to follow-up in the control group did;

‡ All participants lost to follow-up in the treatment group had the event and none of those in the control group did;

Worst plausible analysis: Meta-analysis using the plausible most stringent $RI_{MPD/FU}$ (the incidence of outcome events in participants with missing data relative to those with complete follow-up). We defined a constant $RI_{MPD/FU}$ of 1.0 for control group missing participants, and 1.5, 2, 3, 5 for antibiotics group when the event rate was >40%, 30-40%, 10-30%, <10% respectively.

§ Pooled data using Peto's methods