Appendix 2

Table A Inclusion criteria of abscess and definition of treatment failure/cure as reported in the included trials

Author (year)	Inclusion criteria of abscesses	Definition of treatment failure/cure
RCTs comparing antibiotics versus placebo or standard care		
Daum 2017[9]	A single abscess (defined as a circumscribed, drainable collection of pus) with a greatest diameter of 5.0 cm or less (⩽3 cm for participants 6 to 11 months of age and ⩽4 cm for participants 1 to 8 years of age), evidenced by two or more of the following signs or symptoms for at least 24 hours: erythema, swelling or induration, local warmth, purulent drainage, and tenderness to pain or palpation.	A lack of clinical cure was defined as lack of resolution of signs or symptoms of the infection, an inability to continue taking the study agent because of adverse effects within the first 48 hours, or any one of the following: recurrence at the original site of infection or occurrence of a skin infection at a new body site, unplanned surgical treatment of the skin infection, or hospitalization related to the infection.
Duong 2010[24]	Skin abscesses and were nontoxic, with temperature less than 38.4 °C, skin abscess included the presence of all of the following features: (1) acute onset within 1 week, (2) fluctuance,(3) erythema, (4) induration, and (5) tenderness, with or without purulent drainage.	Treatment failure was defined as the presence of any of the signs or symptoms (erythema, warmth, induration, fluctuance, tenderness, and drainage) at the 10-day follow-up or worsening signs or symptoms before the 10-day follow-up requiring further surgical drainage, change in medication, or hospital admission for intravenous antibiotics. New lesions within 5 cm of the original abscess site were also considered treatment failures. New lesions may consist of folliculitis, furuncles, carbuncles, or abscesses.
Llera 1985[25]	Localized collection of pus causing a fluctuant soft tissue swelling and surrounded by firm granulation tissue and erythema.	It considered treatment failure if any sign of fluctuance, drainage, induration, warmth, or tendemess was present at seven days.

Macfie 1977[28]	Acute superficial abscesses	A recurrence was recorded first, if a further collection of pus appeared at the same site as the original incision, and secondly, if signs of infection, discharge or inflammation reappeared or persisted and became worse following incision.
Rajendran 2007[27]	Diagnostic criteria for an abscess:(1) acute onset within 7 days prior to enrollment; (2) purulent drainage or purulent aspirate; (3) erythema, induration (≥2 cm in diameter), or tenderness; and (4) evidence of lobulated fluid at time of enrollment	Clinical cure: at the 1-week follow-up visit if there was resolution of the following signs and symptoms: purulent wound drainage, erythema, fluctuance, localized warmth, pain/tenderness, and edema/induration Treatment failure, defined as the presence of any of those above symptoms.
Schmitz 2010[26]	Uncomplicated skin abscesses requiring incision and drainage	Treatment failure defined as no improvement after 2 days, development of a new separate lesion or worsening infection (required evidence of an increased diameter of abscess or cellulitis, or the presence of fever or systemic response) within 7 days, leading to an intervention.
Talan 2016[10]	A fluctuant and/or indurated lesion, or findings of a fluid-filled cavity on soft tissue ultrasound evaluation that, when opened reveals purulent material, receiving I&D and having a minimum diameter (along any axis) of at least 2 cm (measured from the borders of induration, if a fluctuant lesion, or borders of the abscess cavity on ultrasound, if not fluctuant)	Clinical failure was defined as fever, an increase in the maximal dimension of erythema by >25% from baseline, or worsening of wound swelling and tenderness by the visit during the treatment period (day 3 or 4); fever, no decrease in the maximal dimension of erythema from baseline, or no decrease in swelling or tenderness by the visit at the end of the treatment period (day 8–10); and fever or more than minimal erythema, swelling, or tenderness by the test-of-cure visit (day 14–21).
RCTs comparing alternative antibiotics		
Bucko 2002[29]	Mild to moderate uncomplicated skin or skin structure infections, at least 2 of the following local signs and symptoms: pain, tenderness, swelling, erythema, associated warmth, purulent drainage/discharge, induration, and regional lymph node swelling or tenderness	Patients were considered clinical cures if their pretreatment signs and symptoms of infection had improved or resolved and they did not need additional antibiotic therapy for the treatment of the skin or skin structure infection clinical failures: at the post treatment visit if they experienced either persistent or worsening signs and symptoms or an improvement only after the patient received additional antimicrobial therapy for the infection.

Giordano 2006[30]	A mild to moderate uncomplicated skin or skin structure infections, which included, but was not limited to, cellulitis, erysipelas, impetigo, simple abscess, wound infection, furunculosis, and folliculitis	Patients were considered clinical failure if they experienced persistent or worsening signs and symptoms, had onset of new USSSI signs/symptoms at the baseline infection site following at least 72 h of antibiotic therapy, or needed additional antimicrobial therapy for the skin infection.
Keiichi 1982[33]	Suppurative skin and soft tissue infections	No details provided
Miller 2015[32]	Patients with uncomplicated skin infections who had two or more of the following signs or symptoms for 24 or more hours: erythema, swelling or induration, local warmth, purulent drainage, and tenderness to pain or palpation. Abscess was defined as a circumscribed, drainable collection of pus.	A lack of clinical cure was defined as a lack of resolution of signs or symptoms of infection, the occurrence of side effects that necessitated discontinuation of treatment with the study medication within the first 48 hours, or any one of the following before the test-of-cure visit: occurrence of a skin infection at a new body site, unplanned surgical treatment of the skin infection, or hospitalization related to the infection.
Montero 1996[31]	Acute skin and/or soft tissue infections	Treatment failure was defined as no change in, or worsening of, signs and symptoms of infection.

USSSI= uncomplicated skin or skin structure infections

Table B Risk of bias of included randomised controlled trials

Author	Adequate randomisation sequence generation	Adequate allocation concealment	Blinding of participants	Blinding of caregivers	Blinding of outcome assessors	Infrequent missing outcome data‡
Bucko 2002a[29]	**Probably yes** Randomised, double-blind*	**Probably yes** Randomised, double-blind†	**Probably yes** Double-blind (details not reported)	**Probably yes** Double-blind (details not reported)	**Probably yes** Double-blind (details not reported)	**Probably yes** There were 8.9% (26/291), 9.2% (26/283), 6.4% (18/283) patients with missing data for cure rate at TOC in three groups, respectively
Bucko 2002b[29]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Probably yes** Double-blind (details not reported)	**Probably yes** Double-blind (details not reported)	**Probably yes** There were 7.2% (20/278), 6.5%(18/277), 9.2%(25/273) patients with missing data for cure rate at TOC in three groups, respectively
Daum 2017[9]	**Definitely yes** Variable-block randomisation was performed by an independent statistics and data-coordinating center	**Definitely yes** Variable-block randomisation was performed by an independent statistics and data-coordinating center	**Definitely yes** Participants and all study staff were unaware	**Definitely yes** Participants and all study staff were unaware	**Definitely yes** Participants and all study staff were unaware	**Probably no** There were 10.5% (28/266), 11.8% (31/263), 14.3% (37/257) patients with missing data in three groups for cure rate at TOC, respectively; **Definitely no** There were 12.0% (32/266), 14.1% (37/263),15.2% (39/257) patients with missing data for cure rate at 1 month in three groups, respectively

Duong 2010[24]	**Definitely yes** Computer randomisation	**Probably yes** Randomised, double-blind	**Definitely yes** The patient, parents, and clinician who assessed the clinical outcome were blinded to group assignment	**Definitely yes** The patient, parents, and clinician who assessed the clinical outcome were blinded to group assignment	**Definitely yes** The patient, parents, and clinician who assessed the clinical outcome were blinded to group assignment	**Probably yes** There were 9.6% (8/84) and 5.1% (4/77) patients in control and TMP groups with missing data for 10d treatment failure rate, respectively; **Definitely no** 37.3% (31/77) and 41.0% (32/84) patients in TMP and control groups with missing data for 30d new lesions, respectively
Giordano 2006[30]	**Definitely yes** Computer randomisation	**Probably yes** Details not reported, investigator-blinded	**Definitely no** Investigator-blinded	**Definitely yes** Investigator-blinded	**Probably yes** Investigator-blinded	**Probably no** There were 10.9% (21/192) and 13% (26/200) patients in Cefdinir and Cephalexin groups with missing data for cure rate at TOC, respectively
Keiichi 1982[33]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Probably yes** Double-blind (details not reported)	**Probably yes** Double-blind (details not reported)	**Definitely yes** Follow up rate was 100%
Llera 1985[25]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** The patient, examining physician, or investigators were blinded to group assignment.	**Definitely yes** The patient, examining physician, or investigators were blinded to group assignment.	**Definitely yes** The patient, examining physician, or investigators were blinded to group assignment.	**Definitely no** There were (31/81) 38% with missing outcome data in two groups

Macfie 1977[28]	**Probably yes** Details not reported, open-label	**Probably no** Details not reported, open-label††	**Definitely no** Open-label	**Definitely no** Open-label	**Definitely no** Open-label	**Probably no** Details not reported
Miller 2015[32]	**Definitely yes** Variable-block randomisation was performed by an independent statistics and data-coordinating center	**Definitely yes** Performed by an independent contract research organization (EMMES) that developed the randomisation code	**Definitely yes** Participants and all study staff were unaware of the study-group assignments	**Definitely yes** Participants and all study staff were unaware of the study-group assignments	**Definitely yes** Participants and all study staff were unaware of the study-group assignments	**Probably no** There were 8.6% (7/127) and 11.3% (13/115) patients with abscess in Clindamycin and TMP-SMX groups with missing data for cure rate at TOC, respectively
Montero 1996[31]	**Probably yes** Details not reported, open-label	**Probably no** Open-label	**Definitely no** Open-label	**Definitely no** Open-label	**Definitely no** Open-label	**Definitely yes** There were 2% (2/100) and 2% (2/100) patients azithromycin and cefaclor groups with missing data for 10-14d treatment failure, respectively
Rajendran 2007[27]	**Definitely yes** A block randomisation scheme	**Probably yes** Sequentially numbered, sealed envelopes	**Definitely yes** All patients, investigators, and clinic staff were blinded to study group assignment	**Definitely yes** All patients, investigators, and clinic staff were blinded to study group assignment	**Definitely yes** All patients, investigators, and clinic staff were blinded to study group assignment	**Definitely yes** There were 2.4% (2/82) and 2.4% (2/84) patients in cephalexin and control groups with missing data for 7d treatment failure, respectively

Schmitz 2010[26]	**Definitely yes** A block randomisation scheme	**Definitely yes** Sealed envelopes	**Definitely yes** Patients and physicians were blinded to treatment	**Definitely yes** Patients and physicians were blinded to treatment	**Definitely yes** Patients and physicians were blinded to treatment	**Probably no** There were 8.3% (8/96) and 12.1% (14/116) patients in TMP/SMX and control groups with missing data for 7d treatment failure, respectively; **Definitely no** There were 52.1% (50/96) and 56.9% (66/116) patients in TMP/SMX and control groups with missing data for 30d new lesions, respectively
Talan 2016[10]	**Definitely yes** Web-based randomisation	**Definitely yes** Using double-blind, Web-based randomisation	**Definitely yes** The treatment arms masked to both the subject and the study staff	**Definitely yes** The treatment arms masked to both the subject and the study staff	**Definitely yes** The treatment arms masked to both the subject and the study staff	**Definitely no** There were 15.3% (96/629) and 16.7% (106/636) patients in placebo and TMP-SMX groups with missing data for cure rate at TOC, respectively

* Method for generating randomisation sequence not clearly reported. We judged that generating randomisation sequence was likely achieved regardless of blinding methods according to instructions. We followed this rule throughout the review.

† Method for allocation concealment not clearly reported. We judged that concealed allocation was likely achieved given it was a randomised double blinded trial, according to instructions. We followed this rule throughout the review.

†† Method for allocation concealment not clearly reported. We judged that concealed allocation was unlikely achieved given it was a randomised open label trial, according to instructions. We followed this rule throughout the review.

‡ We used the following rules to judge the infrequent missing outcome data for all included trials throughout the review: definitely yes: there were less than 5% patients with missing outcome data, and missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups; probably yes: there were 5 to 10% patients with missing outcome data, and missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups; probably no: there were 10% to 15% of missing outcome data; definitely no: there were over 15% patients with missing outcome data, or there were more than 5% absolute difference of missing outcome data between groups.

Table C Safety profile of antibiotics versus placebo or usual care

Outcomes	No. of trials	Events/total		OR(95%CI)	P value of test for overall	I^2	Tau^2	P value of interaction
		Antibiotics	Placebo or usual care					
Over all gastrointestinal side effects								
TMP-SMX vs Placebo	4	303/1064	252/1072	1.28(1.04, 1.58)	0.02	0%	0.00	0.05
Clindamycin vs Placebo	1	49/265	23/255	2.29(1.35, 3.88)	0.002	--	-	
Anaphylactic reaction*								
TMP-SMX vs Placebo	3	7/434	3/455	2.32(0.67,8.06)	0.19	28%	0.00	0.94
Clindamycin vs Placebo	1	7/265	3/255	2.17(0.62, 7.58)	0.22	--	-	
Nausea								
TMP-SMX vs Placebo	3	149/987	108/988	1.49(0.98,2.25)	0.06	11%	0.03	0.48
Clindamycin vs Placebo	1	6/265	6/255	0.96(0.31,3.02)	0.95	--	-	
Diarrhoea								
TMP-SMX vs Placebo	3	111/964	117/948	0.92(0.70,1.22)	0.56	0%	0.00	0.001
Clindamycin vs Placebo	1	43/265	17/255	2.71(1.50,4.89)	0.0009	--	-	

Sepsis*								
TMP-SMX vs Placebo	1	1/630	0/617	7.24(0.14,364.86)	0.32	-	-	
Death*								
TMP-SMX vs Placebo	2	1/891	1/872	0.98(0.06,15.68)	0.99	-	-	-
Clindamycin vs Placebo	1	0/265	0/255	-	-	-	-	

⋆ Data were pooled using Peto's methods