Appendices

Appendix 1. Full search strategy for articles on the effect of postoperative discontinuation of surgical antibiotic prophylaxis on the incidence of surgical site infection

Medline (through PubMed)
Query #	Query
1.	surgical wound infection"[Mesh] OR surgical site infection*[tiab] OR SSI[tiab] OR SSIs[tiab] OR surgical wound infection*[tiab] OR surgical infection*[tiab] OR post-operative wound infection*[tiab] OR post-operative wound infection*[tiab]
2.	antibiotic prophylaxis"[Mesh] OR antimicrobial[tiab] OR antibiotic*[tiab]
3.	(prolong*[tiab] OR duration[tiab] OR short[tiab] OR long[tiab] OR single dose*[tiab] OR single dosage*[tiab] OR single dosis[tiab] OR singular dosage*[tiab] OR singular dosage*[tiab] OR multi dose*[tiab] OR multi dosage*[tiab] OR multiple dosage*[tiab]
4.	trial[ti]) OR randomly[tiab]) OR clinical trial as topic[mesh:noexp]) OR placebo[tiab]) OR randomized[tiab]) OR controlled clinical trial[pt]) OR randomized controlled trial[pt]
5.	1 AND 2 AND 3 AND 4

EMBASE	
Query #	Query
1.	surgical infection/ or (SSI or SSIs).ti,ab,kw. or ((surg* or postoperat* or post-operat*) adj3 infect*).ti,ab,kw.
2.	antibiotic prophylaxis/ or (antimicrobial or antibiotic*).ti,ab,kw.
3.	exp drug dose/ or treatment duration/ or (prolong* or duration*).ti,ab,kw. or ((single or singular or multi*) adj3 (dose* or dosage* or dosis)).ti,ab,kw. or ((short* or long*) adj3 (duration* or course*)).ti,ab,kw.
4.	controlled clinical trial/ or randomized controlled trial/ or exp "clinical trial (topic)"/ or (randomly or randomized or placebo).ti,ab,kw. or trial.ti.
5.	1 and 2 and 3 and 4

Cochrane	Central Register (CENTRAL)
Query #	Query
1.	MeSH descriptor: [surgical wound infection] explode all trees
2.	SSI or SSIs:ti,ab,kw (word variations have been searched)
3.	(surg* or postoperat* or post-operat*) near/3 infect*:ti,ab,kw (word variations have been searched)
4.	#1 or #2 or #3
5.	MeSH descriptor: [antibiotic prophylaxis] explode all trees
6.	antimicrobial or antibiotic*:ti,ab,kw (word variations have been searched)
7.	#5 or #6
8.	prolong* or duration*:ti,ab,kw (word variations have been searched)
9.	(single or singular or multi*) near/3 (dose* or dosage* or dosis):ti,ab,kw (word variations have been searched)
10.	(short* or long*) near/3 (duration* or course*):ti,ab,kw (word variations have been searched)
11.	#8 or #9 or #10
12.	#4 and #7 and #11 in Trials

CINAHL	(Ebsco)
Query #	Query
1.	(MH "surgical wound infection") OR (TI (surgical site infection* OR SSI OR SSIs OR surgical wound infection* OR surgical infection* OR post-operative wound infection* OR postoperative wound infection*) OR AB (surgical site infection* OR SSI OR SSIs OR surgical wound infection* OR surgical infection* OR post-operative wound infe
2.	MH "antibiotic prophylaxis") OR TI (antimicrobial OR antibiotic*) OR AB (antimicrobial OR antibiotic*)
3.	(MH "treatment duration") OR TI (prolong* OR duration OR short OR long OR single dose* OR single dosage* OR single doses OR singular doses OR singular doses OR multi doses OR multi dosage* OR multi doses OR multiple doses OR singular doses OR duration OR short OR long OR single dose* OR single dosage* OR single doses OR singular doses OR singular dosage* OR singular doses OR multiple dosage* OR multiple doses OR multiple dosage* OR multiple doses OR multiple dosage*
4.	(MH "randomized controlled trials") OR (MH "clinical trials+") OR TI trial OR (TI controll* AND trial*) OR AB (TI controll* AND trial*) OR (TI (randomly OR placebo OR randomized) OR AB (randomly OR placebo OR randomized))
5.	S1 AND S2 AND S3 AND S4

WHO regional medical databases					
Query #	Query				
1.	Filter subject descriptor: antibiotic prophylaxis				
2.	(tw:(surgical site infection)) OR (tw:(wound infections)) OR (tw:(wound infection))				

Appendix 2. Criteria for risk of bias assessment

Risk of bias domain	Criteria for judgment
Selection bias	Low risk of bias: A random component was used in the sequence generation process and allocation was concealed
	High risk of bias: A non-random component was used or allocation was inadequately concealed.
	<u>Unclear</u> : Sequence generation or allocation concealment was insufficiently described for judgement.
Performance bias	Low risk of bias: Blinding of patients and investigators was described (e.g. with a placebo control group)
	Hight risk of bias: There was no blinding of patients and investigators.
	<u>Unclear</u> : Blinding of participants and investigators was insufficiently described for judgement
Detection bias	Low risk of bias: Outcome assessor blinding was ensured
	High risk of bias: Outcome assessors were not blinded
	<u>Unclear</u> : Blinding of outcome assessors was insufficiently described.
Attrition bias	Low risk of bias: An intention to treat analysis was conducted or attrition was low or balanced and unlikely to have affected the outcome
	High risk of bias: Attrition was unbalanced or high relative to the event incidence and could have affected the outcome.
	Unclear: Attrition was insufficiently described
Reporting bias	Low risk of bias: No outcomes mentioned in the study registration or protocol where omitted or altered.
	High risk of bias: Outcomes mentioned in the study registration or protocol where omitted or altered.
	<u>Unclear</u> : No registration or protocol was available
Other bias	Low risk of bias, unless other concerns existed on the validity of the study

Appendix	Appendix 3. Studies excluded after full text review								
	Author, year	Reason for exclusion							
1.	Kumar 2013 ¹	Incomparable regimen							
2.	Ahn 2013 ²	Not an RCT							
3.	Fonseca 2006 ³	Incomparable regimen							
4.	Sevin 2007 ⁴	Not an RCT							
5.	Han 2014 ⁵	Not an RCT							
6.	Farran 2008 ⁶	Did not address study question							
7.	Schardey 1997 ⁷	Did not address study question							
8.	Vu 2014 ⁸	Not an RCT							
9.	Basoli 2008 ⁹	Did not address study question							
10.	Safdar 1992 ¹⁰	Incomparable regimen							
11.	Gidiri 2014 ¹¹	Incomparable regimen							
12.	Kato 2007 ¹²	Incomparable regimen							
13.	Dahl A 2006 ¹³	Not an RCT							
14.	Kakimaru 2010 ¹⁴	Not an RCT							
15.	Kato 2006 ¹⁵	Not an RCT							
16.	Pedrini 2005 ¹⁶	Not an RCT							
17.	Righi 1995 ¹⁷	Duplicate of Righi 1996							
18.	Adde 2012 ¹⁸	Incomparable regimen							
19.	Luaces 2010 ¹⁹	Incomparable regimen							
20.	Lacasa 2007 ²⁰	Incomparable regimen							
21.	Jensen 1990 ²¹	Incomparable regimen							
22.	Boffi 1992 ²²	Duplicate of Gazzaniga 1992							
23.	Gazzaniga 1992 ²³	Incomparable regimen							
24.	Mathur 2013 ²⁴	Incomparable regimen							
25.	Kaczmarzyk 2007 ²⁵	Did not address study question							
26.	Vargas-Mena 2012 ²⁶	Not an RCT							
27.	Wu 1998 ²⁷	Did not address study question							
28.	Ahmadi 2005 ²⁸	Did not address study question Did not address study question							
29.	Morimoto 1998 ²⁹	Did not address study question Did not address study question							
		* *							
30.	Morimoto 1993 ³⁰	Not retrievable							
31.	Hashizume 2004 ³¹	Incomparable regimen							
32.	Bonzanini 1993 ³²	Did not address study question							
33.	Fukushima 2014 ³³	Congress abstract							
34.	Badia 2011 ³⁴	Congress abstract							
35.	Hashimoto 2014 ³⁵	Congress abstract							
36.	Ijarotimi 2013 ³⁶	Not retrievable							
37.	Shakya 2010 ³⁷	Not retrievable							
38.	Ko 2010 ³⁸	Not retrievable							
39.	Rajshekhar 2009 ³⁹	Congress abstract							
40.	Patacchiola 2000 ⁴⁰	Did not address study question							
41.	Urbanetz 1994 ⁴¹	Not retrievable							
42.	Cartana 1990 ⁴²	Not retrievable							
43.	Ali 2006 ⁴³	Congress abstract							
44.	Ricart-Hoffiz 2011 ⁴⁴	Congress abstract							
45.	Rolle 1990 ⁴⁵	Not retrievable							
46.	Orlando 2010 ⁴⁶	Congress abstract							
47.	Navarro 1995 ⁴⁷	Did not address study question							
48.	Lee 2012 ⁴⁸	Not retrievable							
49.	Cheshani 2015 ⁴⁹	Not retrievable							
50.	Ali 2012 ⁵⁰	Not retrievable							
51.	Seker 2011 ⁵¹	Not retrievable Not retrievable							
52.	Bencini 1994 ⁵²	Not retrievable Not retrievable							
53.	Lindeboom 2005 ⁵³								
		Did not address study question							
54.	Marcucci 1990 ⁵⁴	Not retrievable							
55.	Shahid 2007 ⁵⁵	Did not address study question							
56.	Cuthbertson 1991 ⁵⁶	Did not address study question							
57.	Akgur 1992 ⁵⁷	Did not address study question							
58.	Garcia 2017 ⁵⁸	Did not address study question							
59.	Ghosh 2017 ⁵⁹	Congress abstract							
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60.	Habibi 2016 ⁶⁰	Congress abstract
61.	Phillips 2016 ⁶¹	Congress abstract
62.	Samson 2017 ⁶²	Congress abstract
63.	Chen 2018 ⁶³	Not retrievable
64.	Yalagachin 2018 ⁶⁴	Did not address study question

Appendix 4. Study characteristics of the included studies for all five comparisons

Author,	Country, design, participants	Mean age,%		Wound class.	CDC SSI definition, Follow-up	Intervention	Control	(1)	0
Comparison	1: Postoper	ative co	ntinuation of sur		ntibiotic pr otic prophy				rgical
Sadraei- Moosavi 2017 ⁶⁵	Iran, Single centre 152*	28, NA	Appendectomy (open, uncomplicated)	II-III	No ^z , NR	1g Ceftriaxone & 0.5g Metronidazole IV preoperatively + 24h postoperatively	1g Ceftriaxone & 0·5g Metronidazole IV preoperatively	No	Yes
Hussain 2012 ⁶⁶	Saudi Arabia, Single centre 377	32, 46%	Appendectomy (open, uncomplicated)	II-III	No ^a , 30 days	Cefuroxime & Metronidazole IV preoperatively + 1x postoperatively	Cefuroxime & Metronidazole IV preoperatively	Yes	Yes
Liberman 1995 ⁶⁷	United States of America, Single centre 99*	26, 17%	Appendectomy (open uncomplicated)	II-III	No ^a , 3 weeks	2g Cefoxitin IV preoperatively + 3x q 6h postoperatively	2g Cefoxitin IV preoperatively	Yes	Yes
Tsang 1992 ⁶⁸	Hong Kong, Single centre 103†	8, 30%	Appendectomy (open, uncomplicated)	II-III	Noª, 4 weeks	1·5 mg/kg Gentamicin IV & 7·5 mg/kg Metronidazole IV preoperatively +2x q 8h postoperatively	1·5 mg/kg Gentamicin IV & 7·5 mg/kg Metronidazole IV preoperatively	No	Yes
Suzuki 2011 ⁶⁹	Japan, Single centre 370	66, 45%	Colorectal surgery	II-III	Nof, 30 days	1g Flomoxef IV preoperatively + 4x q 12h	lg Flomoxef IV preoperatively	Yes	Yes
Fujita 2007 ⁷⁰	Japan, Multi centre 377	61, 38%	Colorectal surgery	II-III	No ^d , NR	1g Cefmetazole IV preoperatively + 2x q 8h	lg Cefmetazole IV preoperatively	Yes	No
Imamura 2012 ⁷¹	Japan, Multi centre 355	65, 32%	Upper GI surgery	II	CDC, 30 days	lg of Cefazolin IV preoperatively +1 x direct postoperative & 4x q 12h postoperative	1g of Cefazolin IV preoperatively	No	Yes
Haga 2012 ⁷²	Japan, Single centre 325	68, 28%	Upper GI surgery	II	CDC, 30 days	1g of Cefazolin IV preoperatively + 5x q 12h postoperatively	lg of Cefazolin IV preoperatively	No	Yes
Balbo 1991 ⁷³	Italy, Multi centre 117	62, 44%	Upper GI surgery	II-III	No ^v , 30 days	2g Mezlocillin IV preoperatively + 2x q 6h postoperatively	2g Mezlocillin iv preoperatively	Yes	Yes
Mohri 2007 ⁷⁴	Japan, Multi centre 486	68, 28%	Upper GI surgery	II	CDC, 6 weeks	1g Cefazolin IV or 1·5 g Ampicillin sulbactam IV preoperatively + 7x q 12h postoperatively		Yes	Yes
Chauhan 2018 ⁷⁵	India, Single centre 210*	-	Laparoscopic Cholecystectomy	II-III	No ^d , 30 days	1g Ceftriaxone IV preoperatively + 4x q 12h postoperatively	lg Ceftriaxone IV preoperatively	No	No
Santibañes 2018 ⁷⁶	Argentina, Single centre 201	50, 47%	Laparoscopic Cholecystectomy	II-III	No ^d , 30 days	Ampicillin sulbactam IV q 6h preoperatively (admission – surgery, < 5 days) + 1g Amoxicillin/Clavulanic acid PO 15x q 8h	(admission until surgery, < 5 days) + 1g Placebo PO 15x q 8h	No	No
Kim 2017 ⁷⁷	South Korea, Multi centre 188	59, 62%	Laparoscopic Cholecystectomy	II-III	Yes, 30 days	1g Cefoxitin IV preoperatively + q 8h IV or PO if tolerated until POD 3	1g Cefoxitin IV preoperatively + placebo q 8h IV or PO if tolerated until POD 3	Yes	Yes
Loozen 2017 ⁷⁸	The Netherlands, Single centre 150	53, 53%	Laparoscopic Cholecystectomy	II-III	Nou	2g Cefazolin IV preoperatively + 0·75g Cefazoline IV & 0·5g Metronidazole IV 9x q 8h	2g Cefazolin IV preoperatively	Yes	Yes
Regimbeau 2014 ⁷⁹	France, Multi centre 414	55, 51%	Open or laparoscopic Cholecystectomy	II-III	CDC, 30 days	2g Amoxycillin clavulanate IV 3dd before surgery & preoperatively + 15x q 8h IV or PO if tolerated	preoperatively	Yes	No
Unemura 2000 ⁸⁰	Japan, Multi centre 242	52, 50%	Laparoscopic cholecystectomy	II-III	Noª, NR	2g of either Flomoxef or Cefotiam or Cefazolin or	2g of either Flomoxef or Cefotiam or Cefazolin or	No	Yes

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						allergy IV	Cefmetazole or Fosfomycn in case of an allergy IV		
						preoperatively + 4x q 12h postoperatively	preoperatively		
Meijer 1993 ⁸¹	The Netherlands, Multi centre 1004	65, 69%	Hepatobiliary surgery	II	Noi, 4-6 weeks	1.5g Cefuroxime IV preoperatively + 0.75g Cefuroxime IV 2x q 8h postoperatively		No	No
Abro 2014 ⁸²	Pakistan, Single centre 208	35, 53%	Mixed general surgery	I-III	No ^j , 35 days	2g Ceftriaxone IV preoperatively + 1g Ceftriaxone IV 2x q 8h postoperatively (& 0·25g Gentamicin & 0·5g Metronidazole when indicated)	2g Ceftriaxone IV preoperatively (& 0·25g Gentamicin & 0·5g Metronidazole when indicated)	No	Yes
Becker 2008 ⁸³	Israel, Single centre 44	65, 31%	Mixed general surgery	Ι	CDC, 30 days	lg Cefazolin IV preoperatively + 3dd postoperatively until drains were removed	1g Cefazolin IV preoperatively	Yes	Yes
Scher 1997 ⁸⁴	United States of America, Single centre 768	NA, NA	Mixed general surgery	II	No ^d , NR	1g of Cefazolin IV preoperatively + 1g Cefazolin IV 3x q 8h postoperatively	lg of Cefazolin IV preoperatively	Yes	Yes
Kow 1995 ⁸⁵	Australia, Single centre 1010*	NA, 50%	Mixed general surgery	II-III	No ^b , 4-6 weeks	2g Cefoxitin IV & 0·5 Metronidazole IV preoperatively + 2x q 6h postoperatively 1g Cefotaxime IV & 0·5g metronidazole IV preoperatively + 2x q	2g Cefoxitin IV & 0.5g Metronidazole IV preoperatively 1g Cefotaxime IV & 0.5g metronidazole IV preoperatively	No	No
Turano 1992 ⁸⁶	Italy, Single centre 3567*	45, NA	Abdominal, Gynaecological and Urological surgery	II-III	Noª, 7 days	1g Cefotaxime IV preoperatively + 2x q 6h after the first dose	1g Cefotaxime IV preoperatively	Yes	Yes
Bates 1992 ⁸⁷	The United Kingdom, Multi centre 900*	55, 58%	Mixed general surgery	II-IV	No ^b , 30 days	0·25g/0·125g Amoxicillin/clavulanic acid IV preoperatively + 2x q 8h postoperatively	0·25g/0·125g Amoxicillin/clavulanic acid IV preoperatively	Yes	No
Aberg 1991 ⁸⁸	Sweden, Single centre 428*	NA, NA	Mixed general surgery	II-III	Noa, 30 days	1.5g Cefuroxime IV	1·5g Cefuroxime IV preoperatively (& 0·5g metronidazole when indicated)	No	No
Sgroi 1990 ⁸⁹	Italy, Single centre 352	54, 46%	Mixed general	II-III	Noª, NR	1 x Cephalosporin§ preoperatively + 2x q 8h postoperatively	1 x Cephalosporin§ preoperatively	Yes	No
Westen 2015 ⁹⁰	Tanzania, Multi centre 176	26, 100%	C-section	II	No ^k , 30 days	1g Ampicillin IV & 0·5g Metronidazole IV preoperatively + 0·5 Ampicillin & 0·5g Metronidazole IV 2x q 8h postoperatively followed by 0·5g Amoxicillin PO and 0·4g metronidazole PO 9x q 8h	preoperatively	Yes	Yes
Shaheen 2014 ⁹¹	Pakistan, Single centre 100	29, 100%	C-section	II	No ¹ , 6 weeks	lg Cefotaxime IV preoperatively + 2 x q 12h postoperatively followed by 0·4g Cefuroxime PO for 5 days	1g Cefotaxime IV preoperatively	Yes	Yes
Lyimo 2013 ⁹²	Tanzania, Single centre 500	NA, 100%	C-section	П	CDC, 30 days	3 mg/kg Gentamicin IV & 0·5g Metronidazole I + preoperatively Metronidazole 0·5g 3x q 8h postoperatively	Metronidazole IV	Yes	Yes

Su 2005 ⁹³	Taiwan, Single centre 532	46, 100%	Gynaecological surgery	II	No ^m , 90 days	1g Cefazolin preoperatively + 3x q 6h postoperatively	1g Cefazolin IV preoperatively	Yes	Yes
Irato 1997 ⁹⁴	Italy, Single centre 84	49 ,NA	Gynaecological surgery	II-III	No ^w , NR	2g cefotetan IV preoperatively + 10x q 12h	2g cefotetan IV preoperatively	Yes	No
Cartaña 1994 ⁹⁵	Spain, Single centre 58	50, 100%	Gynaecological surgery	II	No ^d , 4 days	4g Piperacillin preoperatively + 2x q 6h postoperatively	4g Piperacillin IV preoperatively	Yes	No
Buckley 1990 ⁹⁶	Canada, Single centre 204	77, 74%	Orthopaedic / trauma surgery	Ι	No ^a , 6 weeks	2g Cefazolin IV preoperatively + 1g Cefazolin 3x q 6h postoperatively	2g Cefazolin IV preoperatively	Yes	Yes
Garotta 1991 ⁹⁷	Italy, Multi centre 614	58, 54%	Orthopaedic / trauma surgery	I	No ^c , 1 year	2g Ceftizoxime IV preoperatively + 1x q 12h postoperatively	2g Ceftizoxime IV preoperatively	Yes	No
Hellbusch 2008 ⁹⁸	United States of America, Multi centre 233	NA, 56%	Orthopaedic / trauma surgery	Ι	No°, >21 days	1g<100kg<2g Cefazolin IV preoperatively + 9x q 8h postoperatively followed by 0·5g Cephalexin PO 28x q	1g<100kg<2g Cefazolin IV preoperatively	Yes	Yes
Crist 2018 ⁹⁹	United States of America, Single centre 227	49, 50%	Orthopaedic / trauma surgery	I	Nox	1g<100kg<2g Cefazolin IV preoperatively + 2x q 8h postoperatively	1g<100kg<2g Cefazolin IV preoperatively + 2x q 8h Saline	Yes	Yes
Nooyen 1994 ¹⁰⁰	The Netherlands, Single centre 844	33-86, 86%	Cardiothoracic surgery	Ι	No ^c , NR	20mg/kg Cefuroxime IV preoperatively + 0·75g Cefuroxime IV 9x q 8h postoperatively	20mg/kg Cefuroxime IV preoperatively	Yes	No
Tamayo 2008 ¹⁰¹	Spain, Single centre 838	68, 38%	Cardiothoracic surgery	I	CDC, 12 months	2g Cefazolin IV preoperativel + 1g Cefazolin IV 2x q 8h postoperatively	2g Cefazolin IV preoperatively	No	Yes
Olak 1991 ¹⁰²	The United Kingdom, Single centre 199	63, 29%	Cardiothoracic surgery	II	No ^a , 6 weeks	2g Cefazolin IV preoperatively + 1g Cefazolin IV 5x q 8h postoperatively	2g Cefazolin IV preoperatively	No	Yes
Jiang 2004 ¹⁰³	China, Multi centre 264	55, 22%	Thoracic surgery	II-III	CDC, 30 days	1.5g cefuroxime IV preoperatively + 15x 0.75g q 8h postoperatively	1.5g cefuroxime IV preoperatively	No	No
Hall 1998 ¹⁰⁴	Australia, Single centre 302	70, 28%	Vascular surgery	I	No ^c , 42 days	3·0g/0·1g Ticarcillin Clavulanic acid IV preoperatively + q 6h postoperatively until lines were removed	3·0g/0·1g Ticarcillin Clavulanic acid IV preoperatively	No	Yes
Orlando 2015 ¹⁰⁵	Italy, Multi centre 205	48, 39%	Transplant surgery	Ι	CDC, 30 days	2g Cefazolin IV or 1g Cefotaxime IV preoperatively + q 12h postoperatively until removal of Foley catheter	2g Cefazolin IV or 1g Cefotaxime IV preoperatively	Yes	Yes
Maier 1992 ¹⁰⁶	Germany, Single centre 106	NA,NA	Head and neck surgery	I-II	No ^d , NR	1.5 g Cefuroxime IV preoperatively + 2x q 8h postoperatively	1·5 g Cefuroxime IV preoperatively	Yes	No
Mann 1990 ¹⁰⁷	Germany, Single centre 113	53, 31%	Head and neck surgery	II	No ^a , NR	2g Cefotiam IV & 0.5g Metronidazole IV preoperatively + 2x q 8h postoperatively	2g Cefotiam IV & 0·5g Metronidazole IV preoperatively	Yes	Yes
Rajan 2005 ¹⁰⁸	Australia, Single centre 200	33, 44%	Head and neck surgery	II	No ^d , 30 days	2·2g Amoxicillin/ clavulanic acid IV preoperatively + 1g Amoxicillin/ clavulanic acid PO 14x q 12h postoperatively	2·2g Amoxicillin / clavulanic acid IV preoperatively	Yes	No
Campos 2015 ¹⁰⁹	Brazil, Single centre 74	NA, 16%	Maxillofacial surgery	I-II	No ^e , 6 weeks	2g Cefazolin IV preoperatively + 1g Cefazolin IV 4x q 6h postoperatively	2g Cefazolin IV preoperatively	Yes	Yes
Lindeboom 2003 ¹¹⁰	The Netherlands,	30, 74%	Maxillofacial surgery	II	Nos, 3 months	0·4g Clindamycin IV preoperatively +	0·4g Clindamycin IV preoperatively	Yes	Yes

	Single					Clindamycin IV 4x q			
Cioaca 2002 ¹¹¹	Romania, Single centre 140*	45, 32% 48, 43%	Maxillofacial surgery	II	Noª, 14 days	6h postoperatively 2·4 mg Amoxicillin/ Clavulanic acid IV preoperatively + 15x q 8h postoperatively 2g Cefazolin IV preoperatively + 15x q	2·4 mg Amoxicillin/ Clavulanic acid IV preoperatively 2g Cefazolin IV preoperatively	No	No
Wahab 2013 ¹¹²	India, Single centre 60*	27, 48%	Maxillofacial surgery	II	CDC, 2 months	8h postoperatively 1g Amoxicillin IV preoperatively + 0.5g Amoxicillin IV 2x q 4h postoperatively	1g Amoxicillin IV	No	No
Danda 2010 ¹¹³	India, Single centre 150*	24, 62%	Maxillofacial surgery	II	No ^b , 4 weeks	1g Ampicillin IV preoperatively + Ampicillin 0·5g IV 4x q 6h postoperatively	1g Ampicillin IV preoperatively	No	No
Kang 2009 ¹¹⁴	South Korea, Single centre 56	24, 46%	Maxillofacial surgery	II	CDC, 2 weeks	1g Cefpiramide IV preoperatively + 6x q 12h postoperatively	1g Cefpiramide IV preoperatively	Yes	Yes
Rajabi 2012 ¹¹⁵	Iran, Single centre 291*	26, 38%	Appendectomy (open, uncomplicated)	II-III	No ^a , 10 days after discharge	1g Ceftriaxone IV & 0.5g Metronidazole IV preoperatively + 1g Ceftriaxone IV q 12h & 0.5g Metronidazole IV q 8h For 1 OR 3 days postoperatively	1g Ceftriaxone IV & 0·5g Metronidazole IV preoperatively	No	Yes
Mui 2005 ¹¹⁶	Hong Kong, Single centre 269*	34, 30%	Appendectomy (open, uncomplicated)	II-III	Noª, 30 days	1·5g Cefuroxime IV & 0·5 g Metronidazole IV preoperatively + 2x	1·5g Cefuroxime IV & 0·5 g Metronidazole IV preoperatively	Yes	Yes
Comparis						prophylaxis for multip prophylaxis for one pos		<24	h vs.
Karran 1993 ¹¹⁷	The United Kingdom, Single centre 227	67, 51%	Colorectal surgery	II-III	Nog, 6-8 weeks	1g Imipenem IV preoperatively + 1x 3h postoperatively followed by 0·5 Imipenem IV 2x q 8 h	lg Imipenem IV preoperatively + 1x 3h postoperatively	No	No
Compari	ison 3: Posto	perative				prophylaxis > 24h vs ylaxis <= 24h	postoperative continua	ation	of
Rajabi 2012 ¹¹⁵	Iran, Single centre 194*	26, 39%	Appendectomy (open, uncomplicated)	II-III	No ^a , 10 days after discharge		0.5 g Metronidazole	No	Yes
Mui 2005 ¹¹⁶	Hong Kong, Single centre177*	34, 32%	Appendectomy (open, uncomplicated)	II-III	Noa, 30 days	1.5g Cefuroxime IV & 0.5 g Metronidazole IV preoperatively + 5-	1·5g Cefuroxime IV & 0·5 g Metronidazole IV preoperatively + 2x for 1 day		Yes
	centrery					2dd + metronidazole 400mg 3dd)	postoperatively		
Ishibashi 2014 ¹¹⁸	Japan, Single centre 297	65,36%	Colorectal surgery	II-III	CDC, 30 days	2dd + metronidazole	1g Flomoxef IV + 1x 1h postoperatively	No	Yes
	Japan, Single	65,36% 68,42%		II-III II-III		2dd + metronidazole 400mg 3dd) 1g Flomoxef IV + 1x 1h postoperatively	1g Flomoxef IV + 1x		Yes Yes

	C:1-	ı	ı	1	- 6	TV + 0.5-	W+ 0.5-	1 1	
	Single centre 169				after discharge	IV + 0.5g Metronidazole IV & 0.08g Gentamicin 9x q 8h	IV+ 0·5g Metronidazole IV & 0·08g gentamicin IV 2x q 8h		
Becker 1991 ¹²¹	United States of America, Single centre 40	33, 48%	Colorectal surgery	II-III	No ^b , 56 days	2g Cefoxitin IV preoperatively + 2x q 6h after the initial dose followed by 1g Cefoxitin IV 20x q 6h postoperatively	2g Cefoxitin IV preoperatively + 2x q 6h after the initial dose		No
Fujita 2015 ¹²²	Japan, Single centre 257	68, 13%	Upper GI surgery	II	CDC, 30d	1g Cefmetazole IV 4x	1g Cefmetazole IV 4x q 3h starting preoperatively	Yes	Yes
Lau 1990 ¹²³	Hong Kong, Single centre 203	60, 66%	Open cholecystectomy	II-III	No ^h , 1 year	2g Cefamandole IV preoperatively + 0·5g Cefamandole IV 28x q 6h after the initial dose	2g Cefamandole IV preoperatively + 0·5g Cefamandole IV 2x q 6h after the initial dose	Yes	No
Yang 2001 ¹²⁴	China, Multi centre 731	49, 51%	Mixed general	II-III	No ^d , NR	0.3g Netilmicine IV & 0.5g metronidazole IV when needed + 9x q 8h postoperatively	0.5g metronidazole IV	Yes	No
Bozorgzadeh 1999 ¹²⁵	United States of America, Single centre 300*	27, 13%	Mixed general surgery	II-III	CDC, 30 days	with the first dose given in the emergency	emergency department after determination of the requirement for		No
Hanif 2015 ¹²⁶	India, Single centre 220*	‡, 47%	Mixed general surgery	II-III	No ^d , NR	1g Sulbactam IV & 0.5	1g Sulbactam IV & 0·5 g Cefoperazone IV	Yes	No
Chang 2005 ¹²⁷	Taiwan, Single centre 156	42, 100%	Gynaecological surgery	П	No°, 7 days after discharge	q 6h & 0·06-0·08g	2g Cephalothin IV & 0.08g Gentamicin IV preoperatively + 1g Cephalothin IV 4x q 6h & 0.06-0.08g Gentamicin IV 3x q 8h postoperatively		No
Takemoto 2015 ¹²⁸	United States of America, Single centre 314	58, 55%	Orthopaedic / trauma surgery	I	CDC, 1 year	Cefazolin for drain duration starting preoperatively (average of 3·2 days)	Cefazolin for 24h starting preoperatively	Yes	Yes
Lin 2011 ¹²⁹	Taiwan, Single centre 231	57, 17%	Cardiothoracic surgery	I	CDC, 30 days	8h postoperatively	1 gr Cefazolin preoperatively + 3x q 8h postoperatively	No	Yes
Niederhauser 1997 ¹³⁰	Switzerland, Single centre 53	65, 21%	Cardiothoracic surgery	I	CDC, 3- 540 days	lg of cefazolin preoperatively + 2x q 8h postoperatively followed by Ticarcillin/clavunate 5·2g 6x q 8h & 0·5g Vancomycin q 12h until removal of IABP	1g of cefazolin preoperatively + 2x q 8h postoperatively	Yes	Yes
Liu 2008 ¹³¹	Taiwan, Single centre 53	57, 17%	Head and neck surgery	II	CDC, 30 days	0·3g Clindamycin IV preoperatively +12x q 6h postoperatively	0·3g Clindamycin IV preoperatively + 4x q 6h postoperatively	Yes	Yes
Carroll 2003 ¹³²	United States of America, Single centre 74	62, 38%	Head and neck surgery	II	No ^p , 7 days	0.9g Clindamycin IV preoperatively +15x q 8h after the initial dose	0·9g Clindamycin IV preoperatively + 3x q 8h after the initial dose	Yes	Yes
Righi 1996 ¹³³	Italy, Single centre 162	64, 12%	Head and neck surgery	II	Nos, 20 days	0.6g Clindamycin IV & Cefonicid 1g IV preoperatively + 0.6g Clindamycin IV 9x q 8h & Cefonicid 1g 3x q 12h postoperatively	0.6g Clindamycin IV & Cefonicid 1g IV preoperatively + 0.6g Clindamycin IV 3x q 8h & Cefonicid 1g 1x q 12h postoperatively	Yes	No
Bidkar 2014 ¹³⁴	India, Single centre 78*	29, 58%	Head and neck surgery	I-III	No ^d , 3 weeks	1.5g Cefuroxime preoperatively + 0.75g Cefuroxime 2x q 12h	1·5g Cefuroxime Preoperatively + 0·75g	Yes	Yes

	1	1			1				
						postoperatively followed by 0·2g Cefixime PO 16x q 12h	Cefuroxime 2x q 12h postoperatively		
Abubaker 2001 ¹³⁵	United States of America, Single centre 30	32, 10%	Maxillofacial surgery	II	No ^e , 6 weeks	2m U aqueous Penicillin-G IV q 4h from admission trough the preoperative and intraoperative phase and for 12h postoperatively followed by 0.5g penicillin PO 20x q 6h	2m U aqueous Penicillin-G IV q 4h from admission trough the preoperative and intraoperative phase and for 12h postoperatively	Yes	Yes
Eshghpour 2014 ¹³⁶	Iran, Single centre 50*	27, 66%	Maxillofacial surgery	II	No ^d , 6 weeks	1g Cefazolin IV preoperatively + 1x q 4h after the initial dose followed by 0·5g Amoxicillin PO 21x q 8h	1g Cefazolin IV preoperatively + 1x q 4h after the initial dose		Yes
Jansisyanont 2008 ¹³⁷	Thailand, Multi centre 122*	26, 67% 27, 67%	Maxillofacial surgery	II	CDC, 6 weeks	1·2g Amoxicillin / Clavulanic acid + 0·625g Amoxicillin / clavulanic acid PO 15x q 8h postoperatively 2 million units of aqueous Penicillin IV + 0·5g Amoxicillin PO 15x q 8h postoperatively	1·2g Amoxicillin / Clavulanic acid preoperatively + 1x q 8h postoperatively 2m U of aqueous Penicillin IV preoperatively + 1x q 4h postoperatively	Yes	Yes
Baqain 2004 ¹³⁸	The United Kingdom, Single centre 34	27, 68%	Maxillofacial surgery	II	No ^t , 6 weeks	lg Amoxicillin IV + 0·5g Amoxicillin IV 1x q 3h postoperatively followed by 0·5g Amoxicillin 15x q 8h	1g Amoxicillin IV + 0·5g Amoxicillin IV 1x q 3h postoperatively	No	No
Bentley 1999 ¹³⁹	Canada, Single centre 30	NA,NA	Maxillofacial surgery	П	CDC, 30 days	2m U aqueous Penicillin-G IV preoperatively + 1x q 3h postoperatively after the last intraoperative dose followed by 1m U Penicillin-G IV 8x q 6h followed by 0·3g penicillin-V PO 8x q 6h	2m U aqueous Penicillin-G IV preoperatively + 1x q 3h postoperatively after the last intraoperative dose	No	Yes
Fridrich 1994 ¹⁴⁰	United States of America, Single centre 30*	27, 47%	Maxillofacial surgery	II	No ^d , 8 weeks	2m U Penicillin IV preoperatively + q 4h until IV discontinuation on postoperative day 1 followed by 0·5g Penicillin VK 28x q 6h	2m U Penicillin IV preoperatively + a 2h until participants reached the recovery room, where the final dose was given	Yes	Yes
Compari	son 4: Posto	perative				e prophylaxis > 48h vs ylaxis <= 48h	postoperative continu	ation	of
Togo 2007 ¹⁴¹	Japan, Single centre 180	62, 36%	Hepatobiliary surgery	II	CDC, 30 days	1g Flomoxef IV preoperatively + 1x postoperatively followed by 2g Flomoxef IV 10x q 12h	1g Flomoxef IV preoperatively + 1x postoperatively followed by 2g Flomoxef IV 4x q 12h		Yes
Sugawara 2018 ¹⁴²	Japan, Single centre 86	70, 29%	Hepatobiliary surgery	II-III	CDC, 30 days	Cefazoline IV (or in case of a positive culture, as culture indicated) preoperatively + 12x q8h	Cefazoline IV (or in case of a positive culture, as culture indicated) preoperatively + 6x q8h		Yes
Gupta 2010 ¹⁴³	India, Single centre 227	54, 19%	Cardiothoracic surgery	Ι	CDC, 30 days	Ceftazidime Pentahydrate IV & Amikacin IV preoperatively + for 72h postoperatively	Ceftazidime Pentahydrate IV & Amikacin IV preoperatively + for 48h postoperatively	Yes	Yes

Otani 2004 ¹⁴⁴	Japan, Single centre 40	49, 43%	Thoracic surgery	II-III	No ^d , 14 days	1g Cefmetazole IV preoperatively + 1x directly postoperatively followed by 12 x q 12h	1g Cefmetazole IV preoperatively + 1x directly followed by 2 x q 12h	No	No
Sawyer 1990 ¹⁴⁵	United States of America, Multi centre 50	62, 24%	Head and neck surgery	II		1g Cefazolin IV & 0·5g Metronidazole IV preoperatively + 1g Cefazolin IV 21x q 8h & 0·5g Metronidazole IV 28x q 6 h postoperatively	preoperatively + 1g	No	Yes
Davis 2017 ¹⁴⁶	Canada, Single centre 171*	25, 74%	Maxillofacial surgery	II	CDC, 30 days / 1 year	2g Cefazolin IV preoperatively + 3x q 8h postoperatively followed by 0·5g Cephalexin PO & 0·3g Clindamycin PO 8x q 6h	2g Cefazolin IV preoperatively + 3x q 8h postoperatively	Yes	Yes

Comparison 5: Postoperative continuation of surgical antibiotic prophylaxis > 72h vs postoperative continuation of surgical antibiotic prophylaxis <= 72h

Park 2010 ¹⁴⁷ South Korea, Multi centre 255 58,	Colorectal surgery	II-III	CDC, 21 days	1g Cefotetan IV preoperatively + 15x q 8h postoperatively	1g Cefotetan IV preoperatively + 9x q 8h postoperatively	Yes	Yes
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CDC: Center for Disease Control and Prevention; SSI: Surgical Site infection; Wound class.: CDC Wound Classification; : Timing of preoperative intravenous antibiotic specified and within 60 min prior to incision; : Repeat of surgical antibiotic prophylaxis administration specified when Indicated; *: Included paediatric patients; †: exclusively paediatric patients; No^[letter]: SSI definition deviating from CDC classification. Letter refers to specification in the appendix, pp 12; IV: intravenous; H: Hour; x: times/frequency; q: per/interval; g: gram; NR: not recorded; SSI: surgical site infection; IABP: intra-aortic balloon pumping; <: less than; >: more than; <= less than or equal to; >=more than or equal to; POD: Postoperative day; NA: Not Available; ‡: 75% of the patients is < 40 years; § Various (unspecified) cephalosporins with medium to long halftimes were used

Appendix 5. SSI definitions deviating from the CDC definition

- a Purulent discharge with or without culture
- b Purulent discharge, or serous with a positive culture
- c Discharge with a positive culture
- d Wound infection, not otherwise specified
- e Pus drainage at the fracture site or in the vicinity of the surgical intervention site; b) increased swelling 7 days after the operation; c) presence of a fistula in the area of the surgical intervention or at the site of the fracture, with active drainage; d) other clinical features observed by the evaluator, including typical signs of infection such as fever, oedema and localized redness.
- f Purulent discharge or abscess
- g Purulent discharge, positive bacteriological culture, abscess, peritonitis, septicaemia
- h Purulent discharge, serous discharge + positive bacteriological cultures, serous discharge after the patient had returned home. Intraperitoneal abscess was diagnosed by ultrasonic evidence of an abscess and by laparotomy
- 0: No sign of infection., 1: Minor infection (erythema, stitch abscess or skin edge necrosis)., 2: Major infection (purulent discharge or wound dehiscence).
- Pain at the operative site, persistent fever >38°C wound erythema, tenderness, wound discharge and dehiscence.
- k Presence of erythema, purulent discharge, cellulitis or wound abscess, peritonitis, pelvic abscess or wound dehiscence.
- 1 Superficial or deep infection, pus discharge, abscess formation, wound dehiscence, and hematoma formation
- m Abdominal wound infection or trocar wound infection (including wound discharge or abscess). Pelvic abscess or tuba-ovarian abscess. Vaginal cuff abscess. Postoperative septicaemia.
- n Pelvic cellulitis, vaginal cuff abscess, pelvic abscess, wound infection
- o If the wound appeared red or oedematous or if there was drainage.
- p A wound was considered infected if the colour became red or the wound was swollen. A pink wound that developed purulent discharge was also considered infected.
- q Purulent drainage (either spontaneously or by incision) or muco-cutaneous fistula interpreted as wound infection.
- r Major wound infection was defined as wound breakdown and undermining of tissues sufficient to allow packing of the wound. Lesser complications, such as cellulitis or a tiny fistula, allowing only entry of a cotton-tipped applicator were considered as minor.
- Presence of purulent drainage (either spontaneously or by incision), accompanied by pain or tenderness, localized swelling, redness, and heat or fever (>38·5° C) or an increase in localized swelling after an initial postoperative decrease of oedema, together with pain, discomfort, induration, and an increase in body temperature (>38·5° C).
- t The need for additional antibiotics
- u Wound infection Erythema of incision(s), pus and/or turbid fluid. Intra-abdominal abscess
- v Purulent discharge, endoperitoneal abscess or diffuse peritonitis but not secondary to anastomotic leakage
- w Infiltrate, dehiscence or Purulent secretion of the wound.
- x Purulent drainage at the operative site with the presence of one or more of the classic signs and symptoms of inflammation (rubor, calor, tumor, dolor)
- z Pus discharge from the wound, redness, tenderness and oedema. Intra-abdominal collection was defined as fluid collection inside the peritoneal cavity confirmed by ultrasound or CT

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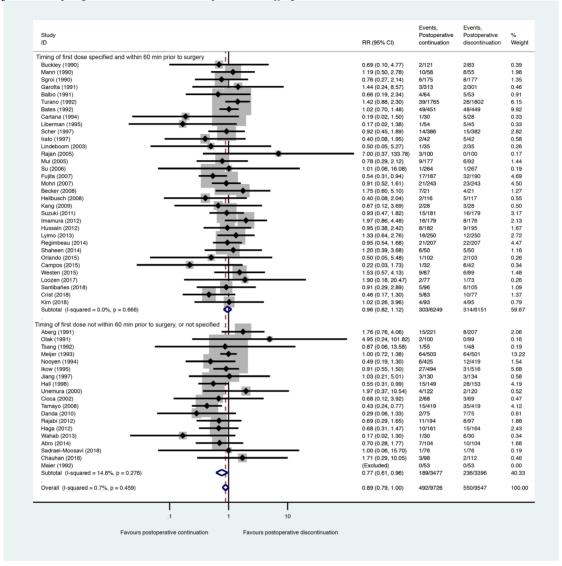
Appendix 6. R Explanatory	sG	s of t	SSI in longer	SSI shorter	ogroup an Relative risk	tau 2 _{MA}	urgical sul	P-Value for	% of heterogeneity
variable	50	11	regimen	regimen	(95%CI)		taa MR	subgroup differences	variance explained
					Overall anal	yses			
Overall analysis	A	52	492 of 9,726	549 of 9,547	0·89 (0·79, 1·00)	0.001	NA	NA	NA
Optimal regimen	В	24	196 of 4,648	186 of 4,552	1·04 (0·85, 1·27)	0.000	NA	NA	NA
			l .		Subgroup ana	lyses	•		
Maxillofacial	A	6	9 of 268	27 of 279	0·38 (0·18, 0·80)	0.000	0.000	0.025	100
surgery	В	3	4 of 95	11 of 105	0·44 (0·14, 1·39)	0.000	0.000	0.137	0
Cardiac surgery	A	2	21 of 844	47 of 838	0·45 (0·27, 0·74)	0.000	0.000	0.006	100
surgery	В	0	NA	NA	NA	NA	NA	NA	NA
Vascular Surgery	A	1	15 of 149	28 of 153	0·55 (0·31, 0·99)	0.000	0.000	0.102	100
Surgery	В	0	NA	NA	NA	NA	NA	NA	NA
	A	6	31 of 738	30 of 553	0·74 (0·44, 1·22)	0.000	0.003	0.458	0
Appendectomy	В	3	18 of 413	20 of 332	0·73 (0·36, 1·47)	0.047	0.000	0.285	0
Colorectal	A	2	32 of 368	48 of 269	0·68 (0·40, 1·15)	0.048	0.000	0.182	100
surgery	В	1	15 of 181	16 of 179	0·93 (0·47, 1·82)	0.000	0.000	0.725	0
Upper GI	A	4	51 of 647	51 of 636	0·98 (0·62, 1·54)	0.058	0.004	0.612	0
surgery	В	3	41 of 486	36 of 472	1·11 (0·63, 1·97)	0.087	0.000	0.812	0
Chole-	A	6	39 of 693	37 of 712	1·06 (0·67, 1·64)	0.000	0.002	0.392	0
cystectomy	В	2	6 of 170	5 of 168	1·19 (0·37, 3·87)	0.000	0.000	0.822	0
Hepatobiliary Surgery	A	1	64 of 503	64 of 501	1·00 (0·72, 1·38)	0.000	0.003	0.470	0
	В	0	NA	NA	NA	NA	NA	NA	NA
Mixed general	A	8	164 of 3617	152 of 3658	1·08 (0·87, 1·34)	0.000	0.000	0.029	100
surgery	В	3	60 of 2172	47 of 2205	1·30 (0·89, 1·88)	0.000	0.000	0.174	0
Caesarean	A	3	31 of 387	23 of 389	1·35 (0·81, 2·28)	0.000	0.000	0.101	100
section	В	3	31 of 387	23 of 389	1·35 (0·81, 2·28)	0.000	0.000	0.281	0
Gynaecological surgery	A	3	4 of 336	11 of 337	0·37 (0·12, 1·17)	0.000	0.000	0.136	100

	В	1	1 of 264	1 of 267	1·01 (0·06, 16·08)	0.000	0.000	0.984	0
Ortho/Trauma	A	4	12 of 633	19 of 578	0·57 (0·28, 1·19)	0.000	0.000	0.233	100
surgery	В	3	9 of 320	17 of 277	0·48 (0·22, 1·06)	0.000	0.000	0.047	0
Thoracic surgery	A	2	5 of 230	3 of 233	1·44 (0·36, 5·87)	0.000	0.003	0.492	0
	В	0	NA	NA	NA	NA	NA	NA	NA
Head and neck	A	3	13 of 211	8 of 208	1·65 (0·41, 6·69)	0.436	0.001	0.302	29
surgery	В	1	10 of 58	8 of 55	1·19 (0·50, 2·78)	0.000	0.000	0.758	0
Transplantation	A	1	1 of 102	2 of 203	0·50 (0·05, 5·48)	0.000	0.004	0.645	0
surgery	В	1	1 of 102	2 of 203	0·50 (0·05, 5·48)	0.000	0.000	0.551	0

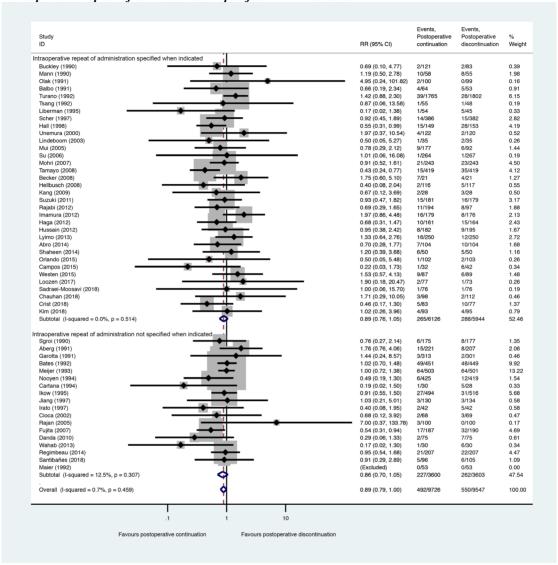
SG: Subgroup, A: Overall analysis, B: Subgroup; Adherence to current best practice standards of SAP, N: Number of studies, SSI: Surgical site infection, 95%CI: 95% confidence interval, NA: Not available, tau²: Tau-squared, MR: Meta-regression, MA: Meta-analysis, % of heterogeneity variance explained: $\left(\frac{\tau^2_{MA(overal)} - \tau^2_{MR}}{\tau^2_{MA(overal)}}\right)$

Appendix 7. Forest plots

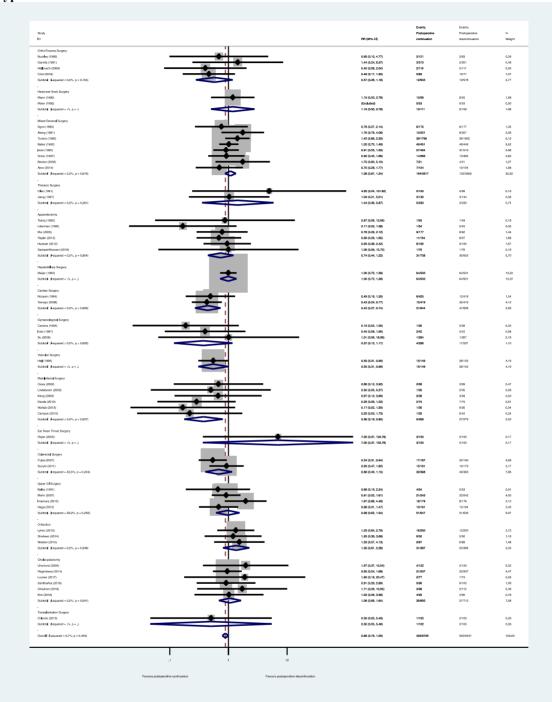
Appendix 7a. Forest plot: Postoperative continuation of surgical antibiotic prophylaxis vs. postoperative discontinuation of surgical antibiotic prophylaxis. Subgroup analysis: *Timing of first dose specified and within 60 min prior to surgery*



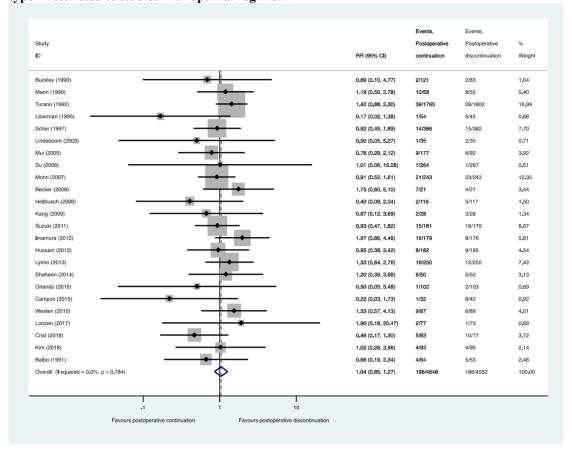
Appendix 7b. Forest plot: Postoperative continuation of surgical antibiotic prophylaxis vs. postoperative discontinuation of surgical antibiotic prophylaxis. Subgroup analysis: Intraoperative repeat of administration specified when indicated



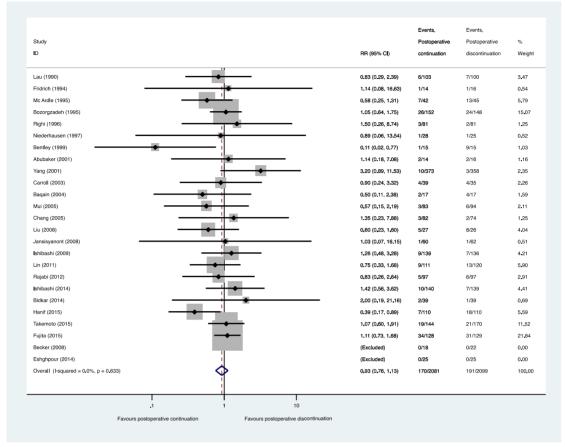
Appendix 7c. Forest plot: Postoperative continuation of surgical antibiotic prophylaxis vs. postoperative discontinuation of surgical antibiotic prophylaxis. Stratified analysis: Procedure type



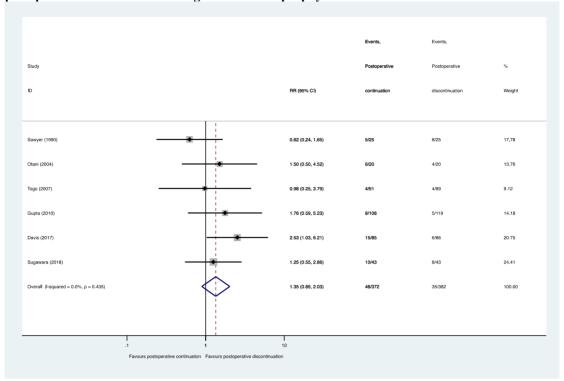
Appendix 7d. Forest plot: Postoperative continuation of surgical antibiotic prophylaxis vs. postoperative discontinuation of surgical antibiotic prophylaxis. Stratified analysis: Procedure type – restricted to studies with optimal regimen.



Appendix 7e. Forest plot: Postoperative continuation of SAP > 24h vs postoperative continuation of $SAP \le 24h$.



Appendix 7f. Forest plot: Postoperative continuation of surgical antibiotic prophylaxis > 48h vs postoperative continuation of surgical antibiotic prophylaxis <= 48h



Appendix 8. Studies reporting adverse events related to SAP

Study	Adverse event definition	Longer	Shorter
		postoperative	postoperative
		regimens	regimens
Mui 2005 ¹¹⁶ ¶	Clostridium difficile confirmed by fecal clostridium toxin	5 of 177	0 of 92
Karran 1993 ¹¹⁷ †	Hypotension, phlebitis, rash, erythema	5 of 114	1 of 113
Turano 1992 ⁸⁶ *	Thrombophlebitis, allergic reaction and gastrointestinal	40 of 1517	10 of 1700
	disturbances		
Bidkar 2014 ¹³⁴ ‡	Gastrointestinal disturbances	19 of 39	1 of 39
Rajan 2005 ¹⁰⁸ *	Nausea, diarrhea, skin rash, pruritus	29 of 100	2 of 100
de Santibanes 2018 ⁷⁶ *	Unspecified	4 of 96	3 of 105
Liu 2008 ¹³¹ ‡	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Carrol 2003 ¹³² ‡	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Righi 1996 ¹³³ ‡	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Maier 1992 ¹⁰⁶ *	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Sawyer 1990 ¹⁴⁵ §	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Kang 2009 ¹¹⁴ *	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Lindeboom 2003110 *	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Suzuki 2011 ⁶⁹ *	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Fujita 2015 ¹²² *	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Imamura 2012 ⁷¹ *	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Mohri 2007 ⁷⁴ *	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Regimbeau 2007 ⁷⁹ *	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Becker 200883 *	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Cartana 1994 ⁹⁵ *	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Eshghpour 2014 ¹³⁶ ‡	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Loozen 2017 ⁷⁸ *	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Rajabi 2012 ¹¹⁵ ¶	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.
Danda 2010 ¹¹³ *	No adverse events attributable to antibiotic use in both the	intervention and c	ontrol group.

^{*} Postoperative continuation vs immediate discontinuation of SAP; † Postoperative continuation for 24 h vs a single dose after surgery; ‡ Postoperative continuation for >24 h $vs \le 24$ h; § Postoperative continuation for >48 h $vs \le 48$ h; ¶ Postoperative continuation vs immediate discontinuation of SAP and Postoperative continuation for >24 h $vs \le 24$ h;

Appendix 9. Studies reporting costs of SAP continuation

Study	Cost included	Cost postoperative continuation	Cost postoperative discontinuation	Absolute difference	Relative difference
Liberman 1995 ⁶⁷ *	Antibiotics	\$ 54.80	\$ 17.90	+ \$ 36,90	3.06
Su 2005 ⁹³ *	Antibiotics	\$ 48,00	\$ 3.50	+ \$ 44,50	13.71
Chang 2005 ¹²⁷ †	Total costs	\$ 1,768.00	\$ 1,728.00	+ \$ 40,00	1.02
Orlando 2015 ¹⁰⁵ *	Antibiotics	\$ 38.80	\$ 3.88	+ \$ 34,92	10,00
Rajan 2005 ¹⁰⁸ *	Total costs	\$ 93.45	\$ 14.50	+ \$ 78,95	6,44

^{*} Postoperative continuation vs immediate discontinuation of SAP; † Postoperative continuation for >24 h $vs \le 24$ h

Appendix 10. Risk of bias evaluation of the included studies

Appendix 10). Risk of bia	s evaluation	of the inclu	ded studies			
	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Sadraei- Moosavi 2018 ⁶⁵	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	All predefined outcomes reported	No concerns
Hussain 2012 ⁶⁶	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Liberman 1995 ⁶⁷	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Tsang 1992 ⁶⁸	High	High	High	Unclear	Unclear	Unclear	Low
Support for judgement	Randomized according to hospital numbers (even -odd)	Randomized according to hospital numbers (even -odd)	No blinding described and no allocation concealment	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Suzuki 2011 ⁶⁹	Low	Unclear	Unclear	Unclear	Low	Unclear	Low
Support for judgement	Random number table	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Missing data balanced in numbers across intervention groups for similar reasons	No protocol or registration	No concerns
Fujita 2007 ⁷⁰	Low	Low	High	High	Low	Unclear	Low
Support for judgement	Central computer randomisation	Central computer randomisation	Not blinded	Not blinded	Low attrition, unlikely to influence outcome	No protocol or registration	No concerns
Imamura 2012 ⁷¹	Low	Low	High	High	Low	Low	Low
Support for judgement	Mersenne twister randomisation	Central randomisation	Not blinded	Not blinded	Intention to treat analysis	All predefined outcomes reported	No concerns
Haga 2012 ⁷²	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Balbo 1991 ⁷³	Unclear	High Based on a	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	randomisation list	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Mohri 2007 ⁷⁴	Low	Low	Low	Low	Low	Unclear	Low
Support for judgement	Central computer randomisation	Central computer randomisation	Blinded investigators and patients	Independent outcome assessor	Balanced in reason and groups, unlikely to affect outcome	No protocol or registration	No concerns
Chauhan 2018 ⁷⁵	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgment	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Santibañes 2018 ⁷⁶	Low	Low	Low	Low	Low	Low	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Blinded investigators and patients	Blinded investigators and patients	Intention to treat analysis	All predefined outcomes reported	No concerns
Kim 2017 ⁷⁷	Low	Low	Low	Low	Low	Low	Low
Support for judgement	Computer randomisation	Central allocation by	Blinded investigators and patients	Blinded investigators and patients	Missing outcomes balanced in	All predefined outcomes reported	No concerns

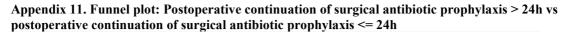
		independent			reason and		
Y 201778		investigator	*** 1	** 1	groups		<u> </u>
Loozen 2017 ⁷⁸	Low	Low	High	Unclear	Low Missing	Low	Low
6	Central	Central		Not	outcomes	All predefined	
Support for judgement	computer	computer	Not blinded	(sufficiently)	balanced in	outcomes	No concerns
juagement	randomisation	randomisation		described	reason and	reported	
Regimbeau					groups		
2014 ⁷⁹	Low	Low	Unclear	Low	Low	Unclear	Low
6	Central	Central	Not	Blinded	T	NI 1	
Support for judgement	computer	computer randomisation	(sufficiently)	outcome	Intention to treat analysis	No protocol or registration	No concerns
juagement	randomisation	based	described	assessor	treat analysis	registration	
Unemura	High	High	Unclear	Unclear	Unclear	Unclear	Low
200080	Randomized by						
	alternately	alternately	Not	Not	Not	N	
Support for judgement	selecting	selecting	(sufficiently)	(sufficiently)	(sufficiently)	No protocol or registration	No concerns
juagement	treatment	treatment	described	described	described	registration	
Meijer 1993 ⁸¹	allocation Low	allocation Low	Low	Low	Low	Unclear	Low
	Central	Central	Blinded	Blinded			20.7
Support for judgement	computer	computer	investigators	outcome	Intention to treat analysis	No protocol or registration	No concerns
Abro 2014 ⁸²	randomisation Unclear	randomisation Unclear	and patients Unclear	assessor Unclear	•	Unclear	Low
A010 2014	Unclear	Officiear	Unclear	Unclear	High High attrition	Unclear	Low
Support for	Not	Not	Not	Not	relative to	No protocol or	
judgement	(sufficiently)	(sufficiently)	(sufficiently)	(sufficiently)	events. Could	registration	No concerns
Jg	described)	described	described	described	have affected outcome		
Becker 2008 ⁸³	Low	Unclear	Low	Unclear	Unclear	Unclear	Low
Support for	Drawing of	Not	Randomisation	Not	Not	No protocol or	
judgement	envelopes	(sufficiently)	after procedure	(sufficiently)	(sufficiently)	registration	No concerns
Scher 1997 ⁸⁴	Low	described Low	Unclear	described Unclear	described Unclear	Unclear	Low
Selici 1997	Central	Central	Not			Gileieur	Eo II
Support for	randomisation	randomisation	(sufficiently)	Not (sufficiently)	Not (sufficiently)	No protocol or	No concerns
judgement	by random number chart*	by random number chart *	described	described	described	registration	Tto concerns
Kow 1995 ⁸⁵	Unclear	Unclear	High	Unclear	Unclear	Unclear	Low
Support for	Not	Not	Not blinded	Not	Not	No protocol or	
judgement	(sufficiently) described	(sufficiently) described	1vot omided	(sufficiently) described	(sufficiently) described	registration	No concerns
Turano 1992 ⁸⁶	Unclear	High	Unclear	Unclear	Unclear	Unclear	Low
Support for	Not	Open	Not	Not	Not	No protocol or	
judgement	(sufficiently)	randomisation	(sufficiently)	(sufficiently)		registration	No concerns
Bates 1992 ⁸⁷	described Low	Unclear	described Unclear	described Low	described Low	Unclear	Low
					Attrition low	Circical	LOW
Support for	Randomized by random number	Not (sufficiently)	Not (sufficiently)	Blinded outcome	and balanced.	No protocol or	No concerns
judgement	table	described	described	assessor	Unlikely to affect outcome	registration	140 concerns
Aberg 1991 ⁸⁸	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for	Not	Not	Not	Not	Not	No protocol or	
judgement	(sufficiently)	(sufficiently)	(sufficiently)	(sufficiently)	(sufficiently)	registration	No concerns
Sgroi 1990 ⁸⁹	described Unclear	described Unclear	described Unclear	described Unclear	described Unclear	Unclear	Low
	Not	Not	Not	Not	Not		LOW
Support for judgement	(sufficiently)	(sufficiently)	(sufficiently)	(sufficiently)	(sufficiently)	No protocol or registration	No concerns
Westen 2015 ⁹⁰	described Unclear	described Low	described Unclear	described Low	described Low	Low	Low
W CSICII 2013		Sequentially			LUW		LUW
Support for	Not (sufficiently)	numbered,	Not (sufficiently)	Blinded outcome	Intention to	All predefined outcomes	No concerns
judgement	(sufficiently) described	opaque, sealed	(sufficiently) described	assessor	treat analysis	reported	No concerns
Shaheen 2014 ⁹¹	Low	envelopes Unclear	Unclear	Unclear	Unclear	Unclear	Low
	LOW	Not	Not	Not	Not		LOW
Support for judgement	Shuffled cards	(sufficiently)	(sufficiently)	(sufficiently)	(sufficiently)	No protocol or registration	No concerns
Lyimo 2013 ⁹²	Low	described Unclear	described	described	described Low	Unclear	Low
	Low	Unclear Not	High	High			Low
Support for	Drawing of	(sufficiently)	Not blinded	Not blinded	Intention to	No protocol or	No concerns
judgement	envelopes	described			treat analysis	registration	

Su 2005 ⁹³	Low	Unclear	Unclear	Unclear	High	Unclear	Low
Support for judgement	Computer randomisation	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Unbalanced attrition. Could have affected outcome	No protocol or registration	No concerns
Irato 199794	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Cartaña 1994 ⁹⁵	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Random number table	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Buckley 199096	Unclear	Unclear	Low	Low	High	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Blinded investigators and patients	Blinded outcome assessors	Unbalanced attrition. Could have affected outcome	No protocol or registration	No concerns
Garotta 1991 ⁹⁷	Low	Low	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Central computer randomisation	Central computer randomisation	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Hellbusch 2008 ⁹⁸	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	High attrition relative to events. Could have affected outcome	No protocol or registration	No concerns
Crist 2018 ⁹⁹	Unclear	Low	Low	Low	High	Unclear	Low
Support for judgement	Not (sufficiently) described	Pharmacy controlled randomisation	Blinded investigators and patients	Blinded investigators and patients	High attrition relative to events. Could have affected outcome	No protocol or registration	No concerns
Nooyen 1994 ¹⁰⁰	Low	Low	Unclear	Unclear	High	Unclear	Low
Support for judgement	Central computer randomisation	Central computer randomisation	Not (sufficiently) described	Not (sufficiently) described	Unbalanced attrition. Could have affected outcome	No protocol or registration	No concerns
Tamayo 2008 ¹⁰¹	Low	Unclear	Unclear	Low	High	Unclear	Low
Support for judgement	Computerized randomisation	Not (sufficiently) described	Not (sufficiently) described	Blinded outcome assessor	High attrition relative to events. Could have affected outcome	No protocol or registration	No concerns
Olak 1991 ¹⁰²	Low	Low Central random	Low Blinded	Low Blinded	Unclear Not	Unclear	Low
Support for judgement	number generation	number generation	investigators and patients	outcome assessor	(sufficiently) described	No protocol or registration	No concerns
Jiang 2004 ¹⁰³	Low	High	Unclear Not	Unclear Not	Unclear Not	Unclear	Low
Support for judgement	Random number list	Open list	(sufficiently) described	(sufficiently) described	(sufficiently) described	No protocol or registration	No concerns
Hall 1998 ¹⁰⁴	Low	Low	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Computer randomisation	Sequentially numbered, opaque, sealed envelopes	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Orlando 2015 ¹⁰⁵	Low	Low	Unclear	Unclear	Low	Low	Low
Support for judgement	Central computer randomisation	Central computer randomisation	Not (sufficiently) described	Not (sufficiently) described	All patients complied with the study protocol	All predefined outcomes reported	No concerns
Maier 1992 ¹⁰⁶	High	High	High	Unclear	Unclear	Unclear	Low
1	Randomisation	Randomisation	No blinding	Not	Not	No protocol or	
Support for judgement Mann 1990 ¹⁰⁷	by even and uneven days Unclear	by even and uneven days Unclear	described and no allocation concealment Unclear	(sufficiently) described Unclear	(sufficiently) described Unclear	registration Unclear	No concerns Low

	Not	Not	Not	Not	Not	<u> </u>	
Support for judgement	(sufficiently) described	(sufficiently) described	(sufficiently) described	(sufficiently) described	(sufficiently) described	No protocol or registration	No concerns
Rajan 2005 ¹⁰⁸	Low	Unclear	Low	Unclear	Unclear	Unclear	Low
Support for judgement	Drawing of envelopes	Not (sufficiently) described	Blinded investigators	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Campos 2015 ¹⁰⁹	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Lindeboom 2003 ¹¹⁰	Low	High	Unclear	Low	Unclear	Unclear	Low
Support for judgement	Random number list	Open list	Not (sufficiently) described	Blinded outcome assessor	Not (sufficiently) described	No protocol or registration	No concerns
Cioaca 2002 ¹¹¹	Unclear	Unclear	Unclear	Low	Low	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Blinded outcome assessor	Attrition low and balanced. Unlikely to affect outcome	No protocol or registration	No concerns
Wahab 2013 ¹¹²	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Danda 2010 ¹¹³	Unclear	Unclear	Low	Low	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Blinded investigators and patients	Blinded outcome assessor	Not (sufficiently) described	No protocol or registration	No concerns
Kang 2009 ¹¹⁴	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Computer randomisation	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Rajabi 2012 ¹¹⁵	Unclear	Unclear	Low	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Mui 2005 ¹¹⁶	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Karran 1993 ¹¹⁷	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	High attrition relative to events. Could have affected outcome	No protocol or registration	No concerns
Ishibashi 2014 ¹¹⁸	Unclear	Unclear	Low	Unclear	Low	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Randomisation after procedure	Not (sufficiently) described	Attrition low and balanced. Unlikely to affect outcome	No protocol or registration	No concerns
Ishibashi 2009 ¹¹⁹	Unclear	Unclear	Low	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Randomisation after procedure	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
McArdle 1995 ¹²⁰	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Becker 1991 ¹²¹	Unclear	Unclear	Low	Low	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Blinded investigators and patients	Blinded outcome assessor	Not (sufficiently) described	No protocol or registration	No concerns
Fujita 2015 ¹²²	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Lau 1990 ¹²³	Unclear	Unclear	Low	Low	High	Unclear	Low

					High attrition		
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Randomisation after procedure	Blinded outcome assessor	relative to events. Could have affected	No protocol or registration	No concerns
** **********					outcome		
Yang 2001 ¹²⁴	Unclear Not	Unclear Not	Unclear Not	Unclear Not	Unclear Not	Unclear	Low
Support for judgement	(sufficiently) described	(sufficiently) described	(sufficiently) described	(sufficiently) described	(sufficiently) described	No protocol or registration	No concerns
Bozorgzadeh 1999 ¹²⁵	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Hanif 2015 ¹²⁶	High	High	Unclear	Unclear Not	Unclear	Unclear	Low
Support for judgement	Randomisation by alternating assignment	Randomisation by alternating assignment	Not (sufficiently) described	(sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Chang 2005 ¹²⁷	Low	Low	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Central computer randomisation	Central computer randomisation	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No concerns
Takemoto 2015 ¹²⁸	Low	Unclear	Low	Low	High	Low	Low
Support for judgement	Computer randomisation	Not (sufficiently) described	Investigators blinded	Outcome assessors blinded	High attrition relative to events. Could have affected outcome	All predefined outcomes reported	No concerns
Lin 2011 ¹²⁹	Low	unclear	Unclear	Low	low	Unclear	Low
Support for judgement	Computer randomisation	Not (sufficiently) described	Not (sufficiently) described	Blinded outcome assessor	Intent-to-treat analysis	No protocol or registration	No concerns
Niederhauser 1997 ¹³⁰	Low	Unclear	Low	Unclear	Low	Unclear	Low
Support for judgement	Randomisation list	Not (sufficiently) described	Randomisation after procedure	Not (sufficiently) described	All participants were analysed	No protocol or registration	No concerns
Liu 2008 ¹³¹	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Computer randomisation	Not (sufficiently) described	Randomisation after procedure	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Carroll 2003 ¹³²	unclear	unclear	Unclear	Unclear	Unclear	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns
Righi 1996 ¹³³	unclear	unclear	Unclear	Unclear	High	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	High attrition relative to events. Could have affected outcome	No protocol or registration	No concerns
Bidkar 2014 ¹³⁴	Low	Unclear	Low	Low	Low	Unclear	Low
Support for judgement	Computer randomisation	Not (sufficiently) described	Blinded investigators	Blinded outcome assessors	All participants were analysed	No protocol or registration	No concerns
Abubaker 2001 ¹³⁵	Unclear	Low	Low	Low	High	Unclear	Low
Support for judgement	Not (sufficiently) described	Central randomisation	Blinded investigators and participants	Blinded outcome assessors	High attrition relative to events. Could have affected outcome	No protocol or registration	No concerns
Eshghpour 2014 ¹³⁶	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	All participants were analysed	No protocol or registration	No concerns
Jansisyanont 2008 ¹³⁷	Unclear	Unclear	Unclear	Unclear	High	Unclear	Low
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	High attrition relative to events. Could	No protocol or registration	No concerns

					have affected							
					outcome							
Baqain 2004 ¹³⁸	Low	Low	Low	low	Low	Unclear	Low					
Support for judgement	Central randomisation by random list	Central randomisation by random list	Blinded investigators and patients	Blinded outcome assessors	All participants were analysed	No protocol or registration	No concerns					
Bentley 1999 ¹³⁹	Unclear	Unclear	Low	Low	Unclear	Unclear	Low					
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Blinded investigators and patients	Blinded outcome assessors	Not (sufficiently) described	No protocol or registration	No concerns					
Fridrich 1994 ¹⁴⁰	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Low					
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	All participants were analysed	No protocol or registration	No concerns					
Togo 2007 ¹⁴¹	Low	Low	Unclear	Unclear	low	unclear	Low					
Support for judgement	Central computer randomisation	Central computer randomisation	Not (sufficiently) described	Not (sufficiently) described	All participants were analysed	No protocol or registration	No concerns					
Sugawara 2018 ¹⁴²	Low	Low	Low	Unclear	Low	Low	Low					
Support for judgement	Central computer randomisation	Central computer randomisation	Randomisation after procedure	Not (sufficiently) described outcome	All participants were analysed	All predefined outcomes reported	No concerns					
Gupta 2010 ¹⁴³	Low	Low	Low	Low	Low	Unclear	Low					
Support for judgement	Randomisation by random number table	Allocation concealed throughout the study	Blinded investigators and patients	Blinded outcome assessors	Attrition low. Unlikely to affect outcome.	No protocol or registration	No concerns					
Otani 2004 ¹⁴⁴	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low					
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns					
Sawyer 1990 ¹⁴⁵	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low					
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns					
Davis 2017 ¹⁴⁶	Low	Unclear	Low	Low	High	Low	Low					
Support for judgement	Randomisation by drawing envelopes	Not (sufficiently) described	Blinded investigators and patients	Blinded outcome assessors	High attrition relative to events. Could have affected outcome	All predefined outcomes reported	No concerns					
Park 2010 ¹⁴⁷	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low					
Support for judgement	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	Not (sufficiently) described	No protocol or registration	No concerns					
		* Information obtained through correspondence with author										





The figure illustrates the distribution of effect estimates of the different studies (x-axis) against their precision (y-axis). Asymmetry across the vertical midline, representing the overall effect estimate of the meta-analysis, indicates publication bias. Both funnel plots show a symmetrical distribution and no indication of publication bias.

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