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The use of triclosan coated sutures to prevent surgical site infections: a systematic review and meta-analysis of the literature

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ABSTRACT

Introduction and objectives

Surgical site infections represent a common and serious complication of all surgery. Sutures can lead to the development of surgical site infections as micro-organisms can colonise the suture as it is implanted the skin. Triclosan coated sutures are antibacterial sutures aimed at reducing surgical site infections.

Our objective is to systematically review and summarise the available evidence assessing the effectiveness of triclosan coated sutures in preventing surgical site infections.

Methods

A systematic review of EMBASE, MEDLINE, AMED and CENTRAL was performed to identify full text randomised controlled trials.

Intervention

Triclosan coated sutures versus non triclosan coated sutures.

Primary outcome

Our primary outcome was the development of surgical site infections at 30 days post operatively. A meta-analysis was performed using a random effects model.

Results

Twenty one RCTs were included involving 11,248 participants. Triclosan coated sutures were used in 5656 participants and non triclosan coated sutures were used in 5592. Triclosan coated sutures significantly reduced the risk of surgical site infections at 30 days (RR 0.74, 95% CI 0.64 to 0.86). Further sensitivity analysis demonstrated that triclosan coated sutures significantly reduced the risk of surgical site infections in both clean and contaminated surgery.

Conclusion

Triclosan coated sutures have been shown to significantly reduced the risk of surgical site infections when compared to standard sutures. This is in agreement with previous work in this area. This study represented the largest review to date in this area. Further work may be required in specific categories of

surgery e.g. dirty or clean contaminated. Heterogeneity of the included studies should be noted when interpreting the results of this review.

Registration

PROSPERO (Reference: CRD42014014856).

Key words

Surgical site infection, triclosan, systematic review

Article summary

Strengths and limitations of this study

Strengths

- Systematic nature of data collection and analysis
- Largest review to date in this topic area
- Analyses performed comparing difference classifications of surgery i.e clean, clean-contaminated, contaminated and dirty.

Limitations

- Heterogenous nature of included studies. E.g. different age of participants, co-morbidities and surgery type.

Original protocol

A protocol for this review was prospectively registered with PROSPERO (Reference: CRD42014014856).

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Competing interests

All authors report no competing interests.

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INTRODUCTION

Surgical site infections (SSIs) represent a common complication throughout all surgical procedures[1]. It is estimated that SSIs account for 5% of all surgical complications[2] and 20% of all healthcare associated infections[3,4]. It is generally believed that the number of surgical procedures, in particular in elective orthopaedics[5], will increase over the next decade, therefore increasing the incidence of SSIs. SSIs are associated with prolonged hospital admission[6] and increased morbidity and mortality[7,8,9]. In addition to having a significant impact on patient care and experience, SSIs also add substantial costs to healthcare providers. It is estimated that SSIs cost UK healthcare services approximately £61 million in 2012[10] and figures from the US highlight the extensive cost of SSIs with an estimated additional $2300 per case[11]. Furthermore, Fleck *et al.* found that the mean cost of treated a SSI following sternal wound incision was $11,200[12]. These are conservative estimates as active surveillance of SSIs not routinely performed[6].

Due to the wide ranging deleterious effects of SSIs and their treatment, particularly in the context of increasing numbers of surgical procedures, there is a clinical need to reduce the incidence of SSIs. SSIs are multifactorial with patient factors such as age, co-morbidities including diabetes, and immunosuppression[7,13-15] contributing to their development along with surgical factors. Many patient factors may not be optimised and hence research focus has been placed on surgical factors, including suture material.

SSIs may arise from suture material when bacteria colonise the material[16] and as it passes through the skin a biofilm[17] is created. This biofilm establishes an immunity from both antimicrobial treatment and the host immune system[6,18]. Once this biofilm develops there is an increased chance of a SSI developing. Research has shown bacteria may colonise monofilament and braided sutures[17,19,20]. With this in mind, considerable work has been carried out since the 1950s in coating suture material with an antimicrobial, including silver[21,22]. Triclosan (polychlorophenoxyphenol) has been used for its antiseptic properties for

many years in toothpaste[24] and soap[5] and has an established safety profile[5]. Despite its widespread use there have been no identified incidences of resistance[24]. Triclosan has been used to successfully coat the following sutures and gained FDA approval in 2002[23]: braided polyglactan 910 (Vicryl Plus), poliglecaprone 25 (Monocryl Plus) and polydioxanone (PDS Plus).

In vitro and *in vivo* studies have shown the effectiveness of triclosan coated sutures[24-26] in killing bacteria associated with SSIs and inhibiting colonisation of suture material, with one study demonstrating a 66% reduction in bacterial colonisation[27]. Since then a large number of randomised control trials (RCTs) have been performed with contrasting results in the effectiveness of triclosan coated sutures in preventing SSIs. Subsequent meta-analyses have also produced conflicting results and hence the true effect remains unclear[6,7,28-33]. The most recent and largest systematic review to date was performed by De Jonge *et al.* and found triclosan coated sutures significantly reduced the incidence of SSIs[33]. This review searched the literature until November 2015 and included 6462 patients from RCTs published in peer-reviewed journals as well as conference abstracts. Performing robust methodological appraisal on conference abstracts is not possible and they do not permit thorough risk of bias assessments. As they have not undergone the formal journal peer-review process, they represent a potentially biased and unreliable source of data. Since this review a number of large, high quality RCTs have been produced[34,35]. Of note, a recent RCT of 2546 patients found that triclosan coated sutures did not reduce the incidence of SSIs; a finding in contrast to the previous systematic review[33,35]. This represents a substantial increase in the number of patients available for meta-analysis since the last review. There is therefore a timely need to undertake a further systematic review and meta-analysis to assimilate the current evidence and inform clinical practice.

This systematic review and meta-analysis aims to determine whether the use of triclosan coated sutures reduces the incidence of SSIs in comparison to standard non-coated sutures.

PICOS statement

The included population is patients of any age and gender undergoing any surgical procedure utilising sutures to close the wound. The intervention studied is the use of triclosan coated sutured and comparison is made with non-triclosan coated sutures. The outcomes assessed are the rates of SSIs, including superficial and deep SSIs. This systematic review will only include RCTs.

METHODS

A systematic review of the available literature was conducted and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance[36]. A protocol for this review was prospectively registered with PROSPERO (Reference: CRD42014014856).

Search methods

Electronic searches were conducted using OVID SP on the following databases: MEDLINE(1946-March Week 5 2018); Excerpta Medica Database (EMBASE) (1974 to 2018 April 10); Allied and Complementary Medicine (AMED) (1985 to March 2018); and Cochrane Central Register of Controlled Trials (CENTRAL). A multi-purpose search was performed for all terms and the search terms were: "Triclosan", "Anti-bacterial agents", "Anti-infective agents, local", "Coated materials, biocompatible", "Biomimetic material", "Sutures", "Vicryl Plus", "Monocryl Plus", "PDS Plus", "Surgical site infection", "Surgical Wound infection". The search was conducted on 10th April 2018.

Selection of Studies

Two authors (IA and AB) independently selected studies for inclusion. Any disagreement was resolved by a third author (ED). Titles and abstracts were screened and full texts obtained for any studies of interest. The eligibility criteria were formed from the PICOS statement and registered on PROSPERO prior to

undertaking the search. Only RCTs published in peer-reviewed journals presenting new data were included.

Data extraction

Data was independently extracted from eligible included studies onto predetermined forms by two authors (IA and AB). Any discrepancies were then resolved. Data extracted included baseline patient characteristics, surgical procedures performed, number of centres, suture material, SSI diagnostic criteria, length of follow up, routine prophylactic antibiotic use and number of SSIs. Data regarding superficial of deep SSI was extracted when possible. Information regarding randomisation, blinding, funding and country of origin was extracted.

Assessment of Risk of Bias

Two authors (IA and AB) independently appraised eligible studies according to the Cochrane Collaboration's risk of bias tool, resolving any discrepancies with a third author (ED)as necessary[37]. Review Manager version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used to generate the summary figures.

Publication bias was assessed following construction of a funnel plot in order to identify the presence or absence of bias of this kind.

Statistical analysis

A random effects model was used to calculate the predominant relative risk (RR) and the 95% confidence intervals of the studies included. A random effects model was used under the assumption all studies represented a clinically heterogeneous population[38]. Statistically heterogeneity was first assessed using a funnel plot and more formally using the I^2 statistic[39]. Forest plots were then generated summarising the results of the meta-analysis using Review Manager 5.3.

Patient and Public Involvement

Patient and public members were not involved in the development and conduct of this review.

RESULTS

The search revealed 255 records of possible relevance. No other sources of records were identified. Removal of duplicates left 242 records to be examined. 209 records were excluded based on title and abstract screening. 26 full texts were assessed for eligibility and 21 studies were included in the meta-analysis (see figure 1)[2,7,11,34,35,40-55].

Study characteristics

Study characteristics are summarised in table 1. Twenty-one RCTs were included in this review involving 11,248 patients[2,7,11,34,35,40-55]. There were 5,656 patients randomised to triclosan coated sutures and 5592 patients to standard sutures. In studies which reported mean age, the mean age was comparable between the two groups (56.63 vs 56.63). Seven studies were multi-centre[2,7,35,40,50,53,55], with the remainder single-centre studies (n=14)[11,34,41-49,51,52,54]. Vicryl was compared with Vicryl Plus in ten studies[11,35,41-43,45,48-51], two studies compared PDS and versus PDS Plus[7,40], one study compared PDS II with PDS II Plus[46], one study compared Monocryl against Monocryl Plus[47], one compared Chinese silk with Vicryl Plus[55], four studies compared Vicryl and Monocryl versus Vicryl Plus and Monocryl Plus[34,52-54], and two studies compared Vicryl and PDS versus Vicryl Plus and PDS Plus[2,44].

To define SSI, the CDC criteria were used by 14 studies[2,7,11,34,35,43-46,50,52-55], clinical diagnosis was used by two studies[41,47], positive wound culture and clinical judgement was used by one study[51], and four did not provide explicit definitions[40,42,48,49]. Twelve studies used a follow up duration of 30 days or one month or four weeks[2,7,11,34,35,40,43-45,51,53,55], two for two weeks[46,47], one for six weeks[54], one for 80 days[42], one for one year[48], one until discharge[49], and one study did not specify a follow-up regime[41]. Routine prophylactic antibodies were used in 15 studies[2,7,11,35,40,41,44,46-53], no prophylactic antibiotics were used in one study[42], one used prophylactic antibiotics in high risk patients only[54], one study used prophylactic antibiotics in 30% of participants[34], and three did specify prophylactic antibiotic use[43,45,55].

Surgical site infection

The risk of developing surgical site infection was significantly reduced in the triclosan group compared to the standard suture group (RR 0.74, 95% CI 0.64 to 0.86). Heterogeneity was low to moderate (χ^2=24.66, P=0·21, I^2=19%). There were 400 instances of SSI amongst 5656 patients in the triclosan coated suture group and 543 SSIs in 5592 patients in the standard suture group. See figure 2.

Sub-group analysis

Seven studies reported superficial and deep infections separately[2,7,34,35,44,48,53]. There were 144/3421 cases of superficial SSI in the triclosan group and 146/3535 cases in the standard suture group, producing a meta-analysis risk ratio of 1.01 (95% CI 0.79 to 1.28). The risk of developing a deep infection was lower in the triclosan group when compared to the standard suture group, however this was not significant (RR 0.75, 95% CI 0.52 to 1.08). There were 60/3421 cases of deep infections in the triclosan group and 84/3535 cases in the standard suture group. See figure 3.

Nine studies reported the incidence of surgical site infection for clean surgery[34,35,41,45,51-55]. Triclosan coated sutures were associated with a significantly lower incidence of SSI when compared to standard sutures (RR 0.72, 95% CI 0.58 to 0.89).

Five studies reported clean contaminated surgery and there was no difference between the two groups (RR 1.01, 95% CI 0.82,1.26)[2,7,42,44,48].

Two studies reported the incidence of surgical site infections in contaminated surgery[11,49]. Triclosan coated sutures were associated with a significantly lower risk of SSI when compared to standard sutures (RR 0.42, 95% CI 0.2 to,0.79).

Two further studies reported the incidence of surgical site infection for dirty surgery[47,50]. There was no significant difference in the incidence of SSIs between the two groups of sutures (RR 0.74, 95% CI 0.46 to 1.18). See figure 4.

Risk of bias

There was a variability in the included studies risk of bias as assessed by the Cochrane risk of bias tool. The results of the risk of bias screening can be seen on figure 1.

Publication bias was assessed using a funnel plot. The distribution of studies in the funnel plot was symmetrical. No evidence was found for publication bias in this analysis (figure 5).

Statistical heterogeneity was assessed using the Tau^2 (0.02) test and the I^2 (22%) test, indicating there is low heterogeneity between the studies included in this review.

DISCUSSION

This large systematic review of 21 randomised clinical trials included 11,248 patients and there were 943 instances of SSI. The subsequent meta-analysis supports the use of triclosan-coated sutures in reducing the risk of surgical site infections. We report a significantly lower risk of SSI when triclosan coated sutures were used, compared to standard sutures in RCTs. Triclosan coated sutures were used in a wide range of surgeries, including both adult and paediatric patients. The use of triclosan coated sutures significantly reduced the risk of SSI in meta-analyses of clean surgery and also contaminated surgery, and whilst this difference was not statistically significant in dirty surgery, the signal was toward reduced risk with triclosan coated sutures. Further subgroup analysis revealed a signal towards reduced risk of deep SSIs with triclosan coated sutures, however this was not statistically significant. Triclosan coated sutures appear to have no effect on the incidence of superficial SSIs.

Our results support the findings of Konstantelias et al who concluded that triclosan coated sutures were associated with a significantly lower risk of SSI when compared to standard sutures [56]. In addition, the authors concluded that triclosan coated sutures significantly reduced the risk of SSI in clean, clean-contaminated, and contaminated surgery; in agreement with our findings [56]. De Jonge et al reported a meta-analysis of 21 RCTs including 6462 patients, also concluding that triclosan coated sutures significantly reduced the risk of SSI compared to standard sutures [33].

The strengths of this current review include the thorough and systematic nature of data collection. This review represents the most up to date review of the literature and is the largest review of RCTs to date, including 11,248 patients from 21 RCTs. A recent RCT in elective hip and knee surgery included 2546 participants, the largest RCT to date in this subject area. This review is the only review to include this important and well-conducted study. In addition, this systematic review only included peer-reviewed studies with published full texts. Previous meta-analyses have included conference abstracts which do not go through the same rigorous peer-review process as full journal publications and thus represent a potential danger to review quality[33]. Furthermore, robust quality and risk of bias assessment is not possible with these abstract publications[57]. A further strength of this review is the detailed and systematic quality assessments, along with robust Cochrane risk of bias assessments, of all included studies[37,57].

The main weakness of this review is the study population. As mentioned above the review includes procedures which were classed as clean, clean- contaminated, contaminated, and dirty. These types of surgery would all have a differing rates of SSI. The authors therefore performed sub-analyses of the different categories of surgery. Routine antibiotic prophylaxis was used in 15 studies[2,7,11,35,40,41,44,46-53] with a variation in the antibiotic agent used and the timing. This is a potential confounder for the frequency of SSI[58]. A proportion of the included studies assessed patients with an underlying malignancy who may have been immunosuppressed. This influences the rate of SSI and is not accounted for in many of the included studies[59]. Another weakness is the heterogeneity in the use of triclosan coated sutures. In some studies, triclosan was used for closure of all surgical layers, whereas in other studies triclosan coated sutures were only used on the superficial layers. This study heterogeneity should be noted when interpreting the meta-analysis result. This review reports trials using CDC criteria for superficial site infections. It is important to note that a stitch abscess does not meet the criteria for a superficial site infections. Patients may present with a stitch abscess to healthcare professionals and undergo treatment. This study does not report the impact of surgical site infections on stitch abscesses.

Our review is the largest review of RCTs to date in terms of patient numbers and demonstrates clinical effectiveness of triclosan coated sutures when compared to standard sutures when assessing SSI rate. SSIs have been shown to have a significant impact on patient quality of life as well as on healthcare providers in terms of resource allocation. The cost of triclosan sutures is variable, however the cost of SSI to patients and healthcare providers is sizeable[10-12]. A robust cost-analysis has not been performed, nevertheless, organisations should consider carefully whether they routinely use triclosan coated sutures in light of these positive meta-analysis findings. This review also identified that triclosan coated sutures significantly reduced the risk of SSIs in clean and contaminated surgery, therefore thoughtful consideration should be paid to whether they are routinely used in this patient population.

Conclusion

This systematic review identified 21 RCTs examining the effect of triclosan in reducing incidence of SSI, compared with non-coated sutures. The subsequent meta-analysis included 11,248 patient and revealed an overall a risk ratio of 0.74 (95% CIs 0.64 to 0.86) of developing SSI in favour of triclosan coated sutures, thereby demonstrating a statistically significant lower risk of SSI following closure of a surgical wound with triclosan coated sutures. Further analysis has demonstrated that triclosan coated sutures significantly reduced the risk of SSIs in clean and contaminated surgery. This study is in agreement with previous smaller and less robust reviews which have produced comparable results. This is the largest review of RCTs in terms of patient numbers to demonstrate the clinical effectiveness of triclosan coated sutures. Further detailed cost effectiveness is required to assess the economic benefit of implementing the use of these sutures. Given the heterogeneous nature of the included population, the implementation of triclosan coated sutures should be carefully considered on a specialty by specialty basis.

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Competing interests

The authors report no competing interests for this study

Ethical Approval

No ethical approval required for this study.

Data Statement

All raw data is available upon request.

Author contributions

- IA: Conception of review, data collection, analysis, production of figures and final manuscript
- AB: Data collection, analysis, production of figures and final manuscript
- SR: Production of figures and revised final manuscript
- WC: Production of figures and revised final manuscript
- ED: Data collection and revision of final manuscript
- NS: Revision of final manuscript
- MR: Conception of idea and revision of final manuscript

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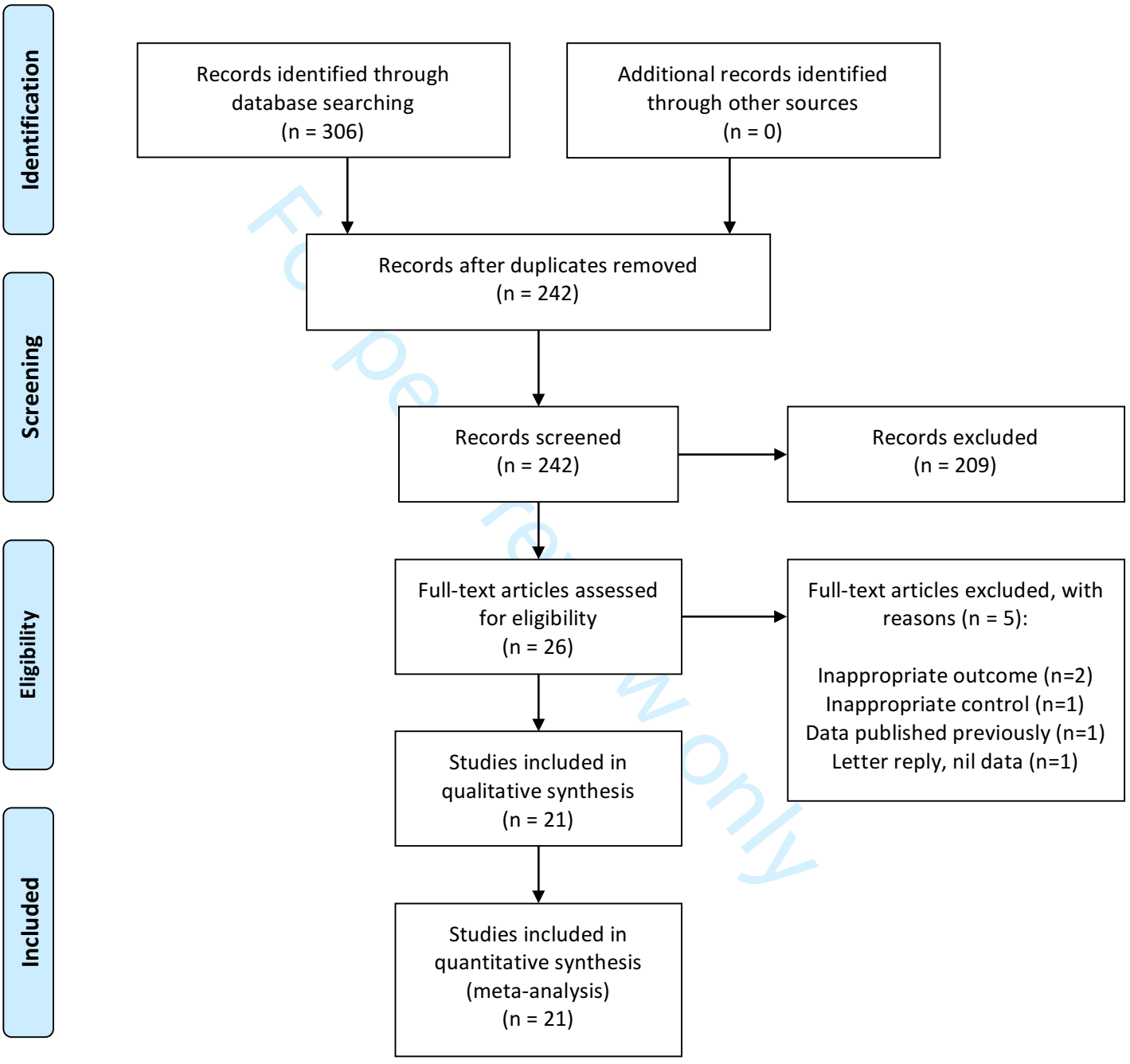
Study	No. of participants	No. of centres	Surgery type	Sutures used	SSI criteria	Duration of follow-up	Routine prophylactic antibiotics?
Baracs 2011	385	7	Elective colorectal surgery	PDS vs PDS Plus	Not stated	30 days	Yes
Chen 2011	241	1	Head and neck surgery	Vicryl vs Vicryl Plus	Local erythema with purulent discharge, wound dehiscence, or skin necrosis	Not stated	Yes
Diener 2014	1185	24	Laparotomy	PDS vs PDS Plus	CDC criteria	30 days	Yes
Ford 2005	147	1	Paediatric general surgery	Vicryl vs Vicryl Plus	Not stated	80 days	No
Galal 2011	450	1	All surgery	Vicryl vs Vicryl Plus	CDC criteria	30 days	Not stated
Ichida 2018	1023	1	Gastroenterologic surgery	Vicryl and PDS II vs Vicryl Plus and PDS Plus	CDC criteria	30 days	Yes
Isik 2011	510	1	Cardiac surgery	Vicryl vs Vicryl Plus	CDC criteria	1 month	Not stated
Justinger 2013	856	1	Laparotomy	PDS II vs PDS II Plus	CDC criteria	2 weeks	Yes
Karip 2016	106	1	Pilonidal sinus excision followed by Karydakis flap repair	Monocryl Plus vs Monocryl	Rash, fever or purulent discharge	2 weeks	Yes
Mattavelli 2015	300	4	Elective colorectal surgery	Vicryl and PDS vs Vicryl Plus and PDS Plus	CDC criteria	30 days	Yes
Mingmalairak 2009	100	1	Appendectomy	Vicryl vs Vicryl Plus	Not stated	30 days, 6 months and 1 year	Yes
Nakamura 2013	410	1	Elective colorectal surgery	Vicryl vs Vicryl Plus	CDC criteria	30 days	Yes
Rasic 2011	184	1	Elective colorectal cancer surgery	Vicryl vs Vicryl Plus	Not stated	To discharge	Yes
Renko 2017	1633	1	Paediatric surgery	Vicryl and Monocryl and PDS vs Vicryl Plus and Monocryl Plus and PDS Plus	CDC criteria	30 days	In 30%
Ruiz-Tovar 2015	110	3	Open colorectal surgery with faecal peritonitis	Vicryl vs Vicryl Plus	CDC criteria	60 days	Yes
Seim 2012	328	1	CABG leg wound	Vicryl vs Vicryl Plus	Positive bacterial culture and clinical judgement	4 weeks	Yes

Sprowson 2018	2546	3	Primary THR or TKR	Vicryl vs Vicryl Plus	CDC criteria	30 days	Yes
Thimour-Bergstrom 2013	392	1	CABG (+/-AVR, MVR) with saphenous vein graft	Vicryl and Monocryl vs Vicryl Plus and Monocryl Plus	CDC criteria	60 days	Yes
Turtiainen 2012	276	3	Non-emergency lower-limb arterial surgery	Vicryl and Monocryl vs Vicryl Plus and Monocryl Plus	CDC criteria	30 days	Yes
Williams 2011	150	1	Mastectomy	Vicryl and Monocryl vs Vicryl Plus and Monocryl Plus	CDC criteria	6 weeks	If considered at risk
Zhang 2011	101	6	Mastectomy	Chinese silk vs Vicryl Plus	CDC criteria	30 days	Not stated

Table 1: Study characteristics

PRISMA 2009 Flow Diagram

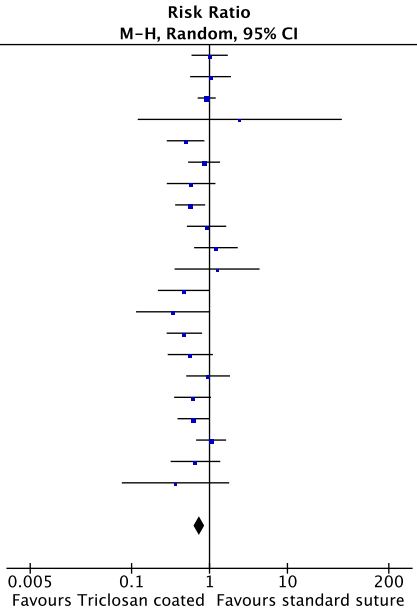


From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

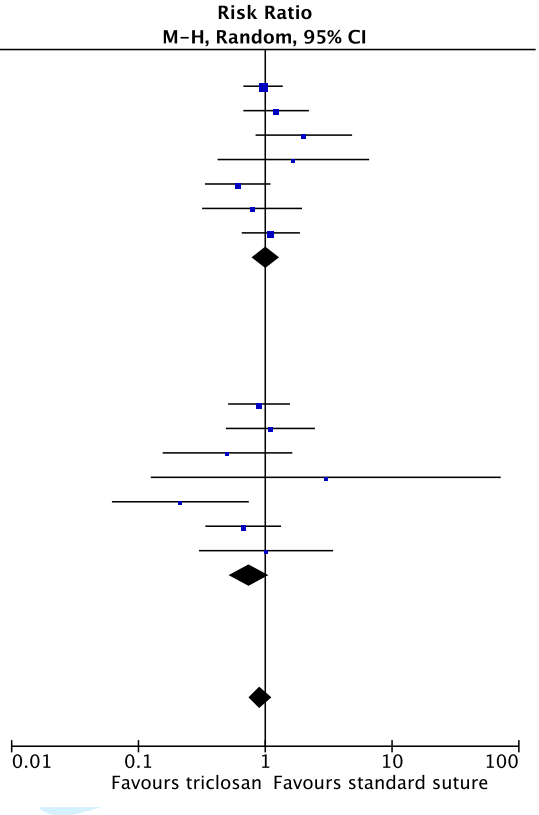
Study or Subgroup	Triclosan coated suture Events	Total	Standard suture Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Baracs 2011	23	188	24	197	5.6%	1.00 [0.59, 1.72]
Chen 2011	17	112	19	129	4.6%	1.03 [0.56, 1.88]
Diener 2014	87	587	96	596	13.9%	0.92 [0.70, 1.20]
Ford 2005	2	91	0	44	0.2%	2.45 [0.12, 49.88]
Galal 2011	17	230	33	220	5.3%	0.49 [0.28, 0.86]
Ichida 2018	30	508	35	505	6.8%	0.85 [0.53, 1.37]
Isik 2011	9	170	31	340	3.4%	0.58 [0.28, 1.19]
Justinger 2013	31	485	42	371	7.5%	0.56 [0.36, 0.88]
Karip 2016	15	52	17	54	4.9%	0.92 [0.51, 1.64]
Mattavelli 2015	18	140	15	141	4.2%	1.21 [0.63, 2.30]
Mingmalairak 2009	5	50	4	50	1.2%	1.25 [0.36, 4.38]
Nakamura 2013	9	206	19	204	3.1%	0.47 [0.22, 1.01]
Rasic 2011	4	91	12	93	1.6%	0.34 [0.11, 1.02]
Renko 2017	20	779	42	778	5.8%	0.48 [0.28, 0.80]
Ruiz-Tovar 2015	10	50	18	51	3.9%	0.57 [0.29, 1.10]
Seim 2012	16	160	17	163	4.1%	0.96 [0.50, 1.83]
Sprowson 2018	21	1323	32	1223	5.5%	0.61 [0.35, 1.05]
Thimour-Bergstrom 2013	23	184	38	190	6.7%	0.63 [0.39, 1.01]
Turtiainen 2012	31	137	30	139	7.5%	1.05 [0.67, 1.63]
Williams 2011	10	66	14	61	3.3%	0.66 [0.32, 1.37]
Zhang 2011	2	47	5	43	0.8%	0.37 [0.07, 1.79]
Total (95% CI)		**5656**		**5592**	**100.0%**	**0.74 [0.64, 0.86]**
Total events	400		543			

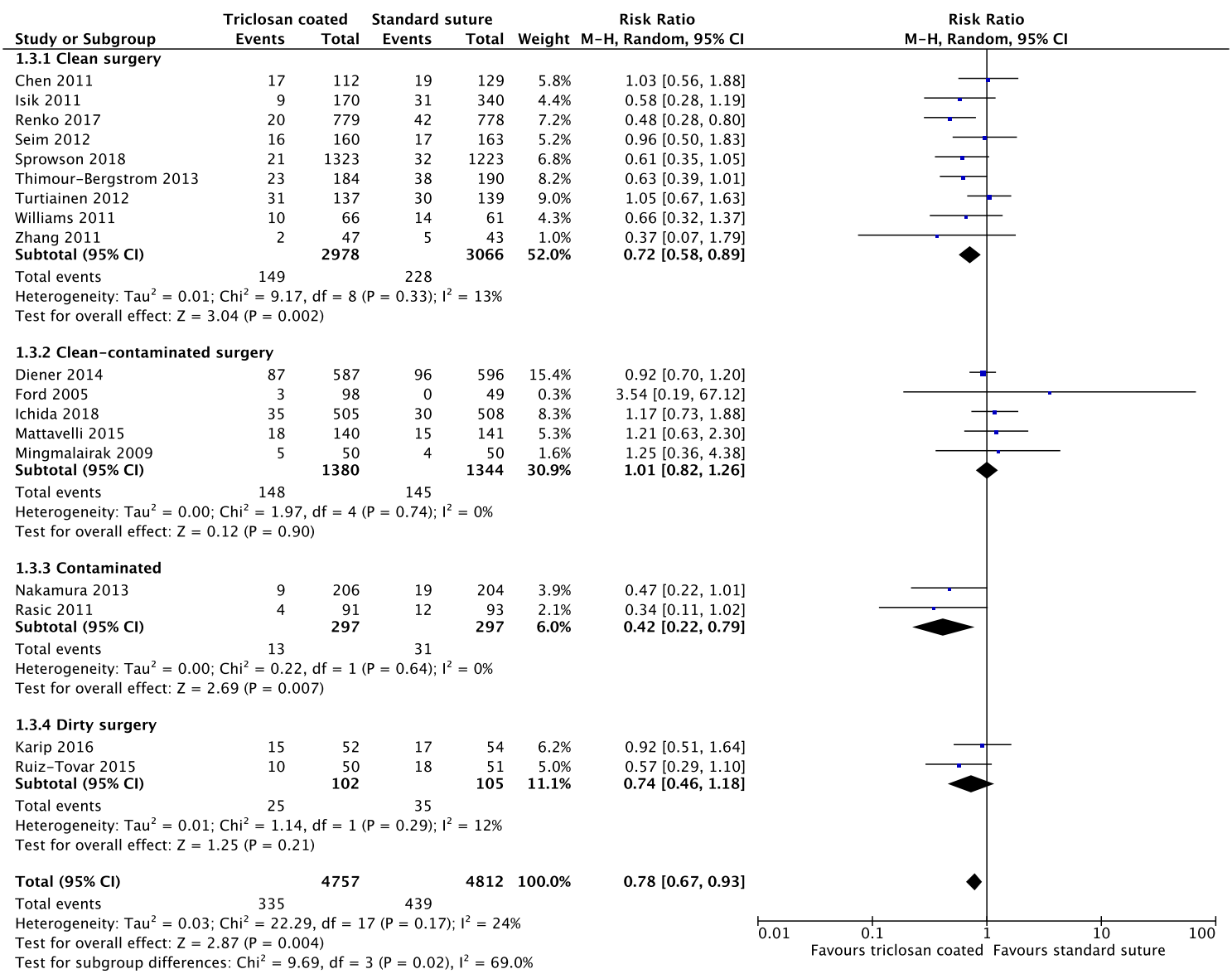
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 24.66$, df = 20 (P = 0.21); $I^2 = 19\%$
Test for overall effect: Z = 4.07 (P < 0.0001)



Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Study or Subgroup	Triclosan coated suture Events	Total	Standard suture Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.2 Superficial infections						
Diener 2014	53	587	56	596	21.0%	0.96 [0.67, 1.37]
Ichida 2018	23	505	19	508	10.1%	1.22 [0.67, 2.21]
Mattavelli 2015	14	140	7	141	5.2%	2.01 [0.84, 4.84]
Mingmalairak 2009	5	50	3	50	2.2%	1.67 [0.42, 6.60]
Renko 2017	17	779	28	778	10.2%	0.61 [0.33, 1.10]
Sprowson 2018	8	1223	11	1323	4.9%	0.79 [0.32, 1.95]
Turtiainen 2012	24	137	22	139	12.2%	1.11 [0.65, 1.88]
Subtotal (95% CI)		**3421**		**3535**	**65.9%**	**1.01 [0.79, 1.28]**
Total events	144		146			
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 6.58$, df = 6 (P = 0.36); $I^2 = 9\%$						
Test for overall effect: Z = 0.07 (P = 0.94)						
1.2.3 Deep infections						
Diener 2014	22	587	25	596	11.1%	0.89 [0.51, 1.57]
Ichida 2018	12	505	11	508	6.0%	1.10 [0.49, 2.46]
Mattavelli 2015	4	140	8	141	3.0%	0.50 [0.16, 1.63]
Mingmalairak 2009	1	50	0	50	0.4%	3.00 [0.13, 71.92]
Renko 2017	3	779	14	778	2.7%	0.21 [0.06, 0.74]
Sprowson 2018	13	1223	21	1323	8.0%	0.67 [0.34, 1.33]
Turtiainen 2012	5	137	5	139	2.8%	1.01 [0.30, 3.43]
Subtotal (95% CI)		**3421**		**3535**	**34.1%**	**0.75 [0.52, 1.08]**
Total events	60		84			
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 6.68$, df = 6 (P = 0.35); $I^2 = 10\%$						
Test for overall effect: Z = 1.53 (P = 0.13)						
Total (95% CI)		**6842**		**7070**	**100.0%**	**0.92 [0.74, 1.13]**
Total events	204		230			
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 15.08$, df = 13 (P = 0.30); $I^2 = 14\%$						
Test for overall effect: Z = 0.81 (P = 0.42)						
Test for subgroup differences: $Chi^2 = 1.73$, df = 1 (P = 0.19), $I^2 = 42.2\%$						




Triclosan coated
Standard suture
Risk Ratio
Risk Ratio
Study or Subgroup Events Total Events Total Weight M-H, Random, 95% CI
M-H, Random, 95% CI
1.3.1 Clean surgery
Chen 2011 17 112 19 129 5.8% 1.03 [0.56, 1.88]
Isik 2011 9 170 31 340 4.4% 0.58 [0.28, 1.19]
Renko 2017 20 779 42 778 7.2% 0.48 [0.28, 0.80]
Seim 2012 16 160 17 163 5.2% 0.96 [0.50, 1.83]
Sprowson 2018 21 1323 32 1223 6.8% 0.61 [0.35, 1.05]
Thimour-Bergstrom 2013 23 184 38 190 8.2% 0.63 [0.39, 1.01]
Turtiainen 2012 31 137 30 139 9.0% 1.05 [0.67, 1.63]
Williams 2011 10 66 14 61 4.3% 0.66 [0.32, 1.37]
Zhang 2011 2 47 5 43 1.0% 0.37 [0.07, 1.79]
Subtotal (95% CI) 2978 3066 52.0% 0.72 [0.58, 0.89]
Total events 149 228
Heterogeneity: Tau² = 0.01; Chi² = 9.17, df = 8 (P = 0.33); I² = 13%
Test for overall effect: Z = 3.04 (P = 0.002)
1.3.2 Clean-contaminated surgery
Diener 2014 87 587 96 596 15.4% 0.92 [0.70, 1.20]
Ford 2005 3 98 0 49 0.3% 3.54 [0.19, 67.12]
Ichida 2018 35 505 30 508 8.3% 1.17 [0.73, 1.88]
Mattavelli 2015 18 140 15 141 5.3% 1.21 [0.63, 2.30]
Mingmalairak 2009 5 50 4 50 1.6% 1.25 [0.36, 4.38]
Subtotal (95% CI) 1380 1344 30.9% 1.01 [0.82, 1.26]
Total events 148 145
Heterogeneity: Tau² = 0.00; Chi² = 1.97, df = 4 (P = 0.74); I² = 0%
Test for overall effect: Z = 0.12 (P = 0.90)
1.3.3 Contaminated
Nakamura 2013 9 206 19 204 3.9% 0.47 [0.22, 1.01]
Rasic 2011 4 91 12 93 2.1% 0.34 [0.11, 1.02]
Subtotal (95% CI) 297 297 6.0% 0.42 [0.22, 0.79]
Total events 13 31
Heterogeneity: Tau² = 0.00; Chi² = 0.22, df = 1 (P = 0.64); I² = 0%
Test for overall effect: Z = 2.69 (P = 0.007)
1.3.4 Dirty surgery
Karip 2016 15 52 17 54 6.2% 0.92 [0.51, 1.64]
Ruiz-Tovar 2015 10 50 18 51 5.0% 0.57 [0.29, 1.10]
Subtotal (95% CI) 102 105 11.1% 0.74 [0.46, 1.18]
Total events 25 35
Heterogeneity: Tau² = 0.01; Chi² = 1.14, df = 1 (P = 0.29); I² = 12%
Test for overall effect: Z = 1.25 (P = 0.21)
Total (95% CI) 4757 4812 100.0% 0.78 [0.67, 0.93]
Total events 335 439
Heterogeneity: Tau² = 0.03; Chi² = 22.29, df = 17 (P = 0.17); I² = 24%
Test for overall effect: Z = 2.87 (P = 0.004)
Test for subgroup differences: Chi² = 9.69, df = 3 (P = 0.02), I² = 69.0%
0.01 0.1 1 10 100
Favours triclosan coated Favours standard suture

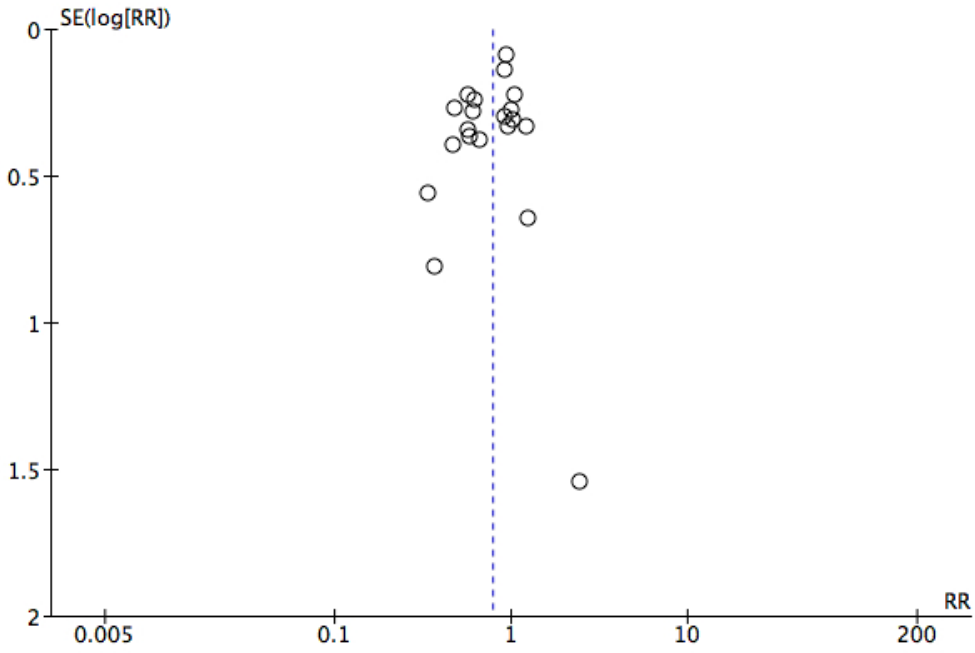


Figure 5: Funnel plot for the including studies

211x141mm (72 x 72 DPI)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3/4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7 and table 1
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5/6/7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5/6/7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6/7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6/7

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6/7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7/8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7/8 table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Figure 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figure 2-5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figure 2-5
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Figure 2-5
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	9/10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	9/10/11
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

PRISMA 2009 Checklist

BMJ Open

The use of triclosan coated sutures to prevent surgical site infections: a systematic review and meta-analysis of the literature

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Primary Subject Heading:	Surgery
Secondary Subject Heading:	Infectious diseases
Keywords:	Surgical site infection, Triclosan, Systematic review

The use of triclosan coated sutures to prevent surgical site infections: a systematic review and meta-analysis of the literature

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ABSTRACT

Introduction and objectives

Surgical site infections (SSIs) represent a common and serious complication of all surgical interventions. Micro-organisms are able to colonise sutures that are implanted in the skin, which is a causative factor of SSis. Triclosan coated sutures are antibacterial sutures aimed at reducing surgical site infections.

Our objective is to update the existing literature by systematically reviewing available evidence to assess the effectiveness of triclosan coated sutures in the prevention of surgical site infections.

Methods

A systematic review of EMBASE, MEDLINE, AMED (Allied and complementary medicine database) and CENTRAL was performed to identify full text randomised controlled trials (RCTs).

Intervention

Triclosan coated sutures versus non triclosan coated sutures.

Primary outcome

Our primary outcome was the development of surgical site infections at 30 days post operatively. A meta-analysis was performed using a random effects model.

Results

Twenty five RCTs were included involving 11,957 participants. Triclosan coated sutures were used in 6008 participants and non triclosan coated sutures were used in 5949. Triclosan coated sutures significantly reduced the risk of surgical site infections at 30 days (RR 0.73, 95% CI 0.65 to 0.82). . Further sensitivity analysis demonstrated that triclosan coated sutures significantly reduced the risk of surgical site infections in both clean and contaminated surgery.

Conclusion

Triclosan coated sutures have been shown to significantly reduced the risk of surgical site infections when compared to standard sutures. This is in agreement with previous work in this area. This study represented the largest review to date in this area. This moderate quality evidence recommends the use

of Triclosan coated sutures in order to reduce the risk of SSIs particularly in clean and contaminated surgical procedures. .

Registration

PROSPERO (Reference: CRD42014014856).Key words

Surgical site infection, triclosan, systematic review

Article summary

Strengths and limitations of this study

Strengths

- Systematic nature of data collection and analysis
- Largest review to date in this topic area
- Analyses performed comparing different classifications of surgery i.e clean, clean-contaminated, contaminated and dirty.

Limitations

- Heterogenous nature of included studies. E.g. different age of participants, co-morbidities and surgery type.

Original protocol

A protocol for this review was prospectively registered with PROSPERO (Reference: CRD42014014856).

Funding statement

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Competing interests

All authors report no competing interests.

Word count: 3620

INTRODUCTION

Surgical site infections (SSIs) represent a common complication throughout all surgical procedures[1]. It is estimated that SSIs account for 5% of all surgical complications[2] and 20% of all healthcare associated infections[3,4]. It is generally believed that the number of surgical procedures, particularly in elective orthopaedics[5], will increase over the next decade, therefore increasing the incidence of SSIs. SSIs are associated with prolonged hospital admission[6] and increased morbidity and mortality[7,8,9]. In addition to having a significant impact on patient care and experience, SSIs also add substantial costs to healthcare providers. It is estimated that SSIs cost UK healthcare services approximately £61 million in 2012[10] and figures from the US highlight the extensive cost of SSIs with an estimated additional $2300 per case[11]. Furthermore, Fleck *et al.* found that the mean cost of treated a SSI following sternal wound incision was $11,200[12]. These are conservative estimates as active surveillance of SSIs not routinely performed[6].

Due to the wide ranging deleterious effects of SSIs and their treatment, particularly in the context of increasing numbers of surgical procedures, there is a clinical need to reduce the incidence of SSIs. SSIs are multifactorial with patient factors such as age, co-morbidities including diabetes, and immunosuppression[7,13-15] contributing to their development, along with surgical factors. Many patient factors may not be optimised and hence research focus has been placed on surgical factors, including suture material.

SSIs may arise when bacteria colonise the suture material[16], creating a biofilm as it passes through the skin[17]. This biofilm establishes an immunity from both antimicrobial treatment and the host immune system[6,17]. Once this biofilm develops there is an increased chance of a SSI developing. Research has shown bacteria may colonise monofilament and braided sutures[18-20]. With this in mind, considerable work has been carried out since the 1950s with regards to coating suture material with an antimicrobial, including silver[21,22]. Triclosan (polychlorophenoxyphenol) has been used for its antiseptic properties for

many years in toothpaste and soap and has an established safety profile[5]. Triclosan has been used to successfully coat the following sutures and gained FDA (US food and drug administration) approval in 2002: braided polyglactan 910 (Vicryl Plus), poliglecaprone 25 (Monocryl Plus) and polydioxanone (PDS Plus).

In vitro and *in vivo* studies have shown the effectiveness of triclosan coated sutures[23-25] in killing bacteria associated with SSIs and inhibiting colonisation of suture material, with one study demonstrating a 66% reduction in bacterial colonisation[26]. Since then a large number of randomised control trials (RCTs) have been performed with contrasting results of the effectiveness of triclosan coated sutures in the prevention of SSIs. Subsequent meta-analyses have also produced conflicting results and hence the true effect remains unclear[6,7,27-32]. The most recent and largest systematic review to date was performed by De Jonge *et al.* and found triclosan coated sutures significantly reduced the incidence of SSIs[32]. This review searched the literature up until November 2015 and included 6462 patients from RCTs published in peer-reviewed journals as well as conference abstracts. Performing robust methodological appraisal of conference abstracts is not possible, they do not permit thorough risk of bias assessments, and as they have not undergone the formal journal peer-review process, they represent a potentially biased and unreliable source of data. Since this review, a number of large, high quality RCTs have been produced[33,34]. Of note, a recent RCT of 2546 patients found that triclosan coated sutures did not reduce the incidence of SSIs; a finding in contrast to the previous systematic review[32,34]. This represents a substantial increase in the number of patients available for meta-analysis since the last review. As a result, we believe it is important to update the existing literature by performing a new, up to date, systematic review and meta-analysis to assimilate the current evidence and inform clinical practice. A new review should include a detailed risk of bias assessment and GRADE assessment of the quality of evidence.

This new systematic review and meta-analysis of the available literature aims to determine whether the use of triclosan coated sutures reduces the incidence of SSIs in comparison to standard non-coated sutures.

PICOS statement

The included population encompasses patients of any age and gender undergoing any surgical procedure utilising sutures to close the wound. The intervention studied is the use of triclosan coated sutured and comparison is made with non-triclosan coated sutures. The outcomes assessed are the rates of SSIs, including superficial and deep SSIs. This systematic review will only include RCTs.

METHODS

A systematic review of the available literature was conducted and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance[35]. A protocol for this review was prospectively registered with PROSPERO (Reference: CRD42014014856).

Search methods

Electronic searches were conducted using OVID SP on the following databases: MEDLINE(1946-March Week 5 2018); Excerpta Medica Database (EMBASE) (1974 to 2018 April 10); Allied and Complementary Medicine (AMED) (1985 to March 2018); and Cochrane Central Register of Controlled Trials (CENTRAL). A multi-purpose search was performed for all terms and the search terms were: "Triclosan", "Anti-bacterial agents", "Anti-infective agents, local", "Coated materials, biocompatible", "Biomimetic material", "Sutures", "Vicryl Plus", "Monocryl Plus", "PDS Plus", "Surgical site infection", "Surgical Wound infection". The search was conducted on 31st May 2019.

Selection of Studies

Two authors (IA and AB) independently selected studies for inclusion. Any discrepancies were resolved by discussion with a third author (ED). Titles and abstracts were screened and full texts obtained for any studies of interest. The eligibility criteria were formed from the PICOS statement and registered on PROSPERO prior to undertaking the search. Only RCTs published in peer-reviewed journals presenting new data were included.

Data extraction

Data was independently extracted from eligible included studies onto predetermined forms by two authors (IA and AB). Any discrepancies were then resolved following discussion between two authors (IA and AB) and a third author. Data extracted included baseline patient characteristics, surgical procedures performed, number of centres, suture material, SSI diagnostic criteria, length of follow up, routine prophylactic antibiotic use and number of SSIs. Data regarding superficial of deep SSI was extracted when possible. Information regarding randomisation, blinding, funding and country of origin was extracted.

Assessment of Risk of Bias

Two authors (IA and AB) independently appraised eligible studies according to the Cochrane Collaboration's risk of bias tool, resolving any discrepancies with a third author (ED)as necessary[36]. Review Manager version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used to generate the summary figures. The parameters used for 'other' sources of bias included source of funding and antibiotic regime.

Two authors (IA and AB) independently assessed the quality of evidence. We used the GRADE considerations (study limitations, consistence of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence[37]. Decisions to upgrade or downgrade body of evidence have been clearly stated in the discussion.

Publication bias was assessed following construction of a funnel plot in order to identify the presence or absence of bias of this kind.

Statistical analysis

A fixed effects model was used to calculate the predominant relative risk (RR) and the 95% confidence intervals of the studies included. Statistically heterogeneity was first assessed using a funnel plot and more formally using the I^2 statistic[36]. Forest plots were then generated summarising the results of the meta-analysis using Review Manager 5.3.

Patient and Public Involvement

Given the design of this study and the retrospective nature, patient and public members were not involved in the development and conduct of this review. With the aid of patient and public members we will produce lay summaries of the results available for patients.

RESULTS

The search revealed 357 records of possible relevance. No other sources of records were identified. Removal of duplicates left 249 records to be examined. 219 records were excluded based on title and abstract screening. 30 full texts were assessed for eligibility and 25 studies were included in the meta-analysis (see figure 1)[2,7,11,33,34,38-57].

Study characteristics

Study characteristics are summarised in table 1. Twenty-five RCTs were included in this review involving 11,957 patients[2,7,11,33,34,38-57]. There were 6008 patients randomised to triclosan coated sutures and 5949 patients to standard sutures. In studies which reported mean age, the mean age reported in 23 out of 25 studies was comparable between the two groups (54.8 vs 54.8). For the studies which reported gender 57% of the included patients were male. Eight studies were multi-centre, with the remainder single-centre studies (n=17). Vicryl was compared with Vicryl Plus in twelve studies[11,34,39-41,43,46-49,54,56], three studies compared PDS and versus PDS Plus[7,38,55], one study compared PDS II with PDS II Plus[44], two study

compared Monocryl against Monocryl Plus[45,57], one compared Chinese silk with Vicryl Plus[53], four studies compared Vicryl and Monocryl versus Vicryl Plus and Monocryl Plus[33,50-52], and two studies compared Vicryl and PDS versus Vicryl Plus and PDS Plus[2,42].

To define SSI, the Centre for disease control (CDC) criteria were used by 18 studies[2,7,11,33,34,41-44,48,50-57], clinical diagnosis or wound cultures was used by three studies studies[39,45,49], and four did not provide explicit definitions[38,40,46,47]. Seventeen studies used a follow up duration of 30 days or one month or four weeks[2,7,11,33,34,38,41-43,46,49,51,53-57], three for six weeks[48,50,52], two for two weeks[44,45], one for 80 days[40], one until discharge[47], and one study did not specify a follow-up regime[39]. Routine prophylactic antibodies were used in 19 studies[2,7,11,34,38,39,42,44-51,54-57], no prophylactic antibiotics were used in one study[40], one used prophylactic antibiotics in high risk patients only[52], one study used prophylactic antibiotics in 30% of participants[33], and three did specify prophylactic antibiotic use[41,43,53].

Surgical site infection

The risk of developing surgical site infection was significantly reduced in the triclosan group compared to the standard suture group (RR 0.73, 95% CI 0.65 to 0.82). Heterogeneity was low to moderate (χ^2=24.66, P=0·21, I^2=17%). There were 420 instances of SSI amongst 6008 patients in the triclosan coated suture group and 581 SSIs in 5949 patients in the standard suture group. See figure 2.

Sub-group analysis

Eight studies reported superficial and deep infections separately[2,7,33,34,42,46,51,57]. There were 152/3507 cases of superficial SSI in the triclosan group and 164/3626 cases in the standard suture group, producing a meta-analysis risk ratio of 0.95 (95% CI 0.72 to 1.25). The risk of developing a deep infection was lower in the triclosan group when compared to the standard suture group, however this was not significant (RR 0.77, 95% CI 0.55 to 1.07). There were 61/3507 cases of deep infections in the triclosan group and 85/3626 cases in the standard suture group. See figure 3.

Ten studies reported the incidence of surgical site infection for clean surgery[33,39,43,49-53,56,58]. Triclosan coated sutures were associated with a significantly lower incidence of SSI (149/3029) when compared to standard sutures (230/1117) (RR 0.71, 95% CI 0.58 to 0.88).

Six studies reported clean contaminated surgery and there was no difference between the two groups (160/1540 vs 156/1504) (RR 1.02, 95% CI 0.83,1.25)[2,7,40,42,46,54].

Four studies reported the incidence of surgical site infections in contaminated surgery[11,47,55,57]. Triclosan coated sutures were associated with a significantly lower risk of SSI (22/438) when compared to standard sutures (55/443) (RR 0.43, 95% CI 0.27 to,0.7).

Two further studies reported the incidence of surgical site infection for dirty surgery[45,48]. There was no significant difference in the incidence of SSIs between the two groups of sutures (25/102 vs 35/105) (RR 0.74, 95% CI 0.46 to 1.18). See figure 4.

Risk of bias

The results of the risk of bias screening can be seen on figure 1. The majority of studies had a clear randomisation sequence generation and allocation concealment using sealed envelopes. Five out of twenty five (20%) had high risk of selection bias, either because the randomisation method was not stated or a quasirandomisation method was used. Two further studies had a risk of selection bias due to unclear allocation concealment methods. Ten out of twenty five studies (40%) had high risk of performance and detection bias due to either absence of blinding of the participants and outcome assessors or the methods of blinding were not stated. Four out of twenty five (16%) were at high risk of other bias due to source of funding. One study had differences in antibiotic regime between the two groups, with one group not receiving any antibiotic prophylaxis.

The distribution of studies in the funnel plot was symmetrical. No evidence was found for publication bias in this analysis (figure 5).

Statistical heterogeneity was assessed using the τ^2 (0.02) test and the I^2 (17%) test, indicating there is low heterogeneity between the studies included in this review based on the recommendations in the Cochrane handbook.

DISCUSSION

This large systematic review of 25 randomised clinical trials included 11,957 patients and there were 1001 instances of SSI. The subsequent meta-analysis supports the use of triclosan-coated sutures in reducing the risk of surgical site infections. We report a significantly lower risk of SSI when triclosan coated sutures were used, compared to standard sutures in RCTs. Triclosan coated sutures were used in a wide range of surgeries, including both adult and paediatric patients. The use of triclosan coated sutures significantly reduced the risk of SSI in meta-analyses of clean surgery and also contaminated surgery.. Further subgroup analysis revealed a non-statistically significant reduction on the risk of developing deep SSIs with triclosan coated sutures. Triclosan coated sutures appear to have no effect on the incidence of superficial SSIs.

Our results support the findings of Konstantelias et al who concluded that triclosan coated sutures were associated with a significantly lower risk of SSI when compared to standard sutures [59]. In addition, the authors concluded that triclosan coated sutures significantly reduced the risk of SSI in clean, clean-contaminated, and contaminated surgery; in agreement with our findings [59]. De Jonge et al reported a meta-analysis of 21 RCTs including 6462 patients, also concluding that triclosan coated sutures significantly reduced the risk of SSI compared to standard sutures [32].

Quality of evidence

Using the GRADE criteria the evidence was graded as 'moderate' quality. The reason for downgrading was due to study limitations. Studies had high risk of selection bias due to unclear randomisation and allocation methods. In addition studies had a high risk of performance and detection bias due to issues with blinding of participants and outcome assessors. The body of evidence was not downgraded for inconsistency as there was narrow point estimates and low study heterogeneity (I^2=17%). There were no

issues with indirectness or imprecision as the outcome measures used are directly aligned to the outcome measures of interest in this review. There were also a large number of participants included in this review with satisfactory event rate numbers. Our symmetrical funnel plot indicated no risk of publication bias. Given the quality of the evidence we are moderately confident in the effect estimate, the true effect is likely to be close to the estimate of the effect.

The strengths of this current review include the thorough and systematic nature of data collection. This review represents the most up to date review of the literature and is the largest review of RCTs to date, including 11,248 patients from 21 RCTs. A recent RCT in elective hip and knee surgery included 2546 participants, the largest RCT to date in this subject [58]. This review is the only review to include this important and well-conducted study. In addition, this systematic review only included peer-reviewed studies with published full texts. Previous meta-analyses have included conference abstracts which do not go through the same rigorous peer-review process as full journal publications and thus represent a potential danger to review quality[32]. Furthermore, robust quality and risk of bias assessment is not possible with these abstract publications[60]. A further strength of this review is the detailed and systematic quality assessments, along with robust Cochrane risk of bias assessments, of all included studies[36,60]. In addition, this new review included further detailed sub group analysis based on superficial vs deep surgical infections and based on type of surgery e.g. clean, clean contaminated, contaminated and dirty surgery.

The main weakness of this review is the study population. As mentioned above the review includes procedures which were classed as clean, clean- contaminated, contaminated, and dirty. These types of surgery would all have a differing rates of SSI. The authors therefore performed sub-analyses of the different categories of surgery. Routine antibiotic prophylaxis was used in 15 studies[2,7,11,38,39,42,44-51,58] with a variation in the antibiotic agent used and the timing. This is a potential confounder for the frequency of SSI[61]. A proportion of the included studies assessed patients with an underlying malignancy who may have

been immunosuppressed. This influences the rate of SSI and is not accounted for in many of the included studies[62]. Another weakness is the heterogeneity in the use of triclosan coated sutures. In some studies, triclosan was used for closure of all surgical layers, whereas in other studies triclosan coated sutures were only used on the superficial layers. This study heterogeneity should be noted when interpreting the meta-analysis result. This review reports trials using CDC criteria for superficial site infections. It is important to note that a stitch abscess does not meet the criteria for a superficial site infections. Patients may present with a stitch abscess to healthcare professionals and undergo treatment. This study does not report the impact of surgical site infections on stitch abscesses.

Our review is the largest review of RCTs to date in terms of patient numbers and demonstrates clinical effectiveness of triclosan coated sutures when compared to standard sutures when assessing SSI rate. SSIs have been shown to have a significant impact on patient quality of life as well as on healthcare providers in terms of resource allocation. The cost of triclosan sutures is variable, however the cost of SSI to patients and healthcare providers is sizeable[10-12]. A robust cost-analysis has not been performed, nevertheless, organisations should consider carefully whether they routinely use triclosan coated sutures in light of these positive meta-analysis findings. This review also identified that triclosan coated sutures significantly reduced the risk of SSIs in clean and contaminated surgery, therefore thoughtful consideration should be paid to whether they are routinely used in this patient population.

Conclusion

This systematic review identified 21 RCTs examining the effect of triclosan in reducing incidence of SSI, compared with non-coated sutures. The subsequent meta-analysis included 11,248 patient and revealed an overall a risk ratio of 0.74 (95% Cis 0.64 to 0.86) of developing SSI in favour of triclosan coated sutures, thereby demonstrating a statistically significant lower risk of SSI following closure of a surgical wound with triclosan coated sutures. Further analysis has demonstrated that triclosan coated sutures

significantly reduced the risk of SSIs in clean and contaminated surgery. This study is in agreement with previous smaller and less robust reviews which have produced comparable results. This is the largest review of RCTs in terms of patient numbers to demonstrate the clinical effectiveness of triclosan coated sutures. Further detailed cost effectiveness is required to assess the economic benefit of implementing the use of these sutures. The evidence considered in this review suggests that triclosan coated sutures are effective in reducing surgical site infections, the use should in particular be considered in clean and contaminated surgery.

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Competing interests

The authors report no competing interests for this study

Ethical Approval

No ethical approval required for this study.

Data Statement

Raw data is available on request by email to the corresponding author.

Author contributions

All authors contributed to the production of this manuscript and meet the ICMJE criteria.

- IA: Conception of review, data collection, analysis, drafted final manuscript
- AB: Data collection, analysis, drafted final manuscript
- SR: Data analysis and revised final manuscript
- WC: Data analysis and revised final manuscript
- ED: Data collection and revision of final manuscript
- NS: Revision of final manuscript
- MR: Conception of idea and revision of final manuscript

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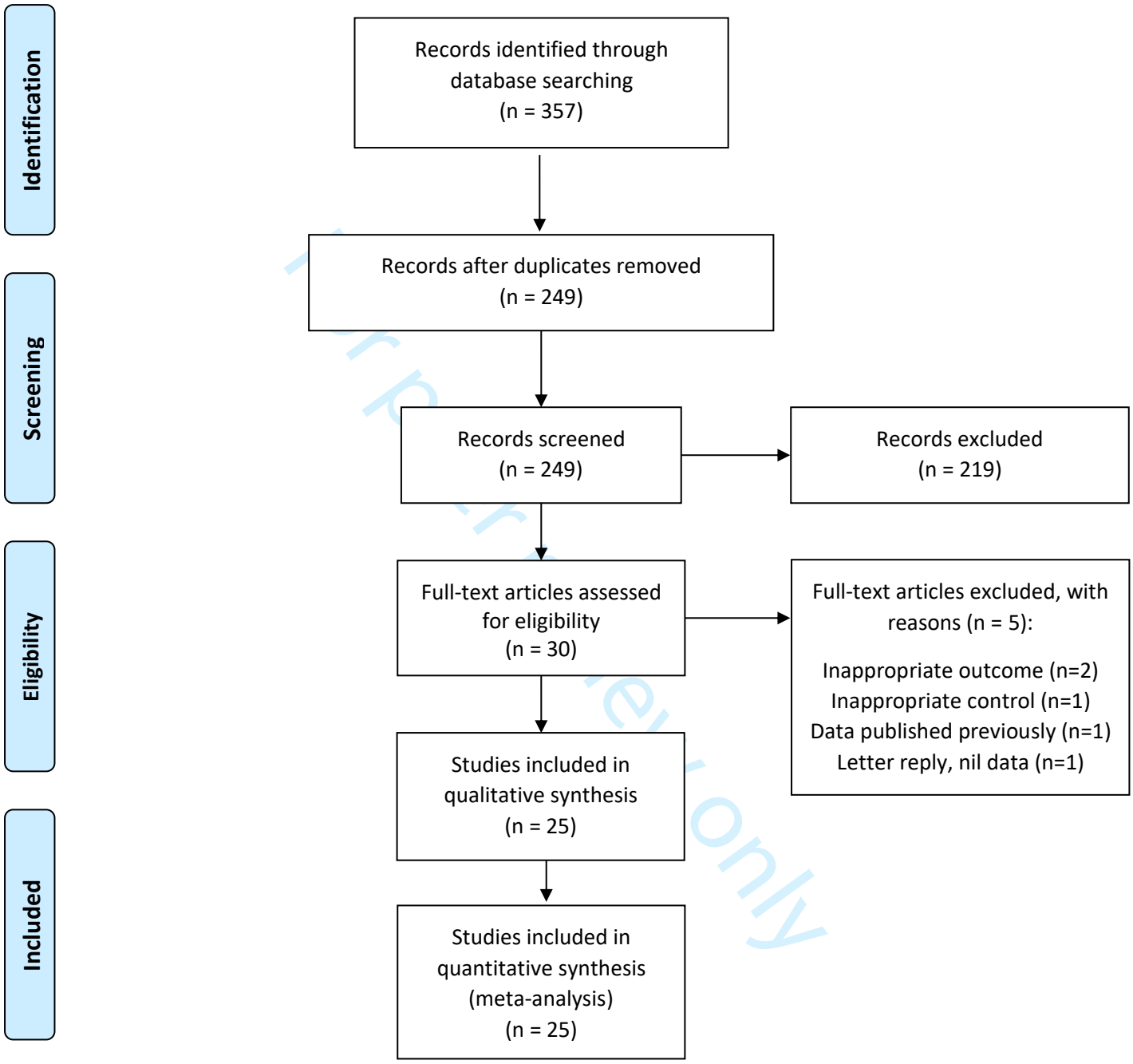
Study	No. of participants	No. of centres	Surgery type	Sutures used	SSI criteria	Duration of follow-up	Routine prophylactic antibiotics?
Arslan 2018	**177**	**1**	**Surgery for pilonidal disease**	**Vicryl vs Vicryl plus**	**CDC criteria**	**30 days**	**Yes**
Baracs 2011	385	7	Elective colorectal surgery	PDS vs PDS Plus	Not stated	30 days	Yes
Chen 2011	241	1	Head and neck surgery	Vicryl vs Vicryl Plus	Local erythema with purulent discharge, wound dehiscence, or skin necrosis	Not stated	Yes
Diener 2014	1185	24	Laparotomy	PDS vs PDS Plus	CDC criteria	30 days	Yes
Ford 2005	147	1	Paediatric general surgery	Vicryl vs Vicryl Plus	Not stated	80 days	No
Galal 2011	450	1	All surgery	Vicryl vs Vicryl Plus	CDC criteria	30 days	Not stated
Ichida 2018	1023	1	Gastroenterologic surgery	Vicryl and PDS II vs Vicryl Plus and PDS Plus	CDC criteria	30 days	Yes
Isik 2011	510	1	Cardiac surgery	Vicryl vs Vicryl Plus	CDC criteria	1 month	Not stated
Justinger 2013	856	1	Laparotomy	PDS II vs PDS II Plus	CDC criteria	2 weeks	Yes
Karip 2016	106	1	Pilonidal sinus excision followed by Karydakis flap repair	Monocryl Plus vs Monocryl	Rash, fever or purulent discharge	2 weeks	Yes
Lin 2018	102	1	Total knee replacement surgery	Vicryl vs Vicryl plus	CDC criteria	30 days	Yes
Mattavelli 2015	300	4	Elective colorectal surgery	Vicryl and PDS vs Vicryl Plus and PDS Plus	CDC criteria	30 days	Yes
Mingmalairak 2009	100	1	Appendectomy	Vicryl vs Vicryl Plus	Not stated	30 days, 6 months and 1 year	Yes
Nakamura 2013	410	1	Elective colorectal surgery	Vicryl vs Vicryl Plus	CDC criteria	30 days	Yes
Rasic 2011	184	1	Elective colorectal cancer surgery	Vicryl vs Vicryl Plus	Not stated	To discharge	Yes
Renko 2017	1633	1	Paediatric surgery	Vicryl and Monocryl and PDS vs Vicryl Plus and Monocryl Plus and PDS Plus	CDC criteria	30 days	In 30%
Roy 2019	110	1	Gastrointestinal surgery	PDS vs PDS plus	CDC criteria	30 days	Yes

Ruiz-Tovar 2015	110	3	Open colorectal surgery with faecal peritonitis	Vicryl vs Vicryl Plus	CDC criteria	60 days	Yes
Seim 2012	328	1	CABG leg wound	Vicryl vs Vicryl Plus	Positive bacterial culture and clinical judgement	4 weeks	Yes
Sprowson 2018	2546	3	Primary THR or TKR	Vicryl vs Vicryl Plus	CDC criteria	30 days	Yes
Tabrizi 2018	320	2	Dental implant surgery	Vicryl vs Vicryl plus	CDC criteria	30 days	Yes
Thimour-Bergstrom 2013	392	1	CABG (+/-AVR, MVR) with saphenous vein graft	Vicryl and Monocryl vs Vicryl Plus and Monocryl Plus	CDC criteria	60 days	Yes
Turtiainen 2012	276	3	Non-emergency lower-limb arterial surgery	Vicryl and Monocryl vs Vicryl Plus and Monocryl Plus	CDC criteria	30 days	Yes
Williams 2011	150	1	Mastectomy	Vicryl and Monocryl vs Vicryl Plus and Monocryl Plus	CDC criteria	6 weeks	If considered at risk
Zhang 2011	101	6	Mastectomy	Chinese silk vs Vicryl Plus	CDC criteria	30 days	Not stated

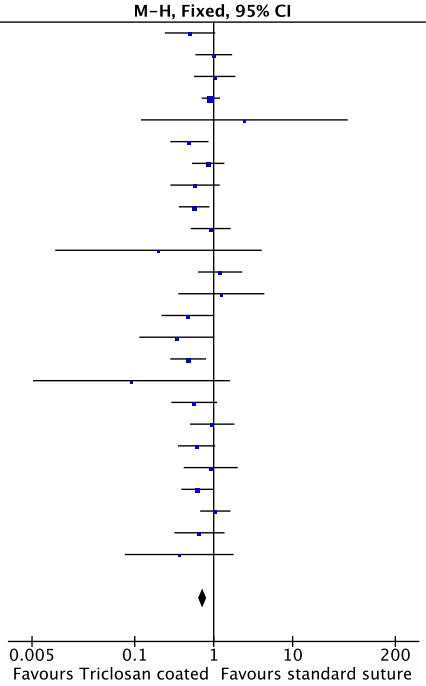
Table 1: Study characteristics

Figure 1: PRISMA flow diagram of search results



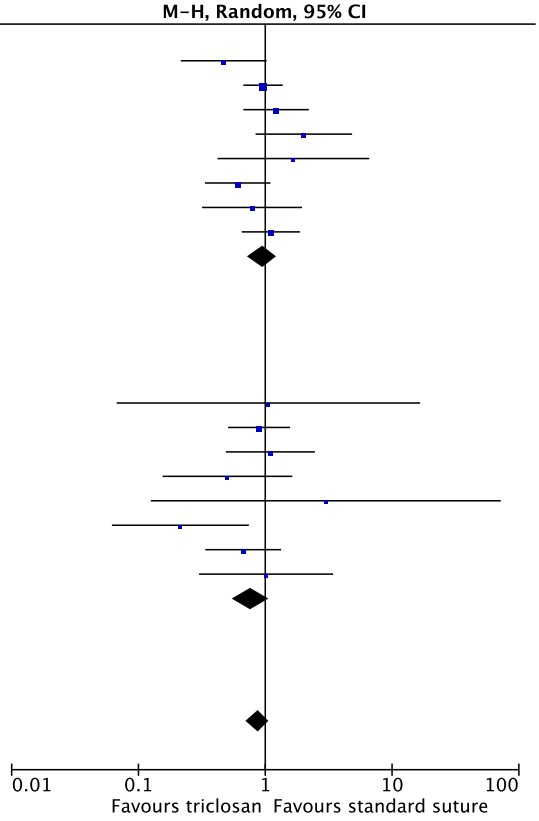
Study or Subgroup	Triclosan coated suture Events	Total	Standard suture Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Arslan 2018	9	86	19	91	3.2%	0.50 [0.24, 1.05]
Baracs 2011	23	188	24	197	4.1%	1.00 [0.59, 1.72]
Chen 2011	17	112	19	129	3.1%	1.03 [0.56, 1.88]
Diener 2014	87	587	96	596	16.5%	0.92 [0.70, 1.20]
Ford 2005	2	91	0	44	0.1%	2.45 [0.12, 49.88]
Galal 2011	17	230	33	220	5.9%	0.49 [0.28, 0.86]
Ichida 2018	30	508	35	505	6.1%	0.85 [0.53, 1.37]
Isik 2011	9	170	31	340	3.6%	0.58 [0.28, 1.19]
Justinger 2013	31	485	42	371	8.3%	0.56 [0.36, 0.88]
Karip 2016	15	52	17	54	2.9%	0.92 [0.51, 1.64]
Lin 2018	0	51	2	51	0.4%	0.20 [0.01, 4.07]
Mattavelli 2015	18	140	15	141	2.6%	1.21 [0.63, 2.30]
Mingmalairak 2009	5	50	4	50	0.7%	1.25 [0.36, 4.38]
Nakamura 2013	9	206	19	204	3.3%	0.47 [0.22, 1.01]
Rasic 2011	4	91	12	93	2.1%	0.34 [0.11, 1.02]
Renko 2017	20	779	42	778	7.3%	0.48 [0.28, 0.80]
Roy 2019	0	55	5	55	1.0%	0.09 [0.01, 1.61]
Ruiz-Tovar 2015	10	50	18	51	3.1%	0.57 [0.29, 1.10]
Seim 2012	16	160	17	163	2.9%	0.96 [0.50, 1.83]
Sprowson 2018	21	1323	32	1223	5.8%	0.61 [0.35, 1.05]
Tabrizi 2018	11	160	12	160	2.1%	0.92 [0.42, 2.02]
Thimour-Bergstrom 2013	23	184	38	190	6.5%	0.63 [0.39, 1.01]
Turtiainen 2012	31	137	30	139	5.2%	1.05 [0.67, 1.63]
Williams 2011	10	66	14	61	2.5%	0.66 [0.32, 1.37]
Zhang 2011	2	47	5	43	0.9%	0.37 [0.07, 1.79]
Total (95% CI)		**6008**		**5949**	**100.0%**	**0.73 [0.65, 0.82]**
Total events	420		581			

Heterogeneity: Chi² = 28.97, df = 24 (P = 0.22); I² = 17%
Test for overall effect: Z = 5.20 (P < 0.00001)

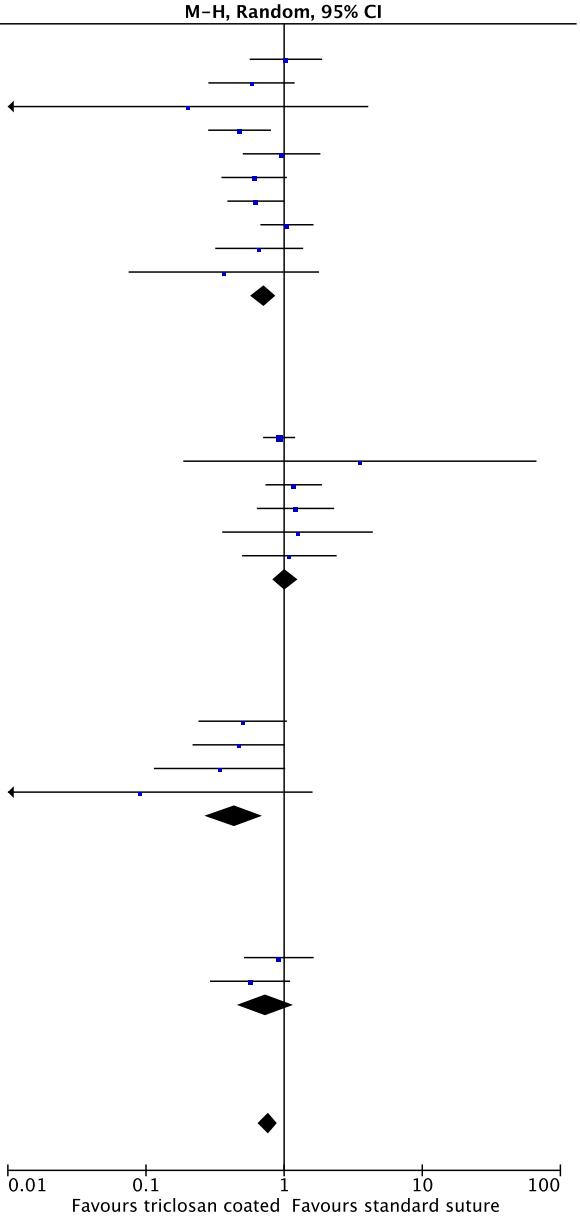


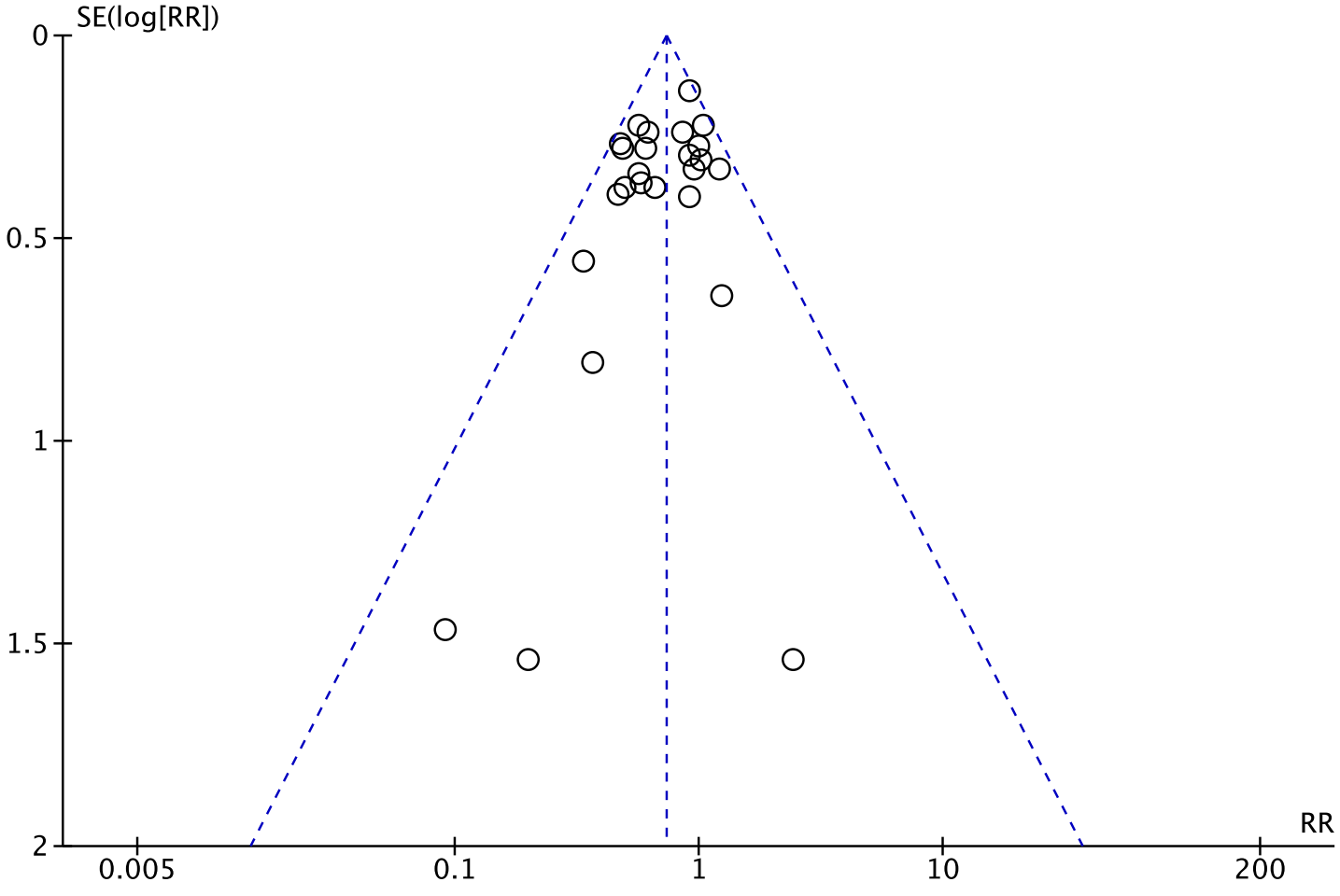
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Study or Subgroup	Triclosan coated suture Events	Total	Standard suture Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.2 Superficial infections						
Arslan 2018	8	86	18	91	6.1%	0.47 [0.22, 1.02]
Diener 2014	53	587	56	596	18.8%	0.96 [0.67, 1.37]
Ichida 2018	23	505	19	508	9.5%	1.22 [0.67, 2.21]
Mattavelli 2015	14	140	7	141	5.0%	2.01 [0.84, 4.84]
Mingmalairak 2009	5	50	3	50	2.2%	1.67 [0.42, 6.60]
Renko 2017	17	779	28	778	9.5%	0.61 [0.33, 1.10]
Sprowson 2018	8	1223	11	1323	4.7%	0.79 [0.32, 1.95]
Turtiainen 2012	24	137	22	139	11.4%	1.11 [0.65, 1.88]
Subtotal (95% CI)		**3507**		**3626**	**67.1%**	**0.95 [0.72, 1.25]**
Total events	152		164			
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 9.95$, df = 7 (P = 0.19); $I^2 = 30\%$						
Test for overall effect: Z = 0.38 (P = 0.70)						
1.2.3 Deep infections						
Arslan 2018	1	86	1	91	0.6%	1.06 [0.07, 16.65]
Diener 2014	22	587	25	596	10.4%	0.89 [0.51, 1.57]
Ichida 2018	12	505	11	508	5.7%	1.10 [0.49, 2.46]
Mattavelli 2015	4	140	8	141	2.9%	0.50 [0.16, 1.63]
Mingmalairak 2009	1	50	0	50	0.4%	3.00 [0.13, 71.92]
Renko 2017	3	779	14	778	2.6%	0.21 [0.06, 0.74]
Sprowson 2018	13	1223	21	1323	7.5%	0.67 [0.34, 1.33]
Turtiainen 2012	5	137	5	139	2.7%	1.01 [0.30, 3.43]
Subtotal (95% CI)		**3507**		**3626**	**32.9%**	**0.77 [0.55, 1.07]**
Total events	61		85			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 6.74$, df = 7 (P = 0.46); $I^2 = 0\%$						
Test for overall effect: Z = 1.58 (P = 0.11)						
Total (95% CI)		**7014**		**7252**	**100.0%**	**0.88 [0.71, 1.08]**
Total events	213		249			
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 17.81$, df = 15 (P = 0.27); $I^2 = 16\%$						
Test for overall effect: Z = 1.20 (P = 0.23)						
Test for subgroup differences: $Chi^2 = 0.95$, df = 1 (P = 0.33), $I^2 = 0\%$						



Study or Subgroup	Triclosan coated Events	Total	Standard suture Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.3.1 Clean surgery						
Chen 2011	17	112	19	129	5.4%	1.03 [0.56, 1.88]
Isik 2011	9	170	31	340	4.1%	0.58 [0.28, 1.19]
Lin 2018	0	51	2	51	0.3%	0.20 [0.01, 4.07]
Renko 2017	20	779	42	778	6.6%	0.48 [0.28, 0.80]
Seim 2012	16	160	17	163	4.9%	0.96 [0.50, 1.83]
Sprowson 2018	21	1323	32	1223	6.3%	0.61 [0.35, 1.05]
Thimour-Bergstrom 2013	23	184	38	190	7.5%	0.63 [0.39, 1.01]
Turtiainen 2012	31	137	30	139	8.2%	1.05 [0.67, 1.63]
Williams 2011	10	66	14	61	4.0%	0.66 [0.32, 1.37]
Zhang 2011	2	47	5	43	1.0%	0.37 [0.07, 1.79]
Subtotal (95% CI)		**3029**		**3117**	**48.3%**	**0.71 [0.58, 0.88]**
Total events	149		230			
Heterogeneity: Tau² = 0.01; Chi² = 9.88, df = 9 (P = 0.36); I² = 9%						
Test for overall effect: Z = 3.16 (P = 0.002)						
1.3.2 Clean-contaminated surgery						
Diener 2014	87	587	96	596	13.6%	0.92 [0.70, 1.20]
Ford 2005	3	98	0	49	0.3%	3.54 [0.19, 67.12]
Ichida 2018	35	505	30	508	7.6%	1.17 [0.73, 1.88]
Mattavelli 2015	18	140	15	141	4.9%	1.21 [0.63, 2.30]
Mingmalairak 2009	5	50	4	50	1.5%	1.25 [0.36, 4.38]
Tabrizi 2018	12	160	11	160	3.5%	1.09 [0.50, 2.40]
Subtotal (95% CI)		**1540**		**1504**	**31.4%**	**1.02 [0.83, 1.25]**
Total events	160		156			
Heterogeneity: Tau² = 0.00; Chi² = 2.00, df = 5 (P = 0.85); I² = 0%						
Test for overall effect: Z = 0.18 (P = 0.86)						
1.3.3 Contaminated						
Arslan 2018	9	86	19	91	4.0%	0.50 [0.24, 1.05]
Nakamura 2013	9	206	19	204	3.7%	0.47 [0.22, 1.01]
Rasic 2011	4	91	12	93	2.0%	0.34 [0.11, 1.02]
Roy 2019	0	55	5	55	0.3%	0.09 [0.01, 1.61]
Subtotal (95% CI)		**438**		**443**	**9.9%**	**0.43 [0.27, 0.70]**
Total events	22		55			
Heterogeneity: Tau² = 0.00; Chi² = 1.55, df = 3 (P = 0.67); I² = 0%						
Test for overall effect: Z = 3.46 (P = 0.0005)						
1.3.4 Dirty surgery						
Karip 2016	15	52	17	54	5.7%	0.92 [0.51, 1.64]
Ruiz-Tovar 2015	10	50	18	51	4.6%	0.57 [0.29, 1.10]
Subtotal (95% CI)		**102**		**105**	**10.3%**	**0.74 [0.46, 1.18]**
Total events	25		35			
Heterogeneity: Tau² = 0.01; Chi² = 1.14, df = 1 (P = 0.29); I² = 12%						
Test for overall effect: Z = 1.25 (P = 0.21)						
Total (95% CI)		**5109**		**5169**	**100.0%**	**0.77 [0.66, 0.91]**
Total events	356		476			
Heterogeneity: Tau² = 0.03; Chi² = 27.52, df = 21 (P = 0.15); I² = 24%						
Test for overall effect: Z = 3.15 (P = 0.002)						
Test for subgroup differences: Chi² = 12.91, df = 3 (P = 0.005), I² = 76.8%						

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1
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RR

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4/5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-9 and table 1
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6/7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6/7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8,9 table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10, Figure 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9,10 Figure 2-5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9,10 Figure 2-5
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10, Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9,10 Figure 2-5
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11, 12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12,13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13, 14

PRISMA 2009 Checklist

FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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BMJ Open

The use of triclosan coated sutures to prevent surgical site infections: a systematic review and meta-analysis of the literature

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Primary Subject Heading:	Surgery
Secondary Subject Heading:	Infectious diseases
Keywords:	Surgical site infection, Triclosan, Systematic review

The use of triclosan coated sutures to prevent surgical site infections: a systematic review and meta-analysis of the literature

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ABSTRACT

Introduction and objectives

Surgical site infections (SSIs) represent a common and serious complication of all surgical interventions. Micro-organisms are able to colonise sutures that are implanted in the skin, which is a causative factor of SSis. Triclosan coated sutures are antibacterial sutures aimed at reducing surgical site infections.

Our objective is to update the existing literature by systematically reviewing available evidence to assess the effectiveness of triclosan coated sutures in the prevention of surgical site infections.

Methods

A systematic review of EMBASE, MEDLINE, AMED (Allied and complementary medicine database) and CENTRAL was performed to identify full text randomised controlled trials (RCTs) on 31/05/2019.

Intervention

Triclosan coated sutures versus non triclosan coated sutures.

Primary outcome

Our primary outcome was the development of surgical site infections at 30 days post operatively. A meta-analysis was performed using a fixed effects model.

Results

Twenty five RCTs were included involving 11,957 participants. Triclosan coated sutures were used in 6008 participants and non triclosan coated sutures were used in 5949. Triclosan coated sutures significantly reduced the risk of surgical site infections at 30 days (RR 0.73, 95% CI 0.65 to 0.82). Further sensitivity analysis demonstrated that triclosan coated sutures significantly reduced the risk of surgical site infections in both clean and contaminated surgery.

Conclusion

Triclosan coated sutures have been shown to significantly reduced the risk of surgical site infections when compared to standard sutures. This is in agreement with previous work in this area. This study represented the largest review to date in this area. This moderate quality evidence recommends the use

of Triclosan coated sutures in order to reduce the risk of SSIs particularly in clean and contaminated surgical procedures.

Registration

PROSPERO (Reference: CRD42014014856).

Key words

Surgical site infection, triclosan, systematic review

Article summary

Strengths and limitations of this study

Strengths

- Systematic nature of data collection and analysis
- Largest review to date in this topic area
- Analyses performed comparing different classifications of surgery i.e clean, clean-contaminated, contaminated and dirty.

Limitations

- Heterogeneous nature of included studies. E.g. different age of participants, co-morbidities and surgery type.

Original protocol

A protocol for this review was prospectively registered with PROSPERO (Reference: CRD42014014856).

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Competing interests

All authors report no competing interests.

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INTRODUCTION

Surgical site infections (SSIs) represent a common complication throughout all surgical procedures[1]. It is estimated that SSIs account for 5% of all surgical complications[2] and 20% of all healthcare associated infections[3,4]. It is generally believed that the number of surgical procedures, particularly in elective orthopaedics[5], will increase over the next decade, therefore increasing the incidence of SSIs. SSIs are associated with prolonged hospital admission[6] and increased morbidity and mortality[7,8,9]. In addition to having a significant impact on patient care and experience, SSIs also add substantial costs to healthcare providers. It is estimated that SSIs cost UK healthcare services approximately £61 million in 2012[10] and figures from the US highlight the extensive cost of SSIs with an estimated additional $2300 per case[11]. Furthermore, Fleck *et al.* found that the mean cost of treated a SSI following sternal wound incision was $11,200[12]. These are conservative estimates as active surveillance of SSIs not routinely performed[6].

Due to the wide ranging deleterious effects of SSIs and their treatment, particularly in the context of increasing numbers of surgical procedures, there is a clinical need to reduce the incidence of SSIs. SSIs are multifactorial with patient factors such as age, co-morbidities including diabetes, and immunosuppression[7,13-15] contributing to their development, along with surgical factors. Many patient factors may not be optimised and hence research focus has been placed on surgical factors, including suture material.

SSIs may arise when bacteria colonise the suture material[16], creating a biofilm as it passes through the skin[17]. This biofilm establishes an immunity from both antimicrobial treatment and the host immune system[6,17]. Once this biofilm develops there is an increased chance of a SSI developing. Research has shown bacteria may colonise monofilament and braided sutures[18-20]. With this in mind, considerable work has been carried out since the 1950s with regards to coating suture material with an antimicrobial, including silver[21,22]. Triclosan (polychlorophenoxyphenol) has been used for its antiseptic properties for

many years in toothpaste and soap and has an established safety profile[5]. Triclosan has been used to successfully coat the following sutures and gained FDA (US food and drug administration) approval in 2002: braided polyglactan 910 (Vicryl Plus), poliglecaprone 25 (Monocryl Plus) and polydioxanone (PDS Plus).

In vitro and *in vivo* studies have shown the effectiveness of triclosan coated sutures[23-25] in killing bacteria associated with SSIs and inhibiting colonisation of suture material, with one study demonstrating a 66% reduction in bacterial colonisation[26]. Since then a large number of randomised control trials (RCTs) have been performed with contrasting results of the effectiveness of triclosan coated sutures in the prevention of SSIs. Subsequent meta-analyses have also produced conflicting results and hence the true effect remains unclear[6,7,27-32]. The most recent and largest systematic review to date was performed by De Jonge *et al.* and found triclosan coated sutures significantly reduced the incidence of SSIs[32]. This review searched the literature up until November 2015 and included 6462 patients from RCTs published in peer-reviewed journals as well as conference abstracts. Performing robust methodological appraisal of conference abstracts is not possible, they do not permit thorough risk of bias assessments, and as they have not undergone the formal journal peer-review process, they represent a potentially biased and unreliable source of data. Since this review, a number of large, high quality RCTs have been produced[33,34]. Of note, a recent RCT of 2546 patients found that triclosan coated sutures did not reduce the incidence of SSIs; a finding in contrast to the previous systematic review[32,34]. This represents a substantial increase in the number of patients available for meta-analysis since the last review. As a result, we believe it is important to update the existing literature by performing a new, up to date, systematic review and meta-analysis to assimilate the current evidence and inform clinical practice. A new review should include a detailed risk of bias assessment and GRADE assessment of the quality of evidence.

This new systematic review and meta-analysis of the available literature aims to determine whether the use of triclosan coated sutures reduces the incidence of SSIs in comparison to standard non-coated sutures.

PICOS statement

The included population encompasses patients of any age and gender undergoing any surgical procedure utilising sutures to close the wound. The intervention studied is the use of triclosan coated sutured and comparison is made with non-triclosan coated sutures. The outcomes assessed are the rates of SSIs, including superficial and deep SSIs. This systematic review will only include RCTs.

METHODS

A systematic review of the available literature was conducted and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance[35]. A protocol for this review was prospectively registered with PROSPERO (Reference: CRD42014014856).

Search methods

Electronic searches were conducted using OVID SP on the following databases: MEDLINE(1946-May Week 4 2019); Excerpta Medica Database (EMBASE) (1974 to 2019 May 31); Allied and Complementary Medicine (AMED) (1985 to May 2019); and Cochrane Central Register of Controlled Trials (CENTRAL). A multi-purpose search was performed for all terms and the search terms were: “Triclosan”, “Anti-bacterial agents”, “Anti-infective agents, local”, “Coated materials, biocompatible”, “Biomimetic material”, “Sutures”, “Vicryl Plus”, “Monocryl Plus”, “PDS Plus”, “Surgical site infection”, “Surgical Wound infection”. The search was conducted on 31st May 2019. A copy of the search strategy can be seen in supplementary file 1.

Selection of Studies

Two authors (IA and AB) independently selected studies for inclusion. Any discrepancies were resolved by discussion with a third author (ED). Titles and abstracts were screened and full texts obtained for any studies of interest. The eligibility criteria were formed from the PICOS statement and registered on PROSPERO prior to undertaking the search. Only RCTs published in peer-reviewed journals presenting new data were included.

Data extraction

Data was independently extracted from eligible included studies onto predetermined forms by two authors (IA and AB). Any discrepancies were then resolved following discussion between two authors (IA and AB) and a third author. Data extracted included baseline patient characteristics, surgical procedures performed, number of centres, suture material, SSI diagnostic criteria, length of follow up, routine prophylactic antibiotic use and number of SSIs. Data regarding superficial of deep SSI was extracted when possible. Information regarding randomisation, blinding, funding and country of origin was extracted.

Assessment of Risk of Bias

Two authors (IA and AB) independently appraised eligible studies according to the Cochrane Collaboration's risk of bias tool, resolving any discrepancies with a third author (ED)as necessary[36]. Review Manager version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used to generate the summary figures. The parameters used for 'other' sources of bias included source of funding and antibiotic regime.

Two authors (IA and AB) independently assessed the quality of evidence. We used the GRADE considerations (study limitations, consistence of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence[37]. Decisions to upgrade or downgrade body of evidence have been clearly stated in the discussion.

Publication bias was assessed following construction of a funnel plot in order to identify the presence or absence of bias of this kind.

Statistical analysis

A fixed effects model was used to calculate the predominant relative risk (RR) and the 95% confidence intervals of the studies included. Statistically heterogeneity was first assessed using a funnel plot and more formally using the I^2 statistic[36]. Forest plots were then generated summarising the results of the meta-analysis using Review Manager 5.3.

Patient and Public Involvement

Given the design of this study and the retrospective nature, patient and public members were not involved in the development and conduct of this review. With the aid of patient and public members we will produce lay summaries of the results available for patients.

RESULTS

The search revealed 357 records of possible relevance. No other sources of records were identified. Removal of duplicates left 249 records to be examined. 219 records were excluded based on title and abstract screening. 30 full texts were assessed for eligibility and 25 studies were included in the meta-analysis (see figure 1)[2,7,11,33,34,38-57].

Study characteristics

Study characteristics are summarised in table 1. Twenty-five RCTs were included in this review involving 11,957 patients[2,7,11,33,34,38-57]. There were 6008 patients randomised to triclosan coated sutures and 5949 patients to standard sutures. In studies which reported mean age, the mean age reported in 23 out of 25 studies was comparable between the two groups (54.8 vs 54.8). For the studies which reported gender 57% of the included patients were male. Eight studies were multi-centre, with the remainder single-centre studies (n=17). Vicryl was compared with Vicryl Plus in twelve studies[11,34,39-41,43,46-49,54,56], three studies compared PDS and versus PDS Plus[7,38,55], one study compared PDS II with PDS II Plus[44], two study

compared Monocryl against Monocryl Plus[45,57], one compared Chinese silk with Vicryl Plus[53], four studies compared Vicryl and Monocryl versus Vicryl Plus and Monocryl Plus[33,50-52], and two studies compared Vicryl and PDS versus Vicryl Plus and PDS Plus[2,42].

To define SSI, the Centre for disease control (CDC) criteria were used by 18 studies[2,7,11,33,34,41-44,48,50-57], clinical diagnosis or wound cultures was used by three studies studies[39,45,49], and four did not provide explicit definitions[38,40,46,47]. Seventeen studies used a follow up duration of 30 days or one month or four weeks[2,7,11,33,34,38,41-43,46,49,51,53-57], three for six weeks[48,50,52], two for two weeks[44,45], one for 80 days[40], one until discharge[47], and one study did not specify a follow-up regime[39]. Routine prophylactic antibodies were used in 19 studies[2,7,11,34,38,39,42,44-51,54-57], no prophylactic antibiotics were used in one study[40], one used prophylactic antibiotics in high risk patients only[52], one study used prophylactic antibiotics in 30% of participants[33], and three did specify prophylactic antibiotic use[41,43,53].

Surgical site infection

The risk of developing surgical site infection was significantly reduced in the triclosan group compared to the standard suture group (RR 0.73, 95% CI 0.65 to 0.82). Heterogeneity was low to moderate (χ^2=24.66, P=0·21, I^2=17%). There were 420 instances of SSI amongst 6008 patients in the triclosan coated suture group and 581 SSIs in 5949 patients in the standard suture group. See figure 2.

Sub-group analysis

Eight studies reported superficial and deep infections separately[2,7,33,34,42,46,51,57]. There were 152/3507 cases of superficial SSI in the triclosan group and 164/3626 cases in the standard suture group, producing a meta-analysis risk ratio of 0.95 (95% CI 0.72 to 1.25). The risk of developing a deep infection was lower in the triclosan group when compared to the standard suture group, however this was not significant (RR 0.77, 95% CI 0.55 to 1.07). There were 61/3507 cases of deep infections in the triclosan group and 85/3626 cases in the standard suture group. See figure 3.

Ten studies reported the incidence of surgical site infection for clean surgery[33,39,43,49-53,56,58]. Triclosan coated sutures were associated with a significantly lower incidence of SSI (149/3029) when compared to standard sutures (230/1117) (RR 0.71, 95% CI 0.58 to 0.88).

Six studies reported clean contaminated surgery and there was no difference between the two groups (160/1540 vs 156/1504) (RR 1.02, 95% CI 0.83,1.25)[2,7,40,42,46,54].

Four studies reported the incidence of surgical site infections in contaminated surgery[11,47,55,57]. Triclosan coated sutures were associated with a significantly lower risk of SSI (22/438) when compared to standard sutures (55/443) (RR 0.43, 95% CI 0.27 to,0.7).

Two further studies reported the incidence of surgical site infection for dirty surgery[45,48]. There was no significant difference in the incidence of SSIs between the two groups of sutures (25/102 vs 35/105) (RR 0.74, 95% CI 0.46 to 1.18). See figure 4.

Risk of bias

The results of the risk of bias screening can be seen on figure 2. The majority of studies had a clear randomisation sequence generation and allocation concealment using sealed envelopes. Five out of twenty five (20%) had high risk of selection bias, either because the randomisation method was not stated or a quasirandomisation method was used. Two further studies had a risk of selection bias due to unclear allocation concealment methods. Ten out of twenty five studies (40%) had high risk of performance and detection bias due to either absence of blinding of the participants and outcome assessors or the methods of blinding were not stated. Four out of twenty five (16%) were at high risk of other bias due to source of funding. One study had differences in antibiotic regime between the two groups, with one group not receiving any antibiotic prophylaxis.

The distribution of studies in the funnel plot was symmetrical. No evidence was found for publication bias in this analysis (figure 5).

Statistical heterogeneity was assessed using the τ^2 (0.02) test and the I^2 (17%) test, indicating there is low heterogeneity between the studies included in this review based on the recommendations in the Cochrane handbook.

DISCUSSION

This large systematic review of 25 randomised clinical trials included 11,957 patients and there were 1001 instances of SSI. The subsequent meta-analysis supports the use of triclosan-coated sutures in reducing the risk of surgical site infections. We report a significantly lower risk of SSI when triclosan coated sutures were used, compared to standard sutures in RCTs. Triclosan coated sutures were used in a wide range of surgeries, including both adult and paediatric patients. The use of triclosan coated sutures significantly reduced the risk of SSI in meta-analyses of clean surgery and also contaminated surgery. Further subgroup analysis revealed a non-statistically significant reduction in the risk of developing deep SSIs with triclosan coated sutures. Triclosan coated sutures appear to have no effect on the incidence of superficial SSIs.

There have been 11 previous reviews in this topic area, the results of these reviews have been summarised in table 2 [27,28,30-32,59-64]. Our results support the findings of Konstantelias et al who concluded that triclosan coated sutures were associated with a significantly lower risk of SSI when compared to standard sutures [32,65]. In addition, the authors concluded that triclosan coated sutures significantly reduced the risk of SSI in clean, clean-contaminated, and contaminated surgery; in agreement with our findings [65]. De Jonge et al reported a meta-analysis of 21 RCTs including 6462 patients, also concluding that triclosan coated sutures significantly reduced the risk of SSI compared to standard sutures [32]. Five out of eleven reviews included a risk of bias assessment[27,31,32,60,64] and only one review assessed the quality of evidence using the GRADE criteria [60].

Quality of evidence

Using the GRADE criteria, the evidence was graded as 'moderate' quality. The reason for downgrading was due to study limitations. Studies had high risk of selection bias due to unclear randomisation and allocation methods. In addition, studies had a high risk of performance and detection bias due to issues

with blinding of participants and outcome assessors. The body of evidence was not downgraded for inconsistency as there was narrow point estimates and low study heterogeneity (I^2=17%). There were no issues with indirectness or imprecision as the outcome measures used are directly aligned to the outcome measures of interest in this review. There were also a large number of participants included in this review with satisfactory event rate numbers. Our symmetrical funnel plot indicated no risk of publication bias. Given the quality of the evidence we are moderately confident in the effect estimate, the true effect is likely to be close to the estimate of the effect.

The strengths of this current review include the thorough and systematic nature of data collection. This review represents the most up to date review of the literature and is the largest review of RCTs to date, including 11,957 patients from 25 RCTs. A recent RCT in elective hip and knee surgery included 2546 participants, the largest RCT to date in this subject [58]. This review is the only review to include this important and well-conducted study. In addition, this systematic review only included peer-reviewed studies with published full texts. Previous meta-analyses have included conference abstracts which do not go through the same rigorous peer-review process as full journal publications and thus represent a potential danger to review quality[32]. Furthermore, robust quality and risk of bias assessment is not possible with these abstract publications[66]. A further strength of this review is the detailed and systematic quality assessments, along with robust Cochrane risk of bias assessments, of all included studies[36,66]. As demonstrated in table 2 five out of eleven reviews assessed risk of bias and one out of eleven reviews assessed the quality of evidence. A strength of this review is the inclusion of a thorough risk of bias and GRADE assessment. In addition, this new review included further detailed sub group analysis based on superficial vs deep surgical infections and based on type of surgery e.g. clean, clean contaminated, contaminated and dirty surgery.

The main weakness of this review is the study population. The review includes procedures which were classed as clean, clean- contaminated, contaminated, and dirty. These types of surgery would all have differing rates of SSI. The authors therefore performed a sub-analyses of the different categories of surgery. Routine antibiotic prophylaxis was used in 15 studies[2,7,11,38,39,42,44-51,58] with a variation in the antibiotic agent used and the timing. This is a potential confounder for the frequency of SSI[67]. A proportion of the included studies assessed patients with an underlying malignancy who may have been immunosuppressed. This influences the rate of SSI and is not accounted for in many of the included studies[68]. Another weakness is the heterogeneity in the use of triclosan coated sutures. In some studies, triclosan was used for closure of all surgical layers, whereas in other studies triclosan coated sutures were only used on the superficial layers. This study heterogeneity should be noted when interpreting the meta-analysis result. This review reports trials using CDC criteria for superficial site infections. It is important to note that a stitch abscess does not meet the criteria for a superficial site infections. Patients may present with a stitch abscess to healthcare professionals and undergo treatment. This study does not report the impact of triclosan coated sutures on stitch abscesses.

Our review is the largest review of RCTs to date in terms of patient numbers and demonstrates clinical effectiveness of triclosan coated sutures when compared to standard sutures when assessing SSI rate. SSIs have been shown to have a significant impact on patient quality of life, as well as an increased burden on healthcare providers in terms of resource allocation. The cost of triclosan sutures is variable, however the cost of SSI to patients and healthcare providers is sizeable[10-12]. A robust cost-analysis has not been performed, nevertheless, organisations should consider carefully whether they routinely use triclosan coated sutures in light of these positive meta-analysis findings. This review also identified that triclosan coated sutures significantly reduced the risk of SSIs in clean and contaminated surgery, therefore thoughtful consideration should be paid to whether they are routinely used in this patient population. The results demonstrate that triclosan coated sutures may not be as effective in reducing SSI rate in 'clean-

contaminated' and 'dirty' surgery. However, a potential explanation for 'dirty' surgery is the low patient numbers included in this subgroup. This is a potential area of future research given the effectiveness of triclosan coated sutures in 'clean' and 'contaminated' surgery.

Conclusion

This systematic review identified 25 RCTs examining the effect of triclosan in reducing incidence of SSI, compared with non-coated sutures. The subsequent meta-analysis included 11,957 patient and revealed an overall a risk ratio of RR 0.73, (95% CI 0.65 to 0.82) of developing SSI in favour of triclosan coated sutures, thereby demonstrating a statistically significant lower risk of SSI following closure of a surgical wound with triclosan coated sutures. Further analysis has demonstrated that triclosan coated sutures significantly reduced the risk of SSIs in clean and contaminated surgery. This study is in agreement with previous smaller and less robust reviews which have produced comparable results. This is the largest review of RCTs in terms of number of included studies and number of participants from RCTs to demonstrate the clinical effectiveness of triclosan coated sutures. Further detailed cost effectiveness is required to assess the economic benefit of implementing the use of these sutures. The evidence considered in this review suggests that triclosan coated sutures are effective in reducing surgical site infections, the use should in particular be considered in clean and contaminated surgery.

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Competing interests

The authors report no competing interests for this study

Ethical Approval

No ethical approval required for this study.

Data Statement

Raw data is available on request by email to the corresponding author.

Author contributions

All authors contributed to the production of this manuscript and meet the ICMJE criteria.

- IA: Conception of review, data collection, analysis, drafted final manuscript
- AB: Data collection, analysis, drafted final manuscript
- SR: Data analysis and revised final manuscript
- WC: Data analysis and revised final manuscript
- ED: Data collection and revision of final manuscript
- NS: Revision of final manuscript
- MR: Conception of idea and revision of final manuscript

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Study	No. of participants	No. of centres	Surgery type	Sutures used	SSI criteria	Duration of follow-up	Routine prophylactic antibiotics?
Arslan 2018	**177**	**1**	**Surgery for pilonidal disease**	**Vicryl vs Vicryl plus**	**CDC criteria**	**30 days**	**Yes**
Baracs 2011	385	7	Elective colorectal surgery	PDS vs PDS Plus	Not stated	30 days	Yes
Chen 2011	241	1	Head and neck surgery	Vicryl vs Vicryl Plus	Local erythema with purulent discharge, wound dehiscence, or skin necrosis	Not stated	Yes
Diener 2014	1185	24	Laparotomy	PDS vs PDS Plus	CDC criteria	30 days	Yes
Ford 2005	147	1	Paediatric general surgery	Vicryl vs Vicryl Plus	Not stated	80 days	No
Galal 2011	450	1	All surgery	Vicryl vs Vicryl Plus	CDC criteria	30 days	Not stated
Ichida 2018	1023	1	Gastroenterologic surgery	Vicryl and PDS II vs Vicryl Plus and PDS Plus	CDC criteria	30 days	Yes
Isik 2011	510	1	Cardiac surgery	Vicryl vs Vicryl Plus	CDC criteria	1 month	Not stated
Justinger 2013	856	1	Laparotomy	PDS II vs PDS II Plus	CDC criteria	2 weeks	Yes
Karip 2016	106	1	Pilonidal sinus excision followed by Karydakis flap repair	Monocryl Plus vs Monocryl	Rash, fever or purulent discharge	2 weeks	Yes
Lin 2018	102	1	Total knee replacement surgery	Vicryl vs Vicryl plus	CDC criteria	30 days	Yes
Mattavelli 2015	300	4	Elective colorectal surgery	Vicryl and PDS vs Vicryl Plus and PDS Plus	CDC criteria	30 days	Yes
Mingmalairak 2009	100	1	Appendectomy	Vicryl vs Vicryl Plus	Not stated	30 days, 6 months and 1 year	Yes
Nakamura 2013	410	1	Elective colorectal surgery	Vicryl vs Vicryl Plus	CDC criteria	30 days	Yes
Rasic 2011	184	1	Elective colorectal cancer surgery	Vicryl vs Vicryl Plus	Not stated	To discharge	Yes
Renko 2017	1633	1	Paediatric surgery	Vicryl and Monocryl and PDS vs Vicryl Plus and Monocryl Plus and PDS Plus	CDC criteria	30 days	In 30%
Roy 2019	110	1	Gastrointestinal surgery	PDS vs PDS plus	CDC criteria	30 days	Yes

Ruiz-Tovar 2015	110	3	Open colorectal surgery with faecal peritonitis	Vicryl vs Vicryl Plus	CDC criteria	60 days	Yes
Seim 2012	328	1	CABG leg wound	Vicryl vs Vicryl Plus	Positive bacterial culture and clinical judgement	4 weeks	Yes
Sprowson 2018	2546	3	Primary THR or TKR	Vicryl vs Vicryl Plus	CDC criteria	30 days	Yes
Tabrizi 2018	320	2	Dental implant surgery	Vicryl vs Vicryl plus	CDC criteria	30 days	Yes
Thimour-Bergstrom 2013	392	1	CABG (+/-AVR, MVR) with saphenous vein graft	Vicryl and Monocryl vs Vicryl Plus and Monocryl Plus	CDC criteria	60 days	Yes
Turtiainen 2012	276	3	Non-emergency lower-limb arterial surgery	Vicryl and Monocryl vs Vicryl Plus and Monocryl Plus	CDC criteria	30 days	Yes
Williams 2011	150	1	Mastectomy	Vicryl and Monocryl vs Vicryl Plus and Monocryl Plus	CDC criteria	6 weeks	If considered at risk
Zhang 2011	101	6	Mastectomy	Chinese silk vs Vicryl Plus	CDC criteria	30 days	Not stated

Table 1: Study characteristics of included RCTs in this review

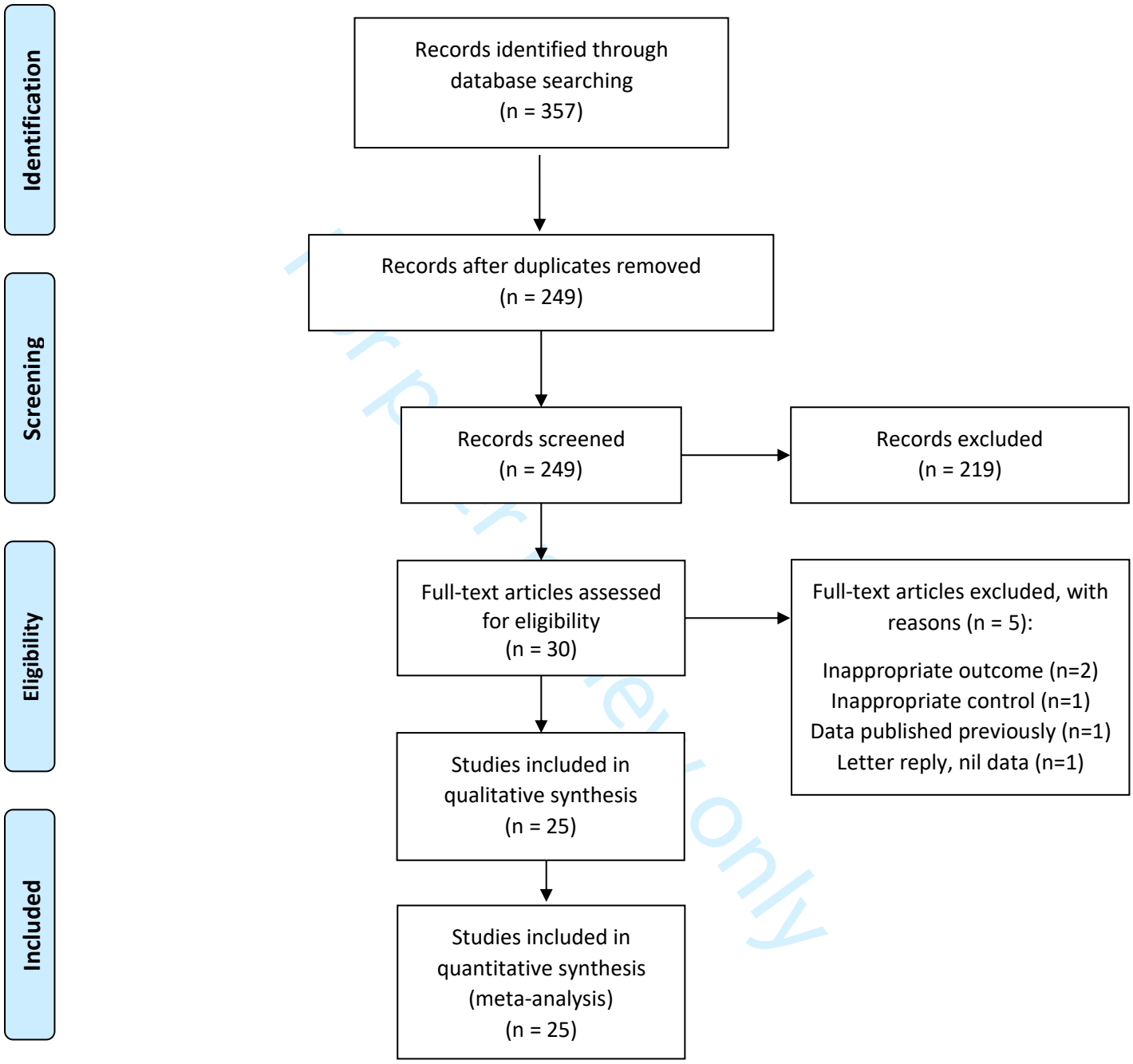
Author	Date	Journal	Number of studies	Number of participants	Findings	Risk of bias	Grade
Wang et al	2013	British Journal of Surgery	17	3720	Triclosan coated sutures significantly reduced SSI rate compared to standard sutures. RR 0.7 (95% CI 0.57, 0.85). Triclosan coated sutures significantly reduced SSI rate in 'clean' and 'clean-contaminated' surgery.	Included	Not included
Edmiston et al	2013	Surgery	13	3568	Triclosan coated sutures significantly reduced SSI rate compared to standard suture. RR 0.734 (95% CI 0.59, 0.91). No subgroup analysis was performed.	Not included	Not included
Daoud et al	2014	Surgical infections	15	4800	Triclosan coated sutures significantly reduced SSI rate compared to standard sutures. RR 0.67 (95% 0.54, 0.84). No subgroup analysis was performed.	Not included	Not included
Apisarnthanarak et al	2015	Infection Control and Hospital Epidemiology	29 (22 RCT and 7 non-RCT)	11942	Triclosan coated sutures significantly reduced SSI rate compared to standard suture. RR 0.65 (95% CI 0.549, 0.769). RR for RCT alone 0.74 (95% CI 0.61, 0.89). Triclosan coated sutures significantly reduced SSI rate for all CDC wound classifications.	Not included	Not included

Guo et al	2015	Journal of Surgical Research	13	5256	Triclosan coated sutures significantly reduced risk of SSI compared to standard suture. RR 0.76 (95% CI 0.65, 0.88). Triclosan coated sutures significantly reduced risk of SSI in abdominal surgery. RR 0.70 (95% CI 0.63, 0.99). There was no significant difference in cardiac and breast surgery.	Included	Not included
Sandini et al	2016	Medicine	6 (only included elective colorectal surgery)	2168	Triclosan coated sutures did not significantly reduce the risk of SSI compared to standard sutures in elective colorectal surgery. OR 0.81 (95% CI 0.58, 1.13)	Included	Not included
Wu et al	2017	European Journal of Microbiology and Infectious Disorders	18 (13 RCTs and 5 non RCTs)	7458	Triclosan coated sutures significantly reduced risk of SSI compared to standard suture in both the RCTs (OR 0.72; 95% CI 0.59, 0.88) and the non- RCTS (OR 0.58; 95% CI 0.40, 0.83). Triclosan coated sutures significantly reduced the risk of SSIS in clean surgery.	Included	Included

De Jonge et al	2017	British Journal of Surgery	21	6462	Triclosan coated sutures significantly reduced risk of SSI compared to standard suture. RR 0.72 (95% CI 0.60, 0.86).	Included	Not included
Leaper et al	2017	British Journal of Surgery	34 (20 RCTs and 14 non-RCTs)	16762	Triclosan coated sutures significantly reduced risk of SSI compared to standard sutures. OR 0.61 (95% CI 0.52, 0.73). No significant difference in SSI rate for 'contaminated' or 'dirty' wounds	Not included	Not included
Konstantelias et al	2017	Acta Chirurgica Belgica 2017	30 (19 RCTs and 11 non-RCTs)	15385	Triclosan coated sutures significantly reduced risk of SSI compared to standard suture. RR 0.68 (95% CI 0.57, 0.81). Triclosan coated sutures significantly reduced risk of SSI in 'clean', 'clean-contaminated' and 'contaminated surgery.'	Not included	Not included
Henriksen et al	2017	Hernia	8 (only included studies reporting abdominal wall closure)	3641	Triclosan coated sutures significantly reduced risk of SSI compared to standard suture in abdominal wall closure. OR 0.67 (95% CI 0.46, 0.98).	Not included	Not included

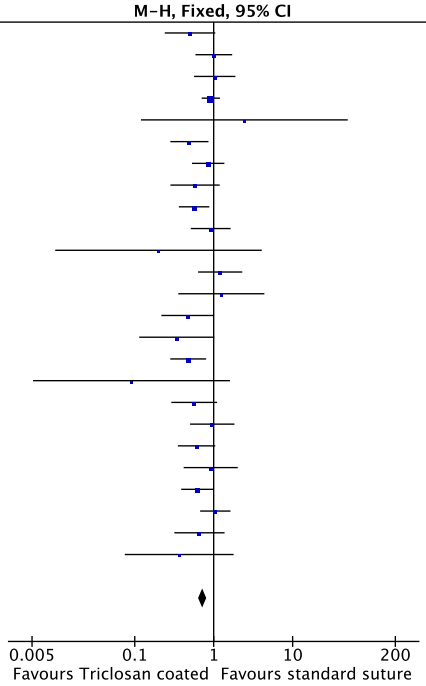
Table 2: A summary of previous systematic reviews on this topic area highlighting number of studies, number of participants and key findings.

Figure 1: PRISMA flow diagram of search results



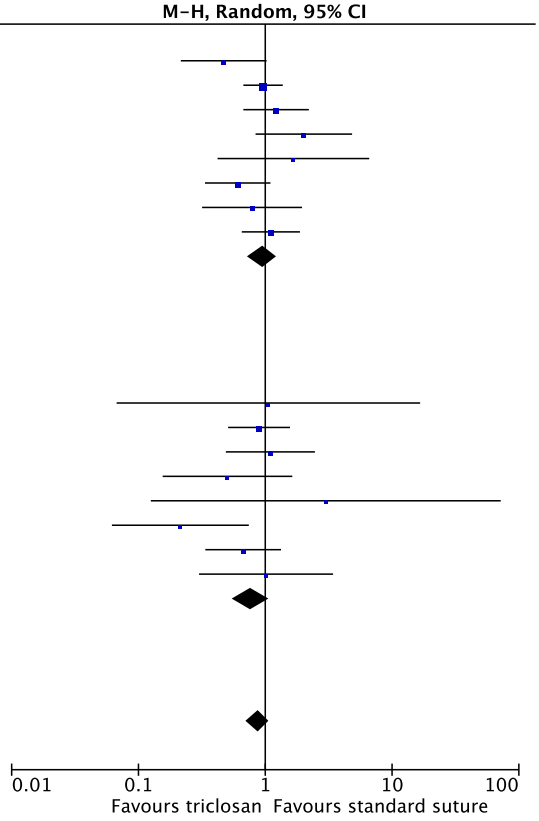
Study or Subgroup	Triclosan coated suture Events	Total	Standard suture Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Arslan 2018	9	86	19	91	3.2%	0.50 [0.24, 1.05]
Baracs 2011	23	188	24	197	4.1%	1.00 [0.59, 1.72]
Chen 2011	17	112	19	129	3.1%	1.03 [0.56, 1.88]
Diener 2014	87	587	96	596	16.5%	0.92 [0.70, 1.20]
Ford 2005	2	91	0	44	0.1%	2.45 [0.12, 49.88]
Galal 2011	17	230	33	220	5.9%	0.49 [0.28, 0.86]
Ichida 2018	30	508	35	505	6.1%	0.85 [0.53, 1.37]
Isik 2011	9	170	31	340	3.6%	0.58 [0.28, 1.19]
Justinger 2013	31	485	42	371	8.3%	0.56 [0.36, 0.88]
Karip 2016	15	52	17	54	2.9%	0.92 [0.51, 1.64]
Lin 2018	0	51	2	51	0.4%	0.20 [0.01, 4.07]
Mattavelli 2015	18	140	15	141	2.6%	1.21 [0.63, 2.30]
Mingmalairak 2009	5	50	4	50	0.7%	1.25 [0.36, 4.38]
Nakamura 2013	9	206	19	204	3.3%	0.47 [0.22, 1.01]
Rasic 2011	4	91	12	93	2.1%	0.34 [0.11, 1.02]
Renko 2017	20	779	42	778	7.3%	0.48 [0.28, 0.80]
Roy 2019	0	55	5	55	1.0%	0.09 [0.01, 1.61]
Ruiz-Tovar 2015	10	50	18	51	3.1%	0.57 [0.29, 1.10]
Seim 2012	16	160	17	163	2.9%	0.96 [0.50, 1.83]
Sprowson 2018	21	1323	32	1223	5.8%	0.61 [0.35, 1.05]
Tabrizi 2018	11	160	12	160	2.1%	0.92 [0.42, 2.02]
Thimour-Bergstrom 2013	23	184	38	190	6.5%	0.63 [0.39, 1.01]
Turtiainen 2012	31	137	30	139	5.2%	1.05 [0.67, 1.63]
Williams 2011	10	66	14	61	2.5%	0.66 [0.32, 1.37]
Zhang 2011	2	47	5	43	0.9%	0.37 [0.07, 1.79]
Total (95% CI)		**6008**		**5949**	**100.0%**	**0.73 [0.65, 0.82]**
Total events	420		581			

Heterogeneity: Chi² = 28.97, df = 24 (P = 0.22); I² = 17%
Test for overall effect: Z = 5.20 (P < 0.00001)

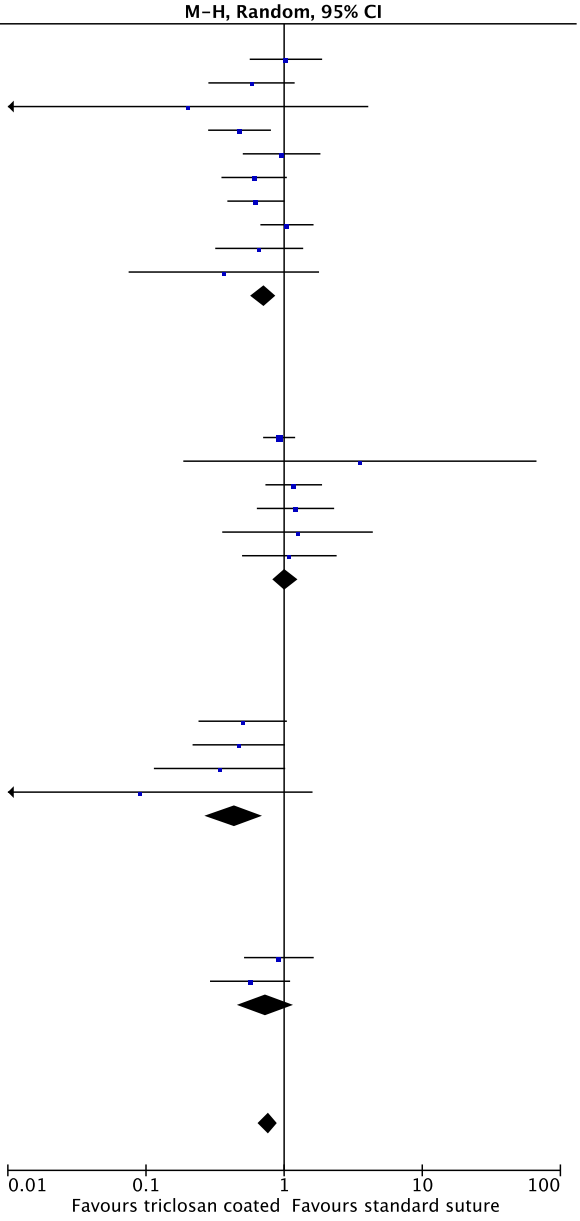


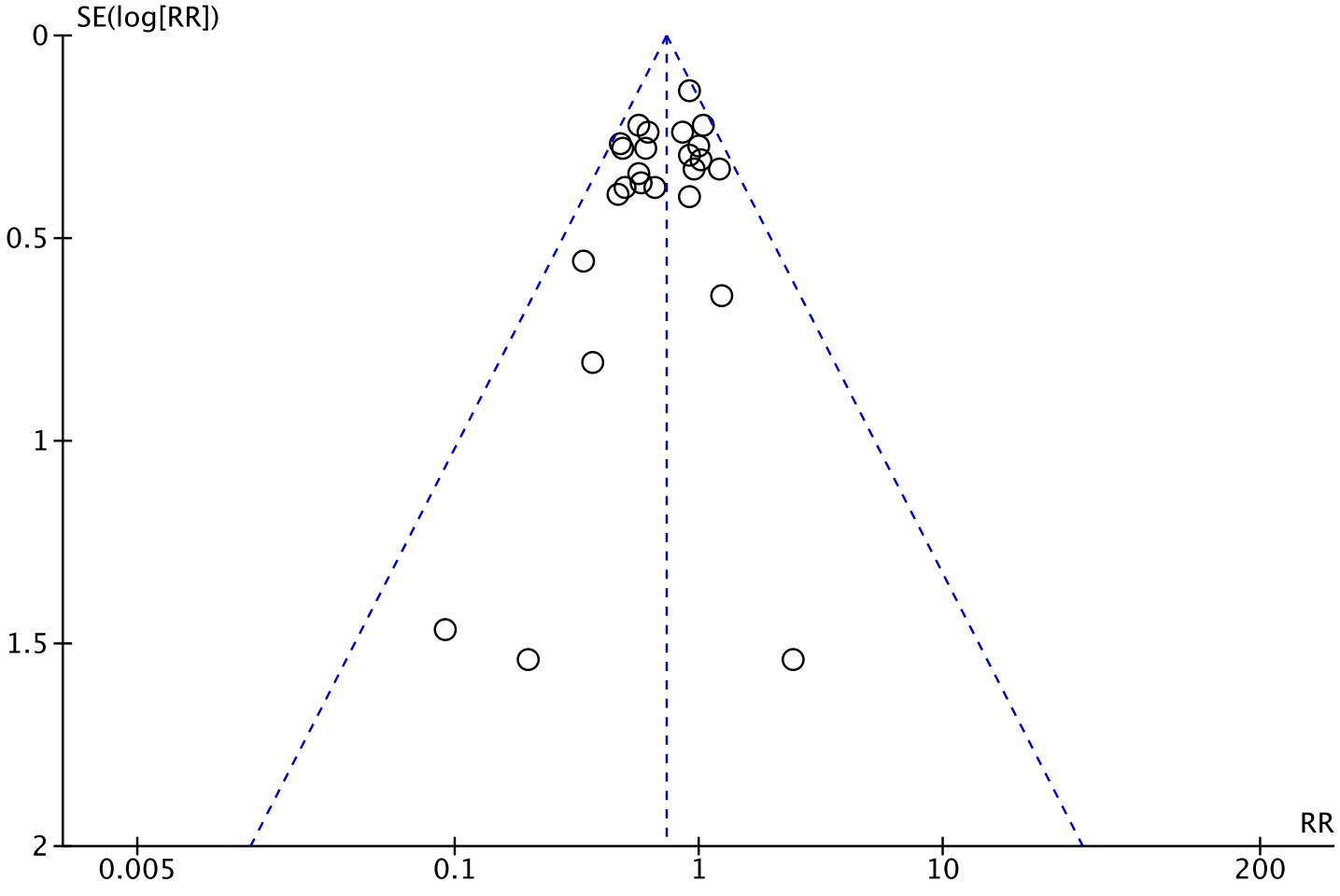
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Study or Subgroup	Triclosan coated suture Events	Total	Standard suture Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.2 Superficial infections						
Arslan 2018	8	86	18	91	6.1%	0.47 [0.22, 1.02]
Diener 2014	53	587	56	596	18.8%	0.96 [0.67, 1.37]
Ichida 2018	23	505	19	508	9.5%	1.22 [0.67, 2.21]
Mattavelli 2015	14	140	7	141	5.0%	2.01 [0.84, 4.84]
Mingmalairak 2009	5	50	3	50	2.2%	1.67 [0.42, 6.60]
Renko 2017	17	779	28	778	9.5%	0.61 [0.33, 1.10]
Sprowson 2018	8	1223	11	1323	4.7%	0.79 [0.32, 1.95]
Turtiainen 2012	24	137	22	139	11.4%	1.11 [0.65, 1.88]
Subtotal (95% CI)		**3507**		**3626**	**67.1%**	**0.95 [0.72, 1.25]**
Total events	152		164			
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 9.95$, df = 7 (P = 0.19); $I^2 = 30\%$						
Test for overall effect: Z = 0.38 (P = 0.70)						
1.2.3 Deep infections						
Arslan 2018	1	86	1	91	0.6%	1.06 [0.07, 16.65]
Diener 2014	22	587	25	596	10.4%	0.89 [0.51, 1.57]
Ichida 2018	12	505	11	508	5.7%	1.10 [0.49, 2.46]
Mattavelli 2015	4	140	8	141	2.9%	0.50 [0.16, 1.63]
Mingmalairak 2009	1	50	0	50	0.4%	3.00 [0.13, 71.92]
Renko 2017	3	779	14	778	2.6%	0.21 [0.06, 0.74]
Sprowson 2018	13	1223	21	1323	7.5%	0.67 [0.34, 1.33]
Turtiainen 2012	5	137	5	139	2.7%	1.01 [0.30, 3.43]
Subtotal (95% CI)		**3507**		**3626**	**32.9%**	**0.77 [0.55, 1.07]**
Total events	61		85			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 6.74$, df = 7 (P = 0.46); $I^2 = 0\%$						
Test for overall effect: Z = 1.58 (P = 0.11)						
Total (95% CI)		**7014**		**7252**	**100.0%**	**0.88 [0.71, 1.08]**
Total events	213		249			
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 17.81$, df = 15 (P = 0.27); $I^2 = 16\%$						
Test for overall effect: Z = 1.20 (P = 0.23)						
Test for subgroup differences: $Chi^2 = 0.95$, df = 1 (P = 0.33), $I^2 = 0\%$						



Study or Subgroup	Triclosan coated Events	Total	Standard suture Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.3.1 Clean surgery						
Chen 2011	17	112	19	129	5.4%	1.03 [0.56, 1.88]
Isik 2011	9	170	31	340	4.1%	0.58 [0.28, 1.19]
Lin 2018	0	51	2	51	0.3%	0.20 [0.01, 4.07]
Renko 2017	20	779	42	778	6.6%	0.48 [0.28, 0.80]
Seim 2012	16	160	17	163	4.9%	0.96 [0.50, 1.83]
Sprowson 2018	21	1323	32	1223	6.3%	0.61 [0.35, 1.05]
Thimour-Bergstrom 2013	23	184	38	190	7.5%	0.63 [0.39, 1.01]
Turtiainen 2012	31	137	30	139	8.2%	1.05 [0.67, 1.63]
Williams 2011	10	66	14	61	4.0%	0.66 [0.32, 1.37]
Zhang 2011	2	47	5	43	1.0%	0.37 [0.07, 1.79]
Subtotal (95% CI)		**3029**		**3117**	**48.3%**	**0.71 [0.58, 0.88]**
Total events	149		230			
Heterogeneity: Tau² = 0.01; Chi² = 9.88, df = 9 (P = 0.36); I² = 9%						
Test for overall effect: Z = 3.16 (P = 0.002)						
1.3.2 Clean-contaminated surgery						
Diener 2014	87	587	96	596	13.6%	0.92 [0.70, 1.20]
Ford 2005	3	98	0	49	0.3%	3.54 [0.19, 67.12]
Ichida 2018	35	505	30	508	7.6%	1.17 [0.73, 1.88]
Mattavelli 2015	18	140	15	141	4.9%	1.21 [0.63, 2.30]
Mingmalairak 2009	5	50	4	50	1.5%	1.25 [0.36, 4.38]
Tabrizi 2018	12	160	11	160	3.5%	1.09 [0.50, 2.40]
Subtotal (95% CI)		**1540**		**1504**	**31.4%**	**1.02 [0.83, 1.25]**
Total events	160		156			
Heterogeneity: Tau² = 0.00; Chi² = 2.00, df = 5 (P = 0.85); I² = 0%						
Test for overall effect: Z = 0.18 (P = 0.86)						
1.3.3 Contaminated						
Arslan 2018	9	86	19	91	4.0%	0.50 [0.24, 1.05]
Nakamura 2013	9	206	19	204	3.7%	0.47 [0.22, 1.01]
Rasic 2011	4	91	12	93	2.0%	0.34 [0.11, 1.02]
Roy 2019	0	55	5	55	0.3%	0.09 [0.01, 1.61]
Subtotal (95% CI)		**438**		**443**	**9.9%**	**0.43 [0.27, 0.70]**
Total events	22		55			
Heterogeneity: Tau² = 0.00; Chi² = 1.55, df = 3 (P = 0.67); I² = 0%						
Test for overall effect: Z = 3.46 (P = 0.0005)						
1.3.4 Dirty surgery						
Karip 2016	15	52	17	54	5.7%	0.92 [0.51, 1.64]
Ruiz-Tovar 2015	10	50	18	51	4.6%	0.57 [0.29, 1.10]
Subtotal (95% CI)		**102**		**105**	**10.3%**	**0.74 [0.46, 1.18]**
Total events	25		35			
Heterogeneity: Tau² = 0.01; Chi² = 1.14, df = 1 (P = 0.29); I² = 12%						
Test for overall effect: Z = 1.25 (P = 0.21)						
Total (95% CI)		**5109**		**5169**	**100.0%**	**0.77 [0.66, 0.91]**
Total events	356		476			
Heterogeneity: Tau² = 0.03; Chi² = 27.52, df = 21 (P = 0.15); I² = 24%						
Test for overall effect: Z = 3.15 (P = 0.002)						
Test for subgroup differences: Chi² = 12.91, df = 3 (P = 0.005), I² = 76.8%						

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10
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RR

Supplementary file 1. Demonstrating the full search strategy and the number of results for each search term. The search was performed on the 31st May 2019.

Database: AMED (Allied and Complementary Medicine) <1985 to May 2019>, Ovid MEDLINE(R) <1946 to May Week 4 2019>, Embase <1974 to 2019 May 30>
Search Strategy:
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1 triclosan.mp. (8754)
2 anti-bacterial agents.mp. (315458)
3 anti-infective agents, local.mp. (16419)
4 coated materials, biocompatible.mp. (13821)
5 biomimtic material.mp. (0)
6 1 or 2 or 3 or 4 or 5 (350648)
7 sutures.mp. (61707)
8 vicryl plus.mp. (129)
9 monocryl plus.mp. (20)
10 PDS plus.mp. (47)
11 7 or 8 or 9 or 10 (61743)
12 surgical site infection.mp. (14995)
13 surgical wound infection.mp. (37378)
14 12 or 13 (48237)
15 6 and 11 and 14 (282)
16 remove duplicates from 15 (233)

****

Then CENTRAL search identified 75, and after duplicates removed this was 16 new. So total 249 records screened.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4/5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-9 and table 1
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6/7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6/7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8,9 table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10, Figure 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9,10 Figure 2-5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9,10 Figure 2-5
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10, Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9,10 Figure 2-5
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11, 12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12,13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13, 14

PRISMA 2009 Checklist

FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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BMJ Open

The use of triclosan coated sutures to prevent surgical site infections: a systematic review and meta-analysis of the literature

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The use of triclosan coated sutures to prevent surgical site infections: a systematic review and meta-analysis of the literature

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ABSTRACT

Introduction and objectives

Surgical site infections (SSIs) represent a common and serious complication of all surgical interventions. Micro-organisms are able to colonise sutures that are implanted in the skin, which is a causative factor of SSis. Triclosan coated sutures are antibacterial sutures aimed at reducing surgical site infections.

Our objective is to update the existing literature by systematically reviewing available evidence to assess the effectiveness of triclosan coated sutures in the prevention of surgical site infections.

Methods

A systematic review of EMBASE, MEDLINE, AMED (Allied and complementary medicine database) and CENTRAL was performed to identify full text randomised controlled trials (RCTs) on 31/05/2019.

Intervention

Triclosan coated sutures versus non triclosan coated sutures.

Primary outcome

Our primary outcome was the development of surgical site infections at 30 days post operatively. A meta-analysis was performed using a fixed effects model.

Results

Twenty five RCTs were included involving 11,957 participants. Triclosan coated sutures were used in 6008 participants and non triclosan coated sutures were used in 5949. Triclosan coated sutures significantly reduced the risk of surgical site infections at 30 days (RR 0.73, 95% CI 0.65 to 0.82). Further sensitivity analysis demonstrated that triclosan coated sutures significantly reduced the risk of surgical site infections in both clean and contaminated surgery.

Conclusion

Triclosan coated sutures have been shown to significantly reduced the risk of surgical site infections when compared to standard sutures. This is in agreement with previous work in this area. This study represented the largest review to date in this area. This moderate quality evidence recommends the use

of Triclosan coated sutures in order to reduce the risk of SSIs particularly in clean and contaminated surgical procedures.

Registration

PROSPERO (Reference: CRD42014014856).

Key words

Surgical site infection, triclosan, systematic review

Article summary

Strengths and limitations of this study

Strengths

- Systematic nature of data collection and analysis
- Largest review to date in this topic area
- Analyses performed comparing different classifications of surgery i.e clean, clean-contaminated, contaminated and dirty.

Limitations

- Heterogeneous nature of included studies. E.g. different age of participants, co-morbidities and surgery type.

Original protocol

A protocol for this review was prospectively registered with PROSPERO (Reference: CRD42014014856).

Funding statement

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Competing interests

All authors report no competing interests.

Word count: 3596

INTRODUCTION

Surgical site infections (SSIs) represent a common complication throughout all surgical procedures[1]. It is estimated that SSIs account for 5% of all surgical complications[2] and 20% of all healthcare associated infections[3,4]. It is generally believed that the number of surgical procedures, particularly in elective orthopaedics[5], will increase over the next decade, therefore increasing the incidence of SSIs. SSIs are associated with prolonged hospital admission[6] and increased morbidity and mortality[7,8,9]. In addition to having a significant impact on patient care and experience, SSIs also add substantial costs to healthcare providers. It is estimated that SSIs cost UK healthcare services approximately £61 million in 2012[10] and figures from the US highlight the extensive cost of SSIs with an estimated additional $2300 per case[11]. Furthermore, Fleck *et al.* found that the mean cost of treated a SSI following sternal wound incision was $11,200[12]. These are conservative estimates as active surveillance of SSIs not routinely performed[6].

Due to the wide ranging deleterious effects of SSIs and their treatment, particularly in the context of increasing numbers of surgical procedures, there is a clinical need to reduce the incidence of SSIs. SSIs are multifactorial with patient factors such as age, co-morbidities including diabetes, and immunosuppression[7,13-15] contributing to their development, along with surgical factors. Many patient factors may not be optimised and hence research focus has been placed on surgical factors, including suture material.

SSIs may arise when bacteria colonise the suture material[16], creating a biofilm as it passes through the skin[17]. This biofilm establishes an immunity from both antimicrobial treatment and the host immune system[6,17]. Once this biofilm develops there is an increased chance of a SSI developing. Research has shown bacteria may colonise monofilament and braided sutures[18-20]. With this in mind, considerable work has been carried out since the 1950s with regards to coating suture material with an antimicrobial, including silver[21,22]. Triclosan (polychlorophenoxyphenol) has been used for its antiseptic properties for

many years in toothpaste and soap and has an established safety profile[5]. Triclosan has been used to successfully coat the following sutures and gained FDA (US food and drug administration) approval in 2002: braided polyglactan 910 (Vicryl Plus), poliglecaprone 25 (Monocryl Plus) and polydioxanone (PDS Plus).

In vitro and *in vivo* studies have shown the effectiveness of triclosan coated sutures[23-25] in killing bacteria associated with SSIs and inhibiting colonisation of suture material, with one study demonstrating a 66% reduction in bacterial colonisation[26]. Since then a large number of randomised control trials (RCTs) have been performed with contrasting results of the effectiveness of triclosan coated sutures in the prevention of SSIs. Subsequent meta-analyses have also produced conflicting results and hence the true effect remains unclear[6,7,27-32]. The most recent and largest systematic review to date was performed by De Jonge *et al.* and found triclosan coated sutures significantly reduced the incidence of SSIs[32]. This review searched the literature up until November 2015 and included 6462 patients from RCTs published in peer-reviewed journals as well as conference abstracts. Performing robust methodological appraisal of conference abstracts is not possible, they do not permit thorough risk of bias assessments, and as they have not undergone the formal journal peer-review process, they represent a potentially biased and unreliable source of data. Since this review, a number of large, high quality RCTs have been produced[33,34]. Of note, a recent RCT of 2546 patients found that triclosan coated sutures did not reduce the incidence of SSIs; a finding in contrast to the previous systematic review[32,34]. This represents a substantial increase in the number of patients available for meta-analysis since the last review. As a result, we believe it is important to update the existing literature by performing a new, up to date, systematic review and meta-analysis to assimilate the current evidence and inform clinical practice. A new review should include a detailed risk of bias assessment and GRADE assessment of the quality of evidence.

This new systematic review and meta-analysis of the available literature aims to determine whether the use of triclosan coated sutures reduces the incidence of SSIs in comparison to standard non-coated sutures.

PICOS statement

The included population encompasses patients of any age and gender undergoing any surgical procedure utilising sutures to close the wound. The intervention studied is the use of triclosan coated sutured and comparison is made with non-triclosan coated sutures. The outcomes assessed are the rates of SSIs, including superficial and deep SSIs. This systematic review will only include RCTs.

METHODS

A systematic review of the available literature was conducted and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance[35]. A protocol for this review was prospectively registered with PROSPERO (Reference: CRD42014014856).

Search methods

Electronic searches were conducted using OVID SP on the following databases: MEDLINE(1946-May Week 4 2019); Excerpta Medica Database (EMBASE) (1974 to 2019 May 31); Allied and Complementary Medicine (AMED) (1985 to May 2019); and Cochrane Central Register of Controlled Trials (CENTRAL). A multi-purpose search was performed for all terms and the search terms were: “Triclosan”, “Anti-bacterial agents”, “Anti-infective agents, local”, “Coated materials, biocompatible”, “Biomimetic material”, “Sutures”, “Vicryl Plus”, “Monocryl Plus”, “PDS Plus”, “Surgical site infection”, “Surgical Wound infection”. The search was conducted on 31st May 2019. A copy of the search strategy can be seen in supplementary file 1.

Selection of Studies

Two authors (IA and AB) independently selected studies for inclusion. Any discrepancies were resolved by discussion with a third author (ED). Titles and abstracts were screened and full texts obtained for any studies of interest. The eligibility criteria were formed from the PICOS statement and registered on PROSPERO prior to undertaking the search. Only RCTs published in peer-reviewed journals presenting new data were included.

Data extraction

Data was independently extracted from eligible included studies onto predetermined forms by two authors (IA and AB). Any discrepancies were then resolved following discussion between two authors (IA and AB) and a third author. Data extracted included baseline patient characteristics, surgical procedures performed, number of centres, suture material, SSI diagnostic criteria, length of follow up, routine prophylactic antibiotic use and number of SSIs. Data regarding superficial of deep SSI was extracted when possible. Information regarding randomisation, blinding, funding and country of origin was extracted.

Assessment of Risk of Bias

Two authors (IA and AB) independently appraised eligible studies according to the Cochrane Collaboration's risk of bias tool, resolving any discrepancies with a third author (ED)as necessary[36]. Review Manager version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used to generate the summary figures. The parameters used for 'other' sources of bias included source of funding and antibiotic regime.

Two authors (IA and AB) independently assessed the quality of evidence. We used the GRADE considerations (study limitations, consistence of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence[37]. Decisions to upgrade or downgrade body of evidence have been clearly stated in the discussion.

Publication bias was assessed following construction of a funnel plot in order to identify the presence or absence of bias of this kind.

Statistical analysis

A fixed effects model was used to calculate the predominant relative risk (RR) and the 95% confidence intervals of the studies included. Statistically heterogeneity was first assessed using a funnel plot and more formally using the I^2 statistic[36]. Forest plots were then generated summarising the results of the meta-analysis using Review Manager 5.3.

Patient and Public Involvement

Given the design of this study and the retrospective nature, patient and public members were not involved in the development and conduct of this review. With the aid of patient and public members we will produce lay summaries of the results available for patients.

RESULTS

The search revealed 357 records of possible relevance. No other sources of records were identified. Removal of duplicates left 249 records to be examined. 219 records were excluded based on title and abstract screening. 30 full texts were assessed for eligibility and 25 studies were included in the meta-analysis (see figure 1)[2,7,11,33,34,38-57].

Study characteristics

Study characteristics are summarised in table 1. Twenty-five RCTs were included in this review involving 11,957 patients[2,7,11,33,34,38-57]. There were 6008 patients randomised to triclosan coated sutures and 5949 patients to standard sutures. In studies which reported mean age, the mean age reported in 23 out of 25 studies was comparable between the two groups (54.8 vs 54.8). For the studies which reported gender 57% of the included patients were male. Eight studies were multi-centre, with the remainder single-centre studies (n=17). Vicryl was compared with Vicryl Plus in twelve studies[11,34,39-41,43,46-49,54,56], three studies compared PDS and versus PDS Plus[7,38,55], one study compared PDS II with PDS II Plus[44], two study

compared Monocryl against Monocryl Plus[45,57], one compared Chinese silk with Vicryl Plus[53], four studies compared Vicryl and Monocryl versus Vicryl Plus and Monocryl Plus[33,50-52], and two studies compared Vicryl and PDS versus Vicryl Plus and PDS Plus[2,42].

To define SSI, the Centre for disease control (CDC) criteria were used by 18 studies[2,7,11,33,34,41-44,48,50-57], clinical diagnosis or wound cultures was used by three studies studies[39,45,49], and four did not provide explicit definitions[38,40,46,47]. Seventeen studies used a follow up duration of 30 days or one month or four weeks[2,7,11,33,34,38,41-43,46,49,51,53-57], three for six weeks[48,50,52], two for two weeks[44,45], one for 80 days[40], one until discharge[47], and one study did not specify a follow-up regime[39]. Routine prophylactic antibodies were used in 19 studies[2,7,11,34,38,39,42,44-51,54-57], no prophylactic antibiotics were used in one study[40], one used prophylactic antibiotics in high risk patients only[52], one study used prophylactic antibiotics in 30% of participants[33], and three did specify prophylactic antibiotic use[41,43,53].

Surgical site infection

The risk of developing surgical site infection was significantly reduced in the triclosan group compared to the standard suture group (RR 0.73, 95% CI 0.65 to 0.82). Heterogeneity was low to moderate (χ^2=24.66, P=0·21, I^2=17%). There were 420 instances of SSI amongst 6008 patients in the triclosan coated suture group and 581 SSIs in 5949 patients in the standard suture group. See figure 2.

Sub-group analysis

Eight studies reported superficial and deep infections separately[2,7,33,34,42,46,51,57]. There were 152/3507 cases of superficial SSI in the triclosan group and 164/3626 cases in the standard suture group, producing a meta-analysis risk ratio of 0.95 (95% CI 0.72 to 1.25). The risk of developing a deep infection was lower in the triclosan group when compared to the standard suture group, however this was not significant (RR 0.77, 95% CI 0.55 to 1.07). There were 61/3507 cases of deep infections in the triclosan group and 85/3626 cases in the standard suture group. See figure 3.

Ten studies reported the incidence of surgical site infection for clean surgery[33,39,43,49-53,56,58]. Triclosan coated sutures were associated with a significantly lower incidence of SSI (149/3029) when compared to standard sutures (230/1117) (RR 0.71, 95% CI 0.58 to 0.88).

Six studies reported clean contaminated surgery and there was no difference between the two groups (160/1540 vs 156/1504) (RR 1.02, 95% CI 0.83,1.25)[2,7,40,42,46,54].

Four studies reported the incidence of surgical site infections in contaminated surgery[11,47,55,57]. Triclosan coated sutures were associated with a significantly lower risk of SSI (22/438) when compared to standard sutures (55/443) (RR 0.43, 95% CI 0.27 to,0.7).

Two further studies reported the incidence of surgical site infection for dirty surgery[45,48]. There was no significant difference in the incidence of SSIs between the two groups of sutures (25/102 vs 35/105) (RR 0.74, 95% CI 0.46 to 1.18). See figure 4.

Risk of bias

The results of the risk of bias screening can be seen on figure 2. The majority of studies had a clear randomisation sequence generation and allocation concealment using sealed envelopes. Five out of twenty five (20%) had high risk of selection bias, either because the randomisation method was not stated or a quasirandomisation method was used. Two further studies had a risk of selection bias due to unclear allocation concealment methods. Ten out of twenty five studies (40%) had high risk of performance and detection bias due to either absence of blinding of the participants and outcome assessors or the methods of blinding were not stated. Four out of twenty five (16%) were at high risk of other bias due to source of funding. One study had differences in antibiotic regime between the two groups, with one group not receiving any antibiotic prophylaxis.

The distribution of studies in the funnel plot was symmetrical. No evidence was found for publication bias in this analysis (figure 5).

Statistical heterogeneity was assessed using the τ^2 (0.02) test and the I^2 (17%) test, indicating there is low heterogeneity between the studies included in this review based on the recommendations in the Cochrane handbook.

DISCUSSION

This large systematic review of 25 randomised clinical trials included 11,957 patients and there were 1001 instances of SSI. The subsequent meta-analysis supports the use of triclosan-coated sutures in reducing the risk of surgical site infections. We report a significantly lower risk of SSI when triclosan coated sutures were used, compared to standard sutures in RCTs. Triclosan coated sutures were used in a wide range of surgeries, including both adult and paediatric patients. The use of triclosan coated sutures significantly reduced the risk of SSI in meta-analyses of clean surgery and also contaminated surgery. Further subgroup analysis revealed a non-statistically significant reduction in the risk of developing deep SSIs with triclosan coated sutures. Triclosan coated sutures appear to have no effect on the incidence of superficial SSIs.

There have been 11 previous reviews in this topic area, the results of these reviews have been summarised in table 2 [27,28,30-32,59-64]. Our results support the findings of Konstantelias et al who concluded that triclosan coated sutures were associated with a significantly lower risk of SSI when compared to standard sutures [32,65]. In addition, the authors concluded that triclosan coated sutures significantly reduced the risk of SSI in clean, clean-contaminated, and contaminated surgery; in agreement with our findings [65]. De Jonge et al reported a meta-analysis of 21 RCTs including 6462 patients, also concluding that triclosan coated sutures significantly reduced the risk of SSI compared to standard sutures [32]. Five out of eleven reviews included a risk of bias assessment[27,31,32,60,64] and only one review assessed the quality of evidence using the GRADE criteria [60].

Quality of evidence

Using the GRADE criteria, the evidence was graded as 'moderate' quality. The reason for downgrading was due to study limitations. Studies had high risk of selection bias due to unclear randomisation and allocation methods. In addition, studies had a high risk of performance and detection bias due to issues

with blinding of participants and outcome assessors. The body of evidence was not downgraded for inconsistency as there was narrow point estimates and low study heterogeneity (I^2=17%). There were no issues with indirectness or imprecision as the outcome measures used are directly aligned to the outcome measures of interest in this review. There were also a large number of participants included in this review with satisfactory event rate numbers. Our symmetrical funnel plot indicated no risk of publication bias. Given the quality of the evidence we are moderately confident in the effect estimate, the true effect is likely to be close to the estimate of the effect.

The strengths of this current review include the thorough and systematic nature of data collection. This review represents the most up to date review of the literature and is the largest review of RCTs to date, including 11,957 patients from 25 RCTs. A recent RCT in elective hip and knee surgery included 2546 participants, the largest RCT to date in this subject [58]. This review is the only review to include this important and well-conducted study. In addition, this systematic review only included peer-reviewed studies with published full texts. Previous meta-analyses have included conference abstracts which do not go through the same rigorous peer-review process as full journal publications and thus represent a potential danger to review quality[32]. Furthermore, robust quality and risk of bias assessment is not possible with these abstract publications[66]. A further strength of this review is the detailed and systematic quality assessments, along with robust Cochrane risk of bias assessments, of all included studies[36,66]. As demonstrated in table 2 five out of eleven reviews assessed risk of bias and one out of eleven reviews assessed the quality of evidence. A strength of this review is the inclusion of a thorough risk of bias and GRADE assessment. In addition, this new review included further detailed sub group analysis based on superficial vs deep surgical infections and based on type of surgery e.g. clean, clean contaminated, contaminated and dirty surgery.

The main weakness of this review is the study population. The review includes procedures which were classed as clean, clean- contaminated, contaminated, and dirty. These types of surgery would all have differing rates of SSI. The authors therefore performed a sub-analyses of the different categories of surgery. Routine antibiotic prophylaxis was used in 15 studies[2,7,11,38,39,42,44-51,58] with a variation in the antibiotic agent used and the timing. This is a potential confounder for the frequency of SSI[67]. A proportion of the included studies assessed patients with an underlying malignancy who may have been immunosuppressed. This influences the rate of SSI and is not accounted for in many of the included studies[68]. Another weakness is the heterogeneity in the use of triclosan coated sutures. In some studies, triclosan was used for closure of all surgical layers, whereas in other studies triclosan coated sutures were only used on the superficial layers. This study heterogeneity should be noted when interpreting the meta-analysis result. This review reports trials using CDC criteria for superficial site infections. It is important to note that a stitch abscess does not meet the criteria for a superficial site infections. Patients may present with a stitch abscess to healthcare professionals and undergo treatment. This study does not report the impact of triclosan coated sutures on stitch abscesses.

Our review is the largest review of RCTs to date in terms of patient numbers and demonstrates clinical effectiveness of triclosan coated sutures when compared to standard sutures when assessing SSI rate. SSIs have been shown to have a significant impact on patient quality of life, as well as an increased burden on healthcare providers in terms of resource allocation. The cost of triclosan sutures is variable, however the cost of SSI to patients and healthcare providers is sizeable[10-12]. A robust cost-analysis has not been performed, nevertheless, organisations should consider carefully whether they routinely use triclosan coated sutures in light of these positive meta-analysis findings. This review also identified that triclosan coated sutures significantly reduced the risk of SSIs in clean and contaminated surgery, therefore thoughtful consideration should be paid to whether they are routinely used in this patient population. The results demonstrate that triclosan coated sutures may not be as effective in reducing SSI rate in 'clean-

contaminated' and 'dirty' surgery. However, a potential explanation for 'dirty' surgery is the low patient numbers included in this subgroup. This is a potential area of future research given the effectiveness of triclosan coated sutures in 'clean' and 'contaminated' surgery.

Conclusion

This systematic review identified 25 RCTs examining the effect of triclosan in reducing incidence of SSI, compared with non-coated sutures. The subsequent meta-analysis included 11,957 patient and revealed an overall a risk ratio of RR 0.73, (95% CI 0.65 to 0.82) of developing SSI in favour of triclosan coated sutures, thereby demonstrating a statistically significant lower risk of SSI following closure of a surgical wound with triclosan coated sutures. Further analysis has demonstrated that triclosan coated sutures significantly reduced the risk of SSIs in clean and contaminated surgery. This study is in agreement with previous smaller and less robust reviews which have produced comparable results. This is the largest review of RCTs in terms of number of included studies and number of participants from RCTs to demonstrate the clinical effectiveness of triclosan coated sutures. Further detailed cost effectiveness is required to assess the economic benefit of implementing the use of these sutures. The evidence considered in this review suggests that triclosan coated sutures are effective in reducing surgical site infections, the use should in particular be considered in clean and contaminated surgery.

Acknowledgements

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Competing interests

The authors report no competing interests for this study

Ethical Approval

No ethical approval required for this study.

Data Statement

Raw data is available on request by email to the corresponding author.

Author contributions

All authors contributed to the production of this manuscript and meet the ICMJE criteria.

- IA: Conception of review, data collection, analysis, drafted final manuscript
- AB: Data collection, analysis, drafted final manuscript
- SR: Data analysis and revised final manuscript
- WC: Data analysis and revised final manuscript
- ED: Data collection and revision of final manuscript
- NS: Revision of final manuscript
- MR: Conception of idea and revision of final manuscript

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Study	No. of participants	No. of centres	Surgery type	Sutures used	SSI criteria	Duration of follow-up	Routine prophylactic antibiotics?
Arslan 2018	**177**	**1**	**Surgery for pilonidal disease**	**Vicryl vs Vicryl plus**	**CDC criteria**	**30 days**	**Yes**
Baracs 2011	385	7	Elective colorectal surgery	PDS vs PDS Plus	Not stated	30 days	Yes
Chen 2011	241	1	Head and neck surgery	Vicryl vs Vicryl Plus	Local erythema with purulent discharge, wound dehiscence, or skin necrosis	Not stated	Yes
Diener 2014	1185	24	Laparotomy	PDS vs PDS Plus	CDC criteria	30 days	Yes
Ford 2005	147	1	Paediatric general surgery	Vicryl vs Vicryl Plus	Not stated	80 days	No
Galal 2011	450	1	All surgery	Vicryl vs Vicryl Plus	CDC criteria	30 days	Not stated
Ichida 2018	1023	1	Gastroenterologic surgery	Vicryl and PDS II vs Vicryl Plus and PDS Plus	CDC criteria	30 days	Yes
Isik 2011	510	1	Cardiac surgery	Vicryl vs Vicryl Plus	CDC criteria	1 month	Not stated
Justinger 2013	856	1	Laparotomy	PDS II vs PDS II Plus	CDC criteria	2 weeks	Yes
Karip 2016	106	1	Pilonidal sinus excision followed by Karydakis flap repair	Monocryl Plus vs Monocryl	Rash, fever or purulent discharge	2 weeks	Yes
Lin 2018	102	1	Total knee replacement surgery	Vicryl vs Vicryl plus	CDC criteria	30 days	Yes
Mattavelli 2015	300	4	Elective colorectal surgery	Vicryl and PDS vs Vicryl Plus and PDS Plus	CDC criteria	30 days	Yes
Mingmalairak 2009	100	1	Appendectomy	Vicryl vs Vicryl Plus	Not stated	30 days, 6 months and 1 year	Yes
Nakamura 2013	410	1	Elective colorectal surgery	Vicryl vs Vicryl Plus	CDC criteria	30 days	Yes
Rasic 2011	184	1	Elective colorectal cancer surgery	Vicryl vs Vicryl Plus	Not stated	To discharge	Yes
Renko 2017	1633	1	Paediatric surgery	Vicryl and Monocryl and PDS vs Vicryl Plus and Monocryl Plus and PDS Plus	CDC criteria	30 days	In 30%
Roy 2019	110	1	Gastrointestinal surgery	PDS vs PDS plus	CDC criteria	30 days	Yes

Ruiz-Tovar 2015	110	3	Open colorectal surgery with faecal peritonitis	Vicryl vs Vicryl Plus	CDC criteria	60 days	Yes
Seim 2012	328	1	CABG leg wound	Vicryl vs Vicryl Plus	Positive bacterial culture and clinical judgement	4 weeks	Yes
Sprowson 2018	2546	3	Primary THR or TKR	Vicryl vs Vicryl Plus	CDC criteria	30 days	Yes
Tabrizi 2018	320	2	Dental implant surgery	Vicryl vs Vicryl plus	CDC criteria	30 days	Yes
Thimour-Bergstrom 2013	392	1	CABG (+/-AVR, MVR) with saphenous vein graft	Vicryl and Monocryl vs Vicryl Plus and Monocryl Plus	CDC criteria	60 days	Yes
Turtiainen 2012	276	3	Non-emergency lower-limb arterial surgery	Vicryl and Monocryl vs Vicryl Plus and Monocryl Plus	CDC criteria	30 days	Yes
Williams 2011	150	1	Mastectomy	Vicryl and Monocryl vs Vicryl Plus and Monocryl Plus	CDC criteria	6 weeks	If considered at risk
Zhang 2011	101	6	Mastectomy	Chinese silk vs Vicryl Plus	CDC criteria	30 days	Not stated

Table 1: Study characteristics of included RCTs in this review

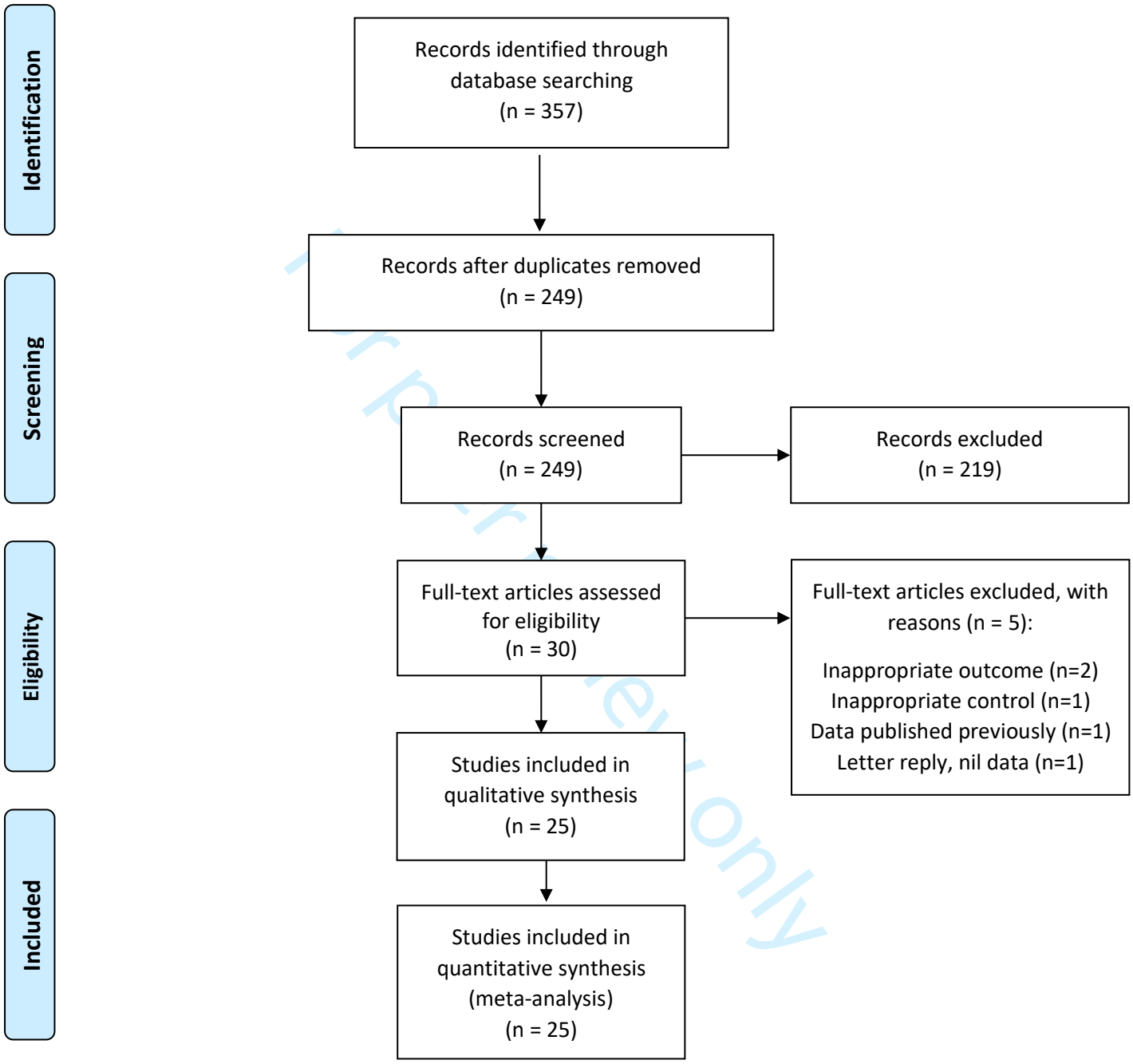
Author	Date	Journal	Number of studies	Number of participants	Findings	Risk of bias	Grade
Wang et al	2013	British Journal of Surgery	17	3720	Triclosan coated sutures significantly reduced SSI rate compared to standard sutures. RR 0.7 (95% CI 0.57, 0.85). Triclosan coated sutures significantly reduced SSI rate in 'clean' and 'clean-contaminated' surgery.	Included	Not included
Edmiston et al	2013	Surgery	13	3568	Triclosan coated sutures significantly reduced SSI rate compared to standard suture. RR 0.734 (95% CI 0.59, 0.91). No subgroup analysis was performed.	Not included	Not included
Daoud et al	2014	Surgical infections	15	4800	Triclosan coated sutures significantly reduced SSI rate compared to standard sutures. RR 0.67 (95% 0.54, 0.84). No subgroup analysis was performed.	Not included	Not included
Apisarnthanarak et al	2015	Infection Control and Hospital Epidemiology	29 (22 RCT and 7 non-RCT)	11942	Triclosan coated sutures significantly reduced SSI rate compared to standard suture. RR 0.65 (95% CI 0.549, 0.769). RR for RCT alone 0.74 (95% CI 0.61, 0.89). Triclosan coated sutures significantly reduced SSI rate for all CDC wound classifications.	Not included	Not included

Guo et al	2015	Journal of Surgical Research	13	5256	Triclosan coated sutures significantly reduced risk of SSI compared to standard suture. RR 0.76 (95% CI 0.65, 0.88). Triclosan coated sutures significantly reduced risk of SSI in abdominal surgery. RR 0.70 (95% CI 0.63, 0.99). There was no significant difference in cardiac and breast surgery.	Included	Not included
Sandini et al	2016	Medicine	6 (only included elective colorectal surgery)	2168	Triclosan coated sutures did not significantly reduce the risk of SSI compared to standard sutures in elective colorectal surgery. OR 0.81 (95% CI 0.58, 1.13)	Included	Not included
Wu et al	2017	European Journal of Microbiology and Infectious Disorders	18 (13 RCTs and 5 non RCTs)	7458	Triclosan coated sutures significantly reduced risk of SSI compared to standard suture in both the RCTs (OR 0.72; 95% CI 0.59, 0.88) and the non- RCTS (OR 0.58; 95% CI 0.40, 0.83). Triclosan coated sutures significantly reduced the risk of SSIS in clean surgery.	Included	Included

De Jonge et al	2017	British Journal of Surgery	21	6462	Triclosan coated sutures significantly reduced risk of SSI compared to standard suture. RR 0.72 (95% CI 0.60, 0.86).	Included	Not included
Leaper et al	2017	British Journal of Surgery	34 (20 RCTs and 14 non-RCTs)	16762	Triclosan coated sutures significantly reduced risk of SSI compared to standard sutures. OR 0.61 (95% CI 0.52, 0.73). No significant difference in SSI rate for 'contaminated' or 'dirty' wounds	Not included	Not included
Konstantelias et al	2017	Acta Chirurgica Belgica 2017	30 (19 RCTs and 11 non-RCTs)	15385	Triclosan coated sutures significantly reduced risk of SSI compared to standard suture. RR 0.68 (95% CI 0.57, 0.81). Triclosan coated sutures significantly reduced risk of SSI in 'clean', 'clean-contaminated' and 'contaminated surgery.'	Not included	Not included
Henriksen et al	2017	Hernia	8 (only included studies reporting abdominal wall closure)	3641	Triclosan coated sutures significantly reduced risk of SSI compared to standard suture in abdominal wall closure. OR 0.67 (95% CI 0.46, 0.98).	Not included	Not included

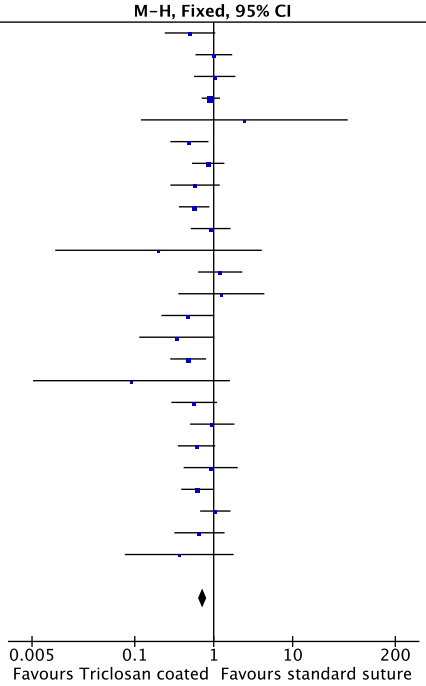
Table 2: A summary of previous systematic reviews on this topic area highlighting number of studies, number of participants and key findings.

Figure 1: PRISMA flow diagram of search results



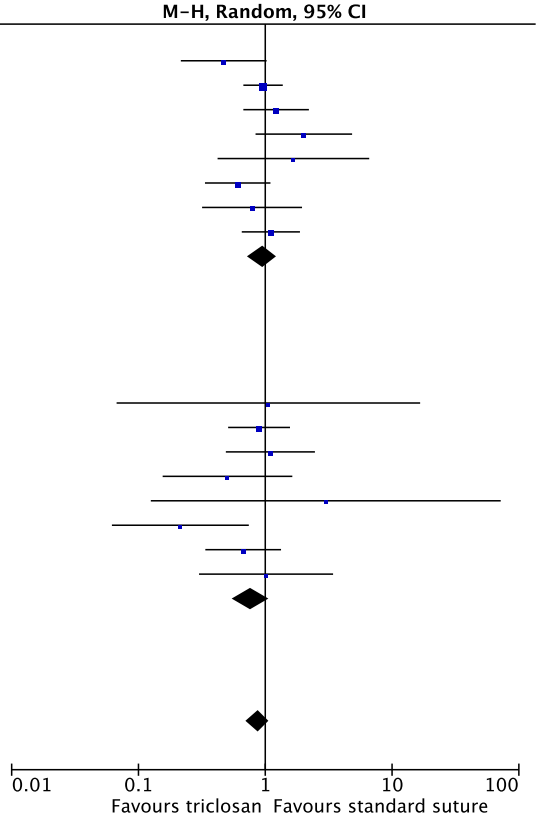
Study or Subgroup	Triclosan coated suture Events	Total	Standard suture Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Arslan 2018	9	86	19	91	3.2%	0.50 [0.24, 1.05]
Baracs 2011	23	188	24	197	4.1%	1.00 [0.59, 1.72]
Chen 2011	17	112	19	129	3.1%	1.03 [0.56, 1.88]
Diener 2014	87	587	96	596	16.5%	0.92 [0.70, 1.20]
Ford 2005	2	91	0	44	0.1%	2.45 [0.12, 49.88]
Galal 2011	17	230	33	220	5.9%	0.49 [0.28, 0.86]
Ichida 2018	30	508	35	505	6.1%	0.85 [0.53, 1.37]
Isik 2011	9	170	31	340	3.6%	0.58 [0.28, 1.19]
Justinger 2013	31	485	42	371	8.3%	0.56 [0.36, 0.88]
Karip 2016	15	52	17	54	2.9%	0.92 [0.51, 1.64]
Lin 2018	0	51	2	51	0.4%	0.20 [0.01, 4.07]
Mattavelli 2015	18	140	15	141	2.6%	1.21 [0.63, 2.30]
Mingmalairak 2009	5	50	4	50	0.7%	1.25 [0.36, 4.38]
Nakamura 2013	9	206	19	204	3.3%	0.47 [0.22, 1.01]
Rasic 2011	4	91	12	93	2.1%	0.34 [0.11, 1.02]
Renko 2017	20	779	42	778	7.3%	0.48 [0.28, 0.80]
Roy 2019	0	55	5	55	1.0%	0.09 [0.01, 1.61]
Ruiz-Tovar 2015	10	50	18	51	3.1%	0.57 [0.29, 1.10]
Seim 2012	16	160	17	163	2.9%	0.96 [0.50, 1.83]
Sprowson 2018	21	1323	32	1223	5.8%	0.61 [0.35, 1.05]
Tabrizi 2018	11	160	12	160	2.1%	0.92 [0.42, 2.02]
Thimour-Bergstrom 2013	23	184	38	190	6.5%	0.63 [0.39, 1.01]
Turtiainen 2012	31	137	30	139	5.2%	1.05 [0.67, 1.63]
Williams 2011	10	66	14	61	2.5%	0.66 [0.32, 1.37]
Zhang 2011	2	47	5	43	0.9%	0.37 [0.07, 1.79]
Total (95% CI)		**6008**		**5949**	**100.0%**	**0.73 [0.65, 0.82]**
Total events	420		581			

Heterogeneity: Chi² = 28.97, df = 24 (P = 0.22); I² = 17%
Test for overall effect: Z = 5.20 (P < 0.00001)

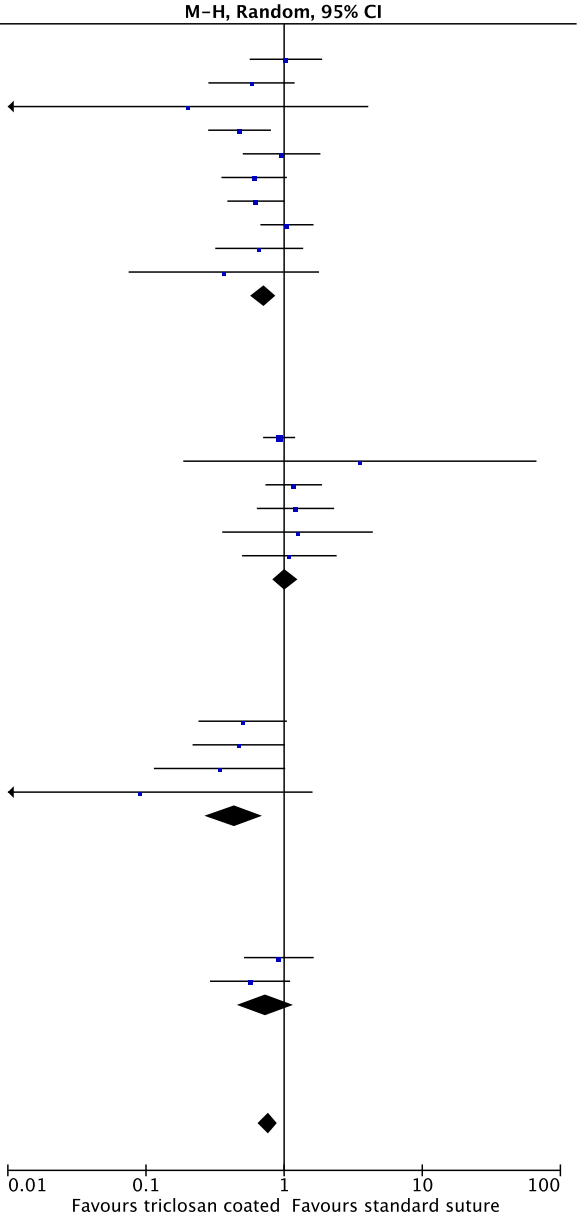


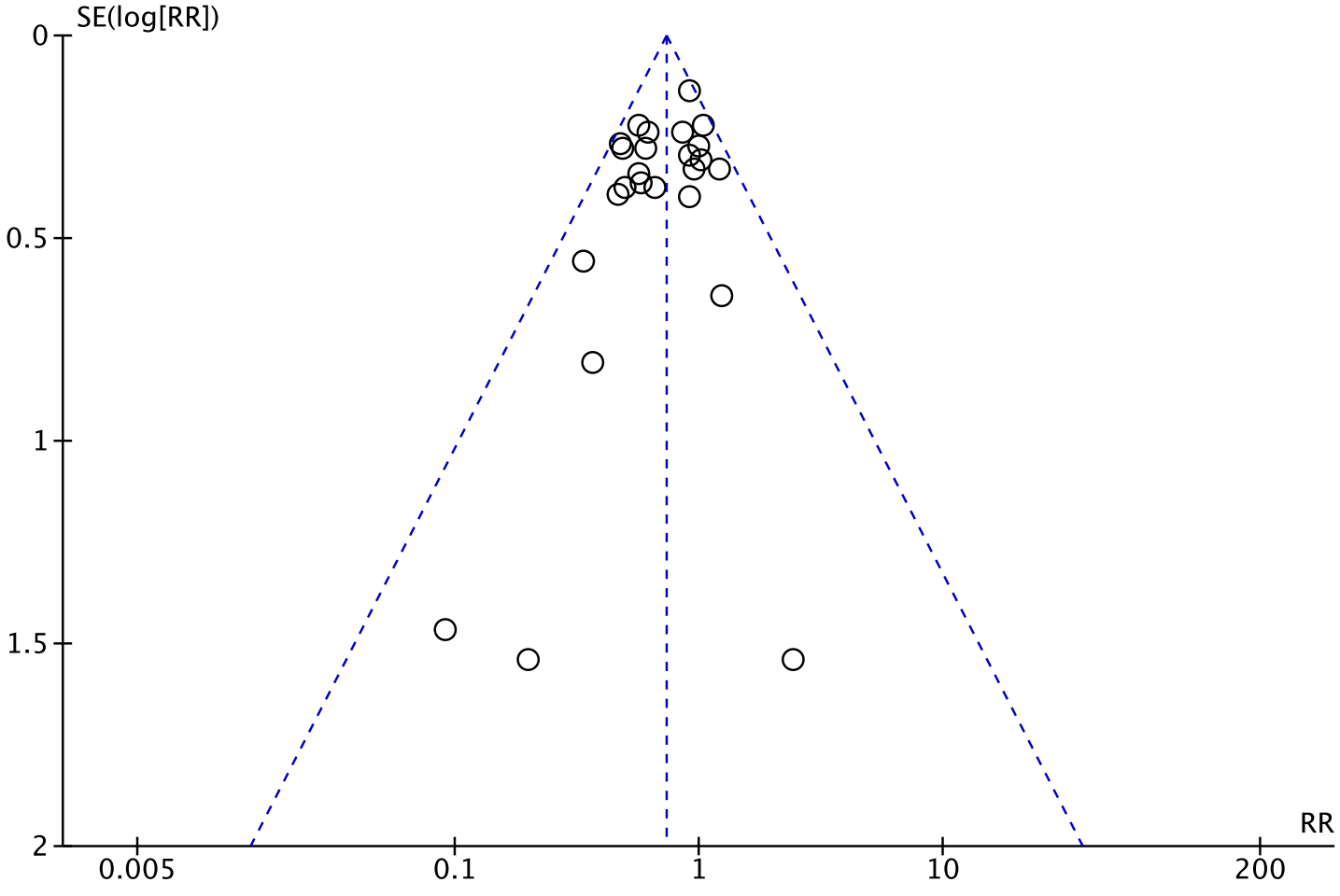
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Study or Subgroup	Triclosan coated suture Events	Total	Standard suture Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.2 Superficial infections						
Arslan 2018	8	86	18	91	6.1%	0.47 [0.22, 1.02]
Diener 2014	53	587	56	596	18.8%	0.96 [0.67, 1.37]
Ichida 2018	23	505	19	508	9.5%	1.22 [0.67, 2.21]
Mattavelli 2015	14	140	7	141	5.0%	2.01 [0.84, 4.84]
Mingmalairak 2009	5	50	3	50	2.2%	1.67 [0.42, 6.60]
Renko 2017	17	779	28	778	9.5%	0.61 [0.33, 1.10]
Sprowson 2018	8	1223	11	1323	4.7%	0.79 [0.32, 1.95]
Turtiainen 2012	24	137	22	139	11.4%	1.11 [0.65, 1.88]
Subtotal (95% CI)		**3507**		**3626**	**67.1%**	**0.95 [0.72, 1.25]**
Total events	152		164			
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 9.95$, df = 7 (P = 0.19); $I^2 = 30\%$						
Test for overall effect: Z = 0.38 (P = 0.70)						
1.2.3 Deep infections						
Arslan 2018	1	86	1	91	0.6%	1.06 [0.07, 16.65]
Diener 2014	22	587	25	596	10.4%	0.89 [0.51, 1.57]
Ichida 2018	12	505	11	508	5.7%	1.10 [0.49, 2.46]
Mattavelli 2015	4	140	8	141	2.9%	0.50 [0.16, 1.63]
Mingmalairak 2009	1	50	0	50	0.4%	3.00 [0.13, 71.92]
Renko 2017	3	779	14	778	2.6%	0.21 [0.06, 0.74]
Sprowson 2018	13	1223	21	1323	7.5%	0.67 [0.34, 1.33]
Turtiainen 2012	5	137	5	139	2.7%	1.01 [0.30, 3.43]
Subtotal (95% CI)		**3507**		**3626**	**32.9%**	**0.77 [0.55, 1.07]**
Total events	61		85			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 6.74$, df = 7 (P = 0.46); $I^2 = 0\%$						
Test for overall effect: Z = 1.58 (P = 0.11)						
Total (95% CI)		**7014**		**7252**	**100.0%**	**0.88 [0.71, 1.08]**
Total events	213		249			
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 17.81$, df = 15 (P = 0.27); $I^2 = 16\%$						
Test for overall effect: Z = 1.20 (P = 0.23)						
Test for subgroup differences: $Chi^2 = 0.95$, df = 1 (P = 0.33), $I^2 = 0\%$						



Study or Subgroup	Triclosan coated Events	Total	Standard suture Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.3.1 Clean surgery						
Chen 2011	17	112	19	129	5.4%	1.03 [0.56, 1.88]
Isik 2011	9	170	31	340	4.1%	0.58 [0.28, 1.19]
Lin 2018	0	51	2	51	0.3%	0.20 [0.01, 4.07]
Renko 2017	20	779	42	778	6.6%	0.48 [0.28, 0.80]
Seim 2012	16	160	17	163	4.9%	0.96 [0.50, 1.83]
Sprowson 2018	21	1323	32	1223	6.3%	0.61 [0.35, 1.05]
Thimour-Bergstrom 2013	23	184	38	190	7.5%	0.63 [0.39, 1.01]
Turtiainen 2012	31	137	30	139	8.2%	1.05 [0.67, 1.63]
Williams 2011	10	66	14	61	4.0%	0.66 [0.32, 1.37]
Zhang 2011	2	47	5	43	1.0%	0.37 [0.07, 1.79]
Subtotal (95% CI)		**3029**		**3117**	**48.3%**	**0.71 [0.58, 0.88]**
Total events	149		230			
Heterogeneity: Tau² = 0.01; Chi² = 9.88, df = 9 (P = 0.36); I² = 9%						
Test for overall effect: Z = 3.16 (P = 0.002)						
1.3.2 Clean-contaminated surgery						
Diener 2014	87	587	96	596	13.6%	0.92 [0.70, 1.20]
Ford 2005	3	98	0	49	0.3%	3.54 [0.19, 67.12]
Ichida 2018	35	505	30	508	7.6%	1.17 [0.73, 1.88]
Mattavelli 2015	18	140	15	141	4.9%	1.21 [0.63, 2.30]
Mingmalairak 2009	5	50	4	50	1.5%	1.25 [0.36, 4.38]
Tabrizi 2018	12	160	11	160	3.5%	1.09 [0.50, 2.40]
Subtotal (95% CI)		**1540**		**1504**	**31.4%**	**1.02 [0.83, 1.25]**
Total events	160		156			
Heterogeneity: Tau² = 0.00; Chi² = 2.00, df = 5 (P = 0.85); I² = 0%						
Test for overall effect: Z = 0.18 (P = 0.86)						
1.3.3 Contaminated						
Arslan 2018	9	86	19	91	4.0%	0.50 [0.24, 1.05]
Nakamura 2013	9	206	19	204	3.7%	0.47 [0.22, 1.01]
Rasic 2011	4	91	12	93	2.0%	0.34 [0.11, 1.02]
Roy 2019	0	55	5	55	0.3%	0.09 [0.01, 1.61]
Subtotal (95% CI)		**438**		**443**	**9.9%**	**0.43 [0.27, 0.70]**
Total events	22		55			
Heterogeneity: Tau² = 0.00; Chi² = 1.55, df = 3 (P = 0.67); I² = 0%						
Test for overall effect: Z = 3.46 (P = 0.0005)						
1.3.4 Dirty surgery						
Karip 2016	15	52	17	54	5.7%	0.92 [0.51, 1.64]
Ruiz-Tovar 2015	10	50	18	51	4.6%	0.57 [0.29, 1.10]
Subtotal (95% CI)		**102**		**105**	**10.3%**	**0.74 [0.46, 1.18]**
Total events	25		35			
Heterogeneity: Tau² = 0.01; Chi² = 1.14, df = 1 (P = 0.29); I² = 12%						
Test for overall effect: Z = 1.25 (P = 0.21)						
Total (95% CI)		**5109**		**5169**	**100.0%**	**0.77 [0.66, 0.91]**
Total events	356		476			
Heterogeneity: Tau² = 0.03; Chi² = 27.52, df = 21 (P = 0.15); I² = 24%						
Test for overall effect: Z = 3.15 (P = 0.002)						
Test for subgroup differences: Chi² = 12.91, df = 3 (P = 0.005), I² = 76.8%						




SE(log[RR])
0
0.5
1
1.5
2
0.005
0.1
1
10
200
RR

Supplementary file 1. Demonstrating the full search strategy and the number of results for each search term. The search was performed on the 31st May 2019.

Database: AMED (Allied and Complementary Medicine) <1985 to May 2019>, Ovid MEDLINE(R) <1946 to May Week 4 2019>, Embase <1974 to 2019 May 30>
Search Strategy:
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1 triclosan.mp. (8754)
2 anti-bacterial agents.mp. (315458)
3 anti-infective agents, local.mp. (16419)
4 coated materials, biocompatible.mp. (13821)
5 biomimtic material.mp. (0)
6 1 or 2 or 3 or 4 or 5 (350648)
7 sutures.mp. (61707)
8 vicryl plus.mp. (129)
9 monocryl plus.mp. (20)
10 PDS plus.mp. (47)
11 7 or 8 or 9 or 10 (61743)
12 surgical site infection.mp. (14995)
13 surgical wound infection.mp. (37378)
14 12 or 13 (48237)
15 6 and 11 and 14 (282)
16 remove duplicates from 15 (233)

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Then CENTRAL search identified 75, and after duplicates removed this was 16 new. So total 249 records screened.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4/5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-9 and table 1
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6/7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6/7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8,9 table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10, Figure 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9,10 Figure 2-5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9,10 Figure 2-5
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10, Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9,10 Figure 2-5
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11, 12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12,13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13, 14

PRISMA 2009 Checklist

FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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