Meta-analysis

Systematic review and meta-analysis of triclosan-coated sutures for the prevention of surgical-site infection

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Background: **Surgical-site infections (SSIs) increase morbidity and mortality in surgical patients and represent an economic burden to healthcare systems. Experiments have shown that triclosan-coated sutures (TCS) are beneficial in the prevention of SSI, although the results from individual randomized controlled trials (RCTs) are inconclusive. A meta-analysis of available RCTs was performed to evaluate the efficacy of TCS in the prevention of SSI.**

Methods: **A systematic search of PubMed, Embase, MEDLINE, Web of Science®, the Cochrane Central Register of Controlled Trials and internet-based trial registries for RCTs comparing the effect of TCS and conventional uncoated sutures on SSIs was conducted until June 2012. The primary outcome investigated was the incidence of SSI. Pooled relative risks with 95 per cent confidence interval (c.i.) were estimated with RevMan 5.1.6.**

Results: **Seventeen RCTs involving 3720 participants were included. No heterogeneity of statistical significance across studies was observed. TCS showed a significant advantage in reducing the rate of SSI by 30 per cent (relative risk 0·70, 95 per cent c.i. 0·57 to 0·85; $P < 0·001$). Subgroup analyses revealed consistent results in favour of TCS in adult patients, abdominal procedures, and clean or clean-contaminated surgical wounds.**

Conclusion: **TCS demonstrated a significant beneficial effect in the prevention of SSI after surgery.**

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Introduction

Surgical-site infections (SSIs) remain a pervasive problem in modern surgery. According to the US Centers for Disease Control and Prevention (CDC), the overall incidence of SSI is estimated as 2·8 per cent in the USA[1], equivalent to 756 000 patients per year. European countries report SSI rates from 1·5 to 20 per cent, owing to the inherent inconsistencies between studies; however, the true rate of SSI is believed to be underestimated, indicating that SSIs represent a significant problem in Europe as well[2]. With its high incidence, SSI places a severe burden on both patients and healthcare systems. SSIs not only lead to a significant increase in morbidity, readmissions, intensive care unit admissions and long-term surgical-site complications, but also result in a greater risk of death in patients having surgical procedures[3]. Furthermore, SSIs challenge healthcare systems by requiring additional hospital bed occupancy, escalated resource costs and increased loss of working hours[2,4,5].

An estimated 40–60 per cent of SSIs are preventable[6]. In spite of the fact that the causes of SSIs are complicated, it is well known that bacterial colonization of suture materials is an important risk factor for the development of SSI[7,8]. Prevention of SSI using sutures impregnated with antimicrobial activity has been attempted. Triclosan, a broad-spectrum antiseptic agent, has been employed to provide sutures with antimicrobial activity. Several products have been introduced into the market, including triclosan-coated polyglactin 910 antimicrobial suture (Vicryl Plus®; Ethicon, Johnson & Johnson, Somerville, New Jersey, USA), triclosan-coated poliglecaprone 25 antimicrobial suture (Monocryl Plus®; Ethicon, Johnson & Johnson) and triclosan-coated polydioxanone antimicrobial suture (PDS Plus®; Ethicon, Johnson & Johnson).

Both *in vitro* and *in vivo* animal experiments have shown that triclosan-coated sutures (TCS) attenuate bacterial colonization[9,10] and exhibit inhibitory activity to a wide

spectrum of pathogens related to SSIs[9–16] without altering the physical properties of sutures, and with no interference with the wound-healing process[17,18]. Several recent clinical trials have also reported results showing a beneficial effect of TCS in the prevention of SSIs[19–24]. Nevertheless, the efficacy of TCS remains unproven and controversial, because several studies[25–29], including a meta-analysis[30], have reported no significant difference in the incidence of SSI between triclosan-coated and uncoated suture groups. However, several recent randomized controlled trials (RCTs)[22–24,27–29,31–36] have been reported since that meta-analysis. The objective of this systematic review was to analyse currently available RCTs comparing the effect of TCS with conventional uncoated sutures on the incidence of SSI following surgical procedures.

Methods

Search strategy

The methodology of this study adhered to the guidelines outlined in the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement[37] (*Fig. 1*). A literature search in PubMed, Embase, MEDLINE, Web of Science®, Cochrane Central Register of Controlled Trials (CENTRAL) databases was carried out with the combination of the following search terms: 'triclosan', 'antimicrobial', 'antiseptic', 'Vicryl Plus', 'Monocryl Plus', 'PDS Plus' and 'suture'. The search was performed by two independent investigators and last updated on 20 June 2012; publication date and publication language were not restricted. Reference lists were examined manually, and internet-based trial registries[38,39] were searched to identify further potentially relevant studies.

Study selection

Studies included in the meta-analysis had to meet all of the following criteria: RCT evaluating the efficacy of TCS in humans; if serial studies of the same population from the same group were retrieved, only the latest report was included. Two investigators identified trials for inclusion independently. If there was any disagreement, a senior investigator was invited for discussion until a consensus was reached.

Risk of bias

Risk of bias and methodological quality of included studies were assessed using the Cochrane Collaboration tool for assessing risk of bias following the principles of the *Cochrane Handbook for Systematic Reviews of Interventions*[40]. Overall risk of bias was determined by the following domains: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; and incomplete outcome data. Studies with all five domains rated as low risk were classified as having a low risk of bias. Studies with any domain assessed as unclear risk or high risk were classified as unclear or high risk of bias respectively. A risk-of-bias table was generated to summarize the results of the assessment.

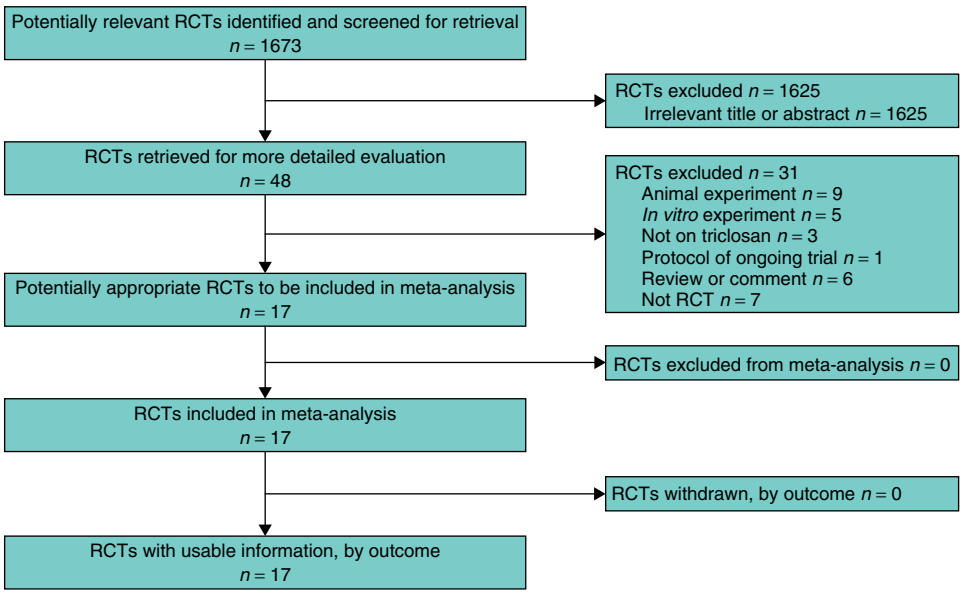

Fig. 1 PRISMA flow diagram for the study. RCT, randomized controlled trial

Table 1 Characteristics of randomized controlled trials involving triclosan-coated sutures

Reference	Year	Sample size		Study design	Blinding	Interventions	Length of follow-up
		TCSs	Control				
Baracs *et al*.[24]	2011	188	197	Multicentre RCT	Double-blinded	PP *versus* P	30 days
DeFazio *et al*.[25]	2005	43	50	Single-centre RCT	Double-blinded	VP *versus* V	6 weeks
Deliaert *et al*.[47]	2009	26	26	Single-centre RCT	Double-blinded	VP *versus* V	4 weeks
Ford *et al*.[48]	2005	98	49	Single-centre RCT	Open-label	VP *versus* V	80 ± 5 days
Galal and El-Hindawy[22]	2011	230	220	Multicentre RCT	Double-blinded	VP *versus* V	30 days*
Isik *et al*.[36]	2012	170	340	Single-centre RCT	Double-blinded	VP *versus* V	1 month
Khachatryan *et al*.[33]	2011	65	68	Single-centre RCT	Open-label	VP *versus* uncoated	NR
Mattavelli *et al*.[34]	2011	108	109	Multicentre RCT	Single-blinded	VP *versus* V	30 days
Mingmalairak *et al*.[26]	2009	50	50	Single-centre RCT	Double-blinded	VP *versus* V	1 year
Rasić *et al*.[23]	2011	91	93	Single-centre RCT	Double-blinded	VP *versus* V	NR
Rozzelle *et al*.[21]	2008	46	38	Single-centre RCT	Double-blinded	VP *versus* V	6 months
Seim *et al*.[28]	2012	160	163	Single-centre RCT	Single-blinded	VP *versus* V	4 weeks
Singh *et al*.[32]	2010	50	50	RCT	Unknown	VP *versus* uncoated	30 days
Turtiainen *et al*.[29]	2012	139	137	Multicentre RCT	Double-blinded	VP/MP *versus* V/M	30 days
Williams *et al*.[35]	2011	66	61	Single-centre RCT	Double-blinded	VP/MP *versus* V/M	6 weeks
Zhang *et al*.[27]	2011	46	43	Multicentre RCT	Open-label	MP *versus* silk	30 days
Zhuang *et al*.[31]	2009	150	300	Single-centre RCT	Unknown	VP *versus* P/silk	12–24 months

*One year for prosthetic surgery. TCS, triclosan-coated suture; RCT, randomized controlled trial; NR, not reported. PP, PDS Plus®; P, PDS®; VP, Vicryl Plus®; V, Vicryl®; MP, Monocryl Plus®; M, Monocryl® (all from Ethicon, Johnson & Johnson, Somerville, New Jersey, USA).

Data abstraction

Two investigators independently extracted data from the included trials. Characteristics of eligible studies were extracted, including publication date, publication status, demographic characteristics of participants, interventions of trials, sample size of intervention groups, study design, surgery type, traditional classification of incision and follow-up period. Outcome data were extracted as events per total number at risk in both the experimental and control arms. The two investigators cross-checked the data abstraction results and reached a consensus on all extracted data. If different results were generated, they would check the data and have a discussion to arrive at a consensus. A senior investigator would be invited to the discussion if disagreement still existed. Missing data were obtained by contacting the corresponding author or by adopting the data as reported in the previous systematic review[30].

Primary outcome endpoint of the meta-analysis and subgroup analyses

The primary outcome investigated was the incidence of SSI. All studies with eligible data were pooled to achieve an overall estimation of the effect of TCS on the incidence of SSIs compared with uncoated sutures.

To verify further the result of overall estimation in more specified populations with relatively uniform background, the following subgroup analyses stratified by characteristics of participants and interventions were performed: age of participants, wound contamination classified by traditional incision classification, and surgery type. Comparisons exclusively between Vicryl Plus® and Vicryl® were also analysed to determine whether triclosan enhanced the antimicrobial property of Vicryl®, which represents one of the most frequently used suture materials worldwide.

According to the CDC, SSIs are defined as infections occurring within 30 days after surgical procedures (or within 1 year if an implant is left in place after the procedure)[41]. Therefore, studies were further stratified by follow-up period within 1 month or longer than 1 month to investigate whether the length of follow-up of individual trials influenced the assessment of SSI. In addition, subgroup analyses by risk of bias and publication status were conducted to evaluate further the credibility and stability of this meta-analysis.

Publication bias

Publication bias of the literature was assessed using funnel plots. An asymmetrical plot suggested possible publication bias.

Statistical analysis

Quantitative data synthesis was performed using RevMan 5.1.6[42]. The existence of statistical heterogeneity among the studies was checked with the χ^2-based Q test. $P > 0{\cdot}100$ for Q test indicated that no significant heterogeneity existed among studies[43]. If no significant heterogeneity was detected, the pooled relative risks

(RRs) with corresponding 95 per cent confidence interval (c.i.) were estimated by the fixed-effects model (Mantel–Haenszel method)[44]. Otherwise, the random-effects model (DerSimonian–Laird method) was employed to generate pooled RRs[45]. The amount of heterogeneity was measured by the I^2 statistic[46]. An I^2 value of less than 25 per cent was defined as low heterogeneity; I^2 between 25 and 50 per cent was considered representative of moderate heterogeneity; and I^2 greater than 50 per cent represented high heterogeneity. The significance of pooled RRs was determined by the Z test, and $P < 0{\cdot}050$ was considered statistically significant. Forest plots were generated to summarize the results of individual meta-analyses.

Sensitivity analysis was carried out by deleting one study each time to examine the influence of individual data sets on the pooled RRs.

Results

Of 1673 citations identified from the database search and other sources, 17 eligible RCTs involving a total of 3720 participants were included in the meta-analysis. The flow diagram of study identification is shown in *Fig. 1*.

The sample size of included RCTs ranged from 52 to 510 participants; 1726 participants were randomized to the TCS group and 1994 to the uncoated sutures group, with follow-up periods varying from 4 weeks to 24 months. The TCS examined included Vicryl Plus®, Monocryl Plus® and PDS Plus®. Detailed characteristics of the included studies are shown in *Table 1*.

The qualities and risks of bias of the included RCTs are summarized in *Table 2*. Three trials were considered as 'high quality and low risk of bias', and six were classified as 'low quality and high risk of bias'. Owing to insufficient information regarding detailed study design and lack of evidence to prove the existence of risk of bias, the remaining eight RCTs were classified as 'moderate quality and unclear risk of bias'. Overall, the qualities of the included studies were acceptable with moderate risk of bias.

Effect of triclosan-coated *versus* uncoated sutures on surgical-site infections

Seventeen trials reported the incidence of SSIs in TCS and control groups[21–29,31–36,47,48]. Meta-analysis of these RCTs favoured TCS with a pooled RR of 0·70 (95 per cent c.i. 0·57 to 0·85; $P < 0{\cdot}001$) without statistical heterogeneity (P for Q test = 0·129, $I^2 = 29$ per cent), indicating that the use of TCS resulted in a significant reduction in the incidence of SSI (*Fig. 2*). Sensitivity analysis reflected that no individual data set significantly altered heterogeneity and the pooled RR of SSI, suggesting that the results from this meta-analysis were stable.

Subgroup analyses

In subgroup analyses stratified by characteristics of participants and interventions, the beneficial effect of TCS on the prevention of SSI was consistently significant in adult patients, abdominal surgery, and clean or

Table 2 Risk of bias summary

Reference	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Baracs *et al.*[24]	+	?	?	?	−	+	+
DeFazio *et al.*[25]	?	+	+	+	?	+	−
Deliaert *et al.*[47]	?	+	+	+	+	−	+
Ford *et al.*[48]	?	?	−	−	−	+	+
Galal and El-Hindawy[22]	+	+	+	+	+	+	+
Isik *et al.*[36]	?	?	?	?	+	?	+
Khachatryan *et al.*[33]	?	?	−	−	?	?	?
Mattavelli *et al.*[34]	?	?	−	−	?	?	?
Mingmalairak *et al.*[26]	+	+	+	+	+	?	+
Rasić *et al.*[23]	+	+	?	?	+	?	?
Rozzelle *et al.*[21]	?	+	+	+	+	+	+
Seim *et al.*[28]	?	+	−	−	+	+	+
Singh *et al.*[32]	?	?	?	?	?	?	?
Turtiainen *et al.*[29]	?	+	+	+	+	+	+
Williams *et al.*[35]	+	+	+	+	+	−	+
Zhang *et al.*[27]	+	+	−	−	+	+	−
Zhuang *et al.*[31]	?	?	?	+	+	?	?

+, Low risk; ?, unclear risk; −, high risk.

Reference	SSI: Triclosan	SSI: Control	Weight (%)	Relative risk
Baracs *et al.*[24]	23 of 188	24 of 197	10·8	1·00 (0·59, 1·72)
DeFazio *et al.*[25]	4 of 43	4 of 50	1·7	1·16 (0·31, 4·37)
Deliaert *et al.*[47]	0 of 26	0 of 26		Not estimable
Ford *et al.*[48]	3 of 98	0 of 49	0·3	3·54 (0·19, 67·12)
Galal and El-Hindawy *et al.*[22]	17 of 230	33 of 220	15·5	0·49 (0·28, 0·86)
Isik *et al.*[36]	9 of 170	19 of 340	5·8	0·95 (0·44, 2·05)
Khachatryan *et al.*[33]	6 of 65	14 of 68	6·3	0·45 (0·18, 1·10)
Mattavelli *et al.*[34]	11 of 108	12 of 109	5·5	0·93 (0·43, 2·01)
Mingmalairak *et al.*[26]	5 of 50	4 of 50	1·8	1·25 (0·36, 4·38)
Rasić *et al.*[23]	4 of 91	12 of 93	5·5	0·34 (0·11, 1·02)
Rozzelle *et al.*[21]	2 of 46	8 of 38	4·0	0·21 (0·05, 0·92)
Seim *et al.*[28]	16 of 160	17 of 163	7·7	0·96 (0·50, 1·83)
Singh *et al.*[32]	6 of 50	16 of 50	7·4	0·38 (0·16, 0·88)
Turtiainen *et al.*[29]	31 of 139	30 of 137	13·9	1·02 (0·65, 1·59)
Williams *et al.*[35]	10 of 66	14 of 61	6·7	0·66 (0·32, 1·37)
Zhang *et al.*[27]	2 of 46	5 of 43	2·4	0·37 (0·08, 1·83)
Zhuang *et al.*[31]	0 of 150	15 of 300	4·8	0·06 (0·00, 1·07)
Total	149 of 1726	227 of 1994	100	0·70 (0·57, 0·85)

Heterogeneity: $\chi^2 = 21{\cdot}26$, 15 d.f., $P = 0{\cdot}129$; $I^2 = 29\%$
Test for overall effect: $Z = 3{\cdot}61$, $P < 0{\cdot}001$

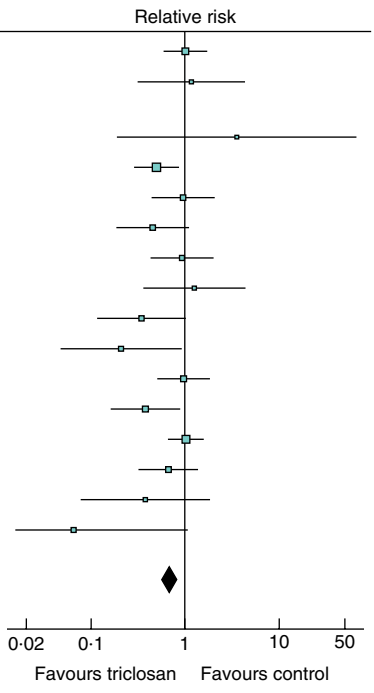

Fig. 2 Forest plot for meta-analysis comparing the incidence of surgical-site infection (SSI) in triclosan-coated and uncoated (control) suture groups. A Mantel–Haenszel fixed-effects model was used for meta-analysis. Relative risk values are shown with 95 per cent confidence intervals

Table 3 Summary of subgroup analysis

	No. of studies	No. of participants	Surgical-site infection: TCSs	Surgical-site infection: Control	Relative risk	*P**	*P* for *Q* test†	I^2 (%)
Overall	17	3720	149 of 1726	227 of 1994	0·70 (0·57, 0·85)	< 0·001	0·129	29
Age group								
Adult	15	3489	144 of 1582	219 of 1907	0·71 (0·58, 0·87)	< 0·001	0·185	25
Paediatric	2	231	5 of 144	8 of 87	0·64 (0·04, 10·1)	0·749	0·087	66
Contamination								
Clean	9	1797	80 of 820	117 of 977	0·73 (0·56, 0·95)	0·021	0·219	26
Clean-contaminated	6	1146	53 of 566	79 of 580	0·69 (0·50, 0·96)	0·026	0·349	10
Contaminated/dirty	2	87	8 of 42	12 of 45	1·10 (0·14, 8·43)	0·928	0·065	71
Type of surgery								
Abdominal	7	1562	53 of 695	85 of 867	0·69 (0·50, 0·97)	0·030	0·169	34
Breast	3	268	12 of 138	19 of 130	0·59 (0·30, 1·14)	0·114	0·522	0
Cardiac	3	933	31 of 380	52 of 553	0·75 (0·49, 1·14)	0·180	0·178	42
Follow-up (months)								
1	9	2402	115 of 1117	156 of 1285	0·79 (0·63, 0·99)	0·037	0·230	25
> 1	6	1001	24 of 453	45 of 548	0·56 (0·35, 0·92)	0·021	0·136	40
Risk of bias								
Low	3	677	32 of 346	51 of 331	0·60 (0·39, 0·90)	0·015	0·395	0
Unclear	8	1749	56 of 715	104 of 1034	0·57 (0·32, 1·00)	0·051	0·034	56
High	6	1294	61 of 665	72 of 629	0·85 (0·62, 1·18)	0·332	0·487	0
Publication status								
Full-length	13	3177	122 of 1460	181 of 1717	0·72 (0·58, 0·90)	0·003	0·116	34
Abstract	4	543	27 of 266	46 of 277	0·61 (0·39, 0·94)	0·026	0·292	20
Vicryl Plus® *versus* Vicryl®	10	2160	71 of 1022	109 of 1138	0·70 (0·53, 0·94)	0·016	0·243	22

Values in parentheses are 95 per cent confidence intervals. TCS, triclosan-coated suture. *Z test; †χ^2 test.

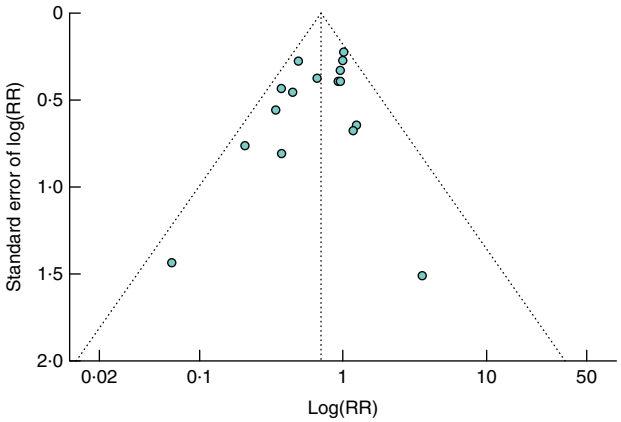

Fig. 3 Funnel plot for the evaluation of publication bias. RR, relative risk. A symmetrical funnel plot suggests no obvious publication bias

clean-contaminated incisions (*Table 3*). This advantageous effect was not observed for paediatric patients, contaminated/dirty incisions, breast surgery or cardiac surgery.

For RCTs that exclusively studied the efficacy of Vicryl Plus® *versus* Vicryl®, pooled estimation favoured Vicryl Plus® (RR 0·70, 95 per cent c.i. 0·53 to 0·94; $P = 0·016$). Moreover, the advantage of TCS over conventional sutures was consistent regardless of length of follow-up.

In analysis stratified by risk of bias, significant statistical heterogeneity was detected in the subgroup of trials with an unclear risk of bias. The superiority of TCS was significant in low-risk studies (RR 0·60, 0·39 to 0·90; $P = 0·015$), whereas studies with unclear risk showed a trend towards a reduced incidence of SSI in the TCS group with a marginal P value of 0·051 (RR 0·57, 0·32 to 1·00). The estimation of studies with a high risk of bias failed to find an advantage for TCS over uncoated sutures (RR 0·85, 0·62 to 1·18; $P = 0·332$). Furthermore, subgroup analysis carried out in studies published as full-length articles or conference abstracts was consistent with the overall estimation.

Publication bias

The distribution of studies in funnel plot was symmetrical. No evidence for a significant publication bias in this meta-analysis was found (*Fig. 3*).

Discussion

This systematic review and meta-analysis found that use of TCS resulted in a 30 per cent reduction in the risk of SSI, especially in adult patients, abdominal procedures, and clean or clean-contaminated incisions. TCS may be favourable in clinical application to reduce the incidence of SSI and the additional medical costs associated with SSIs.

Suture materials play an important role in the development of SSI by providing a local surface for the adherence of microorganisms[49]. Once pathogens have colonized suture materials, a biofilm may subsequently be formed to promote the attachment and reinforce the resistance against attack from the host's immune system and antimicrobial treatment, thus predisposing the wound to infection[50–52]. Accordingly, the strategy of coating sutures with antimicrobial agents, such as silver or antibiotics, to reduce the risk of suture-related SSI has been considered since the 1950s[53–55]. Triclosan, a broad-spectrum antiseptic with an established safety profile, has been used widely in pharmaceutical and hygiene products for human use for over 30 years[56,57]. Recently, TCS materials with antimicrobial activity have been developed to counter the challenge from SSIs.

Following the promising results from *in vitro* and *in vivo* experiments, various clinical trials have demonstrated the advantage of TCS over conventional uncoated sutures in the prevention of SSI. However, results from individual RCTs have been inconclusive and controversial, indicating that the limited sample size of individual RCTs may be underpowered to detect the true effect of TCS. According to calculations, demonstration of a statistically significant difference between TCS and control groups in SSI rates at 2 and 6 weeks after breast surgery would require approximately 13 and three times respectively the number of participants actually randomized in the same trial[35]. Meta-analysis may indeed be helpful in such circumstances as it involves the quantitative synthesis of data from multiple RCTs, thereby providing a more comprehensive estimation with greater statistical power[58]. With data from 3720 surgical patients, this systematic review confirmed the beneficial effect of TCS in SSI prevention.

Application of TCS may have a significant impact on current clinical practice by reducing not only morbidity and risk of death in surgical patients, but also overall indirect costs[59,60]. Previous reports have demonstrated considerable economic loss incurred by SSIs[60,61]. With only a small additional expense, TCS could significantly decrease both the risk of readmission and the length of hospital stay, and subsequently reduce excess costs on medical systems[19,61]. The results of this systematic review justify the routine use of TCS, especially in adult patients, abdominal procedures, and clean or clean-contaminated incisions.

The conclusion of the present meta-analysis is different from that of a previous meta-analysis on the subject[30]. The other study included seven RCTs and found no benefit for

the use of TCS. However, most of the studies analysed were of low quality and high heterogeneity. The limited number of trials also prevented the authors from exploring further the potential effect of TCS in specific populations. In contrast, the present systematic review and meta-analysis provided updated comprehensive estimation of the efficacy of TCS with latest evidence from currently available RCTs. Ten newly published studies[22,23,28,29,31–36] and updated data from two other trials[24,27] have expanded the total sample size from 836 to 3720, significantly improving the power of this meta-analysis. The quality of trials also improved from one with low risk, three with unclear risk and three with high risk, to three studies with low risk, eight with unclear risk and six with high risk. In the present meta-analysis, subgroup analysis revealed a progressive trend of statistical significance in accordance with the improvement of study quality, which may at least partly explain the competing conclusion with the previous study[30] and again emphasizes the importance of methodological quality of RCTs. Moreover, the 17 studies included in this meta-analysis could be categorized by similar clinical settings, thus enabling the authors to improve the problem of heterogeneity by subgroup analyses. Results confirmed by subgroup analyses should be more reliable and more informative, because they describe the efficacy of TCS in a similar clinical situation with more uniform background and less clinical heterogeneity. Importantly, multiple subgroup analyses on quality of study design and potential risk of bias were conducted in this systematic review, and the consistent results further confirm the stability and reliability of the results of the present meta-analysis.

Of note, caution should be exercised when interpreting the results owing to some limitations of this systematic review and meta-analysis. First, the quality of included trials is still not fully satisfactory. As the reliability of a meta-analysis is determined largely by the quality of included trials, the results of this meta-analysis should be interpreted cautiously. Further well designed RCTs of high methodological quality are needed. Second, postoperative SSI is a clinical diagnosis that is highly dependent on assessors. Only five of the trials[22,27,29,35,36] clearly defined the diagnostic criteria for SSI developed by the CDC[62], whereas the remaining studies did not adhere to these criteria. This may introduce clinical heterogeneity, so that potential bias cannot be ruled out. Moreover, although all of the included studies reported the incidence of SSI following surgical procedures as an endpoint, three did not use SSI as the primary outcome[27,47,48]. Heterogeneity of outcome reporting could bring potential bias and may distort the data from these trials. Third, the trials included in this meta-analysis were conducted in different settings of participants and for varying surgical procedures. The results should be interpreted with caution and specified clinical scenarios should be considered. Finally, insufficient individual patient data prevented the authors from conducting a meta-analysis based on detailed individual information. Stratification by risk factors for SSI such as diabetes, steroids and smoking was also not possible owing to lack of available data. These factors could influence the estimation by interacting with the effect of TCS.

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