TITLE: Antibacterial Sutures for Wound Closure After Surgery: A Review of Clinical and Cost-Effectiveness and Guidelines for Use

DATE: 21 November 2014

CONTEXT AND POLICY ISSUES

Surgical site infections (SSIs) account for approximately 20% of all compromised wounds in the Canadian healthcare setting.[1] It is estimated that 6.3% of surgical wounds in Canada result in infection.[2] An overall SSI rate of 2.5% was reported in a sample of hospitalized adults across Canada.[3] In addition to increasing the risk of morbidity, delayed recovery, and prolonged hospital stay,[4] SSIs may increase Canadian healthcare costs associated with surgical procedures.[5] It is estimated that the incidence of SSIs could be reduced by over 50% with the implementation of various evidence-based prevention strategies.[6] Risk factors for SSIs include patient related factors (e.g., diabetes, obesity), category of wound (e.g., clean, clean-contaminated), bacterial species, and hospital-related infection prevention measures.[7] Sutures may act as a medium for bacterial growth and it has been demonstrated by in-vitro[8] and in-vivo animal studies[9] that antimicrobial coating may reduce the risk of SSIs. Antimicrobial sutures, which are currently commercially limited to triclosan coated sutures (TCS) (e.g., Vicryl [polyglactin 910] Plus, Monocryl [poliglecaprone 25] Plus, PDS [polydioxanone] Plus), are targeted for the prevention of SSIs. Although antimicrobial sutures are more costly than conventional sutures,[10] if effective for SSI prevention they may reduce surgery related costs. The reported clinical efficacy of antimicrobial sutures is inconsistent, with some systematic reviews reporting an overall benefit,[11] while others do not.[12] A previous CADTH report summarized evidence suggesting that TCS reduced SSIs compared to non-coated sutures.[13] This report will provide an update and augment a recent CADTH Rapid Response reference list.[14]

RESEARCH QUESTIONS

1. What is the clinical effectiveness of antibacterial sutures for the prevention of surgical site infections?

2. What are the adverse events associated with antibacterial suture use, including the development of drug-resistant bacteria?

3. What are the guidelines for using antibacterial sutures for wound closure?

4. What is the cost-effectiveness of using antibacterial sutures for wound closure?

KEY FINDINGS

Clinical evidence of varying quality suggests that the use of antimicrobial sutures reduces SSI incidence compared to non-antimicrobial sutures, and evidence from one non-Canadian economic evaluation suggests that antimicrobial sutures are cost-effective from healthcare, payer, and societal perspectives for prevention of SSIs. No relevant literature was available on adverse events (including development of drug-resistant bacteria), or guidelines for using antimicrobial sutures for wound closure.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 10), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between April 1, 2014 and October 24, 2014. Additional references were drawn from a previous report on the same topic, including English language documents published between April 1, 2013 and April 1, 2014.

Selection Criteria and Methods

One reviewer screened citations and a second reviewer selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults undergoing surgery Subgroups: Colorectal surgery
Intervention	Antimicrobial or antibacterial sutures
Comparator	Non-antimicrobial/antibacterial sutures
Outcomes	Q1: Surgical site infections Q2: Adverse events/harms Q3: Guidelines Q4: Cost-Effectiveness
Study Designs	Heath technology assessment reports, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, evidence based guidelines.

Exclusion Criteria

Studies were excluded if they did not satisfy the selection criteria, if they were duplicate publications, or if they were published prior to 2013.

Health technology assessments, meta-analyses, systematic reviews, non-randomized studies and evidence-based guidelines were excluded if there was incomplete reporting of methods or if they were superseded by a more recent, rigorous, or updated review or guideline. Randomized controlled trials (RCTs) were excluded if they were described in a systematic review included in this report. Economic evaluations that reported costs and were not cost-effectiveness or cost-utility analyses were also excluded. Articles were excluded if there were duplicate publications of the same study.

Critical Appraisal of Individual Studies

Key methodological aspects relevant to each study design were appraised. Systematic review appraisal followed the AMSTAR checklist[15] and the methods used when conducting the literature search, study selection, quality assessment, data extraction, and for summarizing the data were appraised. For non-randomized studies, the Downs and Black checklist[16] was followed. Appropriateness and comparability of cases and controls, blinding, recruitment time-frames, losses to follow-up, consideration of confounders, and completeness of reporting were appraised.[16] For economic evaluations, Drummond's checklist[17] was used to appraise study design, data collection, and analysis and interpretation of results. For each type of study, numeric scores were not calculated, instead the individual strengths and limitations were described narratively.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 155 citations were identified in the literature search. Following screening of titles and abstracts, 142 citations were excluded and 13 potentially relevant reports from the electronic search were retrieved for full-text review. One potentially relevant publication was retrieved from the grey literature search. Of these 14 potentially relevant articles, five publications were excluded for various reasons, while nine publications met the inclusion criteria and were included in this report. One included systematic review and meta-analysis[18] was assessed within the earlier CADTH report.[13] The study selection process is detailed in the PRISMA flowchart (Appendix 1).

Summary of Study Characteristics

Systematic Reviews and Meta-Analyses

Four systematic reviews[18-21], and four non-randomized studies[10,22-24] regarding the clinical effectiveness of antimicrobial sutures were retrieved and study details are described in Table A1 and A2 in Appendix 2. No relevant evidence-based guidelines were identified.

There was a substantial degree of overlap among the four systematic reviews. Of 23 single RCTs, fourteen appeared in at least two of the four reviews. Nine RCTs were unique to a single

review; six contained within the Wang et al.[18] review and one in each of the other three reviews.[19-21] Only one RCT[25] was contained within all four reviews. These differences were partially attributed to search date ranges and varying inclusion criteria (e.g. only abdominal surgery RCTs included in the Diener et al.[20] study).

The systematic review and meta-analysis by Daoud et al.,[19] included 15 RCTs comparing various TCS to various non-antimicrobial sutures. The primary endpoint of interest was incidence of SSIs, defined by United States Centers for Disease Control and Prevention (CDC) (Appendix 3) or alternate criteria. Sub-group analyses were conducted for mode of blinding, CDC incision class, and operation type. The included trials were published between 2005 and 2013. Twelve studies were multicentre and three were single centre trials. Nine studies were double blinded, two were assessor blind, and four were open-label. Sample sizes ranged from 61 to 856, for a total of 4800 patients; 2323 randomized to treatment and 2477 randomized to control. Length of follow-up ranged from 14 days to 14 months. Thirteen studies included adult populations, one included children, and one included both. Studies focused on general, shunt implant, appendectomy, abdominal, breast, colorectal, vein harvesting, and cardiac surgeries. All four CDC classes of surgical wounds were included.

The systematic review and meta-analysis by Diener et al.,[20] included five RCTs comparing various TCS to various non-antimicrobial sutures. The primary endpoint of interest was incidence of SSIs. Subgroup analysis of all trials excluding the PROUD study was conducted. The included trials were published between 2011 and 2014. The study included two multicentre and three single centre trials. Method of blinding was not reported. Sample sizes ranged from 184 to 1185 for a total of 3020 patients; 1557 randomized to treatment and 1463 randomized to control. Length of follow-up was not reported. Only studies focused on abdominal surgery were included. All four CDC classes of surgical wounds were assessed.

The systematic review and meta-analysis conducted by Sajid et al.,[21] included seven RCTs comparing various TCS to various non-antimicrobial sutures. The primary endpoint of interest was incidence of SSIs. Sub-group analysis was not conducted. The included trials were published between 2005 and 2011. Some form of blinding was used in five of seven studies. Sample sizes ranged from 93 to 510 for a total of 1631 patients; 760 randomized to treatment and 871 randomized to control. Length of follow-up ranged from 30 days to 12 months, and was not recorded for one study. One trial was in children and the remaining six were in adults. Studies were not restricted by type of surgery. All four CDC classes of surgical wounds were included.

The systematic review and meta-analysis conducted by Wang et al.,[18] included 17 RCTs comparing various TCS to various non-antimicrobial sutures. The primary endpoint of interest was incidence of SSIs. Sub-group analyses were conducted for age, wound classification, surgery type, follow-up period, risk of bias, publication status, and brand of suture. The included trials were published between 2005 and 2012. The study included five multicentre, 11 single centre trials, and one trial with unspecified design. Sample sizes ranged from 52 to 450 for a total of 3720 patients, 1726 randomized to treatment and 1994 randomized to control. Length of follow-up ranged from 30 days to two years. Fifteen RCTs were conducted in adults and two were conducted in children. All four CDC classes of surgical wounds were included.

Non-Randomized Studies

The four observational studies [10,22-24] were published between 2013 and 2014. These studies compared various TCS to various non-antimicrobial sutures. The primary endpoint for all studies was incidence of SSIs or wound infection. These studies included patients undergoing pancreaticoduodenectomy[23], colorectal disease surgery[22], gastrointestinal surgery[10], and spinal cord surgery[24]. Follow-up was unreported or 30 days post-surgery.

Economic Evaluation

One economic evaluation[26] was retrieved and study characteristics are described in Appendix 4.

The economic evaluation[26] was conducted in the United States (US) using cost-effectiveness analyses from a hospital, third party payer, and societal perspective. A decision analytic model constructed in TreeAge Pro 2013 and Monte Carlo probabilistic sensitivity analysis were used to compare the cost per SSI prevented of TCS compared to standard non-antimicrobial sutures. The report focused only on abdominal surgeries of unclear wound classification. Data was sourced from public databases, expert opinion, and published resources. The amount of suture used was assumed to be four times the incision length and cost varied depending on whether SSIs were superficial or deep. Exposure to all pathogens was assumed to cause equal risk of SSI. In addition, a 40 hour work week was assumed for productivity losses that did not consider surgical recovery period. Evaluation of consistency of model inputs with current costs, efficacy estimates, and SSI risk was not within the scope of this project.

Summary of Critical Appraisal

Systematic Reviews and Meta-Analyses

Study strengths and limitations are presented in Appendix 5.

All systematic reviews and meta-analyses[18-21] included a comprehensive literature search of multiple bibliographic databases and hand-searching of reference lists of retrieved reports. A priori objectives were stated in all but one review.[20] All reviews assessed included trials for heterogeneity.

The systematic review and meta-analysis by Daoud et al.,[19] was well designed and well conducted with some reporting deficiencies. The authors referred to an earlier review[11] for most of their methods. Clinical trial registries were searched and no search restrictions based on language or date were imposed. The number of authors involved in screening and abstraction was unclear. A full list of included studies including descriptive characteristics was provided. A list of excluded studies was not provided but it was reported that studies were excluded on the basis of lacking peer review or randomization and if only reported as an abstract. Quality was assessed by evaluating concordance with eligibility criteria, using the concentration of evidence criteria proposed by the Centre for Evidence-Based Medicine at the University of Oxford, and applying the Cochrane Collaboration criteria for quality and low risk of bias. However, the results of this assessment were only discussed briefly in the results and outcome data for individual studies was not available in text. The authors considered scientific quality in the formulation of their conclusions. Publication bias was assessed and presented visually and statistically. No external funding was declared, though the review this update was based on had been funded by

Ethicon, a manufacturer of TCS and non-antimicrobial sutures.[11] At the trial level, SSI diagnostic methods and incision class were not universally reported. Authors contacted for verification or request of information were not universally responsive. There was substantial overlap among the reviews (14 common studies included in at least two of the four reviews), which should be considered in perceiving the overall strength and quantity of evidence available.

The systematic review and meta-analysis by Diener et al.,[20] was conducted as a secondary analysis of an RCT and both the primary study and subsequent review were published in the same report. It wasn't clear whether the meta-analysis was planned a priori. In general, the methodology and results were underreported as the focus appeared to be on the primary RCT. Grey literature searching was limited (i.e., the authors only reported cross-searching of reference lists of retrieved reports). No filters were applied based on publication status. The number of authors involved in screening and abstraction was unclear. A list of included studies was provided and characteristics were discussed in text. Characteristics of excluded studies were not discussed or reported. Risk of bias assessment was not completed and no discussion of study quality could be identified. Publication bias was not assessed or discussed. Funding was provided by Johnson and Johnson, who own Ethicon, a manufacturer of TCS and non-antimicrobial sutures.

The systematic review and meta-analysis conducted by Sajid et al.,[21] was well designed and conducted. Two authors and a third arbitrator were involved in screening; it was unclear how many authors participated in data abstraction. A search filter to exclude non-randomized trials was applied during the search. No grey literature search was described. A list of included studies was provided and characteristics were discussed in text. Characteristics of excluded studies were not reported but reason for exclusion was listed in the PRIMSA flow diagram. Risk of bias assessment used the criteria of 'lack of adequate randomisation and intention to treat analysis' to represent high risk of bias. They also conducted further quality assessment based on randomization technique, allocation concealment, power calculations, blinding, and intention-to-treat analysis. The strength of evidence was assessed using GRADE criteria. Publication bias was not assessed or discussed. Funding sources were not declared.

The systematic review and meta-analysis by Wang et al.,[18] was well designed and conducted. Study selection was conducted independently by two authors and a third was consulted to resolve uncertainty. Data abstraction was completed independently by two authors who cross-checked for consistency and resolved differences by discussion. Clinical trial registries were searched but no further grey literature searching was completed. No restrictions were imposed based on status of publication. A full list of studies and respective characteristics was provided. Characteristics of excluded studies were not reported but reason for exclusion was listed in the PRIMSA flow diagram. Risk of bias was assessed using the Cochrane Collaboration tool for assessing risk of bias and a tabular summary was provided. Risk of bias was high in six trials, low in three, and could not be determined in eight. Scientific quality of the studies was adequately considered in formulation of the results with reference to limitations of the analysis and deficiencies within the individual trials. Publication bias was assessed visually. Funding was disclosed and no conflict of interest was reported.

Non-Randomized Studies

Overall the non-randomized studies were adequately designed with some design and reporting deficiencies. All trials established a primary objective a priori. Patient demographics, intervention, and potential confounders were clearly described. Main findings were presented

clearly but no trials reported measures of variability alongside averages. In general, limited adverse event reporting on wound complications was completed up until hospital discharge. Selection and measurement bias could not be controlled due to lack of randomization and blinding. Recruitment for treatment and control groups was conducted over different time periods in all studies, with most studies reporting retrospective enrolment of the control group. This selection approach introduces potential problems including an inability to control for differences in hospital environment and infection control measures during the different time periods. Moreover, the different selection approaches used for the TCS and control groups introduces inconsistency in the sampling methods and may result in group differences related to willingness to participate. Willing patients could not be differentiated from patients who declined to participate and volunteer bias couldn't be assessed. The results may not be generalizable to the general surgical populations, other types of surgery, patient groups (e.g. pediatric populations) or hospital environments. Compliance with wound care protocols was implied though not adequately discussed for the in-hospital period, and compliance in the post-hospital period was not discussed by any study. None of the studies reported sample size calculations in their methods. There was no loss to follow-up reported in any of the studies.

Okada et al.,[23] provided an adequate description for identifying SSIs. Incidence of SSIs was assessed by specially trained physicians but the number of assessors wasn't specified. The CDC criteria were used to classify wounds. Multivariate analysis was not conducted. All patients were followed up to 30 days post-op. Groups were recruited from a single hospital but were not recruited over the same time period. The treatment group was significantly older, and had a higher proportion of diabetics and smokers. The pre-operative care was consistent with CDC guidelines.

Fraccalvieri et al.,[22] provided a description for identifying SSIs but no reference was provided. In general, it was not as comprehensive as the CDC criteria. Groups were not recruited over the same time period. Multivariate analysis was conducted to investigate potential confounders. All patients were followed up to 30 days post-op. There were significant differences between baseline demographics of the case and control groups. Specifically, the treatment group had a higher incidence of anemia, lower body mass index, and a shorter duration of surgery. Pre-operative care and hospital environment wasn't described and could not be assessed. The source of participants was not discussed but it was assumed that a single site was used.

Hoshino et al.,[10] used CDC criteria to identify SSIs. Groups were not recruited over the same time period. Multivariate analysis was conducted to investigate potential confounders. Patients were followed up to 30 days post-op. Most baseline demographics were similar with the exception of C-reactive protein levels. Length of follow-up wasn't indicated. Pre-operative care and hospital environment wasn't described and could not be assessed. The source of participants was not discussed but it was assumed that a single site was used.

Ueno et al.,[24] provided a thorough description for identifying SSIs but did not attribute it to any particular guideline or criteria. In addition they failed to discuss multivariate analyses prior to presentation of the results. Univariate analysis was conducted to investigate potential confounders but multivariate analysis was not undertaken. Most baseline demographics were similar. Length of follow-up wasn't indicated. Pre-operative care and hospital environment was described in detail. Patients were recruited from Departments of Orthopedic Surgery in University Hospitals in Kanagawa Japan.

Economic Evaluation

Study strengths and limitations are presented in Appendix 6.
The research question was clearly stated as an examination of the cost-effectiveness of TCS versus non-antimicrobial sutures for the prevention of SSIs from three viewpoints. The specific brand and suture material was not clarified for the intervention or comparator. The type of economic model was stated but it was not justified. Sources for all model inputs and effectiveness estimates were provided but the method of combining data from multiple sources, as well as the original study design and limitations were not provided and could not be assessed. Also, some model inputs were from non-aggregated sources, limiting generalizability. The primary outcome of cost per SSI prevented was clearly stated and the incremental equation was provided. No value based assessment was undergone so conclusions could only be made about technical efficiency, not allocative efficiency. Productivity costs were viewpoint-specified and clearly stated but the time-frame of productivity losses was not extended beyond duration of hospitalization with the exception of the occurrence of mortality. The methods used to estimate quantities and costs were not discussed; only references to the data sources were given. The currency and price data was recorded as US dollars but no base year was given. No adjustments for currency or inflation were noted. Details of the model were presented visually and the description of model inputs was comprehensive. The time-horizon was not explicitly stated but was assumed to be time to SSI given the stated outcome (prevention of SSI) and the criteria used (CDC Criteria); long term costs were not considered. Discounting to 2013 values using a 3% discount rate was completed. Ranges for efficacy of TCS, cost, and risk of SSI were using in sensitivity analysis to estimate the potential variability in outcome. Justification for these ranges was referenced but not discussed. Outcomes were reported as incremental cost effectiveness ratios but disaggregated results were not provided. The authors provided a clear answer to the research question and the conclusions consider appropriate caveats such as the controversy surrounding the actual efficacy of TCS and SSI risk. The study was conducted from the US perspective, covered only abdominal surgery and did not assess organ/space SSIs. Therefore, generalizability to the Canadian setting, other modes of surgery, and specific contexts (e.g. higher risk hospital environments) is limited.

Summary of Findings

What is the clinical effectiveness of antibacterial sutures for the prevention of surgical site infections?

Detailed results are available in Appendix 7.

Overall, the findings of the four systematic reviews and meta-analyses[18-20] indicated a reduction in the incidence of SSI with the use of TCS compared to non-antimicrobial sutures. The 15 studies retrieved by Daoud et al.,[19] were meta-analyzed resulting in a pooled relative risk (RR) of 0.67 (95% confidence interval [CI], 0.54 to 0.84); I^2 = 88.7%. A statistically significant reduction in risk for SSIs was not observed for several subgroups including: assessor-blind and open-label studies, CDC class IV incisions, and all surgical subgroups with the exception of cerebrospinal fluid shunt implantation or revision. Sensitivity analysis suggested the results were vulnerable to the removal of three specific trials but robust to the removal of up to two trials. The five studies retrieved by Diener et al.,[20] were meta-analyzed resulting in a statistically significant pooled RR of 0.67 (95% CI, 0.47 to 0.98); I^2 = 50%, though the clinical significance is unclear given the imprecision in the result. The seven studies retrieved by Sajid et al.,[21] were meta-analyzed resulting in a statistically significant pooled odds ratio (OR) of 0.61 (95% CI, 0.37

to 0.99); I^2 = 29%, though the clinical significance is unclear. No sub-group analysis was conducted. The evidence was deemed to be of moderate quality suggesting further research may influence the estimate of effect.[21] The 17 studies retrieved by Wang et al.,[18] were meta-analyzed resulting in a pooled RR of 0.70 (95% CI, 0.57 to 0.85); I^2 = 0.29%. Results remained statistically significant for all subgroups except paediatric patients, contaminated or dirty surgery (CDC class III or IV), breast and cardiac surgeries, and trials with unclear or high risk of bias.

The non-randomized studies consistently reported an association between the use of TCS and a reduction in SSIs but this relationship was vulnerable to confounding and some studies did not consider potential confounders. Hoshino et al.,[10] reported reduced incidence of SSIs in the treatment versus control group, however, in multivariate logistic regression analysis, the use of Vicryl Plus was not associated with a reduction in SSIs. Rather, incidence of SSIs was associated with the use of a laparoscope, lower American Society of Anesthesiologists physical status score, and higher class of CDC wound classification. Fraccalvieri et al.,[22] reported a reduced incidence of SSI in the treatment versus control group. This association was persistent in multivariate analysis, showing a significantly higher risk of wound infection in individuals who did not receive TCS. Okada et al.,[23] reported a reduction in superficial and deep SSIs but no difference in organ/space SSIs between groups. They did not conduct multivariate analysis; therefore the effect of TCS in the context of other infection-determining factors could not be assessed.

What are the adverse events associated with antibacterial suture use, including the development of drug-resistant bacteria?

Severe adverse events associated with the use of antimicrobial sutures (including the development of drug-resistant bacteria) were not a reported outcome within any of the clinical evidence retrieved. The Diener review[20] reported 16 deaths in the PROUD study that were not attributed to TCS, but did not report on deaths in the other included RCTs. Sajid et al.,[21] reported a reduced risk (RR = 0.56 [95% CI, 0.32 to 0.98]) of post-operative complications (not including SSIs) with the use of TCS compared to non-antimicrobial sutures, based on pooled results from four RCTs. There was no difference in duration of hospitalization between groups.[21] None of the meta-analyses[18-21] assessed or reported risk of mortality as an outcome. Among the non-randomized studies, Okada et al.,[23] reported no difference in duration of hospitalization between groups.

What are the guidelines for using antibacterial sutures for wound closure?

No relevant literature was identified; therefore, no summary can be provided.

What is the cost-effectiveness of using antibacterial sutures for wound closure?

Detailed results are available in Appendix 8.

The economic evaluation reported that under set circumstances of moderate (15%) SSI risk and variable efficacy (5-50%) costs were saved per SSI prevented from all perspectives. Under circumstances of 5% SSI risk and less than 10% efficacy, and 5% efficacy and less than 10% SSI risk, hospitals and third party payers incurred extra costs per SSI prevented.

From the hospital perspective at 5% to 10% efficacy and 5% risk, or 5% efficacy and up to 10% risk of SSI the excess cost per SSI averted was $1625 to $18870. However, at greater than

10% efficacy and greater than 10% SSI risk cost savings per SSI averted ranged from $3750 to $14309. From the third party payer perspective at 5 to 10% efficacy and 5% risk of SSI, or 5% efficacy and up to 10% risk of SSI, the excess cost per SSI averted was $1071 to $17687. However, at greater than 10% efficacy and greater than 10% SSI risk, cost savings per SSI averted ranged from $4474 to $14577. From the societal perspective costs were saved per SSI averted at greater than 5% efficacy and greater than 5% risk of SSI with savings ranging from $23519 to $54704.

When suture costs were lowered ($5 per inch) in the models, cost savings were increased at lower efficacies, whereas higher priced sutures ($20 per inch) required at least 20% TCS efficacy to be cost-effective from the hospital and payer perspective. From the societal perspective, suture cost had to exceed $20 per inch for extra costs to incur, assuming 5% TCS efficacy (low).

Limitations

Clinical Evidence

The results of the four systematic reviews and meta-analyses[18-20] should be interpreted cautiously due to several limitations. A clear definition for SSI was not reported by all included RCTs and SSI incidence was not universally reported as the primary outcome. All but one study[20] did not impose restrictions on type of surgery. This variability among surgical procedures contributed to heterogeneity amongst trials and limits generalizability. Sub-group analyses on type of surgery were conducted by only one study.[19] Several subgroup analyses may have had an insufficient sample size and event occurrence for robust analysis. In addition, some important patient (e.g. diabetes, immunosuppression) and surgery (e.g. skin preparation) related risk factors were not considered. The impact of industry funding in two trials[19,20] was not evaluated.

The results of the non-randomized studies should be interpreted in light of the following limitations. No trials reported measures of variability alongside averages and there were significant differences in SSI relevant baseline characteristics of the case and control groups. Adverse event reporting was limited and generally restricted to non-critical surgery complications up until hospital discharge. Consequently, long-term morbidity and mortality could not be assessed. Selection bias and measurement bias could not be ruled out due to lack of randomization and blinding, and recruitment of treatment and control groups during different time. The results of the studies are restricted to the respective types of surgeries assessed, which limits generalizability. Similarly, certain patients groups (i.e., pediatrics) and certain hospital environments (e.g. those with poorly established infection prevention protocols) were not evaluated. Compliance with wound care protocols was not assessed post-discharge and could not be controlled for. In addition, no study disclosed sample size calculations. For the trials that did not conduct multivariate analysis, potential confounding by other risk factors for SSIs could not be ruled out. Some studies did not report follow-up duration.

Economic Evidence

The economic evaluation was not conducted in the Canadian context and limited to abdominal surgery, reducing generalizability. Methodology and sources of model inputs lacked transparency, and quality of life factors were not considered so allocative efficiency could not be assessed.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Clinical effectiveness of TCS for adults undergoing surgery was evaluated in a total of 23 RCTs of varying quality aggregated within four systematic reviews and meta-analyses, and 4 non-randomized studies, published between 2013 and 2014. While the overall trend was for a reduction in the incidence of SSIs with the use of TCS versus non-antimicrobial sutures it should be noted that imprecision in the results of two meta-analyses due to the influence of several negative RCTs led to unclear clinical significance. Moreover, they reported subgroup analyses showing a lack of effect in certain categories including non-double blinded trials, CDC class IV wounds, studies that did not classify wounds by CDC criteria; colorectal, appendix, breast and cardiac surgery; pediatric populations, and trials with unclear or high risk of bias. The observational data followed this general trend but the effect observed in one study was vulnerable to multivariate analysis.[10] To reduce uncertainty, further clinical research investigating TCS versus non-antimicrobial sutures may benefit from implementing a more rigorous study design (i.e. double blind) and focusing on a specific surgical area to reduce heterogeneity, especially in the case of systematic reviews. The observations from the clinical evidence retrieved was in agreement with the overall conclusion of the previous CADTH report,[13] which found that the use of TCS reduced the rate of SSI compared to non-antimicrobial sutures.

Cost effectiveness of TCS compared to non-coated sutures for adults undergoing abdominal surgery was assessed by one economic evaluation conducted in the United States. Assuming moderate (15%) SSI risk, TCS at variable efficacies (5-50%) would be considered cost effective relative to non-coated sutures for preventing SSI risk from all perspectives. The generalizability of these findings to the Canadian context and other types of surgery is unknown.

There was no recent evidence to address the issue of harms including the development of bacterial resistance, and no evidence-based guidelines for using TCS for wound closure.

PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca

REFERENCES

1. Canadian Institute for Health Information. Compromised wounds in Canada [Internet]. Ottawa: CIHI; 2013 Aug. (Analysis in brief). [cited 2014 Nov 11]. Available from: https://secure.cihi.ca/free_products/AiB_Compromised_Wounds_EN.pdf

2. Hurd T, Posnett J. Point prevalence of wounds in a sample of acute hospitals in Canada. Int Wound J. 2009 Aug;6(4):287-93.

3. Gravel D, Taylor G, Ofner M, Johnston L, Loeb M, Roth VR, et al. Point prevalence survey for healthcare-associated infections within Canadian adult acute-care hospitals. J Hosp Infect. 2007 Jul;66(3):243-8.

4. Coello R, Charlett A, Wilson J, Ward V, Pearson A, Borriello P. Adverse impact of surgical site infections in English hospitals. J Hosp Infect. 2005 Jun;60(2):93-103.

5. Zoutman D, McDonald S, Vethanayagan D. Total and attributable costs of surgical-wound infections at a Canadian tertiary-care center. Infect Control Hosp Epidemiol. 1998 Apr;19(4):254-9.

6. Umscheid CA, Mitchell MD, Doshi JA, Agarwal R, Williams K, Brennan PJ. Estimating the proportion of healthcare-associated infections that are reasonably preventable and the related mortality and costs. Infect Control Hosp Epidemiol. 2011 Feb;32(2):101-14.

7. Cheadle WG. Risk factors for surgical site infection. Surg Infect (Larchmt). 2006;7 Suppl 1:S7-11.

8. Rothenburger S, Spangler D, Bhende S, Burkley D. In vitro antimicrobial evaluation of Coated VICRYL* Plus Antibacterial Suture (coated polyglactin 910 with triclosan) using zone of inhibition assays. Surg Infect (Larchmt). 2002;3 Suppl 1:S79-S87.

9. Marco F, Vallez R, Gonzalez P, Ortega L, de la Lama J, Lopez-Duran L. Study of the efficacy of coated Vicryl plus antibacterial suture in an animal model of orthopedic surgery. Surg Infect (Larchmt). 2007 Jun;8(3):359-65.

10. Hoshino S, Yoshida Y, Tanimura S, Yamauchi Y, Noritomi T, Yamashita Y. A study of the efficacy of antibacterial sutures for surgical site infection: a retrospective controlled trial. Int Surg [Internet]. 2013 Apr [cited 2014 Oct 29];98(2):129-32. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3723176

11. Edmiston CE, Jr., Daoud FC, Leaper D. Is there an evidence-based argument for embracing an antimicrobial (triclosan)-coated suture technology to reduce the risk for surgical-site infections?: A meta-analysis. Surgery. 2013 Jul;154(1):89-100.

12. Chang WK, Srinivasa S, Morton R, Hill AG. Triclosan-impregnated sutures to decrease surgical site infections: systematic review and meta-analysis of randomized trials. Ann Surg. 2012 May;255(5):854-9.

13. Canadian Agency for Drugs and Technologies in Health. Antimicrobial sutures for wound closure after surgery: a review of the clinical effectiveness, safety, guidelines, and cost-

effectiveness [Internet]. Ottawa: The Agency; 2013 May 16. (Rapid response report: summary with critical appraisal). [cited 2014 Nov 11]. Available from: http://www.cadth.ca/media/pdf/htis/jun-2013/RC0450%20Antib%20Sutures%20Final.pdf

14. Canadian Agency for Drugs and Technologies in Health. Antibacterial sutures for wound closure after surgery: update on clinical effectiveness and guidelines for use [Internet]. Ottawa: The Agency; 2014 Apr 1. (Rapid response report: reference list). [cited 2014 Nov 11]. Available from: http://www.cadth.ca/media/pdf/htis/may-2014/RA0666%20Antibacterial%20Sutures%20Update%20Final.pdf

15. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol [Internet]. 2007;7:10. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1810543/pdf/1471-2288-7-10.pdf

16. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health [Internet]. 1998 Jun;52(6):377-84. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1756728/pdf/v052p00377.pdf

17. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. BMJ. 1996 Aug 3;313(7052):275-83. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2351717

18. Wang ZX, Jiang CP, Cao Y, Ding YT. Systematic review and meta-analysis of triclosan-coated sutures for the prevention of surgical-site infection. Br J Surg. 2013 Mar;100(4):465-73.

19. Daoud FC, Edmiston CE, Jr., Leaper D. Meta-analysis of prevention of surgical site infections following incision closure with triclosan-coated sutures: robustness to new evidence. Surg Infect (Larchmt) [Internet]. 2014 Jun;15(3):165-81. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4063374

20. Diener MK, Knebel P, Kieser M, Schüler P, Schiergens TS, Atanassov V, et al. Effectiveness of triclosan-coated PDS Plus versus uncoated PDS II sutures for prevention of surgical site infection after abdominal wall closure: the randomised controlled PROUD trial. Lancet. 2014 Jul 12;384(9938):142-52.

21. Sajid MS, Craciunas L, Sains P, Singh KK, Baig MK. Use of antibacterial sutures for skin closure in controlling surgical site infections: a systematic review of published randomized, controlled trials. Gastroenterology Report [Internet]. 2013 [cited 2014 Nov 20];1:42-50. Available from: http://gastro.oxfordjournals.org/content/1/1/42.full.pdf+html

22. Fraccalvieri D, Kreisler Moreno E, Flor Lorente B, Torres García A., Muñoz Calero A, Mateo Vallejo F, et al. Predictors of wound infection in elective colorectal surgery. Multicenter observational case-control study. Cir Esp. 2014 Aug;92(7):478-84.

23. Okada N, Nakamura T, Ambo Y, Takada M, Nakamura F, Kishida A, et al. Triclosan-coated abdominal closure sutures reduce the incidence of surgical site infections after pancreaticoduodenectomy. Surg Infect (Larchmt). 2014 Jun;15(3):305-9.

24. Ueno M, Saito W, Yamagata M, Imura T, Inoue G, Nakazawa T, et al. Triclosan-coated sutures reduce wound infections after spinal surgery: a retrospective, nonrandomized, clinical study. Spine J. 2013 Aug 27.

25. Rasic Z, Schwarz D, Adam VN, Sever M, Lojo N, Rasic D, et al. Efficacy of antimicrobial triclosan-coated polyglactin 910 (Vicryl* Plus) suture for closure of the abdominal wall after colorectal surgery. Coll Antropol. 2011 Jun;35(2):439-43.

26. Singh A, Bartsch SM, Muder RR, Lee BY. An economic model: value of antimicrobial-coated sutures to society, hospitals, and third-party payers in preventing abdominal surgical site infections. Infect Control Hosp Epidemiol. 2014 Aug;35(8):1013-20.

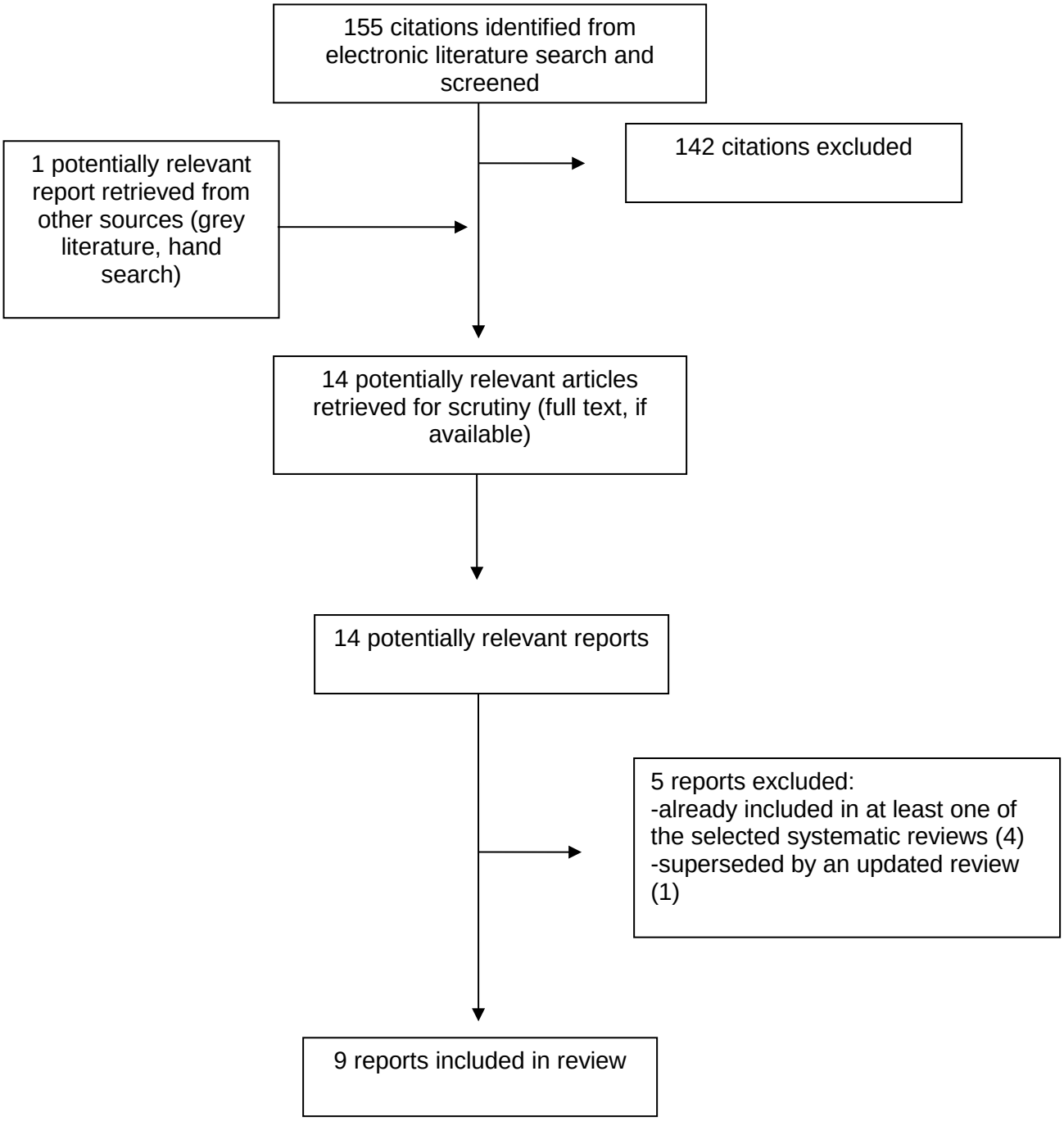
27. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Am J Infect Control. 1992 Oct;20(5):271-4.

28. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. Am J Infect Control. 1999 Apr;27(2):97-132.

29. Garner JS. CDC guideline for prevention of surgical wound infections, 1985. Supersedes guideline for prevention of surgical wound infections published in 1982. (Originally published in November 1985). Revised. Infect Control. 1986 Mar;7(3):193-200.

30. Simmons BP. Guideline for prevention of surgical wound infections. Am J Infect Control. 1983 Aug;11(4):133-43.

APPENDIX 1: Selection of Included Studies



APPENDIX 2: Characteristics of Clinical Studies

Table A1. Characteristics of Included Systematic Reviews and Meta-Analyses

Author, year, funding source	Key inclusion criteria, N studies	Interventions and Comparators, Type of Surgery	Outcomes
Daoud, 2014,[9] No external funding	Head to head RCTs (cut off July 2013); no language, date, or publication restrictions 15 RCTs (n = 4800 patients)	Intervention Vicryl Plus Monocryl Plus PDS Plus Comparator Vicryl Silk Monocryl PDS Surgery type unrestricted	Incidence of SSIs Subgroup analyses: Type of blinding CDC incision class Operation type
Diener, 2014,[17] Johnson & Johnson Medical Limited	RCTs (cut-off July 2013); no language, date, or publication restrictions 5 RCTs (n = 3020 patients)	Intervention Vicryl Plus PDS Plus Comparator Vicryl PDS II Abdominal surgery	Incidence of SSIs Subgroup analysis: Excluding PROUD Trial
Sajid, 2013,[21] Undeclared no conflict of interest stated	RCTs (cut off October 2012); no language or publication status restrictions, filtered to exclude non-randomized studies 7 RCTs (n = 1631)	Intervention Antibiotic sutures Comparator Simple sutures Surgery type unrestricted	Incidence of SSIs Subgroup analyses were not conducted
Wang, 2013,[18] Grants for Key Clinical Centres and Institutes and Science Fund of Ministry of Health of China	RCTs (cut off June 2012); no language or date of publication restrictions 17 RCTs (n= 3720 patients)	Intervention Vicryl Plus Monocryl Plus PDS plus Comparator Vicryl Monocryl PDS Plus Silk Non-antimicrobial Surgery type unrestricted	Incidence of SSIs Subgroup analyses: Age Wound classification Surgery Type Follow-up period Risk of bias Publication status Vicryl® Plus

CDC = United States Centers for Disease Control and Prevention; SSI = surgical site infection.

Table A2. Characteristics of Included Non-Randomized Studies

Author, year, funding source, country	Study Design	Population	Interventions (n) and Comparators (n)	Outcomes
Okada, 2014,[12] Not reported, Japan	Uncontrolled before-after study	Patients undergoing pancreaticoduodenectomy	Intervention Vicryl Plus, n = 88 Comparator Vicryl, n = 110	Incidence of SSIs
Fraccalvieri, 2013,[22] Not reported, Spain	Uncontrolled before-after study	Patients undergoing colorectal disease surgery	Intervention Vicryl Plus, n = 240 Comparator PDS Plus, n = 240	Incidence of SSIs
Hoshino, 2013,[10] Not reported, Japan	Uncontrolled before-after study	Patients undergoing gastrointestinal surgery	Intervention Vicryl Plus, n= 455 Comparator Vicryl, n= 596	Incidence of wound Infections
Ueno, 2013,[24] Not reported, Japan	Case-control study	Patients undergoing spinal cord surgery	Intervention Triclosan coated sutures, n= 200 Comparator Non-coated sutures, n= 205	Incidence of wound infections

SSI = Surgical Site Infection.

APPENDIX 3. Centers of Disease Control and Prevention Criteria

Table A3. Criteria for Defining a SSI*

Superficial Incisional SSI
• Infection occurs within 30 days after the operation *and* • Infection involves only skin or subcutaneous tissue of the incision *and* at least *one* of the following: 1. Purulent drainage, with or without laboratory confirmation, from the superficial incision 2. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision 3. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat and superficial incision is deliberately opened by surgeon, unless incision is culture-negative. 4. Diagnosis of superficial incisional SSI by the surgeon or attending physician. • Do *not* report the following conditions as SSI: 1. Stitch abscess (minimal inflammation and discharge confined to the points of suture penetration). 2. Infection of an episiotomy or newborn circumcision site. 3. Infected burn wound. 4. Incisional SSI that extends into the fascial and muscle layers (see deep incisional SSI). *Note*: Specific criteria are used for identifying infected episiotomy and circumcision sites and burn wounds.
Deep Incisional SSI
• Infection occurs within 30 days after the operation if no implant† is left in place or within 1 year if implant is in place and the infection appears to be related to the operation *and* • infection involves deep soft tissues (e.g., fascial and muscle layers) of the incision *and* at least *one* of the following: 1. Purulent drainage from the deep incision but not from the organ/space component of the surgical site. 2. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38ºC), localized pain, or tenderness, unless site is culture-negative. 3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination. 4. Diagnosis of a deep incisional SSI by a surgeon or attending physician. *Notes:* 1. Report infection that involves both superficial and deep incision sites as deep incisional SSI. 2. Report an organ/space SSI that drains through the incision as a deep incisional SSI.
Organ/Space SSI
• Infection occurs within 30 days after the operation if no implant† is left in place or within 1 year if implant is in place and the infection appears to be related to the operation *and* • infection involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation *and* at least *one* of the following: 1. Purulent drainage from a drain that is placed through a stab wound‡ into the organ/space. 2. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space. 3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination. 4. Diagnosis of an organ/space SSI by a surgeon or attending physician.

SSI = surgical site infection.
*Horan et al.,[27] Mangram et al.,[28] page 252.
†National Nosocomial Infection Surveillance definition: a nonhuman-derived implantable foreign body (e.g. prosthetic heart valve, nonhuman vascular graft, mechanical heart, or hip prosthesis) that is permanently placed in patient during surgery
‡If the area around a stab wound becomes infected, it is not an SSI. It is considered a skin or soft tissue infection, depending on its depth.

Table A4. Surgical Wound Classification*

Class I/Clean
An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tract is not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if they meet the criteria.
Class II/Clean-Contaminated
An operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.
Class III/Contaminated
Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, nonpurulent inflammation is encountered are included in this category.
Class IV/Dirty-Infected
Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

*Garner et al.,[29] and Simmons et al.[30]

APPENDIX 4: Characteristics of Economic Studies

Table A5. Characteristics of Included Economic Evaluations

Author, year, funding source	Population, Perspective, Time Horizon, Methods Used	Interventions and Comparators	Outcomes
Singh, 2014[26], National Institute of General Medical Sciences Models of Infectious Disease Agent Study and the Pennsylvania Department of Health	Individuals undergoing abdominal surgery Hospital, third party payer and societal perspective Time to event Cost-effectiveness analysis, Decision analytic model, Monte Carlo probabilistic sensitivity analysis	Intervention Triclosan coated sutures Comparator Standard 'uncoated' sutures	Cost per SSI prevented

SSI = surgical site infection.

APPENDIX 5: Critical Appraisal of Clinical Evidence

Table A6. Critical Appraisal of Systematic Reviews and Meta-Analyses

Study, Country, Publication Year	Strengths	Limitations
Daoud, 2014[19]	• A priori objectives stated • Heterogeneity assessed • Comprehensive literature search of multiple databases and hand searching of reference lists • Included studies were comprehensively described • Quality assessment was done using multiple methods • Publication bias assessed visually and statistically • Subgroup and sensitivity analysis conducted	• Number of authors involved in screening and abstraction was unclear • Results of quality assessment were not described in adequate detail • Previous industry funding to the research group was not disclosed • Limited grey literature search
Diener, 2014[20]	• Comprehensive literature search of multiple databases and hand searching of reference lists • Focused on a sub-group of surgical procedures	• Unclear whether meta-analysis was planned a priori • Methodology and results underreported • Quality assessment of included trials was not completed • Publication bias not assessed • Influence of industry funding was not assessed • A limited description of included studies was provided • Limited grey literature search
Sajid, 2013[21]	• A priori objectives stated • Comprehensive literature search of multiple databases and hand searching of reference lists • Multiple authors were involved in the screening and abstraction process • Included studies were comprehensively described	• A search filter to exclude non-randomized trials was applied • Risk of bias assessment was unclear and based on limited criteria • Publication bias was not assessed • No funding sources were declared • Limited grey literature search
Wang, 2013[18]	• A priori objectives stated • Comprehensive literature search of multiple databases and hand searching of reference lists • Multiple authors were involved in the screening and abstraction process • Included studies were comprehensively described • Quality assessment was completed • Publication bias was assessed visually • Funding was disclosed • Appropriate subgroup analysis conducted	• Limited grey literature search

Table A7. Critical Appraisal of Non-Randomized Studies

Study, Country, Publication Year	Strengths	Limitations
Okada, 2014[23]	• Primary objective reported a priori • Patient, intervention and comparator were adequately described • Study subjects were representative of the specific surgical population • CDC criteria used to categorize wounds and for pre-operative wound care	• Measures of variability were not presented alongside averages • Lack of randomization and blinding • Recruitment for treatment and control groups conducted over different time-frames • Sample size calculation not reported • Multivariate analysis was not conducted
Fraccalvieri, 2013[22]	• Primary objective reported a priori • Patient, intervention and comparator were adequately described • Study subjects were representative of the specific surgical population • Multivariate analysis conducted	• Measures of variability were not presented alongside averages • Lack of randomization and blinding • Recruitment for treatment and control groups conducted over different time-frames • Sample size calculation not reported • Criteria for SSI was not attributed to any guideline or policy • Pre and post-operative hospital care wasn't described
Hoshino, 2013[10]	• Primary objective reported a priori • Patient, intervention and comparator were adequately described • Study subjects were representative of the specific surgical population • Multivariate analysis conducted	• Measures of variability were not presented alongside averages • Lack of randomization and blinding • Recruitment for treatment and control groups conducted over different time-frames • Sample size calculation not reported • Pre and post-operative hospital care wasn't described
Ueno, 2013[24]	• Primary objective reported a priori • Patient, intervention and comparator were adequately described • Study subjects were representative of the specific surgical population • Pre and post-operative care was described in detail	• Measures of variability were not presented alongside averages • Lack of randomization and blinding • Recruitment for treatment and control groups conducted over different time-frames • Sample size calculation not reported • Criteria for SSI was not attributed to any guideline or policy • Multivariate analysis was not conducted • Length of follow-up not indicated

CDC = United States Centers for Disease Control and Prevention; SSI = surgical site infection.

APPENDIX 6: Critical Appraisal of Economic Studies

Table A8. Critical Appraisal of Economic Evaluations

Study, Publication Year. Country	Strengths	Limitations
Singh, 2013,[26] United States	• Model design and inputs clearly reported • Sensitivity analysis conducted • Discounted costs and benefits • A clear definition for the outcome of interest (SSI) was given • ICERs were reported as the primary outcome	• Incomplete reporting of resources, unit costs, and disaggregated results • Details about intervention and comparator (e.g. brand, material) was not given • Time horizon not specified • Incomplete description of sources of efficacy data • Productivity costs were limited to hospital stay and death (disability and post-hospital recovery not considered) • No adjustments for currency or inflation were noted • Limited generalizability to the Canadian setting • Limited generalizability to different types of surgery • Allocative efficiency could not be assessed as cost utility analysis was not conducted

ICER = incremental cost effectiveness ratio; SSI = surgical site infection.

APPENDIX 7: Summary of Clinical Findings

Table A9. Surgical Site Infections Reported for Systematic Reviews and Meta-Analyses

Author, Publication Year	Treated group, n/N	Control group, n/N	RR or OR (95% CI), Heterogeneity
Daoud, 2014[19]	180/2323	273/2477	RR = 0.67 (0.54 to 0.84), I^2 = 88.7%
Diener, 2014[20]	154/1557	193/1463	RR = 0.67 (0.47 to 0.98), I^2 = 50%
Sajid, 2013[21]	48/760	88/871	OR = 0.61 (0.37 to 0.99), I^2 = 29%
Wang, 2013[18]	149/1726	227/1994	RR = 0.70 (0.57 to 0.85), I^2 = 29%

CI = Confidence Interval; OR = Odds Ratio; RR = Relative Risk.

Table A10. Surgical Site Infections Reported for Non-Randomized Studies

Author, Publication Year	Treated group, n/N	Control group, n/N	Chi^2 Statistic, p-value
Okada, 2014[23]	4/88	16/110	NR, p = 0.034
Fraccalvieri, 2013[22]	35/240	70/240	NR, p = 0.001
Hoshino, 2013[10]	30/455	72/596	NR, p = 0.002
Ueno, 2013[24]	1/200	8/205	NR, p = 0.020

NR = not reported; OR = odds ratio; RR = relative risk

Table A11. Surgical Site Infections by Sub-Group*

Sub-group	N Studies	Treated group n/N	Control group n/N	Relative Risk (95% CI)
Daoud et al.[19]†				
Blinding				
Double blind RCTs	9	132/1585	200/1825	**0.65 (0.51 to 0.82)**
Open label RCTs	4	46/537	53/502	0.85 (0.52 to 1.40)
Single Blind RCTs	2	2/201	20/350	0.23 (0.05 to 1.16)
Wound Class				
CDC Class I	8	75/1089	124/1220	**0.63 (0.48 to 0.83**
CDC Class II	6	61/751	84/683	**0.66 (0.48 to 0.90)**
CDC Class III	4	9/85	19/74	**0.45 (0.22 to 0.91)**
CDC Class IV	1	4/38	1/38	4.0 (0.47 to 34.16)
Diagnostic method (other)	2	31/289	45/437	0.95 (0.62 to 1.48)
Operation Type‡				
Colorectal or appendectomy§	5	58/678	78/644	0.687 (0.470 to 1.004)
Cerebrospinal fluid shunt implantation or revision	1	2/46	8/38	**0.207 (0.044 to 0.961)**
Diener et al.[20]				
Excluding PROUD study	4	67/970	97/865	**0.58 (0.38 to 0.91)**
Wang et al.[18]				
Population				
Adult	15	144/1582	219/1907	**0.71 (0.58 to 0.87)**
Pediatric	2	5/144	8/87	0.64 (0.04 to 10.1)
Wound Class				

Sub-group	N Studies	Treated group n/N	Control group n/N	Relative Risk (95% CI)
Clean	9	80/820	117/977	**0.73 (0.56 to 0.95)**
Clean-contaminated	6	53/566	79/580	**0.69 (0.50 to 0.96)**
Contaminated/dirty	2	8/42	12/45	1.10 (0.14 to 8.43)
Type of Surgery				
Abdominal	7	53/695	85/867	**0.69 (0.50, 0.97)**
Breast	3	12/138	19/130	0.59 (0.30, 1.14)
Cardiac	3	31/380	52/553	0.75 (0.49, 1.14)
Length of Follow-Up				
1 month follow-up	9	115/1117	156/1285	**0.79 (0.63, 0.99)**
>1 month follow-up	6	24/453	45/548	**0.56 (0.35, 0.92)**
Risk of Bias				
Low risk of bias	3	32/346	51/331	**0.60 (0.39, 0.90)**
Unclear risk of bias	8	56/715	104/1034	0.57 (0.32, 1.00)
High risk of bias	6	61/665	72/629	0.85 (0.62, 1.18)
Publication Type				
Full-length publication	13	122/1460	181/1717	**0.72 (0.58, 0.90)**
Abstracts	4	27/266	46/277	**0.61 (0.39, 0.94)**
Type of Suture				
Vicryl Plus versus Vicryl	10	71/1022	109/1138	**0.70 (0.53, 0.94)**

CDC = Centers for Disease Control and Prevention; CI = confidence interval; RCT = randomized controlled trial.
Statistically significant results in bold
*Sajid Meta-Analysis[21] did not conduct sensitivity analysis
†Full data was not available for all sub-groups
‡Results for abdominal, breast, leg, hepatopancreaticobiliary, lower limb revascularization, multiple site, other abdominal, small intestine, sternal, and upper GI surgical subgroups were not statistically significant
§In text and in table relative risks were slightly but not significantly different

APPENDIX 8: Summary of Findings of Economic Studies

Table A12. Results of Cost-Effectiveness Studies

Author, Year, Country	Intervention and Comparator	ICER(Costs per SSI Prevented), SSIs or Deaths Prevented/1000 Surgeries		
		Hospital Perspective†	Third-Party Payer Perspective†	Societal Perspective†
Singh, 2014,[26] United States	TCS versus standard non-coated sutures	$4109 to 13975 saved per SSI prevented 7 to 75 SSIs prevented/1000 surgeries	$4133 to 14297 saved per SSI prevented 7-14 SSIs prevented/1000 surgeries	$40127 to 53244 saved per SSI prevented 0.29 to 3.2 deaths prevented/1000 surgeries

ICER = incremental cost effectiveness ratio; SSI = surgical site infection; TCS = triclosan coated sutures.
†Assuming 15% SSI risk and variable efficacy (5-50%)[26]