EUnetHTA Joint Action 3 WP4

**Rapid assessment of other technologies using the HTA Core Model®
for Rapid Relative Effectiveness Assessment**

ANTIBACTERIAL-COATED SUTURES VERSUS NON-ANTIBACTERIAL-COATED SUTURES FOR THE PREVENTION OF ABDOMINAL, SUPERFICIAL AND DEEP INCISIONAL, SURGICAL SITE INFECTION (SSI)

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Disclaimer

The assessment represents a consolidated view of the EUnetHTA network members and is in no case the official opinion of the participating institutions or individuals.

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Conflict of interest

All authors and dedicated reviewers involved in the production of this assessment have declared they have no conflicts of interest in relation to the technology assessed according to the EUnetHTA Declaration of interest and confidentiality undertaking (DOICU) statement form. One external expert, Professor Kriwanek, has declared *a financial or another relationship with a Developing and/or Producing and/or Distributing Organisation (DPDO) for the technology or comparators undergoing assessment*, and thus has a conflict of interest according to the EUnetHTA guidelines for handling conflict of interest. Professor Kriwanek has attended symposia related to and gave lectures on the topic of antibacterial-coated sutures which were sponsored by the company Johnson & Johnson. This sponsoring included the refunding of accommodation, travel costs and congress fees. He has no other conflicts of interest related to the topic of antibacterial-coated sutures to declare. According to the EUnetHTA guidelines for handling conflict of interest, the involvement of Professor Kriwanek as external expert is acceptable for commenting on the draft assessment without having access to any potentially confidential material.

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LIST OF ABBREVIATIONS

AAZ	Agency for Quality and Accreditation in Health Care and Social Welfare
ABHR	Alcohol-based hand rub
ACROBAT-NRSI	A Cochrane Risk Of Bias Assessment Tool: for Non-Randomized Studies of Interventions
AE	Adverse event
AGENAS	L'Agenzia Nazionale per i Servizi Sanitari Regionali
AMSTAR	A Measurement Tool to Assess Systematic Reviews
ASA	American Society of Anesthesiology
ASC/AST	Active Surveillance Culture/Testing
BMI	Body mass index
BSI	British Standards Institution
CA	Collaborative Assessment
CABG	Coronary artery bypass graft
CADTH	Canadian Agency for Drugs and Technologies in Health
CBGB	Coronary artery bypass graft surgery
CBGC	Coronary artery bypass graft with chest incision
CDC	Centers for Disease Control and Prevention
CE	Conformité Européene
CHA	Chlorhexidine diacetate
CHG	Chlorhexidine gluconate
CHOL	Cholecystectomy
CI	Confidence intervals
CIRC	Infected circumcision site in newborns
COLO	Colon surgery
CONSORT	Consolidated Standards of Reporting Trials
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
CSEC	Caesarean section
CUR	Health Problem and Current Use of the Technology domain
D&C	Drugs and Cosmetics
DI	Deep incisional
DIP	Deep Incisional Primary
DIS	Deep Incisional Secondary
DM	Diabetes Mellitus
DOICU	Declaration of interest and confidentiality undertaking of interest
DPDO	Developing and/or Producing and/or Distributing Organisation
DRG	Diagnosis-related group

e.g.	For example
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EFF	Clinical Effectiveness domain
EP	European Pharmacopoeia
EQ-5D	EuroQol five dimensions questionnaire
ESBL	Extended spectrum beta-lactamase
ETH	Ethical analysis
EU	European Union
EUnetHTA	European network for Health Technology Assessment
FDA	Food and Drug Administration
FiO2	Fraction of inspired oxygen
GDFT	Goal-directed fluid therapy
GDG	Guidelines Development Group
GI	Gastro-intestinal
GL	Guideline
GMDN	Global medical device nomenclature
GRADE	The Grading of Recommendations Assessment, Development and Evaluation
HCAI	Health care-associated infection
HELICS	Hospitals in Europe Link for Infection Control through Surveillance
HPRO	Arthroplasty of hip, hip prosthesis
HTA	Health technology assessment
i.e	That is
ICD	International Classification of Diseases
ICTRP	International Clinical Trials Registry Platform
IQWIG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
ISRCTN	International Standard Randomised Controlled Trial Number
ITT	Intention-to-treat
J&J	Johnson & Johnson
KPRO	Arthroplasty of knee, knee prosthesis
LAM	Laminectomy
LBI-HTA	Ludwig Boltzmann Institute for Health Technology Assessment
LEG	Legal aspects
LMICs	Low- and middle-income countries
LOS	Length of stay
MA	Meta-analysis
MAH	Marketing authorisation holder
MBP	Mechanical bowel preparation
MeSH	Medical Subject Headings

mITT	Modified intention to treat
MK	M Kieser
MKD	M K Diener
MRSA	Methicillin-resistant S. aureus
MWB	M W Büchler
NHSN	National Healthcare Safety Network
NICE	National Institute for Health and Care Excellence
NNT	Number of patients needed to treat to obtain a benefit
No	Number
non-RCTs	Non randomized controlled trials
NPS	National Prevalence Survey
NR	Not reported
NS	Not significant
NSPHMPDB	National School of Public Health, Management and Professional Development
OGYEI	National Institute of Pharmacy and Nutrition
OR	Odds Ratio
OR	Operating room
ORG	Organisational aspects
OS	Organ/space
OS	Overall survival
PCT	Procalcitonin
PD	Pancreaticoduodenectomy
PDS	Polydioxanone
PDS	Post-discharge surveillance
PHLS	Public Health Laboratory Service
PICO	Population-Intervention-Control-Outcome
PMDA	Pharmaceuticals and Medical Devices Agency
pNPWT	Prophylactic negative pressure wound therapy
PP	Per protocol
PROUD	PRevention of abdominal wOUnD infection
QALY	Quality-adjusted life year
QoL	Quality of life
R-AMSTAR	Revised Assessment of Multiple Systematic Reviews
RCT	Randomised Controlled Trial
REA	Relative Effectiveness Assessment
RoB	Risk of Bias
RR	Relative risk
SAE	Serious Adverse Event
SAF	Safety domain

SAP	Surgical antibiotic prophylaxis
SDGC	Study Center of the German Surgical Society
SHEA	The Society for Healthcare Epidemiology of America
SHEA/IDSA	Society for Healthcare Epidemiology of America/Infectious Diseases Society of America
SI	Superficial incisional
SIP	Superficial Incisional Primary
SIS	Superficial Incisional Secondary
SISG	Surgical Infection Study Group
SNHTA	Swiss Network for Health Technology Assessment
SOC	Patients and Social aspects
SR	Systematic review
SR/MA	Systematic review/Meta-analysis
SSI	Surgical site infection
SUKL	State Institute for Drug Control, Czech Republic
TCSs	Triclosan-coated sutures
TEC	Description and Technical Characteristics of Technology domain
TGA	Therapeutic Goods Administration
UK	United Kingdom
UNK	Unknown
US	United States
USP	United States Pharmacopoeia
VASPVT	Valstybinė akreditavimo sveikatos priežiūros veiklai tarnyba
vs	Versus
WBC	White blood cell count
WHO	World Health Organization
WMD	Weighted mean difference
WP	Wound protector
WP4	Work package 4

SUMMARY OF RELATIVE EFFECTIVENESS OF ANTIBACTERIAL-COATED SUTURES

Scope

The objective of this rapid assessment was to evaluate the effectiveness and safety of antibacterial-coated sutures for the prevention of superficial and deep incisional surgical site infection (SSI), compared with non-antibacterial coated sutures, in abdominal surgery in adults.

The scope can be found here: Scope.

Introduction

Description of technology and comparators

Antibacterial-coated sutures are developed with the aim to reduce the risk of SSI by minimizing the risk of colonization of the suture by bacteria commonly associated with such infections. Surgical sutures coated with triclosan and surgical sutures coated with chlorhexidine are currently on the market, and some others are in the development phase [1] (**B0001**).

Triclosan-coated sutures

Plus sutures *(MONOCRYL™ Plus Antibacterial suture*, *Coated VICRYL™ Plus Antibacterial Suture* and *PDS™ Plus Antibacterial suture)* are absorbable sutures which contain the purest form of the antibacterial agent triclosan (Irgacare MP®).

Triclosan prevents/reduces colonization of the suture by bacteria commonly associated with SSI development. In vitro studies have shown that triclosan-coated sutures placed in an agar plate create a zone of inhibition, which can last up to 23 days. Furthermore, in animal studies the antibacterial sutures inhibit bacterial colonization of the suture after direct in vivo challenge with bacteria [2-4,5] (**B0001**).

The zone of bacterial inhibition surrounding the knotted sutures using Vicryl® Plus showed an antimicrobial effect over *Staphylococcus aureus*, *Staphylococcus epidermis* and its Methicillin resistant strains [3,6,7] (**B0001**).

Using zone of inhibition studies, Monocryl® Plus and PDS® Plus antibacterial Suture have been shown to inhibit colonization of the suture by *Staphylococcus aureus*, *Staphylococcus epidermidis*, Methicillin-Resistant *S.aureus*, Methicillin-resistant *S.epidermidis*, *Echerichia coli* and *Klebsiella pneumoniae*. The clinical significance of this finding is unknown [2,4,5] (**B0001**).

Adverse reactions associated with these devices include transient local irritation at the wound site, transient inflammatory foreign body response and erythema and induration during absorption with subcuticular sutures, as well as allergic reaction to Irgacare MP (triclosan). Like all foreign bodies, PDS® Plus Antibacterial Suture may potentiate an existing infection. As with any foreign body, prolonged contact of any suture with salt solutions, such as those found in the urinary or biliary tracts may result in calculus formation. Monocryl™ Plus Antibacterial suture, Coated Vicryl™ Plus Antibacterial Suture and PDS™ Plus Antibacterial suture should not be used in patients with known allergic reactions to Irgacare® MP (triclosan). This suture may be inappropriate in elderly,

malnourished or debilitated patients, or in patients suffering from conditions which may delay wound healing, as with all absorbable sutures (**B0001**).

Chlorhexidine-coated sutures

Antibacterial Surgical Sutures coated with chlorhexidine of different manufacturers are also available on the market. Chlorhexidine has activity against gram-positive and gram-negative organisms, facultative anaerobes, aerobes, and yeast; it is both bacteriostatic and bactericidal, depending on its concentration. The bactericidal effect of chlorhexidine is a result of the binding of this cationic molecule to negatively charged bacterial cell walls and extramicrobial complexes. At low concentrations, this causes an alteration of bacterial cell osmotic equilibrium and leakage of potassium and phosphorous, resulting in a bacteriostatic effect. At high concentrations of chlorhexidine, the cytoplasmic contents of the bacterial cell precipitate and result in cell death (**B0001**).

Comparators

Non-antibacterial coated sutures were used as comparators in this assessment: Vicryl® (Ethicon); Monocryl® (Ethicon) and PDS® II (Ethicon). Adverse effects associated with the use of these devices include wound dehiscence, failure to provide adequate wound support in closure of the sites where expansion, stretching or distension occur, failure to provide adequate wound support in elderly, malnourished or debilitated patients or in patients suffering from conditions which may delay wound healing, infection, minimal acute inflammatory tissue reaction, localized irritation when skin sutures are left in place for longer than 7 days, suture extrusion and delayed absorption in tissue with poor blood supply, calculi formation in urinary and biliary tracts on prolonged contact with salt solutions such as urine and bile occurs, and transitory local irritation at the wound site (**B0001**).

Indications (A0020)

Triclosan-coated sutures

Vicryl® Plus sutures are intended for use in general soft tissue approximation and/or ligation, including microsurgery for vessels less than 2 mm in diameter. The safety and effectiveness of Vicryl® Plus sutures in cardiovascular tissue, ophthalmic surgery and neurological tissue have not been established [3].

Monocryl® Plus Antibacterial Sutures are intended for use in general soft tissue approximation and/or ligation where an absorbable material is indicated [2].

PDS® Plus Antibacterial sutures are intended for use in general soft tissue approximation, including use in paediatric cardiovascular tissue, and in ophthalmic surgery (other than contact with cornea and sclera). These sutures are particularly useful where the combination of an absorbable suture and extended wound support (up to six weeks) is desirable [4].

Chlorhexidine-coated sutures

Assufil® plus sutures are intended for use in all surgical procedures, at the user's discretion [8].

Egycryl extra sutures are intended for use in general soft tissue approximation and/or ligation including ophthalmic surgery, peripheral nerve anastomosis and microsurgery for vessels less than 2 mm in diameter [9].

Neosorb® Plus Synthetic Absorbable Surgical Suture is indicated for use in general soft tissue approximation and/or ligation, but not for use in ophthalmic, cardiovascular and neurological procedures [10].

The claimed benefit of triclosan-coated sutures is to reduce or prevent the risk of SSI. By destroying its cell membrane, triclosan prevents colonization of the most common gram-positive and gram-negative bacteria associated with SSI. Triclosan has been used for several decades and it was shown not to have carcinogenic potential or genotoxicity. It is rapidly absorbed, well distributed, metabolised and excreted from the human body, which reflects a minimal impact on the patient and environment [5] (**B0002**).

Health problem

Surgical wound infection or SSI is a type of healthcare-associated infection in which a wound infection occurs after an invasive (surgical) procedure. SSI is also defined as an infection that occurs within 30 days after the operation and involves the skin and subcutaneous tissue of the incision (superficial incisional) and/or the deep soft tissue (for example, fascia, muscle) of the incision (deep incisional) and/or any part of the anatomy (for example, organs and spaces) other than the incision that was opened or manipulated during an operation (organ/space) [11]. Overall, *Staphylococcus aureus* and *Escherichia coli* were the most commonly reported microorganisms (**A0002**).

SSI occurs after pathogenic organisms multiply in a wound and cause local signs and symptoms: heat, redness, pain and swelling. In serious cases, SSIs manifest with systemic signs of fever or a raised white blood cell count (**A0005**).

SSI is a frequent type of nosocomial infection, accounting for about 14% to 15% of the total number of nosocomial infections and roughly 5% of all surgical complications [12]. The total incidence of SSI is as follows: 5.6 SSIs per 100 surgical procedures in developing countries; 2.6 per 100 surgeries in the United States and 2.9 per 100 surgeries in European countries [13]. The highest cumulative incidence was for colon surgery with 9.5 episodes per 100 operations, followed by 3.5% for coronary artery bypass graft, 2.9% for caesarean section and 1.4% for cholecystectomy [14,15] (**A0002**).

Abdominal surgery presents a particular risk factor for development of SSI. The incidence of SSI following abdominal surgery varies according to the nature of the procedure undertaken (laparoscopic surgery compared with open surgery) and the degree of wound contamination. The frequency of SSI after midline laparotomy varies between 12% and 16%, depending on definition, patient population, and study design [16]. According to the classification of surgery wounds from the CDC, gastric cancer surgery falls into class II (clean-contaminated). In typical class II surgeries, SSI rates are reportedly 5%–15%. In the case of a planned and prepared gastrectomy (i.e., laparotomy), the rate remarkably drops to lower than 5% [17]. Open colon and rectal procedures are classified as clean-contaminated: in elective colorectal operations, the international SSI rates are 4.7%–25% [18] (**A0002**).

A relevant number of SSIs are preventable, by applying various invasive and non-invasive interventions. Measures can be taken in the pre-, intra- and postoperative phases of care to reduce risk of infection. The prevention measures include for example: removal of microorganisms that normally colonise the skin, prevention of the multiplication of microorganisms at the operative site (for example by using prophylactic antimicrobial therapy), enhancing the patient's defences against infection (for example by minimising tissue damage and maintaining normothermia) and preventing access of microorganisms into the incision postoperatively by use of wound dressings (**A0025**)**.**

The WHO panel suggests the use of triclosan-coated sutures for the purpose of reducing the risk of SSI, independent of the type of surgery. Their recommendation is conditional, with moderate quality of evidence noted [15].

According to the Surgical Site Infection Guidelines Update 2016, recently published by the American College of Surgeons and Surgical Infection Society [19], the use of triclosan-coated suture is recommended for wound closure in clean and clean-contaminated abdominal cases when available (**A0025**).

The target population in this assessment are adult patients undergoing elective or emergency setting open (laparotomy) or minimally invasive (i.e. laparoscopic) abdominal surgery. Types of incision used for open abdominal surgery, e.g. midline/transverse/Pfannenstiel, were not used to restrict participant selection (**A0007**).

Methods

For Effectiveness (EFF) and Safety (SAF) domains, a systematic literature search according to the predefined search strategy (without limitations) was performed in October 2016, according to the Cochrane methodology, in standard medical and HTA databases (The Cochrane Central Register of Controlled Trials, The Database of Abstracts of Reviews of Effects, The Health Technology Assessment Database, NHS Economic Evaluation Database, MEDLINE, EMBASE; all via OvidSP, and CINAHL via EBSCOhost). A hand search (of the reference lists of relevant studies) was also done. The following clinical trial registries were searched for ongoing clinical trials and observational studies, in November 2016: ClinicalTrials.gov (http://www.clinicaltrials.gov/), WHO International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/Default.aspx) and the EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/).

A separate Guideline (GL) search (G-I-N, National Guidelines Clearinghouse, TRIP-Database and hand search) was performed as well, in October 2016, with a further update in November 2016.

The manufacturer of triclosan-coated sutures, Ethicon/Johnson & Johnson, was contacted by the assessment coordination team and completed the EUnetHTA submission file for medical devices between 14/09/2016 and 25/10/2016. Three manufacturers of chlorhexidine-coated sutures (Assut Europe, Samyang Genex, Taisier Med) were contacted by the coordination team but did not respond to questions related to their medical devices.

An update of existing systematic reviews (SRs) was not possible, and a new SR of RCTs with a meta-analysis on one critical primary outcome – incidence of total incisional SSIs – was performed. Risk ratios were calculated for dichotomous variables, and when a sufficient number of comparable trials were available, trials were pooled in a meta-analysis. The meta-analysis

combined results of studies (or included only the studies) that were considered clinically homogenous in terms of participants, interventions and outcomes using the RevMan3 software. We have used the odds ratio (OR), along with the appropriate 95% confidence intervals (CI), and the Mantel-Haenszel method for the meta-analysis. Since we expected considerable methodological heterogeneity in the included studies, we have used a random-effects model for the meta-analysis.

For TEC and CUR domains, no quality assessment tool was used, but multiple sources were used in order to validate individual, possibly biased, sources.

The quality of the included systematic review (SR) was assessed using the AMSTAR and R-AMSTAR tools [20, 21].

The results from the included SRs were intended to be included according to the methodology suggested by Whitlock 2008 [22] and Robinson 2014 [23] on how to integrate existing SRs into new SRs. To answer our research questions, only one out of four possible approaches in using existing SRs described in Robinson et al. 2014 [23] was used: (1) using the existing SR(s) listing of included studies as a quality check for the literature search and screening strategy conducted for the new review (Scan References). For all previously published and newly identified primary studies, the risk of bias of included RCTs was evaluated independently by two reviewers. The Cochrane risk of bias assessment approach was used for RCTs [24], on the study level, on one critical primary outcome – the incidence of total incisional SSIs and on safety outcome – incidence of adverse events (AEs). Quality of data in RCTs, related to one critical primary outcome – the incidence of total incisional SSIs – and on safety outcome – incidence of AEs was assessed using the GRADE methodology [25].

Results

Available evidence

From the recently published SR/MA by Sandini et al., 2016 [26], the listing of included studies was used as a quality check for the literature search conducted for the new review (Scan References), according to the methodology suggested by Whitlock 2008 [22] and Robinson 2014 [23]. Using the data extraction and/or analyses from this SR was not possible due to two reasons: the scope was too narrow, including only patients with elective colorectal surgery, and the search strategy was not described.

For the Effectiveness domain, data from 7 RCTs were analysed. For the Safety domain, in addition to the already mentioned RCTs, data from 7 prospective non-randomised studies were included (five observational, one interventional non-randomised clinical pathway driven study and one interventional single arm study).

Clinical effectiveness

Seven RCTs published between 2011 and October 2015 were included in our relative effectiveness assessment, with a total of 3580 patients randomised; 1879 (52.4%) to triclosan-coated sutures and 1707 (47.6%) to non-antibacterial coated sutures.

No RCTs were found investigating other antibacterial-coated sutures.

Diener et al., 2014, reported a total of 29 deaths; the difference between the two groups was not statistically significant: 9 (1.5%) patients died in the intervention group, whereas 20 (3.3%) died in the control group /OR 0.46 (0.21 to 1.01), p=0.48/. All deaths were classified as unrelated to the trial intervention and most of the postoperative deaths were due to septic shock, multiple organ failure or cardiac and pulmonary decompensation [27]. Ruiz-Tovar et al., 2015, reported a total of 9 (8.2%) deaths, affecting 5 patients in the intervention group and 4 patients in the control group (not statistically significant). Mortality causes were multi-organ failure secondary to septic status [28] (**D0001**).

The incidence of total incisional SSIs was significantly lower in triclosan-coated sutures in comparison with non-antibacterial coated sutures in 4 RCTs [28-31]. In three RCTs, the difference was not statistically significant [27,32,33]. The same was true for the incidence of superficial and deep incisional SSIs, specifically analysed in two RCTs [27,33].

The meta-analysis on total incisional SSIs of the data pooled from 7 RCTs comparing triclosan-coated sutures vs non-antibacterial coated sutures demonstrated a statistically significant benefit of triclosan-coated sutures in reducing the risk of total incisional SSIs /**OR 0.65 (95% CI 0.44,0.96), p=0.03/**. Heterogeneity among included RCTs was moderate, I^2 = 61%.

We did not find a significant difference between triclosan-coated sutures in SSIs rates in the colorectal or hepatobiliary or upper-gastrointestinal subgroup (p=0.77).

Data from two RCTs [27,30] comparing PDS Plus vs PDS II showed no statistically significant difference in reducing risk of total incisional SSIs /OR 0.72 (95% CI 0.43,1.21), p=0.22/. Heterogeneity among included RCTs was moderate, I^2 = 69%.

Data from three RCTs [28,29,31] comparing Vicryl Plus vs Vicryl showed that Vicryl Plus significantly reduced the risk of total incisional SSIs /**OR 0.33 (95% CI 0.19,0.58), p=0.0001**/. Heterogeneity among included RCTs was low, I^2 = 0%.

The effect of antibacterial coated sutures was similar to non-antibacterial coated sutures in trials with clean-contaminated wounds and mixed trials with a whole patients sample with the whole range of wound types, and separately in trials with clean, clean-contaminated and contaminated wounds. Heterogeneity among included RCTs was moderate, I^2 =62%, and for the subgroup the difference was high, I^2 =76.1%.

In one trial with dirty wounds [28], the effect of triclosan-coated sutures was statistically significant in reducing the SSIs risk /**OR 0.20 (95% CI 0.07, 0.60), p=0.004**/.

Significant differences were found in high or unclear risk of bias RCTs /**OR 0.50 (95% CI 0.30,0.81), p=0.005,** I^2 =51%/ but not in low risk of bias RCTs /OR 0.96 (0.72,1.28), p=0.76, I^2 =0%/ (**D0005**).

The length of hospital stay was an outcome in all 7 RCTs; only in one RCT the length was statistically different in favour of the triclosan-coated surgical sutures group [29]. In one RCT it was pointed out that with normal wound healing, the average number of nursing days was nine, whereas for SSI patients it was 15 (p = 0.043) [32].

Regarding the other secondary outcomes assessed in our SR, no conclusion could be made due to the lack of or different results of reported data. In two RCTs the difference between the intervention and control group was statistically different, in favour of triclosan-coated sutures [27,29]. The opposite was true for one RCT [30] in which major wound revision was higher in the triclosan-coated sutures group.

Complete abdominal wound dehiscence was reported in two RCTs: in both trials it was statistically significantly lower in the intervention than in the control groups [27,29]. Incisional hernia was reported in one RCT [29], but the difference between the two groups was not statistically significant (**D0005**).

None of the 7 included RCTs specifically assessed the effect of antibacterial-coated sutures on patient body functions and the effect of antibacterial-coated sutures on activities of daily living (**D0011, D0016**).

Quality of life was assessed only in one RCT [27] and did not differ between the groups. (**D0012, D0013).** None of the 7 included RCTs assessed patient satisfaction (**D0017**).

Safety

Out of seven RCTs, four RCTs (with high risk of bias) did not specify AEs as an outcome or report them [28, 30-32]. In two RCTs, AEs were not specified as an outcome, but reported [29,33], and in only one RCT (with unclear risk of bias) SAEs were specified in the study protocol and reported in the published article [27].

In five out of seven prospective non-randomised studies, AEs were neither specified as an outcome nor reported; in two studies, AEs were not specified as outcome but reported [34,35].

Only one RCT [27] reported the frequency of SAEs, which was not statistically different between the intervention (146/583) and control (138/602) group (p=0.39).

In brief, local AEs were mentioned in 2 RCTs: in one RCT [29] postoperative inflammatory reactions to the skin sutures were statistically significantly higher in the comparator group using polyglactin 910 Vicryl (7/91 vs 16/93, p<0.05) than in the intervention group (triclosan-coated polyglactin 910 Vicryl Plus). In another RCT in which two different triclosan-coated sutures were used in the intervention group (triclosan-coated polyglactin - 0 Vicryl Plus and triclosan-coated polydioxanone - PDS Plus) [33], incisional haematoma was statistically higher in the intervention group /OR 4.71 (1.31–16.91), p=0.02/. No significant differences were observed for skin swelling, redness or wound seroma.

Systemic SAEs were reported in three studies [27,34,35], but investigators found a majority of them being unrelated to the intervention. None of them were statistically different between groups (**C0008**).

Upcoming evidence

No ongoing RCTs or other studies with triclosan-coated sutures and chlorhexidine coated sutures in abdominal surgery were identified in the following clinical trials registries: ClinicalTrials.gov (http://www.clinicaltrials.gov/), WHO International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/Default.aspx) and the EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/) after a search performed on 28/11/2016.

Reimbursement

No data about the reimbursement status in corresponding countries have been found during the literature search, and the specific data were not available in the evidence submission file

completed by Johnson & Johnson International [5]. EUnetHTA JA3 Partners were not approached to provide these data.

In Croatia, surgical sutures are financed as a part of the surgical treatment according to a Diagnosis-related Group (DRG) system. Multiple services which are invoiced during one episode of surgical treatment are summarised under one DRG code [36]. In Germany, antibacterial-coated suture material is reimbursable within the DRG-based hospital payment. Hospitals do not receive extra payment when using this type of suture; they rather receive a fixed amount of payment and have to decide for themselves whether they want to use this money for buying antibacterial-coated sutures (**A0021**).

Table 1: Summary table of relative effectiveness of triclosan-coated sutures

	Health benefit* (RCTs only)						**Harm (RCTs and non-RCTs)**	
	Total incisional SSIs (7 RCTs)	**Mortality** (2 RCTs)	**Quality of life** (1 RCT)	**Length of hospital stay** (7 RCTs)	**Wound dehiscence** (2 RCTs)	**Incisional hernia** (1 RCT)	**SAEs** (1 RCTs and 2 non-RCTs)	**AEs** (2 RCTs)
Triclosan-coated sutures **Non-antibacterial coated sutures**	**OR 0.65** **(95% CI 0.44, 0.96), p=0.03** (D0005)	OR 0.46 (0.21 to 1.01); p=0.48 [27] 9 (8.2%) /5 vs 4, not significant/ [28] (D0001)	EQ-5D visual analogue scale p=0.34; EQ-5D index p=0.18 [27] (D0012, D0013)	1.2±1.3 vs 21.4±2.8; **p<0.05** [29] Other 6 RCTs: not significant [27,28,30-33] (D0006)	1 (1.1) vs 7 (7.7); **p=0.027** [29] 9 (1.9) vs 22 (4.5); 0.40 (0.18-0.88), **p=0.01** [27] (D0006)	2 (2.2) vs 5 (5.5); p=0.235 [29] (D0006)	146 vs 138,p=0.39 [27] 8 (0.87) [34] Pancreatic fistula 22 (25) vs 25 (23.7), p=0.71; Delayed gastric emptying 8 (9) vs 15 (14.6); p=0.32 [35] (C0008)	Postoperative inflammatory reactions to the skin sutures: 7 (7.5) vs 16 (17.5); **p<0.05** [29] Overall incision complications 64 (45.7) vs 54 (38.3) 4.71 (1.31–16.91), p=0.21 [33] Incision hematoma13 (9.3) vs 3 (2.1); 4.71 (1.31–16.91), **p=0.02** [33] (C0008)
Quality of body of evidence*	***Moderate***	***Not assessed***	***Not assessed***	***Not assessed***	***Not assessed***	***Not assessed***	***Not assessed****	***Low****

Abbreviations: AE=adverse event; OR=odds ratio

* For health-benefit outcomes: Body functions, Activities of daily living and Patient satisfaction; evidence was not available.

** GRADE, High = We are very confident that the true effect lies close to that of the estimate of the effect; Moderate = We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; Low = Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

*** High Cochrane Risk of Bias and low quality of evidence according the GRADE for RCTs; 2 non-RCTs were not assessed for RoB and quality according the GRADE (observational studies are primarily graded as low quality unless upgraded by review authors to moderate or high quality, if the effect is large enough)

Discussion

Results from our SR, including a meta-analysis performed on the primary outcome related to total incisional SSIs, are based on the data pooled from 7 RCTs comparing triclosan-coated sutures to non-antibacterial coated sutures. A statistically significant benefit of triclosan-coated sutures in reducing the risk of total incisional SSIs was demonstrated. Heterogeneity among included RCTs was moderate and the majority of studies have a high or unclear risk of bias. In subgroup analysis a significant differences were found in high or unclear risk of bias RCTs but not in low risk of bias RCTs. Heterogeneity among included RCTs was moderate, and for subgroups the difference was high. According to the GRADE assessment, the quality of these RCTs was moderate. No clinical studies were found on chlorhexidine-coated sutures.

The choice of the primary outcome (incidence of incisional SSIs, as critical outcome) is representative, according to the guidelines; all RCTs reported this outcome. Mortality was not specified as an outcome or reported in 3 RCTs. The length of hospital stay was an outcome in all 7 RCTs. Regarding the other secondary outcomes assessed in our SR, no conclusion could be made due to the lack of or different results of reported data. None of the 7 included RCTs specifically assessed the effect of antibacterial-coated sutures on patient body functions and the effect of antibacterial-coated sutures on activities of daily living. Quality of life was assessed only in one RCT. None of the 7 included RCTs assessed patient satisfaction.

The population (adults) included in 7 RCTs is representative of patients usually included in such clinical trials. Baseline characteristics show that the studies included similar groups of patients. The majority of patients had clean and clean-contaminated wounds and underwent colorectal surgery. There were a small number of patients with dirty wounds as well as patients with laparoscopic or emergency surgery. SSI was defined according to the Centres for Disease Control and Prevention of Atlanta criteria in 5 trials. Antibiotic prophylaxis was given in all RCTs, but in one trial was followed by further antibiotic treatment for at least 7 days (patients with faecal peritonitis).

Paediatric patients were not within the scope of this assessment. Trial results cannot be directly extrapolated between adults and children, because children have different physiological characteristics and different risk factors for surgical site infections. Future trials should focus on individual types of paediatric surgery to evaluate a potential beneficial effect.

RCTs included patients worldwide. Four were multicentre studies, with a range of 4 to 24 hospitals and 3 single centres. This is representative for the expected use.

No ongoing RCTs or other studies with triclosan-coated sutures and chlorhexidine coated sutures in abdominal surgery were identified in clinical trials registries.

The poor reporting of harms data (safety data is inadequately reported or not reported at all) has major implications for a proper evaluation of the benefit-risk ratio. According to the GRADE assessment, the quality of evidence (in three RCTs with reported AEs) was low. Limitations of data from published studies are obvious, so further research, in form of RCTs including pragmatic RCTs and observational registries studies, is needed on the safety of triclosan-coated sutures and other antibacterial coated sutures already registered on the market, like chlorhexidine-coated sutures. Clear reporting of AEs is needed, including the need to assess the risk of allergy and monitoring possible antimicrobial resistance to the respective antimicrobial agent [15].

Data reporting should be done according to evidence-based reporting guidelines, specifically the CONSORT Statement extension on better reporting of harms in RCTs and trials assessing non-

pharmacological treatments [37,38], as well as the PRISMA harm checklist [39]. New recommendations to improve adverse event reporting for medical devices in clinical trial publication, like the ones recently published on pharmaceuticals, is clearly needed [40].

Conclusion

All the clinical data assessed in this report are related to triclosan-coated sutures. No published clinical studies on chlorhexidine-coated sutures have been identified.

A statistically significant benefit of triclosan-coated sutures in reducing the risk of total incisional SSIs was demonstrated in our SR/MA, based on moderate quality RCTs data.

Comparisons with other antimicrobial sutures are needed, since we did not find any published clinical studies despite the fact that chlorhexidine-coated sutures are already on the market. All studies should be designed as an RCT with the SSI outcome defined according to CDC criteria and sub-specified as superficial, deep and organ space SSIs.

The relative safety of triclosan-coated sutures could not be confirmed due to a lack of reporting of AEs in RCTs and non-RCTs included in our assessment. The same is true for chlorhexidine-coated sutures because no clinical studies were found during our literature search.

Ten years after the launch, the manufacturer Ethicon has not been contacted by any regulatory body concerning the use of IRGACARE®† MP on Plus Sutures.

1 SCOPE

Description	Project scope
Population	• Patients: **Adult patients having elective or emergency open (laparotomy) or minimally invasive abdominal (i.e. laparoscopic) surgery** ICD-10 codes:K20-K31; K35-K38; K40-K46; K55-K64; K65-K66; K70-K76; K80-K86; K91-K92…(types of incision used for open abdominal surgery, e.g. midline/transverse/Pfannenstiel, will not be used to restrict participant selection) • Mesh-terms: Abdomen/surgery; Laparotomy [D007813, E04.406]; Laparoscopy [D010535, E01.370.388.250.520, E04.502.250.520] Abdominal Wound Closure Techniques [E04.987.100]; Suture Techniques; Surgical Wound Infection • Intended use of the technology: Treatment and Prevention
Intervention	**Antibacterial-coated absorbable surgical sutures for abdominal wall closure:** • **Antibacterial Surgical Sutures coated with triclosane**: Antimicrobial triclosan-coated suture Polyglactin 910 - Vicryl Plus, Monocryl Plus Antimicrobial triclosan-coated suture Polyglecaprone and Antimicrobial triclosan-coated suture Polydioxanone - PDS Plus, Ethicon, Johnson & Johnson Company Int. • **Antibacterial Surgical Sutures coated with chlorhexidine**: i.e. Assufil Plus (Assut Europe), Neosorb Plus (Samyang Genex), Egycryl Extra (Taisier-Med) • MeSH-terms: Sutures, Anti-Bacterial Agents, Triclosan, Chlorhexidine
Comparison	• **Non-antibacterial coated absorbable surgical suture** (equivalent standard)**:** absorbable i.e. Vicryl, Monocryl, PDS II, Ethicon, Johnson & Johnson Company Int. • Studies using other methods of wound closure in the comparator arm (e.g. staples, or skin glue) will not be included. • Rationale: Comparators have been chosen based on information from relevant published HTAs, clinical guidelines [12,14,15] and EUnetHTA guidelines [41] and they represent current and usual therapeutic solutions for repairing the abdominal wall after surgical procedures. • Mesh-terms: Sutures [E07.858.690.820]; Catgut [E07.858.690.820.250]
Outcomes	**EFF Domain** ***Primary:*** • Incidence of superficial and deep incisional surgical site infections (SSIs), according to the US Center for Disease Control and Prevention (CDC) criteria [11,42] in patients undergoing abdominal surgery; • Mortality ***Secondary****:* • Quality of life.

Description	Project scope
	• Length of hospital stay. • The proportion of patients requiring secondary surgery for wound-related complications of surgery. • The proportion of patients requiring hospital readmissions for SSI/wound-related complications • The incidence of complete abdominal wound dehiscence within 30 days of surgery. • The incidence of incisional hernia during the period of study follow-up. • Causative microorganism of SSI (Results of microbiological cultures in patients with SSI) • The use of systemic antibiotic therapy within 30 days of surgery. • Patient satisfaction. **SAF Domain** • **Adverse events (AEs)** /Any AEs, Serious AE (SAE), most frequent AEs and SEAs, Death as SAE/ • ***From the Checklist for potential ethical, organisational, patient and social and legal aspects***, if needed. • Rationale: Outcomes will be selected based on the recommendations from the relevant HTAs, clinical guidelines [12,14,15,43] and the EUnetHTA Guidelines on Clinical and Surrogate Endpoints and Safety [41].
Subgroups analysis **(If possible with available data)**	• Emergency versus elective surgery; • Open versus laparoscopic surgery; • The nature of the surgical procedure (e.g. oesophagogastric, hepato-pancreato-biliary, colorectal etc.) • The type of surgical incision (midline, transverse, Pfannenstiel etc.) • The degree of wound contamination, according to the US Centre for Disease Control and Prevention (CDC) criteria [42]; • Antibiotic prophylaxis (received vs not received)
Study design	**Effectiveness:** If suitable evidence syntheses (SRs/HTA reports) are available: • evidence syntheses (SRs/HTA reports) and • primary studies (as described in next bullet) published after the last search date of the latest SR/HTA document If suitable evidence syntheses (SRs/HTA reports) are NOT available: • Randomised controlled trials **Safety:** If suitable evidence syntheses (SRs/HTA reports) are available: • evidence syntheses (SRs/HTA reports) and • primary studies (as described in next bullets) published after the last search date of the latest SR/HTA document If suitable evidence syntheses (SRs/HTA reports) are NOT available:

Description	Project scope
	• Randomised controlled trials • Non-randomised controlled trials • Prospective studies with or without a control group • Medical device adverse event registers and • Postmarketing surveillance data on device-related adverse events **Organisational, ethical, patient and social, legal aspects:** Qualitative and quantitative studies, reports or opinions (according to the EUnetHTA Core HTA Model® 3.0, p. 264) [44]. Only English language studies will be included in this Rapid REA.

2 METHODS AND EVIDENCE INCLUDED

2.1 Assessment Team

Description of the distribution of responsibilities and the workload between authors and co-authors:

AAZ (1st authors):

- Develop first draft of the EUnetHTA project plan;
- Perform the literature search;
- Carry out the assessment: answer assessment elements, fill in the checklist regarding potential "ethical, organisational, patient and social and legal aspects" of the HTA Core Model® for rapid REA;
- Send "draft versions" to reviewers, compile feedback from reviewers and perform changes according to reviewer comments;
- Prepare the final assessment including a final summary of the assessment.

NSPHMPDB (co-authors):

- Review the draft EUnetHTA project plan;
- Check and approve all steps (e.g. literature selection, data extraction, assessment of risk of bias);
- Agree with the 1st author's conclusions;
- Review the draft assessment, propose amendments where necessary (perform additional hand search of literature if needed) and provide written feedback.

2.2 Source of assessment elements

The selection of assessment elements was based on the EUnetHTA Core Model® Application for Rapid Relative Effectiveness (REA) Assessments (4.2) [45]. The Checklist for potential ethical, organisational, patient and social and legal aspects of the HTA Core Model® for rapid REA was filled in as well. Additionally, further assessment elements from the EUnetHTA Core Model® domains: ethical analysis, organisational aspects, patients and social aspects, legal aspects – relevant for medical and surgical interventions – were included if deemed relevant (3.0) [44].

The selected issues (generic questions) were translated into actual research questions (answerable questions).

2.3 Search

For EFF and SAF domains, a systematic literature search according to the predefined search strategy (without limitations) was performed in October 2016, according to the Cochrane methodology, in standard medical and HTA databases (The Cochrane Central Register of Controlled Trials, The Database of Abstracts of Reviews of Effects, The Health Technology Assessment Database, NHS Economic Evaluation Database, MEDLINE, EMBASE, all via OvidSP and CINAHL via EBSCOhost). Additionally, a hand search (according to the reference lists of

relevant studies) was done. The following clinical trials registries were searched for ongoing clinical trials and observational studies, in November 2016: ClinicalTrials.gov (http://www.clinicaltrials.gov/), WHO International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/Default.aspx) and the EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/).

A separate GL search (G-I-N, National Guidelines Clearinghouse, TRIP-Database and hand search) was performed as well in October 2016, with a further update in November 2016.

The manufacturer of triclosan-coated sutures, Ethicon/ Johnson & Johnson, was contacted by LBI-HTA (coordination team) and completed the EUnetHTA submission file for medical devices between 14/09/2016 and 25/10/2016. Three manufacturers of chlorhexidine-coated sutures (Assut Europe, Samyang Genex, Taisier Med) were contacted by LBI-HTA but did not respond to questions related to their medical devices.

Relevant references (after duplicates were removed) were screened and assessed for eligibility independently by two reviewers. References were included or excluded according to the overall research question, Population-Intervention-Control-Outcome (PICO)-scheme (as described in the Project Scope) and the predefined inclusion/exclusion criteria, and presented according to the PRISMA Statement [46].

Inclusion criteria: one or more of the EFF and SAF outcomes are reported; sufficient methodological details are reported to allow critical appraisal of study quality; publication in English; report on humans only.

Exclusion criteria: primary or secondary studies which report preliminary study results; no data provided for our outcomes of interest in an extractable format; papers with RCTs without sufficient methodological details to allow critical appraisal of study quality; papers (publications) published in a language other than English; duplicate of original publication.

Differences in selection results were discussed in order to achieve consensus; a third reviewer was involved in case of disagreement.

Data extraction was performed by one reviewer in pre-defined extraction tables and double-checked regarding completeness and accuracy by a second reviewer. Any differences in extraction results were discussed to achieve consensus; any disagreements were resolved by a third reviewer. Co-authors checked and verified this step as well. An update of existing SRs was not possible and a new SR of RCTs with meta-analysis on one primary outcome – incidence of total incisional SSIs – was performed.

2.4 Study selection

857 records were identified through database searching and 10 additional records were identified through other sources; 699 remained after duplicates were removed. Thirty full-text articles were assessed for eligibility, and after the exclusion of 22 full-text articles, one moderate quality SR and 7 RCTs were included in our SR for EFF domain. For the SAF domain, 7 prospective non-randomised studies were included in addition (five observational, one interventional non-randomised clinical pathway driven study and one interventional single arm study), adding up to a total of 15 studies.

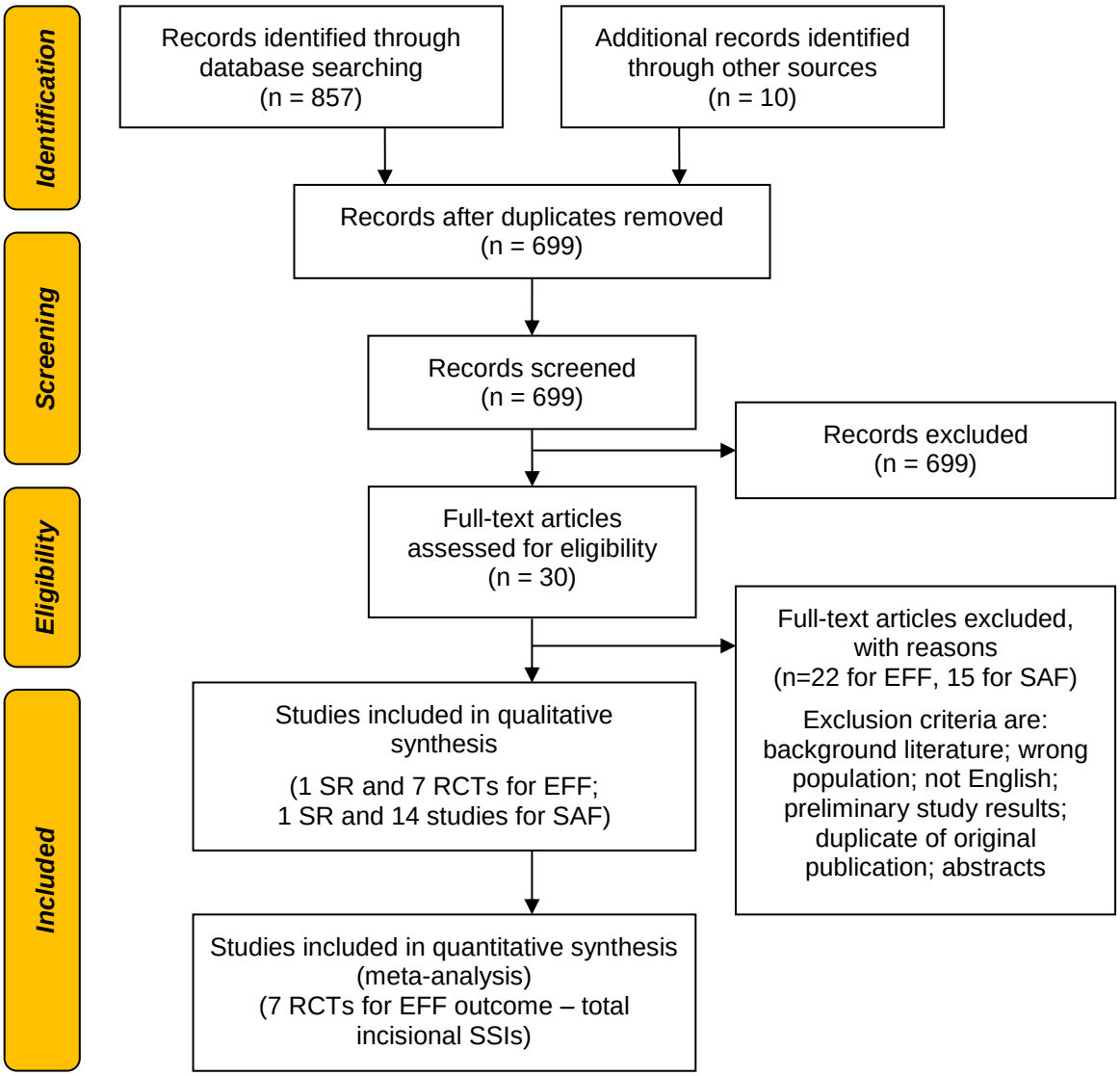

Figure 1: Flow chart

2.5 Quality rating of studies

For TEC and CUR domains, no quality assessment tool was used, but multiple sources were used in order to validate individual, possibly biased sources. Descriptive analysis was performed on different information sources. The completed part of the EUnetHTA Submission file from the manufacturer was used as well.

For assessment elements from other domains (ETH, ORG, SOC, LEG), if deemed relevant: hand search, internet search and contacting manufacturers (part of submission file) was conducted. No quality assessment tool was utilised, but multiple sources were used in order to validate individual, possibly biased sources.

The quality of the included SR was assessed using the AMSTAR and R-AMSTAR tools [20,21].

The results from the included SRs were planned to be included according to the methodology suggested by Whitlock 2008 [22] and Robinson 2014 [23] on how to integrate existing SRs into new SRs. To answer our research questions, only one out of four possible approaches in using

existing SRs, described in Robinson et al. 2014 [23], was used: (1) using the existing SR(s)' listing of included studies as a quality check for the literature search and screening strategy conducted for the new review (Scan References). It was not possible to use the other three approaches: (2) using the existing SR(s) to completely or partially provide the body of included studies for one or more Key Questions in the new review (Use Existing Search); (3) using the data abstraction, risk of bias assessments and/or analyses from existing SRs for one or more Key Questions in the new review (Use Data Abstraction/Syntheses), and (4) using the existing SR(s), including conclusions, to fully or partially answer one or more Key Questions in this SR (Use Complete Review).

For all previously published and newly identified primary studies, the risk of bias of included RCTs was evaluated independently by two reviewers. The Cochrane risk of bias assessment approach was used for RCTs [24], on study level, on one critical primary outcome – the incidence of total incisional SSIs and on safety outcome – incidence of adverse events (AEs). Quality of data in RCTs, related to one critical primary outcome – the incidence of total incisional SSIs – and on safety outcome – incidence of AEs was assessed using the GRADE methodology [25]. This approach specifies four levels of quality: High: further research is very unlikely to change our confidence in the estimate of effect; Moderate: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimates; Low: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: we are very uncertain about the estimate.

2.6 Description of the evidence used

Based on the recently published SR/MA by Sandini et al., 2016 [26] (details can be found in the Appendix 1, Table A6), with the primary aim to compare the effect of triclosan-coated suture with uncoated suture on the incidence of SSI after elective colorectal operation in published RCTs, the listing of included studies was used as a quality check for the literature search conducted for the new review (Scan References), according to the methodology suggested by Whitlock 2008 [22] and Robinson 2014 [23]. Using the data abstraction and/or analyses from this SR was not possible due to two reasons: the scope was too narrow, including only patients with elective colorectal surgery, and the search strategy was not described. The quality of this SR was assessed using AMSTAR and R-AMSTAR tools [20,21]: the total score was 35/44 (Table A6, Appendix 1).

For the Effectiveness domain, data from 7 RCTs were analysed, and for the Safety domain, in addition to the already mentioned RCTs, data from 7 prospective non-randomised studies were included (five observational, one interventional non-randomised clinical pathway driven study and one interventional single arm study (Table 2, Table A7 and Table A8 in the Appendix 1).

Table 2: Main characteristics of studies included

Author and year or study name	Study type / Surgery	Number of patients	Intervention(s)	Main endpoints	Included in clinical effectiveness and/or safety domain
Baracs et al. 2011 [32] NCT01123616	RCT / Open elective for Colorectal	385 / 188 vs 197 (188 vs 197 analysed for total incisional SSIs)	Triclosan-coated polydiaxanone PDS vs triclosan uncoated PDS (fascia closure) Triclosan-coated poliglecaprone 25 (Monocryl Plus) vs triclosan uncoated poliglecaprone 25 (Monocryl) (skin closure)	The number of SSIs after colorectal surgery; the length of the hospital stay, any additional costs, and chances of late SSI after discharge of the patient from the hospital. AEs not specified as outcome nor reported	**Clinical effectiveness and safety domains**
Rasic et al. 2011 [29]	RCT / Open elective for colorectal cancer	184 / 91 vs 93 (91 vs 93 analysed for total incisional SSIs)	Triclosan-coated polyglactin 910 Vicryl* Plus (Ethicon Johnson-Johnson): single-layer mass technique (peritoneum, muscle, and fascia) vs Polyglactin 910 Vicryl*; Skin closure: polyamide (Ethilon, 2–0, Ethicon, Johnson-Johnson)	Duration of operative procedure, duration of hospitalization, biochemical inflammation parameters (white blood cell count – WBC; procalcitonin – PCT; and C-reactive protein – CRP), presence of wound infection, dehiscence, haematoma or inflammatory reactions to the skin sutures (skin inflammation around the suture), postoperative hernias, readmissions and reoperations AEs not specified as outcome but reported.	**Clinical effectiveness and safety domains**
Justinger et al. 2013 [30] NCT00998907	RCT / Open Colorectal; Hepatopancreatobiliar; Small intestine; upper GI tract; vascular; other	967 / 599 vs 408 (485 vs 371 analysed for total incisional SSIs)	Triclosan impregnated 2-0 polydioxanone loop (PDS Plus) vs 2-0 polydioxanone loop without triclosan PDS II (fascia closure) Skin closure: staples	The rate of wound infection – SSIs at the laparotomy incision following the CDC and Prevention criteria. Although not specifically mentioned in the Methods: blood loss, duration of surgery, and duration of hospital stay. From Protocol: number of incisional hernias. AEs not specified as outcome but reported (blood loss).	**Clinical effectiveness and safety domains**

Nakamura et al. 2013 [31] UMIN000003322	RCT / Open elective or laparoscopic: colorectal	410 / 206 vs 204 (206 vs 204 analysed for total incisional SSIs)	Triclosan-coated polyglactin 910 antimicrobial sutures (Vicryl* Plus) (fascia closure) vs Polyglactin 910 sutures (Vicryl*) Skin closure: staples	Number of wound infections; Extra cost owing to the care of infected wound management AEs not specified as outcome nor reported.	**Clinical effectiveness and safety domains**
Diener et al. 2014 [27] DRKS00000390	RCT / Open elective: colon, rectum, stomach, pancreas, liver, combination, other	1224 / 590 vs 600 1185 (587 PDS Plus and 598 PDS II) analysed in mITT analysis for total incisional SSIs; 913 (451 vs 462) in PP analysis for total incisional SSIs	Triclosan-coated polydioxanone sutures (PDS Plus) vs uncoated polydioxanone sutures (PDS II): fascial closure Skin closure: staples	The occurrence of superficial or deep surgical site infection according to the Centres for Disease Control and Prevention criteria within 30 days after the operation; Frequency of wound dehiscence (cutaneous and subcutaneous layer), frequency of burst abdomen (fascial dehiscence), postoperative length of stay in intensive care unit, postoperative length of stay in hospital, 30-day mortality, and quality of life (assessed with the EQ-5D questionnaire) SAEs reported.	**Clinical effectiveness and safety domains**
Mattavelli et al. 2015 [33] NCT01869257	RCT / Elective open colorectal resection	300 / 150 vs 150 (140 vs 141 analysed for total incisional SSIs)	Triclosan-coated polyglactin – 0 Vicryl Plus; Triclosan-coated polydioxanone – PDS Plus vs Polyglactin or polydioxanone suture without triclosan (Vicryl; PDS II) Separate layer technique starting with the peritoneum with triclosan-coated polyglactin 910, followed by the fascia with triclosan-coated polydioxanone, and then the skin with triclosan-coated polyglactin. In cases of subcutaneous fat tissue closure, the technique was interrupted sutures with 3/0 Vicryl Plus.	Overall rate of incisional SSI (superficial and deep incisional SSI); Length of hospital stay and overall incision complication rate, including skin swelling and redness, hematomas, and seromas. AEs not specified as outcome but reported.	**Clinical effectiveness and safety domains**

Ruiz-Tovar et al. 2015 [28]	RCT / Open for faecal peritonitis	110 / 55 vs 55 (50 vs 51 analysed for total incisional SSIs)	Triclosan-coated polyglactin 910 - Vicryl Plus vs Triclosan-uncoated polyglactin 910 Vicryl (for fascial closure). Skin closure: with staples.	Incisional SSIs (including deep and superficial), mortality, hospital stay. AEs not specified as outcome nor reported.	**Clinical effectiveness and safety domains**
Justinger et al. 2009 [47]	Observational study (with historical control) / Open for different abdominal operations	2087 /1043 vs 1045	Triclosan-coated polyglactin 910 antimicrobial sutures –Vicryl Plus vs polydioxanone PDS II	AEs not specified as outcome nor reported.	**Safety domain**
Justinger et al. 2011 [48] NCT00932503	Interventional non-randomized clinical pathway driven study / Open for Hepatobiliary resection	839 / 430 vs 409	Triclosan-coated polyglactin 910 antimicrobial sutures –Vicryl Plus vs polydioxanone PDS II	AEs not specified as outcome nor reported.	**Safety domain**
Hoshino et al. 2013 [49]	Prospective observational study (with historical control) / Open for Digestive tract surgery	1078 / 467 vs 611	Triclosan-coated polyglactin 910 antimicrobial sutures –Vicryl Plus vs polyglactin 910 - Vicryl	AEs not specified as outcome nor reported.	**Safety domain**
Fraccalvieri et al. 2014 [50]	Prospective observational study (with historical control) / Open for Elective colorectal disease	480 / 240 vs 240	Triclosan-coated polyglactin 910 antimicrobial sutures –Vicryl Plus vs polydioxanone PDS II	AEs not specified as outcome nor reported.	**Safety domain**
Jung et al. 2014 [34]	Interventional single arm study / Open for Gastric cancer	916	Triclosan-coated polyglactin 910 antimicrobial sutures –Vicryl Plus	AEs not specified as outcome but reported as AEs.	**Safety domain**
Okada et al. 2014 [35]	Prospective observational study (with historical control) / Open for	198 / 88 vs 110	Triclosan-coated polyglactin 910 antimicrobial sutures –Vicryl Plus vs polyglactin 910 – Vicryl	AEs not specified as outcome but reported.	**Safety domain**

	Pancreaticoduodenectomy				
Nakamura et al. 2016 [51]	Prospective observational study / Laparoscopic for Colon cancer	670 / 382 vs 288	Triclosan-uncoated 0-PDS I and Triclosan-coated 0-PDS Plus	AEs not specified as outcome nor reported.	**Safety domain**

Abbreviations: RCT: randomised controlled trial; nRCT: non-randomised controlled trial; AE: adverse event; SAE: serious adverse event: SSI: surgical site infection

2.7 Deviations from project plan

Subgroup analyses based on the risk of bias criteria was conducted to evaluate possible effects on the critical primary outcome – total incisional SSIs - in 5 RCTs with a high [28,29] or unclear risk of bias [30-32] and two RCTs with a low risk of bias [27,33].

Some deadlines within the timelines were postponed due to several objective reasons.

3 DESCRIPTION AND TECHNICAL CHARACTERISTICS OF TECHNOLOGY (TEC)

3.1 Research questions

Element ID	Research question
B0001	What are antibacterial-coated sutures and the comparator(s), non-antibacterial-coated sutures?
A0020	For which indications have antibacterial-coated sutures received CE marking?
B0002	What is the claimed benefit of antibacterial-coated sutures in relation to non-antibacterial-coated sutures?
B0003	What is the phase of development and implementation of antibacterial-coated sutures and non-antibacterial-coated sutures?
B0004	Who administers antibacterial-coated sutures and non-antibacterial-coated sutures and in what context and level of care are they provided?
A0021	What is the reimbursement status of antibacterial-coated sutures?

3.2 Results

Features of the technology and comparators

[B0001] – What are antibacterial-coated sutures and the comparator(s), non-antibacterial-coated sutures?

A suture is a medical device used to hold skin, internal organs, blood vessels and all other tissues of the human body together, after they have been severed by injury, incision or surgery. Surgical sutures can be classified according to the origin of the suture material as natural or synthetic, according to the structure as monofilament or multifilament and regarding the absorption profile as absorbable or non-absorbable [52].

Antibacterial-coated sutures are developed with the aim of reducing the risk of surgical site infection by minimizing the risk of colonization of the suture by bacteria commonly associated with such infections. Surgical sutures ***coated with triclosan*** and surgical sutures ***coated with chlorhexidine*** are currently on the market, and some others are in the development phase [1].

Main features of triclosan-coated and non-antibacterial-coated sutures can be found in Table 3, with details in Table A3, Table A4 and Table A5 in Appendix 1.

Table 3: Features of the intervention and comparators

	Interventions: Antibacterial coated sutures			**Comparators: Non-antibacterial coated sutures**		
Name	Antibacterial Surgical Suture	Antibacterial Surgical Suture	Antibacterial Surgical Suture	Surgical Suture	Surgical Suture	Surgical Suture
Proprietary name	Coated Vicryl®Plus	Monocryl® Plus	PDS Plus®	Vicryl®	Monocryl®	PDS II®
Manufacturer	Johnson & Johnson International	Johnson & Johnson International	Johnson & Johnson International	Johnson & Johnson International	Johnson & Johnson International	Johnson & Johnson International

Class / GMDN code	Class III / 45401	Class III / 46317	Class III / 47362	Class III	Class III	Class III

Abbreviations: GMDN- Global medical device nomenclature

Sources: [5]

Triclosan-coated sutures

Plus sutures *(MONOCRYL™ Plus Antibacterial suture, Coated VICRYL™ Plus Antibacterial Suture and PDS™ Plus Antibacterial suture)* are absorbable sutures which contain the purest form of the antibacterial agent triclosan (Irgacare MP®).

Triclosan prevents/reduces the colonization of the suture by bacteria commonly associated with SSI development. In vitro studies have shown that triclosan-coated sutures placed in an agar plate create a zone of inhibition, which can last up to 23 days. Furthermore, in animal studies, the antibacterial sutures inhibit bacterial colonization of the suture after direct in vivo challenge with bacteria [2-5].

Triclosan [5-chloro-2-(2,4-dichlorophenoxy)phenol] is a broad-spectrum antibacterial agent that is commercially used in several products such as soaps, deodorants, shower gels and toothpastes due to its antimicrobial efficacy and low toxicity to humans. Triclosan interferes with microbial lipid synthesis and consequently attenuates bacterial growth and colonisation of the suture material in a broad spectrum manner in both in vivo and in vitro studies [1].

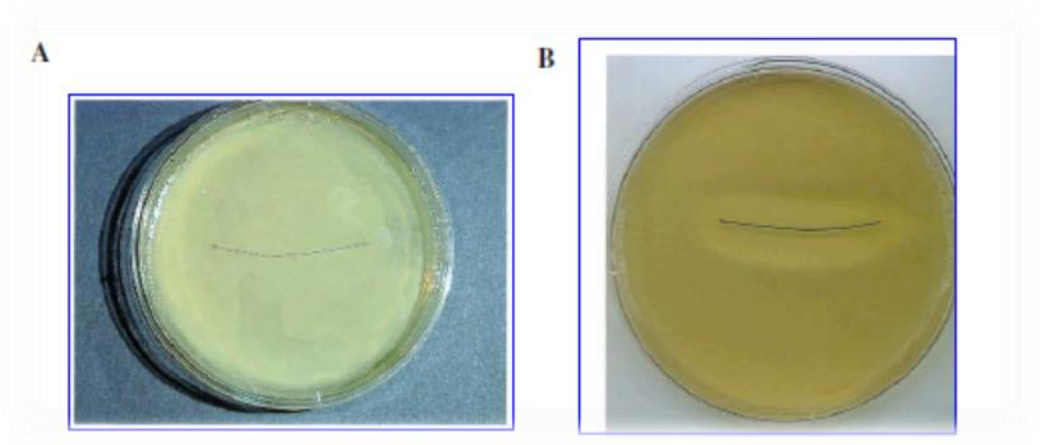

Figure 2: Zone of inhibition around Plus suture: A. suture without Triclosan, B. suture with triclosan [5]

Table 4: Spectrum of antibacterial efficacy

Spectrum of efficacy	Vicryl® Plus	Monocryl® Plus	PDS® Plus
Staphylococcus aureus	+	+	+
Staphylococcus epidermidis	+	+	+
MRSA-*methicillin resistant Staphylococcus aureus*	+	+	+
MRSE-*methicillin resistant Staphylococcus epidermidis*	+	+	+
Escherichia coli	-	+	+

Klebsiella pneumoniae	-	+	+

Source: [5]

Antibacterial triclosan-coated suture Polyglactin 910 – Vicryl® Plus
(Ethicon, Johnson & Johnson International)

Vicryl® Plus is a synthetic absorbable sterile surgical suture. It is composed of a copolymer made from 90% glycolide and 10% L-lactide. Braided Vicryl® Plus sutures are coated with a mixture composed of equal parts of copolymer of glycolide and lactide (polyglactin 370) and calcium stearate. Polyglactin 910 copolymer and Polyglactin 370 with calcium stearate have been found to be non-antigenic, non-pyrogenic and elicit only a slight tissue reaction during absorption. It contains a broad spectrum antibacterial agent Irgacare® MP (Triclosan) with a concentration of ≤ 275 µg/m.

Vicryl® Plus suture elicits a minimal inflammatory reaction in tissues and in-growth of fibrous connective tissue. Absorption of Vicryl® Plus suture is essentially complete between 56 and 70 days [3].

The zone of bacterial inhibition surrounding the knotted sutures using Vicryl® Plus showed an antimicrobial effect over *Staphylococcus aureus*, *Staphylococcus epidermis* and its Methicillin resistant strains [3,6,7]. Furthermore, in animal studies, Vicryl® Plus sutures inhibit bacterial colonization of the suture after direct in vivo challenge with bacteria [3].

Adverse reactions associated with the use of this device include transitory local irritation at the wound site, transitory inflammatory foreign body response, erythema and induration during the absorption process of subcuticular sutures. Like all foreign bodies Vicryl® Plus may potentiate an existing infection [3].

Users should be familiar with surgical procedures and techniques involving absorbable sutures before employing Vicryl® Plus suture for wound closure, as risk of wound dehiscence may vary with the site of application and the suture material used. Surgeons should consider in vivo performance when selecting a suture. As with any foreign body, prolonged contact of any suture with salt solutions, such as urinary or biliary tracts, may result in calculus formation. As an absorbable suture, Vicryl® Plus may act transiently as a foreign body [3,5].

Antibacterial triclosan-coated suture Polyglecaprone 25 - Monocryl® Plus
(Ethicon, Johnson & Johnson International)

Monocryl® Plus is a sterile, synthetic, absorbable, monofilament suture. It is comprised of a copolymer of glycolide and ε-caprolactone. Poliglecaprone 25 copolymer has been found to be non-antigenic, non-pyrogenic and elicits only a slight tissue reaction during absorption. It contains a broad spectrum antibacterial agent, Irgacare® MP (Triclosan) at a concentration of ≤ 2360 µg/m.

The Monocryl® Plus Antibacterial Suture elicits a minimal inflammatory reaction in tissues and is eventually replaced with an in-growth of fibrous connective tissue. Absorption is essentially complete at 91 to 119 days.

Using zone of inhibition studies, Monocryl® Plus Antibacterial Suture has been shown to inhibit colonization of the suture by *Staphylococcus aureus*, *Staphylococcus epidermidis*, Methicillin-resistant *S.aureus*, Methicillin-resistant *S.epidermidis*, *Echerichia coli* and *Klebsiella pneumoniae*. The clinical significance of this finding is unknown [2,5]. Furthermore, in animal studies Monocryll®

Plus sutures inhibit bacterial colonization of the suture after direct in vivo challenge with bacteria [2].

Antibacterial triclosan-coated suture Polydioxanone – PDS® Plus
(Ethicon, Johnson & Johnson International)

PDS® Plus Antibacterial Suture is a sterile synthetic absorbable monofilament suture. It is made from the polyester poly (p-dioxanone). Polydioxanone polymer has been found to be non-antigenic, non-pyrogenic and elicits only a slight tissue reaction during absorption. It contains a broad spectrum antibacterial agent Irgacare® MP (triclosan) at a concentration of ≤ 2360 µg/m.

PDS® Plus Antibacterial Suture elicits a minimal inflammatory reaction in tissues and is eventually replaced with an in-growth of fibrous connective tissue. Absorption is minimal until about the 90th postimplantation day and essentially complete at between 182 and 238 days.

PDS® Plus Antibacterial Suture has been shown to inhibit colonization of the suture by *Staphylococcus aureus*, *Staphylococcus epidermidis,* Methicillin-resistant *S.aureus*, Methicillin-resistant *S.epidermidis*, *Echerichia coli* and *Klebsiella pneumoniae*. The clinical significance of this finding is unknown. Furthermore, in animal studies PDS® Plus sutures inhibit bacterial colonization of the suture after direct in vivo challenge with bacteria [4].

Adverse reactions associated with this device include: transient local irritation at the wound site, transient inflammatory foreign body response and erythema and induration during absorption with subcuticular sutures, as well as allergic reaction to Irgacare MP (triclosan). Like all foreign bodies, PDS® Plus Antibacterial Suture may potentiate an existing infection. As with any foreign body, prolonged contact of any suture with salt solutions, such as those found in the urinary or biliary tracts may result in calculus formation. As an absorbable suture, PDS® Plus may transiently act as a foreign body [4,5].

Contraindications for the use of triclosan-coated sutures under assessment are presented in Table 5.

Table 5: Contraindications for Vicryl® Plus, Monocryl® Plus and PDS® Plus use

Monocryl™ Plus Antibacterial suture	**Coated Vicryl™ Plus Antibacterial Suture**	**PDS™ Plus Antibacterial suture**
Monocryl™ Plus Antibacterial suture, Coated Vicryl™ Plus Antibacterial Suture and PDS™ Plus Antibacterial suture should not be used in patients with known allergic reactions to Irgacare® MP (triclosan).		
Consideration should be taken in the use of absorbable sutures in tissues with poor blood supply as suture extrusion and delayed absorption may occur.		
This suture may be inappropriate in elderly, malnourished or debilitated patients or in patients suffering from conditions which may delay wound healing.		
These sutures (dyed and undyed), being absorbable, should not be used where extended approximation of tissues under stress is required. Undyed Monocryl™ Plus Antibacterial sutures, in particular should not be used to close fascial tissue.	These sutures, being absorbable, should not be used where extended approximation of tissues under stress is required.	These sutures, being absorbable, should not be used where prolonged (beyond 6 weeks) approximation of tissues under stress is required or in conjunction with prosthetic devices, for example, heart valves or synthetic grafts.
The safety and effectiveness of Monocryl™ Plus Antibacterial Sutures has not been established in the	The safety and effectiveness of Coated Vicryl™ Plus Antibacterial	The safety and effectiveness of PDS™Plus Antibacterial Sutures have not been established in

following areas: neural tissue, cardiovascular tissue, microsurgery and ophthalmic surgery.	sutures in cardiovascular tissue, ophthalmic surgery and neurological tissue have not been established.	contact with the central nervous system, in adult cardiac tissue, in large vessels or for contact with cornea and sclera.

Source: [5]

Chlorhexidine-coated sutures

Antibacterial Surgical Sutures coated with Chlorhexidine from different manufacturers are also available on the market. Chlorhexidine has activity against gram-positive and gram-negative organisms, facultative anaerobes, aerobes and yeast; it is both bacteriostatic and bactericidal, depending on its concentration. The bactericidal effect of chlorhexidine is a result of the binding of this cationic molecule to negatively charged bacterial cell walls and extramicrobial complexes. At low concentrations, this causes an alteration of bacterial cell osmotic equilibrium and leakage of potassium and phosphorous, resulting in a bacteriostatic effect. At high concentrations of chlorhexidine, the cytoplasmic contents of the bacterial cell precipitate and result in cell death.

Assufil® Plus (Assut Europe)

Assufil Plus suture is a synthetic absorbable sterile surgical suture device, composed of braided multifilament of polyglycolic acid. Studies on animals have proven that the absorption of Assufil® Plus suture is practically complete within 90 days of implantation.

Assufil® Plus suture may cause local inflammatory reaction associated with erythema formation.

Egycryl Extra (Taisier-Med)

Egycryl Extra is a sterile synthetic absorbable suture with antibacterial based on copolymer made from 90% Glycolide and 10% L-Lactide. Egycryl Extra sutures are coated with an equal combination of copolymer (Glycolide and Lactide), calcium stearate and Chlorhexidine diacetate which act as broad spectrum antibacterial agent with a maximum dose of 60 µg/m. Absorption is essentially complete at between 55 and 70 days.

Using zone of inhibition studies, Chlorhexidine diacetate in coated Egycryl Extra has been shown to inhibit colonization of the suture by *Staphylococcus aureus*, *Staphylococcus epidermidis* and Methicillin-resistant S.epidermidis which are microorganisms known to contribute to surgical site infections. Animal studies have demonstrated that Egycryl extra inhibits bacterial colonization of the suture after direct in vivo challenge with bacteria. The clinical significance of this finding is unknown [9].

Neosorb Plus (Medipac)

Neosorb Plus is a braided, violet, synthetic absorbable polyglactin 910 surgical suture which is coated with an antibacterial agent (CHA-chlorhexide diacetate).

Neosorb Plus Synthetic Absorbable Surgical Suture elicits a minimal acute inflammatory reaction in tissues, which is followed by gradual encapsulation of the suture by fibrous connective tissue. The absorption of the suture is essentially complete at between 56-70 days. Evaluation of antimicrobial efficacy showed that Neosorb Plus suture has a zone of inhibition that is effective

against the pathogens that most often cause surgical site infection – *Staphylococcus aureus* and *Staphylococcus epidermidis* [10].

Comparators: Non-antibacterial-coated sutures

The main characteristics and adverse effects of the non-antibacterial-coated sutures used as comparators in this assessment - Vicryl® (Ethicon); Monocryl® (Ethicon) and PDS® II (Ethicon) - can be found in Table 6 below, with more details in the Appendix 1.

Table 6: Main characteristics and adverse effects of the non-antibacterial-coated sutures

Vicryl® (Ethicon)
The coated Vicryl® Suture (poyglactin 910) is a synthetic absorbable sterile surgical suture composed of a copolymer made from 90% glycolide and 10% L-lactide. It is prepared by coating Coated Vicryl® Suture material with a mixture composed of equal parts of a copolymer of glycolide and lactide (polyglactin 370) and calcium stearate. The copolymers used in this product have been found to be non-antigenic, non-pyrogenic and elicit only a mild tissue reaction during absorption. Coated Vicryl® Sutures elicit a minimal acute inflammatory reaction in tissue and minimal in-growth of fibrous connective tissue. The suture is essentially complete at between 56 and 70 days.
Monocryl® (Ethicon)
Monocryl® (poliglecarpone 25) suture is a monofilament synthetic absorbable surgical suture prepared from a copolymer of glycolide and epsilon-caprolactone. Poliglecarpone 25 copolymer has been found to be non-antigenic, non-pyrogenic and elicits only a slight tissue reaction during absorption. Absorption of Monocryl® absorbable suture is essentially complete at between 91 and 119 days.
PDS® II (Ethicon)
PDS® II (polydioxanone) monofilament synthetic absorbable suture is prepared from the polyester poly (p-dioxanone). Polydioxanone polymer has been found to be non-allergenic, non-pyrogenic and elicits only a slight tissue reaction during absorption.
Vicryl®, Monocryl® and PDS® II
Adverse effects associated with the use of this device include wound dehiscence, failure to provide adequate wound support in closure of the sites where expansion, stretching or distension occur, failure to provide adequate wound support in elderly, malnourished or debilitated patients or in patients suffering from conditions which may delay wound healing, infection, minimal acute inflammatory tissue reaction, localized irritation when skin sutures are left in place for longer than 7 days, suture extrusion and delayed absorption in tissue with poor blood supply, calculi formation in urinary and biliary tracts when prolonged contact with salt solutions such as urine and bile occurs and transitory local irritation at the wound site. Broken needles may result in extended or additional surgeries or residual foreign bodies. Inadvertent needle sticks with contaminated surgical needles may result in transmission of blood-borne pathogens.

Source: [53-55]

[A0020] – For which indications have the antibacterial-coated sutures received CE marking?

Triclosan-coated sutures

Vicryl® Plus sutures are intended for use in general soft tissue approximation and/or ligation, including microsurgery for vessels less than 2 mm in diameter. The safety and effectiveness of Vicryl® Plus sutures in cardiovascular tissue, ophthalmic surgery and neurological tissue have not been established [3].

Monocryl® Plus Antibacterial Sutures are intended for use in general soft tissue approximation and/or ligation where an absorbable material is indicated [2].

PDS® Plus Antibacterial sutures are intended for use in general soft tissue approximation, including use in paediatric cardiovascular tissue, and in ophthalmic surgery (other than contact with cornea and sclera). These sutures are particularly useful where the combination of an absorbable suture and extended wound support (up to six weeks) is desirable [4].

Details can be found in Table A14 and

Table A15, Appendix 2.

Chlorhexidine coated sutures

Assufil® Plus sutures are intended for use in all surgical procedures, at the user's discretion [8].

Egycryl Extra sutures are intended for use in general soft tissues approximation and/or ligation including ophthalmic surgery, peripheral nerve anastomosis and microsurgery for vessels less than 2 mm in diameter [9].

Neosorb® Plus Synthetic Absorbable Surgical Suture is indicated for use in general soft tissue approximation and/or ligation, but not for use in ophthalmic, cardiovascular and neurological procedures [10].

Comparators: Non-antibacterial-coated sutures

Vicryl® sutures are indicated for use in general soft tissues approximation and/or ligation, including use in ophthalmic procedures, but not for use in cardiovascular and neurological tissues [53].

Monocryl® sutures are indicated for use in general soft tissues approximation and/or ligation, but not for use in cardiovascular or neurological tissues, microsurgery or ophthalmic surgery [54].

PDS II® sutures are indicated for use in general soft tissue approximation, including use in paediatric cardiovascular tissue where growth is expected to occur, and in ophthalmic surgery. PDS II suture is not indicated in adult cardiovascular tissue, microsurgery and neural tissue. These sutures are particularly useful where the combination of an absorbable suture and extended wound support (up to six weeks) is desirable [55].

[B0002] – What is the claimed benefit of antibacterial-coated sutures in relation to the comparator(s)?

Triclosan-coated sutures have been documented to reduce bacterial colonization and to inhibit a wide spectrum of pathogens without impeding wound healing or altering suture properties. Chlorhexidine is both bacteriostatic and bactericidal, depending on its concentration; it has activity against gram-positive and gram-negative organisms, facultative anaerobes, aerobes and yeast.

The claimed benefit of triclosan-coated sutures is to reduce or prevent the risk of surgical site infection. By destroying the cell membrane, triclosan prevents colonization of the most common gram-positive and gram-negative bacteria associated with SSI. Triclosan has been used for several decades and it was shown to have no carcinogenic potential or genotoxicity. It is rapidly absorbed, well distributed, metabolised and excreted from the human body, which reflects a minimal impact on the patient and environment [5].

[B0003] – What is the phase of development and implementation of antibacterial-coated sutures and the comparator(s)?

Triclosan-coated sutures are approved for use in a wide range of countries. The first approval was by the US FDA in 2002. The product got the approval from all regulatory agencies that the manufacturer sought approval from, including the US FDA, EU Notified Body (BSI), Japan PMDA, Australia TGA and Health Canada. Dates of the first approval for certain countries are presented in Table 7.

Table 7: Dates of first approval for Plus sutures

	Date of First Approval		
Country	**Vicryl® Plus**	**PDS® Plus**	**Monocryl® Plus**
United States	Dec 19, 2002	Jul 14, 2006	Jun 29, 2005
European Union (CE)	Sep 17, 2004	Apr 3, 2009	May 21 2007
Japan	Dec 18, 2008	Aug 2, 2011	Not pursued
Australia	Oct 9, 2006	Nov 19, 2008	Jan 2, 2008
Canada	Jan 13, 2003	Mar 6, 2008	Nov 22, 2005

Source: [5]

Details can be found in Table A14 and

Table A15, in Appendix 2.

There is no data on any off label use [5].

[B0004] – Who administers the antibacterial-coated sutures and the comparator(s) and in what context and level of care are they provided?

Triclosan-coated sutures as well as non-antibacterial coated sutures are intended for use in hospital operating theatres or ambulances or any qualified environment by qualified personnel, experienced in technical and surgical procedures where the use of suture is required. Care should be taken when handling the suture material to avoid any bending or flattening to the thread due to application of surgical instruments [2-4].

The surgeon uses a surgical needle to penetrate tissue and advance a suture strand to its desired location. The surgeon must select suture materials appropriate for the procedure and must place them in the tissues in a manner consistent with the principles that promote wound healing.

The surgeon's knowledge of the physical characteristics of suture material is important. As the requirements for wound support vary with patient factors, the nature of the procedure and the type of tissue involved, the surgeon needs to select the suture material that will retain its strength until the wound heals sufficiently to withstand stress on its own.

A nurse must maintain the sterility of sutures when storing, handling and preparing them for use. The integrity and strength of each strand must remain intact until it is in the surgeon's hand [6].

[A0021] – What is the reimbursement status of antibacterial-coated sutures?

No data about the reimbursement status in corresponding countries was found during the literature search, and the specific data was not available in the evidence submission file completed by Johnson & Johnson International [5]. EUnetHTA JA3 Partners were not approached to provide reimbursement information.

In Croatia, surgical sutures are financed as a part of the surgical treatment according to a Diagnosis-related Group (DRG) system. Multiple services which are invoiced during one episode of surgical treatment are summarised under one DRG code [36]. In Germany, antibacterial coated suture material is reimbursable within the DRG-based hospital payment. Hospitals do not receive extra payment when using this type of suture; they instead receive a fixed amount of payment and have to decide for themselves whether they want to use this money for buying antibacterial coated sutures.

3.3 Discussion

The majority of data presented are related to triclosan-coated sutures, provided by the manufacturer (J&J) in the submission file. Manufacturers of other antibacterial sutures were contacted as well but they did not provide a specific response.

Since the first approval in 2002, triclosan-coated sutures became an established technology with additional sutures launched in the product range since that time. They are now used in a wide range of surgical procedures and patients to minimize the risk of colonization of the suture by bacteria commonly associated with surgical site infection [5].

Widespread use of triclosan in many contemporary consumer and personal health-care products, like oral and dermal products and also in household items including plastics and textiles, led to major concerns about the possibility that triclosan resistance may contribute to reduced susceptibility to clinically important antimicrobials, due to either cross-resistance or co-resistance mechanisms, and therefore, may represent a potential public health risk. In the last 15 years, because of its relevance, the occurrence of triclosan resistance among different microorganisms, including some of clinical relevance, was the subject of many studies [56].

There is not sufficient evidence to support claims of antibiotic resistance or bacterial resistance to triclosan in patients [57-59].

Recently, there has been a surge in the development of novel sutures with additional properties such as those modified with antimicrobial agents, bioactive molecules like DNA, drugs, antibodies, proteins, growth factors and silver [1].

4 HEALTH PROBLEM AND CURRENT USE OF THE TECHNOLOGY (CUR)

4.1 Research questions

Element ID	Research question
A0002	What is abdominal surgical wound infection within the scope of this assessment?
A0003	What are the known risk factors for abdominal surgical wound infection?
A0004	What is the natural course of abdominal surgical wound infection?
A0005	What are the symptoms and the burden of abdominal surgical wound infection?
A0006	What are the consequences of abdominal surgical wound infection for the society?
A0024	How is abdominal surgical wound infection currently diagnosed according to published guidelines and in practice?
A0025	How is abdominal surgical wound infection currently prevented and managed according to published guidelines and in practice?
A0007	What is the target population in this assessment?
A0023	How many people belong to the target population?
A0011	How much are antibacterial-coated sutures utilised?

4.2 Results

Overview of the disease or health condition

[A0002] – What is abdominal surgical wound infection within the scope of this assessment?

Surgical wound infection or surgical site infection is a type of healthcare-associated infection in which a wound infection occurs after an invasive (surgical) procedure. The United States Centers for Disease Control and Prevention (CDC) defines SSI as an infection that precipitates post-surgery at the surgical site [60].

SSI is also defined as an infection that occurs within 30 days of the operation and involves the skin and subcutaneous tissue of the incision (superficial incisional) and/or the deep soft tissue (for example, fascia, muscle) of the incision (deep incisional) and/or any part of the anatomy (for example, organs and spaces) other than the incision that was opened or manipulated during an operation (organ/space) [61].

SSI occurs after pathogenic organisms multiply in a wound and cause local signs and symptoms: heat, redness, pain and swelling. In serious cases, SSIs are manifested with systemic signs of fever or a raised white blood cell count.

The following terms are used to classify surgical wounds [62]:

Surgical wound classification

- *Clean*: an uninfected operative wound in which no inflammation is encountered and the alimentary, genital or urinary tract is not entered. Clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds after nonpenetrating (blunt) trauma should be included in this category if they meet the criteria.

- *Clean contaminated*: a wound in which the respiratory, alimentary, genital or urinary tract is entered in a controlled manner 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.
- *Contaminated*: open, new, accidental wounds or operations in which there is a significant break in aseptic technique (e.g. gross contamination with GI tract contents) or incisions in which acute nonpurulent inflammation is encountered. Necrotic tissue without evidence of purulent drainage (e.g. dry gangrene) is also included in this category.
- *Dirty* or *Infected*: old traumatic wounds with retained devitalised tissue, or those involving existing infection or visceral perforation. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

According to the US CDC definition, three types of SSI are described, as follows [11,42,60,63]:

Superficial incisional infection*,* which occurs within 30 days of surgery, affecting the skin and/or subcutaneous tissue (but not extending down to the deep fascia). May be indicated by localised (Celsian) signs, such as redness, pain, heat or swelling at the site of the incision or by the drainage of pus (purulent drainage). Microorganisms are isolated from an aseptically-obtained culture.

There are two specific types of superficial incisional SSIs: 1. *Superficial Incisional Primary* (SIP) – a superficial incisional SSI identified in the primary incision in a patient who had an operation with one or more incisions (e.g., C-section incision or chest incision for CBGB); 2. *Superficial Incisional Secondary* (SIS) – a superficial incisional SSI identified in the secondary incision in a patient who had an operation with more than one incision (e.g., donor site incision for CBGB).

Deep incisional infection, which occurs within 30 days of surgery (in the absence of a prosthetic implant) or within one year in the presence of a prosthetic implant, if the infection appears to be related to surgery, affecting the fascial and muscle layer. Infections may be indicated by the presence of fever with tenderness of the wound or purulent discharge from a deep incision but not from organ space. Microorganisms are isolated from an aseptically-obtained culture, an abscess or other evidence of deep infection can be found either on examination, at re-operation or on appropriate radiological imaging. A separation of the edges of the incision exposing the deeper tissues can be noted.

Deep incisional infections pose a specific risk of complete abdominal wound dehiscence (breakdown of both the superficial and deep layers of the abdominal wall along the incision, with subsequent exposure of the abdominal viscera) and incisional hernia (protrusion of abdominal viscera through a gap in the deep layer of the abdominal wall that is covered by intact skin), both of which may require further surgical treatment.

There are two specific types of deep incisional SSIs: 1. *Deep Incisional Primary* (DIP) – a deep incisional SSI identified in a primary incision in a patient who had an operation with one or more incisions (e.g., C-section incision or chest incision for CBGB); 2. *Deep Incisional Secondary* (DIS) – a deep incisional SSI identified in the secondary incision in a patient who had an operation with more than one incision (e.g., donor site incision for CBGB).

Organ or ***space infection***, which involves any part of the anatomy other than the incision that is opened or manipulated during the surgical procedure, for example a joint or the peritoneum.

Figure 3 presents the SSI classification and its frequency.

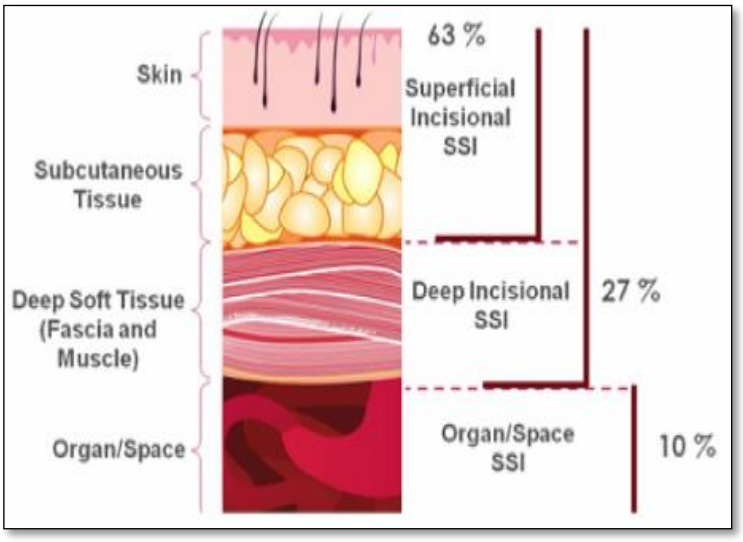

Figure 3: SSI classification [42]

SSI is one of the most common healthcare-associated infections in developed and developing countries. The incidence of SSI in developing countries may not be adequately represented due to the scarcity of published data and the lack of proper surveillance systems in these regions [64, 65].

SSI is a frequent type of nosocomial infection, accounting for about 14% to 15% of the total number of nosocomial infections and roughly 5% of all surgical complications [12]. The total incidence of SSI is as follows: 5.6 SSIs per 100 surgical procedures in developing countries, 2.6 per 100 surgeries in the United States and 2.9 per 100 surgeries in European countries [13].

The WHO reports that in low- and middle-income countries (LMICs) the pooled incidence of SSI was 11.8 per 100 surgical procedures (range 1.2 to 23.6).

The highest cumulative incidence was for colon surgery with 9.5% (episodes per 100 operations), followed by 3.5% for coronary artery bypass graft, 2.9% for caesarean section and 1.4% for cholecystectomy [14,15].

According to the ECDC, the percentage of SSIs per 100 surgical procedures varied from 0.6% to 9.5% depending on the type of procedure. The incidence density of in-hospital SSIs per 1000 post-operative patient-days varied from 0.2 to 5.7 depending on the type of surgical procedure.

The ECDC Annual epidemiological report (2013-2014) reported on 18 364 SSIs in a total of 967 191 surgical procedures performed in 15 EU member states and Norway [66].

Abdominal surgery presents a particular risk factor for development of SSI. The incidence of SSI following abdominal surgery varies according to the nature of the procedure undertaken (laparoscopic [key-hole] surgery compared with open surgery) and the degree of wound contamination. Abdominal wounds are generally closed in at least two layers, with the first encompassing the fascia/muscle layer of the abdominal wall and the second encompassing the skin. In laparoscopic surgery, instruments are inserted into the abdomen using a number of metal or plastic ports that prevent direct contact between instruments and the abdominal wall. In addition, the ports may protect the tissues of the abdominal wall from spilled contents from the GI tract or pus. There are some indications that suggest that the incidence of wound infection

following surgery for perforated appendicitis is seven-fold lower in patients who are treated using a laparoscopic approach [42].

The frequency of SSI after midline laparotomy varies between 12% and 16%, depending on definition, patient population and study design [16]. More specifically, it is reported that 4%–17% of midline laparotomy patients suffer from SSI [17]. An SSI incidence of 10% was reported in patients undergoing either small or large bowel surgery in a second UK-based survey study by Coello et al [67]. The incidence of wound infection following an elective splenectomy in which the gastro-intestinal tract is not entered would be expected to be much lower than that following an emergency laparotomy for a colonic perforation during which contamination of the surgical site is inevitable [42].

According to the classification of surgery wounds from the CDC, gastric cancer surgery falls into class II (clean-contaminated). In typical class II surgeries, SSI rates are reportedly 5%–15%. In the case of a planned and prepared gastrectomy (i.e., laparotomy), the rate remarkably drops to lower than 5% [17].

Open colon and rectal procedures are classified as clean-contaminated, with infective complications at entry portals being especially likely. In elective colorectal operations, the international SSI rates are 4.7%–25% [18].

In the patient groups who develop SSI after bowel surgery, the intraoperative colonization rate has been found to be 85% [68].

Among all abdominal operations, pancreaticoduodenectomy (PD) has the most infectious complications because it is highly invasive, necessitates a longer operation than other abdominal procedures and involves many anastomoses, resulting in a high risk of anastomotic leak [35].

Gastric cancer surgery is one of the most frequently performed surgeries in Korea. According to the CDC classification of surgery wounds, gastric cancer surgery falls into class II (clean-contaminated). In typical class II surgeries, SSI rates are reportedly 5%–15%. In the case of a planned and prepared gastrectomy (i.e. laparotomy), the rate remarkably drops to lower than 5%. However, for cancer patients who suffer from SSIs, the infection can cause them more serious psychological and financial damage than to patients with other diseases and can delay postoperative adjuvant therapy, resulting in deadly outcomes [42,69].

For CHOL operations, the percentage of SSIs was 1.8%, with an inter-country range from 0.7% to 6.0%. In endoscopic CHOL operations, the percentage of SSIs was 1.5%, with an inter-country range from 0.4% to 5.6%. In non-endoscopic CHOL operations, the percentage of SSIs was 4.2%, with an inter-country range from 0.8% to 12.0%.

For COLO operations, the percentage of SSIs was 9.5%, with an inter-country range from 4.0% to 16.1%. In endoscopic COLO operations, the percentage of SSIs was 7.3%, with an inter-country range from 2.7% to 10.3%. In non-endoscopic COLO operations, the percentage of SSIs was 10.7%, with an inter-country range from 4.5% to 17.1%.

For CSEC operations, the percentage of SSIs was 2.2%, with an inter-country range from 0.6% to 7.7% [66].

Two trends were observed for the period of 2011-2014 (in yearly percentages of SSIs), a significantly increasing trend in cholecystectomy operations and one significantly decreasing, in coronary artery bypass grafts and knee prosthesis surgery [66].

The CDC noticed a similar trend in USA. Between 2008 and 2014 there was an overall 17% decrease in SSI in the 10 main surgical procedures. As an example, there was a decrease of 17% in abdominal hysterectomy and 2% in colon surgery [70]. Approximately half of the SSIs are superficial infections, nearly a third are deep incisional infections and the remainder are organ-space infections. According to the CDC, 66% of all surgical infections are exclusively located in the incision, i.e. they are superficial or deep [71].

In the Netherlands, SSIs account for about 25% of healthcare-related infections, making them one of the most common nosocomial infections [72]. One study from Switzerland described a 13-year multicentre SSI surveillance scheme performed from 1998 to 2010. Reported SSI rates were: 18.2% after 7411 colectomies; 6.4% after 6383 appendectomies; 2.3% after 7411 cholecystectomies; 1.7% after 9933 herniorrhaphi [73]. In Italy, the SSI rate reported by the national SSI surveillance system from 355 Italian surgical wards between 2009 and 2011 was 2.6 episodes per 100 procedures (1628 cases/60 460 procedures); 60% of SSIs were diagnosed through 30-day post-discharge surveillance. SSI rates were higher in the colon (9.0%) and for rectal surgery (7.0%), laparotomy (3.1%) and appendectomy (2.1%) [74]. In England, data collected by National Health Service hospitals reported cumulative SSI rates from January 2008 to March 2013. The highest rate was reported among large bowel surgery (8.3%; 95% CI: 7.9–8.7 per 1000 inpatient days), followed by small bowel surgery (4.9%; 95% CI: 4.3–5.7), bile duct, liver and pancreatic surgery (4.9%; 95% CI: 4.1–5.9) and cholecystectomy (4.6%; 95% CI: 3.1–6.6) [15].

[A0003] – What are the known risk factors for abdominal surgical wound infection?

The development of SSI is a multifactorial phenomenon. Risk factors for the development of surgical site infection include patient-related and intervention-related factors [19].

The risk of SSI can be increased by factors that:

- increase the risk of endogenous contamination (e.g., procedures that involve parts of the body with a high concentration of normal flora such as the bowel);
- increase the risk of exogenous contamination (for example, prolonged operations that increase the length of time that tissues are exposed);
- diminish the efficacy of the general immune response (for example, diabetes, malnutrition or immunosuppressive therapy with radiotherapy, chemotherapy or steroids) or local immune response (for example, foreign bodies, damaged tissue or formation of a haematoma).

The extent of contamination during the procedure (clean, clean contaminated, contaminated, dirty) is a major risk factor. It is largely associated with the length of the procedure and with the patient's general condition [75].

Patient-related factors

Known patient-related risk factors are: age, sex, the patient's body mass index (BMI)/obesity, malnutrition, lifestyle (e.g. smoking), surgical history and pre-existing infections [17].

Various predisposing etiopathological factors for SSI also include baseline disease and existence of comorbidities, for example diabetes mellitus, jaundice, nutritional deficiencies, hypoproteinemias, congestive cardiac failure, hepatic failure, renal failure, chemotherapy agents,

steroids and immunosuppression due to diminished efficacy of the general immune response (e.g. as a result of diabetes, malnutrition or immunosuppressive therapy with radiotherapy, chemotherapy) or local immune response (e.g. due to presence of foreign bodies, damaged tissue or formation of a haematoma) [17,62,68,76,77-79].

Other patient-related factors associated with SSI following abdominal surgery include hypoalbuminaemia (low blood albumin), chronic obstructive pulmonary disease and chronic liver disease [80,81].

The incidence of infective complications was almost doubled in patients with sarcopenia (loss of muscle mass and strength) undergoing colorectal cancer resection [82].

Intervention-related factors

The increased risk of SSI is associated with interventions for which there is an elevated risk of endogenous or exogenous contamination. The probability of endogenous contamination is often increased in the procedures performed on the parts of the body with a high concentration of normal flora such as the bowel. Exogenous contamination is more common in prolonged procedures in which tissues are exposed for a longer period of time [62,74,78].

Wound contamination, contaminated instruments, (quality of) surgical technique and the experience of the surgical team, sutures used to close the skin and the presence of foreign bodies including drains have also been reported to be responsible for SSI and cosmetic outcomes [75,83, 84].

Other factors regarding surgery which affect the SSI incidence are pre-surgical preparation (hair removal, skin preparation/sterilization and hand/forearm antisepsis), ventilation of the operation room, type of surgery, duration of procedure, frequent glove changes, refined and aseptic operative techniques and the proper use of antibiotics/ antimicrobial prophylaxis [17].

Intra or postoperative contamination of suture materials appears to be one of the most frequent causes of SSI, whereas a less frequent cause is the presence of contaminated foreign material in the wound [85,86,87].

In a recent unpublished SR conducted by the WHO, a total of 14 observational studies (no RCTs) describing the relationship between surgical volume and the risk of SSI were identified. There was a substantial heterogeneity in the definitions of volume, surgical procedures studied and SSI measurement. Thus, separate meta-analyses were performed to evaluate SSI rates between high vs. low and medium vs. low hospital volume and high vs. low and medium vs. low surgeon volume. A moderate quality of evidence showed that surgical procedures performed in high-/medium-volume hospitals have lower SSI rates compared with low-volume hospitals (OR: 0.69; 95% CI: 0.55-0.87 and OR: 0.80; 95% CI: 0.69-0.94, respectively). In addition, there was a moderate quality of evidence that surgical procedures performed by high- or medium-volume surgeons have lower SSI rates (OR: 0.67; 95% CI: 0.55-0.81 and OR: 0.73; 95% CI: 0.63-0.85, respectively) compared with low volume hospitals. However, there was controversial evidence when high- and medium-volume hospitals were compared and it remains unclear whether there is a linear relationship between procedure/surgeon volume and the SSI rate. Despite robust data on the burden of SSI in some countries or regions, accurate estimates of the global burden in terms of SSI rates and the economic aspects still remain a goal for the future. There is a global need to address changes to SSI definitions, strengthen and validate SSI data quality and to conduct robust SSI economic and burden studies [15].

Basic SSI risk index [60,61]

The basic SSI risk index is used in the National Healthcare Safety Network (NHSN) which assigns surgical patients into categories based upon the presence of three major risk factors:

- operation lasting more than the duration cut point hours, where the duration cut point is the approximate 75th percentile of the duration of surgery in minutes for the operative procedure, rounded to the nearest whole number of hours;
- contaminated (class 3) or dirty/infected (class 4) wound class;
- ASA classification of 3, 4 or 5.

The patient's SSI risk category is the number of these factors present at the time of the operation (see below).

Calculation of basic SSI risk index:

Calculation	Score =0, if:	Score =1, if:
Wound contamination class	W1, W2	W3, W4
ASA classification	A1, A2	A3, A4, A5
Duration of operation T (see Table 8 below)	≤ T	> T
Basic SSI risk index	Sum of scores	

Abbreviations: W1= Clean; W2 = Clean-contaminated; W3 = Contaminated; W4 = Dirty or infected; UNK = Unknown.

The Physical status classification is developed by the American Society of Anesthesiology (ASA) [88]**.**

ASA physical status classification:

ASA score	Description
A1	A1 **Normally healthy patient**
A2	A2 Patient with **mild systemic disease**
A3	A3 Patient with **severe systemic disease** that is not incapacitating
A4	A4 Patient with an **incapacitating systemic disease** that is a constant threat to life
A5	A5 **Moribund** patient who is not expected to survive for 24 hours with or without operation

Table 8 shows the 75th percentile cut-off values for selected NHSN procedures. In case of a reintervention within 72h after the primary procedure, the duration of the reintervention needs to be added to the duration of the primary procedure [89].

Table 8: Cut-off values for duration of operative procedure categories

Category	Description	75th percentile cut-off value, in hours
CHOL	Cholecystectomy: removal of gallbladder; includes	2

	procedures performed using the laparoscope	
COLO	Colon surgery: incision, resection or anastomosis of the large bowel; includes large-to-small and small-to-large bowel anastomosis	3
CSEC	Caesarean section	1

Abbreviations: CHOL= Cholecystectomy; COLO = Colon surgery; CSEC= Caesarean section

[A0004] – What is the natural course of abdominal surgical wound infection?

Healing by primary union or first intention, with minimal oedema and no local infection or serious discharge is a normal pathway of wound healing.

Healing by second intention

When the wound fails to heal by primary union, a more complicated and prolonged healing process takes place. Healing by second intention is caused by infection, excessive trauma, tissue loss or imprecise approximation of tissue. In this case, the wound may be left open and allowed to heal from the inner layer to the outer surface. Granulation tissue forms and contains myofibroblasts.

Delayed primary closure

This is considered to be a safe method of management of contaminated, as well as dirty and infected traumatic wounds with extensive tissue loss and a high risk of infection. The surgeon usually treats these injuries by debridement of nonviable tissues and leaves the wound open, inserting gauze packing which is changed twice a day [89].

SSI pathogenesis

The development of a SSI depends on contamination of the wound site at the end of a surgical procedure and specifically relates to the pathogenicity and inoculum of microorganisms present, balanced against the host's immune response. The number of pathogenic organisms required to cause an SSI is reduced in the presence of the foreign body (e.g. suture material, an implant or drain) [42,62].

The type of the microorganisms responsible for SSIs can be variable, depending on the type and location of the procedure, as well as antimicrobials received by the patient as prophylaxis [72]

Most often, the cause of infections of the surgical intervention port are gram-positive bacteria [90]. Additionally, some typical gram-negative enteric pathogens, primarily *Escherichia coli* and *Klebsiella pneumoniae*, can cause SSIs. Fungi from endogenous and exogenous sources rarely cause SSIs and their pathogenesis is not well understood.

According to the ECDC Annual epidemiological report 2013-2014, data on microorganisms were reported for 7,114 (38.7%) SSIs from 13 countries, using patient- or unit-based surveillance. Overall, *Staphylococcus aureus* (17.0%) and *Escherichia coli* (16.9%) were the most commonly reported microorganisms. The distribution of microorganisms varied by surgical procedure type. For CHOL and COLO operations, the majority of the reported microorganisms were

Enterobacteriaceae. For all other surgical procedure types, gram-positive cocci were the most commonly reported microorganisms [66]. The National Healthcare Safety Network, USA, reported that between 2009 and 2011 among the 1029 facilities that reported one or more SSI, *Staphylococcus aureus* was the most commonly reported pathogen overall (30.4%), followed by coagulase-negative staphylococci (11.7%), *Escherichia coli* (9.4%) and *Enterococcus faecalis* (5.9%) [91].

Antimicrobial-resistant pathogens, such as methicillin-resistant *S.aureus* (MRSA), vancomycin-resistant Enterococcus, gram-negative bacilli or *Candida albicans*, are recognized as a major problem, since they are causing an ever increasing proportion of SSIs [42,92].

Outbreaks or clusters of SSIs have also been caused by unusual pathogens, such as *Rhizopus oryzae*, *Clostridium perfringens*, *Rhodococcus bronchialis*, *Nocardia farcinica*, *Legionella pneumophila* and *Legionella dumoffii*, and *Pseudomonas multivorans*. These rare outbreaks have been related to contaminated adhesive dressings, elastic bandages, colonized surgical personnel, tap water or contaminated disinfectant solutions [42].

Most of the SSIs are caused by contamination of an incision with microorganisms from the patient's own skin or from an opened viscus during surgery (endogenous infection), where endogenous flora typically includes aerobic gram-positive cocci (e.g., staphylococci), but may include faecal flora (e.g., anaerobic bacteria and gram-negative aerobes) when incisions are made near the perineum or groin. If a gastrointestinal organ is opened during an operation and it becomes the source of pathogens, gram-negative bacilli (e.g., E. coli), gram-positive microorganisms (e.g., enterococci) and sometimes anaerobes (e.g., *Bacillus fragilis*) are found in the typical SSI isolates [42].

Infection caused by microorganisms from an outside source following surgery is less common. Exogenous infection occurs when microorganisms from instruments or the theatre environment contaminate the site at operation, when microorganisms from the environment contaminate a traumatic wound or when microorganisms gain access to the wound after surgery, before the skin has sealed [62,12]. Exogenous flora is primarily aerobes, especially gram-positive organisms (e.g. staphylococci and streptococci). Fungi from endogenous and exogenous sources rarely cause SSIs and their pathogenesis is not well understood [42].

Rarely, microorganisms from a distant source of infection, principally through haematogenous spread, can cause an SSI by attaching to a prosthesis or other implant left in an operative site [62].

SSIs are potentiated by the sutures when necrotic or devascularized tissue, hematoma or dead space caused by tissue damage or poor surgical technique are present [93].

The adherence of microorganisms to the suture material is highly variable. There are several variables that affect adherence: the type of microorganisms, the physical and chemical configuration of the different sutures (the structure of suture itself and the chemical composition of the device). The variations in the sutures' capillarity and fluid absorption properties determine bacterial transport along the suture filaments [93,94].

Braided sutures have been shown to be more susceptible to microbial colonization compared with nylon devices and, in a study on an animal model, it was demonstrated that wounds closed with buried absorbable subcutaneous sutures (subcuticular) were more susceptible to infection with Staphylococcus aureus in comparison with transdermal closure, regardless of copious saline

irrigation. Braided suture provides a large surface area with a three dimensional, highly complex architectural matrix for entrapping bacteria and thereby increasing the risk of contamination [94].

After their adhesion, microorganisms can proliferate and create colonies on the suture. A biofilm may subsequently be formed in order to promote the attachment of additional microorganisms and reinforce the resistance against attack from the host's immune system and antimicrobial treatment, predisposing the wound to infection [17,62].

The mechanisms by which microorganisms cause a SSI are different and their mechanistic relationship to SSI development has not been fully determined.

The majority of gram-negative bacteria produce endotoxin. Endotoxin stimulates cytokine production which in turn can trigger the systemic inflammatory response syndrome that sometimes leads to multiple system organ failure. Intraabdominal infection is one of the most common causes of multiple system organ failure in modern surgical care.

Some bacterial surface components, notably polysaccharide capsules, inhibit phagocytosis, thereby eliminating an early host defence response to microbial contamination.

Certain strains of clostridia and streptococci produce potent exotoxins that disrupt cell membranes or alter cellular metabolism.

A variety of microorganisms, including gram-positive bacteria such as coagulasenegative staphylococci, produce glycocalyx and an associated component called "slime," which physically shields bacteria from phagocytes or inhibits the binding or penetration of antimicrobial agents [42].

Effects of the disease or health condition

[A0005] – What are the symptoms and the burden of abdominal surgical wound infection?

The majority of SSI symptoms appear within 30 days ~~of~~ after an operative procedure (most often between the 5th and 10th postoperative day). If a prosthetic implant was implanted during the procedure, SSIs affecting the deeper tissues may occur several months after the operation [62].

Symptoms of the superficial SSI include: infection which affects only skin and subcutaneous tissue of the incision, with typical signs of infection (fever, pain or tenderness, localized swelling, redness, erythema and sense of heat), purulent drainage and present bacterial culture [17].

Symptoms of deep SSI are: infection in deep soft tissues of the incision (e.g. fascial and muscle layers), purulent drainage from the deep incision but not from the organ/space component of the surgical site, spontaneously dehiscing deep wound and isolated bacterial culture. Other signs or symptoms include fever (>38°C) and/or localized pain or tenderness.

Symptoms of organ SSI include infection in any part of the body deeper than the fascial/muscle layers opened or manipulated during the operative procedure: an abscess, purulent drainage from a drain that is placed into the organ/space and isolated bacterial culture.

SSIs may generate psychological, physical and financial stress to patients and, therefore, can have a significant effect on the quality of life of the patient [60,61].

SSIs are associated with considerable morbidity and extended hospital stay. They result in significant increase in readmissions, intensive care unit admissions and long-term surgical-site

complications. In extreme cases, SSIs can result in a greater risk of death from sepsis or other complications in patients having surgical procedures (17% of the mortality after surgery are attributed directly to such infections) [12,17,92].

According to the WHO, there is an increased burden put on healthcare resources. The literature demonstrates that patients with SSIs are twice as likely to spend time in an intensive care unit, five times more likely to be readmitted after discharge, and the risk of death is two times higher [95].

[A0006] – What are the consequences of abdominal surgical wound infection for the society?

The majority of SSIs are closely associated with sutures. Infections associated with implanted medical devices are often difficult to resolve and may require extended hospitalization, antibiotic therapy and additional surgical procedures [90].

Direct costs related to SSIs include prolonged hospitalization and readmission to the hospital (resulting in additional hospital bed occupancy, incurring increased economic costs in terms of bed stay, physician time and nursing care), outpatient visits and visits to the emergency department, additional surgery (ranging from incision and drainage to staged reimplantation), prolonged antibiotic therapy, more use of ancillary services such as radiologic procedures, laboratory tests and home health visits, costs of drugs and durable medical equipment and professional fees.

The indirect costs of SSI, which are difficult to quantify, include lost productivity – not only by the patient, but also by family members or friends who act as caregivers – temporary or permanent loss of functional capacity, impaired mental health (also temporary or permanent), decreased patient satisfaction, reduced referrals and possibly litigation [96].

As a summary, please see Table 9 below.

Table 9: Direct and indirect costs of SSI [96]

Direct costs	Indirect costs
• Prolonged hospitalization and re-admission • Outpatient and emergency care visits • Additional surgical procedures • Incision and drainage • Staged re-implantation • Prolonged antibiotic therapy • Increased use of ancillary services • Home health visits • Radiology and laboratory tests • Drug costs • Durable medical equipment	• Lost productivity (patient and family members) • Temporary or permanent impairment of functional • and mental capacity • Decreased patient satisfaction • Decreased referrals • Increased litigation

The per-case cost of SSI varies widely, from several hundred to tens of thousands of US dollars per case. The major factors influencing total cost are the geographic locale, the type of procedure, and the depth of infection [97].

The cost of treating superficial SSIs is relatively low when compared with intra-abdominal infections. This type of SSIs is managed by removing sutures or staples, establishing local drainage, providing wound care and, on occasion, administering antibiotics. Management may be based on outpatient visits, home health nursing visits or both.

Deep incisional SSIs often require prolonged hospital stay and frequent readmissions with additional procedures that may be necessary. Compared with patients having superficial incisional SSI, both inpatient wound management and parenteral antibiotic therapy are required more often. The costs of deep SSIs management are moderate to high. In cases of organ or space infections, prolonged initial hospitalization and readmissions to the hospital are to be expected, as are further procedures such as resection of an implant or staged reimplantation, with the overall costs being high to extremely high [96].

SSIs can double the length of time a patient stays in hospital and thereby increase the costs of health care. Additional costs attributable to SSI between £814 and £6626 have been reported, depending on the type of surgery and the severity of the infection. The main additional costs are related to re-operation, extra nursing care and interventions and drug treatment costs. The indirect costs, due to loss of productivity, patient dissatisfaction and litigation and reduced quality of life, have been studied less extensively [92].

Reviews of the economic burden of SSIs in Europe show that it represents a substantial burden: the contribution of SSI to the economic costs of surgical procedures was between €1.47-19.1 billion in a comprehensive study by Leaper et al. [98]. The analysis suggested that the true rate of SSIs is likely to have been previously under-reported, and consequently, the associated economic burden was likely to have been underestimated.

The 2008 report on the epidemiology of communicable diseases from the ECDC estimated that the total annual direct healthcare costs of nosocomial infections for the EU-27 was €7 billion, assuming an average hospital cost of €435 per day. Despite robust data on the burden of SSI in some countries or regions, accurate estimates of the global burden in terms of SSI rates and the economic aspects still remain a goal for the future [15].

Current clinical management of the disease or health condition

[A0024] – How is abdominal surgical wound infection currently diagnosed according to published guidelines and in practice?

Diagnosis of an SSI requires not only microbiological evidence but also clinical signs and symptoms of infection. Positive wound cultures in the absence of clinical signs are rarely indicative of SSI since multiple different microorganisms normally colonise skin sites [62]. Perceptive and accurate observation of clinical signs and symptoms by a clinician is crucial [17].

The majority of SSIs become apparent within 30 days of an operative procedure and most often between the 5th and 10th postoperative day. If a prosthetic implant was implanted during the procedure, SSIs affecting the deeper tissues may occur several months after the operation [62].

A large number of SSIs are recognised after discharge, since hospital stays have become increasingly shorter, which made post-discharge surveillance inevitable. Until recently, international consensus was that post-discharge surveillance should be performed up to 30 days after the procedure, or, if an implant was inserted, one year after the operation. In 2013, the CDC linked the duration of post-discharge surveillance to the type of surgery instead of the presence of implants, and the maximum duration of post-discharge surveillance was reduced from one year to 90 days. The ECDC adopted the 90-day post-discharge surveillance for implant surgeries in 2014. As a result of these changes, the international consensus on the recommended duration of post-discharge surveillance has been lost and is currently subject to research. There is still no international agreement about the preferred method of post-discharge surveillance [99].

There is a slight difference (a number of days after procedure when the SSI appears) in SSI diagnostic criteria in US and Europe, as they were published by US CDC in 2016 and ECDC in 2012. A short summary on the ECDC diagnostic criteria is listed below:

European Centre for Disease prevention and Control (ECDC) definitions [61]

Superficial incisional

Infection occurs within 30 days after the operation and involves only the skin and subcutaneous tissue of the incision and at least one of the following:

- purulent drainage with or without laboratory confirmation, from the superficial incision;
- organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision;
- at least one of the following signs or symptoms of infection: pain or tenderness, localised swelling, redness or heat and superficial incision is deliberately opened by surgeon, unless incision is culture-negative;
- diagnosis of superficial incisional SSI made by a surgeon or attending physician.

Deep incisional

Infection occurs within 30 days of the operation if no implant is left in place or within one year if implant is in place and the infection appears to be related to the operation and infection involves deep soft tissue (e.g. fascia, muscle) of the incision and at least one of the following:

- purulent drainage from the deep incision but not from the organ/space component of the surgical site;
- 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 (> 38° C), localised pain or tenderness; unless incision is culture-negative;
- an abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation or by histopathologic or radiologic examination;
- diagnosis of deep incisional SSI made by a surgeon or attending physician.

Organ/space

Infection occurs within 30 days after the operation if no implant is left in place or within one 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 and spaces) other than the incision that was opened or manipulated during an operation and at least one of the following:

- purulent drainage from a drain that is placed through a stab wound into the organ/space;
- organisms isolated from an aseptically obtained culture of fluid or tissue in the

organ/space;

- 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;
- diagnosis of organ/space SSI made by a surgeon or attending physician.

According to the ECDC Annual epidemiological report 2013-2014, the follow-up period was 30 days for superficial SSIs. For deep or organ/space infections following orthopaedic operations with an implant in place (HPRO/KPRO), the follow-up period used in the analysis was 90 days (replacing the previous one-year period), reflecting the upcoming changes in the surveillance [68].

US Centers for Disease Control and Prevention (CDC)

A short summary on the US CDC diagnostic criteria [6] is listed below:

Superficial incisional SSI criteria [60]

Superficial incisional SSIs* must meet the following criteria:

Infection occurs within 30 days of any NHSN operative procedure (where day 1 = the procedure date)

AND

Involves only the skin and subcutaneous tissue of the incision

AND

Patient has at least ***one*** of the following signs or symptoms of infection:

- purulent drainage from the superficial incision, with or without laboratory confirmation.
- organisms isolated from an aseptically-obtained specimen from the superficial incision or subcutaneous tissue by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g. not Active Surveillance Culture/Testing (ASC/AST).
- A superficial incision that is deliberately opened by a surgeon or attending physician** or other designee and culture or non-culture based testing is not performed **AND** the patient has at least ***one*** of the following signs or symptoms: pain or tenderness; localized swelling; erythema; or heat. A culture or non-culture based test that has a negative finding does not meet this criterion.
- diagnosis of a superficial incisional SSI by the surgeon or attending physician* or other designee.

* There are two specific types of superficial incisional SSIs: 1. Superficial Incisional Primary (SIP) – a superficial incisional SSI that is identified in the primary incision in a patient that has had an operation with one or more incisions (e.g., C-section incision or chest incision for CBGB); 2. Superficial Incisional Secondary (SIS) – a superficial incisional SSI that is identified in the secondary incision in a patient that has had an operation with more than one incision (e.g. donor site incision for CBGB)

** The term attending physician for the purposes of application of the NHSN SSI criteria may be interpreted to mean the surgeon(s), infectious disease, other physician on the case, emergency physician or physician's designee (nurse practitioner or physician's assistant).

The following does not qualify as criteria for meeting the NHSN definition of superficial SSI:

- Diagnosis/treatment of cellulitis (redness/warmth/swelling), does not by itself meet the criterion for superficial incisional SSI. An incision that is draining or that has organisms identified by culture or non-culture based testing is not considered cellulitis;

- A stitch abscess alone (minimal inflammation and discharge confined to the points of suture penetration);
- A localized stab wound or pin site infection. While it would be considered either a skin (SKIN) or soft tissue (ST) infection, depending on its depth, it is not reportable under this module. A laparoscopic trocar site for an NHSN operative procedure is not considered a stab wound;
- Circumcision is not an NHSN operative procedure. An infected circumcision site in newborns is classified as CIRC and is not reportable under this module;
- An infected burn wound is classified as BURN and is not reportable under this module.

Deep incisional SSI criteria [60]

Deep incisional SSIs* must meet the following criteria:

Infection occurs within 30 or 90 days of the NHSN operative procedure (where day 1 = the procedure date).

AND

Involves deep soft tissues of the incision (e.g. fascial and muscle layers)

AND

Patient has at least one of the following:

- purulent drainage from the deep incision but not from the organ/space component of the surgical site;
- a deep incision that spontaneously dehisces, or is deliberately opened or aspirated by a surgeon, attending physician** or other designee and organism is identified by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g. not Active Surveillance Culture/Testing (ASC/AST) or culture or non-culture based microbiologic testing method is not performed **AND** the patient has at least ***one*** of the following signs or symptoms: fever (>38°C); localized pain or tenderness. A culture or non-culture based test that has a negative finding does not meet this criterion;
- an abscess or other evidence of infection involving the deep incision that is detected on direct, gross anatomical or histopathologic exam, during reoperation or imaging test.

* There are two specific types of deep incisional SSIs: 1. Deep Incisional Primary (DIP) – a deep incisional SSI that is identified in a primary incision in a patient that has had an operation with one or more incisions (e.g., C-section incision or chest incision for CBGB); 2. Deep Incisional Secondary (DIS) – a deep incisional SSI that is identified in the secondary incision in a patient that has had an operation with more than one incision (e.g. donor site incision for CBGB)

** The term attending physician for the purposes of application of the NHSN SSI criteria may be interpreted to mean the surgeon(s), infectious disease, other physician on the case, emergency physician or physician's designee (nurse practitioner or physician's assistant).

Organ/Space SSI criteria [60]

Organ/Space SSI must meet the following criteria:

Infection occurs within 30 or 90 days of the NHSN operative procedure
(where day 1 = the procedure date).

AND

Infection involves any part of the body deeper than the fascial/muscle layers that is opened or

manipulated during the operative procedure

AND

Patient has at least ***one*** of the following:

- purulent drainage from a drain that is placed into the organ/space (e.g. closed suction drainage system, open drain, T-tube drain, CT guided drainage);
- organisms are isolated from an aseptically-obtained fluid or tissue in the organ/space by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST);
- an abscess or other evidence of infection involving the organ/space that is detected on gross anatomical or histopathologic exam, or imaging test.

AND

Meets at least one criterion for a specific organ/space infection site.

[A0025] – How is abdominal surgical wound infection currently prevented and managed according to published guidelines and in practice?

Prevention of SSI [12,62]

The majority of SSIs are preventable by applying various invasive and non-invasive interventions. The prevention of SSI is, therefore, aimed at minimising the number of microorganisms introduced into the operative site, for example by:

- removing microorganisms that normally colonise the skin;
- preventing the multiplication of microorganisms at the operative site, for example by using prophylactic antimicrobial therapy;
- enhancing the patient's defences against infection, for example by minimising tissue damage and maintaining normothermia;
- preventing access of microorganisms into the incision postoperatively by use of wound dressings.

Measures can be taken in the pre-, intra- and postoperative phases of care to reduce risk of infection.

A short summary of new **WHO Guideline recommendations** [15] is presented below:

1. Preoperative phase

Preoperative bathing

It is good clinical practice for patients to bathe or shower prior to surgery. The panel suggests that either a plain or antimicrobial soap may be used for this purpose. *(Conditional recommendation, moderate quality of evidence)*

The panel decided not to formulate a recommendation on the use of chlorhexidine gluconate (CHG) -impregnated cloths for the purpose of reducing SSI due to the limited and very low quality evidence.

According to upper mentioned NICE guidelines, 2014, bathing is recommended to reduce the microbial load, but not necessarily SSI. Soap should be used. The use of antiseptic soap to prevent SSI is inconclusive.

Decolonization with mupirocin ointment with or without chlorhexidine gluconate body wash for

the prevention of Staphylococcus aureus infection in nasal carriers undergoing surgery

The panel recommends that patients undergoing cardiothoracic and orthopaedic surgery with known nasal carriage of *S. aureus* should receive perioperative intranasal applications of mupirocin 2% ointment with or without a combination of CHG body wash. *(Strong recommendation, moderate quality of evidence)*

The panel suggests considering to treat also patients with known nasal carriage of *S. aureus* undergoing other types of surgery with perioperative intranasal applications of mupirocin 2% ointment with or without a combination of CHG body wash. *(Conditional recommendation, moderate quality of evidence)*

Screening for extended-spectrum beta-lactamase colonization and the impact on surgical antibiotic prophylaxis

The panel decided not to formulate a recommendation due to the lack of evidence. In the absence of evidence, the implementation of routine screening for ESBL to detect faecal colonization prior to surgery would have major cost implications, especially in LMICs.

Optimal timing for preoperative surgical antibiotic prophylaxis

The panel recommends the administration of surgical antibiotic prophylaxis (SAP) prior to the surgical incision when indicated (depending on the type of operation). *(Strong recommendation, low quality of evidence)*

The panel recommends the administration of SAP within 120 minutes before incision, while considering the half-life of the antibiotic. *(Strong recommendation, moderate quality of evidence)*

Mechanical bowel preparation and the use of oral antibiotics

The panel suggests that preoperative oral antibiotics combined with mechanical bowel preparation (MBP) should be used to reduce the risk of SSI in adult patients undergoing elective colorectal surgery. (*Conditional recommendation, moderate quality evidence)*

The panel recommends that MBP alone (without administration of oral antibiotics) should not be used for the purpose of reducing SSI in adult patients undergoing elective colorectal surgery. *(Strong recommendation, moderate quality evidence)*

Hair removal

The panel recommends that in patients undergoing any surgical procedure, hair should either not be removed or, if absolutely necessary, it should be removed only with a clipper. Shaving is strongly discouraged at all times, whether preoperatively or in the operating room (OR). *(Strong recommendation, moderate quality of evidence)*

Surgical site preparation

The panel recommends alcohol-based antiseptic solutions based on CHG for surgical site skin preparation in patients undergoing surgical procedures. *(Strong recommendation, low to moderate quality of evidence)*

Antimicrobial skin sealants

The panel suggests that antimicrobial sealants should not be used after surgical site skin preparation for the purpose of reducing SSI. *(Conditional recommendation, very low quality of evidence)*

Surgical hand preparation

The panel recommends that surgical hand preparation be performed either by scrubbing with a suitable antimicrobial soap and water or using a suitable alcohol-based hand rub (ABHR) before donning sterile gloves. *(Strong recommendation, moderate quality of evidence)*

2. Perioperative phase

The panel suggests not discontinuing immunosuppressive medication prior to surgery for the

purpose of preventing SSI. (*Conditional recommendation, very low quality of evidence*)

Perioperative oxygenation

The panel recommends that adult patients undergoing general anaesthesia with endotracheal intubation for surgical procedures should receive an 80% fraction of inspired oxygen (FiO2) intraoperatively and, if feasible, in the immediate postoperative period for 2-6 hours to reduce the risk of SSI. (*Strong recommendation, moderate quality of evidence*)

Maintaining normal body temperature (normothermia)

The panel suggests the use of warming devices in the operating room and during the surgical procedure for patient body warming with the purpose of reducing SSI. *(Conditional recommendation, moderate quality of evidence)*

Use of protocols for intensive perioperative blood glucose control

The panel suggests the use of protocols for intensive perioperative blood glucose control for both diabetic and non-diabetic adult patients undergoing surgical procedures to reduce the risk of SSI. *(Conditional recommendation, low quality of evidence)*

Maintenance of adequate circulating volume control/normovolemia

The panel suggests the use of goal-directed fluid therapy (GDFT) intraoperatively to reduce the risk of SSI. *(Conditional recommendation, low quality of evidence)*

Drapes and gowns

The panel suggests that either sterile, disposable, non-woven or sterile, reusable, woven drapes and surgical gowns can be used during surgical operations for the purpose of preventing SSI. *(Conditional recommendation, moderate to very low quality of evidence)*

The panel suggests not to use plastic adhesive incise drapes with or without antimicrobial properties for the purpose of preventing SSI. *(Conditional recommendation, low to very low quality of evidence)*

Wound protector devices

The panel suggests considering the use of wound protector (WP) devices in clean-contaminated, contaminated and dirty abdominal surgical procedures for the purpose of reducing the rate of SSI. *(Conditional recommendation, very low quality of evidence)*

Incisional wound irrigation

The panel considers that there is insufficient evidence to recommend for or against saline irrigation of incisional wounds before closure for the purpose of preventing SSI.

The panel suggests considering the use of irrigation of the incisional wound with an aqueous PVP-I solution before closure for the purpose of preventing SSI, particularly in clean and clean contaminated wounds.

The panel suggests that antibiotic incisional wound irrigation before closure should not be used for the purpose of preventing SSI. *(Conditional recommendations/low quality of evidence)*

Prophylactic negative pressure wound therapy

The panel suggests the use of prophylactic negative pressure wound therapy (pNPWT) in adult patients on primarily closed surgical incisions in high-risk wounds, for the purpose of the prevention of SSI, while taking resources into account. *(Conditional recommendation, low quality of evidence)*

Use of surgical gloves

The panel decided not to formulate a recommendation due to the lack of evidence to assess whether double-gloving or changing of gloves during the operation or using specific types of gloves is more effective in reducing the risk of SSI.

Changing of surgical instruments

The panel decided not to formulate a recommendation on this topic due to the lack of evidence.

Antimicrobial-coated sutures

The panel suggests the use of triclosan-coated sutures for the purpose of reducing the risk of SSI, independent of the type of surgery. *(Conditional recommendation, moderate quality of evidence)*

Laminar airflow ventilation systems in the context of operating room ventilation

The panel suggests that laminar airflow ventilation systems should not be used to reduce the risk of SSI for patients undergoing total arthroplasty surgery. *(Conditional recommendation, low to very low quality of evidence)*

3. Postoperative phase

Surgical antibiotic prophylaxis prolongation

The panel recommends against the prolongation of SAP administration after completion of the operation for the purpose of preventing SSI. *(Strong recommendation/moderate quality of evidence)*

Advanced dressings

The panel suggests not using any type of advanced dressing over a standard dressing on primarily closed surgical wounds for the purpose of preventing SSI. *(Conditional recommendation/low quality of evidence)*

Antimicrobial prophylaxis in the presence of a drain and optimal timing for wound drain removal

The panel suggests that perioperative antibiotic prophylaxis should not be continued in the presence of a wound drain for the purpose of preventing SSI. *(Conditional recommendation, low quality of evidence)*

The panel suggests removing the wound drain when clinically indicated. No evidence was found to recommend an optimal timing of wound drain removal for the purpose of preventing SSI. *(Conditional recommendation, very low quality of evidence)*

A short summary of Guidelines for prevention and treatment of surgical site infections (published by NICE in 2008, last updated in 2014), during pre-, intra- and postoperative phases of care [12], is presented below:

1. Information for patients and carers

1.1 Offer patients and carers clear, consistent information and advice throughout all stages of their care. This should include the risks of surgical site infections, what is being done to reduce them and how they are managed.

1.2 Offer patients and carers information and advice on how to care for their wound after discharge.

1.3 Offer patients and carers information and advice about how to recognise a surgical site infection and who to contact if they are concerned. Use an integrated care pathway for healthcare-associated infections to help communicate this information to both patients and all those involved in their care after discharge.

1.4 Always inform patients after their operation if they have been given antibiotics.

2. Preoperative phase

Preoperative showering

2.1 Advise patients to shower or have a bath (or help patients to shower, bath or bed bath)

using soap, either the day before or on the day of surgery.

Hair removal

2.2 Do not use hair removal routinely to reduce the risk of surgical site infection.

2.3 If hair has to be removed, use electric clippers with a single-use head on the day of surgery. Do not use razors for hair removal because they increase the risk of surgical site infection.

Patient theatre wear

2.4 Give patients specific theatre wear that is appropriate for the procedure and clinical setting, and that provides easy access to the operative site and areas for placing devices, such as intravenous cannulas. Consider also the patient's comfort and dignity.

Staff theatre wear

2.5 All staff should wear specific non-sterile theatre wear in all areas where operations are undertaken.

Staff leaving the operating area

2.6 Staff wearing non-sterile theatre wear should keep their movements in and out of the operating area to a minimum.

Nasal decontamination

2.7 Do not use nasal decontamination with topical antimicrobial agents aimed at eliminating *Staphylococcus aureus* routinely to reduce the risk of surgical site infection.

Mechanical bowel preparation

2.8 Do not use mechanical bowel preparation routinely to reduce the risk of surgical site infection.

Hand jewellery, artificial nails and nail polish

2.9 The operating team should remove hand jewellery before operations.

2.10 The operating team should remove artificial nails and nail polish before operations.

Antibiotic prophylaxis

2.11 Give antibiotic prophylaxis to patients before:

- clean surgery involving the placement of a prosthesis or implant
- clean-contaminated surgery
- contaminated surgery

2.12 Do not use antibiotic prophylaxis routinely for clean non-prosthetic uncomplicated surgery.

2.13 Use the local antibiotic formulary and always consider potential adverse effects when choosing specific antibiotics for prophylaxis.

2.14 Consider giving a single dose of antibiotic prophylaxis intravenously on starting anaesthesia. However, give prophylaxis earlier for operations in which a tourniquet is used.

2.15 Before giving antibiotic prophylaxis, consider the timing and pharmacokinetics (for example, the serum half-life) and necessary infusion time of the antibiotic. Give a repeat dose of antibiotic prophylaxis when the operation is longer than the half-life of the antibiotic given.

2.16 Give antibiotic treatment (in addition to prophylaxis) to patients having surgery on a dirty or infected wound.

2.17 Inform patients before the operation, whenever possible, if they will need antibiotic prophylaxis, and afterwards if they have been given antibiotics during their operation.

3. Intraoperative phase

Hand decontamination

3.1 The operating team should wash their hands prior to the first operation on the list using an aqueous antiseptic surgical solution, with a single-use brush or pick for the nails, and ensure that hands and nails are visibly clean.

3.2 Before subsequent operations, hands should be washed using either an alcoholic hand rub or an antiseptic surgical solution. If hands are soiled then they should be washed again with an antiseptic surgical solution.

Incise drapes

3.3 Do not use non-iodophor-impregnated incise drapes routinely for surgery as they may increase the risk of surgical site infection.

3.4 If an incise drape is required, use an iodophor-impregnated drape unless the patient has an iodine allergy.

Sterile gowns

3.5 The operating team should wear sterile gowns in the operating theatre during the operation.

Gloves

3.6 Consider wearing two pairs of sterile gloves when there is a high risk of glove perforation and the consequences of contamination may be serious.

Antiseptic skin preparation

3.7 Prepare the skin at the surgical site immediately before incision using an antiseptic (aqueous or alcohol-based) preparation: povidone-iodine or chlorhexidine are most suitable.

3.8 If diathermy is to be used, ensure that antiseptic skin preparations are dried by evaporation and pooling of alcohol-based preparations is avoided.

Diathermy

3.9 Do not use diathermy for surgical incision to reduce the risk of surgical site infection.

Maintaining patient homeostasis

3.10 Maintain patient temperature in line with 'inadvertent perioperative hypothermia' (NICE clinical guideline 65).

3.11 Maintain optimal oxygenation during surgery. In particular, give patients sufficient oxygen during major surgery and in the recovery period to ensure that a haemoglobin saturation of more than 95% is maintained.

3.12 Maintain adequate perfusion during surgery.

3.13 Do not give insulin routinely to patients who do not have diabetes to optimise blood glucose postoperatively as a means of reducing the risk of surgical site infection.

Wound irrigation and intracavity lavage

3.14 Do not use wound irrigation to reduce the risk of surgical site infection.

3.15 Do not use intracavity lavage to reduce the risk of surgical site infection.

Antiseptic and antimicrobial agents before wound closure

3.16 Do not use intraoperative skin re-disinfection or topical cefotaxime in abdominal surgery to reduce the risk of surgical site infection.

Wound dressings

3.17 Cover surgical incisions with an appropriate interactive dressing at the end of the operation.

4. Postoperative phase

Changing dressings

4.1 Use an aseptic non-touch technique for changing or removing surgical wound dressings.

Postoperative cleansing

4.2 Use sterile saline for wound cleansing up to 48 hours after surgery.

4.3 Advise patients that they may shower safely 48 hours after surgery.

4.4 Use tap water for wound cleansing after 48 hours if the surgical wound has separated or has been surgically opened to drain pus.

Topical antimicrobial agents for wound healing by primary intention

4.5 Do not use topical antimicrobial agents for surgical wounds that are healing by primary intention to reduce the risk of surgical site infection.

Dressings for wound healing by secondary intention

4.6 Do not use Eusol and gauze, or moist cotton gauze or mercuric antiseptic solutions to manage surgical wounds that are healing by secondary intention.

4.7 Use an appropriate interactive dressing to manage surgical wounds that are healing by secondary intention.

4.8 Refer to a tissue viability nurse (or another healthcare professional with tissue viability expertise) for advice on appropriate dressings for the management of surgical wounds that are healing by secondary intention.

Antibiotic treatment of surgical site infection and treatment failure

4.9 When surgical site infection is suspected (i.e. cellulitis), either de novo or because of treatment failure, give the patient an antibiotic that covers the likely causative organisms. Consider local resistance patterns and the results of microbiological tests in choosing an antibiotic.

Debridement

4.10 Do not use Eusol and gauze, or dextranomer or enzymatic treatments for debridement in the management of surgical site infection.

Specialist wound care services

The following recommendation has been taken unchanged from 'Guidance on the use of debriding agents and specialist wound care clinics for difficult to heal surgical wounds' (NICE technology appraisal 24).

4.11 Although there is no direct evidence to support the provision of specialist wound care services for managing difficult to heal surgical wounds, a structured approach to care (including preoperative assessments to identify individuals with potential wound healing problems) is required in order to improve overall management of surgical wounds. To support this, enhanced education of healthcare workers, patients and carers, and sharing of clinical expertise will be required.

In the Surgical Site Infection Guidelines Update 2016, recently published by the American College of Surgeons and Surgical Infection Society [19], the use of triclosan-coated suture is recommended for wound closure in clean and clean-contaminated abdominal cases, when available.

Management of SSI

The appropriate treatment of established SSIs requires careful monitoring and communication between the multidisciplinary postoperative team (surgeons, intensivists, microbiologists, nurses) and the primary care team. Many complications of postoperative wounds do not represent infection but exudation of tissue fluid or an early failure to heal, which is common in patients with a high body mass index (BMI).

In most cases, the SSIs respond to the removal of sutures with drainage of pus if present. Occasionally, there is a need for debridement and open wound care. These procedures, along with parenteral antibiotics, if indicated, usually require a return to secondary care.

Incomplete sealing of the wound edges can often be managed by using a delayed primary or secondary suture or closure with adhesive tape, but in larger open wounds the granulation tissue must be healthy with a low bioburden of colonising or contaminating organisms if healing is to occur.

Extensive wound breakdown may need specialist wound management to reduce bacterial burden in the open wound. Wound bed preparation may be required to encourage healing by secondary intention or facilitate secondary suture.

It is likely that over 15% of postoperative wounds are treated with antibiotics, possibly inappropriately, which can contribute to the problem of antibiotic resistance [12].

Innovative intraoperative strategies such as continuous insulin infusion, hyperoxia, and continuous antibiotic infusion are recognized as modes to reduce the risk of infectious morbidity, thereby improving patient outcomes. These interventions improve wound healing and host defence posture within the surgical wound, creating an environmental inhospitable to wound contamination [94].

Target population

[A0007] – What is the target population of this assessment?

The target population in this assessment are adult patients undergoing elective or emergency setting open (laparotomy) or minimally invasive (i.e. laparoscopic) abdominal surgery. Types of incision used for open abdominal surgery, e.g. midline/transverse/Pfannenstiel, were not used to restrict participant selection [100].

[A0023] – How many people belong to the target population?

It is not possible to estimate the exact size of the target population due to the wide range of procedures included in the abdominal surgery subgroup and the subsequent limitations of publicly available data. However, focusing on a subset estimation of the target population, it is possible to estimate in part the abdominal surgery population, based on 4 of the numerous abdominal procedures: cholecystectomy; colectomy; hysterectomy and appendectomy [5].

The latest update reports on the following EUROSTAT data regarding 2010-2014, by procedure:

Table 10: The number of procedures per year, according to EUROSTAT data [5]

Procedures*	2010	2011	2012	2013	2014
Colectomy	261.540	248.606	253.214	265.765	262.168
Appendectomy	720.957	711.571	728.401	576.762	560.496
Cholecystectomy	1.007.226	1.007.174	1.014.018	884.619	892.507
Hysterectomy	537.989	519.022	515.729	500.986	490.490
Total	**2.527.712**	**2.486.373**	**2.511.362**	**2.228.132**	**2.205.661**

* The table provides a general indication of the volume of procedures across Europe. The extent to which this is performed is influenced by a number of factors: the size of the population, the incidence of the underlying disease, differences in medical practices between countries and the availability of financial and human resources.

In general, all patients undergoing surgery are at risk of complications, including SSIs. The number of reported surgical procedures (CABG, CHOL, COLO, CSEC) listed by country and type of operations is noted in the table below [66]:

Table 11: Number of reporting hospitals and reported surgical procedures by country and type of operation, EU/EEA, 2013–2014

Country	Number of reporting hospitals	No. of CABG procedures	No. of CHOL procedures	No. of COLO procedures	No. of CSEC procedures
Patient-based data					
Austria	48	954	1 133	389	8 390
Estonia	1	304			469
Finland	13				
France	345	1 159	18 010	7 649	28 936
Germany	845	24 955	33 955	16 800	39 093
Hungary	53	402	7 188	1 350	7 591
Italy	126	2 588	13 379	9 194	18 470
Lithuania	23	946	1 760	592	2 883
Malta	1	384			400
The Netherlands	67		8 673	6 647	10 717
Norway	59	4 198	8 880	6 205	18 668
Portugal	37	49	5 509	3 006	3 400
Slovakia	8		1 145		
UK–England	259	11 982	295	6 517	
UK–Northern Ireland	11				11 420
UK–Wales	17				15 277
Subtotal	**1 913**	**47 921**	**99 927**	**58 349**	**165 714**
Unit-based data					
The Czech Republic	1			566	
Romania	8	254	2 695	2 116	653

Country	Number of reporting hospitals	No. of CABG procedures	No. of CHOL procedures	No. of COLO procedures	No. of CSEC procedures
UK–Scotland	33				33 179
Subtotal	**42**	**254**	**2 695**	**2 682**	**33 759**
EU/EEA	**1 955**	**48 175**	**102 622**	**61 031**	**199 546**

Abbreviations: CABG= Coronary artery bypass graft; CHOL= Cholecystectomy; COLO = Colon surgery; CSEC= Caesarean section

Source: Adapted from: WHO. Global Guidelines for the Prevention of Surgical Site Infection. WHO Library Cataloguing-in-Publication Data. World Health Organization, 2016. Country reports from Austria, the Czech Republic, Estonia, Finland, France, Germany, Hungary, Italy, Lithuania, Malta, the Netherlands, Norway, Portugal, Romania, Slovakia and the United Kingdom (England, Northern Ireland, Scotland and Wales).

* Excluded from further analysis because fewer than 20 surgical procedures of this type were reported by this country.

CABG: coronary artery bypass graft, CHOL: cholecystectomy, COLO: colon surgery, CSEC: caesarean section

The ECDC report presents the results of SSI surveillance in Europe for the period from 2010 to 2011, as well as the results of trend analysis for the period between 2008 and 2011. Data for years 2010 and 2011 were received from 20 networks in 16 European countries (15 EU Member States and one EEA country) and included 811 468 surgical operations: 796 495 operations reported using the patient-based protocol, and 14 973 (<2%) operations reported using the unit-based protocol [61].

Cholecystectomy

A total of 80 563 cholecystectomy (CHOL) operations and 1149 (1.4%) SSI was reported within 30 days of the operation. Of these, 679 (59%) were superficial incisional SSI, 258 (22%) were deep incisional SSI, 201 (17%) were organ/space SSI and for 11 (1%) the type of SSI was unknown. A lower cumulative incidence (1.0%) of SSI was reported in laparoscopic CHOL operations compared with non-endoscopic CHOL operations (4.1%). 48% of SSI were detected during hospitalisation. The incidence density was 1.5 in-hospital SSI per 1 000 post-operative patient-days. The most frequently isolated microorganisms were Enterobacteriaceae (50%) followed by gram-positive cocci (37%). The overall CHOL trend analysis in countries contributing data for all years 2008–2011 showed a significant decreasing trend for the incidence density of SSI, but no significant trend for the cumulative incidence of SSI [61].

Colon surgery

A total of 51 526 colon surgery (COLO) operations and 4 893 (9.5%) SSI was reported within 30 days of the operation. Of these, 2 466 (50%) were superficial incisional SSI, 1 446 (30%) were deep incisional SSI, 958 (20%) were organ/space SSI and 23 (<1%) were of unknown type. 80% of SSI were detected during hospitalisation. The incidence density was 6.2 in-hospital SSI per 1000 post-operative patient-days. Enterobacteriaceae (47%) were the most frequently reported microorganisms followed by gram-positive cocci (30%). The overall COLO trend analysis in countries contributing data for all years 2008–2011 showed a significant decrease for the incidence density of SSI, but no significant trend for the cumulative incidence of SSI [61].

Caesarean section

A total of 167 202 caesarean section (CSEC) operations and 4 894 (2.9%) SSI was reported within 30 days of the operation. Of these, 4247 (87%) were superficial incisional SSI, 485 (10%) were deep incisional SSI, 143 (3%) were organ/space SSI and 19 (<1%) were of unknown type. 16% of SSI were detected during hospitalisation. The incidence density was 0.8 in-hospital SSI per 1000 post-operative patient-days. The most frequently isolated microorganisms were gram-positive cocci (54%) followed by Enterobacteriaceae (29%). The overall CSEC trend analysis in countries contributing data for all years 2008–2011 showed a significant decrease of both the cumulative incidence of SSI and the incidence density of SSI [60].

[A0011] – How much are the antibacterial-coated sutures utilised?

Since 2002, antibacterial sutures have been used in a wide range of surgical procedures and patients to minimize the risk of colonization of the suture by bacteria commonly associated with surgical site infection. It is not possible to track the sutures used for each individual patient or procedure. Consequently, data regarding the number of people currently being treated with the technology (MONOCRYL™ Plus Antibacterial suture, Coated VICRYL™ Plus Antibacterial Suture and PDS™ Plus Antibacterial suture) is not available [5].

4.3 Discussion

Surgical wound infection or SSI is a type of healthcare-associated infection in which a wound infection occurs after an invasive (surgical) procedure.

According to the CDC definition, the three types of SSI are described as: *superficial incisional infection*, *deep incisional infection*, and *organ* or *space infection*.

The incidence of SSI in developed countries is different from SSI incidence in developing countries due to inadequate representation, the scarcity of published data and the lack of proper surveillance systems in these regions [64,65].

Every surgical procedure presents a risk of complications, including SSI, but abdominal surgery presents a particular risk factor for development of SSI which is a result of the nature of the procedures and an elevated risk of endogenous contamination (due to high concentration of normal bowel flora) or exogenous contamination.

Overall, *Staphylococcus aureus* and *Escherichia coli* were the most commonly reported microorganisms.

Measures can be taken in the pre-, intra- and postoperative phases of care to reduce risk of infection by applying various invasive and non-invasive interventions. The prevention measures include, for example: removal of microorganisms that normally colonise the skin, prevention of the multiplication of microorganisms at the operative site (for example by using prophylactic antimicrobial therapy), enhancing the patient's defences against infection (for example by minimising tissue damage and maintaining normothermia) and preventing access of microorganisms into the incision postoperatively by use of wound dressings.

The suture material presents a possible matrix for the adherence of bacteria. The adherence of microorganisms to the suture material is highly variable and depends on the type of microorganisms and the physical and chemical configuration of the different sutures (the structure of suture itself and the chemical composition of the device).

After the adhesion, microorganisms can proliferate and create a biofilm, predisposing the wound to infection.

The WHO panel suggests the use of triclosan-coated sutures for the purpose of reducing the risk of SSI, independent of the type of surgery. Their recommendation is *conditional, with moderate quality of evidence* noted [15].

According to the Surgical Site Infection Guidelines Update 2016, recently published by American College of Surgeons and Surgical Infection Society [19] the use of triclosan-coated suture is recommended for wound closure in clean and clean-contaminated abdominal cases when available.

5 CLINICAL EFFECTIVENESS (EFF)

5.1 Research questions

Element ID	Research question
D0001	What is the expected beneficial effect of antibacterial-coated sutures on mortality?
D0005	How do antibacterial-coated sutures affect symptoms and findings (severity, frequency) of abdominal surgical wound infection?
D0006	How do antibacterial-coated sutures affect progression (or recurrence) of abdominal surgical wound infection?
D0011	What is the effect of antibacterial-coated sutures on patients' body functions?
D0016	How does the use of antibacterial-coated sutures affect activities of daily living?
D0012	What is the effect of antibacterial-coated sutures on generic health-related quality of life?
D0013	What is the effect of antibacterial-coated sutures on disease-specific quality of life?
D0017	Were patients satisfied with the antibacterial-coated sutures?

5.2 Results

Included studies

Seven RCTs were included in the clinical effectiveness assessment (Table 2 and Table A7 in the Appendix 1).

These RCTs were published between 2011 and October 2015, with a total of 3580 randomised patients; 1879 (52.4%) to triclosan-coated sutures and 1707 (47.6%) to non-antibacterial coated sutures. No RCTs were found investigating other antibacterial-coated sutures. Four studies were multicentre studies, with a range of 4 to 24 hospitals and 3 single centres. Sample size was calculated in 6 out of 7 trials.

Three RCTs included patients with elective open colorectal surgery [29,32,33] and one RCT included patients with elective open or laparoscopic colorectal surgery [31]. Two RCTs included patients with elective open surgery on different abdominal organs [27,30]. One RCT included patients with open surgery due to faecal peritonitis caused by colorectal anastomotic leak in 42 patients (41.6%), perforated colonic neoplasm in 25 (24.7%) and perforated acute diverticulitis in 34 (33.7%) [28].

Abdominal incision closure in trials intervention groups was performed by one type of triclosan-coated absorbable synthetic sutures in 5 RCTs: polydioxanone (PDS Plus) in 2 RCTs [27,30] and polyglactin 910 (Vicryl Plus) in 3 RCTs [28,29,31]. In the other 2 RCTs, abdominal incision closure in intervention groups was performed by two types of triclosan-coated absorbable synthetic sutures: polydioxanone (PDS Plus) and polyglactin 910 (Vicryl Plus) in the RCT published by Mattavelli et al., 2015 [33], and polydioxanone (PDS Plus) and poliglecaprone (Monocryl Plus) in the RCT published by Baracs et al., 2011 [32]. Mass closure was performed in 3 RCTs [27,29,30]. Skin closure was performed with staples in 4 RCTs [27,28,30,31].

SSI was defined according to the Centres for Disease Control and Prevention of Atlanta criteria in 5 trials. Antibiotic prophylaxis was given in all RCTs [27,29-31], but in the Ruiz-Tovar study the trial was followed by further antibiotic treatment for at least 7 days [28]. According to wound contamination, clean-contaminated wounds were reported in 2 RCTs [32,33] and dirty in 1 RCT [28]. In 3 RCTs [27,30,31] the whole sample of patients with clean, clean-contaminated, contaminated and dirty wounds (so called mixed trials) was reported. In one RCT, the wound contamination was not reported [29]. Patients were followed up for SSI appearance for 30 days after hospital discharge in 5 out of 7 trials.

Five out of seven RCTs (Table A7, Table A10, Table A11 in the Appendix 1) have a high risk of bias [28-32] and two RCTs have an unclear risk of bias [27,33] on the study level; on the critical outcome – incidence of total inscisional SSIs, five RCTs have high [28,29] or unclear risk of bias [30-32] and two RCTs have a low risk of bias [27,33]. According to the GRADE assessment, the quality of these RCTs related to critical outcome – incidence of total incisional SSIs – was moderate (Table A12 in Appendix 1).

Mortality

[D0001] – What is the expected beneficial effect of antibacterial-coated sutures on mortality?

Mortality was not specified as outcome or reported in 3 RCTs [30,32,33]. There were no deaths in 2 RCTs [29,31].

Diener et al., 2014, reported a total of 29 deaths; the difference between the two groups was not statistically significant: 9 (1.5%) patients died in the intervention group, whereas 20 (3.3%) died in the control group /OR 0.46 (0.21 to 1.01; p=0.48). All deaths were classified as unrelated to the trial intervention and most of the postoperative deaths were due to septic shock, multiple organ failure or cardiac and pulmonary decompensation [27].

Ruiz-Tovar et al., 2015, reported total of 9 (8.2%) deaths, affecting 5 patients in the intervention group and 4 patients in the control group (not statistically significant). Mortality causes were multi-organ failure secondary to septic status [28].

Morbidity

[D0005] – How do antibacterial-coated sutures affect symptoms and findings (severity, frequency) of the disease or health condition?

Incidence of total incisional SSIs

Incidence of total incisional SSIs was an outcome in all 7 RCTs. Only 2 RCTs specifically reported the incidence of incisional superficial and incisional deep SSIs in intervention and control groups [27,33] (Table 12).

Incidence of total incisional SSIs was significantly lower in triclosan-coated sutures in comparison with non-antibacterial coated sutures in 4 RCTs [28-31]. In three RCTs, the difference was not statistically significant [27,32,33]. The same was true for the incidence of superficial and deep incisional SSIs, specifically analysed in two RCTs [27,33] (Table 12).

Table 12: Incidence of total, superficial and deep incisional SSIs (data from the published RCTs)

Studies/Total number of SSI	Intervention *number (%)*	Control *number (%)*	OR (95% CI) / p value
Baracs, 2011			
Total incisional / 47	23/188 (12.2%)	24/197 (12.2%)	p=0.982
Superficial / 42	NR	NR	
Deep / 5	NR	NR	
Rasic, 2011			
Total incisional / 16	4/91 (4.3)	12/93 (13.2)	**p=0.035**
Superficial / NR	NR	NR	
Deep / NR	NR	NR	
Justinger, 2013			
Total incisional / 73	31/485 (6.4)	42/371 (11.3)	**p<0.05**
Superficial / NR	NR	NR	
Deep / NR	NR	NR	
Nakamura, 2013			
Total incisional / 28	9/206 (4.3)	19/204 (9.3)	**p=0.047**
Superficial / NR	NR	NR	
Deep / NR	NR	NR	
Diener, 2014			
Total incisional / 183	87/587 (14.8)	96/598 (16.1)	OR 0.91 (0.66–1.25), p=0.64
Superficial / 109	53	56	
Deep / 47	22	25	
Mattavelli, 2015			
Total incisional / 33	18/140 (12.9)	15/141 (10.6)	OR 1.24 (0.60-2.57), p=0.564
Superficial / 21	14	7	OR 2.13 (0.83-5.44), p=0.115
Deep / 12	4	8	OR 0.49 (0.14-1.66), p=0.252
Ruiz-Tovar, 2015			
Total incisional / 23	5/50 (10)	18/51 (35.3)	OR = 0.204 (0.069-0.605); **p = 0.004;** NNT: 3.95
Superficial / NR	NR	NR	
Deep / NR	NR	NR	

NR: not reported; NNT: The number of patients needed to treat to obtain a benefit

Results of meta-analysis for outcome: total incisional SSIs

Meta-analysis was performed only on the primary outcome, total incisional SSIs.

Risk ratios were calculated for dichotomous variables, and when a sufficient number of comparable trials was available, trials were pooled in a meta-analysis. The meta-analysis combined results of studies (or included only the studies) that were considered clinically homogenous in terms of participants, interventions and outcomes using the RevMan3 software. We used the odds ratio (OR), along with the appropriate 95% confidence intervals (CI) and the appropriate Mantel-Haenszel method of meta-analysis. Since we expected considerable methodological heterogeneity in the included studies, we performed a random-effects model of meta-analysis.

The primary meta-analysis on total incisional SSIs included all eligible studies (7 RCTs). The unit of analysis was individual patients. Statistical significance was considered to be $p<0.05$. Forest plots were used for graphical display of the results. The level of heterogeneity was considered as either low (I^2 less than 25%), moderate (I^2 between 25% to 75%) or high (I^2 over 75%) [101]. We planned to conduct the subgroup analyses to evaluate possible effects on the primary outcome – total incisional SSIs - as follows: Emergency versus elective surgery; Open versus laparoscopic surgery; The nature of the surgical procedure (e.g. oesophagogastric, hepato-pancreato-biliary, colorectal, etc.); The type of surgical incision (midline, transverse, Pfannenstiel, etc.); The degree of wound contamination, according to the US CDC criteria [42]; Antibiotic prophylaxis (received vs not received). Finally, we conducted the subgroup analyses based on the nature of the surgical procedure, specifically colorectal surgery performed in all 7 RCTs [27-33] and on the subgroup of patients with hepatobiliary and upper-gastrointestinal tract surgery in two trials [27,30]; on the type of triclosan-coated absorbable synthetic sutures /5 RCTs: polydioxanone (PDS Plus) in 2 RCTs [27,30] and polyglactin 910 (Vicryl Plus) in 3 RCTs [28,29,31] and based on the degree of wound contamination, according to the CDC criteria [42]. Clean-contaminated wounds were reported in 2 RCTs [32,33] and dirty in 1 RCT [28]. Three RCTs [27,30,31] reported the whole sample of patients with clean, clean-contaminated, contaminated and dirty wounds (so-called mixed trials). We performed additional analysis with available data on SSIs separately for patients with clean, clean-contaminated, contaminated and dirty wounds in 5 RCTs [28,30-33]. In the Nakamura trial, more than 99% patients in both groups had clean-contaminated wounds [31].

In addition, we conducted the subgroup analyses based on the risk of bias criteria to evaluate possible effects on the critical primary outcome – total incisional SSIs – in 5 RCTs with a high or unclear risk of bias [28-32] and two RCTs with a low risk of bias [27,33].

Meta-analysis on total incisional SSIs of the data pooled from 7 RCTs comparing triclosan-coated sutures vs non-antibacterial coated sutures demonstrated a significant benefit of triclosan-coated sutures in reducing the risk of total incisional SSIs, **OR 0.65, (95% CI 0.44,0.96), p=0.03.** Heterogeneity among included RCTs was moderate, $I^2 = 61\%$.

Table 13: Meta-analysis comparing the incidence of total incisional SSIs in patients with triclosan-coated sutures vs non-antibacterial coated sutures

Study or Subgroup	Experimental		Control		Weight	**Odds Ratio**
	Events	Total	Events	Total		M-H, Random, 95% CI
Baracs 2011	23	188	24	197	16.1%	1.00 [0.55,1.85]
Diener 2014	87	587	96	598	22.5%	0.91 [0.66,1.25]

Justinger 2013	31	485	42	371	18.8%	0.53 [0.33,0.87]
Mattavelli 2015	18	140	15	141	13.8%	1.24 [0.60,2.57]
Nakamura 2013	9	206	19	204	12.3%	0.44 [0.20,1.01]
Rasic 2011	4	91	12	93	7.9%	0.31 [0.10,1.00]
Ruiz-Tovar 2015	5	50	18	51	8.7%	0.20 [0.07,0.60]
Total 95% CI		1747		1655	100%	**0.65 [0.44,0.96]**
Total events	177		226			

Heterogeneity: Tau^2=0.15; Chi^2=15.28, df=6 (p=0.02); I=61%; Test for overall effect: Z=2.19 (**p=0.03**)

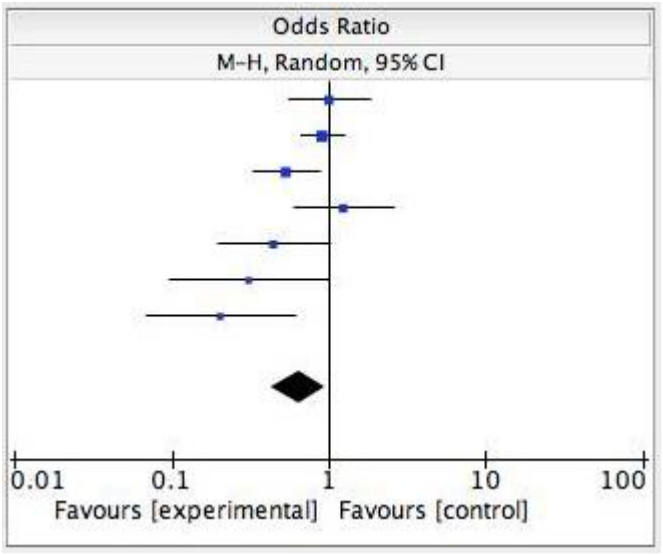

Figure 4: Forest plot of meta-analysis comparing the incidence of total incisional SSIs in patients with triclosan-coated sutures vs non-antibacterial coated sutures

Subgroup analyses based on the nature of the surgical procedure

To evaluate possible effects of the nature of the surgical procedure on the primary outcome – the incidence of total incisional SSIs – we performed the subgroup analysis presented below.

Data from all 7 RCTs performed on patients with abdominal surgery were used, specifically combined in MA on groups or subgroups of patients with colorectal surgery [27-33], hepatobiliary and upper-gastrointestinal tract surgery, available from two RCTs [27,30]. Additional data needed for the Diener RCT was found in the subgroup analysis published in Lancet, October 18, 2014 [102].

We did not find a significant difference of triclosan-coated sutures on the SSI rates in the colorectal or hepatobiliary or upper-gastrointestinal subgroups (p=0.77).

Table 14: Meta-analysis comparing the incidence of total incisional SSIs in patients with colorectal surgery, hepatobiliary and upper-gastrointestinal tract surgery

Study or Subgroup	Experimental		Control		Weight	**Odds Ratio**
	Events	Total	Events	Total		M-H, Random, 95% CI

Colorectal surgery						
Baracs 2011	23	188	24	197	13.1%	1.00 [0.55,1.85]
Diener 2014*	62	344	60	346	16.7%	1.05 [0.71,1.55]
Justinger 2013	17	143	19	100	11.4%	0.58 [0.28,1.17]
Mattavelli 2015	18	140	15	141	11.2%	1.24 [0.60,2.57]
Nakamura 2013	9	206	19	204	10.0%	0.44 [0.20,1.01]
Rasic 2011	4	91	12	93	6.5%	0.31 [0.10,1.00]
Ruiz-Tovar 2015	5	50	18	51	7.1%	0.20 [0.07,0.60]
Subtotal 95% CI		1161		1132	75.9%	0.66 [0.43,1.02]
Total events	138		167			
Heterogeneity: Tau^2=0.19; Chi^2=15.6, df=6 (p=0.02); I^2=60%; Test for overall effect: Z=1.85 (p=0.06)						
Hepatobiliary surgery						
Diener 2014*	4	34	3	40	4.2%	1.64 [0.34,7.92]
Justinger 2013	9	210	14	173	9.4%	0.51 [0.21,1.21]
Subtotal 95% CI		244		213	13.6%	0.75 [0.25,2.24]
Total events	13		17			
Heterogeneity: Tau^2=0.27; Chi^2=1.64, df=1(p=0.20); I^2=39%; Test for overall effect: Z=0.51 (p=0.61)						
Upper-gastrointestinal tract surgery						
Diener 2014*	5	67	15	73	7.3%	0.31 [0.11,0.91]
Justinger 2013	3	59	2	41	3.2%	1.04 [0.17,6.55]
Subtotal 95% CI		126		114	10.5%	0.45 [0.15,1.34]
Total events	8		17			
Heterogeneity: Tau^2=0.14; Chi^2=1.24, df=1 (p=0.26); I^2=20%; Test for overall effect: Z=1.44 (p=0.15)						
Total 95% CI		1532		1459	100.0 %	0.65 [0.46,0.93]
Total events	159		201			

Heterogeneity: Tau^2=0.16; Chi^2=19.78, df=10 (p=0.03); I=49%; Test for overall effect: Z=2.33 (**p=0.02**); Test for subgroup differences: Chi^2=0.52, df=2 (p=0.77); I=0%

* Data from Diener et al, 2014 [102]

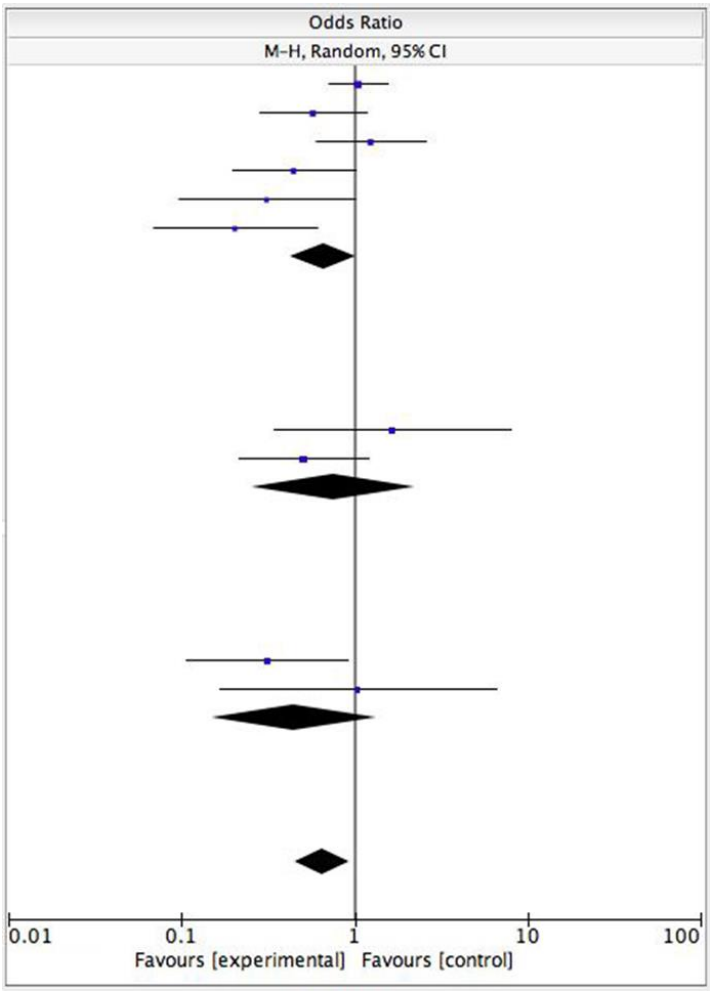

Figure 5: Forest plot of meta-analysis based on the nature of the surgical procedure

Subgroup analyses based on the type of triclosan-coated absorbable synthetic sutures

To evaluate possible effects of the type of triclosan-coated absorbable synthetic sutures on the primary outcome – the incidence of total incisional SSIs – we performed the subgroup analysis presented below. Only Vicryl Plus significantly reduced the risk of total incisional SSIs in comparisons with a non-antibacterial coated suture – Vicryl. Subgroup analyses were performed comparing PDS Plus vs PDS II and Vicryl Plus vs Vicryl sutures. Data from two RCTs [27,30] comparing PDS Plus vs PDS II showed no statistically significant difference in reducing risk of total incisional SSIs, OR 0.72, (95% CI 0.43,1.21), p=0.22. Heterogeneity among included RCTs was moderate, I^2 = 69%. Data from three RCTs [28,29,31] comparing Vicryl Plus vs Vicryl showed that Vicryl Plus significantly reduced risk of total incisional SSIs, **OR 0.33, (95% CI 0.19, 0.58), p=0.0001**. Heterogeneity among included RCTs was low, I^2 = 0%.

Table 15: Meta-analysis comparing the type of triclosan-coated absorbable synthetic sutures on the incidence of total incisional SSIs

Study or Subgroup	Experimental		Control		Weight	**Odds Ratio**
	Events	Total	Events	Total		M-H, Random, 95% CI
PDS Plus						

Diener 2014	87	587	96	598	30.3%	0.91 [0.66,1.25]
Justinger 2013	31	485	42	371	26.1%	0.53 [0.33,0.87]
Subtotal 95% CI		1072		969	56.5%	0.72 [0.43,1.21]
Total events	118		138			
Heterogeneity: Tau^2=0.10; Chi^2=3.24, df=1 (p=0.07); I^2=69%; Test for overall effect: Z=1.24 (p=0.22)						
Vicryl Plus						
Nakamura 2013	9	206	19	204	18.1%	0.44 [0.20,1.01]
Rasic 2011	4	91	12	93	12.1%	0.31 [0.10,1.00]
Ruiz-Tovar 2015	5	50	18	51	13.3%	0.20 [0.07,0.60]
Subtotal 95% CI		347		348	43.5%	**0.33 [0.19,0.58]**
Total events	18		49			
Heterogeneity: Tau^2=0.00; Chi^2=1.28, df=2 (p=0.53); I^2=0%; Test for overall effect: Z=3.81 (**p=0.0001**)						
Total 95% CI		1419		1317	100%	0.50 [0.30,0.83]
Total events	136		187			

Heterogeneity: Tau^2=0.19; Chi^2=11.68, df=4 (p=0.02); I^2=66%; Test for overall effect: Z=2.68 (p=0.007); Test for subgroup differences: Chi^2=3.98, df=1 (p=0.05); I^2=74.9%

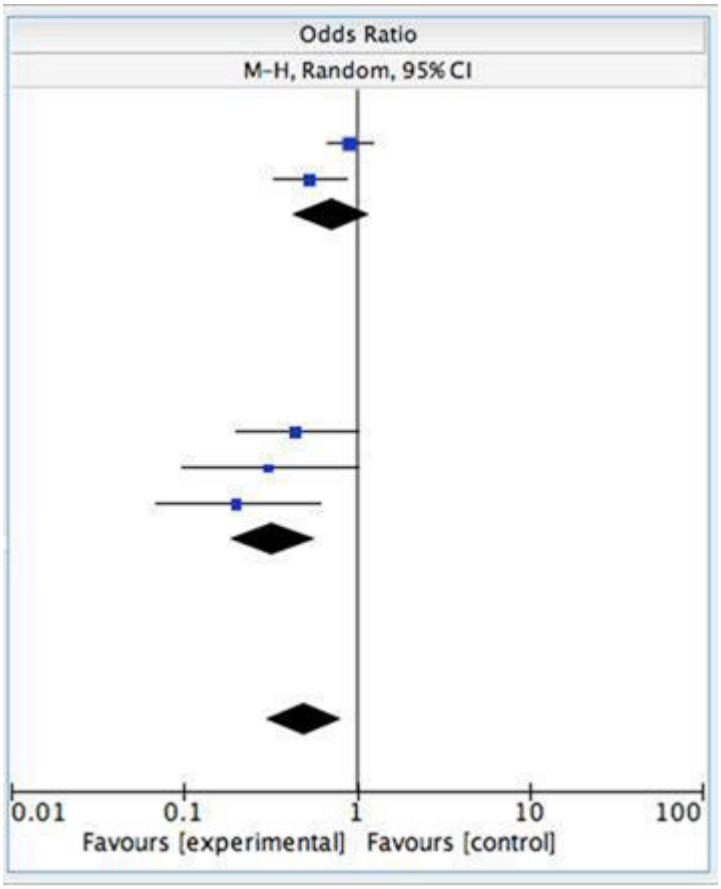

Figure 6: Forest plot of meta-analysis comparing the type of triclosan-coated absorbable synthetic sutures on the incidence of total incisional SSIs

Subgroup analyses based on the degree of wound contamination, according to the US Centre for Disease Control and Prevention (CDC) criteria

To evaluate possible effects of the degree of wound contamination, according to the US CDC criteria, on the primary outcome – the incidence of total incisional SSIs – we performed the subgroup analyses presented below. The effect of antibacterial coated sutures was similar to that of uncoated sutures in trials with clean-contaminated and mixed trials with the whole patients sample with full whole range of wound types, and separately in trials with clean, clean-contaminated and contaminated wounds.

In one trial with dirty wounds [28], the effect of triclosan-coated sutures was statistically significant in reducing the SSI risk, **OR 0.20, (95% CI 0.07, 0.60), p=0.004**. Heterogeneity among included RCTs was moderate, I^2 =62%, and for the subgroup the difference was high, I^2 =76.1% (Table 16).

Clean-contaminated wounds

Meta-analysis of the pooled data from two 2 RCTs [32,33] indicated that triclosan-coated sutures vs non-antibacterial coated sutures had a similar effect on incisional SSIs rates for clean-contaminated wounds, OR 1.10, (95% CI 0.69, 1.75), p=0.70. Heterogeneity among included RCTs was low, I^2 = 0%.

The results did not change with the addition of available subgroup data from the Justinger 2013 and Nakamura trials 2013 [30,31]. In the Nakamura trial, more than 99% patients in both groups had clean-contaminated wounds so data from the whole trial were used.

RCTs with patients with the whole range of wound types – mixed trials

In these trials the rate of SSIs was calculated for the whole sample of patients, with all types of wounds: clean, clean-contaminated, contaminated and dirty. In the Justinger trial the majority of patients in both groups had clean (286/59% vs 245/66%) or clean-contaminated (162/33.4% vs 97/26.1%) wounds; the same was true for patients in the Diener trial: clean wound made for 144/24.5% vs 138/23.1% patients and clean-contaminated for 430/73.3% vs 450/75.3% of patients. In the Nakamura trial, more than 99% patients in both groups had clean-contaminated wounds [27,30,31].

Meta-analysis of the pooled data from 3 RCTs [27,30,31] indicated that triclosan-coated sutures vs non-antibacterial coated sutures also had a similar effect on incisional SSIs rates for the sample of patients with all types of wounds, OR 0.66, (95% CI 0.42,1.03), p=0.07. Heterogeneity among included RCTs was moderate, I^2 =59%.

Dirty wounds

Comparing triclosan-coated sutures vs non-antibacterial coated sutures from one RCT [28], in dirty wounds, triclosan-coated sutures demonstrated a significant benefit in reducing the risk of total incisional SSIs, OR 0.20, (95% CI 0.07,0.60), p=0.004.

Table 16: Meta-analysis based on the degree of wound contamination – RCTs with clean-contaminated wounds vs mixed trials (the whole sample of patients with all types of wounds) vs trial with dirty wounds

Study or Subgroup	Experimental		Control		Weight	Odds Ratio
	Events	Total	Events	Total		M-H, Random, 95% CI
Clean-contaminated						
Baracs 2011	23	188	24	197	17.4%	1.00 [0.55,1.85]
Mattavelli 2015	18	140	15	141	14.8%	1.24 [0.60,2.57]
Subtotal 95% CI		328		328	32.3%	1.10 [0.69,1.75]
Total events	41		39			
Heterogeneity: Tau^2=0.00; Chi^2=0.19, df=1 (p=0.67); I^2=0%; Test for overall effect: Z=0.38 (p=0.70)						
Dirty						
Ruiz-Tovar 2015	5	50	18	51	9.2%	0.20 [0.07,0.60]
Subtotal 95% CI		50		51	9.2%	**0.20 [0.07,0.60]**
Total events	5		18			
Heterogeneity: Not applicable; Test for overall effect: Z=2.87						

(**p=0.004**)						
Mixed RCTs with the whole sample of patients with all types of wounds						
Diener 2014	87	587	96	598	24.9%	0.91 [0.66,1.25]
Justinger 2013	31	485	42	371	20.5%	0.53 [0.33,0.87]
Nakamura 2013	9	206	19	204	13.2	0.44 [0.20,1.01]
Subtotal 95% CI		1278		1173	58.5%	0.66 [0.42,1.03]
Total events	118		138			
Heterogeneity: Tau^2=0.09; Chi^2=4.85, df=2 (p=0.09); I^2=59%; Test for overall effect: Z=1.83 (p=0.07)						
Total 95% CI		1656		1562	100%	**0.69 [0.46,1.03]**
Total events	173		214			

Heterogeneity: Tau^2=0.14; Chi^2=13.08, df=5 (p=0.02); I^2=62; Test for overall effect: Z=1.83 (p=0.07); Test for subgroup differences: Chi^2=8.37, df=2 (p=0.02); I^2=76.1

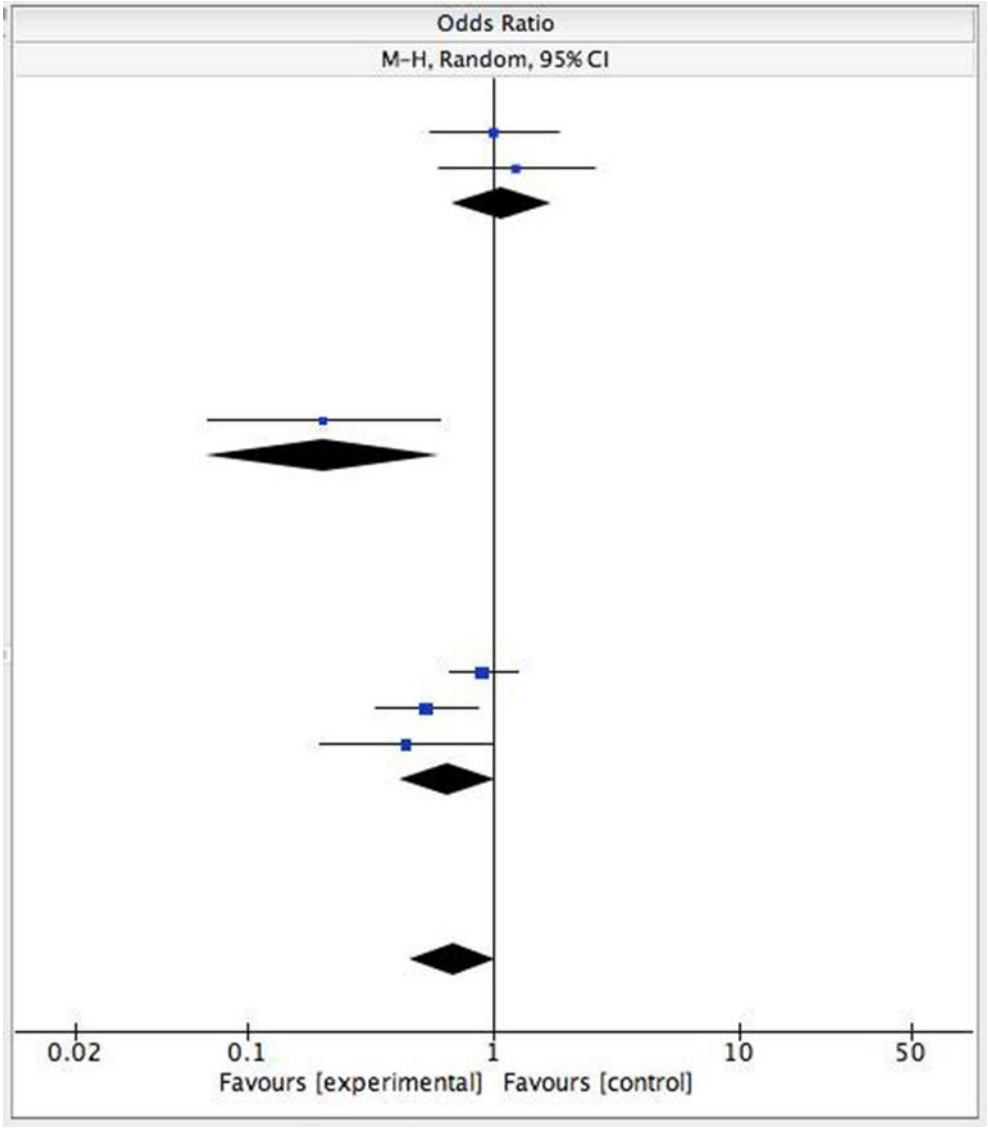

Figure 7: Forest plot of meta-analysis based on the degree of wound contamination, RCTs with clean-contaminated wounds) vs trial with dirty wounds vs mixed trials (the whole sample of patients with all types of wounds)

Data from additional analysis with available data on SSI incidence separately for patients with clean, clean-contaminated, contaminated and dirty wounds in 5 RCTs [28,30] is presented in the table below (Table 17). Results showed that triclosan-coated sutures vs non-antibacterial coated sutures had a statistically significant effect on incisional SSI rates only in patients with dirty wounds **(p=0.004).**

Table 17: Meta-analysis based on the degree of wound contamination, according to the US Centre for Disease Control and Prevention (CDC) criteria, separately for patients with clean, clean-contaminated, contaminated and dirty wounds in 5 RCTs

Study or Subgroup	Experimental		Control		Weight	**Odds Ratio**
	Events	Total	Events	Total		M-H, Random, 95% CI
Clean						

Justinger 2013	14	286	22	245	17.3%	0.52 [0.26,1.04]
Subtotal 95% CI		286		245	17.3%	0.52 [0.26,1.04]
Total events	14		22			
Heterogeneity: Not applicable, Test for overall effect: Z=1.84 (p=0.07)						
Clean-contaminated						
Baracs 2011	23	188	24	197	19.3%	1.00 [0.55,1.85]
Justinger 2013	14	162	16	97	15.7%	0.48 [0.22,1.03]
Mattavelli 2015	18	140	15	141	16.5%	1.24 [0.60,2.57]
Nakamura 2013	9	206	19	204	14.7%	0.44 [0.20,1.01]
Subtotal 95% CI		696		639	66.3%	0.74 [0.45,1.22]
Total events	64		74			
Heterogeneity: Tau^2=0.12; Chi^2=5.57, df=3 (p=0.13); I^2=46%; Test for overall effect: Z=1.17 (p=0.24)						
Contaminated						
Justinger 2013	3	37	4	25	5.9%	0.46 [0.09,2.28]
Subtotal 95% CI		37		25	5.9%	0.46 [0.09,2.28]
Total events	3		4			
Heterogeneity: Not applicable; Test for overall effect: Z=0.95 (p=0.34)						
Dirty						
Ruiz-Tovar 2015	5	50	18	51	10.4%	0.20 [0.07,0.60]
Subtotal 95% CI		50		51	10.4%	**0.20 [0.07,0.60]**
Total events	5		18			
Heterogeneity: Not applicable; Test for overall effect: Z=2.87 (**p=0.004**)						
Total 95% CI		1069		960	100.0%	0.59 [0.39,0.91]
Total events	86		118			

Heterogeneity: Tau^2=0.15; Chi^2=11.31, df=6 (p=0.08); I^2=47%; Test for overall effect: Z=2.39 (**p=0.02**); Test for subgroup differences: Chi^2=4.68, df=3 (p=0.20); I^2=35.9%

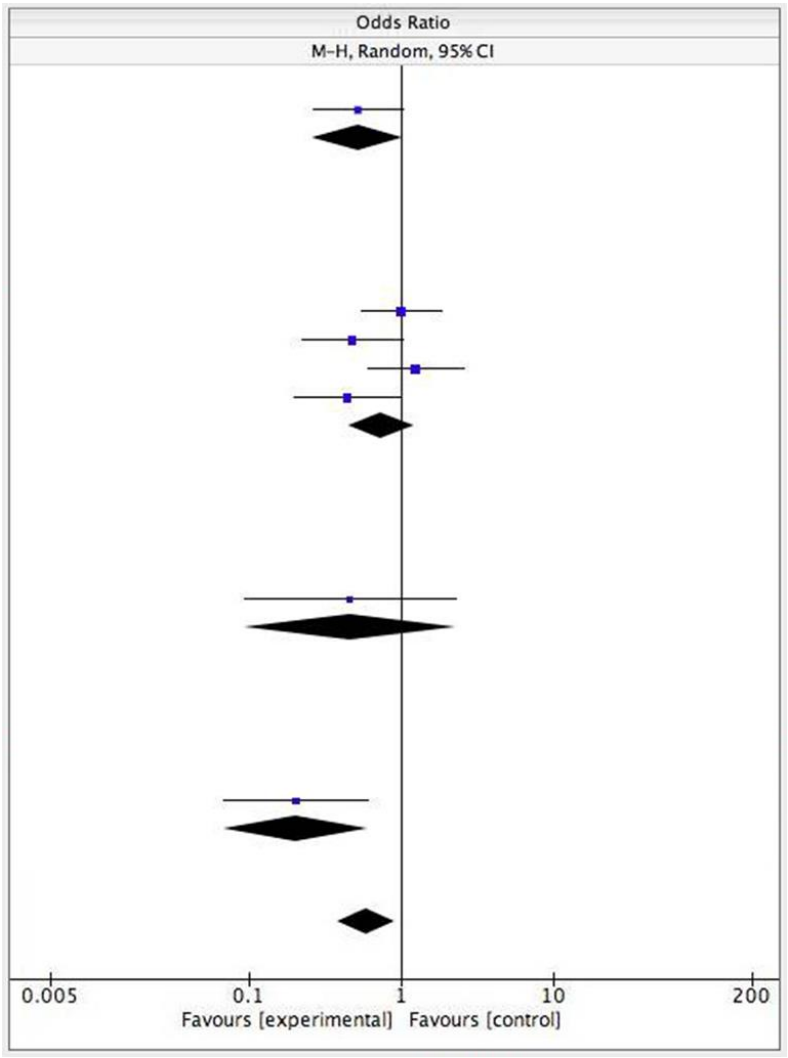

Figure 8: Forest plot of meta-analysis based on the degree of wound contamination, separately for patients with clean, clean-contaminated, contaminated and dirty wounds in 5 RCTs

Subgroup analyses based on the risk of bias criteria

To evaluate possible effects of bias according to the risk criteria on the primary outcome – the incidence of total incisional SSIs – we performed the subgroup analysis presented below on 5 RCTs with a high [28,29] or unclear risk of bias [30-32] and two RCTs with a low risk of bias [27,33] (Table A7, Table A10, Table A11 in the Appendix 1).

Significant differences were found in high or unclear risk of bias RCTs /**OR 0.50 [95% CI 0.30, 0.81], p=0.005,** I^2 =51%/ but not in low risk of bias RCTs /OR 0.96 [0.72,1.28], p=0.76, I^2 =0%/ (Table 18).

Table 18: Meta-analysis comparing the incidence of total incisional SSIs in high or unclear risk of bias RCTs vs low risk of bias RCTs

Study or Subgroup	Experimental		Control		Weight	**Odds Ratio**
	Events	Total	Events	Total		M-H, Random, 95% CI

High or unclear risk of bias						
Baracs 2011	23	188	24	197	16.1%	1.00 [0.55,1.85]
Justinger 2013	31	485	42	371	18.8%	0.53 [0.33,0.87]
Nakamura 2013	9	206	19	204	12.3%	0.44 [0.20,1.01]
Rasic 2011	4	91	12	93	7.9%	0.31 [0.10,1.00]
Ruiz-Tovar 2015	5	50	18	51	8.7%	0.20 [0.07,0.60]
Subtotal 95% CI		1020		916	63.7%	**0.50 [0.30,0.81]**
Total events	72		115			
Heterogeneity: Tau^2=0.15; Chi^2=8.14, df=4 (p=0.09); I^2=51%; Test for overall effect: Z=2.80 (p=**0.005**)						
Low risk of bias						
Diener 2014	87	587	96	598	22.5%	0.91 [0.66,1.25]
Mattavelli 2015	18	140	15	141	13.8%	1.24 [0.60,2.57]
Subtotal 95% CI		727		739	36.3%	0.96 [0.72,1.28]
Total events	105		111			
Heterogeneity: Tau^2=0.00; Chi^2=0.58, df=1 (p=0.45); I^2=0%; Test for overall effect: Z=0.31 (p=0.76)						
Total 95% CI		1747		1655	100.0%	0.65 [0.44,0.96]
Total events	177		226			

Heterogeneity: Tau^2=0.15; Chi^2=15.28, df=6 (p=0.02); I^2=61%; Test for overall effect: Z=2.19 (p=0.03); Test for subgroup differences: Chi^2=5.08, df=1 (p=0.02); I^2=80.3%

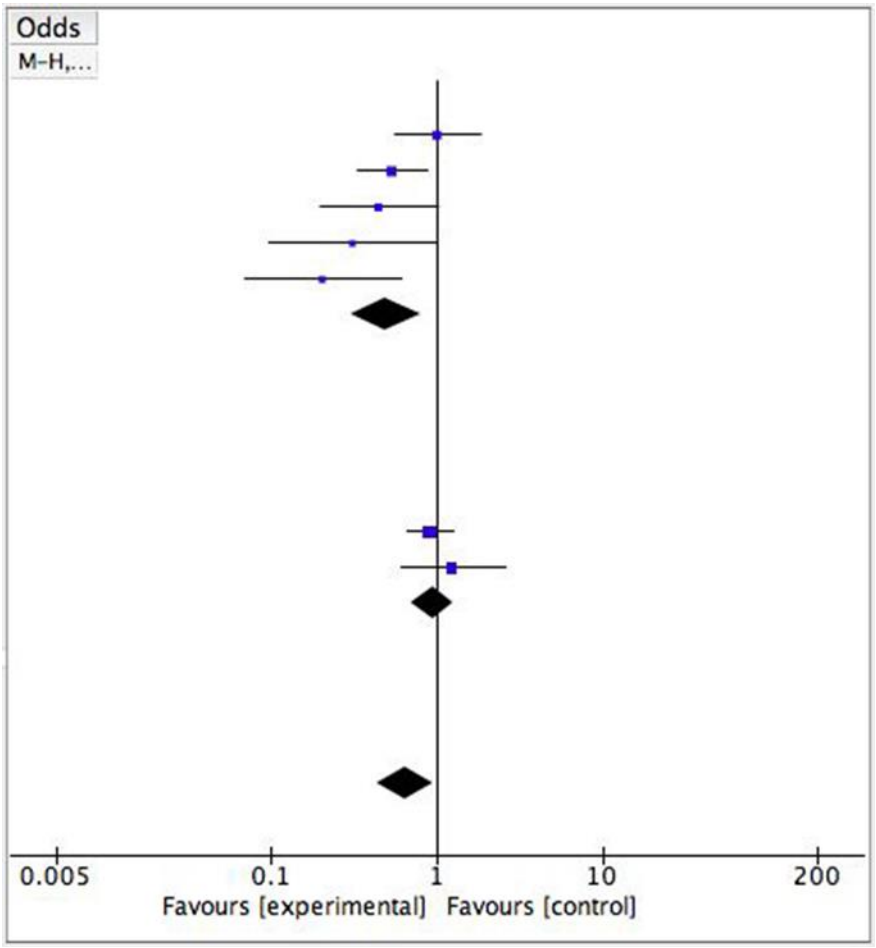

Figure 9: Forest plot of meta-analysis based on the risk of bias criteria

[D0006] – How do antibacterial-coated sutures affect progression (or recurrence) of the disease or health condition?

The length of hospital stay

The length of hospital stay was an outcome in all 7 RCTs; only in one RCT the length was statistically different in favour of the triclosan-coated surgical sutures group [29]. In one RCT it was pointed out that with normal wound healing, the average number of nursing days was nine, whereas for SSI patients it was 15 (p = 0.043) [32] (Table 19).

Table 19: The length of hospital stay in triclosan-coated vs non-antibacterial coated sutures patient groups

Studies	Intervention	Control	p value
Baracs, 2011*			
Length of hospital stay (days)*	NR	NR	NR
Rasic, 2011			
Length of hospital stay (days)	1.2±1.3	21.4±2.8	**p<0.05**
Justinger, 2013			

Length of hospital stay (days)	11 ± 18 (2 - 209)	15 ± 13 (2 - 134)	p=0.30
Nakamura, 2013			
Length of hospital stay (days)	15.2	15.6	p=0.71
Deiner, 2014			
Length of hospital stay (days)	13.0 (7.4)	12.5 (6.3)	p=0.99
Mattavelli, 2015			
Length of hospital stay (days)	12.3	13.5	p=0.546
Ruiz-Tovar, 2015			
Length of hospital stay (days)	9	9.5	NS

NR: not reported; * With normal wound healing, the average number of nursing days was nine, whereas for SSI patients it was 15 (p = 0.043); NS: not significant

The proportion of patients requiring secondary surgery for wound-related complications of surgery

The proportion of patients requiring hospital readmissions for SSI/wound-related complications

The proportion of patients requiring secondary surgery for wound-related complications of surgery is presented in Table 20. In two RCTs the difference between intervention and control group was statistically significant, in favour of triclosan-coated sutures [27,29]. The opposite was true for one RCT [30] in which major wound revision was higher in the triclosan-coated sutures group.

Table 20: The proportion of patients requiring secondary surgery for wound-related complications of surgery

Studies	**Intervention** ***n (%)***	**Control** ***n (%)***	**OR (95% CI) / p value**
Rasic, 2011			
Secondary surgery needed	1 (1)	8 (8.8)	**p<0.05**
Reasons	Wound dehiscence	In 7 patients because of wound dehiscence and in one patient because of peritonitis	
Justinger, 2013			
Secondary surgery needed	8/31 (25.8)	5/42 (11.9)	NR
Reasons	Major wound revision	Major wound revision	
Diener, 2014			
Secondary surgery needed	9 (1.9)	22 (4.5)	0.40 (0.18-0.88), **p=0.01**

Reasons	Complete dehiscence	Complete dehiscence	

NR: not reported

The proportion of patients requiring hospital readmissions for SSI/wound-related complications was not reported in any of the 7 RCTs.

The incidence of complete abdominal wound dehiscence within 30 days of surgery

The incidence of incisional hernia during the period of study follow-up

Complete abdominal wound dehiscence was reported in two RCTs, with a statistically significant difference between the intervention and control groups in both trials [27,29] (Table 21). Incisional hernia was reported in one RCT [29], but the difference between the two groups was not statistically significant.

Table 21: The incidence of complete abdominal wound dehiscence within 30 days of surgery and incisional hernia during the period of study follow-up

Studies	Intervention *n (%)*	Control *n (%)*	OR (95% CI) / p valuae
Rasic, 2011			
Complete wound dehiscence	1 (1.1)	7 (7.7)	**p=0.027**
Incisional hernia	2 (2.2)	5 (5.5)	p=0.235
Deiner, 2014			
Complete wound dehiscence	9 (1.9)	22 (4.5)	0.40 (0.18-0.88), **p=0.01**

Causative microorganism of incisional SSI (results of microbiological cultures in patients with SSI)

The use of systemic antibiotic therapy within 30 days of surgery

Two RCTs did not report a causative microorganism of incisional SSI [27,29] (Table 22).

Ruiz-Tovar, 2015 reported a reduction in the SSIs caused by *Escherichia coli*, *Klebsiella spp*. and *Enterococcus faecalis* in triclosan-coated sutures groups. In the multivariable analysis, the use of triclosan-coated sutures was the only independent variable associated with a reduction in incisional SSIs (p=0.026) [28]. In other RCTs, the difference between the triclosan-coated sutures and non-antibacterial coated sutures groups was not statistically significant or not reported.

Use of systemic antibiotic therapy within 30 days of surgery was reported in two RCTs [27,28].

Table 22: Causative microorganism of SSI and the use of systemic antibiotic therapy within 30 days of surgery

Studies	Intervention *n (%)*	Control *n (%)*	p valuae
Baracs, 2011			

Causative microorganism	Gram-negative organisms (Pseudomonas aeruginosa, Enterococcus faecium, E. coli, Enterococcus spp.)	Gram-negative organisms (Pseudomonas aeruginosa, Enterococcus faecium, E. coli, Enterococcus spp.) Gram-positive bacteria (two cases of S. epidermidis)	NR
Use of systemic antibiotic therapy	NR	NR	NR
Justinger, 2013			
Causative microorganism	Staphylococci 23.1% Enterococci 30.1% Streptococci 5.1% Pseudomonas spp. 5.1%, Enterobacteriacae 2.5% Others 23.1%	Staphylococci 23.1% Enterococci 23.1% Streptococci 5.1%, Enterobacteriacae 5.1% Others	p>0.05
Use of systemic antibiotic therapy	NR	NR	NR
Nakamura, 2013			
Causative microorganism	Enterococcus species (12 of 28 cases)	Bacteroides species (8 of 28 cases)	NS
Use of systemic antibiotic therapy	NR	NR	NR
Diener, 2014			
Causative microorganism	NR	NR	NR
Use of systemic antibiotic therapy	126 (21.5)	112 (18.7)	NR
Mattavelli, 2015			
Causative microorganism	E. coli, E. faecalis, E. avium, Citrobacter koseri, S. aureus , E. cloacae, M. morganii, P. aeruginosa, Proteus vulgaris, K. oxytoca, B. fragilis, Streptococcus anginosus, P. vulgaris	Pseudomonas aeruginosa, Enterobacter cloacae, Klebsiella pneumoniae, Escherichia coli, Staphylococcus aureus, Bacteroides fragilis, Enterococcus faecium, Candida albicans, Morganella morganii	No difference between groups
Use of systemic antibiotic therapy	NR	NR	NR
Ruiz-Tovar, 2015			
Causative microorganism	E. coli: 2 (49%) Klebsiella spp.: 1 (20%) Pseudomonas aeruginosa: 2 (40%) Enterococcus faecalis: 0	E. coli: 16 (88.9%) Klebsiella spp. 5 (27.7%) Pseudomonas aeruginosa: 9 (50%) Enterococcus faecalis: 5 (27.7%)	p=0.006 p=0.003 p=NS p=0.003
Use of systemic antibiotic therapy*	Imipenem or tigecycline	Imipenem or tigecycline	NR

NR: not reported; NS: not significant; * Imipenem 1 g/8 h intravenous; in case of allergies to b-lactams, tigecycline (100mg IV as starting dose, followed by 50mg/12 h IV); both antibiotics were maintained for a minimum of 7 d

[D0011] – What is the effect of antibacterial-coated sutures on patients' body functions?

[D0016] – How does the use of antibacterial-coated sutures affect activities of daily living?

None of the 7 included RCTs specifically assessed the effect of antibacterial-coated sutures on patients' body functions and the effect of antibacterial-coated sutures on activities of daily living.

Health-related quality of life

[D0012] – What is the effect of antibacterial-coated sutures on generic health-related quality of life?

[D0013] – What is the effect of antibacterial-coated sutures on disease-specific quality of life?

Quality of life was assessed in only one RCT [27]. Patient self-assessed quality of life 30 days after the operation, measured on the EQ-5D index, did not differ between the groups. The sub-items with regard to mobility, self-care, usual activities, pain and discomfort, anxiety and depression and the observed general health status on the visual analogue scale also did not differ between the two groups /EQ-5D visual analogue scale N 453 vs 461: mean (SD) 69.2 (20.1) vs 68.2 (19.6) MD 0.96, -1.61 to 3.54, p=0.34); EQ-5D index N 448 vs 448; mean (SD) 0.9 (0.2) vs 0.8 (0.2), MD 0.01, -0.02 to -0.04, p=0.18)/ [27].

Satisfaction

[D0017] – Were patients satisfied with the technology?

None of the 7 included RCTs assessed patient satisfaction.

5.3 Discussion

Despite the fact that the most recently published SR/MA by Sandini et al., 2016 [29], with the primary aim of comparing the effect of triclosan-coated sutures with non-antibacterial coated sutures on the incidence of SSI after elective colorectal operation in published RCTs, already included 6 RCTs relevant for our assessment [27, 29-33], we were not able to update it due to two reasons: the scope was too narrow, including only patients with elective colorectal surgery and the search strategy was not described. We found a Cochrane protocol for a SR with the same scope, published by McCallum et al., 2014 [103], but unfortunately the SR was not performed.

Results from our SR, including a meta-analysis performed on the primary outcome related to total incisional SSIs, are based on the data pooled from 7 RCTs comparing triclosan-coated sutures vs non-antibacterial coated sutures. A statistically significant benefit of triclosan-coated sutures in reducing the risk of total incisional SSIs - OR 0.65 (95% CI 0.44,0.96), p=0.03 - was demonstrated. Heterogeneity among included RCTs was moderate, I^2 = 61%. The majority of studies had a high or unclear risk of bias. In subgroup analysis, significant differences were found in high or unclear risk of bias RCTs - OR 0.50 (95% CI 0.30,0.81), p=0.005, I^2 =51% [29-32] - but not in low risk of bias RCTs - OR 0.96 (0.72,1.28), p=0.76, I^2 =0% [27,33].

No clinical studies were found on chlorhexidine-coated sutures.

A recently published SR/MA by Sandini et al., 2016, did not demonstrate a significant protective effect of triclosan-coated sutures on the occurrence of SSI after elective colorectal resections, so the authors concluded that further large RCTs are needed before introducing this technology into clinical practice [26].

Our subgroup analysis based on the nature of the surgical procedure did not find any significant difference from triclosan-coated sutures on SSI rates in the colorectal or hepatobiliary or upper-gastrointestinal subgroup (p=0.77). In correspondence published in Lancet in 2014 [102], Diener et al. did not note any significant differences in the SSI rates in the colorectal or hepatopancreatobiliary subgroup but did note significant reduction of SSI in the upper-gastrointestinal subgroup after additional analyses performed. The authors said that these results need to be interpreted with caution because of the exploratory nature of these analyses for which no adjustment for multiplicity had been done.

Our subgroup analysis based on the type of triclosan-coated sutures revealed significant differences only in the comparison of Vicryl Plus with Vicryl, which is in accordance with results of the SR/MA published by Wu et al., 2016, and Guo et al., 2016 [104,105] who described different types of surgical procedures and did not only focus on abdominal surgery. Wu et al. explained that this may be due to the relatively small sample sizes in the studies comparing the other triclosan-coated suture types.

In the subgroup analysis based on the type of the surgical wound, we showed that in clean, clean-contaminated, contaminated and mixed trials with all four types of surgical wounds, triclosan-coated sutures have similar effects as non-antibacterial coated sutures. These results were in accordance with other recently published SRs with MAs [104-106]. A statistically significant effect was shown only in one trial including patients with dirty wounds [28]. Ruiz-Tovar, 2015, also reported a reduction in the SSIs caused by *Escherichia coli*, *Klebsiella spp*. and *Enterococcus faecalis* in triclosan-coated suture groups. In the multivariable analysis done by authors, the use of triclosan-coated sutures was the only independent variable associated with a reduction in incisional SSIs (p=0.026) [28].

This study had a high risk of bias, and all patients received systemic antibiotics (imipenem or tigecycline) for a minimum of 7 days due the faecal peritonitis. In an MA published by Wang et al. [107], including 17 RCTs involving 3720 participants with different types of surgical procedures, the results showed a significant advantage in the reduction of the SSI rate by 30% (relative risk 0.70, 95% CI 0.57 to 0.85; p<0.001), and subgroup analyses revealed consistent results in favour of triclosan-coated sutures in adult patients, abdominal procedures and clean or clean-contaminated surgical wounds. Two studies included in this MA with contaminated and dirty procedures failed to demonstrate any advantage of the use of triclosan-coated sutures.

It should be noted that the SR/MA done by Apisarnthanarak et al., 2015, and Wu et al., 2016, [104,106] had different inclusion criteria; they included observational studies in addition to RCTs in the analysis of clinical effectiveness, patients with different types of surgery, data from abstracts and non-English language studies and data from preliminary published results like Mingmalairak et al., 2009 [108].

We decided not to include RCT results published by Mingmalairak et al., 2009, in our SR/MA because we treated this trial as a preliminary report on the first 100 patients, exactly as the authors reported it in the published article (“This is the primary report of the first 100 patients. The sample size was calculated… the sample size in each group was 672 patients at 95% confident

interval. The authors reported the first 100 patients about safety and physical properties to proceed with the complete study. A complete study is required for final conclusion after the safety of the new suture is confirmed.") [108]. We did not contact the authors to find out the status of this study. This study was, unfortunately, not registered in any of the publicly available clinical trial registries, therefore could not be treated properly as an ongoing study. Due to the author statement mentioned above, this trial could not be treated as a so-called "Clinical Trials That Stopped Early" either. It should be noted that the EUnetHTA methods guideline on RCT validity mentions early stopping of trials as a possible reason for bias, but the guideline does not note that such trials should be excluded [41].

Literature data on such trials, also called truncated RCTs, showed that they were associated with greater effect sizes than RCTs not stopped early. This difference was independent of the presence of statistical stopping rules and was greatest in smaller studies [109-111]. Viele et al., 2016, stated that for trials that stop early for success, the statistical superiority of an experimental treatment is straightforward when the early stopping was pre-planned, and it is reasonable to preserve patient resources and time once the primary objective of a trial has been addressed. Early stopping procedures protect against a false conclusion of superiority [112]. Murad et al., 2016, concluded that about half of that trials stopped early to save resources were followed by subsequent trials addressing a similar question, which suggests that researchers may have been sceptical about the decision to stop prior trials. The authors said that a more rigorous threshold for stopping early to save resources is needed [113].

To be completely transparent and to see how our primary result could be changed, we did a meta-analysis including the data from this RCT; the result of MA still showed statistically significant reduction of SSIs risk by triclosan-coated sutures, OR 0.67, 95% CI 0.46,0.98, p=0.04, with moderate heterogeneity (I^2=56%) (Appendix 1, Table A9).

In a recently published WHO Guideline from November 2016 [15], based on a SR/MA published by Wu et al., 2016 [104], the panel suggests the use of triclosan-coated sutures for the purpose of reducing the risk of SSI, independent of the type of surgery (conditional recommendation, moderate quality of evidence). The rationale for the recommendation was: "Overall low to moderate quality evidence shows that antimicrobial-coated sutures have significant benefits in reducing SSI rates in patients undergoing surgical procedures when compared to non-antibacterial coated sutures. The effect seems to be independent of the type of suture, procedure or wound contamination classification. In meta-regression analysis, there was no evidence that the effect of antimicrobial-coated sutures differed between braided and monofilament sutures, clean, cardiac or abdominal surgery, and other surgeries. However, the GDG highlighted that the available trials examined triclosan-coated, absorbable sutures only. There were no studies identified that investigated other antimicrobial agents. Considering the low to moderate quality of the evidence and the low quality of comparisons in the subgroups of the RCTs included in the meta-regression analyses, the GDG agreed that the strength of the recommendation should be conditional."

The length of hospital stay was an outcome in all 7 RCTs included in this SR; only in one RCT the length was statistically different in favour of the triclosan-coated surgical sutures group [32]. In one RCT it was pointed out that the average number of nursing days was nine with normal wound healing, whereas for SSI patients it was 15 (p = 0.043) [32].

Regarding the other secondary outcomes assessed in our SR, no conclusion could be made due to the lack of or different results of reported data. In two RCTs, there was a statistical difference between the intervention and control group in favour of triclosan-coated sutures [27,29]. The

opposite was true for one RCT [30] in which major wound revision was higher in the triclosan-coated sutures group.

Complete abdominal wound dehiscence was reported in two RCTs and was statistically significantly lower in the intervention than in control groups in both trials [27,29].

According to the literature data, early postoperative fascial dehiscence is a surgical emergency. The late complication of fascial disruption is incisional hernia [52].

Incisional hernia was reported in one RCT [29], but the difference between the two groups was not statistically significant. One prospective cohort study in which the incisional hernia was the only outcome, with a follow-up period of 36 months, did not find a significant difference between triclosan-coated polyglactin 910 antimicrobial sutures – Vicryl Plus vs polyglactin 910 – Vicryl /59/389 (15%) vs 56/399 (14%), p=0.685/ [114]. The authors concluded that fast absorbable sutures coated with triclosan do not increase the hernia rate after midline abdominal incision compared to slowly absorbable sutures when wound infection rates are decreased by coating the fast absorbable suture with triclosan. The development of incisional hernia is significantly increased in patients with a BMI >30 kg/m^2.

According to a published SR, the risk of hernia was significantly increased for midline incision compared with transverse incision (relative risk [RR] 1.77, 95% CI, 1.09-2.87) and paramedian incision (RR 3.41, 95% CI 1.02-11.45) [115]. Three separate meta-analyses found that mass closure was associated with a lower incidence of incisional hernia [116-119]. Principles of abdominal wall closure and recommendations could be found in different literature sources [52].

As mentioned above, Ruiz-Tovar, 2015, reported a reduction in the SSIs caused by *Escherichia coli*, *Klebsiella spp*. and *Enterococcus faecalis* in triclosan-coated sutures groups. In other RCTs, the difference between triclosan-coated sutures and non-antibacterial coated sutures groups was not statistically significant or not reported.

Use of systemic antibiotic therapy within 30 days of surgery was reported in two RCTs [27,28].

None of the 7 included RCTs specifically assessed the effect of antibacterial-coated sutures on patients' body functions and the effect of antibacterial-coated sutures on activities of daily living. Quality of life was assessed in only one RCT [27] and did not differ between the groups. None of the 7 included RCTs assessed patient satisfaction.

No ongoing RCTs or other studies with triclosan-coated sutures and chlorhexidine-coated sutures in abdominal surgery were identified in clinical trial registries.

Our SR/MA was focused on adult patients only. Renko et al., 2016, published results of a pragmatic double-blind, randomised, controlled, single centre trial including 1633 children who were undergoing various surgical procedures in Finland. The primary endpoint was the incidence of superficial or deep SSI according to the Centers for Disease Control criteria. The authors concluded that triclosan-coated sutures effectively reduce the occurrence of SSI /20 (3%) of 778 patients in the triclosan group *vs* 42 (5%) of 779 patients in the control group, p=0.004/ [120].

Despite the fact that these results are consistent with previous trials and meta-analyses in adults, Huttner and Diener discussed that triclosan-containing sutures might only be beneficial for specific types of operations and that it cannot be concluded that triclosan-containing sutures reduce SSI for all of these indications. Future trials should focus on individual types of paediatric surgery to evaluate a potential beneficial effect. They also elaborated that trial results cannot be directly extrapolated between adults and children because children have different physiological

characteristics and different risk factors for SSI. Due to these reasons, the authors again stress the need for further high-quality trials in this specific population [121].

Comparisons with other antimicrobial sutures are needed, since we did not find any published clinical studies despite the fact that chlorhexidine-coated sutures are already on the market. All studies should be designed as a RCT, with the SSI outcome defined according to CDC criteria and sub-specified as superficial, deep and organ space SSIs.

6 SAFETY (SAF)

6.1 Research questions

Element ID	Research question
C0008	How safe are antibacterial-coated sutures in relation to the comparator(s)?
C0004	How does the frequency or severity of harms change over time or in different settings?
C0005	What are the susceptible patient groups that are more likely to be harmed through the use of the antibacterial-coated sutures?
B0010	What kind of data/records and/or registry is needed to monitor the use of antibacterial-coated sutures and the comparator(s)?

6.2 Results

Included studies

According to the protocol, in addition to the seven RCTs already mentioned in the Effectiveness domain, 7 prospective non-randomised studies were included for the assessment of safety (Table 2, Table A8 Appendix 1).

Four out of seven RCTs (with high risk of bias) did not specify AEs as an outcome nor reported them [28,30-32]. In two RCTs (one with high and one with unclear risk of bias), AEs were not specified as an outcome, but were reported [29,33], and in only one RCT (with unclear risk of bias) SAEs were specified in the study protocol and reported in the published article [27]. According to the GRADE assessment, the quality of evidence of these three RCTs was low.

Out of 7 prospective non-randomised studies included for the assessment of safety, five were observational studies (four with historical control), one is an interventional non-randomised clinical pathway driven study and one is an interventional single arm study. In five of the studies, AEs were not specified as an outcome nor reported; in two studies, AEs were not specified as outcome but reported [34,35]. Neither the risk of bias nor the quality of evidence according to GRADE [25] (in which observational studies are primarily graded as low quality unless upgraded by review authors to moderate or high quality, if the effect is large enough) were assessed for these studies.

Patient safety

[C0008] – How safe are antibacterial-coated sutures in relation to (the) comparator(s)?

As mentioned above, four out of seven RCTs (with high risk of bias) did not specify AEs as an outcome nor report them [28,30-32]. In two RCTs, AEs were not specified as an outcome but were reported [29,33], and in only one RCT (with unclear risk of bias) SAEs were specified in the study protocol and reported in the published article [27]. In five out of seven prospective non-randomised studies, AEs were not specified as an outcome nor reported; in two studies, AEs were not specified as outcome but were reported [34,35].

All reported AEs are described in Table 23.

Frequency of AEs was not reported in any of the six studies which reported data on AEs. Only one RCT [27] reported the frequency of SAEs, which was not statistically different between the intervention (146/583) and control (138/602) group (p=0.39).

In brief, local AEs were mentioned in 2 RCTs: in one RCT [29] postoperative inflammatory reactions to the skin sutures were statistically significantly higher in the comparator group using polyglactin 910 Vicryl (7/91 vs 16/93, p<0.05) than in the intervention group (triclosan-coated polyglactin 910 Vicryl Plus). In another RCT in which two different triclosan-coated sutures were used in the intervention group (triclosan-coated polyglactin – 0 Vicryl Plus and triclosan-coated polydioxanone – PDS Plus) [33], incisional haematoma was statistically higher in the intervention group - OR 4.71 (1.31–16.91), p = 0.02. No significant differences were observed for skin swelling, redness or wound seroma.

Systemic SAEs were reported in three studies [27,34,35], but investigators found a majority of them were unrelated to the intervention. None of them were statistically different between groups.

Table 23: Frequency and severity of adverse events in 3 RCTs [27,29,33] and 2 non-RCT studies [34,35]

Studies	Intervention *number (%)*	Control *number (%)*	OR (95% CI) / p value
Rasic 2011 (RCT) [29]	**N = 91**	**N =93**	
Total of AEs	NR	NR	NR
Total of SAEs	NR	NR	NR
Frequency of SAEs leading to death	NR	NR	NR
Description of most frequent AE (by arms): Postoperative inflammatory reactions to the skin sutures	 7 (7.5)	 16 (17.5)	 **p<0.05**
Description of SAE (by arms)	NR	NR	NR
Diener 2014 (RCT) [27]	**N = 583**	**N =602**	
Total of AEs	NR	NR	NR
Total of SAEs	146	138	p=0.39
Frequency of SAEs leading to death	NR	NR	NR
Description of most frequent AE (by arms)	NR	NR	NR
Description of SAE (by arms): Anastomotic insufficiency Intra-abdominal fluid collection or abscess Other GI problems Pulmonary Bleeding Cardiovascular Other	 39 (25.8) 14 (9.3) 21 (13.9) 15 (9.9) 12 (7.9) 9 (6.0) 15 (9.9)	 34 (21.5) 7 (4.4) 24 (15.2) 13 (8.2) 14 (8.9) 14 (8.9) 21 (13.3)	p=0.81*
Mattavelli 2015 (RCT) [33]	**N = 140**	**N =141**	
Total of AEs	NR	NR	NR

Total of SAEs	NR	NR	NR
Frequency of SAEs leading to death	NR	NR	NR
Description of most frequent AE (by arms):			
Overall incision complications	64 (45.7)	54 (38.3)	4.71 (1.31–16.91), p = 0.21
Incision hematoma	13 (9.3)	3 (2.1)	4.71 (1.31–16.91), **p = 0.02**
Incision swelling	26 (18.6)	20 (14.2)	1.38 (0.73-2.61), p=0.322
Incision redness	43 (30.7)	38 (26.9)	1.20 (0.71-2.02), p=0.486
Incision seroma	32 (22.9)	31 (22.1)	1.05 (0.60-1.84), p=0.861
Description of SAE (by arms)	NR	NR	NR
Jung 2014 (Non-RCT) [34]	**N= 916**	**No comparator**	
Total of AEs	NR	NA	NA
Total of SAEs	8 (0.87)	NA	NA
Frequency of SAEs leading to death	NR	NA	NA
Description of most frequent AE (by arms)	NR	NA	NA
Description of SAE (by arms):		NA	NA
Respiratory problems: atelectasis, pleural effusion and pneumonia	6	NA	NA
Non-complicated fluid collection in the intra-abdominal cavity	2	NA	NA
Okada 2014 (Non-RCT) [35]	**N=88**	**N=110**	
Total of AEs	NR	NR	NR
Total of SAEs	NR	NR	NR
Frequency of SAEs leading to death	NR	NR	NR
Description of most frequent AE (by arms)	NR	NR	NR
Description of SAE (by arms):			
Pancreatic fistula	22 (25)	25 (23.7)	p=0.71
Delayed gastric emptying	8 (9)	15 (14.6)	p=0.32

Abbreviations: RCT: randomised controlled trial; nRCT: non-randomised controlled trial; AE: adverse event; SAE: serious adverse event; NR: not reported; NA: not applicable

*Significance of subgroup effects

[C0004] – How does the frequency or severity of harms change over time or in different settings?

No published data were found to answer this question related to abdominal surgery.

[C0005] – What are the susceptible patient groups that are more likely to be harmed through the use of antibacterial-coated sutures?

No published data were found to answer this question related to abdominal surgery.

[B0010] – What kind of data/records and/or registry is needed to monitor the use of the technology and the comparator?

Further research related to abdominal surgery in form of RCTs including pragmatic RCTs and observational registries studies is needed on the safety of triclosan-coated sutures and other antibacterial-coated sutures already registered on the market, such as chlorhexidine-coated sutures. As pointed out in a recent WHO guideline [15], clear reporting of AEs is needed, including the need to assess the risk of allergy and monitoring possible emerging antimicrobial resistance to the respective antimicrobial agent.

6.3 Discussion

Wound complications are important causes of early and late postoperative morbidity following laparotomy. Generally, surgical wounds of healthy individuals heal through an orderly sequence of physiologic events that include inflammation, epithelialization, fibroplasia and maturation. Mechanical failure or failure of wound healing at the surgical site can lead to seroma, hematoma, wound dehiscence or hernia. Other complications include SSI and nerve injury [52].

The relative safety of triclosan-coated sutures could not be confirmed due to a lack of reporting of AEs in RCTs and non-RCTs included in our assessment. The same is true for chlorhexidine-coated sutures because no clinical studies were found during our literature search.

In the most recently published SR with meta-analysis [26], which included the six RCTs connected with elective colorectal surgery (out of our 7 RCTs included in the current SR), the authors did not specifically predefine AEs as primary or secondary outcomes nor report them.

In our SR, four out of the seven RCTs included (with high risk of bias) did not specify AEs as an outcome nor report them [28,31,32]. If a study did not report the results for a key outcome that could reasonably be expected for a study of its nature, for example for AEs, it was rated as having a high risk of bias. In three RCTs (one with high and two with unclear risk of bias), AEs were not specified as an outcome but were reported [29,30,33], and in only one RCT (with unclear risk of bias) SAEs were specified in the study protocol and reported in the published article [27]. The definition of SAE and AEs in this RCT is questionable, so published data on SAEs might be not fully relevant. According to the GRADE assessment, the quality of evidence related to harm was low.

In five out of seven prospective non-randomised studies, AEs were not specified as an outcome nor reported; in two studies, AEs were not specified as outcome but reported [34,35].

Local AEs were mentioned in 2 RCTs included in this SR [29,33]. Rasic et al., 2011 [29], found that postoperative inflammatory reactions to the skin sutures were significantly higher in the comparator group using polyglactin 910 Vicryl than in the intervention group (triclosan-coated polyglactin 910 Vicryl Plus, $p<0.05$). Mattavelli et al., 2015, presented a statistically higher frequency of incisional haematoma in the intervention group (triclosan-coated polyglactin – 0 Vicryl Plus and triclosan-coated polydioxanone – PDS Plus) [33]. Such local side effects were not reported previously, and the authors could not find the reason or explain it on the basis of the identified safety reports. They speculated that the release of triclosan in the incision may interfere with some local coagulation pathways or platelet function or might be attributed to the broad use of triclosan-coated sutures in their study. They utilised four sutures to close the peritoneum, fascia, subcutaneous fat tissue and the skin, while previous similar trials used only one or two sutures. No significant differences were observed for skin swelling, redness or wound seroma [33]. Limited evidence was published on possible negative effects on wound healing [122] or contact allergy [123].

Our findings are consistent with other studies that address outcomes reporting bias on safety outcomes. Several studies non-specifically connected with antibacterial-coated sutures have documented underreporting of low-grade AEs, recurrent AEs and inconsistent and incomplete characterisation and reporting of high-grade AEs [124-126]. In a study published by Saini et al, 2014 [127], with the aim of determining the extent and nature of selective non-reporting of harm outcomes in clinical studies that were eligible for inclusion in a cohort of SRs, outcome reporting bias for harms was evident in nearly two thirds of all primary studies included in SRs. In contrast, in the sample of the RCTs analysed in a study published by Huic et al, 2011 [128], in which technologies other than pharmaceuticals were presented in 30% of the total sample, serious and non-serious AEs were mentioned in more than 80% of the published articles.

In conclusion, the sources were not sufficient to answer the questions related to relative safety due to the fact that little evidence was identified on the potential harms of triclosan-coated sutures. Ten years since the launch, Ethicon has not been contacted by any regulatory body concerning the use of IRGACARE®† MP on Plus Sutures. No published clinical studies were found on chlorhexidine-coated sutures.

The poor reporting of harms data (safety data is inadequately reported or not reported at all) has major implications for properly judging the benefit-risk ratio. Limitations of data from published studies are obvious, so further research in the form of RCTs including pragmatic RCTs and observational registries studies is needed on the safety of triclosan-coated sutures and other antibacterial-coated sutures already registered on the market, like chlorhexidine-coated sutures. Clear reporting of AEs is needed, including the need to assess the risk of allergy and monitoring possible antimicrobial resistance to the respective antimicrobial agent [15].

The Huic et al. study [128] and the evaluation of the compliance of 21 trial registries with the WHO Minimum Data Set [129] showed that there is a need for standardisation of mandatory dataset items across the registries in collaboration with the ICMJE. Registry items that differ or are missing from registries, such as the assessment of AEs, should be standardised in order to improve quality and completeness of subsequent publications. Introducing entries addressing safety issues in relation to registered outcome measures was proposed as the solution to this problem.

Data reporting should be according to evidence-based reporting guidelines, specifically the CONSORT Statement extension on better reporting of harms in RCTs and trials assessing non-pharmacological treatments [37,38], as well as the PRISMA harm checklist [39]. New recommendations to improve AE reporting on medical devices in clinical trial publications, like those recently published on pharmaceuticals, are clearly needed [40].

7 POTENTIAL ETHICAL, ORGANISATIONAL, PATIENT AND SOCIAL, AND LEGAL ASPECTS (ETH, ORG, SOC, LEG)

7.1 Research questions

Element ID	Research question
Social 3.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any new social issues?

7.2 Results and 7.3 Discussion

Triclosan is used in many antimicrobial soaps, shampoos and tooth pastes. Therefore, bacteria can develop a resistance to triclosan. If triclosan-coated sutures effectively prevent SSI, it might become necessary to restrict the public use of triclosan-containing products in order to prevent the development of triclosan-resistance. According to the literature, widespread use of triclosan may represent a potential public health risk [56]. Previously published literature pointed out that daily absorption of triclosan from consumer products like commercially available hand soap is higher than a single triclosan suture [130,131]. Several studies assessed the bacterial resistance to triclosan: there is not sufficient evidence to support claims of antibiotic resistance or bacterial resistance to triclosan in patients [57-59]. No study was found on patient values and preferences with regards to this intervention. The GDG is confident that most patients wish to receive this intervention in order to reduce the risk of SSI, but patients must be informed about the small and unconfirmed risk of allergy to triclosan. The GDG emphasised that patients would like to be part of the process by being involved and informed [15].

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[132] EC Design Examination Certificate. Vicryl Plus.

[133] EC Design Examination Certificate. Monocryl Plus.

[134] EC Design Examination Certificate. PDS Plus.

APPENDIX 1: METHODS AND DESCRIPTION OF THE EVIDENCE USED

DOCUMENTATION OF THE SEARCH STRATEGIES

The search was done on 27-28 October, 2016 in the following databases; The Cochrane Central Register of Controlled Trials, The Database of Abstracts of Reviews of Effects, The Health Technology Assessment Database, NHS Economic Evaluation Database, MEDLINE, EMBASE, all via OvidSP, and CINAHL via EBSCOhost.

Database: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

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1 exp Abdomen/su [Surgery] (19448)
2 exp Abdomen/ (99143)
3 exp Surgical Procedures, Operative/ (2734184)
4 Surgical Wound Infection/ (31795)
5 2 and 3 (32470)
6 2 and 4 (1347)
7 5 or 6 (32906)
8 exp Abdominal Wound Closure Techniques/ (403)
9 (abdom$ adj5 (surg$ or operation$ or incision$ or closure)).tw. (34552)
10 (abdom$ adj5 (surgical site infection or surgical wound infection)).tw. (95)
11 exp Digestive System Surgical Procedures/ (315695)
12 Laparotomy/ (17222)
13 Laparoscopy/ (69994)
14 exp Hysterectomy/ (27392)
15 Hysterotomy/ (198)
16 exp Cholecystectomy/ (26251)
17 exp Colon/su [Surgery] (11367)
18 exp Intestine, Small/su [Surgery] (27745)
19 Rectum/su [Surgery] (9577)
20 Appendix/su [Surgery] (971)
21 exp Bile Ducts/su [Surgery] (11831)
22 Gallbladder/su [Surgery] (1865)
23 exp Liver/su [Surgery] (8260)
24 exp Pancreas/su [Surgery] (5410)
25 Spleen/su [Surgery] (2821)
26 Splenectomy/ (20683)
27 Kidney Transplantation/ (85681)

28 exp Kidney/su [Surgery] (8793)

29 exp Ovary/su [Surgery] (2375)

30 exp Cesarean Section/ (39027)

31 Aortic Aneurysm, Abdominal/su [Surgery] (10431)

32 (colectom$ or gastrectom$ or hepatectom$ or pancreatectom$ or pancreaticojejunostom$ or pancreaticoduodenectom$ or gastroplast$ or gastropex$ or hysterectom$ or laparotom$ or cholecystectom$ or appendectom$ or colorectal surger$ or gastroenterologic surger$).tw. (166991)

33 or/1,7-32 (688995)

34 exp Sutures/ (15287)

35 exp Anti-Infective Agents, Local/ (204747)

36 exp Anti-Bacterial Agents/ (619438)

37 34 and (35 or 36) (402)

38 ((antibiotic$ or antiseptic$ or antibacterial$) adj5 suture$).tw. (202)

39 Triclosan/ (2291)

40 vicryl plus.tw. (40)

41 monocryl plus.tw. (5)

42 PDS plus.tw. (13)

43 Chlorhexidine/ (6971)

44 assufil plus.tw. (0)

45 neosorb plus.tw. (0)

46 egycryl extra.tw. (0)

47 ((triclosan or chlorhexidine) adj5 suture$).tw. (87)

48 or/37-47 (9582)

49 33 and 48 (201)

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Database: Embase Classic+Embase <1947 to 2016 Week 43>

Search Strategy:

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1 exp abdominal surgery/ (705994)

2 exp abdomen/ (203605)

3 surgical infection/ (34198)

4 wound closure/ (14571)

5 3 or 4 (48199)

6 2 and 5 (2245)

7 (abdom$ adj5 (surg$ or operation$ or incision$ or closure)).tw. (49815)

8 (abdom$ adj5 (surgical site infection or surgical wound infection)).tw. (158)

9 abdominal hysterectomy/ (9616)

10 hysterotomy/ (1302)

11 exp cholecystectomy/ (44958)

12 exp kidney surgery/ (207328)

13 exp ovary/su [Surgery] (888)

14 abdominal aorta aneurysm/su [Surgery] (11410)

15 (colectom$ or gastrectom$ or hepatectom$ or pancreatectom$ or pancreaticojejunostom$ or pancreaticoduodenectom$ or gastroplast$ or gastropex$ or hysterectom$ or laparotom$ or cholecystectom$ or appendectom$ or colorectal surger$ or gastroenterologic surger$).tw. (245237)

16 exp cesarean section/ (82611)

17 or/1,6-16 (1056467)

18 exp suture/ (63021)

19 antiinfective agent/ (218126)

20 18 and 19 (368)

21 ((antibiotic$ or antiseptic$ or antibacterial$) adj5 suture$).tw. (290)

22 triclosan/ (4082)

23 vicryl plus.tw. (52)

24 monocryl plus.tw. (10)

25 PDS plus.tw. (20)

26 chlorhexidine/ (14701)

27 assufil plus.tw. (0)

28 neosorb plus.tw. (0)

29 egycryl extra.tw. (0)

30 ((triclosan or chlorhexidine) adj5 suture$).tw. (116)

31 or/20-30 (18726)

32 17 and 31 (586)

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Database: EBM Reviews - Cochrane Central Register of Controlled Trials <September 2016>

Search Strategy:

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1 exp Abdomen/su [Surgery] (41)

2 exp Abdomen/ (2504)

3 exp Surgical Procedures, Operative/ (94858)

4 Surgical Wound Infection/ (2625)

5 2 and 3 (1227)

6 2 and 4 (176)

7 5 or 6 (1297)

8 abdominal surgery.kw. (1006)

9 exp Abdominal Wound Closure Techniques/ (37)

10 (abdom$ adj5 (surg$ or operation$ or incision$ or closure)).tw. (5013)

11 (abdom$ adj5 (surg$ site infection or surg$ wound infection)).tw. (29)

12 exp Digestive System Surgical Procedures/ (11169)

13 Laparotomy/ (622)

14 Laparoscopy/ (3260)

15 exp Hysterectomy/ (1571)

16 Hysterotomy/ (7)

17 exp Cholecystectomy/ (1588)

18 exp Colon/su [Surgery] (16)

19 exp Intestine, Small/su [Surgery] (12)

20 Rectum/su [Surgery] (14)

21 Appendix/su [Surgery] (1)

22 exp Bile Ducts/su [Surgery] (8)

23 Gallbladder/su [Surgery] (0)

24 exp Liver/su [Surgery] (11)

25 exp Pancreas/su [Surgery] (13)

26 Spleen/su [Surgery] (0)

27 Splenectomy/ (162)

28 Kidney Transplantation/ (3182)

29 exp Kidney/su [Surgery] (7)

30 exp Ovary/su [Surgery] (6)

31 exp Cesarean Section/ (2373)

32 Aortic Aneurysm, Abdominal/su [Surgery] (34)

33 (abdominal hysterectomy or hysterotomy or cholecystectomy or intestine surgery or kidney surgery or cesarean section).kw. (2897)

34 (colectom$ or gastrectom$ or hepatectom$ or pancreatectom$ or pancreaticojejunostom$ or pancreaticoduodenectom$ or gastroplast$ or gastropex$ or hysterectom$ or laparotom$ or cholecystectom$ or appendectom$ or colorectal surger$ or gastroenterologic surger$).tw. (10931)

35 or/1,7-34 (32223)

36 exp Sutures/ (765)

37 exp Anti-Infective Agents, Local/ (6344)

38 exp Anti-Bacterial Agents/ (20674)

39 36 and (37 or 38) (53)

40 suture.kw. (386)

41 antiinfective agent.kw. (334)

42 40 and 41 (3)

43 ((antibiotic$ or antiseptic$ or antibacterial$) adj5 suture$).tw. (60)

44 Triclosan/ (316)

45 triclosan.kw. (34)

46 vicryl plus.tw. (15)

47 monocryl plus.tw. (4)

48 PDS plus.tw. (6)

49 Chlorhexidine/ (1395)

50 chlorhexidine.kw. (307)

51 assufil plus.tw. (0)

52 neosorb plus.tw. (0)

53 egycryl extra.tw. (0)

54 ((triclosan or chlorhexidine) adj5 suture$).tw. (35)

55 or/39,42-54 (2054)

56 35 and 55 (45)

****

CINAHL with Full Text (EBSCOhost)

S50 (S33 AND S49) 21

S49 (S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48) 1,875

S48 TI ((triclosan or chlorhexidine) N5 suture*) OR AB ((triclosan or chlorhexidine) N5 suture*) 6

S47 TI (egycryl extra) OR AB (egycryl extra) 0

S46 TI (neosorb plus) OR AB (neosorb plus) 0

S45 TI (assufil plus) OR AB (assufil plus) 0

S44 (MH "Chlorhexidine") 1,785

S43 TI (PDS plus) OR AB (PDS plus) 1

S42 TI (monocryl plus) OR AB (monocryl plus) 0

S41 TI (vicryl plus) OR AB (vicryl plus) 1

S40 (MH "Triclosan") 75

S39 TI ((antibiotic* or antiseptic* or antibacterial*) N5 suture*) OR AB ((antibiotic* or antiseptic* or antibacterial*) N5 suture*) 16

S38 S34 AND S37 28

S37 S35 OR S36 6,197

S36 (MH "Antibacterial Agents+") 738

S35 (MH "Antiinfective Agents, Local+") 6,197

S34 (MH "Sutures+") 1,020

S33 S1 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 21,083

S32 TI (colectom* or gastrectom* or hepatectom* or pancreatectom* or pancreaticojejunostom* or pancreaticoduodenectom* or gastroplast* or gastropex* or hysterectom* or laparotom* or cholecystectom* or appendectom* or colorectal surger* or gastroenterologic surger*) OR AB (colectom* or gastrectom* or hepatectom* or pancreatectom* or pancreaticojejunostom* or pancreaticoduodenectom* or gastroplast* or gastropex* or hysterectom* or laparotom* or cholecystectom* or appendectom* or colorectal surger* or gastroenterologic surger*) 7,524

S31 (MH "Aortic Aneurysm, Abdominal/SU") 888

S30 (MH "Cesarean Section+/SU") 0

S29 (MH "Ovary+/SU") 101

S28 (MH "Kidney+/SU") 167

S27 (MH "Kidney Transplantation") 4,549

S26 (MH "Splenectomy") 479

S25 (MH "Spleen/SU") 99

S24 (MH "Pancreas+/SU") 165

S23 (MH "Liver+/SU") 243

S22 (MH "Gallbladder/SU") 0

S21 (MH "Bile Ducts+/SU") 117

S20 (MH "Appendix/SU") 23

S19 (MH "Rectum/SU") 303

S18 (MH "Intestine, Small+/SU") 412

S17 (MH "Colon+/SU") 548

S16 (MH "Cholecystectomy+") 1,403

S15 (MH "Hysterotomy") 0

S14 (MH "Hysterectomy+") 3,035

S13 (MH "Laparoscopy") 3,268

S12 (MH "Laparotomy") 1,009

S11 (MH "Digestive System Surgical Procedures+") 3,991

S10 TI (abdom* N5 ("surgical site infection" OR "surgical wound infection")) OR AB (abdom* N5 ("surgical site infection" OR "surgical wound infection")) 21

S9 TI (abdom* N5 (surg* or operation* or incision* or closure)) OR AB (abdom* N5 (surg* or operation* or incision* or closure)) 1,942

S8 (MH "Abdominal Wound Closure Techniques+") 2,450

S7 (S5 OR S6) 61

S6 (S2 AND S4) 61

S5 (S2 AND S3) 0

S4 (MH "Surgical Wound Infection") 5,112

S3 (MH "Surgical Procedures, Operative+") 40

S2 (MH "Abdomen+") 4,659

S1 (MH "Abdomen+/SU") 1,014

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Database: EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2015>

Search Strategy:

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1 Abdomen su.kw. (0)

2 Abdomen.kw. (93)

3 Surgical Procedures, Operative.kw. (172)

4 Surgical Wound Infection.kw. (213)

5 2 and 3 (6)

6 2 and 4 (8)

7 5 or 6 (13)

8 abdominal surgery.kw. (35)

9 Abdominal Wound Closure Techniques.kw. (10)

10 (abdom$ adj5 (surg$ or operation$ or incision$ or closure)).tw. (305)

11 (abdom$ adj5 (surgical site infection or surgical wound infection)).tw. (5)

12 Digestive System Surgical Procedures.kw. (125)

13 Laparotomy.kw. (59)

14 Laparoscopy.kw. (591)

15 Hysterectomy.kw. (60)

16 Hysterotomy.kw. (1)

17 Cholecystectomy.kw. (109)

18 Colon su.kw. (0)

19 Intestine, Small su.kw. (0)

20 Rectum su.kw. (0)

21 Appendix su.kw. (0)

22 Bile Ducts su.kw. (0)

23 Gallbladder su.kw. (0)

24 Liver su.kw. (0)

25 Pancreas su.kw. (0)

26 Spleen su.kw. (0)

27 Splenectomy.kw. (18)

28 Kidney Transplantation.kw. (145)

29 Kidney su.kw. (0)

30 Ovary su.kw. (0)

31 Cesarean Section.kw. (151)

32 Aortic Aneurysm, Abdominal su.kw. (0)

33 (colectom$ or gastrectom$ or hepatectom$ or pancreatectom$ or pancreaticojejunostom$ or pancreaticoduodenectom$ or gastroplast$ or gastropex$ or hysterectom$ or laparotom$ or cholecystectom$ or appendectom$ or colorectal surger$ or gastroenterologic surger$).tw. (1065)

34 or/1,7-33 (1940)

35 Sutures.kw. (39)

36 Anti-Infective Agents, Local.kw. (79)

37 antiinfective agent.kw. (0)

38 Anti-Bacterial Agents.kw. (681)

39 35 and (36 or 37 or 38) (6)

40 ((antibiotic$ or antiseptic$ or antibacterial$) adj5 suture$).tw. (2)

41 Triclosan.kw. (6)

42 vicryl plus.tw. (0)

43 monocryl plus.tw. (0)
44 PDS plus.tw. (0)
45 Chlorhexidine.kw. (57)
46 assufil plus.tw. (0)
47 neosorb plus.tw. (0)
48 egycryl extra.tw. (0)
49 ((triclosan or chlorhexidine) adj5 suture$).tw. (4)
50 or/39-49 (66)
51 34 and 50 (1)
****

Database: EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2015>

Search Strategy:

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1 exp Abdomen/su [Surgery] (32)
2 exp Abdomen/ (54)
3 exp Surgical Procedures, Operative/ (4679)
4 Surgical Wound Infection/ (118)
5 2 and 3 (37)
6 2 and 4 (3)
7 5 or 6 (39)
8 exp Abdominal Wound Closure Techniques/ (0)
9 (abdom$ adj5 (surg$ or operation$ or incision$ or closure)).tw. (132)
10 (abdom$ adj5 (surg$ site infection or surg$ wound infection)).tw. (0)
11 exp Digestive System Surgical Procedures/ (944)
12 Laparotomy/ (82)
13 Laparoscopy/ (523)
14 exp Hysterectomy/ (116)
15 Hysterotomy/ (0)
16 exp Cholecystectomy/ (111)
17 exp Colon/su [Surgery] (13)
18 exp Intestine, Small/su [Surgery] (9)
19 Rectum/su [Surgery] (13)
20 Appendix/su [Surgery] (0)
21 exp Bile Ducts/su [Surgery] (14)
22 Gallbladder/su [Surgery] (0)
23 exp Liver/su [Surgery] (4)
24 exp Pancreas/su [Surgery] (3)
25 Spleen/su [Surgery] (3)
26 Splenectomy/ (21)

27 Kidney Transplantation/ (175)

28 exp Kidney/su [Surgery] (11)

29 exp Ovary/su [Surgery] (1)

30 exp Cesarean Section/ (64)

31 Aortic Aneurysm, Abdominal/su [Surgery] (65)

32 (colectom$ or gastrectom$ or hepatectom$ or pancreatectom$ or pancreaticojejunostom$ or pancreaticoduodenectom$ or gastroplast$ or gastropex$ or hysterectom$ or laparotom$ or cholecystectom$ or appendectom$ or colorectal surger$ or gastroenterologic surger$).tw. (737)

33 or/1,7-32 (1824)

34 exp Sutures/ (38)

35 exp Anti-Infective Agents, Local/ (68)

36 exp Anti-Bacterial Agents/ (776)

37 34 and (35 or 36) (6)

38 ((antibiotic$ or antiseptic$ or antibacterial$) adj5 suture$).tw. (1)

39 Triclosan/ (5)

40 vicryl plus.tw. (0)

41 monocryl plus.tw. (0)

42 PDS plus.tw. (1)

43 Chlorhexidine/ (23)

44 assufil plus.tw. (0)

45 neosorb plus.tw. (0)

46 egycryl extra.tw. (0)

47 ((triclosan or chlorhexidine) adj5 suture$).tw. (5)

48 or/37-47 (29)

49 33 and 48 (3)

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DESCRIPTION OF THE EVIDENCE USED

Guidelines for diagnosis and management

Table A1: Overview of guidelines

Name of society/organisation issuing guidance	Date of issue	Country/ies to which applicable	Summary of recommendation (Level of evidence/grade of recommendation for the indication under assessment)
The Society for Healthcare Epidemiology of	June 2014	US	Do not routinely use antiseptic-impregnated sutures as a strategy to prevent SSIs (Quality of evidence: II).

America (SHEA)			a. Human volunteer studies involving foreign bodies have demonstrated that the presence of surgical sutures decreases the inoculum required to cause an SSI from 10^6 to 10^2 organisms b. Some trials have shown that surgical wound closure with triclosan-coated polyglactin 910 antimicrobial sutures may decrease the risk of SSI compared with standard sutures. For example, a recent randomized controlled trial of 410 colorectal surgeries concluded that the rate of SSI decreased more than 50% (9.3% in the control group vs 4.3% among cases; *P* p .05). c. In contrast, a recent systematic review and meta-analysis evaluated 7 randomized clinical trials and concluded that neither rates of SSI (odds ratio [OR], 0.77 [95% CI, 0.4–1.51]; P p .45) nor rates of wound dehiscence (OR, 1.07 [95% CI, 0.21–5.43]; P p .93) were statistically different compared with controls.166 In addition, one small study raised concern about higher rates of wound dehiscence while using these sutures. d. The impact of routine use of antiseptic-impregnated sutures on development of resistance to antiseptics is unknown.
National Institute for Health and Care Excellence (NICE)	June 2013	UK	Antimicrobial-coated sutures may reduce surgical site infection risk versus uncoated sutures, although this effect may be specific to particular types of surgery (such as abdominal procedures). Potential Impact on Guidance: Yes* *Evidence Updates are intended to increase awareness of new evidence and do not change the recommended practice as set out in current guidance. Decisions on how the new evidence may impact guidance will not be possible until the guidance is reviewed by NICE following its published processes and methods. For further details of this evidence in the

			context of current guidance, please see the full commentary.
WHO Global Guidelines for the Prevention of Surgical Site Infection give recommendation for Antimicrobial-coated sutures	November 2016	Global	The panel suggest the use of triclosan-caiated sutures for the purpose of reducing the risk of SSI, independent of the type of surgery. (Moderate, Conditional)
American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines, 2016 Update	October 2016	US	Historically, guidelines have not recommended the use of antibiotic suture to decrease SSI, but there is now significant evidence in the literature to support their use. Numerous studies have demonstrated decreased risk with use of triclosan antibiotic sutures compared to standard suture, including multiple randomized controlled trials. Systematic review and meta-analysis on the subject has confirmed this effect. The use of triclosan-coated suture is recommended for wound closure in clean and clean-contaminated abdominal cases when available (Guideline 2.9).

Sources: [5]

Table A2: Summary of HTA recommendations in European countries for the technology in the indication under assessment

European Country	Organisation	Summary of recommendations and restrictions
Sweden (2015)	Stockholms läns landsting	Surgical site infections are common problems in health care. The HTA was performed by a group consisting of an infection specialist, a surgeon and a specialist in infection control and hospital hygiene – all with scientific qualifications – working together with the HTA center. A systematic literature search identified twenty-three articles to be read by the project group. Twelve of those articles were excluded as they did not match the PICO. Eleven RCTs remained and were assessed regarding quality. Results from the nine studies that were of high or medium quality were included in the meta analysis (n=3755) and the level of evidence was assessed using the GRADE system. In these studies patients with various surgical operations were included, the Centers for Disease Control and Prevention (CDC) criteria for

European Country	Organisation	Summary of recommendations and restrictions
		classification of infections or other defined criteria, were used and assessors were blinded. The majority of the patients had antibiotic prophylaxis. The relative risk of superficial SSI with triclosan-coated sutures in nine studies of high or medium quality was 0.78 (95 % CI 0.64-0.95) p=0.01. If only studies of high quality were included there was no statistical significant difference 0.71 (95% CI 0.46-1.10) p=0.13. The conclusion of the assessment was that triclosan-coated sutures had in various operations a limited beneficial effect with significantly lower incidence of superficial or deep postoperative SSI. The level of evidence according to GRADE was low.
Italy (2012)	AGENAS Systematic review	In the studies included, different outcomes and age groups and heterogeneous follow up time coupled with unclear reporting led to a considerable loss of data. Since the available evidence is scarce and heterogeneous there is a need of a large multicenter study to test the equipoise currently visible in the data presented in this review. Until such time clear evidence of dominance of triclosan-coated sutures is not available. Besides, given the higher cost of suture plus antibacterial compared to standard suture, economic studies should be performed to have clear and useful evidence for decisionmaking.
Non European Country	**Organisation**	**Summary of recommendations and restrictions**
Canada (2014)	Canadian Agency of Drugs and Technology in Health	The clinical evidence reviewed in this report was in agreement with the overall conclusions of previous CADTH work, which found the overall pooled evidence in support of benefits of TCS for reducing the risk of SSI and saving costs compared to non-antibacterial sutures. In conclusion, while the totality of evidence suggests that triclosan-coated antibacterial sutures likely reduce the risk of SSI in certain circumstances, such as abdominal surgery, and may result in cost-savings, results of ongoing SRs and clinical studies, and development of evidence-based guidelines such as those currently underway by the CDC52 may help to further clarify the most appropriate clinical indications and methods of application, which remain unclear.

Sources: [5]

Instructions for use data on technologies under assessment

Antibacterial triclosan-coated suture Polyglactin 910 – Vicryl® Plus (Ethicon, Johnson & Johnson International)

Vicryl® Plus is a synthetic absorbable sterile surgical suture. It is composed of a copolymer made from 90% glycolide and 10% L-lactide. The empirical formula of the copolymer is $(C_2H_2O_2)_m(C_3H_4O_2)_n$. Braided Vicryl® Plus sutures are coated with a mixture composed of equal parts of copolymer of glycolide and lactide (polyglactin 370) and calcium stearate. Polyglactin 910 copolymer and Polyglactin 370 with calcium stearate have been found to be nonantigenic, nonpyrogenic and elicit only a slight tissue reaction during absorption. It contains a broad spectrum antibacterial agent Irgacare® MP (triclosan) with a concentration of ≤ 275 µg/m. Vicryl® Plus suture is available undyed and dyed. Dyed sutures are made by adding D&C violet No.2 (Colour index number: 60725) during the polymerisation. It is available in a range of gauge sizes and lengths, non-needled or attached to stainless steel needles of varying types and sizes.

Vicryl® Plus suture elicits a minimal inflammatory reaction in tissues and ingrowth of fibrous connective tissue. Progressive loss of tensile strength and eventual absorption of Vicryl® Plus sutures occurs by means of hydrolysis, where the copolymer degrades to glycolic and lactic acid which are subsequently absorbed and metabolized in the body. Absorption begins as a loss of tensile strength followed by a loss of mass. Coated Vicryl® Plus Antibacterial suture retains approximately 75% of the original tensile strength at two weeks post implantation. At three weeks, approximately 50% of the original strength is retained. At four weeks, approximately 25% of the original strength is retained. All of the original tensile strength is lost by five weeks post implantation. Absorption of Vicryl® Plus suture is essentially complete after between 56 and 70 days [3]. Vicryl® Plus sutures are sterilized by ethylene oxide gas.

These sutures, being absorbable, should not be used where extended approximation of tissues under stress is required. Vicryl® Plus sutures should not be used in patients with known allergic reactions to Irgacare MP (triclosan).

Sutures should be selected and implanted depending on patient condition, surgical experience, surgical technique and wound size. Users should be familiar with surgical procedures and techniques involving absorbable sutures before employing Vicryl® Plus suture for wound closure, as risk of wound dehiscence may vary with the site of application and the suture material used. Surgeons should consider in vivo performance when selecting a suture. As with any foreign body, prolonged contact of any suture with salt solutions, such as urinary or biliary tracts, may result in calculus formation. As an absorbable suture Vicryl® Plus may act transiently as a foreign body.

The use of Vicryl® Plus does not substitute normal observance of hygiene and/or otherwise needed antibiotic treatment. As this is an absorbable suture material, the use of supplemental nonabsorbable sutures should be considered by the surgeon in the closure of the sites which may undergo expansion, stretching or distension or which may require additional support. Skin sutures which must remain in place longer than 7 days may cause localised irritation and should be snipped off or removed as indicated.

Under some circumstances, notably orthopaedic procedures, immobilisation of joints by external support may be employed at the discretion of the surgeon. Consideration should be taken in the use of absorbable sutures in tissues with poor blood supply as suture extrusion and delayed absorption may occur. Subcuticular sutures should be placed as deeply as possible to minimize

the erythema and induration normally associated with the absorption process. This suture may be inappropriate in elderly, malnourished or debilitated patients, or in patients suffering from conditions which may delay wound healing. When handling suture material, care should be taken to avoid damage. Avoid crushing or crimping damage due to application of surgical instruments such as forceps or needle holders. Care should be taken to avoid damage when handling surgical needles.

Vicryl® Plus complies with all the requirements of the United States Pharmacopoeia for Absorbable Surgical Suture and the European Pharmacopoeia for Sterile Synthetic Absorbable Braided Sutures (except for an occasional slight oversize in some gauge) [3].

Table A3: Summary of product characteristics VICRYL® PLUS

Vicryl Plus EC Design Examination Certificate [132]

Product name: Coated VICRYL® PLUS Antibacterial (Polyglactin 910) Sterile Synthetic Absorbable Suture Manufacturer: Ethicon, Johnson & Johnson International	
Suture characteristic	**Range**
Absorbable/Non absorbable	Absorbable
Suture gauge size	1.0-5.0 (metric)
Suture length	5 cm- 250 cm
Suture dyed/undyed	Dyed/Undyed
Suture colour (if dyed)	Violet
Coated/Uncoated	Coated (Copolymer of glycolide and lactide, calcium stearate)
Multifilament/Monofilament	Multifilament
Contains antimicrobials	Irgacare MP (Triclosan)
Triclosan maximum levels	≤ 275 µg/m
Accessories to suture type	N/A
Needled/Non-needled	Needled/Non-Needled
Number of needles per suture	Single Armed/Double Armed
Needle material	420, 420 SS, 4310 SS, ETHALLOY
Needle coating	Silicone, MULTIPASS
Needle shape	Straight/Curve
Needle length	3.5 mm - 110 mm
Needle wire diameter	0.1 mm - 1.55 mm

Antibacterial triclosan-coated suture Polyglecaprone 25 – Monocryl® Plus (Ethicon, Johnson & Johnson International)

Monocryl® Plus is a sterile, synthetic, absorbable, monofilament suture. It is comprised of a copolymer of glycolide and ε-caprolactone. Empirical formula of the polymer is $(C_2H_2O_2)_m$ $(C_6H_{10}O_2)_n$. Poliglecaprone 25 copolymer has been found to be non-antigenic, non-pyrogenic and elicits only a slight tissue reaction during absorption. It contains a broad spectrum antibacterial

agent Irgacare® MP (triclosan) at concentration ≤ 2360 µg/m. Dyed Monocryl® Plus Sutures contain D&C violet No. 2 (Colour index number: 60725). An undyed form is also available. Monocryl® Plus is available in a range of gauge sizes and lengths, non-needled or attached to stainless steel needles of varying types and sizes.

The Monocryl® Plus Antibacterial Suture elicits a minimal inflammatory reaction in tissues and is eventually replaced with an in-growth of fibrous connective tissue. Progressive loss of tensile strength and eventual absorption of Monocryl® Plus Antibacterial Sutures occurs by means of hydrolysis, where the polymer degrades to adipic acid which is subsequently absorbed and metabolized in the body. Absorption begins as a loss of tensile strength followed by a loss of mass. Dyed Monocryl® Plus suture retains 60% of its original strength at 7 days postimplantation, reduced to 30% at 14 days, with all original tensile strength lost by 28 days. At 7 days, the undyed suture retains approximately 50% of its original strength, and approximately 20% at 14 days postimplantation. All of the original tensile strength of the undyed suture is lost by 21 days postimplantation. Absorption is essentially complete at 91 to 119 days.

Dyed and undyed sutures, being absorbable, should not be used where extended approximation of tissues under stress is required. Undyed Monocryl® Plus Antibacterial Sutures, in particular, should not be used to close fascial tissue. Monocryl® Plus Antibacterial Suture complies with all the requirements of the European Pharmacopoeia for Sterile Synthetic Absorbable Monofilament Sutures and the requirements of the United States Pharmacopoeia for Absorbable Surgical Sutures (except for a slight oversize in diameter) [2].

Table A4: Summary of product characteristics MONOCRYL® Plus

Monocryl Plus EC Design Examination Certificate [133]

Product name: MONOCRYL® Plus Antibacterial (poliglecarpone 25) Suture **Manufacturer:** Ethicon, Johnson & Johnson International	
Suture characteristic	**Range**
Absorbable/Non absorbable	Absorbable
Suture gauge size	0.7-0.4
Suture length	45-90 cm
Suture dyed/undyed	Dyed/Undyed
Suture colour (if dyed)	Violet
Coated/Uncoated	Uncoated
Multifilament/Monofilament	Monofilament
Contains antimicrobials	Irgacare MP (Triclosan)
Triclosan maximum levels	≤ 2360 µg/m
Accessories to suture type	N/A
Needled/Non-Needled	Needled
Number of needles per suture	Single Armed/Double Armed
Needle material	420 SS, 455 SS, 4310 SS, ETHALLOY
Needle coating	Silicone, MULTIPASS
Needle shape	Straight/Curve
Needle length	10 mm - 60.3 mm

Needle wire diameter	0.25 mm - 1.3 mm

Antibacterial triclosan-coated suture Polydioxanone – PDS® Plus (Ethicon, Johnson & Johnson International)

PDS® Plus Antibacterial Suture is a sterile synthetic absorbable monofilament suture. It is made from the polyester poly (p-dioxanone). The empirical formula of the polymer is $(C_4H_6O_3)_n$. Polydioxanone polymer has been found to be nonantigenic, nonpyrogenic and elicits only a slight tissue reaction during absorption. It contains a broad spectrum antibacterial agent Irgacare® MP (Triclosan) at concentration ≤ 2360 µg/m. PDS® Plus Antibacterial Sutures are dyed by adding D&C violet No.2 (Colour index number: 60725) during polymerisation. Sutures are also available in the undyed form. It is available in a range of gauge sizes and lengths, attached to stainless steel needles of varying types and sizes.

PDS® Plus Antibacterial Suture elicits a minimal inflammatory reaction in tissues and is eventually replaced with an in-growth of fibrous connective tissue. Progressive loss of tensile strength and eventual absorption of PDS® Plus Antibacterial Sutures occurs by means of hydrolysis, where the polymer degrades to the monomeric acid 2-hydroxyethoxyacetic acid which is subsequently absorbed and eliminated by the body. Absorption begins as a loss of tensile strength followed by a loss of mass. For the sutures M1.5(4-0) and smaller approximately 60% of tensile strength remains 2 weeks postimplantation, 40% at 4 weeks and 35% at 6 weeks. For the sutures M2.0 (3-0) and larger approximately 80% of tensile strength remains 2 weeks postimplantation, 70% at 4 weeks and 60% at 6 weeks. Absorption is minimal until about the 90th postimplantation day and essentially complete between 182 and 238 days.

These sutures, being absorbable, should not be used where prolonged (beyond 6 weeks) approximation of tissues under stress is required or in conjunction with prosthetic devices, for example, heart valves or synthetic grafts. PDS® Plus Antibacterial Suture should not be used in patients with known allergic reactions to Irgacare® MP (triclosan). The safety and effectiveness of PDS® Plus Antibacterial Suture have not been established in contact with the central nervous system, in adult cardiac tissue, in large vessels or for contact with cornea and sclera.

Sutures should be selected and implanted depending on patient condition, surgical experience, surgical technique and wound size. Users should be familiar with surgical procedures and techniques involving absorbable sutures before employing PDS® Plus suture for wound closure, as risk of wound dehiscence may vary with the site of application and the suture material used. Surgeons should consider in vivo performance when selecting a suture. This suture may be inappropriate in elderly, malnourished or debilitated patients, or in patients suffering from conditions which may delay wound healing.

As with any foreign body, prolonged contact of any suture with salt solutions, such as those found in the urinary or biliary tracts, may result in calculus formation. As an absorbable suture PDS® Plus may act transiently as a foreign body. As this is an absorbable suture material, the use of supplemental nonabsorbable sutures should be considered by the surgeon in the closure of the sites which may undergo expansion, stretching or distension, or which may require additional support. Cuticular and vaginal epithelium sutures which remain in place longer than 10 days may cause localised irritation and should be snipped off or removed. Subcuticular sutures should be placed as deeply as possible to minimize the erythema and induration normally associated with the absorption process.

Under some circumstances, notably orthopaedic procedures, immobilisation of joints by external support may be employed at the discretion of the surgeon. Consideration should be taken in the use of absorbable sutures in tissues with poor blood supply as suture extrusion and delayed absorption may occur. When handling suture material, care should be taken to avoid damage. Avoid crushing or crimping damage due to application of surgical instruments such as forceps or needle holders. Care should be taken to avoid damage when handling surgical needles.

This suture complies with all the requirements of the European Pharmacopoeia for Sterile Synthetic Absorbable Monofilament Sutures and the requirements of the United States Pharmacopoeia for Absorbable Surgical Sutures except for a slight oversize in diameter [4].

Table A5: Summary of product characteristics PDS® Plus

PDS Plus EC Design Examination Certificate [134]

Product name: PDS® Plus Antibacterial (poydioxanone) Suture **Manufacturer**: Ethicon, Johnson & Johnson International	
Suture characteristic	**Range**
Absorbable/Non absorbable	Absorbable
Suture gauge size	0.7-0.4 (metric)
Suture length	35-245 cm
Suture dyed/undyed	Dyed/Undyed
Suture colour (if dyed)	Violet
Coated/Uncoated	Uncoated
Multifilament/Monofilament	Monofilament
Contains antimicrobials	Irgacare MP (Triclosan)
Triclosan maximum levels	≤ 2360 µg/m
Accessories to suture type	N/A
Needled/Non-Needled	Needled/Non-needled
Number of needles per suture	Single Armed/Double Armed
Needle material	420 SS, 455 SS, 4310 SS, ETHALLOY
Needle coating	Silicone, CERBERUS, MULTIPASS
Needle shape	Straight/Curve
Needle length	9 mm – 70 mm
Needle wire diameter	0.3 mm - 1.55 mm

Antibacterial Surgical Sutures coated with Chlorhexidine

Assufil® Plus (Assut Europe)

Assufil plus suture is a synthetic absorbable sterile surgical suture device, composed of braided multifilament of polyglycolic acid. The braid of natural white or dyed violet (D&C violet No. 2 ,Color index number: 60725) multifilament is coated with a mixture of poly(glycolide-co-L-lactide), calcium stearate and chlorhexidine diacetate. Assufil® Plus Sutures are available in a range of

gauges sizes and lengths, non-needled or attached to stainless steel needles of different size and shapes. Sutures are sterilized using ethylene oxide.

The progressive loss of the suture tensile strength occurs in consequence of hydrolysis, which degrades the polyglycolic acid to allow absorption and subsequent metabolization in the body.

Assufil® Plus remains approximately 90% of tensile strength 1 week postimplantation, 75% at 2 weeks, 50% at 3 weeks and 30% at 4 weeks. Studies on animals have proved that the absorption of Assufil® Plus suture is practically complete within 90 days from implantation. Assufil® Plus suture may cause local inflammatory reaction associated to erythema formation.

It is recommended that the surgeon considers the possible use of non absorbable sutures for the closure of tissues which may undergo distension or stretching or require additional support. This suture kind may be inappropriate in elderly, malnourished or weakened patients or in patients suffering from conditions which may delay the wound healing process. Care should be taken when handling the suture material to avoid any bending or flattening to the thread due to the application of surgical instruments such as forceps or needleholders [8].

Egycryl Extra (Taisier-Med)

Egycryl extra is a sterile synthetic absorbable suture with antibacterial based on copolymer made from 90% Glycolide and 10% L-Lactide. Egycryl extra sutures are coated with an equal combination of copolymer (Glycolide and Lactide), calcium stearate and Chlorhexidine diacetate which act as broad spectrum antibacterial agent with a maximum dose of 60 µg/m. The sutures are available dyed violet D&C No.2 (CI 60725) and undyed. EGYCRYL extra complies with the requirement of USP and EP. Coated EGYCRYL extra Sutures are available sterile, as braided dyed (violet) and undyed strands in USP sizes 10/0 through 2 (metric size 0.2 through 5) in a variety of lengths with or without needles. Egycryl extra is sterilized by ethylene oxide.

Egycryl extra absorption occurs by means of hydrolysis, where the copolymer degrades to glycolic and lactic acids which are subsequently absorbed and metabolized in the body. Absorption begins as a loss of tensile strength and ends by a total loss of mass. Breaking strength retention: In vivo tests showed that Egycryl extra retain equals to or accounts for more than 65 %(average 75%) of original tensile strength at 2 weeks after implantation. Absorption is essentially complete between 55 and 70 days.

Neosorb Plus (Medipac)

Neosorb Plus is a braided, violet, synthetic absorbable polyglactin 910 surgical suture which is antibacterial (CHA-chlorhexide diacetate) coated.

Neosorb Plus Synthetic Absorbable Surgical Suture elicits a minimal acute inflammatory reaction in tissues, which is followed by gradual encapsulation of the suture by fibrous connective tissue. Progressive loss of tensile strength and eventual absorption of Neosorb Plus Synthetic Absorbable Sutures occurs by means of hydrolysis, where the polymer degrades to glycolic and lactic acids which are subsequently absorbed and metabolized in the body. Absorption begins as a loss of tensile strength without appreciable loss of mass. NEOSORB PLUS retains approximately 50% of the average EP tensile strength requirement at the end of the 3rd post implantation week. The absorption of the suture is essentially complete between 56-70 days.

Comparators: Non-antibacterial-coated sutures

Vicryl® (Ethicon)

The coated Vicryl® Suture (polyglactin 910) is a synthetic absorbable sterile surgical suture composed of a copolymer made from 90% glycolide and 10% L-lactide. It is prepared by coating Coated Vicryl® Suture material with a mixture composed of equal parts of a copolymer of glycolide and lactide (polyglactin 370) and calcium stearate. The copolymers used in this product have been found to be nonantigenic, nonpyrogenic and elicit only a mild tissue reaction during absorption.

The sutures are available undyed (natural) and dyed. Coated Vicryl® Sutures meet U.S.P. except for diameters in the following sizes:

Maximum suture oversize in diameter (mm) from U.S.P	
U.S.P. suture size designation	**Maximum oversize (mm)**
6-0	0.008
5-0	0.016
4-0	0.017
3-0	0.018
2-0	0.004
0	0.022

Coated Vicryl® Sutures are available sterile, as braided dyed (violet) and undyed (natural) strands in sizes 8-0 through 3 (metric sizes 0.4-6), in a variety of lengths, with or without needles. Coated Vicryl® Sutures are also available in size 8-0 (metric size 0.4) with attached beads for use in ophthalmic procedures. They are also available in sizes 4-0 through 2 (metric size 1.5-5.0) attached on removable needles.

Coated Vicryl® Sutures elicit a minimal acute inflammatory reaction in tissue and ingrowth of fibrous connective tissue. Progressive loss of tensile strength and eventual absorption of Coated Vicryl® Suture occurs by means of hydrolysis, where the copolymer degrades to glycolic and lactic acid which are subsequently absorbed and metabolized in the body. Absorption begins as a loss of tensile strength followed by a loss of mass. Implantation studies in rats indicate that Coated Vicryl® Suture retains approximately 75% of the original tensile strength at two weeks post implantation. At three weeks, approximately 50% of the original strength is retained for sizes 6-0 and larger and approximately 40% of its original strength is retained for sizes 7-0 and smaller. At four weeks approximately 25% of the original strength is retained for sizes 6-0 and larger. All of the original tensile strength is lost by five weeks post implantation. Absorption of Coated Vicryl® Suture is essentially complete between 56 and 70 days. These sutures, being absorbable, should not be used where extended approximation of tissues is required.

Users should be familiar with surgical procedures and techniques involving absorbable sutures before employing Coated Vicryl® Suture for wound closure, as risk of wound dehiscence may vary with the site of application and the suture material used. Physicians should consider the in vivo performance when selecting a suture. The use of this suture may be inappropriate in elderly, malnourished, or debilitated patients, or in patients suffering from conditions which may delay

wound healing. As this is an absorbable material, the use of supplemental nonabsorbable sutures should be considered by the surgeon in the closure of the sites which may undergo expansion, stretching or distension, or which may require additional support.

As with any foreign body, prolonged contact of any suture with salt solutions, such as urinary or biliary tracts, may result in calculus formation. As an absorbable suture Coated Vicryl® may act transiently as a foreign body.

Skin sutures which must remain in place longer than 7 days may cause localised irritation and should be snipped off or removed as indicated.

Under some circumstances, notably orthopaedic procedures, immobilisation of joints by external support may be employed at the discretion of the surgeon. Consideration should be taken in the use of absorbable sutures in tissues with poor blood supply as suture extrusion and delayed absorption may occur. Subcuticular sutures should be placed as deeply as possible to minimize the erythema and induration normally associated with the absorption process. When handling suture material, care should be taken to avoid damage. Avoid crushing or crimping damage due to application of surgical instruments such as forceps or needle holders.

Monocryl® (Ethicon)

Monocryl® (poliglecarpone 25) suture is a monofilament synthetic absorbable surgical suture prepared from a copolymer of glycolide and epsilon-caprolactone. Poliglecarpone 25 copolymer has been found to be nonantigenic, nonpyrogenic and elicits only a slight tissue reaction during absorption. Monocryl® sutures are U.S.P except for diameters in the following sizes:

Maximum suture oversize in diameter (mm) from U.S.P	
U.S.P. suture size designation	**Maximum oversize (mm)**
6-0	0.049
5-0	0.033
4-0	0.045
3-0	0.067
2-0	0.055
0	0.088
1	0.066
2	0.099

Monocryl® sutures are available as sterile, monofilament, dyed (violet) strands in sizes 6-0 through 2 (metric sizes 0.7-5) in a variety of lengths, with or without needles. Sutures are also available in sizes 3-0 through 1 (metric sizes 2-4) attached to removable needles.

Monocryl® suture is a monofilament which elicits a minimal acute inflammatory reaction in tissues and ingrowth of fibrous connective tissue. Progressive loss of tensile strength and eventual absorption of Monocryl® sutures occurs by means of hydrolisis. Implantation studies in rats indicate that Monocryl® suture retains approximately 60 to 70% of its original strength at 7 days post implantation, and 30% to 40% of the original tensile strength at 14 days post implantation. Absorption of Monocryl® absorbable suture is essentially complete between 91 and 119 days.

This suture, being absorbable, should not be used where extended approximation of tissues under stress is required.

Users should be familiar with surgical procedures and techniques involving absorbable sutures before employing the Monocryl® suture for wound closure, as risk of wound dehiscence may vary with the site of application and the suture material used. Physicians should consider the in vivo performance when selecting a suture for use in patients. The use of this suture may be inappropriate in elderly, malnourished, or debilitated patients, or in patients suffering from conditions which may delay wound healing.

As this is an absorbable material, the use of supplemental nonabsorbable sutures should be considered by the surgeon in the closure of the sites which may undergo expansion, stretching or distension, or which may require additional support. As with any foreign body, prolonged contact of any suture with salt solutions, such as those found in the urinary or biliary tracts, may result in calculus formation. As an absorbable suture Monocryl® suture may act transiently as a foreign body.

Skin sutures which must remain in place longer than 7 days may cause localised irritation and should be snipped off or removed as indicated. Subcuticular sutures should be placed as deeply as possible to minimize the erythema and induration normally associated with the absorption process. Under some circumstances, notably orthopaedic procedures, immobilization of joints by external support may be employed at the discretion of the surgeon. Consideration should be taken in the use of absorbable sutures in tissues with poor blood supply as suture extrusion and delayed absorption may occur. In handling this or any other suture material, care should be taken to avoid damage from handling. Avoid crushing or crimping damage due to application of surgical instruments such as forceps or needle holders. Monocryl® suture knots must be properly placed to be secure. Adequate knot security requires the accepted surgical technique of flat and square ties with additional throws as warranted by surgical circumstance and the experience of the surgeon. The use of additional throws may be particularly appropriate when knotting monofilaments. Avoid prolonged exposure to elevated temperature.

PDS® II (Ethicon)

PDS® II (polydioxanone) monofilament synthetic absorbable suture is prepared from the polyester poly (p-dioxanone). The empirical formula of the polymer is $(C_4H_6O_3)_n$. Polydioxanone polymer has been found to be nonallergenic, nonpyrogenic and elicits only a slight tissue reaction during absorption.

Maximum suture oversize in diameter (mm) from U.S.P	
U.S.P. suture size designation	**Maximum oversize (mm)**
9-0	0.005
8-0	0.008
7-0	0.020
6-0	0.015
5-0	0.029
4-0	0.029
3-0	0.056

2-0	0.029
0	0.071
1	0.047
2	0.023

PDS® II sutures are available as sterile, monofilament, dyed (violet) strands in sizes 7-0 thru 2 (metric size 0.5-5), in a variety of lengths, with a variety of needles. PDS® II monofilament dyed sutures, sizes 4-0 thru 1 (metric size 1.5-4) are also available attached to removable needles. PDS® II clear sutures are available in sizes 6-0 thru 1 (metric size 0.7-4) in a variety of lenghts with permanently attached needles.

Two important characteristic describe the in vivo performance of absorbable sutures: first, tensile strength, retention and second, the absorption rate (loss of mass). PDS® II suture has been formulated to minimize the variability of these characteristics and to provide wound support through an extended healing period.

Data obtained from implantation studies in rats show that PDS® II suture is essentially absorbed between 182 and 238 days post implantation. The results of implantation indicate that for the sutures M1.5(4-0) and smaller approximately 60% of tensile strength remains 2 weeks postimplantation, 40% at 4 weeks and 35% at 6 weeks. For the sutures M2.0(3-0) and larger approximately 80% of tensile strength remains 2 weeks postimplantation, 70% at 4 weeks and 60% at 6 weeks.

PDS® II suture, being absorbable, is not to be used where prolonged (beyond 6 weeks) approximation of tissues under stress is required or in conjunction with prosthetic devices, for example, heart valves or synthetic grafts. The safety and effectiveness of PDS® II suture have not been established in neural tissue, adult cardiovascular tissue or for use in microsurgery.

Under some circumstances, notably orthopaedic procedures, immobilization of joints by external support may be employed at the discretion of the surgeon. The PDS® II suture knots must be properly placed to be secure. As with others synthetic sutures, knot security requires the standard surgical technique of flat and square ties with additional throws if indicated by surgical circumstance and the experience of the operator.

As with any suture, care should be taken to avoid damage when handling. Avoid the crushing or crimping application of surgical instruments such as forceps or needle holders, to the strands except when grasping the free end of the suture during an instrument tie. Conjunctival and vaginal mucosal sutures remaining in place for extended periods may be associated with localized irritation and should be removed as indicated. Subcuticular sutures should be placed as deeply as possible to minimize the erythema and induration normally associated with the absorption.

Acceptable surgical practice should be followed with respect to drainage and closure of infected wounds. To avoid damaging needle points and swage areas grasp the needle in an area one-third to one-half of the distance from the swaged end to the point. Reshaping needles may cause them to lose strength and be less resistant to bending and breaking. Users should exercise caution when handling surgical needles to avoid inadvertent needle sticks. Prolonged exposure to elevated temperature should be avoided. Due to prolonged suture absorption, some irritation and bleeding has been observed in the conjunctiva and mild irritation has been observed in the vaginal mucosa.

Evidence tables of individual studies included for clinical effectiveness and safety

Table A6: Characteristics and quality of included secondary studies: Systematic reviews

Characteristics of included secondary studies: main study findings and authors conclusions - Sandini et al., 2016 [26]

Author / Year / Reference number / Review time frame / Aim	Study type included Number of included studies (RCTs) Risk of bias Settings	Patients	Intervention	Comparison	Outcomes (Primary and Secondary)	Funding/CoI
Sandini et al., 2016 Aim: To run a new meta-analysis to update the results and to select only RCTs designed for patients undergoing elective colorectal resection or RCTs including also several types of abdominal operation, but in which separate analysis on colorectal patients could be retrieved from the published data or by investigators who responded to our request of additional information.	**RCTs (n=6)** The range of publication year was between 2011 and 2015. In 2 publications, both patients and outcome assessors were blinded to treatment; in 2 studies, only assessors and 2 trials were open-label. 2 RCTs had a high risk of bias; the remaining a low or moderate risk. Three studies were multicentre, with a range of 4 to 24 hospitals and 3 single centres.	With elective colorectal operations Total of 2168 patients, 1102 (50.8%) receiving triclosan-coated material and 1066 (49.2%) uncoated sutures. The mean number of patients/study was 361. Patients were followed up for late SSI	Triclosan-coated sutures: PDS Plus in 3 studies, Vicryl Plus in 2, and both PDS Plus and Vicryl Plus in 1 study Closure of the laparotomy: by a running single-layer mass techniques in 3 trials and miscellaneous techniques in the remaining 3 studies.	Triclosan - uncoated sutures: PDS in 3 studies, Vicryl in 2, and both PDS and Vicryl in 1 study	Primary: to analyse the available RCTs, comparing the effect of triclosan-coated suture with uncoated suture on the incidence of SSI after elective colorectal operation Secondary: length of stay (LOS) in hospital after surgery Moderator analyses were performed according to the following indicators: multicenter or monocenter study, type of suture materials (polydioxanone [PDS] or polyglactin	The authors have no conflicts of interest to disclose.

Lit. search: Between March 1990 and June 2015	Sample size calculated in 4 out of 6 trials.	appearance for 30 days after hospital discharge in 4 out of 6 trials.			[Vicryl]), and outcome masking (double or single-blind, or open-label method). SSI was declared as the primary endpoint of 5/6 of the studies, and SSI was defined according to the Centers for Disease Control and Prevention of Atlanta criteria in 4 trials.	

Results of primary and secondary outcomes

Outcome	Follow up	Trials (Participants) number	Frequency of SSIs	OR (95% CI) or WMD (95% CI)
SSIs	Range 14-30 days after discharge	6 RCTs with 2168 patients (1102 treated and 1066 controls)	11.7% (129/1102) in the triclosan group and 13.4% (143/1066) in control group	*Overall (random-effects model) OR* 0.81 (95% CI 0.58–1.13, P=0.220) Heterogeneity among studies was moderate (I2=44.9%, Q=9.1, P=0.106). No evidence of publication bias was detectable. *OR per RCT*
				Baracs et al. 2011 OR 1.00 (0.59-1.72, p=0.988)
				Rasic et al. 2011 OR 0.34 (0.11-1.02, **p=0.054**)
				Justinger et al. 2013 OR 0.63 (0.34-1.14, p=0.127)
				Nakamura et al. 2013

				OR 0.47 (0.22-1.01, **p=0.054**)
				Diener et al. 2014 OR 1.06 (0.76-1.49, p=0.717)
				Mattavelli et al. 2015 OR 1.21 (0.63-2.30, p=0.564)
Hospital LOS		5 RCTs with 1783 patients (914 treated and 689 controls)		*WMD was - 0.02 in favor of triclosan* *(95% CI -0.11 to -0.07, P=0.668). The tau-squared test for heterogeneity among studies was 0% (Q=1.45, p value of 0.836. Funnel plot suggested no evidence of publication bias.*
Moderator analyses on SSIs				
Single-centre studies vs Multicentre studies				**OR 0.52** (95% CI 0.34–0.80, **p=0.003**) vs OR 1.02 (95% CI 0.83–1.39, p=0.602)
PDS vs Vicryl				OR 0.94 (0.71-1.25, p=0.675) vs 0.62 (0.29-1.36, p=0.236)

"Failed to demonstrate a significant protective effect of triclosan-coated sutures on the occurrence of SSI after elective colorectal resections. Since the present meta-analysis did not completely rule out and solve the conflicting results in the literature on the benefit of impregnated materials on wound infection, further large RCTs that take into account all risk factors and the supplementary preventive strategies are needed before introducing it in a routine clinical use, unless well performed health technology assessment evaluation will prove a dominant cost-effectiveness ratio."

Assessing the quality of included SRs – AMSTAR and R-AMSTAR Criteria

Assessing the quality of included SRs – AMSTAR Criteria *[20]*

Study	**AMSTAR Criteria**										
	(1)	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	**(8)**	**(9)**	**(10)**	**(11)**
Sandini et al., 2016 [29]	Cannot answer	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Cannot answer

Summary of the AMSTAR Assessment. Note: *NA=Not applicable. (1) Was an 'a priori' design provided? (2) Was there duplicate study selection and data extraction? (3) Was a comprehensive literature search performed? (4) Was the status of publication (i.e. grey literature) used as an inclusion criterion? (5) Was a list of studies (included and excluded) provided? (6) Were the characteristics of the included studies provided? (7) Was the scientific quality of the included studies assessed and documented? (8) Was the scientific quality of the included studies used appropriately in formulating conclusions? (9) Were the methods used to combine the findings of studies appropriate? (10) Was the likelihood of publication bias assessed? (11) Was the conflict of interest included?*

R-AMSTAR *[21]*

Sandini et al., 2016 [29]	**R-AMSTAR items**										
	(1)	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	**(8)**	**(9)**	**(10)**	**(11)**
	2	4	4	3	4	3	3	3	3	3	3

Source: [21]

Total score*: 35/44 (final score calculated from judgments provided by 2 independent assessors)

** the R-AMSTAR total score has a range of 11 to 44, 11 signifying that none of the AMSTAR criteria were satisfied, and a score of 44 revealing that all of the criteria of systematic review excellence were verified.*

List of R-AMSTAR items: *(1) Was an 'a priori' design provided? (2) Was there duplicate study selection and data extraction? (3) Was a comprehensive literature search performed? (4) Was the status of publication (i.e. grey literature) used as an inclusion criterion? (5) Was a list of studies (included and excluded) provided? (6) Were the characteristics of the included studies provided? (7) Was the scientific quality of the included studies assessed and documented? (8) Was the scientific quality of the included studies used appropriately in formulating conclusions? (9) Were the methods used to combine the findings of studies appropriate? (10) Was the likelihood of publication bias assessed? (11) Was the conflict of interest included?*

Table A7: Characteristics of randomised controlled studies and Risk of Bias

Evidence Tables of RCTs (n=7) [27-33]

Author, year, reference number: **Baracs et al., 2011** [32]	Author interpretation of results: The implementation of looped PDS decreased the incidence of SSI by one-half, whether the suture was triclosan-coated or not. It seems that patient factors are less important than operative factors in the occurrence of SSI, and there were no differences between elective colon and rectal operations in the development of incisional infections. No beneficial effect of triclosan against gram-positive bacteria, which has been reported in the literature, could be confirmed in our study. We could not show an effect against gram-negative enteric microorganisms. Higher additional costs and longer hospital stay with SSI were confirmed.
Study title/objectives	Surgical Site Infections after Abdominal Closure in Colorectal Surgery Using Triclosan-Coated Absorbable Suture (PDS Plus) vs. Uncoated Sutures (PDS II): A Randomized Multicenter Study / To compare triclosan-coated and uncoated absorbable suture (PDS Plus with PDS II) in elective colorectal operations
Study characteristics	
Study design	A multi-centre-randomized, internet-based study; Randomization: made by computer software (stored in a password protected website and could not be influenced manually. A participating centre could not view the data from the other centres. Four study meetings were held to cross-check and evaluate the data.
Study Registration number	NCT01123616
Country of recruitment	Hungary
Centre	Multicentre: Seven surgical centres (three university clinics and four high-volume hospitals); Coordination was provided by the Surgical Department of The University of Pecs**.**
Ethics Committee Approval	Yes
Sponsor	NR
Study period (study start, study end)	Recruitment: between December 2009 and November 2010
Duration of follow-up (days)	30 days
Inclusion criteria	Patient age between 18 and 80 years with benign or malignant colon or rectal disease undergoing an elective open surgical procedure involving an enterotomy.
Exclusion criteria	Patients with systemic disease influencing local surgical site healing (e.g., type I diabetes mellitus, Child-Pugh class B–C liver cirrhosis, and chronic kidney disease necessitating dialysis) or those having immunosuppressive treatment or inflammatory bowel disease were excluded. Excluded later: acute operations with unprepared bowel and patients who refused to sign the consent form were excluded. Patients with intra-operative findings such as locally incurable tumour or sepsis (abscess, necrotic tumour), or with post-operative findings such as further surgical intervention through the site and patients who withdrew the consent later. Undesirable complications such as sterile surgical site dehiscence and suture breakage during the post-operative period also led to exclusion from the trial.
Sample size calculation	Sample size calculation was done to increase the power of the study to 90% to detect a decrease or the historic 20% SSI rate to < 10%. On this basis, 468 colorectal surgery patients were planned for.

Patient characteristics	
Age of patients	62.6 intervention vs. 63.5 control, p value NS
Sex	110 males intervention vs. 111 control, p value NS
BMI	24.7 vs 25.5, p value NS
Diagnosis	Patients who had underwent elective colon or rectal surgery
Comorbidities (i.e. diabetes and glycaemic control, obesity, hypothermia)	Type II DM 27 vs 26, p value NS; Neoadjuvant th 47 vs 40, p value NS
Target organ for surgery	In 188 patients, the triclosan-coated suture (45 right hemicolectomies, 12 left hemicolectomies, seven transversectomies, one cecal resection, three colotomies, 28 A-P resections of the rectum, 28 sigmoid resections, 61 abdominal resections of the rectum, two subtotal colectomies, one total colectomy) were applied. In 197 cases, uncoated sutures (44 right hemicolectomies, 11 left hemicolectomies, five transversectomies, three colotomies, 27 A-P resections of the rectum, 34 sigmoid resections, 68 abdominal resections of the rectum, five subtotal colectomies) were used.
Type of operative wound	NR specifically, but in introduction state “Open colon and rectal procedures are classified as clean-contaminated…..”
Clean	
Clean-contaminated	Yes
Contaminated	
Dirty-infected	
US CDC criteria	NR
Procedure	
Elective	Yes
Emergency setting	
Open	Yes
Median laparotomy	
Transverse laparotomy	
Other (please specify)	
Laparoscopic	
Antibiotic prophylaxis (Yes/No/Not reported)	Yes
Timing	30min before incision
Dosing (single or multiple)	Single
Antimicrobial agent given	A second-generation cephalosporin and metronidazole
Antibiotic therapy	NR

Duration of surgery	NR
Use of drainage	NR
Intervention	
Type of antibacterial-coated suture material	Triclosan-coated sutures
Description of abdominal wall layers closure (i.e. fascial/muscle layer closure, skin and/or subcutaneous tissue closure…)	For closure of the abdominal fascia, running looped PDS was used. Use of triclosan-coated or uncoated PDS was determined by computer randomization. Separate peritoneal closure and subcutaneous sutures were optional, depending on the surgeon's preference, but if applied, 2-0 suture was used. Interrupted 2-0 poliglecaprone 25 (Monocryl Plus,Ethicon) was employed for the skin closure.
Comparator	
Type of non-bacterial coated suture material	Uncoated suture PDS
Description of abdominal wall layers closure (i.e. fascial/muscle layer closure, skin and/or subcutaneous tissue closure …)	Please see above.
Outcomes	
Primary:	Whether triclosan-coated polydiaxanone is able to reduce the number of SSIs after colorectal surgery.
Secondary:	To determine whether an SSI increases the length of the hospital stay, whether there are any additional costs, and chances of late SSI after discharge of the patient from the hospital
Flow of patients	
No of patients enrolled	468
No of randomized	385
Allocated per arms	Intervention: 188 patients
	Control: 197 patients
Received int. per arms	385
No of analysed per arm	Intervention: 188 patients Control: 197 patients
Statistical analysis	
ITT, modified ITT, Per protocol; other (specify)	Student t-test for continuous variables and a test for independence (chi-square test) for categorical variables. All means were expressed – standard deviation. A p value < 0.05 was considered significant.
Results	
Effectiveness results	
n (%) 95% CI	
Incidence of SSI (superficial +	47: 23/188 (12.2%) intervention vs. 24/197 (12.2%) control, p=0.982; Late surgical SI after discharge by suture type: 4 (17.4%) vs. 9 (37.5%), **p = 0.041**

deep)	In right hemicolectomies, the triclosan-coated suture was significantly inferior to the uncoated one (**p = 0.006**), whereas in resections of the rectum (A-P and abdominal), the coated suture provided significantly (**p = 0.033**) better results. In other types of operations, no significant differences were found.
Incidence of superficial SSI	42 (11.2%)
Incidence of deep SSI	5 (1.3%)
Mortality	NR, Not prespecified as outcome
Quality of Life	NR, Not prespecified as outcome
Length of hospital stay	With normal wound healing, the average number of nursing days was nine, whereas for SSI patients, it was 15 (**p = 0.043**)
Proportion of patients requiring secondary surgery for wound-related complications of surgery	NR, Not prespecified as outcome
Proportion of patients requiring hospital readmissions for SSI/wound-related complications	NR, Not prespecified as outcome
Incidence of complete abdominal wound dehiscence within 30 days of surgery	NR, Not prespecified as outcome
Incidence of incisional hernia during the period of study follow-up	NR, Not prespecified as outcome
Causative microorganism (Results of microbiological cultures in patients with SSI)	Gram-negative organisms (*Pseudomonas aeruginosa*, *Enterococcos faecium*, *E. coli*, *Enterococcus spp*.) were isolated from both groups. Gram-positive bacteria (two cases of *S. epidermidis*) were found only in the uncoated suture group.
The use of systemic antibiotic therapy within 30 days of surgery	NR
Patient satisfaction	NR, Not prespecified as outcome
Safety results	**AE and SAE were not prespecified as outcomes nor reported.**
n (%) 95% CI	
Total of AEs	NR
Total of SAEs	NR
Frequency of SAEs leading to death	NR
Description of most frequent AE (by arms)	NR
Description of SAE (by arms)	NR

Costs (only for national assessment)	NR
Author Disclosure (Conflict of interest)	None exist

RR: relative risk; ITT: intention to treat; NR: not reported; PP: per protocol

Risk of Bias

Study (Author, year): Baracs et al., 2011		
	Judgement (Low, Unclear, **High**)	Support for judgement
Random sequence generation (Selection bias)	Low	Randomization: made by computer software (stored in a password protected website and could not be influenced manually. A participating centre could not view the data from the other centres.
Allocation concealment (Selection bias)	Unclear	See above.
Blinding of participants and personnel (Performance bias)	Unclear	Not reported
Blinding of outcome assessment (Detection bias)	Unclear	Not reported
Incomplete outcome data (Attrition bias)	Low	No drop-out.
Selective reporting (Reporting bias)	High	AE and SAE were not prespecified as outcomes nor reported; so the study does not report the results for a key outcome that could reasonably be expected for a study of its nature. This study was obviously registered retrospectively at NCT01123616. The registration took place in May 2010, but the study completion data is April 2010. Trial registration and trial publication describe different primary outcome measures (quality and quantity of wound discharge vs. SSI).
Other source of bias (Other bias)	Unclear	No conflicting financial interests exist. Funding NR.

Author, year, reference number: **Rasic et al., 2011** [29]	Author interpretation of results: In the Vicryl* Plus group there was a shorter hospital stay (13.2±1.3 days; 21.4±2.8 respectively). In the Vicryl* Plus group inflammatory parameters decreased to normal within the first week whereas in the Vicryl* group remained increased. In the Vicryl* Plus group four patients had a wound discharge, seven had inflammatory reactions to the skin sutures. One dehiscence was noticed. In the Vicryl* group 12 patients had an SSI, 14 patients had inflammatory reactions to the skin sutures and 7 patients had a wound dehiscence. Closure of the abdominal wall using Vicryl*Plus decreases postoperative wound complications, length of hospital stay and is associated with a more rapid return of inflammatory markers to normal.
Study title/objectives	Vicryl Plus for Closure of the Abdominal Wall / To compare the effect of triclosan-coated polyglactin 910 (Vicryl* Plus) or polyglactin 910(Vicryl*) on abdominal wall healing

Study characteristics	
Study design	RCT; Randomization: generated by a computer in blocks of 10. Sealed and numbered opaque envelopes containing suture packets were prepared. The envelopes were kept in the operating theatre and assigned in order.
Study Registration number	NR
Country of recruitment	Croatia
Centre	Single: Department of Surgery, »Sveti Duh« University Hospital, Zagreb, Croatia, by the same surgical team and the same anaesthesiologist
Ethics Committee Approval	Yes
Sponsor	NR
Study period (study start, study end)	Recruitment: 12-month period (September 2008–September 2009)
Duration of follow-up (days)	
Inclusion criteria	Patients diagnosed with colorectal cancer scheduled for elective surgery.
Exclusion criteria	NR
Sample size calculation	NR
Patient characteristics	
Age of patients	58 intervention vs. 57 control
Sex	49 males intervention vs. 50 control
BMI	22.7 vs 22.1, p=0.974
Diagnosis	Patients diagnosed with colorectal cancer scheduled for elective surgery
Comorbidities (i.e. diabetes and glycaemic control, obesity, hypothermia)	22.7 vs 22.1, p=0.974
Target organ for surgery	colorectal
Type of operative wound	NR
Clean	
Clean-contaminated	
Contaminated	
Dirty-infected	
US CDC criteria	NR
Procedure	
Elective	Yes

Emergency setting	
Open	
Median laparotomy	Yes
Transverse laparotomy	
Other (please specify)	
Laparoscopic	
Antibiotic prophylaxis (Yes/No/Not reported)	Yes intravenously
Timing	During induction of anaesthesia
Dosing (single or multiple)	
Antimicrobial agent given	gentamicin 160 mg (Gentamicin, Belupo, Koprivnica, Croatia) and metronidazole 500 mg, (Medazol, Belupo, Koprivnica, Croatia)
Antibiotic therapy	
Duration of surgery	95.5 vs 91.3 min, p=0.8933
Use of drainage	NR
Intervention	
Type of antibacterial-coated suture material	Triclosan-coated polyglactin 910 Vicryl* Plus (Ethicon Johnson- Johnson); Wound closure was performed with a continuous single-layer mass technique (peritoneum, muscle, and fascia)
Description of abdominal wall layers closure (i.e. fascial/muscle layer closure, skin and/or subcutaneous tissue closure…)	Skin was closed with polyamide (Ethilon, 2–0, Ethicon, Johnson-Johnson)
Comparator	
Type of non-bacterial coated suture material	Polyglactin 910 Vicryl* (Ethicon Johnson- Johnson); Wound closure was performed with a continuous single-layer mass technique (peritoneum, muscle, and fascia)
Description of abdominal wall layers closure (i.e. fascial/muscle layer closure, skin and/or subcutaneous tissue closure …)	Skin was closed with polyamide (Ethilon, 2–0, Ethicon, Johnson-Johnson).
Outcomes	
Primary:	
Secondary:	
Not specified as primary or secondary	Duration of operative procedure, duration of hospitalization, biochemical inflammation parameters (white blood cell count – WBC; procalcitonin – PCT; and C-reactive protein – CRP), presence of wound infection, dehiscence, haematoma or inflammatory reactions to the skin sutures (skin inflammation around the suture), postoperative hernias, readmissions and reoperations

Flow of patients	
No of patients enrolled	
No of randomized	184
Allocated per arms	Intervention: 91 patients Control: 93 patients
Received int. per arms	91 vs 93
Lost to follow-up per arms	None
No of analysed per arm	91 vs 93
Statistical analysis	
ITT, modified ITT, Per protocol; other (specify)	Differences between groups were compared by the c2 or Fisher exact test for categorical variables, the Mann--Whitney U-test for continuously variables; A p value < 0.05 was considered statistically significant.
Results	
Effectiveness results	
n (%) 95% CI	
Incidence of SSI (superficial + deep)	4 (4.3%) intervention vs. 12 (13.2%) control, **p<0.05**
Incidence of superficial SSI	NR
Incidence of deep SSI	NR
Mortality	No deaths in either group
Quality of Life	NR
Length of hospital stay	The mean hospitalization period was 1.2±1.3 day in the Vicryl* Plus group and 21.4±2.8 in the Vicryl group (**p<0.05**).
Proportion of patients requiring secondary surgery for wound-related complications of surgery	Re-operation was necessary: in 8 (8.8%) of the control (in 7 patients because of wound dehiscence and in one patient because of peritonitis) vs 1 (1%) needed re-operation in the Vicryl* plus group (wound dehiscence), **P<0.05**
Proportion of patients requiring hospital readmissions for SSI/wound-related complications	NR
Incidence of complete abdominal wound dehiscence within 30 days of surgery	1 (1.1%) intervention vs. 7 (7.7%, **p=0.027**
Incidence of incisional hernia during the period of study follow-up	5 (5.5%) in Vicryl* group compared with 2 (2.2%) in Vicryl* plus group; p=0.235

Causative microorganism (Results of microbiological cultures in patients with SSI)	NR, Not prespecified as outcome
The use of systemic antibiotic therapy within 30 days of surgery	NR, Not prespecified as outcome
Patient satisfaction	NR, Not prespecified as outcome
Safety results	**Not prespecified as outcome**
n (%) 95% CI	
Total of AEs	NR
Total of SAEs	NR
Frequency of SAEs leading to death	NR
Description of most frequent AE (by arms)	Postoperative inflammatory reactions to the skin sutures: 7 (7.5%) intervention vs. 16 (17.5%= control, **p<0.05**
Description of SAE (by arms)	NR
Costs (only for national assessment)	
	NR, Not prespecified as outcome
Author Disclosure (Conflict of interest)	
	NR

RR: relative risk; ITT: intention to treat; PP: per protocol; NR: not reported

Risk of Bias

Study (Author, year): Rasic et al., 2011		
	Judgement (Low, Unclear, **High**)	Support for judgement

Random sequence generation (Selection bias)	Low	Randomization: generated by a computer in blocks of 10. Sealed and numbered opaque envelopes containing suture packets were prepared. The envelopes were kept in the operating theatre and assigned in order.
Allocation concealment (Selection bias)	Low	See above.
Blinding of participants and personnel (Performance bias)	High	Not reported
Blinding of outcome assessment (Detection bias)	High	Not reported
Incomplete outcome data (Attrition bias)	Low	No drop-out.
Selective reporting (Reporting bias)	High	AE and SAE were not prespecified as outcomes nor all reported; so the study does not report the results for a key outcome that could reasonably be expected for a study of its nature.
Other source of bias (Other bias)	Unclear	No conflicting financial interests exist. Funding NR.

Author, year, reference number: **Justinger et al., 2013** [30]	Author interpretation of results: This clinical pathway facilitated trial shows that triclosan impregnation of a 2-0 polydioxanone closing suture can decrease wound infections in patients having a laparotomy for general and abdominal vascular procedures. The use of clinical pathways and altering a single parameter within this pathway in a blinded randomized fashion might be a novel technique for clinical studies.
Study title/objectives	Surgical-site infection after abdominal wall closure with triclosan-impregnated polydioxanone sutures: Results of a randomized clinical pathway facilitated trial / To investigate the effect of triclosan impregnated polydioxanone sutures used for abdominal wall closure on the rate of SSIs
Study characteristics	
Study design	Double-blind randomized trial
Study Registration number	NCT00998907
Country of recruitment	Germany
Centre	Single
Ethics Committee Approval	Yes
Sponsor	This trial was funded by a restricted grant (Johnson&Johnson, Summerville, NJ)
Study period (study start, study end)	September 2009 – September 2011
Duration of follow-up (days)	During hospitalisation and 2 weeks after discharge from hospital
Inclusion criteria	Patients scheduled to undergo a laparotomy, informed consent given, other details NR (from Protocol: Inclusion Criteria: surgical pathologies accessed via midline or transverse abdominal incision; primary fascial closure.
Exclusion criteria	NR (from Protocol: pregnancy, age under 18 years, open abdominal treatmen, known hypersensitivity against PDS/Triclosan)
Sample size calculation	Sample size of 350 patients for each arm was calculated to achieve a power of 1 b = 0.80 for the one-sided v2 test at level a = 0.025 and a low drop-out rate of 5%.

Patient characteristics	
Age of patients	63 ± 13
Sex	Male 525; female 331
BMI	<18: 21; 18–25: 402; 26–30: 303; >30: 130
Diagnosis	Cancer: 118 control group/124 triclosan group
Comorbidities (i.e. diabetes, obesity, hypothermia)	Obesity: 54 control/ 76 triclosan group; Diabetes: 35 control /49 triclosan
Target organ for surgery	Colorectal, Hepatopancreatobiliary, Small intestine; upper GI tract; vascular; other
Type of operative wound	
Clean	245 control / 286 triclosan
Clean-contaminated	97/162
Contaminated	25/37
Dirty-infected	Septic: 4 control/ 0 triclosan
US CDC criteria	Definition of SSI followed the CDC and Prevention criteria
Procedure	Open abdominal surgery; Colorectal resections; 'All patients included in the trial underwent a standardized clinical pathway documented abdominal wall closure after abdominal surgery.' open abdominal exploration and surgery and closure of the incision in a standardized fashion.
Elective	
Emergency setting	
Open	Yes
Median laparotomy	Control 279; triclosan 382
Transverse laparotomy	Control 92; triclosan 103
Other (please specify)	Upper GI tract: control 41; triclosan 59; Hepatopancreatobiliary: control 173; triclosan 210; Small intestine control control 14/triclosan 19; Colorectal, control 100/triclosan 143; Vascular surgery control 24/triclosan 26; other control 19/triclosan 27.
Laparoscopic	
Antibiotic prophylaxis (Yes/No/Not reported)	Yes
Timing	60 minutes before the skin incision
Dosing (single or multiple)	Single dose, although patients having procedures lasting longer than 4 hours received a second dose of antibiotics.
Antimicrobial agent given	Metronidazole and ceftriaxone or metronidazole and clindamycin in case of allergy.
Antibiotic therapy	NR
Duration of surgery	Control: 137 ± 68/ triclosan: 138 ± 65 (minutes)
Use of drainage	NR

Intervention	
Type of antibacterial-coated suture material	Triclosan impregnated 2-0 polydioxanone loop (PDS Plus)
Description of abdominal wall layers closure (i.e. fascial layer closure, skin closure…)	***Fascia*** was closed with either a 2-0 polydioxanone loop or a triclosan impregnated 2-0 polydioxanone loop. The abdominal wall was closed with a continuous suture, with a suture/wound length ratio of 4:1, with a stitch length of approximately 1 cm, taking the fascia at approximately 1.5 cm distance from the midline incision. The peritoneum was not closed separately. No subcutaneous sutures were used. The skin was closed with staples.
Comparator	
Type of non-bacterial coated suture material	2-0 polydioxanone loop without triclosan
Description of abdominal wall layers closure (i.e. fascial layer closure, skin closure…)	***Fascia*** was closed with either a 2-0 polydioxanone loop or a triclosan im- pregnated 2-0 polydioxanone loop. The abdominal wall was closed with a continuous suture, with a suture/wound length ratio of 4:1, with a stitch length of approximately 1 cm, taking the fascia at approximately 1.5 cm distance from the midline incision. The peritoneum was not closed separately. No subcutaneous sutures were used. The skin was closed with staples.
Outcomes	
Primary	The rate of wound infection; SSIs at the laparotomy incision following the CDC and Prevention criteria. Wound infection was identified by the presence of erythema, induration, pain and discharge of serous or contaminated fluid.
Secondary	Although not specifically mentioned in the Methods: blood loss, duration of surgery and duration of hospital stay were described in the Results. From Protocol: number of incisional hernias
Not specified as primary or secondary	
Flow of patients	
No of patients enrolled	1042
No of randomized	967
Allocated per arms	408 control; 559 triclosan group per protocol
Received int. per arms	408 control; 559 triclosan
Lost to follow-up per arms	Overall 111; not reported per arms, although can be calculated: 37 control; 74 triclosan
No of analysed per arm	856 evaluated; 371 control; 485 triclosan
Statistical analysis	
ITT, modified ITT, Per protocol; other (specify)	Per protocol; Differences between groups were calculated by χ^2 or Fisher exact test for categorical variables, Mann- Whitney U test for continuously variables.

Results	
Effectiveness results	
n (%) 95% CI	
Incidence of SSI (superficial + deep)	Incidence of wound infection: control 42 (11.3%) / triclosan 31 (6.4%), p<0.05
Incidence of superficial SSI	NR
Incidence of deep SSI	NR
Mortality	NR, Not prespecified as outcome, Quote: 'Ten patients died postoperatively…' group not specified.
Quality of Life	NR, Not prespecified as outcome
Length of hospital stay	Control: 15 ± 13 (2 - 134); triclosan: 11 ± 18 (2 - 209) (days), p=0.30
Proportion of patients requiring secondary surgery for wound-related complications of surgery	Five patients in the PDS II group and eight patients in the PDS Plus group had major surgical wound revisions (PDS II: 5/42 [11.9%]; PDS Plus: 8/31 [25.8%])
Incidence of complete abdominal wound dehiscence within 30 days of surgery	NR, Not prespecified as outcome
Incidence of incisional hernia during the period of study follow-up	NR, Not prespecified as outcome in article, but was in Protocol
Causative microorganism (Results of microbiological cultures in patients with SSI)	**Control group**: Staphylococci 23.1% Enterococci 23.1% Streptococci 5.1%, Enterobacteriacae 5.1% Others **Triclosan group**: Staphylococci 23.1% Enterococci 30.1% Streptococci 5.1% Pseudomonas spp. 5.1%, Enterobacteriacae 2.5% Others 23.1%. No difference between groups, p>0.05
The use of systemic antibiotic therapy within 30 days of surgery	NR
Patient satisfaction	NR, Not prespecified as outcome
Safety results	**Not prespecified as outcome nor reported**
n (%) 95% CI	
Total of AEs	NR
Total of SAEs	NR
Frequency of SAEs leading to death	NR
Description of most frequent AE (by arms)	NR

Description of SAE (by arms)	NR
Costs (only for national assessment)	Not assessed/reported
Author Disclosure (Conflict of interest)	NR

RR: relative risk; ITT: intention to treat; PP: per protocol; NR: not reported

Risk of Bias

Study (Author, year): Justinger et al., 2013		
	Judgement (Low, Unclear, **High**)	**Support for judgement**
Random sequence generation (Selection bias)	Unclear	Quote: 'Patients were randomized in blocks of 50 to 100 patients'. No further details provided.
Allocation concealment (Selection bias)	Unclear	Not reported
Blinding of participants and personnel (Performance bias)	Low	Quote: 'surgeons, patients, as well as wound monitors were blinded towards the use of either PDS II or PDS Plus. PDS II and PDS Plus sutures cannot be distinguished from each other in terms of physical properties such as color, feel of the suture, or tying properties. ' Blinding probably preformed adequately.
Blinding of outcome assessment (Detection bias)	Low	Quote: '… wound monitors were blinded towards the use of either PDS II or PDS Plus. PDS II and PDS Plus sutures cannot be distinguished from each other in terms of physical properties such as color, feel of the suture, or tying properties.'
Incomplete outcome data (Attrition bias)	Low	111 patients lost after being operated, reasons explained but not specified to groups/sutures performed. Still, the attrition rate is unlikely to have large effect on the results.
Selective reporting (Reporting bias)	High	Outcomes analysed and reported in the Results were not adequately reported in the Methods. AEs or SAEs were not prespecified in the registered protocol nor reported; so the study does not report the results for a key outcome that could reasonably be expected for a study of its nature.
Other source of bias (Other bias)	Unclear	This trial was funded by a restricted grant from a pharmaceutical company Johnson & Johnson, but transparently stated and unlikely to affect the results. Declaration of interests

		not provided.

Author, year, reference number: **Nakamura et al., 2013** [31]	Author interpretation of results: Triclosan-coated sutures can reduce the incidence of wound infections and the costs in colorectal surgery.
Study title/objectives	Triclosan-coated sutures reduce the incidence of wound infections and the costs after colorectal surgery: A randomized controlled trial / To assess the value of triclosan-coated polyglactin sutures in colorectal surgery
Study characteristics	
Study design	RCT; Randomization: Patients were randomly assigned by the envelope method into the 2 groups, and data were collected prospectively.
Study Registration number	UMIN000003322
Country of recruitment	Japan
Centre	Single: Department of Surgery of Teine-Keijinkai Hospital (a 550-bed private hospital that performs 7,500 surgeries annually) in Sapporo, Japan
Ethics Committee Approval	Yes
Sponsor	NR
Study period (study start, study end)	Recruitment: between April 2009 and March 2011
Duration of follow-up (days)	30 days
Inclusion criteria	No specific inclusion criteria
Exclusion criteria	Five patients were excluded from the study before the randomization because of the absence of informed consent
Sample size calculation	The assumed expected wound infection rates of 4% to 5% for the study group and 10% to 11% for the control group. With a 2-sided alpha = 005, the study was expected to have 80% power to detect a relative risk reduction of 5%; a total of 400 patients were estimated to be needed. The G*Power 3 software (Heinrich-Heine University, Dusseldorf, Germany) was used to calculate the sample size.
Patient characteristics	
Age of patients	69.4 intervention vs. 70.2 control
Sex	130 males intervention vs. 92 control
BMI	23.2 vs 23.4
Diagnosis	Patients who had undergone elective colorectal operations
Comorbidities (i.e. diabetes and glycaemic control, obesity, hypothermia)	Renal impairment, COPD, DM - in diabetic patients, a glycemic control protocol was not used in this study; steroid use

Target organ for surgery	colorectal
Type of operative wound	
Clean	0 vs 0
Clean-contaminated	205 vs 2013
Contaminated	1 vs 1
Dirty-infected	0 vs 0
US CDC criteria	Yes
Procedure	
Elective	Yes
Emergency setting	
Open	87 vs 96
Median laparotomy	
Transverse laparotomy	
Other (please specify)	
Laparoscopic	119 vs 108
Antibiotic prophylaxis (Yes/No/Not reported)	Yes intravenously
Timing	30 min before incision; every 3 h of operative time; and after operative time, for 48 h in both groups
Dosing (single or multiple)	Multiple
Antimicrobial agent given	Cephalosporin
Antibiotic therapy	NR
Duration of surgery	238 vs 230 min p=0.36
Use of drainage	NR
Intervention	
Type of antibacterial-coated suture material	Triclosan-coated polyglactin 910 antimicrobial sutures (Vicryl* Plus; Ethicon, Somerville, NJ)
Description of abdominal wall layers closure (i.e. fascial/muscle layer closure, skin and/or subcutaneous tissue closure…)	Wound closure was achieved by the technique of interrupted sutures and surgical staples for skin by 7 trained surgeons
Comparator	
Type of non-bacterial coated suture material	Polyglactin 910 sutures (Vicryl*)

Description of abdominal wall layers closure (i.e. fascial/muscle layer closure, skin and/or subcutaneous tissue closure …)	Wound closure was achieved by the technique of interrupted sutures and surgical staples for skin by 7 trained surgeons
Outcomes	
Primary:	Number of wound infections
Secondary:	Extra cost owing to the care of infected wound management
Flow of patients	
No of patients enrolled	415
No of randomized	410
Allocated per arms	Intervention: 206 patients; Control: 204 patients
Received int. per arms	Intervention: 206 patients; Control: 204 patients
Lost to follow-up per arms	0
No of analysed per arm	Intervention: 206 patients; Control: 204 patients
Statistical analysis	
ITT, modified ITT, Per protocol; other (specify)	ITT;
Results	
Effectiveness results	
n (%) 95% CI	
Incidence of SSI (superficial + deep)	28 infected cases: 12 were laparoscopic surgeries and only 3 cases had stoma. 9/206 (4.3%) Intervention vs. 19/204 (9.3%) control, **p=0.047**; Wound infection rate in the laparoscopic approach vs. open approach: 12/227 (5.3%) vs. 16/183 (8.7%), p=0.16
Incidence of superficial SSI	NR
Incidence of deep SSI	NR
Mortality	
Quality of Life	
Length of hospital stay	Days (median): 11 vs. 11.5, p=0.08; days (mean): 15.2 vs. 15.6, p=0.71
Proportion of patients requiring secondary surgery for wound-	NR

related complications of surgery	
Proportion of patients requiring hospital readmissions for SSI/wound-related complications	NR
Incidence of complete abdominal wound dehiscence within 30 days of surgery	NR
Incidence of incisional hernia during the period of study follow-up	NR
Causative microorganism (Results of microbiological cultures in patients with SSI)	Enterococcus species (12 of 28 cases), Bacteroides species (8 of 28 cases); no differences were found between the study groups
The use of systemic antibiotic therapy within 30 days of surgery	NR
Patient satisfaction	NR
Safety results	**Not prespecified as outcome nor reported**
n (%) 95% CI	
Total of AEs	NR
Total of SAEs	NR
Frequency of SAEs leading to death	NR
Description of most frequent AE (by arms)	NR
Description of SAE (by arms)	NR
Costs (only for national assessment)	Costs of wound infections: $18,370 vs. $60,814 During the study, wound infection developed in 28 patients. The median additional cost of wound-infection management in the inpatient and outpatient settings was $2,310. The actual entire cost, therefore, of 9 patients in the study group was $18,370 (theoretically; $2,310 3 9 patients = $20,790), and that of 19 patients in the control group was $60,814 (theoretically; $2,310 3 19 patients = $43,890). As a result, $42,444 were saved in wound care in the study group (Table VI). The triclosan-coated polyglactin 910 antimicrobial sutures, however, cost $10.80 more than the equivalent nonantimicrobial sutures, so the material costs for the the 206 patients in the study group in were $2,225 more than those in the control group ($10.80 3 206 patients). In summary, the actual savings using triclosan-coated sutures was at least $40,219 ($42,444 to $2,225) in this study period.

Author Disclosure (Conflict of interest)	NR

RR: relative risk; ITT: intention to treat; PP: per protocol; NR: not reported

Risk of Bias

Study (Author, year): Nakamura et al., 2013		
	Judgement (Low, Unclear, **High**)	Support for judgement
Random sequence generation (Selection bias)	Unclear	Patients were randomly assigned by the envelope method into the 2 groups.
Allocation concealment (Selection bias)	Unclear	See above.
Blinding of participants and personnel (Performance bias)	High	None of the surgeons was blinded to the closure method used with either conventional sutures or triclosan-coated sutures. The 7 trained physicians were, however, blinded to the assessment of the wound infections at the bedside, according to the CDC guidelines.
Blinding of outcome assessment (Detection bias)	Low	See above.
Incomplete outcome data (Attrition bias)	Low	No drop-out. ITT analysis.
Selective reporting (Reporting bias)	High	AE and SAE were not prespecified as outcomes nor reported; so the study does not report the results for a key outcome that could reasonably be expected for a study of its nature.
Other source of bias (Other bias)	Unclear	No conflicting financial interests exist. Funding NR.

Author, year, reference number: **Diener et al., 2014** [27]	Author interpretation of results: “Consequently, this finding delivers two messages to both surgeons and industry: first, the results of the PROUD trial underpin the unambiguous necessity of large and high-level clinical trials for valid assessment of surgical techniques, materials, and strategies. Second, although surgical innovation partly relies on the development of new materials, to start marketing without clear proof of effectiveness is the wrong approach. The question of whether triclosan-coated sutures can reduce the occurrence of surgical site infection remains open. Further assessment will necessitate further large, multicentre randomised controlled trials in high-risk and low-risk groups after median laparotomy—for example, in contaminated versus clean surgical procedures and in obese patients. These trials should apply validated criteria for endpoint assessment, such as the Centers for Disease Control and Prevention criteria for surgical site infection.”
Study title/objectives	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 / To obtain reliable data for the effectiveness of triclosan-coated PDS Plus sutures for abdominal wall closure, compared with non-coated PDS II sutures, in the prevention of surgical site infections
Study characteristics	
Study design	Randomised controlled parallel adaptive group-sequential superiority trial
Study Registration number	German Clinical Trials Register, number DRKS00000390
Country of recruitment	Germany
Centre	Multicentre (24 German hospitals, secondary and tertiary care centres)
Ethics Committee Approval	Yes
Sponsor	Johnson & Johnson
Study period (study start, study end)	Between April 7, 2010, and Oct 19, 2012
Duration of follow-up (days)	Time points for assessment of the primary endpoint at discharge or day 10 postoperatively (whichever occurred first) and on day 30 postoperatively
Inclusion criteria	Adult patients (aged ≥18 years) who underwent elective midline abdominal laparotomy for any reason
Exclusion criteria	Impaired mental state, language problems, and participation in another intervention trial that interfered with the intervention or outcome of this trial
Sample size calculation	Based on an assumed surgical site infection rate of 12% in the PDS II group and a reduction of this rate by 50% in the PDS Plus group, which was defined as clinically relevant. In a fixed sample size design, a sample size of 750 randomised patients was needed to achieve a power of 80% for the $\chi 2$ test at a two-sided significance level of 5% and to account for a 5% dropout rate. To cope with the uncertainty about the treatment effect, an adaptive group-sequential design was implemented prospectively. This design allowed for early termination for efficacy or futility or recalculation of the sample size if the study was continued after the interim analysis. In the protocol, the first interim analysis was planned once the primary outcome was available for 375 patients. On the basis of the results of

	this interim analysis, the data safety monitoring board recommended that a further interim analysis should be done after 1200 patients were enrolled. The decision rules of the adaptive group-sequential design were adjusted to ensure control of the overall one-sided type I error rate by 2.5%. The study was stopped after this second interim analysis, and the results for pooled data are reported in the Results section.
Patient characteristics	
Age of patients	64.7 (11.8) vs 65.0 (12.1)
Sex	Male 361 (61.5%) vs 368 (61.5%)
BMI	26.1 (4.3) vs 26.1 (4.6)
Diagnosis	Patients with elective midline abdominal laparotomy for any reason
Comorbidities (i.e. diabetes and glycaemic control, obesity, hypothermia)	Anaemia, DM, COPD, chronic renal failure, liver cirrhosis, malignant disease, current immunosuppressive therapy, chronic inflammatory disease
Target organ for surgery	Colon (189 vs 214), rectum (145 vs 117), stomach (67 vs73), pancreas (32 vs 37), liver (2 vs 3), combination (33 vs 37), other (119 vs 117)
Type of operative wound	
Clean	144 (24.5%) vs 138 (23.1%)
Clean-contaminated	430 (73.3%) vs 450 (75.3%)
Contaminated	11 (1.9%) vs 9 (1.5%)
Dirty-infected	2 (0.3%) vs 1 (0.2%)
US CDC criteria	

Procedure	
Elective	Yes
Emergency setting	
Open	
Median laparotomy	Yes
Transverse laparotomy	
Other (please specify)	
Laparoscopic	No
Antibiotic prophylaxis (Yes/No/Not reported)	Yes (578 (98.5%) vs 586 (98.0%)
Timing	Before the incision
Dosing (single or multiple)	See below.
Antimicrobial agent given	Antibiotic prophylaxis or therapy had to be completed and documented according to the recently updated German national guidelines from the Paul-Ehrlich-Gesellschaft fur Chemotherapie e.V.
Antibiotic therapy	Yes, please see above.
Duration of surgery	179.3 min (87.1) vs 185.2 min (90.9)
Use of drainage	NR
Intervention	

Type of antibacterial-coated suture material	Fascial closure after midline laparotomy with triclosan-coated polydioxanone sutures (PDS Plus PDP9262T; needle: CTX 48 mm 1/2 circle)
Description of abdominal wall layers closure (i.e. fascial/muscle layer closure, skin and/or subcutaneous tissue closure…)	Fascial closure was achieved by continuous mass closure with use of two loops—one each from the cranial and the caudal end of the incision in a continuous suture technique. No suture material or suture techniques apart from those described in the protocol were permitted. No subcutaneous drains were allowed. Skin closure was done with surgical skin staples.
Comparator	
Type of non-bacterial coated suture material	Fascial closure was done with use of uncoated polydioxanone sutures (PDS II Z1950G; needle: CTX 48 mm 1/2 circle) (Johnson & Johnson Medical GmbH, Norderstedt, Germany)
Description of abdominal wall layers closure (i.e. fascial/muscle layer closure, skin and/or subcutaneous tissue closure …)	Fascial closure was achieved by continuous mass closure with use of two loops—one each from the cranial and the caudal end of the incision in a continuous suture technique. No suture material or suture techniques apart from those described in the protocol were permitted. No subcutaneous drains were allowed. Skin closure was done with surgical skin staples.
Outcomes	
Primary	The occurrence of superficial or deep surgical site infection according to the Centres for Disease Control and Prevention criteria within 30 days after the operation
Secondary	Frequency of wound dehiscence (cutaneous and subcutaneous layer), frequency of burst abdomen (fascial dehiscence), postoperative length of stay in intensive care unit, postoperative length of stay in hospital, 30-day mortality, and quality of life (assessed with the EQ-5D questionnaire)
Not stated as primary or secondary	
Flow of patients	
No of patients enrolled	1224

No of randomized	1224 patients
Allocated per arms	607 to PDS Plus, and 617 to PDS II
Received int. per arms	590 vs 600
Lost to follow-up per arms	39 for mITT (34 were excluded from the analysis because they did not receive one of the study interventions, and a further five were excluded because of missing case report form data after randomisation) and 136 vs 136 for PP analysis; Dropout rates did not differ between the two study groups.
No of analysed per arm	1185 (587 PDS Plus and 598 PDS II) in mITT; 913 (451 vs 462) in PP
Statistical analysis	
ITT, modified ITT, Per protocol; other (specify)	Modified intention to treat, mITT; Additionally, a per-protocol analysis of those patients without major protocol violations was done. The primary endpoint was assessed with a logistic regression model that included the covariates age, body-mass index (BMI), centre, and surgeon's expertise (board-certified *vs* no certificate). Missing values for the primary outcome variable were replaced by random imputation with probability equal to the surgical site infection rate recorded for the complete cases in the respective treatment group. Multiple imputation was done as a sensitivity analysis. Point estimates were expressed as odds ratios for binary variables and differences of the means for continuous variables, each with corresponding 95% CIs; logistic regression modelling was used to identify potential risk factors for the occurrence of surgical site infections. Two-sided p values are reported throughout. Calculations were done with SAS version 9.1.
Results	
Effectiveness results	
n (%) 95% CI	
Incidence of SSI (superficial + deep)	The occurrence of surgical site infections did not differ between the PDS Plus group (87 [14.8%] of 587) and the PDS II group (96 [16.1%] of 598; OR 0.91, 95% CI 0.66–1.25; p=0.64)
Incidence of superficial SSI	53 out of 587 vs 56 out of 598

Incidence of deep SSI	22 out of 587 vs 25 out of 598
Mortality	9 (1.5%) vs 20 (3.3%) OR 0.46 (0.21 to 1.01; p=0.48); All deaths were classified as unrelated to the trial intervention and most of the postoperative deaths were due to septic shock, multiple organ failure, or cardiac and pulmonary decompensation.
Quality of Life	Patient self-assessed quality of life, 30 days after operation, measured on the EQ-5D index, did not differ between the groups. The sub-items with regard to mobility, self-care, usual activities, pain and discomfort, anxiety and depression, and the observed general health status on the visual analogue scale, also did not differ between the two groups. EQ-5D visual analogue scale N 453 vs 461: mean (SD) 69.2 (20.1) vs 68.2 (19.6) MD 0.96, -1.61 to 3.54, p=0.34); EQ-5D index N 448 vs 448; mean (SD) 0.9 (0.2) vs 0.8 (0.2), MD 0.01, -0.02 to -0.04, p=0.18)
Length of hospital stay	13.0 (7.4) vs 12.5 (6.3), MD 0.47 (-0.32 to 1.25; p=0.99)
Proportion of patients requiring secondary surgery for wound-related complications of surgery	The reoperation rate because of burst abdomen was lower in the PDS Plus group than in the PDS II group.
Proportion of patients requiring hospital readmissions for SSI/wound-related complications	Not prespecified in protocol as outcome
*Incidence of complete abdominal wound dehiscence within 30 days of surgery	*147 (14.9%) of 989 patients; 66 (13.4%) vs 81 (16.3%), OR 0.80 (0.56 to 1.14; p=0.21) (see definitions above)
Incidence of incisional hernia during the period of study follow-up	Not prespecified in protocol as outcome
Causative microorganism (Results of microbiological cultures in patients with SSI)	Not prespecified in protocol as outcome

The use of systemic antibiotic therapy within 30 days of surgery	126 (21.5%) vs 112 (18.7%)
Patient satisfaction	Not prespecified in protocol as outcome
Safety results*	**Definition of AE and SAE not given or probably not appropriate in article, definition of SAE given in Protocol: A serious adverse event (SAE) is any adverse event occurring at any time during the period of observation, that results in death, is immediately life-threatening, requires or prolongs hospitalization and/or results in persistent or significant disability or incapacity. From the moment the subject has signed informed consent until the regular end of the trial at 30 days follow up or until premature withdrawal of the patient, all SAE must be documented on a “serious adverse event form” available from the investigator study file. The following conditions are expected after the initial operation and will therefore not be classified as complication: pain, nausea, vomiting, urinary tract infection, hyper-/hypotension, imbalances of blood sugar or electrolytes and other lab values out of range, if they are not exceeding the duration and extent that can be expected after surgery. SAE need to be reported to the SDGC once they are noticed by the investigator within a time frame of five days. The safety analysis will be based on the set of all patients for which one of the interventions was applied. SAE will be tabulated, absolute and relative frequencies will be presented; severity and relationship to the intervention will be given and compared between the groups. The Data Safety Monitoring Board will be provided an annual report of SAE during the conduction of the trial.
n (%) 95% CI	
Total of AEs	NR, Not prespecified in protocol as outcome, please see above
Total of SAEs	Serious adverse events did not differ between the groups—146 of 583 (25.0%) patients treated with PDS Plus had at least one serious adverse event, compared with 138 of 602 (22.9%) patients treated with PDS II; p=0.39)
Frequency of SAEs leading to death	NR
Description of most frequent AE (by arms)	NR, Not prespecified in protocol as outcome, please see above

Description of SAE (by arms)	PDS Plus group n=583; PDS II n=602: Burst abdomen 8 (5.3%) vs 10 (6.3%); anastomotic insufficiency 39 (25.8%) vs 34 (21.5%); intra-abdominal fluid collection or abscess 14 (9.3%) vs 7 (4.4%); bleeding 12 (7.9%) vs 14 (8.9%); pulmonary 15 (9.9%) vs 13 (8.2%); cardiovascular 9 (6.0) vs 14 (8.9%); renal 7 (4.6%) vs 8 (5.1%); other GI problems 21 (13.9%) vs 24 (15.2%); Other 15 (9.9%) vs 21 (13.3%); not assessable 4 (2.6%) vs 3 (1.9%)
Costs (only for national assessment)	NR, Not prespecified in protocol as outcome
Author Disclosure (Conflict of interest)	MKD has received payments for lectures given during meetings organised by Johnson & Johnson. All other authors declare that they have no competing interests.

RR: relative risk; ITT: intention to treat; PP: per protocol; NR: not reported

Risk of Bias

Study (Author, year): Diener et al., 2014		
	Judgement (Low, **Unclear**, High)	Support for judgement
Random sequence generation (Selection bias)	Low	A central web-based randomisation tool was used to randomly assign eligible participants by permuted block randomisation with a 1:1 allocation ratio and block size 4 before mass closure to either triclosan-coated sutures (PDS Plus) or uncoated sutures (PDS II) for abdominal fascia closure.
Allocation concealment (Selection bias)	Low	After randomisation, suture packages were opened and sutures were handed out by the scrub nurse in such a way that the surgeon could not see the packaging.
Blinding of participants and personnel (Performance bias)	Low	Patients, surgeons, and the outcome assessors were masked to group assignment.
Blinding of outcome assessment (Detection bias)	Low	See above.
Incomplete outcome data (Attrition bias)	Low	The drop-out rate was not considerable: Modified intention to treat, mITT was done; Additionally, a per-protocol analysis of those patients without major protocol violations was done. Missing values for the primary outcome variable were replaced by random imputation with probability equal to the surgical site infection rate recorded for the complete cases in the respective treatment group. Multiple imputation was done as a sensitivity analysis.

Selective reporting (Reporting bias)	Unclear	AE were not prespecified as outcome, just SAE according to the protocol; In published article intensity of SAEs was recorded as mild, moderate and severe – data normaly connected with AEs; specification of SAEs was not given in details. No differences were recorded in demographics or the results for the primary and secondary endpoints between the modified intention-to-treat and per-protocol analysis
Other source of bias (Other bias)	Low	Funding: Johnson & Johnson Medical Limited. The PROUD trial was designed, managed, and analysed by the Study Centre of the German Surgical Society, with the support of the Institute of Medical Biometry and Informatics of the University of Heidelberg. The single-centre protocol of this trial was approved by the ethics committee of the University of Heidelberg, Germany, on March 22, 2010 (reference number S-064/2010). After acquisition of funding from Johnson & Johnson, a substantial amendment was written and approved by the ethics committee of the University of Heidelberg on Sept 29, 2010 (reference number S-064/2010), and by the ethic committees of all other participating centres between Dec 8, 2010, and Jan 11, 2011. The final study protocol was published and internationally registered. Funding of project and data management, biometry and statistical analysis, case payment, material (sutures, case report forms, digital cameras, trial master file, and investigator site file), trial committees, investigator meetings, and internet tools was provided by Johnson & Johnson Medical Limited (Scotland, UK). Investigators received no financial incentives from the funding source. PROUD was an investigator-initiated trial and the funder had no role in study design, data collection, data analysis, data interpretation, or the writing of the report. MKD, MK, and MWB had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Author, year, reference number: **Mattavelli et al., 2015** [33]	Author interpretation of results: The present trial failed to demonstrate a protective effect of triclosan-coated sutures on the occurrence of SSI. Our data suggest that the extensive use of such sutures have some local side effects. Given the conflicting results in the literature on the benefit and harm of triclosan-impregnated materials on incision healing, further large RCTs are needed before introducing it in a routine clinical use. Our results showed that in patients treated with triclosan-coated sutures there was an increase of wound hematomas. Such local side effects were not reported previously. The reason is unknown and difficult to explain on the basis of the identified safety reports. It can be speculated that the release of triclosan in the incision may interfere with some local coagulation pathways or platelet function. This minor side effect might be attributed to the broad use of triclosan-coated sutures in our study. In fact, we utilized four sutures to close peritoneum, fascia, subcutaneous fat tissue, and skin while previous similar trials used only one or two sutures.
Study title/objectives	Multi-Center Randomized Controlled Trial on the Effect of Triclosan-Coated Sutures on Surgical Site Infection after Colorectal Surgery / To evaluate the effect of a triclosan-coated sutures on the incidence of surgical site infections (SSIs) after elective colorectal operations.
Study characteristics	
Study design	Multi-center, randomized, controlled trial

Study Registration number	NCT01869257
Country of recruitment	Italy
Centre	Four university referral hospitals in Italy, Monza Pavia Rome Varese
Ethics Committee Approval	Ethical committees of all four centers approved the protocol.
Sponsor	Quotes:'This was an independent, unsponsored study; each hospital purchased the sutures.' 'This trial was funded by a research grant of the University of Milano-Bicocca. '
Study period (study start, study end)	Enrollment: between January 2010 and March 2013, other stages NR
Duration of follow-up (days)	30 days after hospital discharge
Inclusion criteria	Candidates for elective colorectal resection with a clean-contaminated field
Exclusion criteria	Younger than 18 years, pregnancy, emergency operations, ongoing infections, American Society of Anesthesiologists (ASA) score 3, any organ insufficiency, Karnofsky performance status < 70, intra-operative evidence of gross contamination of the surgical field, and denied written consent
Sample size calculation	With the planned sample size of 140 patients per arm, the expected width of the two-sided 95% confidence interval for the difference in proportions was 0.17. A dropout rate of 7% for discontinuation of intervention was anticipated, therefore, the target was a total sample size of 300 patients.
Patient characteristics	
Age of patients	Mean age 69
Sex	Male, female
BMI	Mean 24,8
Diagnosis	Cancer: 118 control group/124 triclosan group
Comorbidities (i.e. diabetes, obesity, hypothermia)	Obesity: 15 control/19 triclosan group; Diabetes: 18 control /21 triclosan
Target organ for surgery	Colon
Type of operative wound	
Clean	
Clean-contaminated	Quote: 'Patients were eligible if they were candidates for elective colorectal resection with a clean-contaminated field.'
Contaminated	
Dirty-infected	Gross contamination of the surgical field – exclusion criteria.
CDC criteria	
Procedure	
Elective	Yes
Emergency setting	Emergency operations were reported as exclusion criteria.

Open	
Median laparotomy	
Transverse laparotomy	
Other (please specify)	Right colectomy (49/49), transverse resection (9 control/5 triclosan), left colectomy (55/55), anterior resection of rectum (23 control /29 triclosan), abdominal–perineal resection (5 control /2 triclosan)
Laparoscopic	26 control /26 triclosan
Antibiotic prophylaxis (Yes/No/Not reported)	Yes
Timing	Single pre-operative dose: 30 min before skin incision; Multiple doses: pre-operative dose followed by three consecutive doses every 8 h after the operation. A second dose of antibiotic during surgery was administered in cases in which the duration of the operation was longer than 4 h, intra-operative contamination, or bleeding more than 500 mL
Dosing (single or multiple)	Single: 37 control / 41 triclosan; multiple: 104 control / 99 triclosan; second intraoperative dose 19 control /26 triclosan
Antimicrobial agent given	Penicillin plus b-lactamase inhibitors (PPBLI): 25/23; Cefazolin: 54/61; Cefoxitin: 45/28; Piperacillin: 11/12; Other: 6/16; Metronidazole in combination: 98/99
Antibiotic therapy	NR
Duration of surgery	140 control/ 145 triclosan (in minutes)
Use of drainage	129 control/ 128 triclosan
Intervention	
Type of antibacterial-coated suture material	Triclosan-coated polyglactin – 0 Vicryl Plus; Triclosan-coated polydioxanone – PDS Plus.
Description of abdominal wall layers closure (i.e. fascial layer closure, skin closure…)	Abdominal incision was sutured by a separate layer technique starting with the peritoneum with triclosan- coated polyglactin 910, followed by the fascia with triclosan-coated polydioxanone, and then the skin with triclosan-coated polyglactin. The skin closure was by interrupted sutures, while the peritoneum and the fascia by a running suture. In cases of subcutaneous fat tissue closure, the technique was interrupted sutures with 3/0 Vicryl Plus.
Comparator	
Type of non-bacterial coated suture material	Polyglactin or polydioxanone suture without triclosan.
Description of abdominal wall layers closure (i.e. fascial layer closure, skin closure…)	The identical suturing technique was used in the control group; subcutaneous fat closure used 3/0 Vicryl.
Outcomes	
Primary:	Overall rate of incisional SSI (superficial and deep incisional SSI)
Secondary:	Length of hospital stay and overall incision complication rate, including skin swelling and redness, hematomas, and seromas.
Not stated as primary or	

secondary	
Flow of patients	
No of patients enrolled	300
No of randomized	300
Allocated per arms	150
Received int. per arms	150 control / 150 triclosan
Lost to follow-up per arms	0
No of analysed per arm	141 control/ 140 triclosan (19 (9/10), after randomization, 19 patients (9 in the control arm and 10 in the triclosan arm) underwent relaparotomy with discontinuation of intervention)
Statistical analysis	
ITT, modified ITT, Per protocol; other (specify)	χ^2 test or Fisher exact test when appropriate and t-test were applied for categorical and continuous variables, respectively. A multivariable logistic model was applied including the treatment variable and evaluating the most important risk factors emerging from the literature in a one-step model.
Results	
Effectiveness results	
n (%) 95% CI	
Incidence of SSI (superficial + deep)	33 (11,7%); control 15 (10.6%) vs triclosan 18 (12.9%); difference between control and triclosan 2.2 (- 5.3– 9.7), OR 1.24 (0.60-2.57, p=0.564
Incidence of superficial SSI	21 (7); control 7 (4.7%) vs triclosan 14 (10.0%); difference between control and triclosan **5**.0 (- 1.1– 11.2), OR 2.13 (0.83-5.44, p=0.115
Incidence of deep SSI	12 (4); control 8 (5.7%) vs triclosan 1 (2.9%); difference between control and triclosan **-**2.8 (- 7.5– 1.9), OR 0.49 (0.14-1.66, p=0.252
Mortality	Not assessed, Not prespecified as outcome
Quality of Life	Not assessed, Not prespecified as outcome
Length of hospital stay	Control: 13.5 – 10.4; Triclosan: 12.3 – 6.5 (in days) p=0.546
Proportion of patients requiring secondary surgery for wound-related complications of surgery	NR
Incidence of complete abdominal wound dehiscence within 30 days of surgery	Not assessed, Not prespecified as outcome
Incidence of incisional hernia during the period of study follow-up	Not assessed, Not prespecified as outcome
Causative microorganism (Results	**Control group**: Pseudomonas aeruginosa, Enterobacter cloacae, Klebsiella pneumoniae, Escherichia coli, Staphylococcus aureus,

of microbiological cultures in patients with SSI)	Bacteroides fragilis, Enterococcus faecium, Candida albicans, Morganella morganii; **Triclosan group**: E. coli, E. faecalis, E. avium, Citrobacter koseri, S. aureus , E. cloacae, M. morganii, P. aeruginosa, Proteus vulgaris, K. oxytoca, B. fragilis, Streptococcus anginosus, P. vulgaris.
The use of systemic antibiotic therapy within 30 days of surgery	Not assessed, Not prespecified as outcome
Patient satisfaction	Not assessed, Not prespecified as outcome
Safety results	Not prespecified as outcome
n (%) 95% CI	
Total of AEs	Overall incision complications: control: 54 (38.3); triclosan 64 (45.7), odds ratio: 1.36; 95% CI: 0.84–2.18; p = 0.21 Incision hematoma: 3 (2.1) / 13 (9.3), odds ratio: 4.71; 95% CI: 1.31–16.91; **p = 0.02** Incision swelling: 20 (14.2)/ 26 (18.6); OR 1.38 (0.73-2.61), p=0.322 Incision redness: 38 (26.9)/ 43 (30.7); OR 1.20 (0.71-2.02), p=0.486 Incision seroma: 31 (22.1)/ 32 (22.9); OR 1.05 (0.60-1.84), p=0.861
Total of SAEs	NR
Frequency of SAEs leading to death	NR
Description of most frequent AE (by arms)	Incision hematoma in the triclosan group vs control: Odds ratio: 4.71; 95% CI: 1.31–16.91; p = 0.02
Description of SAE (by arms)	NR
Costs (only for national assessment)	Not assessed/reported
Author Disclosure (Conflict of interest)	No competing financial interests exist

RR: relative risk; ITT: intention to treat; NR: not reported; PP: per protocol

Risk of Bias

Study (Author, year): Mattavelli et al., 2015		
	Judgement	**Support for judgement**

	(Low, **Unclear**, High)	
Random sequence generation (Selection bias)	Low	A computer generated randomization list was used
Allocation concealment (Selection bias)	Low	A computer generated randomization list was used; assignment was done by sealed, opaque, numbered envelopes that were opened in sequence by a registered nurse not involved in the study.
Blinding of participants and personnel (Performance bias)	Unclear	Patients and outcome assessors were blinded to the allocation for the full period of evaluation; however, operating surgeons were not blinded to the material used.
Blinding of outcome assessment (Detection bias)	Low	Quote: 'Outcome assessors were blinded…'
Incomplete outcome data (Attrition bias)	Low	No losses to follow up
Selective reporting (Reporting bias)	Unclear	The trial was registered in May 2013. According to the journal article, however, "patient enrolment took place between January 2010 and March 2013." Thus, it is well possible that trial outcomes were selected and defined after inspection of the data. Because of this retrospective trial registration, the trial is rated as 'unclear'.
Other source of bias (Other bias)	Low	None noticed. Quotes: 'This was an independent, unsponsored study; each hospital purchased the sutures.' 'This trial was funded by a research grant of the University of Milano-Bicocca. '

Author, year, reference number: **Ruiz-Tovar et al., 2015** [28]	Author interpretation of results: The use of triclosan-coated sutures in faecal peritonitis surgery reduces the incidence of incisional SSIs.
Study title/objectives	Association between Triclosan-Coated Sutures for Abdominal Wall Closure and Incisional Surgical Site Infection after Open Surgery in Patients Presenting with Fecal Peritonitis: A Randomized Clinical Trial / To evaluate the effect of triclosan-coated sutures used in abdominal wall closure in patients with faecal peritonitis
Study characteristics	
Study design	RCT
Study Registration number	NR
Country of recruitment	Spain
Centre	Multicentre: three surgeons' experiences at General University Hospital of Elche (Alicante, Spain) and University Hospital Ramon y Cajal (Madrid, Spain)
Ethics Committee Approval	Yes
Sponsor	NR
Study period (study start, study end)	November 2007 and November 2013
Duration of follow-up (days)	All incisions were inspected by an epidemiology nurse who was blinded to group allocation at 5, 30, and 60 d after surgery

Inclusion criteria	Intra-operative diagnosis of faecal peritonitis secondary to acute diverticulitis perforation, neoplastic tumour perforation, or colorectal anastomotic leak of previous elective colorectal resection; without any other selection criterion other than diagnosis of faecal peritonitis
Exclusion criteria	Post-operative mortality
Sample size calculation	"…on an expected superficial SSI incidence of 30% in the control group (non-triclosan suture) based on epidemiology data at our institutions. With 80% power and a p value of 0.05, it was necessary to include 48 patients in each group to demonstrate a 50% reduction in superficial SSIs in the experimental group (triclosan suture). A possible loss of patients at follow-up because of perioperative mortality was calculated in 15%; therefore, 14 additional patients were added to the sample."
Patient characteristics	
Age of patients	Mean age of 64.7 – 15.9
Sex	62%male and 38% female
BMI	NR
Diagnosis	Faecal peritonitis
Comorbidities (i.e. diabetes, obesity, hypothermia)	Diabetes mellitus (34%), high blood pressure (48%), dyslipidemias (32%), cardiopathies (21%; 15% ischemic cardiopathy and 6% atrial fibrillation), chronic obstructive pulmonary diseases (11%), and non-decompensated liver cirrhosis (1%)
Target organ for surgery	Aetiology of faecal peritonitis was colorectal anastomotic leak in 42 patients (41.6%), perforated colonic neoplasm in 25 (24.7%), and perforated acute diverticulitis in 34 (33.7%)
Type of operative wound	
Clean	
Clean-contaminated	
Contaminated	
Dirty-infected	Yes
US CDC criteria	Yes (evaluated according to the U.S. Centres for Disease Control and Prevention (CDC) definition of SSIs, i.e., an incisional SSI must have at least one of the following: purulent drainage; positive culture; pain, tenderness, redness, and swelling)
Procedure	
Elective	
Emergency setting	
Open	Yes (Hartmann technique or a diverting stoma)
Median laparotomy	
Transverse laparotomy	
Other (please specify)	
Laparoscopic	
Antibiotic prophylaxis (Yes/No/Not reported)	Yes
Timing	Peri-operative followed by a minimum 7 days

Dosing (single or multiple)	Multiple
Antimicrobial agent given	Imipenem 1 g/8 h intravenous; in case of allergies to b-lactams, tigecycline (100mg IV as starting dose, followed by 50mg/12 h IV)
Antibiotic therapy	Both antibiotics were maintained for a minimum of 7 d, One hundred and one patients were treated with imipenem and 9 with tigecycline; there were no differences in the SSI rate depending on the antibiotic treatment received
Duration of surgery	NR
Use of drainage	NR
Intervention	
Type of antibacterial-coated suture material	Abdominal wall closure with ***triclosan-coated*** sutures (group 1)
Description of abdominal wall layers closure (i.e. fascial layer closure, skin closure…)	The **fascial layer** was closed with a polyglactin 910 antimicrobial loop suture size number 2; Subcutaneous tissue was not sutured in any of the groups; skin was closed with staples in all patients
Comparator	
Type of non-bacterial coated suture material	***Sutures without triclosan*** (group 2)
Description of abdominal wall layers closure (i.e. fascial layer closure, skin closure…)	The **fascial layer**: identical sutures from the same manufacturer without triclosan were used; Subcutaneous tissue was not sutured in any of the groups; skin was closed with staples in all patients
Outcomes	
Primary	
Secondary	
Not stated as primary or secondary	Incisional SSIs (including deep and superficial), mortality, hospital stay
Flow of patients	
No of patients enrolled	110 patients were included in the study; 76 were operated on at University Hospital Ramon y Cajal and 34 at General University Hospital Elche
No of randomized	110
Allocated per arms	55 in group 1 and 55 in group 2
Received int. per arms	55 in group 1 and 55 in group 2
Lost to follow-up per arms	Nine patients because they presented with multi-organ failure secondary to septic status and died post-operatively (4 in group 1 and 5 in group 2); Because all of the deceased patients died before 96 h postoperative, SSIs could not be evaluated
No of analysed per arm	50 patients were analysed in group 1 and 51 in group 2

Statistical analysis	
ITT, modified ITT, Per protocol; other (specify)	Per protocol. Comparison of variables was performed with the Student t-test (Mann-Whitney test was used for non-Gaussian variables). Comparison of qualitative variables was performed with the w2 test; in those cases with fewer than five observations in the cell, Fisher exact probability method was used. The effect was quantified with risk ratio (RR); $p < 0.05$ was considered significant.
Results	
Effectiveness results	
n (%) 95% CI	
Incidence of SSI (superficial + deep)	10% in group 1 and 35.3% in group 2 (**p = 0.004**; odds ratio [OR] = 0.204; 95% confidence interval [CI] 0.069–0.605); The number of patients necessary to treat (NNT) to obtain a benefit was 3.95.
Incidence of superficial SSI	
Incidence of deep SSI	
Organ/space SSI	Organ/space SSI was 8% in group 1 and 10% in group 2 (NS)
Mortality	8.2%, affecting 5 patients in group 1 and 4 patients in group 2 (not significant [NS]); Mortality causes were multi-organ failure secondary to septic status.
Quality of Life	NR
Length of hospital stay	9 d (range, 7–32 d) in group 1 and 9.5 d (range, 7–54 d) in group 2 (NS)
Proportion of patients requiring secondary surgery for wound-related complications of surgery	NR
Incidence of complete abdominal wound dehiscence within 30 days of surgery	NR
Incidence of incisional hernia during the period of study follow-up	NR
Causative microorganism (Results of microbiological cultures in patients with SSI)	Incision was opened by a surgeon and a microbiologic culture was obtained in all cases; E. coli: Group 1 (n=5): 2 (49%) vs Group 2 (n=18): 16 (88.9%), p=0.006; Klebsiella spp. 1 (20%) vs 5 (27.7%); pseudomonoas aerurinosa 2 (40%) vs 9 (50%), p=NS; Enterococcus faecalis: 0 vs 5 (27.7%), p=0.003: A reduction in the SSIs caused by Escherichia coli and Enterococcus faecalis was observed; In the multivariable analysis, the use of triclosan-coated sutures was the only independent variable associated with a reduction in incisional SSIs (p=0.026)
The use of systemic antibiotic therapy within 30 days of surgery	Imipenem 1 g/8 h intravenous; in case of allergies to b-lactams, tigecycline (100mg IV as starting dose, followed by 50mg/12 h IV); Both antibiotics were maintained for a minimum of 7 d
Patient satisfaction	NR
Safety results	**AEs not specified as outcome nor reported**
n (%) 95% CI	

Total of AEs	NR
Total of SAEs	NR
Frequency of SAEs leading to death	NR
Description of most frequent AE (by arms)	NR
Description of SAE (by arms)	NR
Costs (only for national assessment)	NR
Author Disclosure (Conflict of interest)	No competing financial interests exist.

OR: odds ratio; ITT: intention to treat; PP: per protocol; NR: not reported; NNT: number needed to treat

Risk of Bias

Study (Author, year): Ruiz-Tovar et al., 2015		
	Judgement (Low, Unclear, **High**)	Support for judgement
Random sequence generation (Selection bias)	Low	"The patients were randomized by means of a sequentially numbered container method into two groups: Fascial closure without triclosan-coated sutures (group 1) or sutures with triclosan (group 2). The randomization was performed by the surgeon when the intra-operative diagnosis of fecal peritonitis was achieved. The randomization was stratified for etiology of fecal peritonitis (acute diverticulitis perforation, neoplastic tumor perforation, or colorectal anastomotic leak) and performed depending on the intra-operative findings"
Allocation concealment (Selection bias)	Low	"The patients were randomized by means of a sequentially numbered container method into two groups: Fascial closure without triclosan-coated sutures (group 1) or sutures with triclosan (group 2). The opacity of the container prevents from selecting a particular number. The randomization was performed by the surgeon when the intra-operative diagnosis of fecal peritonitis was achieved."
Blinding of participants and personnel (Performance bias)	Low	Those who made the diagnosis were not blinded to the treatment, but were blinded to the selection of the patient from the sequentially numbered container. Epidemiology nurse who evaluated the outcome of the surgical incision was the only person blinded to the allocated

		treatment.
Blinding of outcome assessment (Detection bias)	Low	Epidemiology nurse who evaluated the outcome of the surgical incision was blinded to the allocated treatment.
Incomplete outcome data (Attrition bias)	Unclear	Nine patients died because they presented with multi-organ failure secondary to septic status and died post-operatively (4 in group 1 and 5 in group 2); Because all of the deceased patients died before 96 h postoperative, SSIs could not be evaluated. Missing data were not imputed using appropriate methods. The characteristics of the dropped-out participants compared with the completed participants have not been reported. Per protocol analysis.
Selective reporting (Reporting bias)	High	Bias due to selective outcome reporting: AEs not mentioned as aim or outcome nor reported; not pre-specified primary or secondary endpoints; so the study does not report the results for a key outcome that could reasonably be expected for a study of its nature.
Other source of bias (Other bias)	High	No competing financial interests exist; Funding not reported; Small sample size

Table A8: Characteristics of other relevant studies included in Safety domain: nRCTs for SAF Domain [34,35,47-51]

Study author/Year	Justinger et al. 2009	Justinger et al. 2011	Hoshino et al. 2013	Fraccalvieri et al. 2014	Jung et al. 2014	Okada et al. 2014	Nakamura et al. 2016
Design	Observational study (with historical control)	Interventional non-randomized clinical pathway driven study NCT00932503	Prospective observational study (with historical control)	Prospective observational study (with historical control)	Interventional single arm study	Prospective observational study (with historical control)	Prospective observational study
Country	Germany	Germany	Japan	Spain	Korea	Japan	Japan
Single or Multicentre	Single	Single	Single	Multicentre	Multicentre	Single	Single
No of patients	2087 / 1043 vs 1045	839 / 430 vs 409	1078 / 467 vs 611	480 / 240 vs 240	916	198 / 88 vs 110 control	670 /382 vs 288
Diagnosis	Different abdominal operations	Hepatobiliary resection	Digestive tract surgery	Elective colorectal disease	Gastric cancer	Pancreaticoduodenectomy	Colon cancer
Follow-up period	NR	NR	30 days	30 days	30 days	30 days	30 days
Open or	Open	Open	Open	Open	Open	Open	Laparoscopic

laparoscopic surgery							
Type of suture material	Triclosan-coated polyglactin 910 antimicrobial sutures -Vicryl Plus vs polydioxanone PDS II	Triclosan-coated polyglactin 910 antimicrobial sutures -Vicryl Plus vs polydioxanone PDS II	Triclosan-coated polyglactin 910 antimicrobial sutures -Vicryl Plus vs polyglactin 910 - Vicryl	Triclosan-coated polyglactin 910 antimicrobial sutures -Vicryl Plus vs polydioxanone PDS II	Triclosan-coated polyglactin 910 antimicrobial sutures -Vicryl Plus	Triclosan-coated polyglactin 910 antimicrobial sutures - Vicryl Plus vs polyglactin 910 - Vicryl	Triclosan-uncoated 0-PDS I and Triclosan-coated 0-PDS Plus
Site of suture	Fascia; skin with surgical staples	Fascia; skin with surgical staples	Fascia	Abdominal wall	Two layer; skin with surgical staples	Fascia; skin with surgical staples	Fascia and dermal
Adverse events	**Not specified as outcome nor reported**	**Not specified as outcome nor reported**	**Not specified as outcome nor reported**	**Not specified as outcome nor reported**	**Not specified as outcome but reported as AEs**	**Not specified as outcome but reported**	**Not specified as outcome nor reported**
Reported/ Not reported	**Not reported**	**Not reported**	**Not reported**	**Not reported**	**Reported**	Reported (not specifically as AEs) *Pancreatic fistula* 22/88 (25%) vs 25/110 (23.7%), p=0.71 *Delayed gastric emptying* 8/88 (9%) vs 15/110 (14.6%), p=0.32	**Not reported**
Total of AEs							
Total of SAEs					8 patients (0.87%) Respiratory problems: atelectasis, pleural effusion and pneumonia: n=6 Non-complicated fluid collection in the		

					intra-abdominal cavity after the operation: n=2		
Frequency of SAEs leading to death							
Description of most frequent AE (by arms)							
Description of SAE (by arms)					A total of eight patients (0.87%) had adverse symptoms, four in postoperative day 3 and four during the surveillance period between day 3 and day 30, and they dropped out from the study. These eight subjects required other antibiotics and additional treatment due to significant adverse symptoms, and had to be hospitalized for a longer time. However, all of these symptoms were caused by general anaesthesia or gastrectomy. No symptom was		

					directly related to triclosan-coated sutures.		
Author Disclosure (Conflict of interest)	Not reported	None	Not reported	Not reported	No conflict of interest	No conflict of interest	No competing financial interest exist

Table A9: Meta-analysis comparing the incidence of total incisional SSIs in patients with triclosan-coated sutures vs antibacterial-uncoated sutures with additional data from interim-analysis of Mingmalairak et al., 2009 [108]

Study or Subgroup	Experimental		Control		Weight	Odds Ratio
	Events	Total	Events	Total		M-H, Random, 95% CI
Baracs 2011	23	188	24	197	15.2%	1.00 [0.55,1.85]
Diener 2014	87	587	96	598	21.7%	0.91 [0.66,1.25]
Justinger 2013	31	485	42	371	17.9%	0.53 [0.33,0.87]
Mattavelli 2015	18	140	15	141	12.9%	1.24 [0.60,2.57]
Mingmalairak 2009	5	50	4	50	5.7%	1.28 [0.32,5.07]
Nakamura 2013	9	206	19	204	11.4%	0.44 [0.20,1.01]
Rasic 2011	4	91	12	93	7.2%	0.31 [0.10,1.00]
Ruiz-Tovar 2015	5	50	18	51	8.0%	0.20 [0.07,0.60]
Total 95% CI		1797		1705	100.0%	**0.67 [0.46,0.98]**
Total events	182		230			

Heterogeneity: Tau^2=0.14; Chi^2=15.87, df=7 (p=0.03); I=56%; Test for overall effect: Z=2.08 (**p=0.04**)

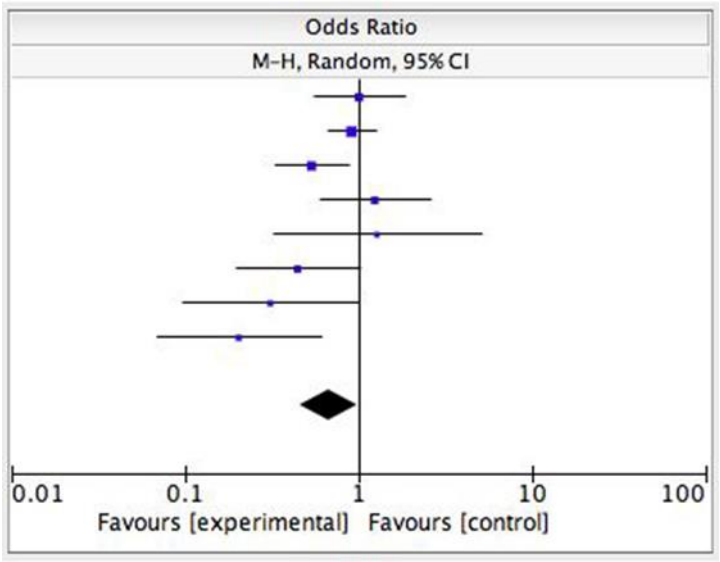

Figure 10: Forest plot of meta-analysis comparing the incidence of total incisional SSIs in patients with triclosan-coated sutures vs non-antibacterial coated sutures with additional data from interim-analysis of Mingmalairak et al, 2009

List of ongoing and planned studies

No ongoing RCTs or other studies with triclosan-coated sutures and chlorhexidine-coated sutures in abdominal surgery were identified in the below mentioned clinical trials registries.

- **ClinicalTrials.gov , https://clinicaltrials.gov/**

None identified on triclosan-coated sutures; None identified on chlorhexidine-coated sutures.

- **ISRCTN, http://www.isrctn.com/**

None identified on triclosan-coated sutures; None identified on chlorhexidine-coated sutures.

- **International Clinical Trials Registry Platform (ICTRP),** http://apps.who.int/trialsearch/, last access 28/11/2016

None identified on triclosan-coated sutures; None identified on chlorhexidine-coated sutures.

Risk of bias tables

Table A10: Risk of bias – study level (RCTs)

Trial	Adequate generation of randomisation sequence	Adequate allocation concealment	Blinding		Incomplete outcome data	Selective outcome reporting unlikely	No other aspects which increase the risk of bias	Risk of bias – study level
			Patient	Medicinal personnel and other staff				
Baracs 2011	Low	Unclear	Unclear	Unclear	Low	High	Unclear	High
Rasic 2011	Low	Low	High	High	Low	High	Unclear	High
Justinger 2013	Unclear	Unclear	low	Low	Low	High	Unclear	High
Nakamura 2013	Unclear	Unclear	High	Low	Low	High	Unclear	High
Diener 2014	Low	Low	Low	Low	Low	Unclear	Low	Unclear
Mattavelli 2015	Low	Low	Unclear	Low	Low	Unclear	Low	Unclear
Ruiz-Tovar 2015	Low	Low	Low	Low	Unclear	High	High	High
Comments: Specific details could be found in Table A7 above, Appendix 1								

Table A11: Risk of bias – outcome level (RCTs)

Outcome Trial	**Blinding – outcome assessors**	**ITT principle adequately realized**	**Selective outcome reporting unlikely**	**No other aspects according to risk of bias**	**Risk of bias – outcome level**
Incidence of total incisional SSIs					
Baracs 2011	Unclear	Low	Low	Unclear	Unclear
Rasic 2011*	High	Low	Low	Unclear	High
Justinger 2013	Low	Low	Low	Unclear	Unclear
Nakamura 2013	Low	Low	Low	Unclear	Unclear
Diener 2014	Low	Low	Low	Low	Low
Mattavelli 2015	Low	Low	Low	Low	Low
Ruiz-Tovar 2015*	Low	Unclear	Low	High	High
Incidence of AEs					
Baracs 2011**	Unclear	NA	High	Unclear	High
Rasic 2011***	High	Unclear	High	Unclear	High
Justinger 2013**	Low	NA	High	Unclear	High
Nakamura 2013**	Low	NA	High	Unclear	High
Diener 2014***	Low	Unclear	Unclear	Low	Unclear
Mattavelli 2015***	Low	Unclear	Unclear	Low	Unclear
Ruiz-Tovar 2015**	Low	NA	High	High	High

Abbreviations: AE: adverse event; NA: not applicable

*Rasic 2011; blinding of outcome assessment not reported; Ruiz-Tovar 2015; small sample size, funding not reported

**AEs (and SAEs) were not prespecified as outcomes nor reported; so the study does not report the results for a key outcome that could reasonably be expected for a study of its nature (Details in Table A7, Appendix 1).

***Details in Table A7, Appendix 1

Table A12: GRADE assessment on outcomes: Incidence of total incisional SSIs and Incidence of AEs

Outcome Trial	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Quality**	**Importance**
Incidence of total incisional SSIs							
7 RCTs	Not serious	Moderate heterogeneity *Serious, -1	Not serious	Not serious	Not serious	Moderate	Critical
Incidence of AEs							
3 RCTs	Not serious	**Serious, -1	Not serious	**Serious, -1	Not serious	Low	Important

Abbreviations: AE: adverse event

*Meta-analysis: Heterogeneity: Tau^2=0.15; Chi^2=15.28, df=6 (p=0.02); **I=61%** (Table 13)

**Differences in the way the outcomes are defined and measured (clinical and methodological heterogeneity); few events, not reported or wide confidence intervals (Details in Table 23 and Table A7, Appendix 1)

Applicability tables

Table A13: Summary table characterising the applicability of a body of studies

Domain	Description of applicability of evidence
Population	The population (adults) included in 7 RCTs is representative of patients usually included in such clinical trials. Baseline characteristics show that the studies included similar groups of patients. The majority of patients have clean and clean contaminated wounds and underwent colorectal surgery. There were a small number of patients with dirty wounds as well as patients with laparoscopic or emergency surgery. SSI was defined according to the Centres for Disease Control and Prevention of Atlanta criteria in 5 trials. Antibiotic prophylaxis was given in all RCTs but in one trial it was followed by further antibiotic treatment for at least 7 days (patients with faecal peritonitis). Paediatric patients were not in the scope of this assessment.
Intervention	Seven RCTs published between 2011 and October 2015 were included in our relative effectiveness assessment, with a total of 3580 patients randomised; 1879 (52.4%) to triclosan-coated sutures and 1707 (47.6%) to antibacterial-uncoated sutures. No clinical studies were found on chlorhexidine-coated sutures. Mass closure was performed in 3 RCTs.
Comparators	Most commonly used CE marked approved comparators – antibacterial-uncoated sutures – were used in all RCTs included in the assessment. In some studies, skin closure was performed by surgical staples.
Outcomes	The choice for primary outcome (incidence of incisional SSIs) is representative, according the guidelines and all RCTs reported this outcome. Mortality was not specified as outcome or reported in 3 RCTs. The length of hospital stay was an outcome in all 7 RCTs. Regarding the other secondary outcomes assessed in our SR, no conclusion could be made due to the lack of or different results of reported data. None of the 7 included RCTs specifically assessed the effect of antibacterial-coated sutures on patients' body functions and the effect of antibacterial-coated sutures on activities of daily living. Quality of life was assessed only in one RCT. None of the 7 included RCTs assessed patients' satisfaction. Relative safety of triclosan-coated sutures could not be confirmed due to a lack of reporting of AEs in RCTs and non-RCTs included in our assessment. The same is true for chlorhexidine-coated sutures because no clinical studies were found during our literature search at all.
Setting	RCTs included patients worldwide. Four studies were multicentre, with a range of 4 to 24 hospitals and 3 single centres. This is representative for the expected use.

APPENDIX 2: REGULATORY AND REIMBURSEMENT STATUS

Table A14: Regulatory status in major market countries

Organisation issuing approval	Verbatim wording of the (expected) indication(s)	(Expected) Date of approval	Launched (yes/no). If no include proposed date of launch
EU	MONOCRYL™ Plus Antibacterial sutures are intended for use in general soft tissue approximation and/or ligation where an absorbable material is indicated	May 21, 2007	Yes
EU	Coated VICRYL™ PLUS Antibacterial Sutures are intended for use in general soft tissue approximation and/or ligation. The safety and effectiveness of Coated VICRYL™ PLUS Antibacterial sutures in cardiovascular tissue, ophthalmic surgery and neurological tissue have not been established	Sep 17, 2004	Yes
EU	PDS™ PLUS Antibacterial Sutures are intended for use in general soft tissue approximation, including use in paediatric cardiovascular tissue, and in ophthalmic surgery (other than contact with cornea and sclera). These sutures are particularly useful where the combination of an absorbable suture and extended wound support (up to 6 weeks) is desirable	Apr 3, 2009	Yes
Japan	Coated VICRYL™ PLUS as above	Dec 18, 2008	Yes
Japan	PDS™ PLUS as above	Aug 2, 2011	Yes
Australia	MONOCRYL™ Plus	Jan 2, 2008	Yes
Australia	Coated VICRYL™ PLUS as above	Oct 9, 2006	Yes
Australia	PDS™ PLUS as above	Nov 19, 2008	Yes
Canada	MONOCRYL™ Plus	Nov 22, 2005	Yes
Canada	Coated VICRYL™ PLUS as above	Jan 13, 2003	Yes
Canada	PDS™ PLUS as above	Mar 6, 2008	Yes
US	MONOCRYL™ Plus	Jun 29, 2005	Yes
US	Coated VICRYL™ PLUS as above	Dec 19, 2002	Yes
US	PDS™ PLUS as above	Jul 14, 2006	Yes

Sources: [5]

Table A15: CE mark data (Vicryl® Plus, Monocryl® Plus, PDS® Plus)

Medical device	Manufacturer	CE Number	First issued	Date	Expiry date	Risk class
Triclosan-coated sutures						
Vicryl® Plus	Ethicon, Johnson & Johnson International	CE 73804	17 September 2004	3 August 2016	4 July 2018	III

Monocryl® Plus	Ethicon, Johnson & Johnson International	CE 518537	21 May 2007	03 March 2015	20 May 2017	III
PDS® Plus	Ethicon, Johnson & Johnson International	CE 536533	3 April 2009	3 August 2016	01 September 2017	III

Source: [132-134]

APPENDIX 3: CHECKLIST FOR POTENTIAL ETHICAL, ORGANISATIONAL, PATIENT AND SOCIAL AND LEGAL ASPECTS

1	**Ethical**	
1.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any new ethical issues?	Yes/**No**
	If answered with 'yes', please provide a short statement explaining why.	
1.2	Does comparing the new technology to the defined, existing comparators point to any differences that may be ethically relevant?	Yes/**No**
	If answered with 'yes', please provide a short statement explaining why.	
2	**Organisational**	
2.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) require organisational changes?	Yes/**No**
	If answered with 'yes', please provide a short statement explaining why.	
2.2	Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be organisationally relevant?	Yes/**No**
	If answered with 'yes', please provide a short statement explaining why.	
3	**Social**	
3.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any new social issues?	**Yes**/No
	If answered with 'yes', please provide a short statement explaining why. Triclosan is used in many antimicrobial soaps, shampoos, and toothpastes. Bacteria can develop resistance to triclosan. If triclosan-coated sutures effectively prevent surgical site infection, it might become necessary to restrict the public use of triclosan-containing products in order to prevent the development of triclosan-resistance. According to the literature, "widespread use of triclosan may represent a potential public health risk" [56].	
3.2	Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be socially relevant?	Yes/**No**
	If answered with 'yes', please provide a short statement explaining why.	
4	**Legal**	
4.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any legal issues?	Yes/**No**
	If answered with 'yes', please provide a short statement explaining why.	
4.2	Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be legally relevant?	Yes/**No**
	If answered with 'yes', please provide a short statement explaining why.	