Appendix 2: Evidence table

Author, year, reference	Design, scope, setting, population	Objective	SSI definition	Type of surgery	Study methods	Intervention	Results
Daeschlein, 2014 [11]	Prospective, blinded RCT Germany Population: 128 adults (male and female) receiving trauma surgery Exclusion criteria: infected wounds, AIDS, HBV/HCV, known drug users	To measure the number of bacteria at the base of the wound, along the wound margin, and on the wound sutures in patients undergoing surgery with and without the use of a cyanoacrylate-based adhesive sealant.	Modified CDC definition, observed by the attending surgeon; not primary study measure. Follow-up: 3 months postoperatively.	Trauma surgery	After assessing eligibility, patients were randomized by opening a sealed envelope, which contained pre-set computer generation number sequence. Skin antisepsis was performed using a 70% propanol-based product for 1-3 minutes. The control group was covered with a sterile drape prior to incision. The ntervention group received an application of cyanoacrylate sealant (IntéguSeal®) after antisepsis, but before draping. Follow-up: 3 months. Three intraoperative swabs were taken from each surgical site and incubated for colony-forming unit data.	Group 1: no sealant Group 2: cyanoacrylate sealant	SSI: Group 1: 0/66 Group 2: 0/62 OR: NA CI: NA This study was financed through the routine research grant of the Institute for Hygiene and Environmental Medicine. The authors have no competing interests to report.

Author, year, reference	Design, scope, setting, population	Objective	SSI definition	Type of surgery	Study methods	Intervention	Results
Doorly, 2015 [8]	Prospective, randomized trial Single institution, multicentre; USA Population: patients undergoing clean-contaminated colorectal procedures Exclusion: less than 18 years, pregnancy, history of hypersensitivity to cyanoacrylate-formaldehyde-acetone, emergent surgery, laparotomy within 60 days (or planned), sepsis, neutropenia, previous abdominal wound infection, serum creatinine > 3mg/dL, chemotherapy/radiation within 30 days, steroid use, HIV	To assess the role of a skin antimicrobial sealant for reducing the rate of superficial and deep wound SSI in a blended case mix of open and laparoscopic clean-contaminated procedures.	CDC criteria	Clean-conta-minated colorectal procedures	Consenting patients were blinded to allocation; randomization occurred via sealed envelopes containing either "InteguSeal®" or "Control". Enrolled patients received the same mechanical bowel preparation and prophylactic antibiotics. Abdomen was prepped with hair removal by clippers and ChloraPrep® (chlorhexidine gluconate 2%, isopropyl alcohol 70%; CareFusion, San Diego, CA, USA) prior to sealant application (in the intervention group). SCIP and a standardized enhanced recovery protocol implemented for all. Follow-up at 4 weeks.	I: cyanoacrylate sealant C: no sealant The sealant was provided by the InteguSeal® manufacturer.	SSI: I: 7/50 C: 5/50 *P*=0.545

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Dromzee, 2012 [9]	Prospective randomized trial June 2010 – June 2011; paediatric orthopaedic unit, France Population: children and adolescents undergoing scoliosis correction Exclusion criteria: previous spinal surgery and surgery indicated for anterior or combined procedures.	To explore the use of a antimicrobial sealant applied before the surgical incision to reduce SSI in patients with scoliosis.	Not specified	Spine	Randomization by random number table; impossible to blind surgical attendants. All patients showered with povidone-iodine the day before and the morning of surgery. Skin was cleaned and prepared in the operating room with 2 consecutive applications of one-step alcohol povidone-iodine 5% solution. Patients were draped either after skin preparation (control) or after the sealant dried (intervention).	Group 1: drape only after skin preparation (n=28) Group 2: drape after sterile, film-forming cyanoacrylate liquid application (IntéguSeal®; n=28)	SSI Group 1: 1/28 Group 2: 5/28 *P*=0.096 "No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript."

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Falk-Brynhildsen, 2014 [4]	RCT May 2010-October 2011; Sweden Population: patients scheduled for elective CABG, with the saphenous vein used for at least two CABG with or without another concomitant cardiac procedure. Exclusion: emergency operation, previous cardiac surgery, long-term corticosteroid treatment and/or antibiotic treatment within 14 days preoperatively skin disease, infection, or preoperative use of an intra-aortic balloon pump.	To compare the use of microbial skin sealant *vs.* bare skin at the saphenous vein harvesting site in patients undergoing CABG with regard to bacterial growth on the skin and in the surgical wound, including the postoperative wound infection rate.	Primary endpoint was bacterial growth on the wound-adjacent skin or from the subcutaneous wound tissue. Secondary endpoint – SSI: defined as wound complications requiring physician-prescribed antibiotic treatment (telephone call via dedicated nurse) Follow-up: 2 months	Coronary artery bypass graft with saphenous vein harvesting site	Patients were randomized via computer-generated block randomization by an external statistician allocated to two groups: bare skin (control) or microbial skin sealant (intervention). After preoperative disinfection with chlorhexidine 0.5% in ethanol 70%, or nurse-applied microbial skin sealant (InteguSeal®) on the saphenous vein harvest site (in intervention group) prior to incision.	Sealant group: cyanoacrylate sealant Control: no sealant	SSI: I: 7/61 C: 14/64 P=0.120 Kimberly Clark Health Care supported the investigators by providing InteguSeal® to be studied in an elective cardiac surgery population. Kimberly Clark provided no financial support to any author.

Author, year, reference	Design, scope, setting, population	Objective	SSI definition	Type of surgery	Study methods	Intervention	Results
Iyer, 2011 [5]	Prospective RCT 2008; New Zealand Population: patients undergoing CABG	To report the effect of pretreatment with an n-butyl cyanoacrylate-based microbial skin sealant in a population undergoing cardiac surgery and discuss its potential use in decreasing infections in other kinds of surgical procedures.	Southampton score divides wounds into 5 grades: 0=normal healing; 1= normal with bruising or erythema; 2=erythema with other signs of inflammation; 3=haemo-serous discharge; 4=purulent discharge; 5=deep or severe infection with or without tissue breakdown.	CABG	Hair removal was performed using an electric clipper the day before surgery. Patients washed with soap on the morning of surgery and the skin was disinfected with an alcohol-based povidone-iodine solution and left to dry for 3 minutes before a one-layer application of antimicrobial sealant, which was applied on the intervention leg on a random basis. No sham application was applied on the other leg. Wounds were examined daily during postoperative stay. In the case of infection, swabs were taken; if no infection was present, a culture swab was applied to a segment of the incision before discharge. Findings were recorded and 1-2 blinded assessors followed up at 4 weeks.	Group 1: Cyanoacrylate-based sealant (InteguSeal®) Group 2: No sealant	SSI Group 1: 1/47 Group 2: 12/47 *P*=0.0011 "Authors have nothing to disclose with regard to commercial support."

Author, year, reference	Design, scope, setting, population	Objective	SSI definition	Type of surgery	Study methods	Intervention	Results
Towfigh, 2008 [10]	Prospective randomized multicentre trial Six teaching hospitals; USA Population: adult patients undergoing open inguinal hernia repair Exclusion criteria: sensitivity to cyanoacrylate, existence of infection or use of antibiotics, chemotherapy, diabetes with HbA > 7 within 90 days, pregnant, nursing, participation in other studies	To compare the safety and effectiveness of antimicrobial sealant in reducing the incidence of surgical incision bacterial contamination relative to surgical skin preparation alone.	Not specified	Hernia repair	Patients were randomized using a 1:1 allocation; each site was supplied with sealed envelopes and the schedule was blocked within the centre to ensure an even distribution. It was not possible to blind the surgeon to the assigned study group. All patients underwent intraoperative microbial wound sampling at 2 stages during the operation; colony-forming units were quantified. Follow-up at 2 and 4 weeks postoperatively for signs of infection.	Group 1: cyanoacrylate sealant Group 2: control	SSI Group 1: 0/68 Group 2: 3/80 OR: 0.45 95% CI: 0.238-0.88 *P*=0.02 Funding given for IntéguSeal® applicator, standardized microbial sampling supplies and facility reimbursement of study-related costs.

Author, year, reference	Design, scope, setting, population	Objective	SSI definition	Type of surgery	Study methods	Intervention	Results
Vierhout, 2014 [6]	Discontinued RCT The Netherlands Population: patients undergoing vascular reconstruction Exclusion: thrombectomies through inguinal incision, patients under 18 years and those with a previous groin incision or vascular reconstruction done cranially to the site of incision.	To investigate whether the use of cyanoacrylate skin sealant at the site of surgery could reduce the incidence of SSI in the groin after vascular procedures.	Southampton wound sssessment scale greater than grade III, erythema plus inflammation and clear or sero-sanguinous discharge (G3) or pus (G4).	Vascular reconstruction	Randomization was completed in a 1:1 ratio by the drawing of a sealed envelope in the operating room 30 minutes before surgery by the surgeon. All patients received cefazolin (2 g intravenous) before incision. Hair removal by clipper done before disinfection with chlorhexidine (0.5% in 70% isopropyl alcohol) and draped with sterile disposable drapes. Intervention group patients received application of cyanoacrylate-based sealant (IntéguSeal®) prior to draping and after skin preparation.	Group 1: control Group 2: cyanoacrylate sealant	SSI: Group 1: 2/22 Group 2: 1/25 *P* = NS

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Von Eckardstein, 2011 [7]	Randomized, controlled, parallel-group, multi-centre, open-label clinical trial April 2006 to February 2009; 5 centres in Asia, Europe, Latin America and the USA Population: adult patients undergoing CABG Exclusion criteria: complex procedures, sensitivity to cyanoacrylate, isopropyl alcohol or iodine; abnormal skin condition; antimicrobial-impregnated incise drapes; chemotherapy, immunosuppressive therapy; steroid or	To determine if the use of this skin sealant before CABG could reduce surgical wound contamination by skin microflora and decrease post-procedure infections	CDC criteria	Cardiac	Randomization in a 1:1 ratio using a computer-generated randomization schedule balanced by randomly permuted blocks; allocations were concealed in a sealed envelope. Surgical site was prepared with either povidone-iodine or iodine 0.7% in isopropyl alcohol. In the experimental group, sealant was applied after drying. Microbial samples were tested for the total bacterial burden and all patients were monitored 30 days postoperatively for SSI.	Group 1: cyanoacrylate sealant (InteguSeal®) Group 2: control	SSI: Group 1: 9/146 Group 2: 14/147 Risk reduction: 35.3% This clinical study was initiated and funded by the Kimberly Clark Corporation.

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Waldow, 2012 [14]	Single-centre quasi-randomized prospective trial October 2010-April 2011; Germany Population: 998 consecutive adult patients undergoing elective cardiac surgical procedures with median sternotomy	To evaluate the prophylactic effect of a cyanoacrylate-based antimicrobial skin sealant on the incidence of postoperative mediastinitis or any other form of chest skin incision SSI after elective cardiac surgery.	CDC criteria	Elective cardiac	Hair removal by hair clipping and the application of an antiseptic alcohol-based (chlorhexidine-free) solution on the skin surface prior to incision. All measures were performed according to written internal hygienic and perioperative standards valid in the institution. Group assigned to receive a cyanoacrylate-based antimicrobial skin sealant (IntéguSeal®) as a drape accessory. All patients were prospectively subdivided into two registries by alternating administration of the antimicrobial sealant every second day of surgery regardless of the operation schedule. SSI follow-up: 30 days	Group 1: cyanoacrylate-based sealant included with standard pre-operative disinfection Group 2: standard preoperative preparation	Group 1: 53/488 Group 2: 57/495 *P* = NS The work was supported by Kimberly-Clark Health Care, which provided investigators with the original IntéguSeal® product to be studied in an elective cardiac surgery population. Kimberly-Clark did not provide any financial support to any author of this publication.

SSI: surgical site infection; CDC: Centers for Disease Control and Prevention; HIV: human immunodeficiency virus; I: intervention; C: control; AIDS: acquired immunodeficiency syndrome; HBV/HCV: hepatitis B virus/hepatitis C virus; NA: not applicable; RCT: randomized controlled trial; CABG: coronary artery bypass graft; OR: odds ratio; CI: confidence interval; SCIP: surgical care improvement project; NS: not significant.