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**Current Opinion in Infectious Diseases: Skin and soft tissue infections**

**Evidence update on prevention of surgical site infection**

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## **ABSTRACT**

Purpose of review: surgical site infection (SSI) is a common health care associated infection and complicates up to 10-20% of operations with considerable health care resources. Apart from the widely adopted use of appropriate hair removal, antibiotic prophylaxis, avoidance of hypothermia and peri-operative glycaemic control to reduce SSIs this review has considered new research and systematic reviews, and whether their findings should be included in guidelines.

Recent findings: The efficacy of preoperative bathing/showering, antibiotic prophylaxis for clean surgery and perioperative oxygen supplementation to reduce the risk of SSI is still in doubt. By contrast, the use of 2% chlorhexidine in alcohol skin preparation, postoperative negative pressure wound therapy and antiseptic surgical dressings do show promise.

Antimicrobial sutures in independent meta-analyses were found to reduce the risk of SSI after all classes of surgery (except dirty) whereas the use of wound guards, or diathermy skin incision (compared with scalpel incision), did not.

Summary: The incidence of SSI after surgery is not falling. Based on this review of published trials and evidence-based systematic reviews some advances might be included into these care bundles. More research is needed together with improved compliance with care bundles.

Key words: surgical site infection, antiseptics, antibiotic prophylaxis, surgical dressings, antimicrobial sutures

## **INTRODUCTION. Epidemiology and costs of SSIs**

Current epidemiological data indicates that the overall prevalence of Health Care Associated Infections (HCAIs) in England is 6.4% (CI 4.7-8.7%) with surgical site infections (SSIs) being the third most common category (15.7%)<sup>1,2</sup>. SSIs could be considered as being the most preventable HCAI, particularly when a care bundle approach, as there are many associated risk factors to target. A High Impact Intervention (HII) care bundle<sup>3</sup> issued by the Department of Health (DH, United Kingdom) is based on a guideline for the prevention and treatment of SSIs published by the National Institute for Health and Clinical Excellence (NICE): a combination of systematic review, other published guidance, and expert advice<sup>4</sup>. The HII care bundle incorporates core interventions of rational antibiotic prophylaxis, appropriate pre-operative hair removal, avoidance of perioperative hypothermia and perioperative glycaemic control in patients who have diabetes, together with other recommendations which are not of a level IA evidence base. An evidence update from NICE has since made no substantial changes to the recommendations published in the original guideline<sup>5</sup>. Despite the introduction of this directive, and its recommendations, having been circulated for over five years no evaluation of compliance with it or its effectiveness has been published<sup>6</sup>.

The national SSI surveillance system, established and administered by Public Health England to enable hospitals to compare their SSI rates against a national benchmark, aims to use SSI data to improve the quality of patient care<sup>2</sup>. Participating hospitals undertake surveillance in at least one of 17 categories of surgical procedures. In addition, the DH has mandated that acute NHS hospital trusts which perform orthopaedic surgery should undertake a minimum of three months of surveillance each year in at least one specified category<sup>7</sup>. It has been suggested that the true prevalence of SSI is underestimated, depending on surgical specialty, accepted and validated definitions and the comprehensiveness of postoperative surveillance<sup>8-9</sup>. When close post-discharge surveillance is included, particularly with the involvement of unbiased, trained and validated observers, SSIs have been reported to complicate 10-20% of surgical operations indicating that there is widespread underestimation of SSI rates across all classes of surgery<sup>10-18</sup>.

SSIs are associated with over a third of postoperative deaths; they can range from a relatively trivial, short-lived, wound discharge (e.g., after open hernia surgery) to being life threatening (e.g., mediastinitis and sternal wound dehiscence)<sup>19</sup>. In between there are the cosmetically

unacceptable scars which may cause pain, prolonged duration, and expense of hospitalisation, and poor emotional wellbeing<sup>20</sup>. Apart from the unrecorded indirect costs related to loss of productivity, reduced quality of life, and expensive litigation the actual cost of an SSI can involve many days of inpatient treatment and added procedures which can run into many thousands of pounds<sup>21, 22</sup>. An example of this is the morbidity and mortality which may follow sternal infection after cardiac surgery<sup>23</sup>. There is a paucity of prospective cost-benefit analysis of SSIs, but retrospective analyses clearly identify that the economic costs of SSI are substantial<sup>24</sup>.

There has been further research published since the NICE guideline recommendations were introduced: some presents new data or promising new technology which could be considered for guideline inclusion and the HII for SSIs; some has been shown to be clearly unhelpful in the prevention of SSIs and the rest has not added to the evidence already in place. Much of this is reflected in a NICE evidence update<sup>5</sup>. Review of the most relevant aspects of this new information is the topic of this article.

### **Preoperative bathing and skin preparation**

Ensuring personal hygiene of the operative team and surgical patient on the day of surgery is not controversial but the role of preoperative bathing and skin preparation with antiseptics to prevent SSIs is unproven. A Cochrane review of seven randomised controlled trials (RCTs; (n=10,157 patients)<sup>25</sup> found that preoperative showering or bathing with chlorhexidine was found to be no more effective than placebo, soap or no washing. Most of the studies included were over 20 years old. A further systematic review of 10 studies (n=7,351)<sup>26</sup> examined the effects of the number of antiseptic showers, and type of antiseptics. No definitive conclusions could be made about the optimal number of preoperative showers but in eight of the studies, chlorhexidine led to a reduction in skin surface bioburden. There were many methodological flaws in the trials, many being underpowered. In addition, skin bacteria did not seem to necessarily correlate with SSI risk. Another systematic review of 20 randomised and non-randomised studies (n=9,520)<sup>27</sup> evaluated three types of skin antiseptic (povidone-iodine, alcohol, or chlorhexidine) for patient skin preparation, operative team hand scrub procedure, preoperative showering or the use of antiseptic-impregnated incise drapes, prior to thoracic, cardiac, plastic, orthopaedic, neurological, abdominal, or pelvic surgery. Significant heterogeneity precluded meta-analysis but preoperative showering appeared to reduce skin

surface bioburden but the effect on SSIs was inconclusive. Again there were multiple flaws in the studies including inconsistencies in the formulation, strength and application of antiseptics, with mixed quality and randomisation and the inclusion of a wide range of procedures.

The benefits of preoperative bathing or showering with antiseptics to prevent SSIs are uncertain and only further large trials can improve this evidence base

### **Patient antiseptic skin preparation**

It is conventional practice to prepare patients' skin at the surgical site immediately before incision using an antiseptic (such as povidone-iodine or chlorhexidine; aqueous or alcohol-based). A Cochrane review<sup>28</sup> compared different preoperative skin preparations for preventing SSI after caesarean section in five randomised, quasi-randomised, and cluster-randomised trials (n=1462). In women who received skin preparation preoperatively the use of incisional drapes made no significant difference to SSI rates (RR=1.29, 95% CI 0.97 to 1.71, p=0.084). One trial (n=79) comparing alcohol scrub plus a povidone-iodine incise drape versus povidone-iodine scrub without drape reported no infections in either group. No conclusions can be confidently drawn because of heterogeneity and low numbers of patients studied, which reflects the conclusions of the systematic review mentioned earlier<sup>27</sup>. This latter review included an RCT (n=849)<sup>29</sup> which compared alcoholic 2% chlorhexidine, administered from a disposable device, with a conventional aqueous povidone-iodine skin preparation. The chlorhexidine group significantly reduced SSIs but the comparison with an aqueous-based antiseptic was flawed; nevertheless, this device has had a wide uptake in surgery in general. The most effective antiseptic for skin preparation before surgical incision is uncertain, but alcohol-based antiseptics are likely to be more effective than aqueous solutions.

### **Antibiotic prophylaxis in breast and hernia surgery**

Antibiotic prophylaxis for breast or hernia surgery remains controversial. A Cochrane review assessed 17 RCTs (n=7843) for the effect of antibiotic prophylaxis on SSIs in adult patients undergoing elective open inguinal or femoral hernia repair. SSIs were significantly lower

with antibiotic prophylaxis (3.1% versus 4.5% respectively; OR=0.64, 95% CI 0.50 to 0.82, p=0.00042) although infections after herniorrhaphy (no mesh) were not significantly different

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Two studies have assessed antibiotic prophylaxis to prevent surgical site infection after breast cancer surgery. A Cochrane review<sup>31</sup> examined seven RCTs (n=1945) which compared preoperative or perioperative antibiotic prophylaxis with none or placebo. A significantly reduced incidence of SSI was found after prophylactic antibiotics (RR=0.72, 95% CI 0.53 to 0.97, p=0.031). However, a double-blind RCT (n=254)<sup>32</sup> found no difference in SSIs between placebo and antibiotic (17/127; 13.4%; p=0.719). There were flaws in the studies; some were old and various antibiotics were used. The risk of antimicrobial resistance and its cost have to be considered and prophylactic use in clean surgery is still not clear cut.

### **Negative pressure wound therapy (NPWT)**

NPWT is widely used in the treatment of chronic wounds to promote wound healing, wound debridement, alleviate exudate and odour and improve quality of life<sup>33,34</sup>. It delivers intermittent or continuous negative pressure (ranging from <50mmHg to >125mmHg) to the wound site which is covered with a foam or gauze dressing and sealed with an occlusive drape. Success has been reported in complex wounds<sup>35</sup> with emerging evidence to show that its use in high risk, post-operative incisions prevents SSIs<sup>36-40</sup>. The likely modes of action are through holding wound edges together (thereby reducing the likelihood of surgical dehiscence), stimulation of perfusion, reduction of lateral tension, haematoma and oedema, and protection of the surgical site from exogenous sources of micro-organisms.

A retrospective analysis of surgery for colorectal, pancreatic and peritoneal surface malignancies<sup>36</sup> found that patients treated with postoperative NPWT developed fewer superficial incisional SSIs compared with those who had a standard dressing (6.7% vs 19.5%, p< 0.015). After clean-contaminated surgery, NPWT was associated with fewer superficial incisional SSIs (6.0% vs 27.4%, p<0.001), total SSIs (16.0% vs 5.5%, p<0.011), and need for postoperative wound interventions (16.0% vs 35.5%, p<0.011). The authors concluded there was a benefit but their results require validation by prospective randomized studies. In a prospective study of obese patients (BMI ≥ 30) having cardiac surgery through median sternotomy<sup>37</sup> it was found that NPWT reduced the incidence of SSI (4%) when compared to

standard wound dressings (16%;  $p = 0.027$ ; OR 4.57; 95% CI, 1.23 - 16.94). SSIs caused by Gram positive skin flora were found in one patient having NPWT compared with 10 in the standard group ( $p = 0.009$ ; OR 11.39; 95% CI, 1.42 - 91.36). Portable NPWT devices have been successfully used to decrease incidence of groin wound infection in patients after vascular surgery<sup>38</sup>. In patients treated conventionally, with a skin adhesive or absorbent dressing, 19/63 (30%) groin incisions developed an SSI; whereas 3/52 (6%) groin incisions treated with the NPWT device did so ( $p = .0011$ ). A further retrospective review of patients undergoing open colectomy<sup>39</sup> showed that 69/254 (27.2%) developed an SSI; 4 (12.5%) occurred in patients who had wounds treated with NPWT and 65 (29.3%) in patients having conventional wound care. In an orthopaedic study, patients with blunt, high-energy fractures of the lower limb were randomised in a multicentre RCT ( $n=249$ ) to standard dressings or NPWT<sup>40</sup>. Significantly more infections were seen in the standard dressings group (23/122; 19%) than the NPWT group.

However, a study of ventral hernia repair<sup>41</sup> suggested that NPWT conferred no effect on the development of an SSI in patients after repair of potentially contaminated and infected hernias (25.8% SSIs with standard incisional wound care; 20.4% after NPWT;  $p = 0.50$ ). A 12 months follow up showed no differences between the groups in late wound complications (31.4% standard care; 28.6% after NPWT;  $p = 0.74$ ). As these early studies are relatively small, with some controversial findings, further well powered and designed RCTs and systematic reviews are needed before the use of NPWT can be routinely recommended to reduce the risk of SSI.

### **Perioperative oxygen supplementation**

Optimal oxygenation during surgery is part of best practice to ensure a haemoglobin saturation of more than 95%. A systematic review and meta-analysis of seven RCTs ( $n=2,728$ ) examined the role of perioperative oxygen supplementation ( $FiO_2 = 0.8$ ) for 2 hours postoperatively in the recovery room to reduce SSIs. No significant difference was seen in the rate of SSIs between supplemented oxygen and control groups (15.5% versus 17.5% respectively; odds ratio=0.85, 95% CI 0.52 to 1.38,  $p=0.51$ ). However, 2 subgroup analyses did show a significant benefit, when studies of neuraxial anaesthesia were excluded and in colorectal surgery, which justifies further research.



Flaws in the trials included heterogeneity of antibiotic use, definition of SSI, patient population, and duration of perioperative oxygen supplementation.

### **Antiseptic surgical dressings**

It is conventional to cover incisions with a dressing at the end of an operation. Whether a dressing is necessary at all, or whether it should be a transparent polyurethane or absorptive island dressing, is unclear. A Cochrane review of 16 RCTs (n=2578)<sup>43</sup> investigated the value of wound dressings for the prevention of SSIs and found that there was no evidence that covering wounds reduced SSIs. There were many methodological flaws in these trials, including heterogeneity, small size and poor scientific quality; many were old studies.

There are many studies of antiseptic dressing use in chronic wound management, although many are of poor quality, but few have been used to prevent SSI. However, silver Nylon dressings have been investigated in a small RCT (n=110) involving patients undergoing colorectal surgery<sup>44</sup> for prevention of SSI. Infections were lower when silver Nylon dressings had been used (7/55; 13%) compared with gauze (18/54; 33%; p=0.011). Again there were many flaws and further evidence is needed to advocate the use of antiseptic dressings.

### **Wound guards**

The concept of a wound barrier, used during surgery to protect the wound edges from contamination, is attractive, but wound guards, based on semi-rigid plastic rings inserted into the incision with drapes attached to the circumference, have not been part of routine surgical practice. A systematic review and meta-analysis<sup>45</sup> found 10 RCTs and 2 controlled trials (n=1933) of the use of wound guards to prevent SSIs after open abdominal, mostly colorectal, surgery. Most studies were old and of poor quality, with variable definitions and risk of bias, but an exploratory meta-analysis using a random effects model suggested a potentially significant benefit (RR=0.60, 95% CI 0.41 to 0.86, p=0.005). The same group have since published an acceptable RCT, the ROSSINI trial, which showed definitively that there was no benefit conferred by wound edge protection devices in the prevention of SSI<sup>46</sup>.

### **Scalpel or diathermy for skin incision**

The use of diathermy for surgical incision may allow quicker surgical access and less bleeding than the use of a scalpel, but the effect on wound complications and SSIs has been investigated in a Cochrane review<sup>47</sup> of 9 RCTs (n=1901). No difference was seen between patients whose abdominal incisions were made with diathermy or with a scalpel (RR=0.90, 95% CI 0.68 to 1.18, p=0.44; 7 RCTs, n=1559). The trials were flawed by being underpowered, with heterogeneity, and definitions were not consistent. The use of diathermy to reduce the risk of SSI needs further evaluation in good quality studies.

### **Antimicrobial sutures**

There is laboratory-based evidence that antimicrobial sutures (impregnated or coated with the broad spectrum antiseptic triclosan) can effectively and safely deliver an antimicrobial into tissues. Several flawed and underpowered early studies showed some promise but now there are three independently undertaken systematic reviews and meta-analyses which found level 1A evidence for their use. The first<sup>48</sup> identified 17 RCTs (n=3720). In a fixed effects model antimicrobial sutures significantly reduced SSIs by 30% (RR=0.70, 95% CI 0.57 to 0.85, p<0.001). Sub-analyses suggested that the effect was only significant after abdominal surgery but not after breast or cardiac surgery. Some studies were flawed by being underpowered with varying definitions of SSI and use of unconventional comparators. The second<sup>49</sup> identified 13 RCTs (n=3568) of better quality and one additional trial of colorectal surgery. In a fixed effects model there was a significant reduction of SSIs associated with the use of antimicrobial sutures (RR=0.73, 95% CI 0.59 to 0.91, p=0.005). The third meta-analysis<sup>50</sup> identified 15 RCTs (n=4800) using PRISMA guidelines. In a fixed effects model the use of antimicrobial sutures significantly reduced SSIs by 33% (RR=0.67, 95 CI 0.53 to 0.84, p<0.0005) with no evidence of publication bias, a sensitivity analysis robust up to removal of three trials and the effect being significant in subsets of clean, clean-contaminated and contaminated surgery. This evidence presents a strong case for the use of antimicrobial-coated sutures to reduce SSIs.

### **CONCLUSION**

Evidence-based medicine, derived from systematic reviews and meta-analysis, provides the strongest data for the compilation of guidelines. Wherever there are gaps in knowledge recommendations have to be based on operator experience, patient preferences and data form

less convincing cohort and non-comparative studies. However, many of the RCTs included in meta-analysis are also of less than perfect scientific quality and guidelines should reflect that.

It is interesting that many aspects of current research to prevent SSIs involve a return to the use of antiseptics which has commented on before <sup>51, 52</sup> and is timely bearing in mind the world-wide concern of rising antibiotic resistance and the lack of new antibiotic groups entering the research train <sup>53</sup>.

There is an attractive logic to having several evidence-based interventions in a care bundle because when enacted together they might act with a summation effect and reduce the risk of an SSI to a very low level. However, unless there is near-complete to complete compliance with a bundle there seems little point introducing innovations which may have large resource implications to implement.

#### Key points

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