

Surgical site infections 2



New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective

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Surgical site infections (SSIs) are the most common health-care-associated infections in developing countries, but they also represent a substantial epidemiological burden in high-income countries. The prevention of these infections is complex and requires the integration of a range of preventive measures before, during, and after surgery. No international guidelines are available and inconsistencies in the interpretation of evidence and recommendations in national guidelines have been identified. Considering the prevention of SSIs as a priority for patient safety, WHO has developed evidence-based and expert consensus-based recommendations on the basis of an extensive list of preventive measures. We present in this Review 16 recommendations specific to the intraoperative and postoperative periods. The WHO recommendations were developed with a global perspective and they take into account the balance between benefits and harms, the evidence quality level, cost and resource use implications, and patient values and preferences.

Introduction

Surgical site infections (SSIs) are largely preventable, but they represent a considerable burden for health-care systems, particularly in low-income and middle-income countries. For these reasons, and the fact that no general set of international recommendations exists, WHO prioritised the development of evidence-based global guidelines for the prevention of SSIs. A panel of international experts developed recommendations on the basis of predetermined research questions and the results of related systematic literature reviews. The description of the intended audience for these recommendations, the methods used, and the first group of recommendations regarding preoperative preventive measures are provided in paper 1 of this Series,¹ which should be read in conjunction with this Review. We present here the recommendations (table) to be applied in the intraoperative and postoperative periods. Important topics such as asepsis in the operating room and sterilisation are not mentioned because they were not the object of formal recommendations, but they are included and extensively reviewed in the WHO guidelines, as cornerstones of SSI prevention.

Recommendation 1: 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 h, to reduce the risk of SSI (strong recommendation, moderate quality of evidence).

Adequate surgical site tissue oxygenation is thought to have a role in preventing SSIs. A high partial pressure of oxygen in the blood achieved through the administration

of high-concentration oxygen (hyperoxia, defined as oxygen at 80% FiO₂) provides more adequate oxygenation at the surgical incision—particularly at infected tissue,⁴ which has a lower oxygen tension than non-infected tissue⁵—and might enhance oxidative killing by neutrophils.⁶ We did a systematic review to assess the effect of high FiO₂ (80%) compared with standard FiO₂ (30–35%) for the prevention of SSI.

We identified 15 randomised controlled trials (RCTs)^{7–21} comparing the perioperative administration of 80% FiO₂ with 30–35% FiO₂ in adults. We did a meta-analysis that included studies in which patients underwent general anaesthesia with endotracheal intubation and mechanical ventilation.^{7–17} Ventilation control (and therefore the actual administration of FiO₂) with a facemask or nasal cannulae in neuraxial anaesthesia was considered to be a different intervention from mechanical ventilation. Furthermore, a meta-regression analysis showed that the type of anaesthesia independently modified the effect of hyperoxygenation. The 11 RCTs included in the meta-analysis showed that increased perioperative FiO₂ is beneficial in reducing SSI compared with standard perioperative FiO₂ (odds ratio [OR] 0.72; 95% CI 0.55–0.94). The quality of the evidence was rated as moderate.

On the basis of this evidence, patients undergoing general anaesthesia with endotracheal intubation for surgical procedures should receive 80% FiO₂ intraoperatively and, if feasible, for 2–6 h in the immediate postoperative period. The expert panel noted that the benefits of this intervention can be observed only when implemented by both intubation during the operation, and using a high-flux mask in the immediate postoperative period (figure). The benefits are also

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This is the second in a Series of two papers about surgical site infections

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	Key research question	Recommendations for prevention of SSIs	Strength of recommendation (quality of evidence retrieved†)	Notes for implementation in low-income and middle-income countries
(1) Perioperative oxygenation	How safe and effective is the perioperative use of high fraction of inspired oxygen in reducing the risk of SSI?	Adult patients undergoing general anaesthesia with endotracheal intubation for surgical procedures should receive 80% fraction of inspired oxygen intraoperatively and, if feasible, in the immediate postoperative period for 2–6 h	Strong recommendation (moderate)	Oxygen availability is low; oxygen and high-flow masks are an additional cost for the health-care facility or patient
(2) Maintaining normal body temperature (normothermia)	In surgical patients, should systemic body warming vs no warming be used for the prevention of SSI?	Warming devices are suggested for use in the operating room and during the surgical procedure for patient body warming	Conditional recommendation (moderate)	Availability of warming devices is low, particularly in low-resource settings; they are an additional cost for the health-care facility and require maintenance; simple blankets might function as efficiently as electrical devices
(3) Use of protocols for intensive perioperative blood glucose control	Do protocols aiming to maintain optimal perioperative blood glucose concentrations reduce the risk of SSI; and what are the optimal perioperative glucose target concentrations in diabetic and non-diabetic patients?	Protocols are suggested to be used for intensive perioperative blood glucose control for both diabetic and non-diabetic adult patients undergoing surgical procedures	Conditional recommendation (low)	Monitoring blood glucose adequately and treating hypoglycaemic events might be hard as medical staff training is required; availability, purchase, and storage (refrigerator) of insulin might cause financial burden
(4) Maintenance of adequate circulating volume control (normovolaemia)	Does the use of specific fluid management strategies during surgery affect the incidence of SSI?	Goal-directed fluid therapy is suggested for use intraoperatively	Conditional recommendation (low)	Some types of intravenous fluids might not be available; expertise in anaesthesia and medical staff training are required for the management of goal-directed fluid therapy and are often unavailable
(5) Disposable non-woven vs reusable woven drapes and gowns	Is SSI incidence affected by the use of disposable non-woven drapes and gowns vs reusable, woven drapes and gowns?‡	Either sterile disposable non-woven or sterile reusable woven drapes and surgical gowns can be used during surgical operations	Conditional recommendation (moderate to very low)	Availability of disposable drapes and gowns may be low and costs might cause a high financial burden, whereas labour costs for reprocessing reusable items may be less of an issue; the ecological effect of the additional clinical waste generated by use of single-use drapes and gowns should also be considered
(6) Adhesive incise drapes	Does the use of disposable adhesive incise drapes reduce the risk of SSI?	Plastic adhesive incise drapes with or without antimicrobial properties should not be used	Conditional recommendation (low to very low)	This recommendation avoids inappropriate resource allocation, because plastic adhesive incise drapes (in particular with antimicrobial properties) usually have an increased cost and they are not readily available in low-income and middle-income countries
(7) Wound-protector devices	Does the use of wound-protector devices reduce the incidence of SSI in open abdominal surgery?	Consider the use of wound-protector devices in clean-contaminated, contaminated, and dirty abdominal surgical procedures	Conditional recommendation (very low)	Wound-protector device availability is low and it is an additional cost for the health-care facility or patients; staff training is required; conflicting results exist from cost-effectiveness studies
(8) Incisional wound irrigation§ with an aqueous povidone-iodine solution	Does intraoperative wound irrigation with an aqueous povidone-iodine solution reduce the risk of SSI?	Consider the use of irrigation of the incisional wound with an aqueous povidone-iodine solution before closure, particularly in clean and clean-contaminated wounds	Conditional recommendation (low)	Availability of sterile products might be low; pulse pressure devices are scarce and have high costs, including purchase, waste disposal, procurement, energy, and machine maintenance

(Table continues on next page)

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maximised when normothermia and normovolaemia are maintained. In low-resource settings in which medical oxygen is scarce and its increased use could place a burden on available resources, this recommendation might not be considered as a priority by policymakers.

Recommendation 2: 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).

Hypothermia is defined as a core temperature less than 36°C. It commonly occurs during and after surgical procedures lasting more than 2 h because of impairment

of thermoregulation by anaesthesia, combined with exposure to a cold environment (the operating room).^{22,23} Unintended hypothermia is considered to be an adverse event of general and regional anaesthesia and might be associated with increased cardiac complications, blood loss due to impaired coagulation, impaired wound healing, decreased drug metabolism, decreased immune function, and an increased risk of SSI.^{22,24–27} We did a systematic review to assess the effectiveness of perioperative body warming on the prevention of SSIs.

We found two RCTs^{28,29} comparing the effect of preoperative and intraoperative body warming on SSIs in adults with no body warming. Meta-analysis showed that body warming was significantly associated with a reduced risk of SSIs (OR 0.33; 95% CI 0.17–0.62); the quality of the evidence was rated as moderate. However, in developing

	Key research question	Recommendations for prevention of SSIs	Strength of recommendation (quality of evidence retrieved†)	Notes for implementation in low-income and middle-income countries
	(Continued from previous page)			
(9)	Incisional wound irrigation with antibiotics Does intraoperative wound irrigation with antibiotics reduce the risk of SSI?	Antibiotic incisional wound irrigation before closure should not be used	Conditional recommendation (low)	This recommendation leads to a cost reduction because of reduced antibiotic use; it also contributes to preventing antimicrobial resistance
(10)	Prophylactic negative-pressure wound therapy Does prophylactic negative-pressure wound therapy reduce the incidence of SSI compared with the use of conventional dressings?	Prophylactic negative-pressure wound therapy on primarily closed surgical incisions is suggested in high-risk wounds, while taking resources into account	Conditional recommendation (low)	Prophylactic negative-pressure wound therapy device availability is low and is an additional cost for the health-care facility or patients (also because it can prolong hospital stay); however, evidence of cost-effectiveness in gynaecological patients has been shown; could construct a non-portable, locally made device at low cost
(11)	Antimicrobial-coated sutures Are antimicrobial-coated sutures effective to prevent SSI; if yes, when should they be used?	Triclosan-coated sutures are suggested to be used in all types of surgery	Conditional recommendation (moderate)	Antimicrobial-coated suture availability is low and they are an additional cost for the health-care facility or patient
(12)	Laminar airflow ventilation systems in the context of operating room ventilation Is the use of laminar airflow in the operating room associated with the reduction of overall or deep SSI; does the use of fans or cooling devices increase incidence of SSI; is natural ventilation an acceptable alternative?¶	Laminar airflow ventilation systems should not be used for patients undergoing total arthroplasty surgery	Conditional recommendation (low to very low)	In particular for the construction of future health-care facilities, this recommendation will reduce costs
(13)	Antimicrobial prophylaxis in the presence of a drain In the presence of drains, does prolonged antibiotic prophylaxis prevent SSI?	Perioperative surgical antibiotic prophylaxis should not be continued because of the presence of a wound drain for the purpose of preventing SSI	Conditional recommendation (low)	This recommendation leads to a cost reduction because of reduced antibiotic use; it also contributes to preventing antimicrobial resistance
(14)	Optimal timing for wound drain removal When using drains, how long should they be kept in place to minimise SSI as a complication?	The wound drain should be removed when clinically indicated; no evidence was found to make a recommendation on the optimal exact timing	Conditional recommendation (very low)	This recommendation has the potential to reduce costs because of a shortened hospital stay as a result of early drain removal
(15)	Wound dressings In surgical patients, should advanced dressings vs standard sterile wound dressings be used for the prevention of SSI?	No type of advanced dressing should be used over a standard dressing on primarily closed surgical wounds	Conditional recommendation (low)	This recommendation avoids inappropriate resource allocation, because advanced dressings are expensive and poorly available in low-income and middle-income countries
(16)	Surgical antibiotic prophylaxis prolongation Does continued postoperative surgical antibiotic prophylaxis reduce the risk of SSI compared with preoperative and (if necessary) intraoperative prophylaxis only?	Surgical antibiotic prophylaxis administration should not be prolonged after completion of the operation	Strong recommendation (moderate)	This recommendation leads to a cost reduction because of reduced antibiotic use; it also contributes to preventing antimicrobial resistance

SSI=surgical site infection. *WHO recommendations for preoperative measures are included in paper 1¹ of this surgical site infections Series, to be read in combination with this Review. †The Grading of Recommendations Assessment, Development, and Evaluation method^{2,3} was used to assess the quality of the retrieved evidence. ‡We could not assess separately the use of sterile disposable non-woven vs sterile reusable woven drapes and sterile disposable non-woven vs sterile reusable woven gowns, because no specific evidence was retrieved. §We could not assess saline irrigation of incisional wounds before closure, because insufficient evidence was found. ¶We could not assess the use of fans or cooling devices vs conventional operating room ventilation, or whether natural ventilation an acceptable alternative to conventional ventilation, because insufficient evidence was retrieved.

Table: Summary of the WHO recommendations for intraoperative and postoperative measures to prevent SSIs*

countries, the equipment and maintenance costs of electrical body-warming equipment represent a substantial financial burden, and availability and procurement are additional issues. Blankets can be considered as a low-cost, effective option in low-resource settings.

Recommendation 3: use of intensive protocols for perioperative blood glucose control

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

A rise in blood glucose concentration is commonly observed in the operative and postoperative periods

because of a surgical stress response, resulting in increased secretion of catabolic hormones (eg, catecholamines or cortisol), inhibition of insulin secretion, and insulin resistance.³⁰ Observational studies have shown that hyperglycaemia is associated with an increased risk of SSIs in both diabetic and non-diabetic patients.^{31–33} Although the importance of perioperative blood glucose control is agreed upon, there is controversy regarding the best treatment options, the optimal target concentration of blood glucose, and the optimal timing of glucose control. The concern is due to the risk of developing hypoglycaemia, which is also associated with increased morbidity and mortality.^{34–37} We did a systematic review to investigate whether the

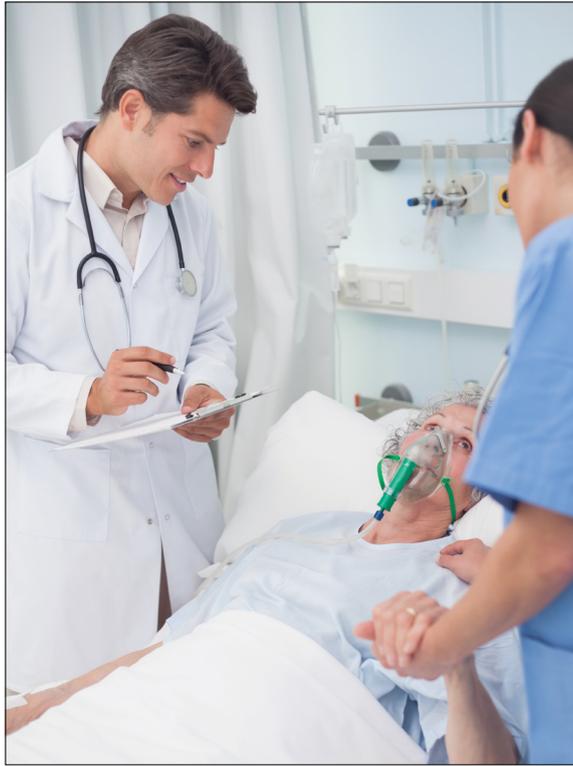


Figure: Patient receiving oxygen in the immediate postoperative period
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use of intensive protocols for perioperative blood glucose control is more effective in reducing the risk of SSI in both diabetic and non-diabetic patients than conventional protocols with less stringent target blood glucose concentrations.

We identified 15 RCTs^{38–52} in adults. Overall, an intensive protocol with strict blood glucose target concentrations was associated with significantly decreased SSI incidence compared with a conventional protocol (OR 0.43; 95% CI 0.29–0.64). Because of the heterogeneity of the timing of application of the protocols (intraoperative *vs* intraoperative-and-postoperative *vs* postoperative), study population (patients with diabetes *vs* patients without diabetes *vs* mixed population), and the upper limit of the target concentration of blood glucose (≤ 110 mg/dL [6.1 mmol/L] *vs* 110–150 mg/dL [6.1–8.3 mmol/L]), we decided to do separate meta-analyses for each of these comparisons. No significant difference in the effect on SSI reduction was observed between studies of patients with and without diabetes in meta-regression analyses ($p=0.590$). There was some evidence that the SSI reduction effect was smaller in studies that used intensive blood glucose control intraoperatively only (OR 0.88; 0.45–1.74) compared with studies that used intensive blood glucose controls postoperatively or both intraoperatively and postoperatively (OR 0.37; 0.25–0.55; $p=0.049$ for difference between these ORs).

No significant difference was observed ($p=0.328$) between studies that used low upper limit target blood glucose concentrations (≤ 110 mg/dL; 6.1 mmol/L), versus studies with high upper limit concentrations (110–150 mg/dL; 6.1–8.3 mmol/L). The overall quality of the evidence was rated as low. Further analysis of adverse events showed no difference between the use of an intensive protocol and a conventional protocol in the risk of death (OR 0.74; 95% CI 0.45–1.23; $p=0.2$) or stroke (OR 1.37; 0.26–7.20; $p=0.7$). However, there was an overall increased risk of hypoglycaemia (OR 5.55; 2.58–11.96). Meta-regression analyses showed no difference in the risk of hypoglycaemia between studies that used low or high upper limit target blood glucose concentrations ($p=0.413$).

In conclusion, using a protocol with strict blood glucose target concentrations is associated with a substantial benefit for the reduction of SSI prevalence, but neither the optimal blood glucose target concentration nor the perioperative timing of glucose control could be defined. However, it should be noted that hypoglycaemia is a possible serious side-effect associated with these intensive protocols and close reliable monitoring of blood glucose concentrations is crucial for this intervention.

Recommendation 4: maintenance of adequate circulating volume control (normovolaemia)

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

Adequate intravascular volume is an essential component of tissue perfusion and an important aspect of tissue oxygenation.⁵³ In unbalanced fluid states—ie, hypovolaemia and hypervolaemia—tissue oxygenation is compromised and might increase the risk of SSI.⁵⁴ The optimal type of fluid (colloid or crystalloid) or strategy of fluid management (goal-directed, liberal, or restrictive) remain controversial topics, partly because of the absence of a universal definition of normovolaemia or a standardised method for its assessment. We did a systematic review to assess whether specific fluid management strategies for the maintenance of normovolaemia are more effective in reducing the risk of SSI than standard fluid regimens administered during surgery.

We identified 24 RCTs^{55–78} comparing specific strategies of fluid management with standard management. Because of substantial heterogeneity in the type of specific fluid management strategy used, separate meta-analyses were done for GDFT or restrictive fluid regimens versus standard regimens in the preoperative, intraoperative, and postoperative periods. GDFT refers to a haemodynamic treatment based on the titration of fluid and inotropic drugs according to cardiac output or similar parameters. Restrictive fluid management refers to the administration of a regimen with a reduced volume

of fluids in the bolus or over time, compared with local standard fluid maintenance. A meta-analysis of 14 RCTs⁵⁵⁻⁶⁸ showed that intraoperative GDFT was significantly associated with lower incidence of SSIs than standard intraoperative fluid management (OR 0.56; 95% CI 0.35–0.88). Meta-analysis of five RCTs⁶⁹⁻⁷³ showed that restrictive intraoperative fluid management did not significantly affect SSI incidence compared with standard intraoperative management (OR 0.73; 0.41–1.28). Meta-analysis of two RCTs^{76,77} showed that postoperative GDFT was associated with a decreased risk of SSI compared with standard postoperative management (OR 0.24; 0.11–0.52). One RCT⁷⁴ showed that preoperative GDFT did not significantly affect SSI incidence compared with standard preoperative management (OR 0.47; 0.13–1.72).

Considering the evidence (rated as low quality), the panel suggested the use of GDFT intraoperatively to prevent SSI. Its postoperative use might also be beneficial to reduce SSI. However, restrictive fluid management and preoperative GDFT were not associated with the reduction of SSI compared with standard fluid management.

Recommendations 5 and 6: drapes and gowns

The panel suggests that either sterile disposable non-woven or sterile reusable woven drapes and surgical gowns be used during surgical operations for the purpose of preventing SSI (conditional recommendation, moderate to very low quality of evidence); and suggests that plastic adhesive incise drapes with or without antimicrobial properties should not be used (conditional recommendation, low to very low quality of evidence).

Drapes and gowns are available for single-use or multiple-use, with varying compositions. Adhesive plastic incise drapes are used on a patient's skin after surgical site preparation, with or without antimicrobial impregnation, and the surgeon performs the incision of the drape and the skin simultaneously. In available guidelines, there are conflicting recommendations on the use of plastic adhesive drapes, mainly discouraging their use.⁷⁹ There are no recommendations on the use of single-use or reusable drapes and gowns for the purpose of SSI prevention. We did a systematic review to investigate the use of sterile disposable or reusable drapes and surgical gowns, and separately the use of plastic adhesive incise drapes, for the purpose of SSI prevention.

We identified 11 studies⁸⁰⁻⁹⁰ (four RCTs^{81,86,89,90}). Meta-analysis of five studies (one RCT,⁸¹ one quasi-RCT,⁸² and three observational studies^{80,83,84}) comparing sterile disposable non-woven drapes and gowns with sterile reusable woven drapes and gowns showed no difference in the SSI risk (RCTs, moderate quality evidence: OR 0.85; 95% CI 0.66–1.09; observational studies, very low quality evidence: OR 1.56; 0.89–2.72). Meta-analysis of four studies (one RCT,⁸⁶ one quasi-RCT,⁸⁵ and two observational studies^{87,88}) comparing adhesive iodine-impregnated incise

drapes with no drapes showed no difference in the SSI risk (RCTs: OR 2.62; 0.68–10.04; observational studies: OR 0.49; 0.16–1.49). Similarly, meta-analysis of two RCTs^{89,90} comparing non-impregnated adhesive incise drapes to no drapes showed no difference in the SSI risk (OR 1.10; 0.68–1.78). The quality of the evidence was rated low to very low.

Considering the evidence, including potential issues of availability and costs in low-resource settings and the ecological effect, the expert panel suggested that either sterile disposable non-woven or sterile reusable woven drapes and gowns can be used. However, adhesive incise drapes (with or without antimicrobial properties) should not be used for the purpose of preventing SSI.

Recommendation 7: wound-protector devices

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

Wound-protector devices (or wound-edge protectors) are comprised of a non-adhesive plastic sheath attached to a single or double rubber ring that firmly secures the sheath to the wound edges. They facilitate the retraction of the incision during surgery and are aimed at reducing wound-edge contamination to a minimum during abdominal surgical procedures. Notably, they have been on the market despite scarce evidence supporting their usefulness. We did a systematic review to assess the effectiveness of wound-protector devices for the reduction of SSI risk compared with conventional wound protection in abdominal surgery.

We found 11 studies (ten RCTs,⁹¹⁻¹⁰⁰ and one prospective controlled trial¹⁰¹) in adults. Meta-analysis showed that the use of a wound-protector device (single-ring or double-ring) was associated with a significantly lower risk of SSI than with conventional wound protection (OR 0.42; 95% CI 0.28–0.62). Meta-regression analyses showed no evidence of a difference in the effect between single-ring and double-ring wound-protector devices or between clean-contaminated, contaminated, or dirty surgery and other surgery.

Considering the evidence (rated as very low quality), the panel suggests the use of wound-protector devices in clean-contaminated, contaminated, and dirty abdominal surgical procedures for the prevention of SSI. The panel highlighted that wound-protector device use should not always be prioritised in low-resource settings over other interventions that prevent SSI, because of their scarce availability and associated costs.

Recommendations 8 and 9: incisional wound irrigation

The panel suggests considering the use of irrigation of the incisional wound with an aqueous povidone-iodine solution before closure for the purpose of preventing SSI, particularly

in clean and clean-contaminated wounds (conditional recommendation, low quality of evidence); but the panel suggests that antibiotic incisional wound irrigation before closure should not be done (conditional recommendation, low quality of evidence); insufficient evidence was available to recommend for or against saline irrigation of incisional wounds before closure for the purpose of preventing SSIs.

Intraoperative wound irrigation refers to the flow of a solution across the surface of an open wound. It is a widely practised procedure and considered to help prevent SSIs.^{102–104} Among other benefits, wound irrigation is intended to physically remove cellular debris, surface bacteria, and body fluids, to dilute possible contamination, and to function as a local antibacterial agent when an antiseptic or antibiotic agent is used. Practices vary depending on the patient population, the surface of application, and solutions used. We did a systematic review to investigate whether intraoperative wound irrigation (with or without active agents or pressured application) affects the incidence of SSI. Studies investigating the topical application of antibiotics or antiseptics (eg, powder, gels, sponges) were not included. We also excluded studies in which surgical antibiotic prophylaxis was not administered appropriately (ie, preoperatively and intravenous) or wound irrigation represented a therapeutic intervention for a pre-existent infection rather than a prophylactic measure.

We identified 21 RCTs^{105–125} comparing wound irrigation with no wound irrigation in patients undergoing various surgical procedures, and the results were substantially heterogeneous. The panel decided to restrict the recommendation to incisional wound irrigation, because too little (and heterogeneous) evidence was available to address other applications of irrigation—ie, intraperitoneal or mediastinal irrigation.

Moderate to very low quality evidence from four studies using irrigation with a saline solution administered with different methods provided conflicting results.^{110,113,115,117} Irrigation with saline solution using pulse pressure or applied with force had a marked benefit in terms of SSI reduction.^{110,115,117} A meta-analysis of seven RCTs^{105–108} showed a significant benefit of irrigation of the incisional wound with aqueous povidone-iodine solutions in different concentrations compared with irrigation with a saline solution (OR 0·31; 95% CI 0·13–0·73; $p=0\cdot007$). Further stratification according to the wound contamination class and povidone-iodine solution showed that the effect was attributable to incisional wound irrigation in clean and clean-contaminated procedures with povidone-iodine 10% and povidone-iodine 0·35%. A meta-analysis of five studies^{119–121,123,124} showed no significant difference between antibiotic irrigation of the incisional wound and no irrigation or irrigation with a saline solution (OR 1·16; 0·64–2·12; $p=0\cdot63$).

The panel concluded that the evidence was insufficient to recommend for or against saline irrigation of incisional wounds for the purpose of preventing SSIs.

By contrast, incisional wound irrigation with an aqueous povidone-iodine solution might have a benefit, particularly in clean and clean-contaminated wounds. Finally, antibiotic incisional wound irrigation before closure should not be used for the purpose of preventing SSI. The expert panel strongly emphasised that this practice is associated with an unnecessary risk of antimicrobial resistance.

Allergic reactions and metabolic adverse events should be considered as potential harms of iodine uptake. Although the panel recognises that saline and povidone-iodine solutions are readily available in most settings, sterile products might be scarce in low-income and middle-income countries. In many settings, the availability and costs of pulse-pressure devices represent a high financial burden, including not only their purchase, but also waste disposal, procurement, energy, and machine maintenance.

Recommendation 10: prophylactic negative-pressure wound therapy

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

pNPWT consists of a closed sealed system connected to a vacuum pump, which maintains negative pressure on the wound surface. Although used for several other purposes since the late 1990s, it is also applied on primarily closed surgical incisions to prevent SSIs. We did a systematic review to establish whether the use of pNPWT is more effective in reducing the risk of SSIs than the use of conventional wound dressings.

We identified 19 publications describing 20 studies (six RCTs^{126–130} and 14 observational studies^{131–144}). Overall, meta-analyses of RCTs and observational studies showed that pNPWT has a significant benefit in reducing the risk of SSI in patients with a primarily closed surgical incision compared with conventional postoperative wound dressings (RCTs: OR 0·56; 95% CI 0·32–0·96; observational studies: OR 0·30; 0·22–0·42). When stratified by type of surgery, this effect was observed in abdominal (nine observational studies;^{132–136,140,141,143,144} OR 0·31; 0·19–0·49) and cardiac (two observational studies;^{137,138} OR 0·29; 0·12–0·69) surgery, but it was not statistically significant in orthopaedic or trauma surgery. Stratification by wound contamination class showed a significant benefit in reducing SSI prevalence with the use of pNPWT in clean surgery (eight observational studies;^{131,135,137–139,141,142,144} OR 0·27; 95% CI 0·17–0·42) and in clean-contaminated surgery (eight observational studies;^{132–134,136,140,141,143,144} OR 0·29; 0·17–0·50).

On the basis of the low-quality evidence available, the panel suggests the use of pNPWT on primarily closed surgical incisions in high-risk conditions (eg, poor tissue perfusion due to surrounding soft tissue or skin

damage, decreased blood flow, bleeding or haematoma, dead space, or intraoperative contamination) for the purpose of the prevention of SSIs, taking available resources into account. The panel highlighted that the use of pNPWT might not be prioritised in low-resource settings compared with other interventions to prevent SSI considering its poor availability and potential associated costs.

Recommendation 11: antimicrobial-coated sutures

The panel suggests the use of triclosan-coated sutures to reduce the risk of SSIs, independent of the type of surgery (conditional recommendation, moderate quality of evidence).

Sutures with antimicrobial properties were developed with the aim to prevent microbial colonisation of the suture material in operative incisions. Early studies showed a reduction of the number of bacteria in vitro and wound infections in animals^{145–147} using triclosan-coated sutures and this effect was subsequently confirmed in clinical studies. Several novel antimicrobial coatings are now available, but still no clinical studies have been done that compare the efficacy with non-coated sutures.^{148,149} We did a systematic review to assess whether the use of antimicrobial-coated sutures is more effective in reducing the risk of SSIs than the use of non-coated sutures.

We found 18 studies (13 RCTs^{150–162} and five cohort studies^{163–167}). All studies investigated triclosan-coated sutures and focused on adult patients, apart from one¹⁵² done in a paediatric population. The overall meta-analysis showed that antimicrobial-coated sutures have a significant benefit in reducing SSI incidence in patients undergoing surgical procedures compared with non-coated sutures (RCTs: OR 0.72; 95% CI 0.59–0.88; observational studies: OR 0.58; 0.40–0.83). When considering specific types of sutures, only the meta-analyses of the studies comparing triclosan-coated polyglactin 910 suture with polyglactin 910 suture featuring a braided suture construction showed that the use of antimicrobial-coated sutures significantly reduces SSI prevalence compared with the non-coated sutures (OR 0.62; 0.44–0.88 for RCTs; OR 0.58; 0.37–0.92 for observational studies). In meta-regression analysis, we found no evidence that the effect of antimicrobial coating of sutures differed between braided and monofilament sutures ($p=0.380$), or between clean ($p=0.690$), cardiac ($p=0.900$), or abdominal ($p=0.832$) surgeries and other surgical procedures.

We highlighted that the quality of the evidence was moderate to low and that many studies had several limitations, including industry sponsorship or conflicts of interest with a commercial entity. On the basis of the evidence but also considering these limitations, the panel suggests the use of antimicrobial-coated sutures for the purpose of reducing the risk of SSI. Because the effect appears to be independent of the type of

procedure or wound contamination classification, this recommendation applies to any type of surgery. Availability and costs should be considered in low-income and middle-income countries. Further studies are needed also on sutures coated with an alternative antimicrobial agent to triclosan.

Recommendation 12: 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 SSIs for patients undergoing total arthroplasty surgery (conditional recommendation, low to very low quality of evidence).

Conventional ventilation systems pass air with a mixed or turbulent flow into the operating room. These systems aim to homogenise the fresh air, the air, and aerosols and particles within the room. Laminar airflow systems pass the fresh air unidirectionally with a steady velocity and approximately parallel streamlines to create a zone in which the air, aerosols, and particles within the room are driven out. Systems with laminar airflow are frequently used in an environment where contamination with particles is a serious adverse event—eg, orthopaedic implant surgery. However, laminar airflow systems are complex and expensive and require careful maintenance. In many settings in low-income countries, neither conventional nor laminar flow systems are affordable or maintained effectively on a regular basis and often, natural ventilation is the only option.

We did a systematic review to assess whether a laminar airflow ventilation system is more effective in reducing the risk of SSI than a conventional ventilation system. We also investigated whether fans or cooling devices and natural ventilation are acceptable alternatives to conventional ventilation for the prevention of SSI. We only identified one observational study¹⁶⁸ that compared natural ventilation with conventional ventilation in the operating room. No difference was observed in the risk of SSI following both total hip and knee arthroplasty. One systematic review¹⁶⁹ and eight observational studies^{168,170–176} comparing laminar airflow with conventional ventilation were identified. Most studies focused on total hip and knee arthroplasty and only a few single studies were available for other types of surgery.^{170,171,173} Meta-analyses showed that laminar airflow ventilation has no benefit compared with conventional ventilation in reducing the SSI incidence in total hip (OR 1.29; 95% CI 0.98–1.71) or knee (OR 1.08; 0.77–1.52) arthroplasty. The quality of the evidence was rated as very low. Considering these results and associated costs, the expert panel decided to suggest that laminar airflow ventilation systems should not be used as a preventive measure to reduce the risk of SSI in patients undergoing total arthroplasty surgery.

Recommendations 13 and 14: antimicrobial prophylaxis in the presence of a drain and optimal timing for wound drain removal

The panel suggests not continuing perioperative antibiotic prophylaxis because of the presence of a wound drain (conditional recommendation, low quality of evidence). They also suggest removing the wound drain when clinically indicated, but they found no evidence to recommend an optimal time for wound drain removal (conditional recommendation, very low quality of evidence).

Drainage tubes are widely used in surgery to remove any fluid or blood that collects in the wounds and cavities created by the surgical procedure and thus might cause complications. However, drains might adversely affect surgical outcomes—eg, affecting anastomotic healing by causing infection in the anastomotic area and the abdominal wound. Many systematic reviews investigating the effect of drains on the related infection risk compared with no wound drainage have been published with conflicting results. The optimal time for drain removal after surgery might influence this risk, but it remains unknown. Furthermore, in most cases, antibiotic prophylaxis is continued postoperatively when a drain is used, but this practice is not evidence-based and raises serious concerns in terms of contributing to the emergence of antimicrobial resistance. We did a systematic review to investigate whether prolonged antibiotic prophylaxis in the presence of a wound drain is more effective in reducing the risk of SSIs than standard perioperative prophylaxis alone. The review also assessed whether the early removal of wound drains more effectively prevents SSIs than late removal.

Regarding the first question, seven RCTs^{177–183} were identified. The meta-analysis showed that prolonged antibiotic prophylaxis in the presence of a wound drain has no benefit in reducing SSI compared with perioperative prophylaxis alone (OR 0.79; 95% CI 0.53–1.20). We identified 11 RCTs^{184–194} comparing early with late removal of closed wound drains. However, there was heterogeneity in the study definitions for early and late drain removal. For the purposes of the analysis, early removal was considered to be from postoperative day 1 to day 5. Two main groups were identified for defining late wound drain removal—ie, drain removal at postoperative day 6 or later (three studies^{187,189,192}) and removal on the basis of drainage volume (six studies^{184–187,188,190,191}). Studies not falling into these categories were excluded from the analysis. The meta-analysis showed that early drain removal does not affect SSI incidence compared with late removal (OR 0.86; 0.49–1.50).

On the basis of this low to very low quality evidence, the panel suggests that antibiotic prophylaxis should not be continued in the presence of a wound drain for the purpose of preventing SSI. Given the results and very low quality of the evidence about optimal timing for removal, wound drains should be removed when clinically indicated.

Recommendation 15: wound 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 SSIs (conditional recommendation, low quality of evidence).

A wide variety of wound dressings are available. Advanced dressings are mainly hydrocolloid, hydrogels, fibrous hydrocolloid, or polyurethane matrix hydrocolloid dressings and vapour-permeable films. A Cochrane review¹⁹⁵ and its update¹⁹⁶ on the effect of dressings for the prevention of SSI found no evidence to suggest that one dressing type was better than any other. We did a systematic review to assess whether the use of advanced dressings is more effective in reducing the risk of SSIs than standard wound dressings.

We identified ten RCTs^{197–206} in adult patients undergoing various types of surgical procedures. There were variations in the definition of SSIs, the duration of postoperative follow-up, and in the type of dressing (hydrocolloid, hydroactive and silver-impregnated, or polyhexamethylene biguanide-impregnated dressings). Overall, the meta-analysis showed that advanced dressings do not significantly reduce SSI occurrence compared with standard dressings (OR 0.80; 95% CI 0.52–1.23); the quality of the evidence was rated as low. In specific meta-analyses, hydrocolloid, silver-impregnated, and hydroactive dressings were non-effective in reducing the risk of SSI compared with standard dressings. On the basis of the evidence, the panel recommended that advanced dressings should not be used for the prevention of SSIs.

Recommendation 16: postoperative surgical antibiotic prophylaxis prolongation

The panel recommends against the prolongation of surgical antibiotic prophylaxis (SAP) administration after completion of the operation for the purpose of preventing SSIs (strong recommendation, moderate quality of evidence).

The preventive effect of the routine use of SAP has long been recognised; however, the necessary duration of SAP to achieve the desired effect has been a matter of debate. Most guidelines recommend a maximum postoperative SAP duration of 24 h, but increasing evidence shows that using only a single preoperative dose (and possible additional intraoperative doses according to the duration of the operation) might be non-inferior. Despite this, surgeons still often routinely continue SAP up to several days after surgery, which leads to serious concerns for the risk of antimicrobial resistance. We did a systematic review to investigate whether prolonged SAP in the postoperative period is more effective in reducing the risk of SSIs than perioperative prophylaxis (defined as a single dose before incision and possible intraoperative additional dose[s] according to the duration of the operation).

We found 69 RCTs^{177–180,183,207–270} investigating the optimal duration of antibiotic prophylaxis in a variety of surgical

procedures. The overall meta-analysis, which pooled studies using any prolonged SAP regimens, showed no benefit in terms of reducing the SSI incidence compared with a single dose of antibiotic prophylaxis (OR 0.89; 95% CI 0.77–1.03). However, a meta-analysis of studies showed that SAP continuation might be beneficial in reducing SSI compared with a single prophylactic dose in cardiac (OR 0.43; 0.25–0.76)^{232,233} and orthognathic (OR 0.30; 0.10–0.88)^{242–244} surgery. Considering the low quality of the evidence and the results of the overall meta-analysis (moderate quality), the expert panel decided to strongly recommend against SAP prolongation, also because of the widespread risk of antimicrobial resistance. Continuing antibiotic administration in cardiac and orthognathic surgery has potential benefit, but further well designed RCTs on this topic are needed.

Conclusion

We discuss the evidence for a broad range of intraoperative and postoperative preventive measures identified by an expert panel as potentially contributing to reducing the risk of SSI. For some of these, the evidence shows no benefit and the panel advises against the adoption of these interventions, particularly when considering resource implications or other consequences, such as antimicrobial resistance. However, the panel identified a range of key measures for SSI prevention to be implemented in the intraoperative and postoperative periods, together with other preoperative measures discussed in paper 1 of this Series. Adoption of the recommendations should be facilitated by sound implementation strategies and practical tools. Notably, careful assessment of feasibility and cost implications in low-resource settings is needed.

Contributors

BA led the writing of and BZ, PB, NZK, SdJ, MA, DP, and JSS contributed to the manuscript. All authors contributed to the development of the WHO Global Guidelines for the Prevention of Surgical Site Infection. BZ, PB, NZK, SdJ, FdV, SMG, SG, EDW, XW, MAB, EPD, ME, PG, XG, JR, and JSS contributed to the performance and interpretation of some systematic reviews and meta-analyses.

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For the full WHO Guidelines for the Prevention of Surgical Site Infection see <http://www.who.int/gpsc/ssi-guidelines/en/index.html>

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