Surgical site infections 2

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

Benedetta Allegranzi, Bassim Zayed, Peter Bischoff, N Zeynep Kubilay, Stijn de Jonge, Fleur de Vries, Stacey M Gomes, Sarah Gans, Elon D Wallert, Xiuwen Wu, Mohamed Abbas, Marja A Boermeester, E Patchen Dellinger, Matthias Egger, Petra Gastmeier, Xavier Guirao, Jianan Ren, Didier Pittet, Joseph S Solomkin, and the WHO Guidelines Development Group

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.

Lancet Infect Dis 2016

Published Online November 2, 2016 http://dx.doi.org/10.1016/S1473-3099(16)30402-9

See Online/Series http://dx.doi.org/10.1016/S1473-3099(16)30398-X

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

Members of the WHO Guidelines Development Group are listed at the end of the paper

Infection Prevention and Control Global Unit, Service Delivery and Safety, WHO, Geneva, Switzerland (B Allegranzi MD, N Z Kubilay MD, B Zayed MD); **Institute of Hygiene and Environmental Medicine, Charité-University Medicine, Berlin, Germany** (P Bischoff MD, Prof P Gastmeier MD); **Department of Surgery, Academic Medical Center Amsterdam, Amsterdam, Netherlands** (S de Jonge MD, F de Vries MD, S Gans MD, E D Wallert BSc, Prof M A Boermeester MD); **OASIS Global, Cincinnati, OH, USA** (S Gomes MS, Prof J S Solomkin MD); **Jinling Hospital, Medical School of Nanjing University, Nanjing, Jiangsu, China** (X Wu MD, Prof J Ren MD); **Infection Control Programme, University of Geneva Hospitals and Faculty of Medicine, Geneva, Switzerland** (M Abbas MD, Prof D Pittet MD); **Department of Surgery, University of Washington, Seattle, WA, USA** (Prof E P Dellinger MD); **Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland** (Prof M Egger MD); **Parc Taulí Hospital Universitari, Barcelona, Spain** (X Guirao MD);

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 (FiO_2) 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% FiO_2) provides more adequate oxygenation at the surgical incision—particularly at infected tissue,[4] which has a lower oxygen tension than non-infected tissue[5]—and might enhance oxidative killing by neutrophils.[6] We did a systematic review to assess the effect of high FiO_2 (80%) compared with standard FiO_2 (30–35%) for the prevention of SSI.

We identified 15 randomised controlled trials (RCTs)[7–21] comparing the perioperative administration of 80% FiO_2 with 30–35% FiO_2 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 FiO_2) 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 FiO_2 is beneficial in reducing SSI compared with standard perioperative FiO_2 (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% FiO_2 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

	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)

WHO Collaborating Centre on Patient Safety (Infection Control and Improving Practices), University of Geneva Hospitals and Faculty of Medicine, Geneva, Switzerland (Prof D Pittet); **and University of Cincinnati College of Medicine, Cincinnati, OH, USA** (Prof J S Solomkin)

Correspondence to: Dr Benedetta Allegranzi, Infection Prevention and Control Global Unit, Service Delivery and Safety, WHO, 1211 Geneva 27, Switzerland **allegranzib@who.int**

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 1[1] 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

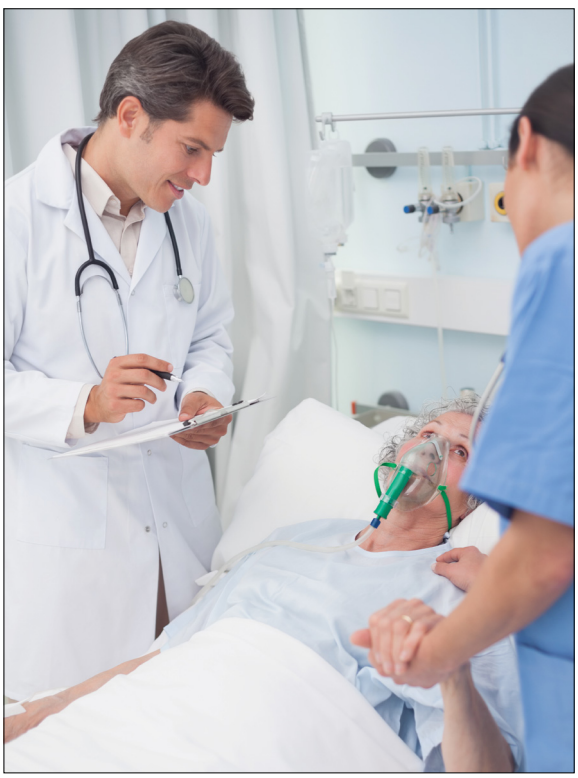

Figure: **Patient receiving oxygen in the immediate postoperative period**
Courtesy of Shutterstock.

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 RCTs[55–68] 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 RCTs[69–73] 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 RCT[74] 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 studies[80–90] (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 trial[101]) 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=0·007). 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=0·63).

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 one[152] 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 study[168] 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 review[169] 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 review[195] and its update[196] 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 polyhexamethalene 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.

WHO Guidelines Development Group

Hanan H Balky (King Saud bin Abdulaziz University for Health Sciences, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia); Marja A Boermeester (Academic Medical Center Amsterdam, Amsterdam, Netherlands); Nizam Damani (Southern Health and Social Service Trust, Portadown, UK); E Patchen Dellinger (University of Washington, Seattle, WA, USA); Mazen S Ferwana (King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia); Petra Gastmeier (Charité-University Medicine Berlin, Berlin, Germany); Xavier Guirao (Parc Taulí Hospital Universitari, Barcelona, Spain); Nordiah Jalil (Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia); Robinah Kaitiritimba (Uganda National Health Consumers' Organization, Kampala, Uganda); Regina Kamoga (Community Health and Information Network, Kampala, Uganda); Claire Kilpatrick (Imperial College London CIPM, S3 Global, London, UK); Shaheen Mehtar (Stellenbosch University, Stellenbosch, South Africa; Infection Control Africa Network, Cape Town, South Africa); Babacar Ndoye (Infection Control Africa Network Board, Dakar, Senegal); Peter Nthumba (AIC Kijabe Hospital, Kijabe, Kenya; University of Bern, Bern, Switzerland; London School of Hygiene & Tropical Medicine, London, UK); Leonardo Pagani (Bolzano Central Hospital, Bolzano, Italy; Annecy-Genevois Hospital Centre, Annecy, France); Didier Pittet (University of Geneva Hospitals, Geneva, Switzerland); Jianan Ren (Nanjing University, Nanjing, China); Joseph S Solomkin (University of Cincinnati College of Medicine and OASIS Global, Cincinnati, OH, USA); Akeau Unahalekhaka (Chiang Mai University, Chiang Mai, Thailand); Andreas F Widmer (Basel University, Basel, Switzerland).

Declaration of interests

MA received grants and non-financial support from the Innovative Medicines Initiative Joint Undertaking under the Combatting Bacterial Resistance in Europe (COMBACTE-Net) grant agreement (no. 115523). These resources are composed of financial contributions from the European Union's 7th Framework Programme (FP7/2007–2013) and the European Federation of Pharmaceutical Industries and Associations companies' in-kind contribution during the study. MAB has previously received a research grant from Johnson & Johnson, and also grants or honoraria for delivering lectures on surgical site infection or serving on scientific advisory boards for Abbott/Mylan, Acelity, Bard, Baxter, GlaxoSmithKline, Ipsen, and Johnson & Johnson. EPD received honoraria from WHO during the study and previously received personal fees from Merck, Baxter, Ortho-McNeil, Targanta, Schering-Plough, Astellas, Allergan, Care Fusion, Durata, Pfizer, Applied Medical, Rib-X, Affinium, Tetraphase, Televancin, R-Pharm, Cubist, 3M, and Melinta, and grants from Motif, and other from Microdermis. ME received personal fees from WHO during the study. XG previously received personal fees from MSD, Pfizer, AstraZeneca, and Novartis. All other authors declare no competing interests.

Acknowledgments

This article should be read in combination with the first paper in this Series on the new WHO recommendations on preoperative measures to be implemented for the prevention of SSI. These papers are an abbreviated version of the full WHO Global Guidelines for the Prevention of Surgical Site Infection, which was published simultaneously on Nov 3, 2016. The development of the guidelines was supervised by a WHO steering committee and we thank the following members: Sergey Eremin, Edward Kelley, Walter Johnson, and Valeska Stempliuk. We thank the following experts who served on the Systematic Reviews Expert Group: Jasper Atema, Nizam Damani, Miranda van Rijen, Jan Kluytmans, Sandra Pequeño, and Caroline Landelle. We are grateful to the following experts who served as external peer reviewers of the draft guideline documents: Emmanuel Ameh, Kamal Itani, Fernando Otaíza, Val Robertson, and Ilker Uçkay. We also thank Rosemary Sudan for editing assistance, and Tomas Allen and Jose Luis Garnica Carreno who provided assistance for the systematic review searches. Funding for the development of these guidelines was mainly provided by WHO; the Swiss Government and OASIS Global (Cincinnati, OH, USA) also provided essential financial support. The systematic reviews done by the external expert teams were done free of charge as in-kind contributions by the following institutions: Amphia Hospital Breda (Breda, Netherlands); Academic Medical Center Amsterdam (Amsterdam, Netherlands); University of Berlin (Berlin, Germany); University of Cincinnati (Cincinnati, OH, USA); Hospital Universitari Parc Tauli, Sabadell (Barcelona, Spain); Jinling Hospital and the Medical School of Nanjing University (Nanjing, China).

References

1 Allegranzi B, Bischoff P, de Jonge S, et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis* 2016; published online Nov 2. http://dx.doi.org/10.1016/S1473-3099(16)30398-X.

2 Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 2011; **64:** 401–06.

3 Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011; **64:** 383–94.

4 Hopf HW, Hunt TK, Rosen N. Supplemental oxygen and risk of surgical site infection. *JAMA* 2004; **291:** 1956.

5 Hays RC, Mandell GL. PO2, pH, and redox potential of experimental abscesses. *Proc Soc Exp Biol Med* 1974; **147:** 29–30.

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

6 Allen DB, Maguire JJ, Mahdavian M, et al. Wound hypoxia and acidosis limit neutrophil bacterial killing mechanisms. *Arch Surg* 1997; **132:** 991–96.

7 Meyhoff CS, Wetterslev J, Jorgensen LN, et al. Effect of high perioperative oxygen fraction on surgical site infection and pulmonary complications after abdominal surgery: the PROXI randomized clinical trial. *JAMA* 2009; **302:** 1543–50.

8 Myles PS, Leslie K, Chan MT, et al. Avoidance of nitrous oxide for patients undergoing major surgery: a randomized controlled trial. *Anesthesiology* 2007; **107:** 221–31.

9 Belda FJ, Aguilera L, García de la Asunción J, et al. Supplemental perioperative oxygen and the risk of surgical wound infection: a randomized controlled trial. *JAMA* 2005; **294:** 2035–42.

10 Bickel A, Gurevits M, Vamos R, Ivry S, Eitan A. Perioperative hyperoxygenation and wound site infection following surgery for acute appendicitis: a randomized, prospective, controlled trial. *Arch Surg* 2011; **146:** 464–70.

11 Greif R, Akça O, Horn EP, Kurz A, Sessler DI, and the Outcomes Research Group. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. *N Engl J Med* 2000; **342:** 161–67.

12 Mayzler O, Weksler N, Domchik S, Klein M, Mizrahi S, Gurman GM. Does supplemental perioperative oxygen administration reduce the incidence of wound infection in elective colorectal surgery? *Minerva Anestesiol* 2005; **71:** 21–25.

13 Pryor KO, Fahey TJ 3rd, Lien CA, Goldstein PA. Surgical site infection and the routine use of perioperative hyperoxia in a general surgical population: a randomized controlled trial. *JAMA* 2004; **291:** 79–87.

14 Schietroma M, Cecilia EM, Carlei F, et al. Prevention of anastomotic leakage after total gastrectomy with perioperative supplemental oxygen administration: a prospective randomized, double-blind, controlled, single-center trial. *Ann Surg Oncol* 2013; **20:** 1584–90.

15 Schietroma M, Cecilia EM, Sista F, Carlei F, Pessia B, Amicucci G. High-concentration supplemental perioperative oxygen and surgical site infection following elective colorectal surgery for rectal cancer: a prospective, randomized, double-blind, controlled, single-site trial. *Am J Surg* 2014; **208:** 719–26.

16 Stall A, Paryavi E, Gupta R, Zadnik M, Hui E, O'Toole RV. Perioperative supplemental oxygen to reduce surgical site infection after open fixation of high-risk fractures: a randomized controlled pilot trial. *J Trauma Acute Care Surg* 2013; **75:** 657–63.

17 Thibon P, Borgey F, Boutreux S, Hanouz JL, Le Coutour X, Parienti JJ. Effect of perioperative oxygen supplementation on 30-day surgical site infection rate in abdominal, gynecologic, and breast surgery: the ISO2 randomized controlled trial. *Anesthesiology* 2012; **117:** 504–11.

18 Duggal N, Poddatoori V, Noroozkhani S, Siddik-Ahmad RI, Caughey AB. Perioperative oxygen supplementation and surgical site infection after cesarean delivery: a randomized trial. *Obstet Gynecol* 2013; **122:** 79–84.

19 Gardella C, Goltra LB, Laschansky E, et al. High-concentration supplemental perioperative oxygen to reduce the incidence of postcesarean surgical site infection: a randomized controlled trial. *Obstet Gynecol* 2008; **112:** 545–52.

20 Scifres CM, Leighton BL, Fogertey PJ, Macones GA, Stamilio DM. Supplemental oxygen for the prevention of postcesarean infectious morbidity: a randomized controlled trial. *Am J Obstet Gynecol* 2011; **205:** 267. e1–9.

21 Williams NL, Glover MM, Crisp C, Acton AL, Mckenna DS. Randomized controlled trial of the effect of 30% versus 80% fraction of inspired oxygen on cesarean delivery surgical site infection. *Am J Perinatol* 2013; **30:** 781–86.

22 Sessler DI. Mild perioperative hypothermia. *N Engl J Med* 1997; **336:** 1730–37.

23 Díaz M, Becker DE. Thermoregulation: physiological and clinical considerations during sedation and general anesthesia. *Anesth Prog* 2010; **57:** 25–32.

24 Sessler DI, Rubinstein EH, Moayeri A. Physiologic responses to mild perianesthetic hypothermia in humans. *Anesthesiology* 1991; **75:** 594–610.

25 Rajagopalan S, Mascha E, Na J, Sessler DI. The effects of mild perioperative hypothermia on blood loss and transfusion requirement. *Anesthesiology* 2008; **108:** 71–77.

26 Leslie K, Sessler DI, Bjorksten AR, Moayeri A. Mild hypothermia alters propofol pharmacokinetics and increases the duration of action of atracurium. *Anesth Analg* 1995; **80:** 1007–14.

27 Frank SM, Cattaneo CG, Wieneke-Brady MB, et al. Threshold for adrenomedullary activation and increased cardiac work during mild core hypothermia. *Clin Sci (Lond)* 2002; **102:** 119–25.

28 Kurz A, Sessler DI, Lenhardt R, and the Study of Wound Infection and Temperature Group. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. *N Engl J Med* 1996; **334:** 1209–15.

29 Melling AC, Ali B, Scott EM, Leaper DJ. Effects of preoperative warming on the incidence of wound infection after clean surgery: a randomised controlled trial. *Lancet* 2001; **358:** 876–80.

30 McAnulty GR, Robertshaw HJ, Hall GM. Anaesthetic management of patients with diabetes mellitus. *Br J Anaesth* 2000; **85:** 80–90.

31 Ata A, Lee J, Bestle SL, Desemone J, Stain SC. Postoperative hyperglycemia and surgical site infection in general surgery patients. *Arch Surg* 2010; **145:** 858–64.

32 Kao LS, Phatak UR. Glycemic control and prevention of surgical site infection. *Surg Infect (Larchmt)* 2013; **14:** 437–44.

33 Kotagal M, Symons RG, Hirsch IB, et al. Perioperative hyperglycemia and risk of adverse events among patients with and without diabetes. *Ann Surg* 2015; **261:** 97–103.

34 Blondet JJ, Beilman GJ. Glycemic control and prevention of perioperative infection. *Curr Opin Crit Care* 2007; **13:** 421–27.

35 Buchleitner AM, Martínez-Alonso M, Hernández M, Solà I, Mauricio D. Perioperative glycaemic control for diabetic patients undergoing surgery. *Cochrane Database Syst Rev* 2012; **9:** CD007315.

36 Griesdale DE, de Souza RJ, van Dam RM, et al. Intensive insulin therapy and mortality among critically ill patients: a meta-analysis including NICE-SUGAR study data. *CMAJ* 2009; **180:** 821–27.

37 Kao LS, Meeks D, Moyer VA, Lally KP. Peri-operative glycaemic control regimens for preventing surgical site infections in adults. *Cochrane Database Syst Rev* 2009; **(3):** CD006806.

38 Emam IA, Allan A, Eskander K, et al. Our experience of controlling diabetes in the peri-operative period of patients who underwent cardiac surgery. *Diabetes Res Clin Pract* 2010; **88:** 242–46.

39 Kirdemir P, Yildirim V, Kiris I, et al. Does continuous insulin therapy reduce postoperative supraventricular tachycardia incidence after coronary artery bypass operations in diabetic patients? *J Cardiothorac Vasc Anesth* 2008; **22:** 383–87.

40 Yuan J, Liu T, Zhang X, et al. Intensive versus conventional glycemic control in patients with diabetes during enteral nutrition after gastrectomy. *J Gastrointest Surg* 2015; **19:** 1553–58.

41 Albacker T, Carvalho G, Schricker T, Lachapelle K. High-dose insulin therapy attenuates systemic inflammatory response in coronary artery bypass grafting patients. *Ann Thorac Surg* 2008; **86:** 20–27.

42 Cao SG, Ren JA, Shen B, Chen D, Zhou YB, Li JS. Intensive versus conventional insulin therapy in type 2 diabetes patients undergoing D2 gastrectomy for gastric cancer: a randomized controlled trial. *World J Surg* 2011; **35:** 85–92.

43 Lazar HL, McDonnell MM, Chipkin S, Fitzgerald C, Bliss C, Cabral H. Effects of aggressive versus moderate glycemic control on clinical outcomes in diabetic coronary artery bypass graft patients. *Ann Surg* 2011; **254:** 458–63, discussion 463–64.

44 Abdelmalak BB, Bonilla A, Mascha EJ, et al. Dexamethasone, light anaesthesia, and tight glucose control (DeLiT) randomized controlled trial. *Br J Anaesth* 2013; **111:** 209–21.

45 Bilotta F, Spinelli A, Giovannini F, Doronzio A, Delfini R, Rosa G. The effect of intensive insulin therapy on infection rate, vasospasm, neurologic outcome, and mortality in neurointensive care unit after intracranial aneurysm clipping in patients with acute subarachnoid hemorrhage: a randomized prospective pilot trial. *J Neurosurg Anesthesiol* 2007; **19:** 156–60.

46 Chan RP, Galas FR, Hajjar LA, Bello CN, Piccioni MA, Auler JO Jr. Intensive perioperative glucose control does not improve outcomes of patients submitted to open-heart surgery: a randomized controlled trial. *Clinics (Sao Paulo)* 2009; **64:** 51–60.

47 Desai SP, Henry LL, Holmes SD, et al. Strict versus liberal target range for perioperative glucose in patients undergoing coronary artery bypass grafting: a prospective randomized controlled trial. *J Thorac Cardiovasc Surg* 2012; **143:** 318–25.

48 Gandhi GY, Nuttall GA, Abel MD, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery: a randomized trial. *Ann Intern Med* 2007; **146:** 233–43.

49 Grey NJ, Perdrizet GA. Reduction of nosocomial infections in the surgical intensive-care unit by strict glycemic control. *Endocr Pract* 2004; **10** (suppl 2)**:** 46–52.

50 Okabayashi T, Shima Y, Sumiyoshi T, et al. Intensive versus intermediate glucose control in surgical intensive care unit patients. *Diabetes Care* 2014; **37:** 1516–24.

51 Cao S, Zhou Y, Chen D, et al. Intensive versus conventional insulin therapy in nondiabetic patients receiving parenteral nutrition after D2 gastrectomy for gastric cancer: a randomized controlled trial. *J Gastrointest Surg* 2011; **15:** 1961–68.

52 Zheng R, Gu C, Wang Y, et al. Impacts of intensive insulin therapy in patients undergoing heart valve replacement. *Heart Surg Forum* 2010; **13:** E292–98.

53 Kreimeier U. Pathophysiology of fluid imbalance. *Crit Care* 2000; **4** (suppl 2)**:** S3–7.

54 Silva JM Jr, de Oliveira AM, Nogueira FA, et al. The effect of excess fluid balance on the mortality rate of surgical patients: a multicenter prospective study. *Crit Care* 2013; **17:** R288.

55 Forget P, Lois F, de Kock M. Goal-directed fluid management based on the pulse oximeter-derived pleth variability index reduces lactate levels and improves fluid management. *Anesth Analg* 2010; **111:** 910–14.

56 Gan TJ, Soppitt A, Maroof M, et al. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. *Anesthesiology* 2002; **97:** 820–26.

57 Harten J, Crozier JE, McCreath B, et al. Effect of intraoperative fluid optimisation on renal function in patients undergoing emergency abdominal surgery: a randomised controlled pilot study (ISRCTN 11799696). *Int J Surg* 2008; **6:** 197–204.

58 Mayer J, Boldt J, Mengistu AM, Röhm KD, Suttner S. Goal-directed intraoperative therapy based on autocalibrated arterial pressure waveform analysis reduces hospital stay in high-risk surgical patients: a randomized, controlled trial. *Crit Care* 2010; **14:** R18.

59 Mythen MG, Webb AR. Perioperative plasma volume expansion reduces the incidence of gut mucosal hypoperfusion during cardiac surgery. *Arch Surg* 1995; **130:** 423–29.

60 Pillai P, McEleavy I, Gaughan M, et al. A double-blind randomized controlled clinical trial to assess the effect of Doppler optimized intraoperative fluid management on outcome following radical cystectomy. *J Urol* 2011; **186:** 2201–06.

61 Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. *N Engl J Med* 2003; **348:** 5–14.

62 Scheeren TW, Wiesenack C, Gerlach H, Marx G. Goal-directed intraoperative fluid therapy guided by stroke volume and its variation in high-risk surgical patients: a prospective randomized multicentre study. *J Clin Monit Comput* 2013; **27:** 225–33.

63 Senagore AJ, Emery T, Luchtefeld M, Kim D, Dujovny N, Hoedema R. Fluid management for laparoscopic colectomy: a prospective, randomized assessment of goal-directed administration of balanced salt solution or hetastarch coupled with an enhanced recovery program. *Dis Colon Rectum* 2009; **52:** 1935–40.

64 Smetkin AA, Kirov MY, Kuzkov VV, et al. Single transpulmonary thermodilution and continuous monitoring of central venous oxygen saturation during off-pump coronary surgery. *Acta Anaesthesiol Scand* 2009; **53:** 505–14.

65 Venn R, Steele A, Richardson P, Poloniecki J, Grounds M, Newman P. Randomized controlled trial to investigate influence of the fluid challenge on duration of hospital stay and perioperative morbidity in patients with hip fractures. *Br J Anaesth* 2002; **88:** 65–71.

66 Wakeling HG, McFall MR, Jenkins CS, et al. Intraoperative oesophageal Doppler guided fluid management shortens postoperative hospital stay after major bowel surgery. *Br J Anaesth* 2005; **95:** 634–42.

67 Benes J, Chytra I, Altmann P, et al. Intraoperative fluid optimization using stroke volume variation in high risk surgical patients: results of prospective randomized study. *Crit Care* 2010; **14:** R118.

68 Lopes MR, Oliveira MA, Pereira VO, Lemos IP, Auler JO Jr, Michard F. Goal-directed fluid management based on pulse pressure variation monitoring during high-risk surgery: a pilot randomized controlled trial. *Crit Care* 2007; **11:** R100.

69 Brandstrup B, Tønnesen H, Beier-Holgersen R, et al. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial. *Ann Surg* 2003; **238:** 641–48.

70 Holte K, Foss NB, Andersen J, et al. Liberal or restrictive fluid administration in fast-track colonic surgery: a randomized, double-blind study. *Br J Anaesth* 2007; **99:** 500–08.

71 Kabon B, Akça O, Taguchi A, et al. Supplemental intravenous crystalloid administration does not reduce the risk of surgical wound infection. *Anesth Analg* 2005; **101:** 1546–53.

72 Lobo DN, Bostock KA, Neal KR, Perkins AC, Rowlands BJ, Allison SP. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. *Lancet* 2002; **359:** 1812–18.

73 Nisanevich V, Felsenstein I, Almogy G, Weissman C, Einav S, Matot I. Effect of intraoperative fluid management on outcome after intraabdominal surgery. *Anesthesiology* 2005; **103:** 25–32.

74 Wilson J, Woods I, Fawcett J, et al. Reducing the risk of major elective surgery: randomised controlled trial of preoperative optimisation of oxygen delivery. *BMJ* 1999; **318:** 1099–103.

75 Boyd O, Grounds RM, Bennett ED. A randomized clinical trial of the effect of deliberate perioperative increase of oxygen delivery on mortality in high-risk surgical patients. *JAMA* 1993; **270:** 2699–707.

76 McKendry M, McGloin H, Saberi D, Caudwell L, Brady AR, Singer M. Randomised controlled trial assessing the impact of a nurse delivered, flow monitored protocol for optimisation of circulatory status after cardiac surgery. *BMJ* 2004; **329:** 258.

77 Pearse R, Dawson D, Fawcett J, Rhodes A, Grounds RM, Bennett ED. Early goal-directed therapy after major surgery reduces complications and duration of hospital stay. A randomised, controlled trial [ISRCTN38797445]. *Crit Care* 2005; **9:** R687–93.

78 Vermeulen H, Hofland J, Legemate DA, Ubbink DT. Intravenous fluid restriction after major abdominal surgery: a randomized blinded clinical trial. *Trials* 2009; **10:** 50.

79 National Institute for Health and Care Excellence (NICE). Surgical site infections: prevention and treatment. 2008. http://www.nice.org.uk/nicemedia/pdf/CG74NICEGuideline.pdf (accessed June 16, 2016).

80 Castro Ferrer MJ, Maseda Alvarez MM, Rodríguez García JI. Comparison of sterile, disposable surgical drapes. *Enferm Clin* 2004; **14:** 3–6.

81 Bellchambers J, Harris JM, Cullinan P, Gaya H, Pepper JR. A prospective study of wound infection in coronary artery surgery. *Eur J Cardiothorac Surg* 1999; **15:** 45–50.

82 Belkin NL. Are "barrier" drapes cost effective? *Todays Surg Nurse* 1998; **20:** 18–23.

83 Gallagher MM, Santini L, Magliano G, et al. Feasibility and safety of a simplified draping method for pacing procedures. *Europace* 2007; **9:** 890–93.

84 Treggiari M, Benevento A, Caronno R, Dionigi R. The evaluation of the efficacy of drapes and gowns of nonwoven fabric versus drapes and gowns of cotton in reducing the incidence of postoperative wound infections. *Minerva Chir* 1992; **47:** 49–54 (in Italian).

85 Al-Qahtani SM, Al-Amoudi HM, Al-Jehani S, et al. Post-appendectomy surgical site infection rate after using an antimicrobial film incise drape: a prospective study. *Surg Infect (Larchmt)* 2015; **16:** 155–58.

86 Segal CG, Anderson JJ. Preoperative skin preparation of cardiac patients. *AORN J* 2002; **76:** 821–28.

87 Swenson BR, Camp TR, Mulloy DP, Sawyer RG. Antimicrobial-impregnated surgical incise drapes in the prevention of mesh infection after ventral hernia repair. *Surg Infect (Larchmt)* 2008; **9:** 23–32.

88 Yoshimura Y, Kubo S, Hirohashi K, et al. Plastic iodophor drape during liver surgery operative use of the iodophor-impregnated adhesive drape to prevent wound infection during high risk surgery. *World J Surg* 2003; **27:** 685–88.

89 Chiu KY, Lau SK, Fung B, Ng KH, Chow SP. Plastic adhesive drapes and wound infection after hip fracture surgery. *Aust N Z J Surg* 1993; **63:** 798–801.

90 Ward HR, Jennings OG, Potgieter P, Lombard CJ. Do plastic adhesive drapes prevent post caesarean wound infection? *J Hosp Infect* 2001; **47:** 230–34.

91 Baier P, Kiesel M, Kayser C, Fischer A, Hopt UT, Utzolino S. Ring drape do not protect against surgical site infections in colorectal surgery: a randomised controlled study. *Int J Colorectal Dis* 2012; **27:** 1223–28.

92 Mihaljevic AL, Schirren R, Özer M, et al. Multicenter double-blinded randomized controlled trial of standard abdominal wound edge protection with surgical dressings versus coverage with a sterile circular polyethylene drape for prevention of surgical site infections: a CHIR-Net trial (BaFO; NCT01181206). *Ann Surg* 2014; **260:** 730–37.

93 Pinkney TD, Calvert M, Bartlett DC, et al, and the West Midlands Research Collaborative, and the ROSSINI Trial Investigators. Impact of wound edge protection devices on surgical site infection after laparotomy: multicentre randomised controlled trial (ROSSINI Trial). *BMJ* 2013; **347:** f4305.

94 Redmond HP, Meagher PJ, Kelly CJ, Deasy JM. Use of an impervious wound-edge protector to reduce the postoperative wound infection rate. *Br J Surg* 1994; **1811:** 81.

95 Sookhai S, Redmond HP, Deasy JM. Impervious wound-edge protector to reduce postoperative wound infection: a randomised, controlled trial. *Lancet* 1999; **353:** 1585.

96 Cheng KP, Roslani AC, Sehha N, et al. ALEXIS O-Ring wound retractor vs conventional wound protection for the prevention of surgical site infections in colorectal resections(1). *Colorectal Dis* 2012; **14:** e346–51.

97 Horiuchi T, Tanishima H, Tamagawa K, et al. Randomized, controlled investigation of the anti-infective properties of the Alexis retractor/protector of incision sites. *J Trauma* 2007; **62:** 212–15.

98 Lee P, Waxman K, Taylor B, Yim S. Use of wound-protection system and postoperative wound-infection rates in open appendectomy: A randomized prospective trial. *Arch Surg* 2009; **144:** 872–75.

99 Reid K, Pockney P, Draganic B, Smith SR. Barrier wound protection decreases surgical site infection in open elective colorectal surgery: a randomized clinical trial. *Dis Colon Rectum* 2010; **53:** 1374–80.

100 Theodoridis TD, Chatzigeorgiou KN, Zepiridis L, et al. A prospective randomized study for evaluation of wound retractors in the prevention of incision site infections after cesarean section. *Clin Exp Obstet Gynecol* 2011; **38:** 57–59.

101 Brunet P, Bounoua F, Bugnon PY, Gautier-Benoit C. Intérêt des champs à anneau en chirurgie abdominale. *Lyon Chir* 1994; **90:** 438–41.

102 Whiteside OJ, Tytherleigh MG, Thrush S, Farouk R, Galland RB. Intra-operative peritoneal lavage—who does it and why? *Ann R Coll Surg Engl* 2005; **87:** 255–58.

103 Diana M, Hübner M, Eisenring MC, Zanetti G, Troillet N, Demartines N. Measures to prevent surgical site infections: what surgeons (should) do. *World J Surg* 2011; **35:** 280–88.

104 Pivot D, Tiv M, Luu M, Astruc K, Aho S, Fournel I. Survey of intraoperative povidone-iodine application to prevent surgical site infection in a French region. *J Hosp Infect* 2011; **77:** 363–64.

105 Sindelar WF, Mason GR. Irrigation of subcutaneous tissue with povidone-iodine solution for prevention of surgical wound infections. *Surg Gynecol Obstet* 1979; **148:** 227–31.

106 Rogers DM, Blouin GS, O'Leary JP. Povidone-iodine wound irrigation and wound sepsis. *Surg Gynecol Obstet* 1983; **157:** 426–30.

107 Sindelar WF, Brower ST, Merkel AB, Takesue EI. Randomised trial of intraperitoneal irrigation with low molecular weight povidone-iodine solution to reduce intra-abdominal infectious complications. *J Hosp Infect* 1985; **6** (suppl A): 103–14.

108 Lau WY, Fan ST, Chu KW, Yip WC, Chong KK, Wong KK. Combined topical povidone-iodine and systemic antibiotics in postappendicectomy wound sepsis. *Br J Surg* 1986; **73:** 958–60.

109 Baker DM, Jones JA, Nguyen-Van-Tam JS, et al. Taurolidine peritoneal lavage as prophylaxis against infection after elective colorectal surgery. *Br J Surg* 1994; **81:** 1054–56.

110 Cervantes-Sánchez CR, Gutiérrez-Vega R, Vázquez-Carpizo JA, Clark P, Athié-Gutiérrez C. Syringe pressure irrigation of subdermic tissue after appendectomy to decrease the incidence of postoperative wound infection. *World J Surg* 2000; **24:** 38–41, discussion 41–42.

111 Ko W, Lazenby WD, Zelano JA, Isom OW, Krieger KH. Effects of shaving methods and intraoperative irrigation on suppurative mediastinitis after bypass operations. *Ann Thorac Surg* 1992; **53:** 301–05.

112 Cheng MT, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH. Efficacy of dilute betadine solution irrigation in the prevention of postoperative infection of spinal surgery. *Spine* 2005; **30:** 1689–93.

113 Al-Ramahi M, Bata M, Sumreen I, Amr M. Saline irrigation and wound infection in abdominal gynecologic surgery. *Int J Gynaecol Obstet* 2006; **94:** 33–36.

114 Chang FY, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH. Can povidone-iodine solution be used safely in a spinal surgery? *Eur Spine J* 2006; **15:** 1005–14.

115 Hargrove R, Ridgeway S, Russell R, Norris M, Packham I, Levy B. Does pulse lavage reduce hip hemiarthroplasty infection rates? *J Hosp Infect* 2006; **62:** 446–49.

116 Kokavec M, Fristáková M. Efficacy of antiseptics in the prevention of post-operative infections of the proximal femur, hip and pelvis regions in orthopedic pediatric patients. Analysis of the first results. *Acta Chir Orthop Traumatol Cech* 2008; **75:** 106–09 (in Slovak).

117 Nikfarjam M, Weinberg L, Fink MA, et al. Pressurized pulse irrigation with saline reduces surgical-site infections following major hepatobiliary and pancreatic surgery: randomized controlled trial. *World J Surg* 2014; **38:** 447–55.

118 Tanaka K, Matsuo K, Kawaguchi D, et al. Randomized clinical trial of peritoneal lavage for preventing surgical site infection in elective liver surgery. *J Hepatobiliary Pancreat Sci* 2015; **22:** 446–53.

119 Pitt HA, Postier RG, MacGowan AW, et al. Prophylactic antibiotics in vascular surgery. Topical, systemic, or both? *Ann Surg* 1980; **192:** 356–64.

120 Freischlag J, McGrattan M, Busuttil RW. Topical versus systemic cephalosporin administration in elective biliary operations. *Surgery* 1984; **96:** 686–93.

121 Juul P, Merrild U, Kronborg O. Topical ampicillin in addition to a systemic antibiotic prophylaxis in elective colorectal surgery. A prospective randomized study. *Dis Colon Rectum* 1985; **28:** 804–06.

122 Silverman SH, Ambrose NS, Youngs DJ, Shepherd AF, Roberts AP, Keighley MR. The effect of peritoneal lavage with tetracycline solution on postoperative infection. A prospective, randomized, clinical trial. *Dis Colon Rectum* 1986; **29:** 165–69.

123 Moesgaard F, Nielsen ML, Hjortrup A, et al. Intraincisional antibiotic in addition to systemic antibiotic treatment fails to reduce wound infection rates in contaminated abdominal surgery. A controlled clinical trial. *Dis Colon Rectum* 1989; **32:** 36–38.

124 Ruiz-Tovar J, Cansado P, Perez-Soler M, et al. Effect of gentamicin lavage of the axillary surgical bed after lymph node dissection on drainage discharge volume. *Breast* 2013; **22:** 874–78.

125 Ruiz-Tovar J, Santos J, Arroyo A, et al. Effect of peritoneal lavage with clindamycin-gentamicin solution on infections after elective colorectal cancer surgery. *J Am Coll Surg* 2012; **214:** 202–07.

126 Gillespie BM, Rickard CM, Thalib L, et al. Use of negative-pressure wound dressings to prevent surgical site complications after primary hip arthroplasty: a pilot RCT. *Surg Innov* 2015; **22:** 488–95.

127 Howell RD, Hadley S, Strauss E, Pelham FR. Blister formation with negative pressure dressings after total knee arthroplasty. *Curr Orthop Pract* 2011; **22:** 176–79.

128 Masden D, Goldstein J, Endara M, Xu K, Steinberg J, Attinger C. Negative pressure wound therapy for at-risk surgical closures in patients with multiple comorbidities: a prospective randomized controlled study. *Ann Surg* 2012; **255:** 1043–47.

129 Stannard JP, Robinson JT, Anderson ER, McGwin G Jr, Volgas DA, Alonso JE. Negative pressure wound therapy to treat hematomas and surgical incisions following high-energy trauma. *J Trauma* 2006; **60:** 1301–06.

130 Stannard JP, Volgas DA, McGwin G 3rd, et al. Incisional negative pressure wound therapy after high-risk lower extremity fractures. *J Orthop Trauma* 2012; **26:** 37–42.

131 Adogwa O, Fatemi P, Perez E, et al. Negative pressure wound therapy reduces incidence of postoperative wound infection and dehiscence after long-segment thoracolumbar spinal fusion: a single institutional experience. *Spine J* 2014; **14:** 2911–17.

132 Blackham AU, Farrah JP, McCoy TP, Schmidt BS, Shen P. Prevention of surgical site infections in high-risk patients with laparotomy incisions using negative-pressure therapy. *Am J Surg* 2013; **205:** 647–54.

133 Bonds AM, Novick TK, Dietert JB, Araghizadeh FY, Olson CH. Incisional negative pressure wound therapy significantly reduces surgical site infection in open colorectal surgery. *Dis Colon Rectum* 2013; **56:** 1403–08.

134 Chadi SA, Kidane B, Britto K, Brackstone M, Ott MC. Incisional negative pressure wound therapy decreases the frequency of postoperative perineal surgical site infections: a cohort study. *Dis Colon Rectum* 2014; **57:** 999–1006.

135 Condé-Green A, Chung TL, Holton LH 3rd, et al. Incisional negative-pressure wound therapy versus conventional dressings following abdominal wall reconstruction: a comparative study. *Ann Plast Surg* 2013; **71:** 394–97.

136 Gassman A, Mehta A, Bucholdz E, et al. Positive outcomes with negative pressure therapy over primarily closed large abdominal wall reconstruction reduces surgical site infection rates. *Hernia* 2015; **19:** 273–78.

137 Grauhan O, Navasardyan A, Hofmann M, Müller P, Stein J, Hetzer R. Prevention of poststernotomy wound infections in obese patients by negative pressure wound therapy. *J Thorac Cardiovasc Surg* 2013; **145:** 1387–92.

138 Grauhan O, Navasardyan A, Tutkun B, et al. Effect of surgical incision management on wound infections in a poststernotomy patient population. *Int Wound J* 2014; **11** (suppl 1)**:** 6–9.

139 Matatov T, Reddy KN, Doucet LD, Zhao CX, Zhang WW. Experience with a new negative pressure incision management system in prevention of groin wound infection in vascular surgery patients. *J Vasc Surg* 2013; **57:** 791–95.

140 Pauli EM, Krpata DM, Novitsky YW, Rosen MJ. Negative pressure therapy for high-risk abdominal wall reconstruction incisions. *Surg Infect (Larchmt)* 2013; **14:** 270–74.

141 Pellino G, Sciaudone G, Candilio G, et al. Preventive NPWT over closed incisions in general surgery: does age matter? *Int J Surg* 2014; **12** (suppl 2)**:** S64–68.

142 Reddix RN Jr, Leng XI, Woodall J, Jackson B, Dedmond B, Webb LX. The effect of incisional negative pressure therapy on wound complications after acetabular fracture surgery. *J Surg Orthop Adv* 2010; **19:** 91–97.

143 Selvaggi F, Pellino G, Sciaudone G, et al. New advances in negative pressure wound therapy (NPWT) for surgical wounds of patients affected with Crohn's disease. *Surg Technol Int* 2014; **24:** 83–89.

144 Soares KC, Baltodano PA, Hicks CW, et al. Novel wound management system reduction of surgical site morbidity after ventral hernia repairs: a critical analysis. *Am J Surg* 2015; **209:** 324–32.

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

146 Rothenburger S, Spangler D, Bhende S, Burkley D. In vitro antimicrobial evaluation of Coated VICRYL* Plus Antibacterial Suture (coated polyglactin 910 with triclosan) using zone of inhibition assays. *Surg Infect (Larchmt)* 2002; **3** (suppl 1)**:** S79–87.

147 Storch ML, Rothenburger SJ, Jacinto G. Experimental efficacy study of coated VICRYL plus antibacterial suture in guinea pigs challenged with *Staphylococcus aureus*. *Surg Infect (Larchmt)* 2004; **5:** 281–88.

148 Matl FD, Zlotnyk J, Obermeier A, et al. New anti-infective coatings of surgical sutures based on a combination of antiseptics and fatty acids. *J Biomater Sci Polym Ed* 2009; **20:** 1439–49.

149 Obermeier A, Schneider J, Wehner S, et al. Novel high efficient coatings for anti-microbial surgical sutures using chlorhexidine in fatty acid slow-release carrier systems. *PLoS One* 2014; **9:** e101426.

150 Baracs J, Huszár O, Sajjadi SG, Horváth OP. 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. *Surg Infect (Larchmt)* 2011; **12:** 483–89.

151 Diener MK, Knebel P, Kieser M, et al. Effectiveness of triclosan-coated PDS Plus versus uncoated PDS II sutures for prevention of surgical site infection after abdominal wall closure: the randomised controlled PROUD trial. *Lancet* 2014; **384:** 142–52.

152 Ford HR, Jones P, Gaines B, Reblock K, Simpkins DL. Intraoperative handling and wound healing: controlled clinical trial comparing coated VICRYL plus antibacterial suture (coated polyglactin 910 suture with triclosan) with coated VICRYL suture (coated polyglactin 910 suture). *Surg Infect (Larchmt)* 2005; **6:** 313–21.

153 Galal I, El-Hindawy K. Impact of using triclosan-antibacterial sutures on incidence of surgical site infection. *Am J Surg* 2011; **202:** 133–38.

154 Isik I, Selimen D, Senay S, Alhan C. Efficiency of antibacterial suture material in cardiac surgery: a double-blind randomized prospective study. *Heart Surg Forum* 2012; **15:** E40–45.

155 Justinger C, Slotta JE, Ningel S, Gräber S, Kollmar O, Schilling MK. Surgical-site infection after abdominal wall closure with triclosan-impregnated polydioxanone sutures: results of a randomized clinical pathway facilitated trial (NCT00998907). *Surgery* 2013; **154:** 589–95.

156 Mingmalairak C, Ungbhakorn P, Paocharoen V. Efficacy of antimicrobial coating suture coated polyglactin 910 with tricosan (Vicryl plus) compared with polyglactin 910 (Vicryl) in reduced surgical site infection of appendicitis, double blind randomized control trial, preliminary safety report. *J Med Assoc Thai* 2009; **92:** 770–75.

157 Nakamura T, Kashimura N, Noji T, et al. Triclosan-coated sutures reduce the incidence of wound infections and the costs after colorectal surgery: a randomized controlled trial. *Surgery* 2013; **153:** 576–83.

158 Rasić Z, Schwarz D, Adam VN, et al. Efficacy of antimicrobial triclosan-coated polyglactin 910 (Vicryl* Plus) suture for closure of the abdominal wall after colorectal surgery. *Coll Antropol* 2011; **35:** 439–43.

159 Seim BE, Tønnessen T, Woldbaek PR. Triclosan-coated sutures do not reduce leg wound infections after coronary artery bypass grafting. *Interact Cardiovasc Thorac Surg* 2012; **15:** 411–15.

160 Thimour-Bergström L, Roman-Emanuel C, Scherstén H, Friberg Ö, Gudbjartsson T, Jeppsson A. Triclosan-coated sutures reduce surgical site infection after open vein harvesting in coronary artery bypass grafting patients: a randomized controlled trial. *Eur J Cardiothorac Surg* 2013; **44:** 931–38.

161 Turtiainen J, Saimanen EI, Mäkinen KT, et al. Effect of triclosan-coated sutures on the incidence of surgical wound infection after lower limb revascularization surgery: a randomized controlled trial. *World J Surg* 2012; **36:** 2528–34.

162 Williams N, Sweetland H, Goyal S, Ivins N, Leaper DJ. Randomized trial of antimicrobial-coated sutures to prevent surgical site infection after breast cancer surgery. *Surg Infect (Larchmt)* 2011; **12:** 469–74.

163 Chen SY, Chen TM, Dai NT, et al. Do antibacterial-coated sutures reduce wound infection in head and neck cancer reconstruction? *Eur J Surg Oncol* 2011; **37:** 300–04.

164 Hoshino S, Yoshida Y, Tanimura S, Yamauchi Y, Noritomi T, Yamashita Y. A study of the efficacy of antibacterial sutures for surgical site infection: a retrospective controlled trial. *Int Surg* 2013; **98:** 129–32.

165 Laas E, Poilroux C, Bézu C, et al. Antibacterial-coated suture in reducing surgical site infection in breast surgery: a prospective study. *Int J Breast Cancer* 2012; **2012:** 819578.

166 Okada N, Nakamura T, Ambo Y, et al. Triclosan-coated abdominal closure sutures reduce the incidence of surgical site infections after pancreaticoduodenectomy. *Surg Infect (Larchmt)* 2014; **15:** 305–09.

167 Ueno M, Saito W, Yamagata M, et al. Triclosan-coated sutures reduce wound infections after spinal surgery: a retrospective, nonrandomized, clinical study. *Spine J* 2015; **15:** 933–38.

168 Song KH, Kim ES, Kim YK, et al. Differences in the risk factors for surgical site infection between total hip arthroplasty and total knee arthroplasty in the Korean Nosocomial Infections Surveillance System (KONIS). *Infect Control Hosp Epidemiol* 2012; **33:** 1086–93.

169 Gastmeier P, Breier AC, Brandt C. Influence of laminar airflow on prosthetic joint infections: a systematic review. *J Hosp Infect* 2012; **81:** 73–78.

170 Bosanquet DC, Jones CN, Gill N, Jarvis P, Lewis MH. Laminar flow reduces cases of surgical site infections in vascular patients. *Ann R Coll Surg Engl* 2013; **95:** 15–19.

171 Brandt C, Hott U, Sohr D, Daschner F, Gastmeier P, Rüden H. Operating room ventilation with laminar airflow shows no protective effect on the surgical site infection rate in orthopedic and abdominal surgery. *Ann Surg* 2008; **248:** 695–700.

172 Dale H, Hallan G, Hallan G, Espehaug B, Havelin LI, Engesaeter LB. Increasing risk of revision due to deep infection after hip arthroplasty. *Acta Orthop* 2009; **80:** 639–45.

173 Jeong SJ, Ann HW, Kim JK, et al. Incidence and risk factors for surgical site infection after gastric surgery: a multicenter prospective cohort study. *Infect Chemother* 2013; **45:** 422–30.

174 Namba RS, Inacio MC, Paxton EW. Risk factors associated with surgical site infection in 30,491 primary total hip replacements. *J Bone Joint Surg Br* 2012; **94:** 1330–38.

175 Namba RS, Inacio MC, Paxton EW. Risk factors associated with deep surgical site infections after primary total knee arthroplasty: an analysis of 56,216 knees. *J Bone Joint Surg Am* 2013; **95:** 775–82.

176 Pedersen AB, Svendsson JE, Johnsen SP, Riis A, Overgaard S. Risk factors for revision due to infection after primary total hip arthroplasty. A population-based study of 80,756 primary procedures in the Danish Hip Arthroplasty Registry. *Acta Orthop* 2010; **81:** 542–47.

177 Becker A, Koltun L, Sayfan J. Impact of antimicrobial prophylaxis duration on wound infection in mesh repair of incisional hernia—preliminary results of a prospective randomized trial. *Eur Surg* 2008; **40:** 37–40.

178 Hall JC, Christiansen KJ, Goodman M, et al. Duration of antimicrobial prophylaxis in vascular surgery. *Am J Surg* 1998; **175:** 87–90.

179 Mohri Y, Tonouchi H, Kobayashi M, Nakai K, Kusunoki M, and the Mie Surgical Infection Research Group. Randomized clinical trial of single- versus multiple-dose antimicrobial prophylaxis in gastric cancer surgery. *Br J Surg* 2007; **94:** 683–88.

180 Orlando G, Manzia TM, Sorge R, et al. One-shot versus multidose perioperative antibiotic prophylaxis after kidney transplantation: a randomized, controlled clinical trial. *Surgery* 2015; **157:** 104–10.

181 Oxman DA, Issa NC, Marty FM, et al. Postoperative antibacterial prophylaxis for the prevention of infectious complications associated with tube thoracostomy in patients undergoing elective general thoracic surgery: a double-blind, placebo-controlled, randomized trial. *JAMA Surg* 2013; **148:** 440–46.

182 Seker D, Ugurlu C, Ergul Z, Akinci M. Single dose prophylactic antibiotics may not be sufficient in elective pilonidal sinus surgery: an early terminated study. *Turk Klin J Med Sci* 2011; **31:** 186–90.

183 Suzuki T, Sadahiro S, Maeda Y, Tanaka A, Okada K, Kamijo A. Optimal duration of prophylactic antibiotic administration for elective colon cancer surgery: a randomized, clinical trial. *Surgery* 2011; **149:** 171–78.

184 Ackroyd R, Reed MR. A prospective randomized trial of the management of suction drains following breast cancer surgery with axillary clearance. *Breast* 1997; **6:** 271–74.

185 Baas-Vrancken Peeters MJ, Kluit AB, Merkus JW, Breslau PJ. Short versus long-term postoperative drainage of the axilla after axillary lymph node dissection. A prospective randomized study. *Breast Cancer Res Treat* 2005; **93:** 271–75.

186 Barton A, Blitz M, Callahan D, Yakimets W, Adams D, Dabbs K. Early removal of postmastectomy drains is not beneficial: results from a halted randomized controlled trial. *Am J Surg* 2006; **191:** 652–56.

187 Clegg-Lamptey JN, Dakubo JC, Hodasi WM. Comparison of four-day and ten-day post-mastectomy passive drainage in Accra, Ghana. *East Afr Med J* 2007; **84:** 561–65.

188 Dalberg K, Johansson H, Signomklao T, et al. A randomised study of axillary drainage and pectoral fascia preservation after mastectomy for breast cancer. *Eur J Surg Oncol* 2004; **30:** 602–09.

189 Gupta R, Pate K, Varshney S, Goddard J, Royle GT. A comparison of 5-day and 8-day drainage following mastectomy and axillary clearance. *Eur J Surg Oncol* 2001; **27:** 26–30.

190 Inwang R, Hamed H, Chaudary MA, Fentiman IS. A controlled trial of short-term versus standard axillary drainage after axillary clearance and iridium implant treatment of early breast cancer. *Ann R Coll Surg Engl* 1991; **73:** 326–28.

191 Kopelman D, Klemm O, Bahous H, Klein R, Krausz M, Hashmonai M. Postoperative suction drainage of the axilla: for how long? Prospective randomised trial. *Eur J Surg* 1999; **165:** 117–20, discussion 121–22.

192 Parikh HK, Badwe RA, Ash CM, et al. Early drain removal following modified radical mastectomy: a randomized trial. *J Surg Oncol* 1992; **51:** 266–69.

193 Strahovnik A, Fokter SK, Kotnik M. Comparison of drainage techniques on prolonged serous drainage after total hip arthroplasty. *J Arthroplasty* 2010; **25:** 244–48.

194 Zamora-Navas P, Collado-Torres F, de la Torre-Solís F. Closed suction drainage after knee arthroplasty. A prospective study of the effectiveness of the operation and of bacterial contamination. *Acta Orthop Belg* 1999; **65:** 44–47.

195 Dumville JC, Walter CJ, Sharp CA, Page T. Dressings for the prevention of surgical site infection. *Cochrane Database Syst Rev* 2011; **7:** CD003091.

196 Dumville JC, Gray TA, Walter CJ, Sharp CA, Page T. Dressings for the prevention of surgical site infection. *Cochrane Database Syst Rev* 2014; **9:** CD003091.

197 Biffi R, Fattori L, Bertani E, et al. Surgical site infections following colorectal cancer surgery: a randomized prospective trial comparing common and advanced antimicrobial dressing containing ionic silver. *World J Surg Oncol* 2012; **10:** 94.

198 Burke NG, Green C, McHugh G, McGolderick N, Kilcoyne C, Kenny P. A prospective randomised study comparing the jubilee dressing method to a standard adhesive dressing for total hip and knee replacements. *J Tissue Viability* 2012; **21:** 84–87.

199 Dickinson Jennings C, Culver Clark R, Baker JW. A prospective, randomized controlled trial comparing 3 dressing types following sternotomy. *Ostomy Wound Manage* 2015; **61:** 42–49.

200 Krieger BR, Davis DM, Sanchez JE, et al. The use of silver nylon in preventing surgical site infections following colon and rectal surgery. *Dis Colon Rectum* 2011; **54:** 1014–19.

201 Martín-Trapero C, Martín-Torrijos M, Fernández-Conde L, et al. Surgical site infections. Effectiveness of polyhexamethylene biguanide wound dressings. *Enferm Clin* 2013; **23:** 56–61 (in Spanish).

202 Michie DD, Hugill JV. Influence of occlusive and impregnated gauze dressings on incisional healing: a prospective, randomized, controlled study. *Ann Plast Surg* 1994; **32:** 57–64.

203 Ozaki CK, Hamdan AD, Barshes NR, et al. Prospective, randomized, multi-institutional clinical trial of a silver alginate dressing to reduce lower extremity vascular surgery wound complications. *J Vasc Surg* 2015; **61:** 419–27.

204 Shinohara T, Yamashita Y, Satoh K, et al. Prospective evaluation of occlusive hydrocolloid dressing versus conventional gauze dressing regarding the healing effect after abdominal operations: randomized controlled trial. *Asian J Surg* 2008; **31:** 1–5.

205 Vogt KC, Uhlyarik M, Schroeder TV. Moist wound healing compared with standard care of treatment of primary closed vascular surgical wounds: a prospective randomized controlled study. *Wound Repair Regen* 2007; **15:** 624–27.

206 Wynne R, Botti M, Stedman H, et al. Effect of three wound dressings on infection, healing comfort, and cost in patients with sternotomy wounds: a randomized trial. *Chest* 2004; **125:** 43–49.

207 Hussain MI, Alam MK, Al-Qahatani HH, Al-Akeely MH. Role of postoperative antibiotics after appendectomy in non-perforated appendicitis. *J Coll Physicians Surg Pak* 2012; **22:** 756–59.

208 Liberman MA, Greason KL, Frame S, Ragland JJ. Single-dose cefotetan or cefoxitin versus multiple-dose cefoxitin as prophylaxis in patients undergoing appendectomy for acute nonperforated appendicitis. *J Am Coll Surg* 1995; **180:** 77–80.

209 Mui LM, Ng CS, Wong SK, et al. Optimum duration of prophylactic antibiotics in acute non-perforated appendicitis. *ANZ J Surg* 2005; **75:** 425–28.

210 Rajabi-Mashhadi MT, Mousavi SH, Mh KM, Ghayour-Mobarhan M, Sahebkar A. Optimum duration of perioperative antibiotic therapy in patients with acute non-perforated appendicitis: a prospective randomized trial. *Asian Biomed* 2012; **6:** 891–94.

211 Tsang TM, Tam PK, Saing H. Antibiotic prophylaxis in acute non-perforated appendicitis in children: single dose of metronidazole and gentamicin. *J R Coll Surg Edinb* 1992; **37:** 110–12.

212 Cuthbertson AM, McLeish AR, Penfold JC, Ross H. A comparison between single and double dose intravenous Timentin for the prophylaxis of wound infection in elective colorectal surgery. *Dis Colon Rectum* 1991; **34:** 151–55.

213 Fujita S, Saito N, Yamada T, et al. Randomized, multicenter trial of antibiotic prophylaxis in elective colorectal surgery: single dose vs 3 doses of a second-generation cephalosporin without metronidazole and oral antibiotics. *Arch Surg* 2007; **142:** 657–61.

214 Fujita T, Daiko H. Optimal duration of prophylactic antimicrobial administration and risk of postoperative infectious events in thoracic esophagectomy with three-field lymph node dissection: short-course versus prolonged antimicrobial administration. *Esophagus* 2015; **12:** 38–43.

215 Haga N, Ishida H, Ishiguro T, et al. A prospective randomized study to assess the optimal duration of intravenous antimicrobial prophylaxis in elective gastric cancer surgery. *Int Surg* 2012; **97:** 169–76.

216 Imamura H, Kurokawa Y, Tsujinaka T, et al. Intraoperative versus extended antimicrobial prophylaxis after gastric cancer surgery: a phase 3, open-label, randomised controlled, non-inferiority trial. *Lancet Infect Dis* 2012; **12:** 381–87.

217 Regimbeau JM, Fuks D, Pautrat K, et al, and the FRENCH Study Group. Effect of postoperative antibiotic administration on postoperative infection following cholecystectomy for acute calculous cholecystitis: a randomized clinical trial. *JAMA* 2014; **312:** 145–54.

218 Meijer WS, Schmitz PI, and the Galant Trial Study Group. Prophylactic use of cefuroxime in biliary tract surgery: randomized controlled trial of single versus multiple dose in high-risk patients. *Br J Surg* 1993; **80:** 917–21.

219 Aberg C, Thore M. Single versus triple dose antimicrobial prophylaxis in elective abdominal surgery and the impact on bacterial ecology. *J Hosp Infect* 1991; **18:** 149–54.

220 Abro AH, Pathan AH, Siddiqui FG, Syed F, Laghari AA. Single dose versus 24-hours antibiotic prophylaxis against surgical site infections. *J Liaquat Univ Med Health Sci* 2014; **13:** 27–31.

221 Bates T, Roberts JV, Smith K, German KA. A randomized trial of one versus three doses of Augmentin as wound prophylaxis in at-risk abdominal surgery. *Postgrad Med J* 1992; **68:** 811–16.

222 Kow L, Toouli J, Brookman J, McDonald PJ. Comparison of cefotaxime plus metronidazole versus cefoxitin for prevention of wound infection after abdominal surgery. *World J Surg* 1995; **19:** 680–86, discussion 686.

223 Turano A, and the Multicenter Study Group. New clinical data on the prophylaxis of infections in abdominal, gynecologic, and urologic surgery. *Am J Surg* 1992; **164** (suppl)**:** 16S–20S.

224 Lyimo FM, Massinde AN, Kidenya BR, Konje ET, Mshana SE. Single dose of gentamicin in combination with metronidazole versus multiple doses for prevention of post-caesarean infection at Bugando Medical Centre in Mwanza, Tanzania: a randomized, equivalence, controlled trial. *BMC Pregnancy Childbirth* 2013; **13:** 123.

225 Shaheen S, Akhtar S. Comparison of single dose versus multiple doses of anitibiotic prophylaxis in elective caesarian section. *J Postgrad Med Inst* 2014; **28:** 83–86.

226 Westen EH, Kolk PR, van Velzen CL, et al. Single-dose compared with multiple day antibiotic prophylaxis for cesarean section in low-resource settings, a randomized controlled, noninferiority trial. *Acta Obstet Gynecol Scand* 2015; **94:** 43–49.

227 Cartaña J, Cortes J, Yarnoz MC, Rossello JJ. Antibiotic prophylaxis in Wertheim-Meigs surgery. A single dose vs three doses. *Eur J Gynaecol Oncol* 1994; **15:** 14–18.

228 Su HY, Ding DC, Chen DC, Lu MF, Liu JY, Chang FY. Prospective randomized comparison of single-dose versus 1-day cefazolin for prophylaxis in gynecologic surgery. *Acta Obstet Gynecol Scand* 2005; **84:** 384–89.

229 Buckley R, Hughes GN, Snodgrass T, Huchcroft SA. Perioperative cefazolin prophylaxis in hip fracture surgery. *Can J Surg* 1990; **33:** 122–27.

230 Garotta F, Pamparana F, and the Ceftizoxime Orthopedic Surgery Italian Study Group. Antimicrobial prophylaxis with ceftizoxime versus cefuroxime in orthopedic surgery. *J Chemother* 1991; **3** (suppl 2)**:** 34–35.

231 Hellbusch LC, Helzer-Julin M, Doran SE, et al. Single-dose vs multiple-dose antibiotic prophylaxis in instrumented lumbar fusion—a prospective study. *Surg Neurol* 2008; **70:** 622–27, discussion 627.

232 Nooyen SM, Overbeek BP, Brutel de la Rivière A, Storm AJ, Langemeyer JJ. Prospective randomised comparison of single-dose versus multiple-dose cefuroxime for prophylaxis in coronary artery bypass grafting. *Eur J Clin Microbiol Infect Dis* 1994; **13:** 1033–37.

233 Tamayo E, Gualis J, Flórez S, Castrodeza J, Eiros Bouza JM, Alvarez FJ. Comparative study of single-dose and 24-hour multiple-dose antibiotic prophylaxis for cardiac surgery. *J Thorac Cardiovasc Surg* 2008; **136:** 1522–27.

234 Olak J, Jeyasingham K, Forrester-Wood C, Hutter J, al-Zeerah M, Brown E. Randomized trial of one-dose versus six-dose cefazolin prophylaxis in elective general thoracic surgery. *Ann Thorac Surg* 1991; **51:** 956–58.

235 Maier W, Strutz J. Perioperative single dose prevention with cephalosporins in the ENT area. A prospective randomized study. *Laryngorhinootologie* 1992; **71:** 365–69 (in German).

236 Mann W, Maurer J. Perioperative short-term preventive antibiotics in head-neck surgery. *Laryngorhinootologie* 1990; **69:** 158–60 (in German).

237 Rajan GP, Fergie N, Fischer U, Romer M, Radivojevic V, Hee GK. Antibiotic prophylaxis in septorhinoplasty? A prospective, randomized study. *Plast Reconstr Surg* 2005; **116:** 1995–98.

238 Campos GB, Lucena EE, da Silva JS, Gomes PP, Germano AR. Efficacy assessment of two antibiotic prophylaxis regimens in oral and maxillofacial trauma surgery: preliminary results. *Int J Clin Exp Med* 2015; **8:** 2846–52.

239 Cioacă RE, Bucur A, Coca-Nicolae C, Coca CA. Comparative study of clinical effectiveness of antibiotic prophylaxis in aseptic mouth, jaw, and facial surgery. *Mund Kiefer Gesichtschir* 2002; **6:** 356–59 (in German).

240 Lindeboom JA, Tuk JG, Kroon FH, van den Akker HP. A randomized prospective controlled trial of antibiotic prophylaxis in intraoral bone grafting procedures: single-dose clindamycin versus 24-hour clindamycin prophylaxis. *Mund Kiefer Gesichtschir* 2005; **9:** 384–88.

241 Lindeboom JA, Baas EM, Kroon FH. Prophylactic single-dose administration of 600 mg clindamycin versus 4-time administration of 600 mg clindamycin in orthognathic surgery: a prospective randomized study in bilateral mandibular sagittal ramus osteotomies. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003; **95:** 145–49.

242 Danda AK, Wahab A, Narayanan V, Siddareddi A. Single-dose versus single-day antibiotic prophylaxis for orthognathic surgery: a prospective, randomized, double-blind clinical study. *J Oral Maxillofac Surg* 2010; **68:** 344–46.

243 Kang SH, Yoo JH, Yi CK. The efficacy of postoperative prophylactic antibiotics in orthognathic surgery: a prospective study in Le Fort I osteotomy and bilateral intraoral vertical ramus osteotomy. *Yonsei Med J* 2009; **50:** 55–59.

244 Wahab PU, Narayanan V, Nathan S, Madhulaxmi. Antibiotic prophylaxis for bilateral sagittal split osteotomies: a randomized, double-blind clinical study. *Int J Oral Maxillofac Surg* 2013; **42:** 352–55.

245 Karran SJ, Sutton G, Gartell P, Karran SE, Finnis D, Blenkinsop J. Imipenem prophylaxis in elective colorectal surgery. *Br J Surg* 1993; **80:** 1196–98.

246 Akgür FM, Cahit Tanyel F, Büyükpamukçu N, Hiçsönmez A. Prophylactic antibiotics for colostomy closure in children: short versus long course. *Pediatr Surg Int* 1992; **7:** 279–81.

247 Ishibashi K, Kuwabara K, Ishiguro T, et al. Short-term intravenous antimicrobial prophylaxis in combination with preoperative oral antibiotics on surgical site infection and methicillin-resistant *Staphylococcus aureus* infection in elective colon cancer surgery: results of a prospective randomized trial. *Surg Today* 2009; **39:** 1032–39.

248 Ishibashi K, Ishida H, Kuwabara K, et al. Short-term intravenous antimicrobial prophylaxis for elective rectal cancer surgery: results of a prospective randomized non-inferiority trial. *Surg Today* 2014; **44:** 716–22.

249 McArdle CS, Morran CG, Pettit L, Gemmell CG, Sleigh JD, Tillotson GS. Value of oral antibiotic prophylaxis in colorectal surgery. *Br J Surg* 1995; **82:** 1046–48.

250 Lau WY, Yuen WK, Chu KW, Chong KK, Li AK. Systemic antibiotic regimens for acute cholecystitis treated by early cholecystectomy. *Aust N Z J Surg* 1990; **60:** 539–43.

251 Takemoto RC, Lonner B, Andres T, et al. Appropriateness of twenty-four-hour antibiotic prophylaxis after spinal surgery in which a drain is utilized: a prospective randomized study. *J Bone Joint Surg Am* 2015; **97:** 979–86.

252 Lin MH, Pan SC, Wang JL, et al. Prospective randomized study of efficacy of 1-day versus 3-day antibiotic prophylaxis for preventing surgical site infection after coronary artery bypass graft. *J Formos Med Assoc* 2011; **110:** 619–26.

253 Niederhäuser U, Vogt M, Vogt P, Genoni M, Künzli A, Turina MI. Cardiac surgery in a high-risk group of patients: is prolonged postoperative antibiotic prophylaxis effective? *J Thorac Cardiovasc Surg* 1997; **114:** 162–68.

254 Carroll WR, Rosenstiel D, Fix JR, et al. Three-dose vs extended-course clindamycin prophylaxis for free-flap reconstruction of the head and neck. *Arch Otolaryngol Head Neck Surg* 2003; **129:** 771–74.

255 Liu SA, Tung KC, Shiao JY, Chiu YT. Preliminary report of associated factors in wound infection after major head and neck neoplasm operations—does the duration of prophylactic antibiotic matter? *J Laryngol Otol* 2008; **122:** 403–08.

256 Righi M, Manfredi R, Farneti G, Pasquini E, Cenacchi V. Short-term versus long-term antimicrobial prophylaxis in oncologic head and neck surgery. *Head Neck* 1996; **18:** 399–404.

257 Bidkar VG, Jalisatigi RR, Naik AS, et al. Perioperative only versus extended antimicrobial usage in tympanomastoid surgery: a randomized trial. *Laryngoscope* 2014; **124:** 1459–63.

258 Abubaker AO, Rollert MK. Postoperative antibiotic prophylaxis in mandibular fractures: a preliminary randomized, double-blind, and placebo-controlled clinical study. *J Oral Maxillofac Surg* 2001; **59:** 1415–19.

259 Baqain ZH, Hyde N, Patrikidou A, Harris M. Antibiotic prophylaxis for orthognathic surgery: a prospective, randomised clinical trial. *Br J Oral Maxillofac Surg* 2004; **42:** 506–10.

260 Bentley KC, Head TW, Aiello GA. Antibiotic prophylaxis in orthognathic surgery: a 1-day versus 5-day regimen. *J Oral Maxillofac Surg* 1999; **57:** 226–30, discussion 230–32.

261 Eshghpour M, Khajavi A, Bagheri M, Banihashemi E. Value of prophylactic postoperative antibiotic therapy after bimaxillary orthognathic surgery: a clinical trial. *Iran J Otorhinolaryngol* 2014; **26:** 207–10.

262 Fridrich KL, Partnoy BE, Zeitler DL. Prospective analysis of antibiotic prophylaxis for orthognathic surgery. *Int J Adult Orthodon Orthognath Surg* 1994; **9:** 129–31.

263 Jansisyanont P, Sessirisombat S, Sastravaha P, Bamroong P. Antibiotic prophylaxis for orthognathic surgery: a prospective, comparative, randomized study between amoxicillin-clavulanic acid and penicillin. *J Med Assoc Thai* 2008; **91:** 1726–31.

264 Bozorgzadeh A, Pizzi WF, Barie PS, et al. The duration of antibiotic administration in penetrating abdominal trauma. *Am J Surg* 1999; **177:** 125–31.

265 Chang WC, Hung YC, Li TC, Yang TC, Chen HY, Lin CC. Short course of prophylactic antibiotics in laparoscopically assisted vaginal hysterectomy. *J Reprod Med* 2005; **50:** 524–28.

266 Becker JM, Alexander DP. Colectomy, mucosal proctectomy, and ileal pouch-anal anastomosis. A prospective trial of optimal antibiotic management. *Ann Surg* 1991; **213:** 242–47.

267 Togo S, Tanaka K, Matsuo K, et al. Duration of antimicrobial prophylaxis in patients undergoing hepatectomy: a prospective randomized controlled trial using flomoxef. *J Antimicrob Chemother* 2007; **59:** 964–70.

268 Gupta A, Hote MP, Choudhury M, Kapil A, Bisoi AK. Comparison of 48 h and 72 h of prophylactic antibiotic therapy in adult cardiac surgery: a randomized double blind controlled trial. *J Antimicrob Chemother* 2010; **65:** 1036–41.

269 Sawyer R, Cozzi L, Rosenthal DI, Maniglia AJ. Metronidazole in head and neck surgery—the effect of lengthened prophylaxis. *Otolaryngol Head Neck Surg* 1990; **103:** 1009–11.

270 Scher KS. Studies on the duration of antibiotic administration for surgical prophylaxis. *Am Surg* 1997; **63:** 59–62.