

---

# Prevention of Periprosthetic Joint Infection: What Is the Current Evidence?

# 4

Simon S. Jameson and Mike R. Reed

---

## Abstract

Periprosthetic joint infection is a disastrous complication following routine joint replacement surgery. The cause is often multi-factorial. In order to minimise risk, a team-based approach should be followed to optimise modifiable patient risk factors and adhere to best surgical practice, informed by robust evidence. This chapter discusses the current best evidence.

---

## Keywords

Surgical site infection • Periprosthetic joint infection

---

## Introduction

Periprosthetic joint infection (PJI) is a major, but infrequent complication of arthroplasty surgery and is associated with substantial morbidity and economic cost [1–3]. A number of patient, surgical and environmental specific risk factors may contribute to the development of a PJI [4, 5] (Table 4.1). The common pathogenic organisms responsible for orthopaedic SSIs are shown in

Fig. 4.1 [6]. In this chapter we discuss the current evidence for best surgical practice to reduce the risk of PJI.

---

## Modifiable Patient Risk Factors

Patient-related factors, such as diabetes mellitus (DM) and rheumatoid disease (RA), are modifiable and certain aspects of management can be optimised to reduce infection.

## Diabetes Mellitus

Wound infection has been shown to be more common in patients with diabetes after arthroplasty, and in non-diabetic patients who developed transient post-operative hyperglycaemia [7]. Hyperglycaemia is associated with increased

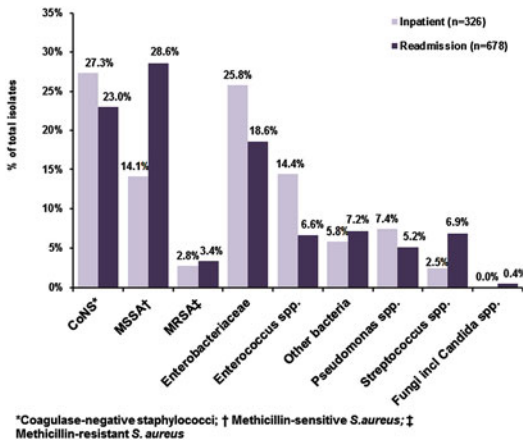
---

S.S. Jameson, PhD, FRCS (T&O)  
Department of Trauma and Orthopaedics, James  
Cook University Hospital, Middlesbrough, UK

M.R. Reed, MD, FRCS (T&O) (✉)  
Department of Trauma and Orthopaedics,  
Northumbria Healthcare, Woodhorn Lane,  
Ashington, Northumberland  
NE63 9JJ, UK  
e-mail: [mike.reed@nhs.net](mailto:mike.reed@nhs.net)

**Table 4.1** Risk factors for surgical site infection

Patient factors	Operative factors
<i>Systemic:</i>	ASA score >2
Obesity	Long duration
Diabetes	Poor surgical technique
Immunosuppression	Contaminated or dirty wound
Smoking	Lack of systemic antibiotic prophylaxis
Rheumatoid arthritis	Lack of local antibiotics/antiseptic
Psoriasis	Hypothermia
Poor nutritional status	Poor diabetic control
Advanced age	MSSA/MRSA colonisation
<i>Local:</i>	
Previous arthroplasty	
Arthroplasty following fracture	
Type of joint	
Peri-operative wound complications	



**Fig. 4.1** Micro-organisms reported as causing SSIs (all orthopaedic patients, England). SSI surgical site infection, MSSA methicillin-sensitive *Staphylococcus aureus*, MRSA methicillin-resistant *Staphylococcus aureus* (Adapted with permission from the Health Protection Agency)

monocyte susceptibility to apoptosis [8] and impaired neutrophil function (impaired chemotactic, phagocytic and bactericidal capability) [9]. Blood glucose levels above 11.1 mmol/l are associated with SSIs in cardiac surgery [10], and in general surgical patients immediate post-operative hyperglycaemia is associated with SSI [11]. The potential to improve *in vivo* neutrophil phagocytic function by aggressive glucose control (using infusion delivery) has also been demonstrated in cardio-pulmonary bypass patients [12]. However,

the effect on SSI is likely to be modest – a recent large study of 40,000 patients undergoing knee replacement found no additional risk for patients with either controlled or uncontrolled diabetes, compared to non diabetics [13].

### Rheumatoid Arthritis

RA is an independent risk factor for infection in arthroplasty, but also for revision and subsequent re-infection. This is especially significant as RA patients often present earlier for arthroplasty.

Local and systemic corticosteroids have been shown to delay wound-healing, increase the risk of wound infection [14] and cause adrenal insufficiency. A recent Cochrane review has questioned the historical practice of providing long-term users with additional perioperative steroids (which may amplify immunosuppression at time of surgery) [15].

Although disease-modifying antirheumatic drugs (DMARDs) increase the risk of prosthetic joint infection [5], the British Society for Rheumatology (BSR) guidelines suggest that in most cases these should not be stopped prior to joint replacement [16]. Methotrexate is a commonly used first-line drug [17] and, despite its inclusion within the DMARD group, is not considered by some authors to increase wound infection risk and should not be discontinued

prior to orthopaedic surgery [18]. Other randomised trials show a clear reduction in risk when methotrexate is stopped prior to joint replacement [19]. However, nitrous oxide should be excluded from the anaesthetic regimen as the interaction can induce immunosuppression [20].

Tumour necrosis factor (TNF)-alpha is an inflammatory cytokine (highly concentrated in the synovial tissue of RA patients) implicated in joint destruction [21]. Any increase in risk of infection in patients who received anti-TNF therapy prior to surgery is debatable [22, 23]. The BSR state that the potential benefit of preventing post-operative infections (by stopping treatment) should be balanced against the risk of a peri-operative disease flare. If anti-TNF therapy is to be withheld, it should be discontinued 5–20 days before surgery (3–5 times the drug half-life), restarting when there is good wound healing and no evidence of infection [24].

The recent consensus statement on PJI recommends all disease-modifying drugs should be stopped prior to surgery – specifically methotrexate should be stopped a week before surgery, and recommenced 2 weeks after surgery [25]. The authors discuss each case with the rheumatology team.

### Patient Weight and Obesity

The effect of obesity (body mass index, BMI  $\geq 30$  kg/m<sup>2</sup>) on SSI is well documented [26]. Self-reported wound complications and reoperations after hip replacement are 1.5–3 times higher in obese patients [27] and there is a 3–7 times higher risk of PJI [28, 29]. Increased length and complexity of surgery and poorer vascularisation of the subcutaneous layer may contribute to this elevated risk. Obese patients also require a significantly higher fraction of inspired oxygen (FiO<sub>2</sub>) to reach an adequate arterial oxygen level [30]. In super obese patients ( $\geq 50$  kg/m<sup>2</sup>) bariatric surgery may be indicated. In patients that underwent both bariatric surgery and lower limb arthroplasty, the wound infection rate was 3.5 times lower in patients who had bariatric surgery first [31]. Communication with the

anaesthetist to evaluate the risk and to discuss increased doses of peri-operative antibiotics is recommended [32].

Low BMI (<18 kg/m<sup>2</sup>) may also increase the risk of PJI, most likely as a result of poor nutrition [29]. As with obese patients, referral to a dietician may be necessary prior to surgery.

### Smoking

Smoking is associated with impaired wound healing and infection [33]. Patients randomised to a cessation programme 6–8 weeks prior to arthroplasty had significantly fewer wound complications (5 % vs. 31 %), shorter length of stay, fewer re-operations and cardiovascular benefits [34]. A large non-randomised study found a 3.2 times greater risk of developing wound complications in patients who smoked [35].

### Screening for and Decolonisation of *Staphylococcus aureus*

The costs associated with treatment of infections due to methicillin-resistant organisms are 1.5 times higher compared to sensitive organisms [36]. A methicillin-resistant *Staphylococcus aureus* (MRSA) screening programme for all planned NHS surgery was implemented in April 2009, with a positive result prompting decolonisation prior to admission.

Nasal carriers of methicillin-sensitive *Staphylococcus aureus* (MSSA) also have an increased risk of SSI. In a large, randomised, multi-centre trial, the risk of developing a *S. aureus* infection in MSSA-carrier patients who were decolonised on admission to hospital (mupirocin nasal ointment and chlorhexidine soap) fell by nearly 60 % compared with placebo – a significant reduction from 7.7 to 3.4 % [37]. Nasal carriage of MSSA is common (~20 %) [37] and UK hospitals are beginning to decolonise patient carriers prior to joint replacement – this has been demonstrated to be cost effective [38].

## Other Considerations

Urogenital and periodontal foci of infection are important sources for haematogenous spread of sepsis and must be eradicated prior to joint replacement [39]. Pre-operative serum albumin levels of less than 3.5 g/dl also increase the risk of post-operative infection [40].

---

## Pre-operative Phase Surgical Risk Factors

### Patient Preparation Prior to Theatre

Admission to hospital prior to surgery should ideally be the same day to reduce the risk of colonization of the patient's skin with possibly resistant hospital-acquired bacterial strains. Patients should shower with soap on the morning of surgery [41]. Washing with an antiseptic reduces skin bacteria (microflora), but there is little evidence of a reduction in risk of SSI [42, 43]. There is no evidence that removing hair reduces the risk of SSI [44]. Dry shaving with a razor may irritate the skin and increase the bacterial count so if hair removal is necessary, electric clippers or depilatory creams on the day of surgery are favoured [41, 45].

Patients should be pre-warmed prior to surgery, to avoid hypothermia during the operation and particularly in recovery [46, 47]. A UK randomised trial published in the *Lancet* demonstrated pre-warming reduces the risk of infection by approximately 65 % in clean surgery [48].

### Antibiotic Prophylaxis

The role of parenteral prophylactic antibiotics has been studied and accepted across most surgical specialties [49, 50], and may be the single most significant factor in the prevention of deep wound infection following lower limb arthroplasty [51].

Although many different groups of antibiotics can be used for prophylaxis, there is insufficient evidence of a significant difference in the efficacy

of cephalosporins, teicoplanin or penicillin-derivatives, or a benefit of one generation of cephalosporins over another [52]. Cephalosporin use has been associated with *Clostridium difficile* colitis, especially in the elderly, but rates are low after joint replacement (1.7 per 1000 replacements) [53].

Aminoglycosides, such as gentamicin, can be administered locally (in the cement) or parenterally. In a review of 15,000 primary total hip replacements from the Norwegian Arthroplasty Register the lowest risk of revision was found in patients who received both systemic and local (in cement) antibiotics [54]. Although there were no significant differences in superficial wound infection, a meta-analysis examining the benefit of antibiotic-laden bone cement (ALBC) in over 6000 arthroplasties identified a lower deep infection rate [55]. ALBC is used in primary arthroplasties throughout Europe but only approved for use in revision arthroplasty after PJI in North America. Despite concerns, there remains no good evidence of changing microbial profiles and greater resistance following routine prophylactic use of ALBC [56]. Preventing deep infection with antibiotic prophylaxis and ALBC has shown improvements in health outcomes among hospitalized patients, with reduced mortality risk and lower costs [57].

The National Institute for Health and Care Excellence (NICE) recommends a single intravenous dose of antibiotic prophylaxis on starting anaesthesia, with a repeat dose if the operation is longer than the half-life of the antibiotic, or if blood loss is a significant [58]. The American Academy of Orthopaedic Surgeons (AAOS) state that the administration of antibiotic should precede the skin incision by 1 h and duration of prophylaxis should not exceed the 24 h. Rates of infection have been found to be lowest for patients who received an antibiotic within 2 h of the incision [49], and there was no difference between 1- and 3-day courses of prophylactic antibiotics in terms of deep-infection rate [59]. In over 32,000 major procedures (including THR and TKR), risk of SSI was not significantly associated with prophylactic antibiotic timing [60]. Administration of antibiotics as early as possible

in the anaesthetic room, and well before (at least 5 min) tourniquet inflation (in order to limit any further rise in tissue antibiotic concentration) seems logical [61].

Unfortunately, there are risks of prophylaxis and there is a delicate balance between reducing risk of SSI and the adverse effects of antibiotics, such as anaphylaxis, interactions with other drugs and antibiotic-associated diarrhoea, including *Clostridium difficile* (CDAD) and thrush. However, whilst recommended antibiotic prophylaxis has shifted from cephalosporins to dual therapy in order to reduce the incidence of CDAD, data suggests acute kidney injury is higher and SSI has remained unchanged [62–65].

The choice of antibiotic should take into account resistance patterns and cover micro-organisms most likely to cause SSI. Patients undergoing high-risk surgery who are MRSA positive should receive a suitable antibiotic active against local strains of MRSA. The combination of vancomycin and cefazolin appear to reduce the incidence of MRSA infections, but the number needed to treat to prevent a single MRSA infection is very high [66]. Another study of over 6000 joint replacements concluded that Gentamicin 4.5 mg/kg alone should not be used as prophylaxis for primary joint arthroplasty as it did not reduce CDAD significantly but increased the risk of other postoperative complications [67].

The most suitable prophylaxis should be the most-narrow spectrum to cover the most common organisms and should be cost-effective. A team-based approach to antibiotic prophylaxis policy is desirable, with knowledge of evidence and information about resistance and drug costs informing recommendations about specific drug regimens.

---

## Peri-operative Phase Surgical Risk Factors

### Theatre Etiquette

The World Health Organisation recommends that all surgical staff should keep doors to the operating room closed, except as needed for the passage of

equipment, personnel and the patient. Staff should store essential equipment in the operating room to decrease theatre traffic [68]. Frequency of theatre door-opening is a positive predictor of raised bacterial counts [69]. The International Consensus on Periprosthetic Joint Infection Meeting in 2013 reiterated the importance of this: of the 207 questions asked, only the question ‘should operating room traffic should be kept to a minimum?’ received a unanimous vote with 100 % agreement among the assembled 400 international PJI experts [25].

Although chlorhexidine gluconate has not been demonstrated to reduce SSI rates, it is associated with a more prolonged and effective reduction in colony forming units following surgical hand scrub than povidone-iodine. Alcohol rub used in preparation for surgery may be as effective as hand scrubbing in preventing SSIs [70]. There is no evidence to suggest that any particular alcohol rub is better than another [71, 72].

### Surgical Site Preparation in Theatre

Skin moisturisers appear to inhibit the ability of aqueous preparations to decolonise the skin, and may increase skin bacteria counts. Avoidance of oil based moisturisers and de-greasing with alcohol pre-wash is recommended [73].

A large randomised trial of 849 patients undergoing clean-contaminated surgery in which pre-operative skin preparation was performed with either 2 % chlorhexidine-alcohol or aqueous povidone-iodine and paint found that the rate of SSI was significantly lower in the chlorhexidine-alcohol group [74]. However, when 41 variables were examined in over 4000 cardiac patients, risk of SSI was not influenced by skin preparation (alcohol betadine or chlorhexadine) [75]. There are currently a number of ongoing clinical trials examining the influence of skin preparations [76]. Further data are likely to emerge in the next few years but the current evidence for skin preparation in joint replacement is limited. NICE support the use of either povidone-iodine or chlorhexidine, but state that alcohol-based solutions may be more effective than aqueous solutions [44].

## Theatre Design

Airborne contaminants are said to be the largest single contributor to infection [77]. One billion skin cells are shed daily per person [78] with up to 10 % carrying bacteria [79]. For orthopaedic surgery, laminar-flow ventilation systems have been advocated although they are not in universal use. These employ high-efficiency particulate air filters where particles greater than 0.3  $\mu\text{m}$  are removed (5  $\mu\text{m}$  for conventional theatres). Ultra-clean air can reduce bacterial and particle concentrations [80]. Evidence from the past supports ultra-clean air in conjunction with prophylactic antibiotics to reduce infections after joint arthroplasty [81]. There is no dispute that the air within an effective laminar flow theatre is extremely clean. However, more recent evidence has questioned the benefit. Brandt et al. found laminar flow to have no protective effect against SSI in 99,230 patients [82]. When 88,311 arthroplasty patients from the New Zealand joint registry where analysed, revision rates for deep infection were significantly higher in laminar flow theatres, despite adjustment for other known variables [83]. A systematic review of 123,788 joint replacements found laminar flow did not reduce the occurrence of SSI [84]. However, before abandoning laminar flow the interaction with forced air warming should be examined. A recent study demonstrated that air from outside the canopy may be drawn into the surgical wound area when forced air warming (FAW) devices are used, and deep infection rates were reduced when FAW was abandoned in favour of contemporary conductive fabric warming in joint replacement [85]. The infection control hazards associated with forced air warming have recently been collated and many units, including the authors', use alternative warming systems [86].

## Operating Personnel Clothing

NICE recommends double gloving in arthroplasty surgery [87]. Glove perforation increases the risk of transmission of blood-borne diseases and breaks the asepsis barrier, potentially allowing contamination of the wound and thus increasing

the risk of infection [88, 89]. Studies have shown that use of a blunt needle compared to sharp needle during surgery reduces glove perforation rates significantly [90, 91]. Most perforations are unnoticed (61.5 %) and are caused by shearing rather than penetration by sharps [88]. A Cochrane systematic review supported the use of double gloving, despite no evidence of a reduction in SSI [92]. Surgical teams should use scrub staff assisted closed gloving to reduce the risk of gown contamination [93]. Glove changing at regular intervals is an effective way to decrease the length of exposure to bacterial contamination [89]. Latex-free gloves have significantly higher perforation rates when compared with latex gloves [94].

Modern space suits contribute to a higher revision rate for infection compared with a normal theatre gown and mask, when analysed independently of laminar flow [83].

## Surgical Drapes

If an incise drape is to be used, NICE recommend that an incise drape impregnated with iodophore should be placed unless the patient has an iodine allergy. Although a Cochrane review concluded that these drapes did not make any difference to infection rates [95], only one trial involved orthopaedic surgery, which showed no difference in post-operative wound infection rates following hip fracture surgery with or without non-impregnated Opsite (Smith & Nephew Wound Management, Hull, United Kingdom) [96].

## Surgical Equipment

Commonly used equipment can become decontaminated in the theatre environment during a procedure, and may be a source of surgical field contamination. Davis et al. found contamination rates of 11.4 % for sucker tips, 9.4 % for skin (outside) blades, 3.2 % for inside blades, 28.7 % for outside gloves used for preparation and draping the patient and 14.5 % for light handles within the laminar flow zone [97].

Pulsatile lavage removes between 57 and 87 % of all organisms from wounds [98, 99]. When

combined with 0.05 % chlorhexidine its efficacy can be increased to 98 % and was responsible for a 0.45 % infection rate after hip replacement at one unit [100]. A randomised trial of dilute betadine solution irrigation has shown reduction of SSI in spinal surgery [101] and a recent cohort study supports its use in arthroplasty surgery [102].

### Body Core Temperature

Peri-operative hypothermia is common during major surgery and causes vasoconstriction resulting in a reduction in subcutaneous tissue perfusion, and an increased risk of infection [103]. Peri-operative hypothermia is associated with increased blood loss, cardiac events, increased transfusion requirements and longer peri-operative hospital stay [104]. Heat loss in theatre is largely conductive and convective, with a small amount of radiated heat. Laminar flow significantly increases convective heat loss in exposed patients, mitigated by active warming.

Warming patients undergoing clean general surgery significantly reduced wound infection from 14 to 5 % [48]. In a further general surgery study, when patients were randomized to either hypothermia or normothermia the trial had to be stopped prematurely due to the profound treatment benefit of normothermia (SSI at 2 weeks: 5.8 % vs. 18.8 %). A similar report of cholecystectomy patients found nearly a six-fold difference in the incidence of wound infection between normothermic and hypothermic patients [105]. The importance of maintaining perioperative normothermia has been recognised in the recent NICE guidelines [106]. However, it is notable that FAW has never been proven to reduce SSIs in orthopaedic implant surgery, and their effect on laminar flow and clean air needs further study [86].

### Oxygen Delivery and Fluid Management

Increasing tissue oxygen concentrations has been hypothesised to increase the killing potential of phagocytes and thus decrease infective complications in the perioperative period [107]. Enhancement of tissue oxygen delivery can be

achieved via improvement of cardiac output and/or oxygen content of the blood. Increased subcutaneous oxygen concentrations can be achieved by increasing the inspired oxygen concentration intra-operatively (from 30 to 80 %), and by providing supplemental oxygen post-operatively. There are studies supporting the use of supplemental oxygen to reduce wound infections in general surgery, but these have never been extrapolated to arthroplasty surgery [108–110].

Both hypovolaemia and hypervolaemia (oedema) can be detrimental to tissue oxygenation. Current guidance would support optimal tissue oxygenation by maintenance of a normovolaemic state throughout the peri- and early post-operative period by judicious use of intravenous fluids [111, 112].

### Anaesthetic Technique

The question of whether regional anaesthesia is superior to general anaesthesia has yet to be adequately assessed, although a recent retrospective population based study found significantly lower 30-day SSI rates in patients undergoing lower limb arthroplasty under a spinal anaesthetic [113]. An RCT examining the potentially beneficial effect of nitrous oxide avoidance failed to show a reduction in SSI. Co-administered anaesthetic and sedative agents may impair immune responses directly, thereby increasing infection [114], and regional anaesthesia may offer particular benefits such as improved tissue oxygen delivery (through vasodilation). Randomised controlled trials are required to address whether choice of agent (such as use of an alpha2 adrenergic versus GABAergic sedative) affects outcome [114, 115]

A recent systematic review and meta-analysis found a significant advantage of haemodynamic goal-directed fluid therapy on surgical site infection rates, based on 3550 patients in 18 RCTs [116].

### Anaemia and Blood Transfusion

In a prospective cohort study preoperative anaemia was associated with increased postoperative infections in patients undergoing hip arthroplasty.

This effect was associated with an increase in postoperative blood transfusion [117].

There are no specific recommendations from NICE regarding transfusions. Though it is clear blood loss is primarily a surgical responsibility, regional anaesthetic techniques and attention to perioperative normothermia are associated with reduced blood loss. Transfusion-related immunomodulation is recognised in trauma patients [118], with a 5 % increase risk of infection for every unit of red cells given [119]. A significant increase in infection rates following hip replacement is seen in patients receiving allogeneic RBCs, with higher risk with more units transfused [120]. There is clearly a risk-benefit balance between immunosuppression and enhancing oxygen supply to hypoperfused tissue. If possible, blood transfusion should be avoided intra-operatively [121] and, if anticipated, should be administered at least 48 h prior to surgery to maximise oxygen transportation of transfused blood. Addressing pre-operative anaemia reduces postoperative transfusion requirements [122].

The use of antifibrinolytics, such as tranexamic acid, prevent blood loss following major arthroplasty [123]. Although there is insufficient data to comment on their ability to prevent postoperative infection, they may indirectly reduce the risk by reducing transfusion requirement and improving the wound environment.

Recent evidence suggests that white cell depleted blood reduces infection risk compared to normal blood [124], and red blood cell transfusions in the UK are routinely filtered.

## Surgical Factors

Prolonged operating time, reflecting the complexity of surgery or the inexperience of the surgeon, may increase the risk of infection. However, when adjusted for confounding factors such as BMI and diabetes this effect is modest with an increased risk of only 7 % for every additional 15 min [29].

Closed suction drains are a potential entry point of infection, but there is no evidence of any association with wound infection risk [125].

There is also insufficient evidence to recommend that a particular wound dressing is more effective than others in reducing the rates of SSI [126].

---

## Post-operative Period

### Thromboembolic Prophylaxis

NICE guidelines state that patients undergoing lower limb joint replacements should have either prophylactic low molecular weight heparin (LMWH) or an orally active direct factor Xa inhibitor for 28 (or 35) days following hip arthroplasty and 14 days following a knee arthroplasty. No increased risk of infection was found with LMWH [127] but prolonged ooze is a recognised risk [128], and each day of prolonged wound drainage increases risk of wound infection by 29–42 % following arthroplasty [128]. Wound-related complications following arthroplasty may increase in patients who receive rivaroxaban, a factor Xa inhibitor, for thromboprophylaxis [129].

### Dental Care and Other Procedures

It has been suggested that patients requiring dental care post-arthroplasty should receive prophylactic antibiotics [130]. Other authors argue that there is little evidence to suggest that bacteraemia associated with dental procedures causes prosthetic joint infection [131] – simple tasks, such as brushing teeth and chewing, can produce a greater bacteraemia than one dental procedure and it would be better practice for the surgeon to ensure dentition and oral health are up to standard prior to elective orthopaedic surgery. Currently in the UK, the British Dental Association does not recommend antibiotics. The routine use of amoxicillin antibiotic prophylaxis prior to dental procedures for patients with TJA may not be cost-effective in those where the risk of infection with dental work is low [132].

Table 4.2 summarises the evidence for methods to reduce PJI.



**Table 4.2** Methods for reducing surgical site infection in joint replacement

Risk factor	Summary
<i>Patient factors</i>	
Diabetes mellitus	Aggressive glucose control
Rheumatoid arthritis	DMARDs and methotrexate should not be stopped Peri-operative steroids are generally not required Balance the risks and benefits of stopping anti-TNF – stop at 3-5 half lives pre-operative, restart after wound healing and no evidence of infection Nitrous oxide should be avoided in patients on methotrexate
Obesity	Dietician input to encourage weight loss Adjust peri-operative antibiotic doses appropriately In super-obese consider bariatric surgery prior to surgery
Smoking	Consider a smoking cessation programme
Carrier screening	MRSA and MSSA screening based on local guidelines, and decolonise prior to admission
<i>Pre-operative factors</i>	
Patient preparation	Shower on day of surgery If shaving required, use electric clippers on day of surgery Avoid oil-based skin moisturisers
Antibiotics	Prophylactic antibiotics should be given as early as possible in the anaesthetic room, and continued for 24 h post-operatively (antibiotic type dependent on local guidelines) Administer antibiotics at least 5 min prior to tourniquet inflation If cementation is required, antibiotic-impregnated should be used
<i>Peri-operative factors</i>	
Theatre	Use laminar flow where possible Keep theatre door opening to a minimum
Personnel	Hand wash with antiseptic surgical solution, using a single-use brush or pick for the nails Before subsequent operations hands should be washed with either an alcoholic hand rub or an antiseptic surgical solution Double glove and change gloves regularly Polypropylene non-woven gowns with adequate mask and hat coverage
Skin preparation	Use an alcohol pre-wash followed by a 2 % chlorhexadine-alcohol scrub solution
Anaesthetic	Maintain normothermia Maintain normovolaemia A higher inspired oxygen concentration peri-operatively and for 6 h post-operative may be of benefit
Drapes	Use of iodine-impregnated incise drapes may be of benefit (in patients without allergy)
Blood transfusion	Optimise pre-operative haemoglobin If possible, transfusion should be avoided intra-operatively and if anticipated should be given more than 48 h prior to surgery Antifibrinolytics may indirectly reduce SSI by reducing the need for transfusion
<i>Post-operative factors</i>	
Dental procedures	Insufficient evidence to recommend the use of prophylactic antibiotics for patients undergoing routine dental procedures following joint replacement
<i>Other</i>	
Surveillance	Initiatives have shown the benefit of collecting and analysing data with appropriate feedback mechanism to prompt changes in practice [133]

Abbreviations: *DMARDs* disease-modifying anti-rheumatic drugs, *TNF* tumour necrosis factor, *MRSA* methicillin-resistant *Staphylococcus aureus*, *MSSA*, methicillin-sensitive *Staphylococcus aureus*, *SSI* surgical site infection

## Conclusion

A PJI following routine arthroplasty surgery can have disastrous consequences for the patient and is costly to healthcare providers. Given the wide variety of infection prevention tactics available a team-based approach is essential in order to reduce infection rates. Every possible step must be exercised to reduce contamination of the surgical wound and to optimise the patient's capacity to eradicate any colony forming units entering the wound. Common-sense approaches are required to minimise or correct physiological disturbances and attention should be given to theatre design and etiquette, identification and control of MSSA carriers and the appropriate and timely use of prophylactic antibiotics. It is important to emphasize the need to educate the patient and all members of the healthcare team, and to increase awareness of the importance of their participation in preventive efforts.

## References

- Darouiche RO. Treatment of infections associated with surgical implants. *N Engl J Med*. 2004;350(14):1422–9 [Review].
- Edwards C, Counsell A, Boulton C, Moran CG. Early infection after hip fracture surgery: risk factors, costs and outcome. *J Bone Joint Surg Br*. 2008;90(6):770–7.
- Bozic KJ, Ries MD. The impact of infection after total hip arthroplasty on hospital and surgeon resource utilization. *J Bone Joint Surg Am*. 2005;87(8):1746–51. [Research Support, Non-U.S. Gov't].
- Gurkan I, Wenz JF. Perioperative infection control: an update for patient safety in orthopedic surgery. *Orthopedics*. 2006;29(4):329–39; quiz 40–1. [Review].
- Moucha CS, Clyburn T, Evans RP, Prokuski L. Modifiable risk factors for surgical site infection. *J Bone Joint Surg Am*. 2011;93(4):398–404 [Review].
- Health-Protection-Agency. Sixth report of the mandatory surveillance of surgical site infection in orthopaedic surgery; 2011. [www.hpa.org.uk](http://www.hpa.org.uk).
- Mraovic B, Donghun S, Jacovides C, Parvizi J. Perioperative hyperglycemia and postoperative infection after lower limb arthroplasty. *J Diabetes Sci Technol*. 2011;5(2):413–8.
- Komura T, Sakai Y, Honda M, Takamura T, Matsushima K, Kaneko S. CD14+ monocytes are vulnerable and functionally impaired under endoplasmic reticulum stress in patients with type 2 diabetes. *Diabetes*. 2010;59(3):634–43.
- Turina M, Fry DE, Polk Jr HC. Acute hyperglycemia and the innate immune system: clinical, cellular, and molecular aspects. *Crit Care Med*. 2005;33(7):1624–33. [Research Support, Non-U.S. Gov't Review].
- Golden SH, Peart-Vigilance C, Kao WH, Brancati FL. Perioperative glycemic control and the risk of infectious complications in a cohort of adults with diabetes. *Diabetes Care*. 1999;22(9):1408–14. [Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.].
- Ata A, Lee J, Bestle SL, Desemone J, Stain SC. Postoperative hyperglycemia and surgical site infection in general surgery patients. *Arch Surg*. 2010;145(9):858–64.
- Rassias AJ, Marrin CA, Arruda J, Whalen PK, Beach M, Yeager MP. Insulin infusion improves neutrophil function in diabetic cardiac surgery patients. *Anesth Analg*. 1999;88(5):1011–6. [Clinical Trial Randomized Controlled Trial Research Support, U.S. Gov't, P.H.S.].
- Adams AL, Paxton EW, Wang JQ, Johnson ES, Bayliss EA, Ferrara A, et al. Surgical outcomes of total knee replacement according to diabetes status and glycemic control, 2001 to 2009. *J Bone Joint Surg Am*. 2013;95(6):481–7.
- Wicke C, Halliday B, Allen D, Roche NS, Scheuenstuhl H, Spencer MM, et al. Effects of steroids and retinoids on wound healing. *Arch Surg*. 2000;135(11):1265–70. [Comparative Study].
- Yong SL, Marik P, Esposito M, Coulthard P. Supplemental perioperative steroids for surgical patients with adrenal insufficiency. *Cochrane Database Syst Rev*. 2009;(4):CD005367. [Meta-Analysis Review].
- Luqmani R, Hennell S, Estrach C, Basher D, Birrell F, Bosworth A, et al. British Society for Rheumatology and British Health Professionals in Rheumatology guideline for the management of rheumatoid arthritis (after the first 2 years). *Rheumatology (Oxford)*. 2009;48(4):436–9. [Practice Guideline Research Support, Non-U.S. Gov't].
- Kameda H, Kanbe K, Sato E, Ueki Y, Saito K, Nagaoka S, et al. Continuation of methotrexate resulted in better clinical and radiographic outcomes than discontinuation upon starting etanercept in patients with rheumatoid arthritis: 52-week results from the JESMR study. *J Rheumatol*. 2011;38(8):1585–92.
- Grennan DM, Gray J, Loudon J, Fear S. Methotrexate and early postoperative complications in patients with rheumatoid arthritis undergoing elective orthopaedic surgery. *Ann Rheum Dis*. 2001;60(3):214–7. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't].
- Carpenter MT, West SG, Vogelgesang SA, Casey Jones DE. Postoperative joint infections in rheumatoid arthritis patients on methotrexate therapy. *Orthopedics*. 1996;19(3):207–10.

20. Sanders RD, Weimann J, Maze M. Biologic effects of nitrous oxide: a mechanistic and toxicologic review. *Anesthesiology*. 2008;109(4):707–22 [Review].
21. Choy EH, Panayi GS. Cytokine pathways and joint inflammation in rheumatoid arthritis. *N Engl J Med*. 2001;344(12):907–16. [Research Support, Non-U.S. Gov't Review].
22. Dixon WG, Lunt M, Watson KD, Hyrich KL, Symmons DP. Anti-TNF therapy and the risk of serious post-operative infection: results from the BSR Biologics register (BSRBR). *Ann Rheum Dis*. 2007;66(Suppl II):118.
23. Bibbo C, Goldberg JW. Infectious and healing complications after elective orthopaedic foot and ankle surgery during tumor necrosis factor-alpha inhibition therapy. *Foot Ankle Int*. 2004;25(5):331–5. [Clinical Trial Comparative Study Controlled Clinical Trial].
24. Ding T, Ledingham J, Luqmani R, Westlake S, Hyrich K, Lunt M, et al. BSR and BHPR rheumatoid arthritis guidelines on safety of anti-TNF therapies. *Rheumatology (Oxford)*. 2010;49(11):2217–9.
25. Parvizi J, Gehrke T, Chen AF. Proceedings of the international consensus on periprosthetic joint infection. *Bone Joint J*. 2013;95-B(11):1450–2.
26. Dowsey MM, Choong PF. Early outcomes and complications following joint arthroplasty in obese patients: a review of the published reports. *ANZ J Surg*. 2008;78(6):439–44 [Review].
27. Jameson SS, Mason JM, Baker PN, Elson DW, Deehan DJ, Reed MR. The impact of body mass index on patient reported outcome measures (PROMs) and complications following primary hip arthroplasty. *J Arthroplasty*. 2014;29(10):1889–98.
28. Namba RS, Paxton L, Fithian DC, Stone ML. Obesity and perioperative morbidity in total hip and total knee arthroplasty patients. *J Arthroplasty*. 2005;20(7 Suppl 3):46–50. [Research Support, Non-U.S. Gov't].
29. 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(10):1330–8.
30. Fleischmann E, Kurz A, Niedermayr M, Schebesta K, Kimberger O, Sessler DI, et al. Tissue oxygenation in obese and non-obese patients during laparoscopy. *Obes Surg*. 2005;15(6):813–9. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.].
31. Kulkarni A, Jameson SS, James P, Woodcock S, Muller S, Reed MR. Does bariatric surgery prior to lower limb joint replacement reduce complications? *Surgeon*. 2011;9(1):18–21.
32. Freeman JT, Anderson DJ, Hartwig MG, Sexton DJ. Surgical site infections following bariatric surgery in community hospitals: a weighty concern? *Obes Surg*. 2011;21:836–40.
33. Kwiatkowski TC, Hanley Jr EN, Ramp WK. Cigarette smoking and its orthopedic consequences. *Am J Orthop (Belle Mead NJ)*. 1996;25(9):590–7 [Review].
34. Moller AM, Villebro N, Pedersen T, Tonnesen H. Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial. *Lancet*. 2002;359(9301):114–7. [Clinical Trial Multicenter Study Randomized Controlled Trial Research Support, Non-U.S. Gov't].
35. Moller AM, Pedersen T, Villebro N, Munksgaard A. Effect of smoking on early complications after elective orthopaedic surgery. *J Bone Joint Surg Br*. 2003;85(2):178–81.
36. Parvizi J, Pawasarat IM, Azzam KA, Joshi A, Hansen EN, Bozic KJ. Periprosthetic joint infection: the economic impact of methicillin-resistant infections. *J Arthroplasty*. 2010;25(6 Suppl):103–7. [Multicenter Study].
37. Bode LG, Kluytmans JA, Wertheim HF, Bogaers D, Vandendroucke-Grauls CM, Roosendaal R, et al. Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. *N Engl J Med*. 2010;362(1):9–17. [Multicenter Study Randomized Controlled Trial Research Support, Non-U.S. Gov't].
38. van Rijen MM, Bode LG, Baak DA, Kluytmans JA, Vos MC. Reduced costs for *Staphylococcus aureus* carriers treated prophylactically with mupirocin and chlorhexidine in cardiothoracic and orthopaedic surgery. *PLoS One*. 2012;7(8):e43065.
39. Schmalzried TP, Amstutz HC, Au MK, Dorey FJ. Etiology of deep sepsis in total hip arthroplasty. The significance of hematogenous and recurrent infections. *Clin Orthop Relat Res*. 1992;280:200–7.
40. Greene KA, Wilde AH, Stulberg BN. Preoperative nutritional status of total joint patients. Relationship to postoperative wound complications. *J Arthroplasty*. 1991;6(4):321–5.
41. Leaper D, Burman-Roy S, Palanca A, Cullen K, Worster D, Gautam-Aitken E, et al. Prevention and treatment of surgical site infection: summary of NICE guidance. *BMJ*. 2008;337:a1924. [Research Support, Non-U.S. Gov't].
42. Webster J, Osborne S. Preoperative bathing or showering with skin antiseptics to prevent surgical site infection. *Cochrane Database Syst Rev*. 2006;(2):CD004985. [Meta-Analysis Review].
43. Jakobsson J, Perlkvist A, Wann-Hansson C. Searching for evidence regarding using preoperative disinfection showers to prevent surgical site infections: a systematic review. *Worldviews Evid Based Nurs*. 2010;28.
44. Excellence NifHaC. Surgical site infection: evidence Update June 2013. 2013 [07/05/2015]; Available from: <http://www.evidence.nhs.uk/document?ci=http%3A%2F%2Farms.evidence.nhs.uk%2Fresources%2FHub%2F1006598&q=Surgical%20site%20infection%20evidence%20update&ReturnUrl=%2Fsearch%3Fq%3DSurgical%2Bsite%2Binfection%2Bevidence%2Bupdate>.
45. Tanner J, Woodings D, Moncaster K. Preoperative hair removal to reduce surgical site infection.

- Cochrane Database Syst Rev. 2006;(3):CD004122. [Meta-Analysis Review].
46. van der Horst MW, Wiewel ELVVM, van der Hoeven CWP, Loer SA, Boer C. Preoperative warming reduces the incidence of hypothermia in total hip- and knee replacement surgery under spinal anesthesia. *Eur J Anaesthesiol.* 2010;27(47):7.
  47. Just B, Trevien V, Delva E, Lienhart A. Prevention of intraoperative hypothermia by preoperative skin-surface warming. *Anesthesiology.* 1993;79(2):214–8.
  48. 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(9285):876–80. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't].
  49. Classen DC, Evans RS, Pestotnik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *N Engl J Med.* 1992;326(5):281–6. [Clinical Trial Randomized Controlled Trial Research Support, U.S. Gov't, P.H.S.].
  50. Prokuski L, Clyburn TA, Evans RP, Moucha CS. Prophylactic antibiotics in orthopaedic surgery. *Instr Course Lect.* 2011;60:545–55.
  51. Hanssen AD, Osmon DR. Prevention of deep wound infection after total hip arthroplasty: the role of prophylactic antibiotics and clean air technology. *Semin Arthroplasty.* 1994;5(3):114–21 [Review].
  52. AlBuhairan B, Hind D, Hutchinson A. Antibiotic prophylaxis for wound infections in total joint arthroplasty: a systematic review. *J Bone Joint Surg Br.* 2008;90(7):915–9. [Meta-Analysis Review].
  53. Jenkins PJ, Teoh K, Simpson PM, Dave J, Simpson AH, Breusch S. *Clostridium difficile* in patients undergoing primary hip and knee replacement. *J Bone Joint Surg Br.* 2010;92(7):994–8.
  54. Engesaeter LB, Lie SA, Espehaug B, Furnes O, Vollset SE, Havelin LI. Antibiotic prophylaxis in total hip arthroplasty: effects of antibiotic prophylaxis systemically and in bone cement on the revision rate of 22,170 primary hip replacements followed 0-14 years in the Norwegian Arthroplasty Register. *Acta Orthop Scand.* 2003;74(6):644–51.
  55. Wang J, Zhu C, Cheng T, Peng X, Zhang W, Qin H, et al. A systematic review and meta-analysis of antibiotic-impregnated bone cement use in primary total hip or knee arthroplasty. *PLoS One.* 2013;8(12), e82745.
  56. Hansen EN, Adeli B, Kenyon R, Parvizi J. Routine use of antibiotic laden bone cement for primary total knee arthroplasty: impact on infecting microbial patterns and resistance profiles. *J Arthroplasty.* 2014;29(6):1123–7.
  57. Merollini KM, Crawford RW, Whitehouse SL, Graves N. Surgical site infection prevention following total hip arthroplasty in Australia: a cost-effectiveness analysis. *Am J Infect Control.* 2013;41(9):803–9.
  58. Swoboda SM, Merz C, Kostuik J, Trentler B, Lipsett PA. Does intraoperative blood loss affect antibiotic serum and tissue concentrations? *Arch Surg.* 1996;131(11):1165–71. discussion 71-2.
  59. Mauerhan DR, Nelson CL, Smith DL, Fitzgerald Jr RH, Slama TG, Petty RW, et al. Prophylaxis against infection in total joint arthroplasty. One day of cefuroxime compared with three days of cefazolin. *J Bone Joint Surg Am.* 1994;76(1):39–45. [Clinical Trial Comparative Study Multicenter Study Randomized Controlled Trial Research Support, Non-U.S. Gov't].
  60. Hawn MT, Richman JS, Vick CC, Deierhoi RJ, Graham LA, Henderson WG, et al. Timing of surgical antibiotic prophylaxis and the risk of surgical site infection. *JAMA Surg.* 2013;148(7):649–57.
  61. Bannister GC, Auchincloss JM, Johnson DP, Newman JH. The timing of tourniquet application in relation to prophylactic antibiotic administration. *J Bone Joint Surg Br.* 1988;70(2):322–4. [Research Support, Non-U.S. Gov't].
  62. Challagundla SR, Knox D, Hawkins A, Hamilton D, W V Flynn R, Robertson S, et al. Renal impairment after high-dose flucloxacillin and single-dose gentamicin prophylaxis in patients undergoing elective hip and knee replacement. *Nephrol Dial Transplant.* 2013;28(3):612–9.
  63. Ross AD, Boscainos PJ, Malhas A, Wigderowitz C. Peri-operative renal morbidity secondary to gentamicin and flucloxacillin chemoprophylaxis for hip and knee arthroplasty. *Scott Med J.* 2013;58(4):209–12.
  64. Bailey O, Torkington MS, Anthony I, Wells J, Blyth M, Jones B. Antibiotic-related acute kidney injury in patients undergoing elective joint replacement. *Bone Joint J.* 2014;96-B(3):395–8.
  65. Craxford S, Bayley E, Needoff M. Antibiotic-associated complications following lower limb arthroplasty: a comparison of two prophylactic regimes. *Eur J Orthop Surg Traumatol.* 2014;24(4):539–43.
  66. Sewick A, Makani A, Wu C, O'Donnell J, Baldwin KD, Lee GC. Does dual antibiotic prophylaxis better prevent surgical site infections in total joint arthroplasty? *Clin Orthop Relat Res.* 2012;470(10):2702–7.
  67. Sprowson A, Symes T, Khan SK, Oswald T, Reed MR. Changing antibiotic prophylaxis for primary joint arthroplasty affects postoperative complication rates and bacterial spectrum. *Surgeon.* 2013;11(1):20–4.
  68. World Health Organization. Surgical care at the district hospital. <http://www.who.int/surgery/publications/en/SCDH.pdf?ua=1> (date last accessed 18 March 2016).
  69. Scaltriti S, Cencetti S, Rovesti S, Marchesi I, Bargellini A, Borella P. Risk factors for particulate and microbial contamination of air in operating theatres. *J Hosp Infect.* 2007;66(4):320–6. [Research Support, Non-U.S. Gov't].
  70. Parienti JJ, Thibon P, Heller R, Le Roux Y, von Theobald P, Bensadoun H, et al. Hand-rubbing

- with an aqueous alcoholic solution vs traditional surgical hand-scrubbing and 30-day surgical site infection rates: a randomized equivalence study. *JAMA*. 2002;288(6):722–7. [Clinical Trial Comparative Study Randomized Controlled Trial Research Support, Non-U.S. Gov't].
71. Tanner J, Swarbrook S, Stuart J. Surgical hand antisepsis to reduce surgical site infection. *Cochrane Database Syst Rev*. 2008(1):CD004288. [Meta-Analysis Review].
72. Jarral OA, McCormack DJ, Ibrahim S, Shipolini AR. Should surgeons scrub with chlorhexidine or iodine prior to surgery? *Interact Cardiovasc Thorac Surg*. 2011;12:1017–21.
73. Mahadeva D, Rankin KS, Muller SD. Skin moisturisers and surgical site preparation: a slippery problem? *J Hosp Infect*. 2007;67(4):386–8. [Letter Research Support, Non-U.S. Gov't].
74. Darouiche RO, Wall Jr MJ, Itani KM, Otterson MF, Webb AL, Carrick MM, et al. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. *N Engl J Med*. 2010;362(1):18–26. [Multicenter Study Randomized Controlled Trial].
75. Raja SG, Rochon M, Jarman JW. Brompton Harefield Infection Score (BHIS): development and validation of a stratification tool for predicting risk of surgical site infection after coronary artery bypass grafting. *Int J Surg*. 2015;16(Pt A):69–73.
76. U.S.-National-Institutes-of-Health. *ClinicalTrials.org*. 2015 [16/09/15]; Available from: <https://clinicaltrials.gov/ct2/results?term=skin+preparation&Search=Search>.
77. Lidwell OM. Air, antibiotics and sepsis in replacement joints. *J Hosp Infect*. 1988;11 Suppl C:18–40 [Review].
78. Whyte W. The role of clothing and drapes in the operating room. *J Hosp Infect*. 1988;11 Suppl C:2–17. [Review].
79. Noble WC. Dispersal of skin microorganisms. *Br J Dermatol*. 1975;93(4):477–85 [Review].
80. Hansen D, Krabs C, Benner D, Brauksiepe A, Popp W. Laminar air flow provides high air quality in the operating field even during real operating conditions, but personal protection seems to be necessary in operations with tissue combustion. *Int J Hyg Environ Health*. 2005;208(6):455–60.
81. Lidwell OM, Elson RA, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, et al. Ultraclean air and antibiotics for prevention of postoperative infection. A multicenter study of 8,052 joint replacement operations. *Acta Orthop Scand*. 1987;58(1):4–13. [Clinical Trial Research Support, Non-U.S. Gov't].
82. Brandt C, Hott U, Sohr D, Daschner F, Gastmeier P, Ruden 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(5):695–700. [Comment Multicenter Study Research Support, Non-U.S. Gov't].
83. Hooper GJ, Rothwell AG, Frampton C, Wyatt MC. Does the use of laminar flow and space suits reduce early deep infection after total hip and knee replacement?: the ten-year results of the New Zealand Joint Registry. *J Bone Joint Surg Br*. 2011;93(1):85–90.
84. Zheng H, Barnett AG, Merollini K, Sutton A, Cooper N, Berendt T, et al. Control strategies to prevent total hip replacement-related infections: a systematic review and mixed treatment comparison. *BMJ Open*. 2014;4(3), e003978.
85. McGovern PD, Reed MR. Forced air warming and ultra-clean ventilation do not mix: an investigation of theatre ventilation, patient warming and joint replacement infection in orthopaedics. *J Bone Joint Surg Br*. 2011;93(11):1537–44.
86. Wood AM, Moss C, Keenan A, Reed MR, Leaper DJ. Infection control hazards associated with the use of forced-air warming in operating theatres. *J Hosp Infect*. 2014;88(3):132–40.
87. Demircay E, Unay K, Bilgili MG, Alataca G. Glove perforation in hip and knee arthroplasty. *J Orthop Sci*. 2010;15(6):790–4.
88. Chan KY, Singh VA, Oun BH, To BH. The rate of glove perforations in orthopaedic procedures: single versus double gloving. A prospective study. *Med J Malaysia*. 2006;61:3–7 Suppl B.
89. Al-Maiyah M, Bajwa A, Mackenney P, Port A, Gregg PJ, Hill D, et al. Glove perforation and contamination in primary total hip arthroplasty. *J Bone Joint Surg Br*. 2005;87(4):556–9. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't].
90. Mingoli A, Sapienza P, Sgarzini G, Luciani G, De Angelis G, Modini C, et al. Influence of blunt needles on surgical glove perforation and safety for the surgeon. *Am J Surg*. 1996;172(5):512–6; discussion 6–7. [Clinical Trial Comparative Study Randomized Controlled Trial].
91. Wright KU, Moran CG, Briggs PJ. Glove perforation during hip arthroplasty. A randomised prospective study of a new taperpoint needle. *J Bone Joint Surg Br*. 1993;75(6):918–20. [Clinical Trial Comparative Study Randomized Controlled Trial].
92. Tanner J, Parkinson H. Double gloving to reduce surgical cross-infection. *Cochrane Database Syst Rev*. 2006;(3):CD003087. [Meta-Analysis Review].
93. Newman JB, Bullock M, Goyal R. Comparison of glove donning techniques for the likelihood of gown contamination. An infection control study. *Acta Orthop Belg*. 2007;73(6):765–71.
94. Aldlyami E, Kulkarni A, Reed MR, Muller SD, Partington PF. Latex-free gloves: safer for whom? *J Arthroplasty*. 2010;25(1):27–30.
95. Webster J, Alghamdi AA. Use of plastic adhesive drapes during surgery for preventing surgical site infection. *Cochrane Database Syst Rev*. 2007(4):CD006353. [Meta-Analysis Review].

96. 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(10):798–801. [Clinical Trial Randomized Controlled Trial].
97. Davis N, Curry A, Gambhir AK, Panigrahi H, Walker CR, Wilkins EG, et al. Intraoperative bacterial contamination in operations for joint replacement. *J Bone Joint Surg Br.* 1999;81(5):886–9.
98. Hope PG, Kristinsson KG, Norman P, Elson RA. Deep infection of cemented total hip arthroplasties caused by coagulase-negative staphylococci. *J Bone Joint Surg Br.* 1989;71(5):851–5.
99. Taylor GJ, Leeming JP, Bannister GC. Effect of antiseptics, ultraviolet light and lavage on airborne bacteria in a model wound. *J Bone Joint Surg Br.* 1993;75(5):724–30.
100. Taylor GJ, Bannister GC, Calder S. Perioperative wound infection in elective orthopaedic surgery. *J Hosp Infect.* 1990;16(3):241–7.
101. 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 (Phila Pa 1976).* 2005;30(15):1689–93.
102. Brown NM, Cipriano CA, Moric M, Sporer SM, Della Valle CJ. Dilute betadine lavage before closure for the prevention of acute postoperative deep periprosthetic joint infection. *J Arthroplasty.* 2012;27(1):27–30.
103. Sessler DI, Akca O. Nonpharmacological prevention of surgical wound infections. *Clin Infect Dis.* 2002;35(11):1397–404. [Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.].
104. Sessler DI. Complications and treatment of mild hypothermia. *Anesthesiology.* 2001;95(2):531–43. [Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S. Review].
105. Flores-Maldonado A, Medina-Escobedo CE, Rios-Rodriguez HM, Fernandez-Dominguez R. Mild perioperative hypothermia and the risk of wound infection. *Arch Med Res.* 2001;32(3):227–31.
106. <https://www.nice.org.uk/guidance/cg65>.
107. Babior BM. The respiratory burst of phagocytes. *J Clin Invest.* 1984;73(3):599–601. [Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S. Review].
108. Pryor KO, Fahey 3rd TJ, 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(1):79–87. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't].
109. Belda FJ, Aguilera L, Garcia de la Asuncion J, Alberti J, Vicente R, Ferrandiz L, et al. Supplemental perioperative oxygen and the risk of surgical wound infection: a randomized controlled trial. *JAMA.* 2005;294(16):2035–42. [Clinical Trial Randomized Controlled Trial Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.].
110. Greif R, Akca O, Horn EP, Kurz A, Sessler DI. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. *N Engl J Med.* 2000;342(3):161–7. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.].
111. Arkllic CF, Taguchi A, Sharma N, Ratnaraj J, Sessler DI, Read TE, et al. Supplemental perioperative fluid administration increases tissue oxygen pressure. *Surgery.* 2003;133(1):49–55. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.].
112. Mauermann WJ, Nemergut EC. The anesthesiologist's role in the prevention of surgical site infections. *Anesthesiology.* 2006;105(2):413–21; quiz 39–40. [Review].
113. Chang CC, Lin HC, Lin HW. Anesthetic management and surgical site infections in total hip or knee replacement: a population-based study. *Anesthesiology.* 2010;113(2):279–84.
114. Sanders RD, Hussell T, Maze M. Sedation & immunomodulation. *Crit Care Clin.* 2009;25(3):551–70, ix. [Review].
115. Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F, et al. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. *JAMA.* 2009;301(5):489–99. [Comparative Study Multicenter Study Randomized Controlled Trial Research Support, Non-U.S. Gov't].
116. Dalfino L, Giglio MT, Puntillo F, Marucci M, Brienza N. Haemodynamic goal-directed therapy and postoperative infections: earlier is better. A systematic review and meta-analysis. *Crit Care.* 2011;15(3):R154.
117. Myers E, O'Grady P, Dolan AM. The influence of preclinical anaemia on outcome following total hip replacement. *Arch Orthop Trauma Surg.* 2004;124(10):699–701.
118. Morales CH, Escobar RM, Villegas MI, Castano A, Trujillo J. Surgical site infection in abdominal trauma patients: risk prediction and performance of the NNIS and SENIC indexes. *Can J Surg.* 2011;54(1):17–24. [Comparative Study Evaluation Studies].
119. Alexander JW, Solomkin JS, Edwards MJ. Updated recommendations for control of surgical site infections. *Ann Surg.* 2011;253(6):1082–93 [Review].
120. Steinitz D, Harvey EJ, Leighton RK, Petrie DP. Is homologous blood transfusion a risk factor for infection after hip replacement? *Can J Surg.* 2001;44(5):355–8. [Clinical Trial].
121. Kendall SJ, Weir J, Aspinall R, Henderson D, Rosson J. Erythrocyte transfusion causes immunosuppression after total hip replacement. *Clin Orthopaedics Relat Res.* 2000;(381):145–55. [Research Support, Non-U.S. Gov't].
122. Foundation TH. Cutting the need for blood transfusions in knee and hip replacement surgery. 2013 [07/05/2015];

Available from: [http://www.health.org.uk/public/cms/75/76/4780/3092/Could%20quality%20be%20cheaper\\_Airedale%20NHS%20Foundation%20Trust%20case%20study.pdf?realName=52EQeC.pdf](http://www.health.org.uk/public/cms/75/76/4780/3092/Could%20quality%20be%20cheaper_Airedale%20NHS%20Foundation%20Trust%20case%20study.pdf?realName=52EQeC.pdf).

123. Sukeik M, Alshryda S, Haddad FS, Mason JM. Systematic review and meta-analysis of the use of tranexamic acid in total hip replacement. *J Bone Joint Surg Br.* 2011;93(1):39–46. [Meta-Analysis Review].
124. Bilgin YM, van de Watering LM, Eijssman L, Versteegh MI, Brand R, van Oers MH, et al. Double-blind, randomized controlled trial on the effect of leukocyte-depleted erythrocyte transfusions in cardiac valve surgery. *Circulation.* 2004;109(22):2755–60.
125. Cochrane-Library. Wound drains in orthopaedic surgery (surgery on the joints or limbs). 2008 [07/05/2015]; Available from: [http://www.cochrane.org/CD001825/MUSKINJ\\_wound-drains-in-orthopaedic-surgery--surgery-on-the-joints-or-limbs](http://www.cochrane.org/CD001825/MUSKINJ_wound-drains-in-orthopaedic-surgery--surgery-on-the-joints-or-limbs).
126. The-Cochrane-Library. No recommendations regarding type of wound dressing for the prevention of surgical site infection. 2014; Available from: [http://www.cochrane.org/CD003091/WOUNDS\\_no-recommendations-regarding-type-of-wound-dressing-for-the-prevention-of-surgical-site-infection](http://www.cochrane.org/CD003091/WOUNDS_no-recommendations-regarding-type-of-wound-dressing-for-the-prevention-of-surgical-site-infection).
127. Jameson SS, Charman S, Reed MR, Gregg PJ, Van der Meulen J. The effect of aspirin and LMWH on venous thromboembolism after hip replacement: a non-randomised comparison in the National Joint Registry. *J Bone Joint Surg Br.* 2011;93(11):1465–70.
128. Patel VP, Walsh M, Sehgal B, Preston C, DeWal H, Di Cesare PE. Factors associated with prolonged wound drainage after primary total hip and knee arthroplasty. *J Bone Joint Surg Am.* 2007;89(1):33–8.
129. Jensen CD, Steval A, Partington PF, Reed MR, Muller SD. Return to theatre following total hip and knee replacement, before and after the introduction of rivaroxaban: a retrospective cohort study. *J Bone Joint Surg Br.* 2011;93(1):91–5.
130. Tong D, Theis JC. Antibiotic prophylaxis and invasive dental treatment in prosthetic joint patients. *N Z Med J.* 2008;121(1280):45–52.
131. Oswald TF, Gould FK. Dental treatment and prosthetic joints: antibiotics are not the answer! *J Bone Joint Surg Br.* 2008;90(7):825–6. [Comment Editorial].
132. Slover JD, Phillips MS, Iorio R, Bosco J. Is routine antibiotic prophylaxis cost effective for total joint replacement patients? *J Arthroplasty.* 2015;30(4):543–6.
133. Frampton L. The value of SSI surveillance. *Clin Serv J.* 2013:43–6. [http://www.icnetplc.com/files/icnetplc/case-study/official\\_copy\\_-\\_the\\_value\\_of\\_ssi\\_surveillance.docx.pdf](http://www.icnetplc.com/files/icnetplc/case-study/official_copy_-_the_value_of_ssi_surveillance.docx.pdf).