SIGN
Scottish Intercollegiate Guidelines Network

NHS
Quality Improvement Scotland

104

Antibiotic prophylaxis in surgery

A national clinical guideline

July 2008

KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1^{++}	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1^{+}	Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1^{-}	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2^{++}	High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2^{+}	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2^{-}	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, eg case reports, case series
4	Expert opinion

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A	At least one meta-analysis, systematic review, or RCT rated as 1^{++}, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1^{+}, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2^{++}, directly applicable to the target population, and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 1^{++} or 1^{+}
C	A body of evidence including studies rated as 2^{+}, directly applicable to the target population and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 2^{++}
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2^{+}

GOOD PRACTICE POINTS

☑	Recommended best practice based on the clinical experience of the guideline development group.

NHS Quality Improvement Scotland (NHS QIS) is committed to equality and diversity. This guideline has been assessed for its likely impact on the six equality groups defined by age, disability, gender, race, religion/belief, and sexual orientation.

For the full equality and diversity impact assessment report please see the "published guidelines" section of the SIGN website at **www.sign.ac.uk/guidelines/published/numlist.html**. The full report in paper form and/or alternative format is available on request from the NHS QIS Equality and Diversity Officer.

Every care is taken to ensure that this publication is correct in every detail at the time of publication. However, in the event of errors or omissions corrections will be published in the web version of this document, which is the definitive version at all times. This version can be found on our web site **www.sign.ac.uk**

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ISBN 978 1 905813 34 6

Published July 2008

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1 Introduction

1.1 THE NEED FOR A GUIDELINE

The first Scottish Intercollegiate Guidelines Network (SIGN) guideline on antibiotic prophylaxis in surgery (SIGN 45)[1] was published in July 2000 to provide evidence based recommendations to reduce inappropriate prophylactic antibiotic prescribing. Evidence from the Scottish Surveillance of Healthcare Associated Infection Programme (SSHAIP) on surgical site infection indicates a high compliance with the guideline's recommendations.[2] The original guideline addressed risk factors for surgical site infection (SSI), benefits and risks of antibiotic prophylaxis, indications for surgical antibiotic prophylaxis as well as recommendations on administration of intravenous prophylactic antibodies.

A review was considered timely in light of the ever increasing need to use antibiotics wisely, complicated by the increasing prevalence of more resistant organisms such as meticillin-resistant *Staphylococcus aureus* (MRSA).

This update is an opportunity to expand and review the evidence base supporting the recommendations and to widen the range of surgical procedures covered. New topics include non-intravenous routes of administration and multiresistant carriage in patients undergoing surgery. SIGN 45 made recommendations for antibiotic prophylaxis in adults. Recommendations for common surgical procedures in children have been included in this guideline.

1.1.1 UPDATING THE EVIDENCE

The guideline is based on a series of key questions that form the basis of the systematic literature search. Key questions were posed to update all sections of SIGN 45 as well as new topics *(see Annex 1)*. Where no new evidence was identified to support an update, the guideline text and recommendations are reproduced verbatim from SIGN 45. The original supporting evidence was not re-appraised by the current guideline development group.

The evidence in SIGN 45 was appraised using an earlier grading system. Details of how the grading system was translated to SIGN's current grading system are available on the SIGN website (**www.sign.ac.uk**).

1.2 REMIT OF THE GUIDELINE

1.2.1 OVERALL OBJECTIVES

The goals of prophylactic administration of antibiotics to surgical patients are to:

- reduce the incidence of surgical site infection
- use antibiotics in a manner that is supported by evidence of effectiveness
- minimise the effect of antibiotics on the patient's normal bacterial flora
- minimise adverse effects
- cause minimal change to the patient's host defences.

It is important to emphasise that surgical antibiotic prophylaxis is an adjunct to, not a substitute for, good surgical technique. Antibiotic prophylaxis should be regarded as one component of an effective policy for the control of healthcare associated infection.

Most of the recommendations in this guideline apply to elective surgery but some emergency operations are included (*see section 3.1.2*).

The guideline is not intended to provide every surgical specialty with a comprehensive text on preventing SSI, but rather to provide the evidence for current practice pertaining to antibiotic use, and to provide a framework for audit and economic evaluation.

The prevention of SSI by antibiotics encompasses a range of procedures and routes of administration (oral, intramuscular, topical) but most evidence relates to the intravenous route.

The risk factors for surgical site infection, the benefits and risks of antibiotic prophylaxis and the general principles of antibiotic administration described in this guideline are based on evidence in adults, but apply equally to children. If the evidence is not applicable it has been stated in the text.

The guideline does **not** cover the following:

- prevention of endocarditis after surgery or instrumentation (this is already covered by a UK guideline which is regularly updated)[3]
- use of antiseptics for the prevention of wound infection after elective surgery
- treatment of anticipated infection in patients undergoing emergency surgery for contaminated or dirty operations
- administration of oral antibiotics for bowel preparation or to achieve selective decontamination of the gut
- most topical antibiotic administration, for example, in wounds or for perineal lavage
- use of antibiotics for prophylaxis in patients with prosthetic implants undergoing dental surgery or other surgery that may cause bacteraemia
- transplant surgery.

1.2.2 BACKGROUND

The term surgical site infection is used to encompass the surgical wound and infections involving the body cavity, bones, joints, meninges and other tissues involved in the operation (*see Annexes 2 and 3*). In procedures that require the insertion of implants or prosthetic devices the term also encompasses infections associated with these devices. Throughout this guideline the term surgical site infection (SSI) is used, unless the evidence relates specifically to surgical wound infection.

Prophylactic administration of antibiotics inhibits growth of contaminating bacteria,[4-6] and their adherence to prosthetic implants, thus reducing the risk of infection. In a survey of antibiotic use in one district general hospital in 1978, this indication accounted for approximately one third of all antibiotics prescribed.[7] Data to update this finding were not identified. Administration of antibiotics also increases the prevalence of antibiotic-resistant bacteria,[8] and predisposes the patient to infection with organisms such as *Clostridium difficile*, a cause of antibiotic-associated colitis.[9]

SSI is one of the most common healthcare associated infections (HAI), with one UK study from 2001 showing the consequences to be an average additional hospital stay of 6.5 days at a cost of £3,246 per patient.[10] The consequences for the patient include a longer and more painful stay in hospital. SSI is an important outcome measure for surgical procedures.

National mandatory surveillance of SSI was introduced in the UK from 2002 and results indicate the incidence of SSI varies by clinical procedure.[2] Of the seven categories of surgery included, operations for fractured neck of femur led to infection most frequently (2.5%) and knee replacements least frequently (0.7%). These data also suggest that up to 70% of SSIs occur after discharge from hospital. The latest prevalence survey of HAI in Scotland indicated that SSIs were the second most common type of HAI, accounting for 16%.[11]

1.2.3 TARGET USERS OF THE GUIDELINE

This guideline will be of interest to surgeons, anaesthetists, theatre nurses, pharmacists, radiologists, microbiologists, infection control nurses, specialists in public health, specialists in clinical effectiveness and clinical governance, and general practitioners.

1.3 DEFINITIONS

Prophylactic antibiotic treatment	The use of antibiotics before, during, or after a diagnostic, therapeutic, or surgical procedure to prevent infectious complications.[12]
Therapeutic antibiotic treatment	The use of substances that reduce the growth or reproduction of bacteria, including eradication therapy.[13] This term is used to describe antimicrobial therapy prescribed to clear infection by an organism or to clear an organism that is colonising a patient but is not causing infection.

1.4 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

1.4.1 ADDITIONAL ADVICE TO NHSSCOTLAND FROM NHS QUALITY IMPROVEMENT SCOTLAND AND THE SCOTTISH MEDICINES CONSORTIUM

NHS QIS processes multiple technology appraisals (MTAs) for NHSScotland that have been produced by the National Institute for Health and Clinical Excellence (NICE) in England and Wales.

The Scottish Medicines Consortium (SMC) provides advice to NHS Boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and any major new indications for established products.

No SMC advice or NHS QIS validated NICE MTAs relevant to this guideline were identified.

2 Key recommendations

The following recommendations were highlighted by the guideline development group as being clinically very important. They are the key clinical recommendations that should be prioritised for implementation. The clinical importance of these recommendations is not dependent on the strength of the supporting evidence.

The key recommendations were identified using a web based Delphi Decision Aid (http://armstrong.wharton.upenn.edu/delphi2/). Guideline development group members scored recommendations and good practice points on the general principles of antibiotic prophylaxis from 0 to 10 (with 0 being least important and 10 most important). Recommendations for specific surgical interventions (*see section 5*) were not included. The mean scores were calculated and recommendations achieving over 75% of the maximum score were identified as key. Eleven of the 35 guideline development group members responded covering the specialities of clinical effectiveness, clinical microbiology, hepatobiliary surgery, implementation, infection control, obstetrics, paediatric anaesthetics, pharmaceutical public health, and radiology.

2.1 BENEFITS AND RISKS OF ANTIBIOTIC PROPHYLAXIS

C **Patients with a history of anaphylaxis, laryngeal oedema, bronchospasm, hypotension, local swelling, urticaria or pruritic rash, occurring immediately after a penicillin therapy are potentially at increased risk of immediate hypersensitivity to beta-lactams and should not receive prophylaxis with a beta-lactam antibiotic.**

☑ Local policies for surgical prophylaxis that recommend beta-lactam antibiotics as first line agents should also recommend an alternative for patients with allergy to penicillins or cephalosporins.

These recommendations are important for patient safety. The risk of penicillin hypersensitivity is important and failure to implement these recommendations may have clinically-disastrous results. Another issue is over-diagnosis of an allergy, resulting in failure to use a beta-lactam when it would have been suitable.

D **The duration of prophylactic antibiotic therapy should be single dose except in special circumstances** *(for example, prolonged surgery, major blood loss or as indicated in sections 5.2, 5.3 and 6.4)***.**

There is still a tendency to give prolonged courses of antibiotics. This recommendation is important to prevent over-prescribing, but if a second dose were administered there would be no major consequences for the patient.

2.2 ADMINISTRATION OF PROPHYLACTIC ANTIBIOTICS

C **The antibiotics selected for prophylaxis must cover the expected pathogens for that operative site.**

☑ The choice of antibiotic should take into account local resistance patterns.

Although it appears self evident that the antimicrobial agent chosen should be suitable for the organisms likely to be encountered, it is easily forgotten in routine prescribing.

☑ A single standard therapeutic dose of antibiotic is sufficient for prophylaxis under most circumstances.

2.3 IMPLEMENTING THE GUIDELINE

- ☑ All aspects of antibiotic prophylaxis, for example, where prophylaxis is not given when recommended, should be clearly recorded in the case records.

- ☑ Locally agreed protocols should clearly indicate where to document antibiotic prophylaxis in the patient records *(for example, the "once only" section of the drug chart, integrated care pathway or anaesthetic chart).*

- ☑ Recording the minimum data set will facilitate audit of the appropriateness of surgical antibiotic prophylaxis.

Recording antibiotic prophylaxis is a legal requirement, although it is not always done. These recommendations will ensure that it is a routine part of local audit and risk management.

3 Risk factors for surgical site infection

3.1 FACTORS AFFECTING THE INCIDENCE OF SURGICAL SITE INFECTION

There are many risk factors for SSI, which can be classified as patient or operation characteristics (*see Table 1*).[14]

Table 1 Factors that influence the risk of SSI[14]

	Risk factor
Patient	Extremes of age
	Poor nutritional state
	Obesity (> 20% ideal body weight)
	Diabetes mellitus
	Smoking
	Coexisting infections at other sites
	Bacterial colonisation (eg nares colonisation with *S. aureus*)
	Immunosuppression (steroid or other immunosuppressive drug use)
	Prolonged postoperative stay
Operation	Length of surgical scrub
	Skin antisepsis
	Preoperative shaving
	Preoperative skin preparation
	Length of operation
	Antimicrobial prophylaxis
	Operating theatre ventilation
	Inadequate instrument sterilisation
	Foreign material in surgical site
	Surgical drains
	Surgical technique including haemostasis, poor closure, tissue trauma
	Postoperative hypothermia[15]

The US Centres for Disease Control's (CDC) NNIS (National Nosocomial Infections Surveillance) risk index is the method of risk adjustment most widely used internationally.[16] Risk adjustment is based on three major risk factors:

- the American Society of Anesthesiologists (ASA) score, reflecting the patient's state of health before surgery[17]
- wound class, reflecting the state of contamination of the wound
- duration of operation, reflecting technical aspects of the surgery.

3.1.1 COMORBIDITIES/ASA SCORE

The American Society of Anesthesiologists has devised a preoperative risk score based on the presence of comorbidities at the time of surgery (*see Table 2*).[17] An ASA score > 2 is associated with increased risk of wound infection and this risk is additional to that of classification of operation and duration of surgery.[16]

Table 2 ASA classification of physical status[17]

ASA score	Physical status
1	A normal healthy patient
2	A patient with a mild systemic disease
3	A patient with a severe systemic disease that limits activity, but is not incapacitating
4	A patient with an incapacitating systemic disease that is a constant threat to life
5	A moribund patient not expected to survive 24 hours with or without operation

3.1.2 WOUND CLASS

Operations can be categorised into four classes (*see Table 3*) with an increasing incidence of bacterial contamination and subsequent incidence of postoperative infection.[16]

Table 3 Classification of operation[16]

Class	Definition
Clean	Operations in which no inflammation is encountered and the respiratory, alimentary or genitourinary tracts are not entered. There is no break in aseptic operating theatre technique.
Clean-contaminated	Operations in which the respiratory, alimentary or genitourinary tracts are entered but without significant spillage.
Contaminated	Operations where acute inflammation (without pus) is encountered, or where there is visible contamination of the wound. Examples include gross spillage from a hollow viscus during the operation or compound/ open injuries operated on within four hours.
Dirty	Operations in the presence of pus, where there is a previously perforated hollow viscus, or compound/open injuries more than four hours old.

This guideline applies to all elective operations in the clean, clean-contaminated or contaminated categories. Recommendations for prophylaxis of emergency surgery are limited to clean operations (for example, emergency repair of abdominal aortic aneurysm or open fixation of a closed fracture) and clean-contaminated operations (for example emergency caesarean section and facial trauma).

The guideline development group considered that antibiotic therapy for emergency operations with contaminated or dirty wounds is standard therapy rather than prophylaxis and as such is beyond the scope of this guideline.

3.1.3 DURATION OF SURGERY

Duration of surgery is positively associated with risk of wound infection and this risk is additional to that of the classification of operation.[16] In this study operations that lasted longer than the 75th percentile for the procedure were classified as prolonged.

3.1.4 EXTRINSIC RISK FACTORS

Guidelines for the prevention of SSI, outlining optimum practice, have been published by the CDC.[14] Extrinsic risks or patient care practices include preoperative skin care, perioperative practices and postoperative wound care (*see Table 1).*

3.1.5 PROCEDURE SPECIFIC RISKS

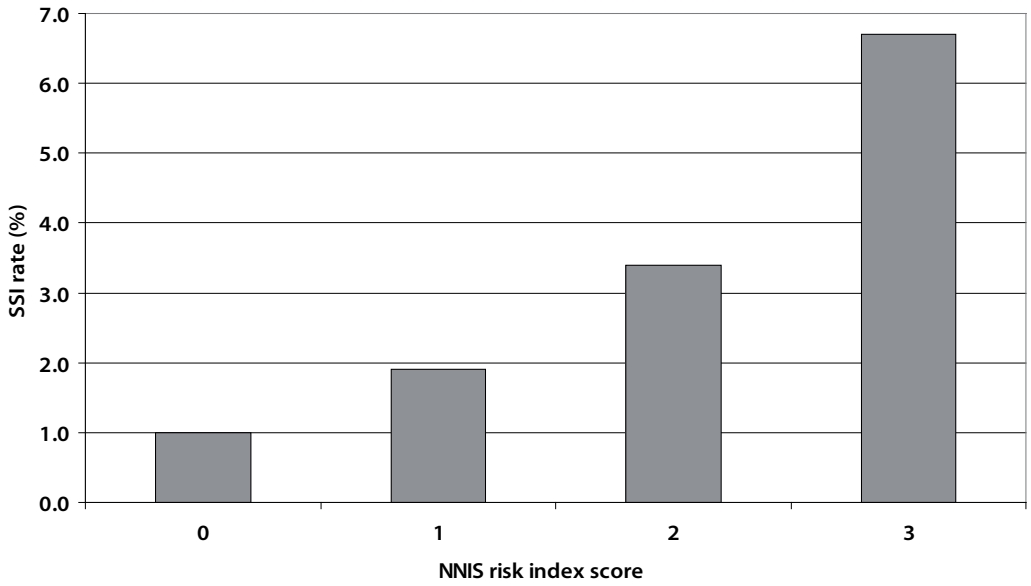
Some surgical procedures are associated with specific risks, for example, the insertion of an orthopaedic implant increases the risk of SSI.[18] Procedures performed endoscopically have been associated with a lower risk of infection.[18]

3.2 PROBABILITY OF SURGICAL SITE INFECTION

Previous guidelines have referred to patients who are at high risk of SSI but have not provided clear information about prediction of risk. This section is intended to illustrate how comorbidity, wound class and duration of operation add to the risk defined by type of operative wound.

The NNIS risk index is scored as zero, one, two or three according to the number of risks present (ASA score, wound class, duration of operation). The infection rate increases with increasing risk score (*see Figure 1*).[16]

Figure 1 SSI rate with increasing NNIS risk index score



The aim of this guideline is to identify the operations for which routine prophylaxis is supported by evidence. However, the ultimate decision rests with the surgeon's assessment of risk and benefit. Giving prophylaxis to patients who are having procedures for which this guideline does not recommend prophylaxis can be justified if the surgeon believes the patient to be at particularly high risk from SSI. In this case the criteria used for risk assessment should be recorded (*see section 8.4.2*).

4 Benefits and risks of antibiotic prophylaxis

☑ The final decision regarding the benefits and risks of prophylaxis for an individual patient will depend on:

- the patient's risk of SSI
- the potential severity of the consequences of SSI
- the effectiveness of prophylaxis in that operation (*see section 5*)
- the consequences of prophylaxis for that patient (*for example, increased risk of colitis*).

4.1 BENEFITS OF PROPHYLAXIS

In many ways, the value of surgical antibiotic prophylaxis in terms of the incidence of SSI after elective surgery is related to the severity of the consequences of SSI. For example, in the presence of an anastomosis of the colon, prophylaxis reduces postoperative mortality.[19] In total hip replacement surgery prophylaxis reduces long term postoperative morbidity.[20] For most operations, however, prophylaxis only decreases short term morbidity. 3

Surgical site infection increases the length of hospital stay.[10] The additional length of stay is dependent on the type of surgery.[21,22] Prophylaxis has the potential to shorten hospital stay. There is little direct evidence that it does so as few randomised trials have included hospital length of stay as an outcome measure. There is evidence to indicate that prevention of wound infection is associated with faster return to normal activity after discharge from hospital.[23]

4.2 RISKS OF PROPHYLAXIS

One of the aims of rationalising surgical antibiotic prophylaxis is to reduce the inappropriate use of antibiotics thus minimising the consequences of misuse.

4.2.1 PENICILLIN ALLERGY

Penicillin and cephalosporin antibiotics are often the cornerstone of antibiotic prophylaxis. If a patient has been wrongly attributed with a penicillin allergy, optimal management may be compromised. Patient history is integral to evaluation of allergy.

Important details of an allergic reaction include:[24]

- signs
- symptoms
- severity
- prior reactions
- time course of allergic event
- temporal proximity to and route of other administered drugs
- other medications being taken
- adverse drug events to other medication.

4

☑ Patients with a history of penicillin allergy should be reviewed to exclude a non-immunological adverse reaction, (*for example, diarrhoea, vomiting, non-specific maculopapular rash*) or, an experience wrongly attributed to the antibiotic (*for example, ampicillin and Epstein-Barr virus infection*).

Cross-reactivity between penicillins and cephalosporins is generally quoted at 10%. This reflects data collected prior to 1980,[25] and is confounded by the impurity of the antibiotics in use and tends to overestimate cross-sensitivity. Cross-reactivity between penicillins and second generation cephalosporins is low.[25] 4

Studies investigating penicillin allergy, cross-reactivity with cephalosporins and methods to support the decision to use a beta-lactam in patients with penicillin allergy focused on the use of skin tests to confirm hypersensitivity to specific antibiotics.[26-28]

In patients allergic to penicillins, challenge tests can be used to demonstrate cross-reactions with cephalosporins[29] and carbapenems.[30] The frequency of these relationships and their clinical significance is uncertain. 2+

Type 1 IgE mediated allergic reactions typically occur within minutes to an hour following exposure.[25,31] When reactions are a consequence of previous exposures/sensitisations, they may be seen up to 72 hours (see *Table 4*).[25,31] As this reaction may be life threatening, the potential risks of cross-reactivity generally outweigh the potential benefits of using a cephalosporin. 4

Table 4 Classification scheme for adverse drug reactions (adapted from Gell and Coombs)[31]

Classification	Time of onset *(hours)*	Mediators	Clinical signs	Comments
Allergic immediate (Type I)	< 1	Antibiotic-specific IgE antibodies	Anaphylaxis and/or hypotension, laryngeal oedema, wheezing, angioedema or urticaria	Much more likely with parenteral than oral administration; fatal outcome in 1 per 50,000 to 1 per 100,000 treatment courses with penicillin; accelerated reactions occurring 1-72 hours after exposure may be IgE mediated
Late (Type II)	> 72	IgG, complement	Increased clearance of red blood cells and platelets by lymphoreticular system	IgE not involved
Type III	> 72	IgG and IgM immune complexes	Serum sickness, tissue injury	Tissue lodging of immune complexes; drug fever; IgE not involved
Type IV	≥ 72		Contact dermatitis	IgE not involved; not allergic
Other (idiopathic)	Usually > 72	Unknown	Maculopapular or morbilliform rashes	1-4% of patients receiving penicillins and cephalosporins; not truly allergic

Other symptomatologies show either no or extremely weak association with subsequent reactions.

C **Patients with a history of anaphylaxis, laryngeal oedema, bronchospasm, hypotension, local swelling, urticaria or pruritic rash, occurring immediately after a penicillin therapy are potentially at increased risk of immediate hypersensitivity to beta-lactams and should not receive prophylaxis with a beta-lactam antibiotic.**

☑ Local policies for surgical prophylaxis that recommend beta-lactam antibiotics as first line agents should also recommend an alternative for patients with allergy to penicillins or cephalosporins.

4.2.2 ANAPHYLAXIS

No evidence was identified on how to reduce the risk of anaphylactic shock in patients receiving prophylactic antibiotics.

4.2.3 ANTIBIOTIC-ASSOCIATED DIARRHOEA

No evidence was identified on how to reduce the incidence of antibiotic-associated diarrhoea (AAD) in patients receiving prophylactic antibiotics.

A single randomised controlled trial (RCT) suggested that the yeast *Saccharomyces boulardi*, in addition to standard antibiotics, reduced the risk of antibiotic-associated diarrhoea in children from 23% to 8% compared to placebo (number needed to treat; NNT = 8). The incidence of *Clostridium difficile* was also reduced.[32] A meta-analysis of the use of *S. boulardi* for preventing antibiotic-associated diarrhoea in adults was inconclusive, as the studies were heterogeneous and used different definitions of antibiotic-associated diarrhoea.[33] 1+

Treatment with *S. boulardi* may increase the risk of fungaemia especially in immunocompromised patients. More research is required before a recommendation on the use of *S. boulardi* can be made.[33]

A study of yoghurt to prevent AAD in adults showed that yogurt twice daily for eight days whilst receiving intravenous antibiotics reduced the incidence of AAD from 23 out of 97 to 13 out of 105 patients (p = 0.04, NNT = 9). It is unclear whether this treatment would be useful during a short course of prophylactic antibiotic. The level of active *Lactobacillus* in the yoghurt is also difficult to assess.[34] 1++

4.2.4 *Clostridium difficile* ASSOCIATED DIARRHOEA

Five per cent of healthy adults are reported to be carrying *Clostridium difficile (C. diff)* on arrival at hospital.[35] Patients who have been treated with broad spectrum antibiotics are at greatest risk of *C. diff* associated disease. The risk of contracting *C. diff* is raised for patients who:[36, 37]

- are elderly
- have a serious underlying illness that compromises their immune system
- have a prolonged stay in healthcare settings
- have recently had gastrointestinal surgery
- are in hospital when there is an outbreak.

The number of death certificates in England and Wales mentioning *C. diff* associated diarrhoea (CDAD) has been on the increase since 1999. In 2005 3,807 death certificates mentioned *C. diff*, a 69% increase from 2004. *C. diff* was the underlying cause of death in a similar proportion of cases each year (around 5%).[38]

The prevalence of *C. diff* associated diarrhoea is related to total antibiotic usage and, in particular, to the use of third generation cephalosporins.[39-41] 2+

In epidemiological studies of *C. diff* colitis, surgical antibiotic prophylaxis is the single most common indication for use of antibiotics,[9] and even single dose prophylaxis increases the risk of carriage of *C. diff*.[42] 2+

It is not clear how many patients have *C. diff* induced diarrhoea following antibiotic prophylaxis. No evidence was identified on how to prevent or reduce *C. diff* associated diarrhoea in patients requiring prophylactic antibiotic treatment.

A meta-analysis of inconsistent and poor quality studies was unable to draw a conclusion about the efficacy of antibiotic treatment for *C. diff* associated diarrhoea, nor about the antibiotic of choice for treating *C. diff* associated diarrhoea.[35] | 1++

4.2.5 ANTIBIOTIC RESISTANCE

Rates of antibiotic resistance are increasing in all hospitals.[43,44] The prevalence of antibiotic resistance in any population is related to the proportion of the population that receives antibiotics, and the total antibiotic exposure.[45-47]

Increased antibiotic use leads to more resistance as demonstrated by a variety of large and small scale studies.[48-50]

Three uncontrolled observational studies showed that when antibiotics were given for surgical prophylaxis there was an increased risk of the patients treated acquiring antibiotic resistant strains following treatment.[51-53] Two trials of patient exposure to a single dose of either ciprofloxacin or vancomycin showed an absolute increase in the number of people with resistant organisms following treatment compared to pre-treatment (4 *versus* 8%).[51,52] Prolonged prophylaxis (>48 hour) in coronary artery bypass graft (CABG) surgery was associated with an increased risk of acquired antibiotic resistance (odds ratio; OR of 1.6). No information was available about patient selection and only 41% of patients had cultures taken.[53] | 3

A small study comparing short term (24 hour) with longer term (five day) prophylaxis following excision of head and neck lesions found significantly fewer patients with wounds infected by MRSA in the short term group (4/33 compared with 13/31, p=0.01).[54] | 2+

D **The duration of prophylactic antibiotic therapy should be single dose except in special circumstances** *(for example prolonged surgery, major blood loss or as indicated in sections 5.2, 5.3 and 6.4)***.**

4.2.6 MULTIRESISTANCE CARRIAGE

No evidence was identified to show whether carriage of multiresistant organisms is associated with more frequent postoperative surgical site infection than carriage of sensitive strains.

In medical patients, carriage of MRSA is strongly predictive of subsequent MRSA infection in the short- or long-term.[55-58] | 2+ 3

Extrapolation of this data to surgical patients suggests that MRSA carriage may be a risk factor for SSI. Preoperative care and choice of prophylactic antibiotic may need to be modified where patients are colonised with MRSA (*see section 6.1.1*).

☑ Carriage of multiresistant organisms should be recognised as a potential risk factor for surgical site infection during high risk operations (*for example orthopaedic implant, heart valve, vascular graft or shunt or CABG*).

☑ For patients with suspected multiresistance carriage undergoing high risk operations preoperative care should include:

- screening for relevant organisms
- changing the antibiotic of choice for prophylaxis.

5 Indications for surgical antibiotic prophylaxis

5.1 INTRODUCTION

Section 5.2 summarises the recommended indications for surgical antibiotic prophylaxis. The recommendations are based on the evidence for the clinical effectiveness of prophylactic antibiotics in reducing the incidence of SSI.

Antibiotic prophylaxis should be used where evidence of benefit exists and should not be considered if there is evidence of a lack of efficacy.

There is a paucity of evidence for surgical antibiotic prophylaxis in children. Section 5.3 summarises the recommended indications for surgical antibiotic prophylaxis in children (birth to 16 years of age). Where no evidence was identified, recommendations for common paediatric procedures, the general principles of antibiotic prophylaxis for clean-contaminated surgery and insertion of prosthetic devices are extrapolated from evidence of efficacy in adults. Where there is no significant difference from practice in adults and no specific recommendations are made for children, the recommendations in section 5.2 should apply.

Four different recommendations have been made regarding surgical antibiotic prophylaxis:

- **Highly recommended**: prophylaxis unequivocally reduces major morbidity, reduces hospital costs and is likely to decrease overall consumption of antibiotics
- **Recommended**: prophylaxis reduces short term morbidity, reduces hospital costs and may decrease overall consumption of antibiotics
- **Should be considered**: prophylaxis should be considered for all patients. Local policy makers may wish to identify exceptions, as prophylaxis may not reduce hospital costs and could increase consumption of antibiotics, especially if given to patients at low risk of infection. Any local policy that recommends restriction of prophylaxis to "high-risk" patients must specify and justify the threshold of risk. Moreover, such a policy requires continuous documentation of wound infection rates in order to provide evidence that the risk of surgical site infection in patients who do not receive prophylaxis is below the specified risk threshold. In addition, for clean-contaminated procedures or procedures involving insertion of prosthetic device, good quality evidence for the clinical effectiveness of surgical antibiotic prophylaxis is lacking. This is either because trials have not been done or have been done with such small numbers of patients that important treatment effects cannot be excluded.[15]
- **Not recommended**: prophylaxis has not been proven to be clinically effective and as the consequences of infection are short term morbidity, it is likely to increase hospital antibiotic consumption for little clinical benefit.

The recommendations are presented in tabular form in sections 5.2 and 5.3, which also lists the odds ratio (OR) for the risk of wound infection and numbers needed to treat (NNT), ie the number of patients that must receive prophylaxis in order to prevent one wound infection. The method of calculation of NNT from baseline risk and odds ratio is given in Annex 6.

Where possible the ORs and NNTs have been taken from published meta-analyses. In some cases, however, data from pooled trials has been combined without formal meta-analysis. In other cases, NNTs and ORs from individual trials are presented *(see supporting material for this guideline on the SIGN website: **www.sign.ac.uk**)*.

A negative NNT indicates that the treatment has a harmful effect and is referred to as the number needed to harm (NNTH).

5.2 RECOMMENDED INDICATIONS FOR SURGICAL ANTIBIOTIC PROPHYLAXIS TO PREVENT SSI

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
HEAD AND NECK **Intracranial**						
Craniotomy	A	Antibiotic prophylaxis is **recommended**	0.24	17	Wound infection	1++[59]
Cerebrospinal fluid *(CSF)* **shunt**	A	Antibiotic prophylaxis is **recommended**	0.48 0.52	16 16	Wound and shunt infection	1+[60, 61]
Spinal surgery	A	Antibiotic prophylaxis is **recommended**	0.36	28	Wound infection	1++[62]
Ophthalmic						
Cataract surgery	A	Antibiotic prophylaxis is **highly recommended**	0.36	451	Endophthalmitis	1++[63]
Glaucoma or corneal grafts	B	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence about cataract surgery*			1+[63]
Lacrimal surgery	C	Antibiotic prophylaxis is **recommended**	0.03	9	Wound infection	2+[64]
Penetrating eye injury	B	Antibiotic prophylaxis is **recommended**	0.20	18	Endophthalmitis	1+[65, 66]
Facial						
Open reduction and internal fixation of compound mandibular fractures	A	Antibiotic prophylaxis is **recommended**	0.26	5	Wound infection	1++, 1+[67-69]
	A	The duration of prophylactic antibiotics should not be more than 24 hours				1++[69]
Intraoral bone grafting procedures	B	Antibiotic prophylaxis is **recommended**	*There was no direct comparison of prophylactic antibiotic with no antibiotic*			1++[70]

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
HEAD AND NECK **Facial**						
	A	Antibiotic prophylaxis is **recommended**	0.21	4	Wound infection	1+[71-74]
Orthognathic surgery	A	The duration of prophylactic antibiotics should not be more than 24 hours				1+[71, 73]
	B	Broad spectrum antibiotics appropriate to oral flora should be given				1+[71-74]
Facial surgery *(clean)*	☑	Antibiotic prophylaxis is **not recommended**				
Facial plastic surgery *(with implant)*	☑	Antibiotic prophylaxis **should be considered**	*Effectiveness is inferred from evidence about other procedures involving insertion of prosthetic devices*			4[75]
Ear, nose and throat - *benign*						
Ear surgery *(clean/clean-contaminated)*	A	Antibiotic prophylaxis is **not recommended**	*There was no subgroup of analysis of clean and clean-contaminated surgery*			1++[76]
Routine nose, sinus and endoscopic sinus surgery	A	Antibiotic prophylaxis is **not recommended**				1+[77]
Complex septorhinoplasty *(including grafts)*	A	The duration of prophylactic antibiotics should not be more than 24 hours				1++[78]
Tonsillectomy	☑	Antibiotic prophylaxis is **not recommended**	*No studies were identified showing evidence of effectiveness of prophylaxis*			
Adenoidectomy *(by curettage)*	A	Antibiotic prophylaxis is **not recommended**				1+[79]

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
HEAD AND NECK **Ear, nose and throat -** *benign*						
Grommet insertion	B	Antibiotic prophylaxis (a single dose of topical antibiotic) is **recommended**	0.46	13	Otorrhea	1^{++},1^{+},2^{++}[80-82]
Head and neck						
Head and neck surgery *(clean, benign)*	D	Antibiotic prophylaxis is **not recommended**				4[83, 84]
Head and neck surgery *(clean, malignant; neck dissection)*	C	Antibiotic prophylaxis **should be considered**	1.28 0.12	-29 9	Wound infection	2^{+}[85, 86]
Head and neck surgery *(contaminated/clean-contaminated)*	A	Antibiotic prophylaxis is **recommended**	0.37	6	Wound infection	1^{++}[87-90]
	C	The duration of prophylactic antibiotics should not be more than 24 hours				2^{+}[54, 85]
	D	Ensure broad spectrum antimicrobial cover for aerobic and anaerobic organisms				4[84]

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
THORAX						
Breast cancer surgery	A	Antibiotic prophylaxis **should be considered**				1++[91]
Breast reshaping procedures	C	Antibiotic prophylaxis **should be considered**	0.66	14	Infection at 6 weeks	2+[92]
Breast surgery with implant *(reconstructive or aesthetic)*	C	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence about breast cancer surgery and other procedures involving insertion of prosthetic devices*			1++[91], 4[75]
Cardiac pacemaker insertion	A	Antibiotic prophylaxis is **recommended**	0.26	38	Any infection	1++[93]
Open heart surgery	C	Antibiotic prophylaxis is **recommended**	0.03 2.52 0.06	5 -27 3	Wound infection	2+[94-96]
	C	The duration of prophylactic antibiotics should not be more than 48 hours				2++,2+,4[53,97,98]
Pulmonary resection	A	Antibiotic prophylaxis is **recommended**	0.20	6	Surgical site infection	1+[99, 100]
UPPER GASTROINTESTINAL						
Oesophageal surgery	D	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence about other clean-contaminated procedures*			4[101]
Stomach and duodenal surgery	A	Antibiotic prophylaxis is **recommended**	0.17	5	Wound infection	1+[102-104]

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
UPPER GASTROINTESTINAL						
Gastric bypass surgery	D	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence about other clean-contaminated procedures*			4[75]
Small intestine surgery	D	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence about other clean-contaminated procedures*			4[75]
HEPATOBILIARY						
Bile duct surgery	A	Antibiotic prophylaxis is **recommended**	0.30	11	Wound infection	1++[105]
Pancreatic surgery	B	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence about biliary surgery*			1++[105]
Liver surgery	B	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence about biliary surgery*			1++[105]
Gall bladder surgery *(open)*	A	Antibiotic prophylaxis is **recommended**	0.30	11	Wound infection	1++[105]
Gall bladder surgery *(laparoscopic)*	A	Antibiotic prophylaxis is **not recommended**				1+[106]
	☑	Antibiotic prophylaxis **should be considered** in high risk* patients				

High risk: *intraoperative cholangiogram, bile spillage, conversion to laparotomy, acute cholecystitis/pancreatitis, jaundice, pregnancy, immunosuppression, insertion of prosthetic devices*

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
LOWER GASTROINTESTINAL						
Appendicectomy	A	Antibiotic prophylaxis is **highly recommended**	0.33 0.43	11 103	Wound infection Intra-abdominal abscesses	1++[107]
Colorectal surgery	A	Antibiotic prophylaxis is **highly recommended**	0.24	4	Wound infection Intra-abdominal abscesses	1++[108]
ABDOMEN						
Hernia repair-groin *(inguinal/femoral with or without mesh)*	A	Antibiotic prophylaxis is **not recommended**				1++[109, 110]
Hernia repair-groin *(laparoscopic with or without mesh)*	B	Antibiotic prophylaxis is **not recommended**	*Effectiveness is inferred from evidence about open inguinal/femoral hernia repair*			1++[109, 110]
Hernia repair *(incisional with or without mesh)*	C	Antibiotic prophylaxis is **not recommended**	*Effectiveness is inferred from evidence about open inguinal/femoral hernia repair*			1++[109, 110]
Open/laparoscopic surgery with mesh *(eg gastric band or rectoplexy)*	B	Antibiotic prophylaxis is **not recommended**	*Effectiveness is inferred from evidence about open inguinal/femoral hernia repair*			1++[109, 110]
	☑	Antibiotic prophylaxis **should be considered** in high risk patients *(see section 3.1)*				
Diagnostic endoscopic procedures	D	Antibiotic prophylaxis is **not recommended**				4[111]

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
ABDOMEN						
Therapeutic endoscopic procedures *(endoscopic retrograde cholangio-pancreatography and percutaneous endoscopic gastrostomy)*	D	Antibiotic prophylaxis **should be considered** in high risk* patients				4[111]
		***High risk:** pancreatic pseudocyst, immunosupression, incomplete biliary drainage (eg primary sclerosing cholangitis or cholangiocarcinoma)*				
Spleen						
Splenectomy	☑	Antibiotic prophylaxis is **not recommended**	*Post-splenectomy prophylaxis is covered elsewhere*[112]			
	☑	Antibiotic prophylaxis **should be considered** in high risk* patients				
		***High risk:** immunosuppression*				
Gynaecological						
Abdominal hysterectomy	A	Antibiotic prophylaxis is **recommended**				1++[113,114]
Vaginal hysterectomy	A	Antibiotic prophylaxis is **recommended**	0.17	4	Pelvic infection	1+[115, 116]
Caesarean section	A	Antibiotic prophylaxis is **highly recommended**	0.41	19	Wound infection	1++[117]
Assisted delivery	A	Antibiotic prophylaxis is **not recommended**				1++[118]
Perineal tear	D	Antibiotic prophylaxis is **recommended** for third/fourth degree perineal tears involving the anal sphincter/rectal mucosa			Wound infection	4[119]

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
ABDOMEN **Gynaecological**						
Manual removal of the placenta	D	Antibiotic prophylaxis **should be considered**				4[120]
	D	Antibiotic prophylaxis is **recommended** for patients with proven chlamydia or gonorrhoea infection				4[120]
Induced abortion	A	Antibiotic prophylaxis is **highly recommended**	0.58	25	Upper genital tract infection	1++[121]
Evacuation of incomplete miscarriage	A	Antibiotic prophylaxis is **not recommended**				1++[122]
Intrauterine contraceptive device *(IUCD)* **insertion**	A	Antibiotic prophylaxis is **not recommended**				1++[123]
Urogenital						
Transrectal prostate biopsy	A	Antibiotic prophylaxis is **recommended**	0.76	27	Bacteriuria	I+[124, 125]
Shock wave lithotripsy	A	Antibiotic prophylaxis is **recommended**	0.45	28	Urinary tract infection	1++[126]
Percutaneous nephrolithotomy	B	Antibiotic prophylaxis is **recommended** for patients with stone ≥ 20 mm or with pelvicalyceal dilation	0.24	4	Urosepsis	1+[127]
	B	Oral quinolone for one week preoperatively is recommended				1+[127]
Endoscopic ureteric stone fragmentation/removal	B	Antibiotic prophylaxis is **recommended**	0.13 2.75	10 -15	Bacteriuria Post-operative fever	1+,2+[128,129]
Transurethral resection of the prostate	A	Antibiotic prophylaxis is **highly recommended**	0.35	8	Bacteriuria Infective complications	1++[130]

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
ABDOMEN **Urogenital**						
Transurethral resection of bladder tumours	D	Antibiotic prophylaxis is **not recommended**				4[131]
Radical cystectomy	☑	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence that SSI is high post-cystectomy*			3[132]
LIMB						
Arthroplasty	B	Antibiotic prophylaxis is **highly recommended**	0.27 0.25	42 57	Hip infection Joint infection	1++,1+, 2++[133,134,135,136]
	B	Antibiotic-loaded cement is recommended in addition to intravenous antibiotics				2++[135, 136]
	B	Up to 24 hours of antibiotic prophylaxis should be considered				2++[136]
Open fracture	A	Antibiotic prophylaxis is **highly recommended**	0.41	14	Wound infection	1++[137]
Open surgery for closed fracture	A	Antibiotic prophylaxis is **highly recommended**	0.36	38	Deep wound infection	1++[138]
Hip fracture	A	Antibiotic prophylaxis is **highly recommended**	0.55	23	Deep wound infection	1++[139]
Orthopaedic surgery *(without implant)*	D	Antibiotic prophylaxis is **not recommended**	*Effectiveness is inferred from evidence about other clean-contaminated procedures*			4[75]
Lower limb amputation	A	Antibiotic prophylaxis is **recommended**	0.32	5	Wound infection	1+[140]

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
LIMB						
Vascular surgery *(abdominal and lower limb arterial reconstruction)*	A	Antibiotic prophylaxis is **recommended**	0.12 0.10	18 4	Wound infection Wound infection	1++[141]
Soft tissue surgery of the hand	☑	Antibiotic prophylaxis **should be considered**	*Effectiveness is inferred from evidence about orthopaedic and vascular surgery*			1++[137, 38]
NON-OPERATIVE INTERVENTIONS						
Intravascular catheter insertion:						
▪ **non-tunnelled central venous catheter** *(CVC)*	D	Antibiotic prophylaxis **is not recommended**				4[142]
▪ **tunnelled CVC**	A	Antibiotic prophylaxis is **not recommended**				1++[143]
GENERAL						
Clean-contaminated procedures *–where no specific evidence is available*	D	Antibiotic prophylaxis is **recommended**				4[75]
Insertion of a prosthetic device or implant *–where no specific evidence is available*	D	Antibiotic prophylaxis is **recommended**				4[75]

5.3 RECOMMENDED INDICATIONS FOR SURGICAL ANTIBIOTIC PROPHYLAXIS TO PREVENT SSI IN CHILDREN

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
HEAD AND NECK						
Craniotomy	B	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence in adults*			1++[59]
CSF shunt	A	Antibiotic prophylaxis is **recommended**	0.48 0.52	16 16	Wound and shunt infection	1+[60, 61]
Spinal surgery	B	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence in adults*			1++[62]
Tonsillectomy	☑	Antibiotic prophylaxis is **not recommended**	*No studies were identified showing evidence of effectiveness of prophylaxis*			
Cleft lip and palate	☑	Antibiotic prophylaxis is **recommended** for major cleft palate repairs				
Adenoidectomy *(by curettage)*	A	Antibiotic prophylaxis is **not recommended**				1+[79]
Grommet insertion	B	Antibiotic prophylaxis (a single dose of topical antibiotic) is **recommended**	0.46	13	Otorrhea	1++, 1+, 2++[80-82]
THORAX						
Open heart surgery	D	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence in adults*			2+[94-96]
Closed cardiac procedures *(clean)*	☑	Antibiotic prophylaxis is **not recommended**				

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
THORAX						
Interventional cardiac catheter device placement	☑	Antibiotic prophylaxis is **highly recommended**	*Effectiveness is inferred from evidence about other procedures involving insertion of a prosthetic device in adults*			4[75]
GASTROINTESTINAL						
Appendicectomy	A	Antibiotic prophylaxis is **highly recommended**	0.64 0.29	47 64	Wound infection Intra-abdominal abscesses	1++[107]
Colorectal surgery	B	Antibiotic prophylaxis is **highly recommended**	*Effectiveness is inferred from evidence in adults*			1++[108]
Insertion of percutaneous endoscopic gastrostomy *(PEG)*	B	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence in adults*			1+[144]
Splenectomy	☑	Antibiotic prophylaxis is **not recommended**	*Post-splenectomy prophylaxis is covered elsewhere*[112]			
UROGENITAL						
Circumcision *(routine elective)*	☑	Antibiotic prophylaxis is **not recommended**				
Hypospadias repair	B	Where a urinary catheter has been inserted, antibiotic prophylaxis **should be considered** until the catheter is removed.	0.26 0.21	4 6	Urinary tract infection Wound infection	1+[145,146]

Operation		*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
UROGENITAL						
Hydrocoeles/hernia repair	C	Antibiotic prophylaxis is **not recommended**	*Effectiveness is inferred from evidence about open inguinal/femoral hernia repair in adults*			1^{++}[109, 110]
Shock wave lithotripsy	B	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence in adults*			1^{++}[126]
Percutaneous nephrolithotomy	C	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence in adults*			1^{+}[127]
Endoscopic ureteric stone fragmentation/removal	C	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence in adults*			1^{+},2^{+}[128, 129]
Cystoscopy	☑	Antibiotic prophylaxis is **not recommended**				
	☑	Antibiotic prophylaxis should be considered if there is a high risk of UTI				
Nephrectomy	☑	Antibiotic prophylaxis is **not recommended**				
Pyeloplasty	☑	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence about other clean-contaminated procedures in adults*			4[75]
Surgery for vesicoureteric reflux *(endoscopic or open)*	☑	Antibiotic prophylaxis is **recommended**	*Effectiveness is inferred from evidence about other procedures involving insertion of a prosthetic device in adults*			4[75]

Operation	*Recommendation*	*Odds Ratio*	*NNT*	*Outcome*	*Evidence level*
NON-OPERATIVE INTERVENTIONS					
Intravascular catheter insertion:					
▪ **non-tunnelled central venous catheter** *(CVC)*	D Antibiotic prophylaxis is **not recommended**	*Effectiveness is inferred from evidence in adults*			4[142]
▪ **tunnelled CVC**	A Antibiotic prophylaxis is **not recommended**	*Effectiveness is inferred from evidence in adults*			1++[143]
GENERAL					
Clean-contaminated procedures *–where no specific evidence is available*	D Antibiotic prophylaxis is **recommended**				4[75]
Insertion of a prosthetic device or implant *–where no specific evidence is available*	D Antibiotic prophylaxis is **recommended**				4[75]

5.4 ANTIBIOTIC PROPHYLAXIS TO PREVENT CHEST OR URINARY TRACT INFECTION

Two meta-analyses were identified comparing the efficacy of ceftriaxone with other antibiotics in reducing surgical site infection. The risk reduction (RR) of respiratory tract infection (RTI) and urinary tract infection (UTI) after prophylactic antibiotic treatment was analysed.[147,148]

One meta-analysis of 48 non-placebo controlled RCTs (including breast, cardiovascular, maxillofacial, neurological, orthopaedic, abdominal, obstetric and urologic surgery) showed that RTIs were reduced after antibiotic prophylaxis in clean and clean-contaminated surgery.[148] UTIs were reduced only in clean-contaminated surgery (RTI, OR -0.30; UTI, OR -0.54),[148] although a second meta-analysis of 43 non-placebo controlled RCTs (including abdominal, colorectal, orthopaedic, cardiothoracic, obstetric and gynaecological surgery and appendicectomy) showed that prophylactic antibiotics during surgery prevent UTI but not RTI.[147] 1+

There was no significant reduction in RTI after antibiotic prophylaxis compared to placebo in an RCT of head and neck surgery.[149]

Another meta-analysis compared cephalosporins at any dosage with placebo and multiple doses with 24 hour antibiotic coverage in orthopaedic surgery.[139] Postoperative UTI was shown to be prevented in three studies of antibiotic prophylaxis compared to placebo. The included studies were all of patients with orthopaedic/hip fracture. These patients may be elderly, and have an indwelling catheter or asymptomatic bacteriuria. They may also be at high risk of *C. diff* infection, so antibiotics should be used cautiously. 1++

A **Prophylactic antibiotic treatment during surgery solely for the prevention of urinary or respiratory tract infection is not recommended.**

6 Administration of prophylactic antibiotics

6.1 CHOICE OF ANTIBIOTIC

Although a wide range of organisms can cause infection in surgical patients, SSI is usually due to a small number of common pathogens (except in the presence of implanted biomaterial: *see Annex 4*). Only these need to be covered by the antibiotic that is prescribed.[14] | 4

C **The antibiotics selected for prophylaxis must cover the expected pathogens for that operative site.**

The antibiotics chosen for prophylaxis can be those used for active treatment of infection. The chosen antibiotics must reflect local, disease-specific information about the common pathogens and their antimicrobial susceptibility.

☑ Local antibiotic policy makers have the experience and information required to make recommendations about specific drug regimens based on an assessment of evidence, local information about resistance and drug costs.

☑ The choice of antibiotic should take into account local resistance patterns.

Three meta-analyses were identified comparing cephalosporins to other antibiotics.[147,148,150] All were of non-uniformity studies tailored to the trial antibiotic. Details about dosage were lacking.

In meta-analyses of heterogeneous studies, perioperative antibiotic prophylaxis with ceftriaxone showed a decrease in the relative risk of SSI of 30% compared to other cephalosporins,[147] and a 22% reduction compared to a range of antibiotics.[148] Given the heterogeneity of the studies the conclusion that ceftriaxone is better cannot be sustained for any particular surgical site. | 1^{++} 1^{+}

The increased risk of *C. diff* associated disease with third-generation cephalosporins should also be considered (*see section 4.2.4*).[39-41] | 2^{+}

A meta-analysis of antibiotic prophylaxis for cardiac surgery showed no difference in effectiveness between beta-lactams and glycopeptides in reducing the risk of SSI. Beta-lactams were superior to glycopeptides for reducing the risk of deep sternal wound infection. Glycopeptides were more effective than beta-lactams for reducing the risk of leg SSI at leg vein harvest sites.[150] | 1^{+}

☑ Narrow spectrum, less expensive antibiotics should be the first choice for prophylaxis during surgery.

A history of a serious adverse event should preclude administration of a particular antibiotic (*see section 4.2.1*). Annex 5 shows a table of the antibiotics most frequently used for surgical prophylaxis.

6.1.1 MULTIRESISTANCE CARRIAGE

MRSA carriage may be a risk factor for SSI (*see section 4.2.6*). SSI can cause major morbidity in patients undergoing high risk procedures (*see Table 5).*

☑ Patients known to carry MRSA should have a course of eradication therapy prior to high risk surgery.

Table 5 Non-general surgery reported as high risk of major morbidity for patients who are MRSA positive

Surgery	Outcome
Cardiothoracic surgery	Deep sternal wound infection[151]
Orthopaedic surgery	Deep wound infection[151]
Neurosurgery	Wound and shunt infection[151]
Vascular surgery	Prosthetic graft infection[155]

A meta-analysis of perioperative prophylaxis with intranasal mupirocin in adult non-general surgery (cardiothoracic, orthopaedic and neurosurgery) showed a decrease in the incidence of SSI in two RCTs (RR 0.80; confidence interval, CI, 0.58 to 1.10) and three non-randomised controlled trials (RR 0.40; CI 0.29 to 0.56). There was no decrease in SSI in general surgery.[151] In one of the trials the overall SSI rate caused by *S. aureus* was similar in both the placebo and mupirocin arms.[152] In a study of orthopaedic surgery the rate of endogenous *S. aureus* wound infections (defined as infections caused by an isolate identical to the nasal strain already carried) was five times lower after perioperative intranasal mupirocin, although there was no overall reduction in SSI rate by *S. aureus*.[153] 1+

A further observational study in orthopaedic surgery showed using intranasal mupirocin produced a reduction in SSI rates.[154] 2+

B **Intranasal mupirocin should be used prophylactically for adult patients undergoing surgery with a high risk of major morbidity who are identified with *S. aureus* or MRSA.**

☑ In the presence of known mupirocin resistance another topical preparation may be used.

A meta-analysis of antibiotic prophylaxis for cardiac surgery showed that glycopeptides are more effective than beta-lactams for preventing SSI caused by MRSA.[150] 1+

☑ Where antibiotic prophylaxis is indicated, patients undergoing high risk surgery who are MRSA positive should receive a suitable antibiotic active against local strains of MRSA.

A **A glycopeptide should be considered for antibiotic prophylaxis in patients undergoing high risk surgery who are MRSA positive.**

6.2 TIMING OF ADMINISTRATION

The time taken for an antibiotic to reach an effective concentration in any particular tissue reflects its pharmacokinetic profile and the route of administration.[156] 1+

Antibiotic prophylaxis administered too late or too early reduces the efficacy of the antibiotic and may increase the risk of SSI.[19,157-159] 1+

Administration of prophylaxis more than three hours after the start of the operation significantly reduces its effectiveness.[160] 1+

A non-systematic review of the literature indicated that intravenous antibiotic should be given ≤30 minutes pre-operatively for all categories of surgery except caesarean section.[14] 4

A systematic review indicated that the benefits and harms of giving antibiotic post-cord clamp following caesarean section cannot be determined from the available evidence.[161] 1++

B **Intravenous prophylactic antibiotics should be given ≤30 minutes before the skin is incised.**

6.3 DOSAGE SELECTION

It is generally accepted as good practice that the dosage of an antibiotic required for prophylaxis is the same as that for the therapy of infection.

☑ A single standard therapeutic dose of antibiotic is sufficient for prophylaxis under most circumstances.

6.4 DURATION OF PROPHYLAXIS

For many types of commonly performed surgery there is consistent evidence that a single dose of antimicrobial with a long enough half-life to achieve activity throughout the operation is adequate.[108,162,163] 1++ 1+ 2+

The *in vitro* activity of antibiotics, which may be considered for antibiotic prophylaxis, are shown in Annex 5.

There is evidence from several studies of antibiotic prophylaxis during surgery that longer dosage duration has no increased benefit over a short course (*see Table 6*).

Table 6 Operations where shorter duration (usually single dose) of antibiotic prophylaxis is as effective as longer duration

Operation	Evidence level
Open reduction and internal fixation of compound mandibular fractures[69]	1++
Orthognathic surgery[71,73]	1+
Complex septorhinoplasty[78]	1++
Head and neck surgery *(contaminated/clean-contaminated)* [54,85]	2+
Breast reshaping procedures[92]	2+
Cardiac surgery *(< 240 min)* [98]	2++
Caesarean section[117]	1++
Endoscopic ureteric stone fragmentation/removal[129]	2+

B **A single dose of antibiotic with a long enough half-life to achieve activity throughout the operation is recommended.**

In arthroplasty there is evidence from a very large observational cohort that 24 hours of antimicrobial prophylaxis is associated with lower rates of re-operation than a single dose.[136] 2++

B **Up to 24 hours of antibiotic prophylaxis should be considered for arthroplasty.**

6.4.1 ADDITIONAL DOSAGE DURING THE OPERATION

A single cohort study looking at cardiac operations showed that one dosage of cefazolin is as effective as two for short cardiac surgeries (< 240 min), but intraoperative redosing with cefazolin in operations longer than four hours resulted in a 16% decrease in overall infection rate bringing the infection rate down to similar to shorter surgeries.[98] 2++

C **An additional intraoperative dosage of antibiotic is recommended for cardiac surgery longer than four hours when using an antibiotic with pharmacokinetics equivalent to cefazolin.**

Apart from the above example, no evidence was identified for additional intraoperative dosage.

☑ Additional dosage may be indicated for longer surgery or shorter-acting agents to maintain activity for the duration of the operation.

6.4.2 BLOOD LOSS, FLUID REPLACEMENT AND ANTIBIOTIC PROPHYLAXIS

Serum antibiotic concentrations are reduced by blood loss and fluid replacement, especially in the first hour of surgery when drug levels are high.[49,164,165] 3

The precise effects of blood loss and fluid replacement are difficult to predict and will depend upon the particular antibiotic used, the time and rate of blood loss and fluid replacement.

A small pharmacokinetic analysis of cloxacillin levels in children undergoing major facial and neck surgery showed that the associated massive blood loss led to serum cloxacillin concentrations below therapeutic levels for significant proportions of surgery.[49]

In a small prospective study of 11 adults undergoing elective surgical spinal instrumentation procedures with an expected large blood loss there was a significant correlation between blood loss and tissue cefazolin concentration. Where there was significant blood loss (>1,500 ml) and the surgery lasted over three hours the tissue concentration of cefazolin fell below the minimum inhibitory concentration.[166] 3

☑ In the event of major intraoperative blood loss in adults (>1,500 ml) additional dosage of prophylactic antibiotic should be considered after fluid replacement.

☑ In the event of major intraoperative blood loss in children (25 ml/kg) additional dosage of prophylactic antibiotic should be considered after fluid replacement.

6.5 ROUTE OF ADMINISTRATION

Systemic antibiotic prophylaxis, typically given by the parenteral intravenous route (IV), has historically proven to be a reliable and effective prophylaxis against SSI in all types of surgery.

☑ Prophylactic antibiotics for surgical procedures should be administered intravenously.

6.5.1 ORAL ADMINISTRATION

Serum and tissue concentrations after oral administration are determined in part by the rate of absorption, which varies between individuals. There is relatively little evidence about the effectiveness of orally administered antibiotic prophylaxis. A further problem is that often the correct time of administration is difficult to guarantee in practice, because, for example, it occurs outwith the theatre environment.

Administration of fluoroquinolones by the oral route achieves comparable serum and tissue levels to antibiotic prophylaxis via the IV route.[127,167-175]

Intensive antibiotic use and in particular fluoroquinolones and cephalosporins contributes significantly to the two major antibiotic resistance issues that confront hospitals today, namely MRSA and *C. diff*.[174-178] In any patient known to be carrying MRSA it is unwise to prescribe these agents, as this may lead to overgrowth of MRSA and higher subsequent risk of infection. Similarly, as short a course of prophylactic antibiotic as possible will keep the risk of symptomatic *C. diff* to a minimum.

6.5.2 TOPICAL ADMINISTRATION

High-risk surgery

There is evidence that supplementary application of resorbable gentamicin-impregnated collagen fleeces after abdominoperineal excision of rectal cancer[179] or gentamicin-collagen implant between the two halves of the sternum after cardiac surgery, may minimise wound infection after surgery.[180,181] 1+

Results from studies on the use of intranasal mupirocin to prevent SSI are inconsistent due to small sample size, design differences and mixed surgical groups. A meta-analysis suggests that its use should be considered in non-general surgery, for example, cardiothoracic or orthopaedic procedures (*see section 6.1.1*).[151] 1+

B **Intranasal mupirocin should be used prophylactically for patients undergoing high risk surgery who are identified with *S. aureus* or MRSA.**

Additional work is needed to determine whether intranasal mupirocin should be combined with screening for nasal carriage in order that a targeted approach for its use be adopted.

Grommet insertion

The level of otorrhea was 8.75% in patients receiving topical antibiotics for five days after grommet insertion compared to 30% in the non-treatment group. This was not significantly different to the rate of infection following the use of oral antibiotics for five days.[80] Topical administration of a single dose of antibiotic was more effective than no treatment in preventing postoperative otorrhea (p = 0.029).[82] A single topical application was not significantly different to topical treatment for five days for reducing postoperative infection after grommet placement (8.4% and 8.2%), but was more effective than no treatment (16.5%). There was no significant difference between single application and five days.[81] 1++ 1+ 2++

B **A single dose of topical antibiotic is recommended for insertion of grommets.**

6.5.3 OTHER ROUTES OF ADMINISTRATION

Joint replacement

A large retrospective study showed that a combination of IV prophylactic antibiotic and antibiotic-impregnated bone cement is more effective than IV prophylaxis alone in reducing the risk of SSI. Compared to the combined regimen, patients who received antibiotic prophylaxis only systemically had a 1.4 times higher revision rate with all reasons for revision as the end point (p = 0.001), 1.3 times higher with aseptic loosening (p = 0.02) and 1.8 times higher with infection as the end point (p = 0.01).[136] 2++

B **In addition to intravenous antibiotics, impregnated cement is recommended for cemented joint replacements.**

Cataract surgery

During cataract surgery prophylactic cefuroxime administered intracamerally reduces the risk of developing endophthalmitis to one fifth of the risk if no prophylactic antibiotic is used.[182] 1++

A **Intracameral antibiotic prophylaxis is recommended for cataract surgery.**

Penetrating eye injuries

Prophylactic antibiotics (vancomycin and ceftazidime) administered intravitreally prevent severe intraocular infection after open globe injury (compared to no intravitreal antibiotics, (p = 0.03).[65] In eyes with an intraocular foreign body, intracameral or intravitreal administration of gentamicin and clindamycin following primary repair reduces the incidence of endophthalmitis compared to balanced salt solution (p = 0.04).[66] 1+

B **Intracameral or intravitreal intraocular antibiotic prophylaxis is recommended at completion of surgery for penetrating eye injuries** *(dependent on extent of injury and the presence or absence of an intraocular foreign body).*

Ventriculoperitoneal shunt infection

In adults, intraventrical prophylactic antibiotic at time of insertion of a ventriculoperitoneal (VP) shunt reduced the shunt infection from 6% to 0.4% (RR 0.7, p = 0.0001).[183] 2-

6.5.4 ANTIBIOTIC-IMPREGNATED DEVICES IN NEUROSURGERY

An RCT of permanent-impregnated CSF shunts compared to non-impregnated shunts in adults and children showed a significant reduction in infection rate when the impregnated device was used (10/60 versus 3/50, $p = 0.038$).[184] The overall shunt infection rate was high in this study. Two cohort studies of impregnated CSF shunts in children showed a 2.4-fold reduction in infection rate in 145 patients compared to 208 historical controls,[185] and 1/31 patients with shunt infection compared to 7/46 historical controls.[186] A six centre RCT of antibiotic-impregnated external ventricular drains showed a 50% risk reduction in colonisation of the catheter (17.9% compared to 36.7% control catheters, $p < 0.0012$) and a 70% reduction in positive CSF cultures from patients with antibiotic-impregnated catheters (1.3% compared to 9.4% of control, $p = 0.002$).[187] There is insufficient evidence to recommend the routine use of antimicrobial-impregnated CSF shunts.

1+
2+

C **Routine use of impregnated devices in neurosurgery is not recommended.**

☑ Impregnated devices may be considered if local CSF infection rates are high.

6.5.5 ANTIMICROBIAL-IMPREGNATED CENTRAL VENOUS CATHETERS

A meta-analysis of antimicrobial-impregnated and heparin-bonded central venous catheters (CVC) identified 11 studies, only one of which reported on antibiotic-impregnated CVCs.[188] Using antimicrobial-impregnated or heparin-bonded CVCs reduces catheter related bloodstream infections by 2.32% (95% CI 1.04% to 3.61%)[188]. There is insufficient evidence to recommend the routine use of antimicrobial-impregnated CVCs.

1++

The use of impregnated CVCs should not replace best clinical practice for inserting CVCs.[189]

4

A **Routine use of antimicrobial-impregnated central venous catheters is not recommended.**

7 Provision of information

7.1 PROVIDING INFORMATION AND SUPPORT

This section reflects the issues likely to be of most concern to patients and their carers. These points are provided for use by health professionals when discussing antibiotic prophylaxis with patients and carers and in guiding the production of locally produced information materials.

7.2 HEALTHCARE ASSOCIATED INFECTION

Patients, carers, relatives and the public have the right to receive high quality oral and written information on HAI. This will help them to understand the issues and the steps taken to control the risks. It will help them to ask informed questions and contribute to control. Guidance on providing information about HAI is available from the Healthcare Associated Infection Task Force.[190]

☑ Healthcare professionals should provide information to patients and carers about HAI to raise awareness and reduce anxiety.

7.2.1 COMBATING HEALTHCARE ASSOCIATED INFECTION IN HOSPITAL

A set of " top five tips" to combat healthcare associated infection in hospital was issued by the Chief Medical Officer in 2004 as advice for hospital visitors.[191]

- Think about keeping patients safe before you visit. If you or someone at home has a cold or are feeling unwell, especially if it's diarrhoea, stay away until you're better.
- Think about what you take in to patients. Food is a treat best saved until they get home. Don't sit on the bed and keep the number of visitors to a minimum at any one time.
- The most important thing you can do is to wash and dry your hands before visiting the ward, particularly after going to the toilet. If there is alcohol hand gel provided at the ward door or at the bedside, use it.
- Never touch dressings, drips, or other equipment around the bed.
- Don't be afraid to raise concerns with members of staff in your hospital. Busy doctors can sometimes forget simple things like cleaning hands before examining a patient. No NHS worker should take offence at a gentle and polite reminder.

7.3 SURGICAL SITE INFECTION

7.3.1 PREOPERATIVE INFORMATION

Explain to patients that surgical operations carry risks, one of which is the risk of infection at the site of surgery, known as surgical site infection (SSI). The risk of SSI is different for different surgical procedures. Antibiotic prophylaxis can reduce the risk of surgical site infection. Not all operations require antibiotic prophylaxis and not all surgical site infections are preventable.

Antibiotic prophylaxis carries a small risk of anaphylaxis. Overuse of antibiotics can lead to the development of micro-organisms that are resistant to certain antibiotics.

☑ All surgical departments should have information leaflets for patients about specific surgical procedures.

☑ Healthcare professionals should discuss the risks and benefits of antibiotic prophylaxis to reduce the risk of SSI with the patient.

☑ Patients should receive preoperative advice and information on how to reduce the risk of SSI.

7.3.2 MRSA CARRIAGE

The risks and benefits of antibiotic prophylaxis are different for patients known to carry MRSA. Preoperative care and choice of antibiotic may also be different. Information leaflets on MRSA are available from the Scottish Government, the Health Protection Agency, the Association of Medical Microbiologists and the Centers for Disease Control and Prevention (*see section 7.4.3*).

☑ Patients known to carry MRSA should receive information about the associated risks and about modification to procedures that may minimise the risks.

7.3.3 POSTOPERATIVE INFORMATION

It is estimated that around 70% of postoperative infections present in the community after discharge.[192] Patient information on monitoring surgical wounds for infection is available from the Health Protection Agency (*see section 7.4.3*).

☑ Healthcare professions should give patients advice and information on postoperative wound care and monitoring surgical wound for infection.

☑ Local information leaflets should be available.

7.4 SOURCES OF FURTHER INFORMATION

7.4.1 NATIONAL ORGANISATIONS

Association of Medical Microbiologists
Microbiology Department, Charing Cross Hospital, London W6 8RF
www.amm.co.uk • Email: honsec@amm.co.uk

Health Protection Agency Central Office
7th Floor, Holborn Gate, 330 High Holborn, London, WC1V 7PP
Tel: 020 7759 2700/2701 • Fax: 020 7759 2733
www.hpa.org.uk • Email: webteam@hpa.org.uk

Health Protection Scotland
Clifton House, Clifton Place, Glasgow, G3 7LN
Tel: 0141 300 1100 • Fax: 0141 300 1170
www.hps.scot.nhs.uk • Email: hpsenquiries@hps.scot.nhs.uk

NHS 24 Health Information
Tel: 08454 242424
www.nhs24.com

NHS24.com provides comprehensive up-to-date health information and self care advice for people in Scotland.

Scottish Patient Safety Programme
National Coordinator, Patient Safety Programme, Patients and Quality Division,
The Scottish Government, St Andrew's House, Regent Road, Edinburgh EH1 3DG
Tel: 0131 623 4317
www.patientsafetyalliance.scot.nhs.uk/programme/ • Email: jane.murkin@nhs.net

The Patient Safety Programme aims to improve the safety of hospital care across the country by using evidence based tools and techniques to improve the reliability and safety of everyday health care systems and processes.

7.4.2 INTERNATIONAL ORGANISATIONS

Centers for Disease Control and Prevention
1600 Clifton Rd, Atlanta, GA 30333, USA
Tel: (404) 639-3311/Public Inquiries: (404) 639-3534/(800) 311-3435
www.cdc.gov

7.4.3 USEFUL PUBLICATIONS

Monitoring surgical wounds for infection: Information for patients

Health Protection Agency
www.hpa.org.uk/infections/topics_az/surgical_site_infection/SSI_leaflet_FINAL.pdf

MRSA: Information for patients

Health Protection Agency
www.hpa.org.uk/infections/topics_az/staphylo/MRSA_leaflet.pdf

MRSA: Information for patients in hospital

Health Protection Agency
www.hpa.org.uk/infections/topics_az/surgical_site_infection/SSI_leaflet_FINAL.pdf

MRSA patient information leaflet

Centers for Disease Control and Prevention
www.cdc.gov/ncidod/dhqp/pdf/ar/MRSAPatientInfoSheet.pdf

The facts about MRSA

Association of Medical Microbiologists
www.amm.co.uk/files/factsabout/fa_mrsa.htm

The facts about *Clostridium difficil*e infection

Association of Medical Microbiologists
www.amm.co.uk/files/factsabout/fa_cdiff.htm

The facts about vancomycin-resistant enterococci (VRE)

Association of Medical Microbiologists
www.amm.co.uk/files/factsabout/fa_vre.htm

Allergy and allergy tests: A guide for patients and relatives

The Royal College of Pathologists
www.rcpath.org/resources/pdf/allergy_doc.pdf

8 Implementing the guideline

This section provides advice on the resource implications associated with implementing the key clinical recommendations, and advice on audit as a tool to aid implementation.

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

8.1 COST EFFECTIVENESS OF ANTIBIOTIC PROPHYLAXIS

The aims of this section are:

- to outline the cost considerations related to surgical antibiotic prophylaxis
- to provide some "rules of thumb" that a decision maker can use to estimate the likely cost effectiveness of embarking upon a particular preventative strategy for surgical site infection.

Very few prospective randomised trials of surgical prophylaxis have included economic evaluation within the trial design. There are some evaluations that combine evidence of effectiveness of prophylaxis with estimates of the additional costs of treating wound infection. As described in section 5.1, the effectiveness of prophylaxis can be estimated using an odds ratio for risk of wound infection. This, together with the rate of wound infection for that procedure in the hospital, is used to calculate the "numbers needed to treat" (NNT, the number of patients who must receive prophylaxis in order to prevent one wound infection, *see Annex 6*).[193]

Table 7 estimates likely odds ratios for various baseline infection risks that can be generalised to most surgical operations. The numbers in the body of the table are the NNTs for the corresponding odds ratios at that particular baseline risk.

Table 7 Translating odds ratios to NNTs

Expected baseline risk %	Odds ratio				
	0.5	**0.4**	**0.3**	**0.2**	**0.1**
20.0	11	9	8	7	6
15.0	15	12	10	9	8
10.0	21	17	15	13	11
7.5	28	23	20	17	15
5.0	41	34	29	25	22
2.5	81	67	58	50	45
1.3	161	134	115	100	89
1.0	201	167	143	125	111
0.8	268	223	191	167	148
0.5	401	334	286	250	222
0.3	801	667	572	500	445

8.2 POSSIBLE COST-EFFECTIVENESS DECISION RULES FOR IMPLEMENTING ANTIBIOTIC PROPHYLAXIS

The following worked examples illustrate the application of two possible decision rules for implementing antibiotic prophylaxis:

Rule 1: Prophylaxis should be given if it is likely to reduce overall antibiotic *consumption* in the hospital.

Rule 2: Prophylaxis should be given if it is likely to reduce overall hospital *costs*.

Note: these decision rules are addressing the "worst case" for assessing the cost effectiveness of prophylaxis, which is that prophylaxis can only be justified on the grounds that it saves hospital resources. This ignores the undoubted health gain to the patient from avoiding surgical site infection and any effects resulting from antibiotic resistance arising from population exposure to antibiotics.

Rule 1: Prophylaxis should be given if it is likely to reduce overall antibiotic *consumption* in the hospital.

Example A: Calculating antibiotic consumption in relation to antibiotic prophylaxis

Suppose that the antibiotic treatment regimen used for SSI following a specific surgical procedure is usually 3 doses per day for 7 days, the total number of doses (the therapeutic antibiotic consumption) would be 21.

The method for calculating how many doses of prophylaxis must be given in order to prevent one SSI is as follows:

Suppose the odds ratio of wound infection with prophylaxis versus no prophylaxis for the operation = 0.3

Baseline risk of wound infection without prophylaxis =10%

Using the equation in Annex 6, the NNT =15

From Table 7 at a baseline risk of 10%, the NNT =15

Therefore 15 patients must receive one dose of prophylaxis in order to prevent one wound infection, which would take 21 doses to treat. Therefore it would be reasonable to give prophylactic doses of antibiotic.

An alternative way of looking at this is:

To minimise overall hospital consumption of antibiotic usage, if 21 doses of therapeutic antibiotic would need to be given for treatment of an SSI, fewer than 21 people would need to be given prophylactic doses to prevent one SSI.

Table 7 shows that the expected baseline risk at which NNT>21 for an odds ratio of 0.3 is about 7%.

If the baseline risk of wound infection after the specific surgery in a hospital is less than 7% it would be reasonable to be concerned that giving prophylaxis routinely would increase overall hospital consumption of antibiotics.

If the baseline risk is more than 7% it would be reasonable to assume that giving prophylaxis would not increase overall antibiotic consumption.

☑ Use NNTs to compare when the consumption of prophylactic antibiotics would be lower than the consumption of therapeutic antibiotics.

Focusing debate about prophylaxis on the likelihood of reducing overall antibiotic consumption highlights the importance of aiming to restrict prophylaxis to a single dose. Every additional prophylactic dosage that is administered increases the baseline risk of wound infection that is required for prophylaxis to reduce overall antibiotic consumption.

If a second prophylactic dosage is administered after the operation and does not further reduce the risk of wound infection, then in example A, 30 doses instead of 15 are being administered to prevent one wound infection. As the NNT is the number of patients who must be treated, this remains at 15 with each patient now receiving two antibiotic doses.

This two-dose regimen would only reduce overall antibiotic consumption if the number of patients treated to prevent one wound infection is seven or lower, then the number of prophylactic doses (14) would be less than the number of doses needed to treat one wound infection (15). This would be the case if the baseline risk of wound infection were at least 15% (*see Table 7*).

Rule 2: Prophylaxis should be given if it is likely to reduce overall hospital *costs*

Example B: Calculation of the cost per wound infection avoided

> Table 7 can also be used to calculate the number of patients who must receive prophylaxis in order to prevent one wound infection (the NNT).
>
> Multiplying NNT by the cost of prophylaxis gives the cost of preventing one wound infection.
>
> For example, for the specific surgery, if the odds ratio = 0.3 and the estimated baseline risk of wound infection =10%, then the NNT =15
>
> If prophylaxis costs eg £5 per patient then it costs £75 (ie £5 x 15) to prevent one wound infection.
>
> This provides a threshold value. If the decision maker believes that it is good value to spend up to £75 to prevent a wound infection then prophylaxis should be implemented.

The prophylaxis cost of avoiding one wound infection of £75 is far less than estimated costs of treating a wound infection published in 1992, which ranged from £367 to £1,404,[22] and prophylaxis should be considered.

8.2.1 CALCULATING THE COMPARATIVE COSTS OF PROPHYLAXIS

The following points must be remembered when calculating the comparative costs of prophylaxis.

- Cost of prophylaxis should include the resource and drug costs of prophylaxis and the costs of increased prevalence of antibiotic resistance from antibiotic exposure.
- Calculations are highly sensitive to the costs of the particular antibiotic used for the prophylaxis.
- The minimal effective dose should be used. Increasing the number of doses above this minimum level of effectiveness adds to cost without improving effectiveness.
- The method of administration may influence the cost of prophylaxis.[194]
- Inappropriate or incorrect use of antibiotic prophylaxis may have adverse cost implications.[195,196]

8.3 IMPLEMENTATION

Guideline implementation should be supported by a programme of continuing education, evaluation of current literature and regular examination of antibiotic susceptibility patterns in local NHS boards.[197] 4

The following factors have been shown to increase the effectiveness of implementation strategies.

- Local guidelines or protocols should be developed by a multidisciplinary group of all stakeholders (for example, surgeons, anaesthetists, speciality pharmacists, microbiologists, infection control specialists).[198-201]
- Local guidelines or protocols should be flexible to allow for clinical judgement.[199]
- Local guidelines or protocols should be clear and easy to follow.[202]
- Regular audit, locally owned by stakeholders, with feedback of non-adherence to local guideline (including specific clinician feedback).[203] This should be actively discussed and acted upon on a regular basis.
- Active involvement and support from local senior staff or respected opinion leaders for the implementation strategy programme.[204, 205]

4

Recommended indications for surgical antibiotic prophylaxis are available from the SIGN website as surgery specific QRGs. These can be annotated for use as local implementation tools.

8.3.1 IMPLEMENTATION TOOLS FOR PREVENTING INAPPROPRIATE PRESCRIBING

Introduction of special forms for prescribing perioperative antimicrobial prophylaxis has been shown to reduce inappropriate prescribing from 64% to 21%.[140]

Use of specific antibiotic order forms[206] reduced inappropriate prescribing and was one of the recommendations of the Infectious Diseases Society of America (IDSA).[207,208] 4

Tools described include:

- standardised perioperative antibiotic prescribing forms[200,209,210]
- integrated dispensing processes[198, 200]
- personalised antibiotic kits[211,212]
- reminders[204]
- automated alerts for re-dosing during prolonged procedures.[212]

4

Prescribing antibiotic prophylaxis in the single dose section of drug prescription forms is also associated with a lower proportion of inappropriate additional dosage.[213] 3

D **Inappropriate prolongation of surgical prophylaxis can be reduced by use of specific prescribing forms for surgical prophylaxis, or recording of prophylaxis in single dose sections of existing drug prescription charts.**

8.4 AUDITING CURRENT PRACTICE

8.4.1 DOCUMENTATION

☑ All aspects of antibiotic prophylaxis, for example, where prophylaxis is not given when recommended, should be clearly recorded in the case records.

☑ Locally agreed protocols should clearly indicate where to document antibiotic prophylaxis in the patient records *(for example, the "once only" section of the drug chart, integrated care pathway or anaesthetic chart)*.

8.4.2 MINIMUM DATA SET FOR AUDIT OF SURGICAL ANTIBIOTIC PROPHYLAXIS

A minimum data set to document the administration of surgical antibiotic prophylaxis is summarised below.

- Date
- Operation performed
- Classification of operation (clean/clean-contaminated/ contaminated)
- Elective or emergency
- Patient weight (especially children)
- Any previous adverse reactions/allergies to antibiotics
- Justification for prophylaxis (eg, evidence of a high risk of SSI) if given for an operation where prophylaxis is not routinely indicated
- Justification for not giving prophylaxis (eg, procedure not in local guideline, patient on antibiotic treatment)
- Time of antibiotic administration
- Name of antibiotic
- Dosage of antibiotic
- Route of administration
- Time of surgical incision
- Duration of operation
- Second dosage indicated?
- Second dosage given?
- Postoperative antibiotic prophylaxis indicated?
- Postoperative antibiotic prophylaxis given?
- Antibiotic prophylaxis continued for > 24 hrs
- Documentation recorded appropriately (in correct place, clarity)
- Name of anaesthetist
- Name of surgeon

☑ Record the minimum data set to facilitate audit of the appropriateness of surgical antibiotic prophylaxis.

The majority of successful implementation strategies used short term audits and active feedback to stakeholders.[198,200,205,211]

A good quality systematic review of non-analytical studies showed that statistical process control can help change management and improve healthcare processes.[214]

3
4

An example of statistical process control is the PDSA (Plan, Do, Study, Act) cycle. Measurement of compliance (for example, using run and control charts) to give timely feedback to healthcare professionals is recommended by the Patient Safety Alliance (www.patientsafetyalliance.scot.nhs.uk) to achieve effective, embedded change. Further information on PDSA is available from NHSScotland Clinical Governance (www.clinicalgovernance.scot.nhs.uk/section2/pdsa.asp).

D **Short period audits held at regular intervals, with stakeholder feedback, are recommended.**

☑ The use of statistical process control to achieve effective, embedded change should be considered.

In the UK, the national mandatory surveillance of SSI dataset includes data items on surgical antibiotic prophylaxis, which indicate compliance with the SIGN guideline. The Surgical Site Infection Surveillance Protocol and Resource Pack is available from the SSHAIP website (www.hps.scot.nhs.uk/haiic/sshaip/guidelinedetail.aspx?id=31554).

8.4.3 CORE INDICATORS FOR AUDIT

Process measures:

- Was prophylaxis given for an operation included in local guidelines?
- If prophylaxis was given for an operation not included in local guidelines, was a clinical justification for prophylaxis recorded in the case notes?
- Was the first dosage of prophylaxis given within 30 minutes of the start of surgery?
- Were the choice, dosage and route of administration consistent with local guidelines for that procedure?
- Was the prescription written in the "once-only" section of the drug prescription chart?
- Was the duration of prophylaxis greater then 24 hours?

Outcome measures:

- Surgical site infection rate = number of SSIs occurring postoperatively/total number of operative procedures.
- Rate of SSIs occurring postoperatively in patients who receive inappropriate prophylaxis (as defined in guideline) compared with rate of this infection in patients who receive appropriate prophylaxis, expressed as a ratio.
- Rate of *C. diff* infections occurring postoperatively in patients who receive inappropriate prophylaxis (as defined in guideline) compared with rate of this infection in patients who receive appropriate prophylaxis, expressed as a ratio.

☑ For audit, surgical site infections should be described following the CDC criteria (*see Annex 2*).

8.4.4 AUDIT OF ANTIMICROBIAL PRESCRIBING

A point prevalence survey of antimicrobial prescribing performed in 10 Scottish hospitals used the Glasgow Antimicrobial Audit Tool (GAAT). Regional differences were seen and data collected may usefully inform local and national audit and support prescribing initiatives.[215]

9 The evidence base

9.1 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by a SIGN Information Officer. Databases searched include Medline, Embase, Cinahl, and the Cochrane Library. For most searches the year range covered was 2001-2007. Internet searches were carried out on various websites including the US National Guidelines Clearinghouse. The Medline version of the main search strategies can be found on the SIGN website, in the section covering supplementary guideline material. The main searches were supplemented by material identified by individual members of the development group.

9.1.1 LITERATURE SEARCH FOR ECONOMIC ISSUES

A SIGN Information Officer conducted a literature search of the NHS Economics Evaluations Database (NEED) for studies that highlighted economic issues related to antibiotic prophylaxis.

9.1.2 LITERATURE SEARCH FOR PATIENT ISSUES

At the start of the guideline development process, a SIGN Information Officer conducted a literature search for qualitative and quantitative studies that addressed patient issues of relevance to antibiotic prophylaxis in surgery. Databases searched include Medline, Embase, CINAHL and PsycINFO, and the results were summarised and presented to the guideline development group. A copy of the Medline version of the patient search strategy is available on the SIGN website.

9.2 RECOMMENDATIONS FOR RESEARCH

The guideline development group was not able to identify sufficient evidence to answer all of the key questions asked in this guideline. The following areas for further research have been identified:

9.2.1 SURGICAL ANTIBIOTIC PROPHYLAXIS IN ADULTS

General

- The efficacy of antibiotic prophylaxis during open surgery compared to laparoscopic surgery.
- The criteria for defining a surgical site infection in trauma and orthopaedics.

Intracranial surgery

- neural tube defects
- intracranial pressure monitors, external ventricular drains and implants
- baclofen pumps
- vagal nerve stimulators
- spinal cord stimulators
- deep brain stimulators
- impregnated CSF shunts.

Ophthalmic surgery

- trabeculectomy
- squint
- dacryocystorhinostomy
- elective posterior segment surgery.

Facial surgery

- facial skin surgery, soft tissue reconstruction and aesthetic surgeries
- facial plastic surgery with implant.

Ear, nose and throat surgery

- tonsillectomy
- adenoidectomy by methods other than curettage
- comparison of topical and oral antibiotics for grommet insertion.

Urological surgery

- urological implants (prosthetics, stents, pumps)
- radical nephrectomy
- radical cystectomy
- radical prostatectomy.

Thorax

- breast surgery.

Surgery of the limb

- soft tissue surgery of the hands
- varicose veins
- vascular grafts
- arterovenous surgery.

Non-operative interventions

- interventional radiological procedures
  - solid organ embolisation
  - percutaneous biliary procedures
  - percutaneous urological intervention
  - endovascular stent graft
- vascular stents, endovascular coil placement
- coronary stents.

9.2.2 SURGICAL ANTIBIOTIC PROPHYLAXIS IN CHILDREN

Further research into the efficacy of antibiotic prophylaxis for all surgical interventions in children, in the form of clinical trials, particularly multicentre trials, is recommended.

Research underpinning the following factors needs to be addressed

- Choice of antibiotic and duration of prophylaxis, as therapy may be carried on for longer in children than studies in adults would recommend.
- Factors such as host responses, antibiotic pharmacodynamics/pharmacokinetics may be different enough to have a separate policy.
- Rates of SSIs and their relation to practice, including prophylaxis.

9.2.3 PRINCIPLES OF ANTIBIOTIC PROPHYLAXIS

Further research is required to address areas where there is insufficient evidence to make recommendations or support current clinical practice. The following areas have been identified as especially important. Research into antibiotic prophylaxis to prevent SSI should use the CDC definitions (*see Annexes 2 and 3*).

- The pharmacodynamics, pharmacokinetics and duration of antibiotic prophylaxis.
- The risks of *C. diff* associated diarrhoea.
- The preoperative implications of MRSA and other multiresistant organisms.
- The harms and benefits of administering prophylactic antibiotics post-cord clamp.
- The timing of administration of prophylactic antibiotics.
- The requirement for additional dosage during operation by:
  - surgery type
  - antibiotic.
- Evaluation of the efficacy and need for topical administration of prophylactic antibiotics
- Economic evaluation of prophylaxis for different operations.

9.3 REVIEW AND UPDATING

This guideline was issued in 2008 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: **www.sign.ac.uk**.

10 Development of the guideline

10.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of NHS Quality Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising clinicians using a standard methodology based on a systematic review of the evidence. The views and interests of NHS Quality Improvement Scotland as the funding body have not influenced any aspect of guideline development, including the final recommendations. Further details about SIGN and the guideline development methodology are contained in "SIGN 50: A Guideline Developer's Handbook", available at **www.sign.ac.uk**

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The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN Executive.

Guideline development and literature review expertise, support and facilitation were provided by the SIGN Executive.

10.2.1 PATIENT INVOLVEMENT

In addition to the identification of relevant patient issues from a broad literature search, SIGN involves patients and carers throughout the guideline development process in several ways. SIGN recruits a minimum of two patient representatives to guideline development groups by inviting nominations from the relevant "umbrella", national and/or local patient focused organisations in Scotland. Where organisations are unable to nominate, patient representatives are sought via other means, for example, from consultation with health board public involvement staff.

Further patient and public participation in guideline development was achieved by involving patients, carers and voluntary organisation representatives at the National Open Meeting (*see section 10.3.1*). Patient representatives were invited to take part in the peer review stage of the guideline and specific guidance for lay reviewers was circulated. Members of the SIGN patient network were also invited to comment on the draft guideline section on provision of information.

10.2.2 ACKNOWLEDGEMENTS

SIGN would like to offer special acknowledgement to Ms Jennifer Blair, lay representative, who sadly died during the development of this guideline.

SIGN is grateful to the following former members of the guideline development group and others who have contributed to the development of the guideline.

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Dr Gavin Stark	*General Practitioner, Victoria Street Medical Group, Aberdeen*
Dr Olivia Wu	*Research Fellow, University of Glasgow*

10.3 CONSULTATION AND PEER REVIEW

10.3.1 NATIONAL OPEN MEETING

A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents its draft recommendations for the first time. The national open meeting for this guideline was held on 26th March 2007 and was attended by 56 representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

10.3.2 SPECIALIST REVIEW

This guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. The guideline group addresses every comment made by an external reviewer, and must justify any disagreement with the reviewers' comments.

SIGN is very grateful to all of these experts for their contribution to the guideline.

Mr Kim Ah-See	*Consultant Otolaryngologist/Head and Neck Surgeon, Aberdeen Royal Infirmary*
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Mr I Graeme Conn	*Consultant Urological Surgeon, Southern General Hospital, Glasgow*

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Mr Christopher Driver	*Consultant in Paediatric Surgery, Aberdeen Royal Infirmary*
Mr Jonothan Earnshaw	*Consultant General and Vascular Surgeon, Gloucestershire Royal Infirmary*
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Mr Joe McManners	*Consultant Oral and Maxillofacial Surgeon, Falkirk and District Royal Infirmary*
Dr Allan Merry	*General Practitioner, South Beach Surgery, Ardrossan*
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Professor Hamish Simpson	*Professor of Trauma and Orthopaedics, University of Edinburgh*
Mr Patrick Walsh	*Consultant Breast Surgeon, Raigmore Hospital, Inverness*
Professor George Youngson	*Professor of Paediatric Surgery, Royal Aberdeen Children's Hospital*

10.3.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group including the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows:

Dr Keith Brown	*Chair of SIGN; Co-Editor*
Mr Andrew de Beaux	*Royal College of Surgeons of Edinburgh*
Dr Safia Qureshi	*SIGN Programme Director; Co-Editor*
Dr Sara Twaddle	*Director of SIGN; Co-Editor*

Abbreviations

AAD	antibiotic-associated diarrhoea
ASA	American Society of Anesthesiologists
BHS	beta-haemolytic streptococci
CABG	coronary artery bypass graft
CDAD	*Clostridium difficile* associated diarrhoea
CDC	Centers for Disease Control
C. diff	*Clostridium difficile*
CI	confidence interval
CNS	coagulase negative staphylococci
CSF	cerebrospinal fluid
CVC	central venous catheter
ERCP	endoscopic retrograde cholangiopancreatography
GAAT	Glasgow Antimicrobial Audit Tool
HAI	healthcare associated infection
Ig	immunoglobulin gamma
IDSA	Infectious Diseases Society of America
IUCD	intrauterine contraceptive device
IV	intravenous
MACE	Malone antegrade continence enema
MRSA	meticillin-resistant *Staphylococcus aureus*
MRSE	meticillin-resistant *Staphylococcus epidermis*
MSSA	meticillin-sensitive *Staphylococcus aureus*
MTA	multiple technology appraisal
NCBI	National Centre for Biotechnology Information
NEED	NHS Economics Evaluations Database
NICE	National Institute for Health and Clinical Excellence
NNIS	National Nosocomial Infections Surveillance
NNT	number needed to treat
NNTH	number needed to harm
OR	odds ratio
PDSA	Plan, Do, Study, Act
PEG	percutaneous endoscopic gastrostomy
RCT	randomised controlled trial
RR	risk reduction
RTI	respiratory tract infection
S. aureus	*Staphylococcus aureus*

S. boulardi	*Saccharomyces boulardi*
SIGN	Scottish Intercollegiate Guidelines Network
SMC	Scottish Medicines Consortium
SSHAIP	Scottish Surveillance of Healthcare Associated Infection Programme
SSI	surgical site infection
UTI	urinary tract infection
VP	ventriculoperitoneal
VRE	vancomycin-resistant enterococci

Annex 1

Key questions used to develop the guideline

The guideline is based on a series of structured key questions that, where possible, define the *population* concerned, the *intervention* (or diagnostic test, etc) under investigation, the type of *control* used, and the *outcomes* used to measure the effectiveness of the interventions. These questions form the basis of the systematic literature search.

THE KEY QUESTIONS USED TO DEVELOP THE GUIDELINE

RISK FACTORS FOR SURGICAL SITE INFECTION	
Key question	*See guideline section*
1. What factors increase or decrease the risk of SSI in patients receiving antibiotic prophylaxis? *Consider*: ▪ comorbidities such as diabetes, high BMI, disabilities ▪ immunosupression ▪ infection of site ▪ smoking ▪ perioperative hypothermia ▪ hypo-oxygenation ▪ early goal directed therapy.	3
BENEFITS AND RISKS OF ANTIBIOTIC PROPHYLAXIS	
Key question	*See guideline section*
2. What is the likelihood that those people with a penicillin allergy are allergic to cephalosporins? What is the best definition of penicillin allergy?	4.2.1
3. What is the evidence that administering antibiotic prophylaxis during surgery increases the risk of the following in the patient? ▪ anaphylaxis ▪ antibiotic-induced diarrhoea ▪ *Clostridium difficile*.	4.2.2-4.2.4
4. What is the evidence that administering antibiotic prophylaxis during surgery increases antibiotic-resistant strains in the general population?	4.2.5
5. What is the evidence that multiresistance carriage in patients undergoing surgical procedures increases the incidence of SSI?	4.2.6
6. Is there evidence that changing the prophylactic antibiotic, when MRSA carriage is known, changes management of SSI?	6.1.1

INDICATIONS FOR SURGICAL ANTIBIOTIC PROPHYLAXIS	
Key question	*See guideline section*
7. Is antibiotic prophylaxis recommended to prevent surgical site infection during neurosurgery? ▪ craniotomy ▪ CSF shunt ▪ spinal ▪ neural tube defects ▪ intracranial pressure monitors, external ventricular drains and implants ▪ baclofen pumps ▪ vagal nerve stimulators ▪ spinal cord stimulators ▪ deep brain stimulators.	5.2
8. Is antibiotic prophylaxis recommended to prevent surgical site infection during ophthalmic surgery? ▪ cataract ▪ cataract/lens implant ▪ vitreoretinal ▪ ocular plastics ▪ glaucoma ▪ squint correction ▪ penetrating keratoplasties ▪ lacrimal ▪ primary repair.	5.2
9. Is antibiotic prophylaxis recommended to prevent surgical site infection during oral and maxillofacial surgery? ▪ facial trauma ▪ temperomandibular joint surgery and prostheses ▪ orthognathic.	5.2
10. Is antibiotic prophylaxis recommended to prevent surgical site infection during ear, nose and throat surgery? ▪ head and neck ▪ ear ▪ nose/sinus ▪ tonsils ▪ grommets.	5.2
11. Is antibiotic prophylaxis recommended to prevent surgical site infection during breast surgery? ▪ mastectomy ▪ biopsy ▪ localisation biopsy ▪ breast reshaping ▪ breast reconstruction.	5.2
12. Is antibiotic prophylaxis recommended to prevent surgical site infection during cardiothoracic surgery? ▪ cardiac pacemaker insertion ▪ heart surgery ▪ coronary artery bypass grafting ▪ prosthetic valve surgery ▪ pulmonary resection.	5.2

13. Is antibiotic prophylaxis recommended to prevent surgical site infection during gastrointestinal surgery ▪ oesophageal ▪ liver ▪ gall bladder ▪ bile duct ▪ pancreatic ▪ spleen (not post splenectomy) ▪ gastric ▪ small bowel ▪ appendix ▪ colorectal ▪ bariatric surgery (gastric band) ▪ endoscopic ultrasound ▪ PEG tubes ▪ ERCP ▪ laparoscopic procedures.	5.2
14. Is antibiotic prophylaxis recommended to prevent surgical site infection during hernia repair? ▪ incisional ▪ groin ▪ laparoscopic ▪ open.	5.2
15. Is antibiotic prophylaxis recommended to prevent surgical site infection during urological surgery? ▪ transrectal prostate biopsy ▪ stones - percutaneous lithotripsy - ureteric and bladder stones - extracorpeal shock wave lithotripsy ▪ transurethral resection of prostate ▪ transurethral resection of bladder tumour ▪ implants (prosthetics, stents, pumps, Teflon) ▪ radical nephrectomy ▪ radical cystectomy ▪ radical prostatectomy.	5.2
16. Is antibiotic prophylaxis recommended to prevent surgical site infection during obstetric and gynaecological surgury ▪ caesarean section (before or after clamp) ▪ hysterectomy ▪ induced abortion ▪ trans-vaginal tape (urinary stress incontinence) ▪ assisted delivery ▪ perineal tear ▪ removal of placenta (manual).	5.2
17. Is antibiotic prophylaxis recommended to prevent surgical site infection during orthopaedic surgery? ▪ primary arthroplasty upper and lower limb ▪ fracture fixation open fracture ▪ fracture fixation closed fracture ▪ surgical hip fracture repair ▪ surgery without implant (elective or emergency) ▪ surgery with implant (artificial or graft) (elective or emergency) ▪ bone tumour surgery.	5.2

18. Is antibiotic prophylaxis recommended to prevent surgical site infection during vascular surgery? ▪ lower limb amputation ▪ vascular surgery (abdominal and lower limb) ▪ varicose veins ▪ vascular grafts ▪ arterovenous surgery.	5.2
19. Is antibiotic prophylaxis recommended to prevent surgical site infection during non-operative interventional procedures? ▪ interventional radiological procedures - solid organ embolisation - percutaneous biliary procedures - percutaneous urological intervention - endovascular stent graft ▪ intravascular catheter insertion ▪ vascular stents, endovascular coil placement ▪ coronary stents.	5.2
20. Is antibiotic prophylaxis recommended to prevent surgical site infection during plastic surgery? ▪ facial skin surgery, soft tissue reconstruction and aesthetic surgeries ▪ plastic surgery (implant or no implant) ▪ soft tissue surgery of the hands.	5.2
21. Is antibiotic prophylaxis recommended to prevent surgical site infection during paediatric surgery? ▪ neurosurgery ▪ cleft lip/palate ▪ cardiothoracic ▪ colostomy, MACE (Malone antegrade continence enema) stoma ▪ appendix ▪ hernia ▪ hydroceles ▪ circumcision ▪ hypospadias ▪ urological (percutaneous lithotripsy, cystoscopy, nephrectomy, pyleoplasty).	5.3
22. Should antibiotic prophylaxis be used to prevent chest/respiratory, UTI, catheter and blood stream infections in patients undergoing surgical procedures?	5.4

ADMINISTRATION OF PROPHYLACTIC ANTIBIOTICS

Key question	*See guideline section*
23. In patients undergoing surgical procedures which of the following antibiotics are most effective at preventing surgical site infection? Consider: ▪ β-lactam, quinolones, cephalasporins, glycopeptides ▪ MRSA carriage.	6.1
24. What is the optimum time to administer prophylactic antibiotics to prevent SSI?	6.2
25. In patients undergoing surgical procedures are multiple or single doses of antibiotics more effective at preventing surgical site infection?	6.4
26. What is the evidence that patients undergoing surgical procedures in excess of two hours require an additional dose of antibiotic to prevent surgical site infection? *Consider*: ▪ half-life of antibiotic ▪ fluid/blood loss.	6.4.1 6.4.2
27. In patients undergoing surgical procedures and receiving antibiotic prophylaxis which of the following routes is most effective at preventing surgical site infection? *Consider*: ▪ IV ▪ oral ▪ topical (bone cement, mesh, grafts, eardrops) ▪ rectal ▪ intraperitoneal washout.	6.5

IMPLEMENTING THE GUIDELINE

Key question	*See guideline section*
28. What strategies exist to increase the effectiveness of guideline implementation?	8

Annex 2

CDC criteria for defining a surgical site infection[216]

Superficial incisional SSI

Infection occurs within 30 days after the operation and infection involves only skin of subcutaneous tissue of the incision *and* at least one of the following:

1. purulent drainage, with or without laboratory confirmation, from the superficial incision
2. organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision
3. at least one of the following signs or symptoms of infection:
   - pain or tenderness
   - localised swelling
   - redness
   - heat

   and superficial incision deliberately opened by a surgeon, unless incision is culture-negative
4. diagnosis of superficial incisional SSI by the surgeon or attending physician.

Do *not* report the following conditions as SSI:

1. stitch abscess (minimal inflammation and discharge confined to the points of suture penetration)
2. infection of an episiotomy or newborn circumcision site
3. infected burn wound
4. incisional SSI that extends into the fascial and muscle layers (see deep incisional SSI).

Note:
Specific criteria are used for identifying infected episiotomy and circumcision sites and burn wounds.

Deep incisional SSI

Infection occurs within 30 days after the operation if no implant is left in place or within one year if implant is in place and the infection appears to be related to the operation and infection involves deep soft tissues (eg fascial and muscle layers) of the incision and at least one of the following:

1. purulent drainage from the deep incision but not from the organ/space component of the surgical site
2. a deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms:
   - fever (>38°C)
   - localised pain
   - tenderness

   unless site is culture-negative
3. an abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathological or radiological examination
4. diagnosis of deep incisional SSI by a surgeon or attending physician.

Notes:
Report infection that involves both superficial and deep incision sites as deep incisional SSI.
Report an organ/space SSI that drains through the incision as deep incisional SSI.

Annex 2

(continued)

Organ/space SSI
Infection occurs within 30 days after the operation if no implant is left in place or within one year if implant is in place and the infection appears to be related to the operation and infection involves any part of the anatomy (eg organs or spaces), other than the incision, which was opened or manipulated during an operation and at least one of the following: 1. purulent discharge from a drain that is placed through a stab wound into the organ/space 2. organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space 3. an abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiological examination 4. diagnosis of an organ/space SSI by a surgeon or attending physician.

Annex 3

CDC classification of site-specific organ/space surgical site infection[216]

- arterial or venous infection
- breast abscess or mastitis
- disc space
- ear, mastoid
- endocarditis
- endometritis
- eye, other than conjunctivitis
- gastrointestinal tract
- intra-abdominal, not specified elsewhere
- intracranial, brain abscess or dura
- joint or bursa
- mediastinitis
- meningitis or ventriculitis
- myocarditis or pericarditis
- oral cavity (mouth, tongue or gums)
- osteomyelitis
- other infections of the lower respiratory tract (eg abscess or emyema)
- other male or female reproductive tract
- sinusitis
- spinal abscess without meningitis
- upper respiratory tract
- vaginal cuff

Annex 4

Table of common pathogens

SSI organism	*Antibiotic susceptibility*
SURGICAL SITE INFECTION FOR A SKIN WOUND AT ANY SITE	
Staphylococcus aureus	30-60% remain susceptible to flucloxacillin, macrolides and clindamycin
Beta-haemolytic streptococci (BHS)	90% remain susceptible to penicillins, macrolides and clindamycin
ADDITIONAL PATHOGENS (*to S. aureus and BHS*) by site of infection	
Head and neck surgery	
Oral anaerobes	95% remain susceptible to metronidazole and co-amoxiclav. Penicillin can no longer be relied upon.
Operations below the diaphragm	
Anaerobes	95% remain susceptible to metronidazole and co-amoxiclav. Penicillin can no longer be relied upon.
E. coli and other enterobacteriaceae	Complex resistance problems. However, approximately 80-90% of *E. coli* remain susceptible to second generation cephalosporins, beta-lactam drugs combined with a beta-lactamase inhibitor, or gentamicin.
Insertion of a prosthesis, graft or shunt	
Coagulase negative staphylococci (CNS) *Staphylococcus aureus* *Diphtheroids*	30-60% of *S. aureus* remain susceptible to flucloxacillin, macrolides or clindamycin, depending on the site of insertion. Although two thirds of CNS are meticillin-resistant, prophylaxis with beta-lactam antibiotics is still appropriate (see below).
MRSE, MRSA and glycopeptide prophylaxis	
The increasing prevalence of meticillin-resistant *S. aureus* (MRSA) raises the issue of glycopeptide prophylaxis against MRSA and meticillin-resistant *S. epidermis* (MRSE) infections, usually when inserting large joint prostheses, vascular or cardiac grafts or shunts (*see section 6.1.1*).	

Annex 5

In vitro activity of antibiotics, which may be considered for antibiotic prophylaxis *(reproduced by kind permission of V Wallroth, V Weston and T Hills)*[217]

	Gram positive							Anaerobes			Gram negative					
	Staphylococcus aureus MSSA	*Staph. aureus MRSA*	*Staph. epidermidis*	*Haemolytic streptococci (Strep. A,C,G and Strep B)*	*Enterococcus faecalis*	*Enterococcus faecium*	*Streptococcus pneumoniae*	*Clostridium perfringens*	*Clostridium difficile*	*Bacteroides fragilis*	*Haemophilus influenzae*	*Escherichia coli*	*Klebsiella species (and other 'coliforms')*	*ESBL positive Escherichia coli and other ESBL positive 'coliforms'*	*Pseudomonas aeruginosa*	*Moraxella catarrhalis*
Penicillins																
Benzylpenicillin	—	—	—	✓	✓	—	✓	✓	—	—	—	—	—	—	—	—
Ampicillin/ Amoxicillin	—	—	—	✓	✓	—	✓	✓	—	—	?	?	?	—	—	—
Co-amoxiclav	✓	—	—	✓	✓	—	✓	✓	—	✓	✓	✓	?	—	—	✓
Flucloxacillin	✓	—	?	✓	—	—	—	—	—	—	—	—	—	—	—	—
Cephalosporins																
Cefradine	✓	—	?	✓	—	—	✓	—	—	—	—	✓	?	—	—	—
Cefuroxime	✓	—	?	✓	—	—	✓	—	—	—	✓	✓	✓	—	—	✓
Ceftriaxone	✓	—	—	✓	—	—	✓	—	—	—	✓	✓	✓	—	—	✓
Ceftazidime	—	—	—	—	—	—	—	—	—	—	✓	✓	✓	—	✓	✓
Macrolides/Lincosamides																
Erythromycin	✓	?	—	✓	—	—	✓	—	—	—	—	—	—	—	—	—
Clarithromycin	✓	?	—	✓	—	—	✓	—	—	—	—	—	—	—	—	—
Clindamycin	✓	?	?	✓	—	—	—	✓	—	✓	—	—	—	—	—	—
Aminoglycosides																
Gentamicin	✓	✓	?	—	—	—	—	—	—	—	—	✓	✓	?	✓	—
Diaminopyrimidines																
Trimethoprim	?	?	—	—	?	?	—	—	—	—	?	✓	✓	—	—	—
Quinolones																
Ciprofloxacin	✓	—	—	—	—	—	—	—	—	—	✓	✓	✓	—	✓	✓
Levofloxacin	✓	—	—	—	—	—	✓	—	—	—	✓	✓	✓	—	✓	✓
Glycopeptides																
Vancomycin IV	✓	✓	✓	✓	✓	✓	✓	—	—	—	—	—	—	—	—	—
Teicoplanin	✓	✓	✓	✓	✓	✓	✓	—	—	—	—	—	—	—	—	—
Vancomycin PO	—	—	—	—	—	—	—	—	✓	—	—	—	—	—	—	—
Nitroimidazoles																
Metronidazole	—	—	—	—	—	—	—	✓	✓	✓	—	—	—	—	—	—
Tetracyclines																
Doxycycline	✓	✓	?	?	?	?	✓	—	—	—	✓	—	—	—	—	✓

✓ in vitro activity (ie usually sensitive)
— inappropriate therapy *or* usually resistant
? variable sensitivity

Annex 6

Calculating the cost effectiveness of antibiotic prophylaxis

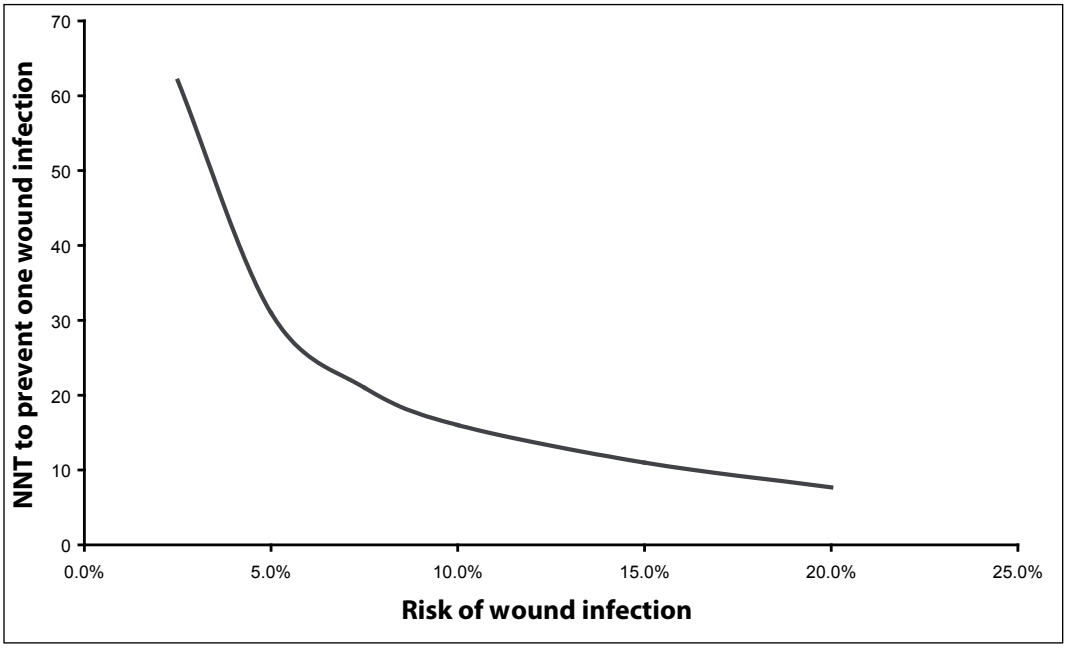
Three concepts are used in calculating the cost effectiveness of using antibiotic prophylaxis:

Odds Ratio (OR)
The OR for a particular procedure is the number of wound infections occurring following prophylaxis divided by the number of wound infections occurring without prophylaxis. An odds ratio of 1 indicates no effect from prophylaxis.
Expected Baseline Risk
This is the number of wound infections occurring within the hospital for a particular surgical procedure each year, divided by the total number of times the surgical procedure is performed in the year. The expected baseline risk multiplied by 100 is the percentage risk of wound infection for that procedure.
Numbers Needed to Treat (NNT)
The NNT is the number of patients who must be given antibiotic prophylaxis in order to prevent one wound infection.

The method of calculating NNT from expected baseline risk and odds ratio is given in Cook and Sackett:[193]

$$\text{NNT} = \frac{1-[\text{expected baseline risk} \times (1-\text{odds ratio})]}{1-(\text{expected baseline risk}) \times \text{expected baseline risk} \times (1-\text{odds ratio})}$$

The relationship between the baseline risk of wound infection and NNT is not a straight line. The NNT falls steeply as the risk of wound infection increases. The figure below shows the numbers of patients needed to be treated with antibiotic prophylaxis to prevent one wound infection in caesarean section surgery based on the results of a meta-analysis of randomised controlled clinical trials.[113, 218] The odds ratio of wound infection with prophylaxis is 0.35.



Annex 7

Unlicensed use of licensed medicines

Some recommendations within this guideline may be for drugs used outwith the terms of their license ("off label"), for example, intranasal mupirocin for patients undergoing surgery with a high risk of major morbidity, who are identified with S. *aureus* or MRSA (*see sections 6.1.1 and 6.5.2*). The definition of an "off label" drug is a medicine with a UK Marketing Authorisation, which is prescribed for:

- an indication not specified within the marketing authorisation
- administration via a different route
- administration of a different dose.

Any practitioner prescribing an unlicensed medicine or a licensed medicine for an unlicensed indication must take responsibility for their actions. The prescriber carries the burden of the patient's welfare and in the event of adverse reactions, may be called upon to justify the decisions that they have taken.

Use of unlicensed medicines may be necessary when there are no other available products, such as is the case with many drugs prescribed for children, which are rarely tested in that population. Alternatively an unlicensed medicine or a licensed medicine for an unlicensed indication may be more cost effective.

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ISBN 978 1 905813 34 6

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