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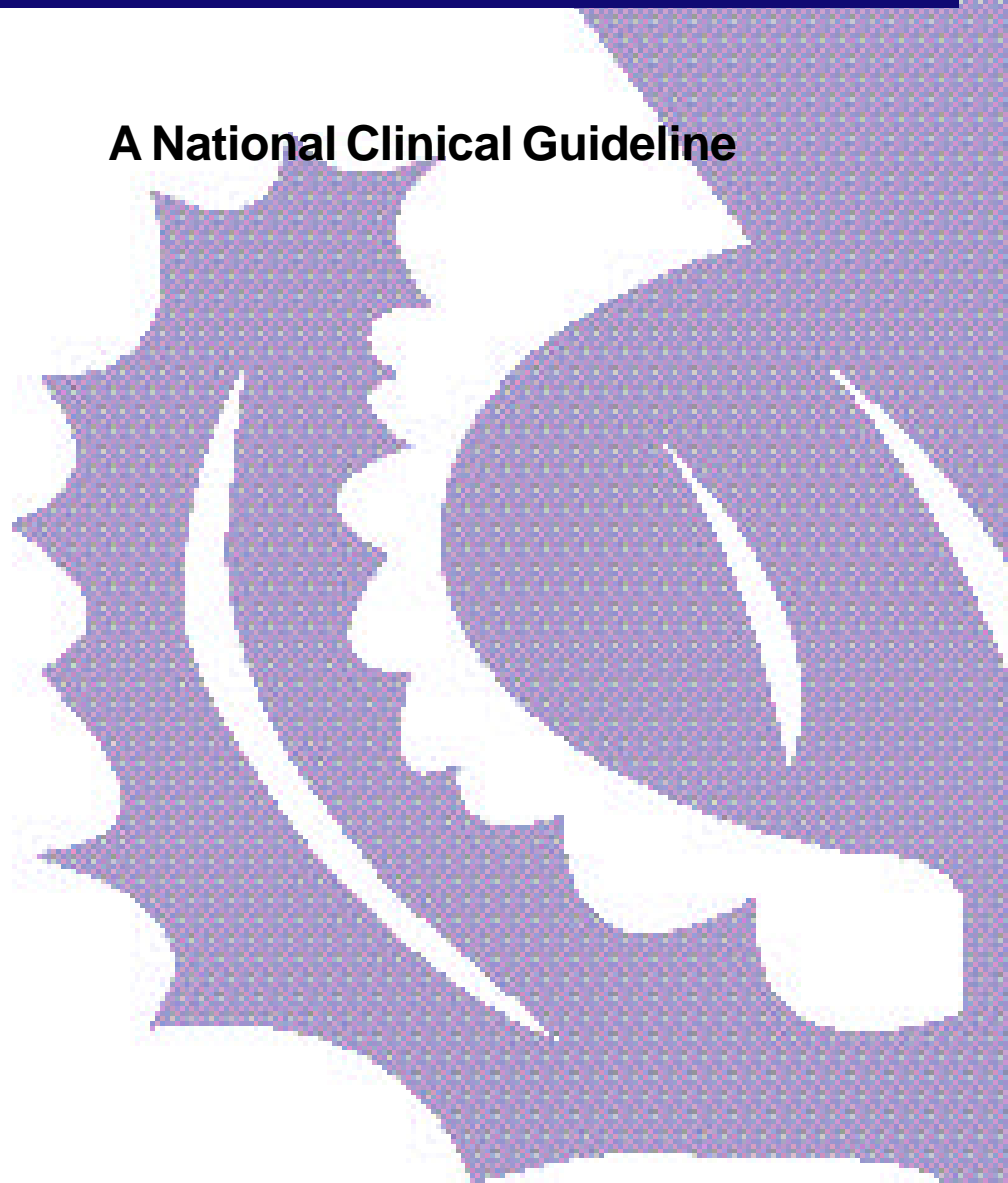
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Scottish
Intercollegiate
Guidelines
Network

Antibiotic Prophylaxis in Surgery

A National Clinical Guideline

July 2000



KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

The definitions of the types of evidence and the grading of recommendations used in this guideline originate from the US Agency for Health Care Policy and Research¹ and are set out in the following tables.

STATEMENTS OF EVIDENCE

<i>Ia</i>	Evidence obtained from meta-analysis of randomised controlled trials.
<i>Ib</i>	Evidence obtained from at least one randomised controlled trial.
<i>IIa</i>	Evidence obtained from at least one well-designed controlled study without randomisation.
<i>IIb</i>	Evidence obtained from at least one other type of well-designed quasi-experimental study.
<i>III</i>	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.
<i>IV</i>	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

GRADES OF RECOMMENDATIONS

A	Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. <i>(Evidence levels Ia, Ib)</i>
B	Requires the availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation. <i>(Evidence levels IIa, IIb, III)</i>
C	Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. <i>(Evidence level IV)</i>

GOOD PRACTICE POINTS

<input checked="" type="checkbox"/>	Recommended best practice based on the clinical experience of the guideline development group.
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Scottish Intercollegiate Guidelines Network

Antibiotic Prophylaxis in Surgery

July 2000



S I G N

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Notes for users of the guideline

DEVELOPMENT OF LOCAL GUIDELINES

It is intended that this guideline will be adopted after local discussion involving clinical staff and management. The Area Clinical Effectiveness Committee should be fully involved. Local arrangements may then be made for the derivation of specific local guidelines to implement the national guideline in individual hospitals, units, and practices, and for securing compliance with them. This may be done by a variety of means, including patient-specific reminders, continuing education and training, and clinical audit.

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STATEMENT OF INTENT

This report is not intended to be construed or to serve as a standard of medical care. Standards of medical 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.

These parameters of practice should be considered guidelines only. Adherence to them 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 regarding a particular clinical procedure or treatment plan must be made by the doctor in light of the clinical data presented by the patient and the diagnostic and treatment options available.

Significant departures from the national guideline as expressed in the local guideline should be fully documented and the reasons for the differences explained. Significant departures from the local guideline should be fully documented in the patient's case notes at the time the relevant decision is taken.

A background paper on the legal implications of guidelines is available from the SIGN Secretariat.

REVIEW OF THE GUIDELINE

This guideline was issued in July 2000 and will be reviewed in 2002, or sooner if new evidence becomes available. Any amendments or updates to the guideline in the interim period will be noted on the SIGN website: www.sign.ac.uk. Comments are invited to assist the review process. All correspondence and requests for further information regarding the guideline should be addressed to:

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Abbreviations

ASA	American Society of Anesthesiologists
BHS	Beta-haemolytic Streptococci
CI	Confidence interval
CNS	Coagulase-negative Streptococci
CSF	Cerebrospinal fluid
IDSA	Infectious Diseases Society of America
IV	Intravenous
MRSE	Methicillin-resistant <i>Staphylococcus epidermis</i>
MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
NNT	Number needed to treat
OR	Odds ratio
RCT	Randomised controlled trial
SIGN	Scottish Intercollegiate Guidelines Network
SSI	Surgical site infection
UTI	Urinary tract infection
VRE	Vancomycin-resistant Enterococcus

Summary of recommendations

PRINCIPLES 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 surgical site infection
 - the potential severity of the consequences of surgical site infection
 - the effectiveness of prophylaxis in that operation
 - the consequences of prophylaxis for that patient (*e.g. increased risk of colitis*).
- 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 microbiology, and drug costs.
- Treatment policies should be based on local information about the epidemiology of drug-resistant bacteria. Implementation of a prophylaxis policy should not trigger an automatic change in treatment policy.
- C** Inappropriate prolongation of surgical prophylaxis can be reduced by use of specific order forms for surgical prophylaxis, or recording of prophylaxis in single dose sections of existing drug prescription charts.

ADMINISTRATION OF INTRAVENOUS PROPHYLACTIC ANTIBIOTICS

- C** The antibiotics selected for prophylaxis must cover the common pathogens.
- B** Patients with a history of anaphylaxis or urticaria or rash occurring immediately after penicillin therapy are at increased risk of immediate hypersensitivity to penicillins and should not receive prophylaxis with a beta-lactam antibiotic.
- 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.
- A** Prophylaxis should be started preoperatively in most circumstances, ideally within 30 minutes of the induction of anaesthesia.
- A** Antibiotic prophylaxis should be administered immediately before or during a procedure.
- Prophylactic antibiotics should be administered intravenously.
- The single dose of antibiotic for prophylactic use is, in most circumstances, the same as would be used therapeutically.
- B** An additional dose of prophylactic agent is not indicated in adults, unless there is blood loss of up to 1500 ml during surgery or haemodilution of up to 15 ml/kg.
- Fluid replacement bags should not be primed with prophylactic antibiotics because of the potential risk of contamination and calculation errors.

INDICATIONS FOR SURGICAL ANTIBIOTIC PROPHYLAXIS

CARDIOTHORACIC SURGERY

Antibiotic prophylaxis is recommended in:

- A – **Cardiac pacemaker insertion**
- B – **Open heart surgery**, including coronary artery bypass grafting and prosthetic valve surgery
- A – **Pulmonary resection**

ENT SURGERY

Antibiotic prophylaxis is recommended in:

- A – **Head and neck surgery** (clean-contaminated/contaminated)

Antibiotic prophylaxis is not recommended in:

- A – **Ear surgery** (clean)
- C – **Head and neck surgery** (clean)
- C – **Nose or sinus surgery**
- C – **Tonsillectomy**

GENERAL SURGERY

Antibiotic prophylaxis is highly recommended in:

- A – **Colorectal surgery**

Antibiotic prophylaxis is recommended but local policy makers may identify exceptions in:

- A – **Appendicectomy**
- A – **Biliary surgery** (open)
- C – **Breast surgery**
- C – **Clean-contaminated procedures** (*extrapolated from specific clean-contaminated procedures*)
- A – **Endoscopic gastrostomy**
- A – **Gastroduodenal surgery**
- C – **Oesophageal surgery**
- C – **Small bowel surgery**
- C – **Laparoscopic or non-laparoscopic hernia repair with mesh**

Antibiotic prophylaxis is not recommended in:

- A – **Laparoscopic or non-laparoscopic hernia surgery without a mesh**
- C – **Laparoscopic cholecystectomy**

NEUROSURGERY

Antibiotic prophylaxis is recommended in:

- A – **Craniotomy**
- A – **CSF shunt**

OBSTETRICS & GYNAECOLOGY

Antibiotic prophylaxis is recommended but local policy makers may identify exceptions in:

- A** – **Caesarean section**
- A** – **Hysterectomy** (abdominal or vaginal)
- A** – **Induced abortion**

OPHTHALMOLOGY

Antibiotic prophylaxis is recommended but local policy makers may identify exceptions in:

- C** – **Cataract surgery**

ORTHOPAEDIC SURGERY

Antibiotic prophylaxis is highly recommended in:

- A** – **Total hip replacement***
- B** – **Prosthetic knee joint replacement***

Antibiotic prophylaxis is recommended in:

- A** – **Closed fracture fixation**
- A** – **Hip fracture repair**
- A** – **Spinal surgery**

Antibiotic prophylaxis is recommended but local policy makers may identify exceptions in:

- C** – **Insertion of prosthetic device*** (*extrapolated from trials of specific devices*)

Antibiotic prophylaxis is not recommended in:

- C** – **Orthopaedic surgery without prosthetic device** (elective)

** regardless of use of antibiotic cement*

UROLOGY

Antibiotic prophylaxis is recommended in:

- A** – **Transrectal prostate biopsy**

Antibiotic prophylaxis is recommended but local policy makers may identify exceptions in:

- A** – **Shock-wave lithotripsy**
- A** – **Transurethral resection of the prostate**

Antibiotic prophylaxis is not recommended in:

- C** – **Transurethral resection of bladder tumours**

VASCULAR SURGERY

Antibiotic prophylaxis is recommended in:

- A** – **Lower limb amputation**
- A** – **Vascular surgery** (abdominal and lower limb)



1 Introduction

1.1 BACKGROUND

Infection of the incised skin or soft tissues is a common but potentially avoidable complication of any surgical procedure. Some bacterial contamination of a surgical site is inevitable, either from the patient's own bacterial flora or from the environment. A UK survey of 157 hospitals carried out in 1993/94 found that the prevalence of wound infection was 2.6% amongst 12,947 patients in eight surgical specialties, varying from 1.5% in neurosurgery to 6.2% in vascular surgery.²

In procedures that require the insertion of implants or prosthetic devices, the term surgical site infection is used to encompass the surgical wound and the implant. Surgical site infection also encompasses infections involving the body cavity (e.g. a subphrenic abscess), bones, joints, meninges and other tissues involved in the operation (see annexes 2 and 3). 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 bacteria³⁻⁵ and their adherence to prosthetic implants, thus reducing the risk of infection. In a survey of antibiotic use in one district general hospital, this indication accounted for approximately one third of all antibiotics prescribed.⁶ Administration of antibiotics also increases the prevalence of antibiotic-resistant bacteria⁷ and predisposes the patient to infection with organisms such as *Clostridium difficile*, a cause of antibiotic-associated colitis.⁸

1.2 GOALS OF ANTIBIOTIC PROPHYLAXIS

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 hospital-acquired infection.

1.3 THE NEED FOR A GUIDELINE

The proposal for a SIGN guideline on surgical antibiotic prophylaxis arose out of a multidisciplinary meeting in November 1997 involving clinicians, pharmacists, microbiologists, nurses, and medical managers, to discuss strategies to address the escalating problems of inappropriate antibiotic prescribing and its impact on drug resistance in hospitals. Participants at this meeting identified antibiotic surgical prophylaxis as representing one of the areas where there was greatest variation in practice across Scotland which might be addressed by evidence-based practice guidelines.

The need for guidelines on surgical antibiotic prophylaxis has been confirmed by the findings of a series of audits. For example, an audit carried out in Aberdeen found that 62% of patients received more than three doses of prophylaxis for general or orthopaedic surgery,⁹ whereas another audit in Tayside found that only 12% continued prophylaxis for more than 24 hours.¹⁰

A survey of antibiotic control measures published by the British Society for Antimicrobial Chemotherapy in 1994 found that policies for surgical prophylaxis existed in only 51% of the hospitals surveyed and compliance was monitored in only half of these.¹¹

There have been a large number of studies of surgical prophylaxis to provide scientific evidence to guide clinicians as to the surgical indications, choice, route, and duration of antibiotic prophylaxis, and a number of guidelines have been published on this topic.¹² The existing guidelines were reviewed by the SIGN guideline development group against the accepted criteria for appraisal of clinical guidelines.¹³ There were a number of methodological criticisms of these guidelines, none of which originated in the UK and do not reflect current UK practice. In addition, the guidelines contain little or no guidance on implementation or audit of current guidelines.¹⁴ There was considerable variation between the guidelines both in the range of operations that were covered and in the recommendations about indications for prophylaxis. Some important general issues, such as risk of adverse drug reactions, were not discussed adequately, links to evidence were often unclear, and some of the guidelines were constructed by single discipline groups. The Infectious Diseases Society of America (IDSA) guideline¹⁵ is the only one to link recommendations to the evidence base. However, even in this guideline the level of evidence supporting each recommendation is not always clear.

It was agreed therefore that it was appropriate for the multidisciplinary SIGN guideline development group to review the evidence on surgical antibiotic prophylaxis and to develop recommendations for the NHS in Scotland according to the SIGN guideline development methodology.¹⁶

1.4 REMIT OF THE GUIDELINE

The remit of this guideline is confined to the administration of **intravenous** antibiotics and does not cover administration of antibiotics by other routes (e.g. oral or intra-incisional injection). The aim of this guideline is to reduce the incidence of surgical site infection and 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 7.4.2*). Most of the recommendations apply to elective surgery but some emergency operations are included (*see definition in section 2.1.1*).

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 guideline addresses the following key questions:

1. What are the risk factors for SSI? (*section 2*)
2. What are the benefits and risks of perioperative antibiotic prophylaxis? (*section 3*)
3. For which operations is there evidence that prophylaxis reduces the risk of SSI? (*section 4*)
4. When and how should antibiotic prophylaxis be administered? (*section 5*)
5. How many doses of prophylactic antibiotics should be administered? (*section 5*)
6. What factors determine the cost-effectiveness of prophylaxis and how should these be used to formulate overall recommendations for prophylaxis? (*sections 5 and 6*)
7. What factors should be considered in the implementation and audit of local guidelines for surgical antibiotic prophylaxis? (*section 7*).

The guideline does **not** cover the following types of surgery:

- prevention of urinary tract or respiratory tract infections after elective surgery, with the exception of urinary tract infection after transurethral resection of the prostate
- prevention of endocarditis after surgery or instrumentation (this is already covered by a UK guideline which is regularly updated^{17,18})
- use of antiseptics or topical antibiotics (e.g. tetracycline peritoneal lavage, subconjunctival injections for cataract surgery) 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
- use of antibiotics for prophylaxis in patients with prosthetic implants undergoing dental surgery or other surgery that may cause bacteremia
- transplant surgery.

Nor does the guideline address choice of antibiotic. There is a huge quantity of trials comparing the efficacy of different antibiotic regimens for prophylaxis. For example, a systematic review of antibiotic prophylaxis for colorectal surgery found 147 trials for this indication alone.¹⁹ These trials generally show equivalence between regimens and the group did not feel that it would be possible to use this evidence to support recommendations for specific drug regimens. Previous guidelines have recommended drug classes (e.g. first and second generation cephalosporins), but this type of recommendation was not thought to be helpful to clinicians.

- ☑ 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 microbiology and drug costs.

2 Risk factors for surgical site infection

2.1 FACTORS AFFECTING THE INCIDENCE OF SURGICAL SITE INFECTION

2.1.1 CLASSIFICATION OF OPERATION

Operations can be categorised into four classes (see *Table 1*) with an increasing incidence of bacterial contamination and subsequent incidence of postoperative infection.²⁰

Table 1

CLASSIFICATION OF OPERATION

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.

The 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 (e.g. emergency repair of abdominal aortic aneurysm or open fixation of a closed fracture) and emergency caesarean section, which is a clean-contaminated operation. The guideline development group consider that emergency operations with contaminated or dirty wounds require antibiotic therapy rather than prophylaxis and as such are beyond the scope of this guideline.

2.1.2 INSERTION OF PROSTHETIC IMPLANTS

Insertion of any prosthetic implant increases the risk of infection of the wound and surgical site.²¹ The implant has a detrimental effect on the patient's host defences. As a result, a lower bacterial inoculum is needed to cause infection of a prosthetic implant than of viable tissue. Thus the chance of infection is increased.

2.1.3 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.²⁰ In this study by Culver *et al*, operations that lasted longer than the 75th percentile for the procedure were classified as prolonged. The 75th percentile is based on data from the USA. These times have not been evaluated or confirmed by studies in the UK.

2.1.4 CO-MORBIDITIES

The American Society of Anesthesiologists (ASA) has devised a preoperative risk score based on the presence of co-morbidities at the time of surgery (see *Table 2*).²² 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.²⁰

Table 2

ASA CLASSIFICATION OF PHYSICAL STATUS

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

2.2 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 co-morbidity and duration of operation add to the risk defined by type of operative wound.

Duration of surgery and co-morbidities have as great an impact on the risk of wound infection as the operation classification.

The presence of the two risk factors co-morbidity (as indicated by an ASA score >2) and duration of operation (>75th percentile) can be used to calculate a "risk index", where:

Risk index 0 = when neither risk factor is present

Risk index 1 = when either one of the risk factors is present

Risk index 2 = when both risk factors are present.

For example, *Table 3* was derived from a large epidemiological study of hospital-acquired infection in which a risk score from a previous study was validated and refined.^{19,23} In this study, the risk of wound infection with a clean wound plus both additional risk factors was greater than the risk for a contaminated wound with no additional risk factors (5.4% versus 3.4%).

Table 3

PROBABILITY OF WOUND INFECTION BY TYPE OF WOUND AND RISK INDEX²⁰

Operation classification	Risk Index		
	0	1	2
Clean	1.0%	2.3%	5.4%
Clean-contaminated	2.1%	4.0%	9.5%
Contaminated	3.4%	6.8%	13.2%

3 Benefits and risks of antibiotic prophylaxis

3.1 BENEFITS OF PROPHYLAXIS

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.²⁴ In total hip replacement surgery prophylaxis reduces long-term postoperative morbidity.²⁵ However, for most operations prophylaxis only decreases short-term morbidity.

Surgical wound infection increases the length of hospital stay.²⁶ The additional length of stay is dependent on the type of surgery, e.g., about three days for cholecystectomy or hysterectomy but 11-16 days for major orthopaedic procedures.²⁷⁻²⁹ Prophylaxis therefore has the potential to shorten hospital stay, but there is little direct evidence as few randomised trials have included hospital length of stay as an outcome measure. Nonetheless, there is limited evidence to show that prevention of wound infection is associated with faster return to normal activity after discharge from hospital.³⁰

Evidence level III

3.2 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.

Rates of antibiotic resistance are increasing in all hospitals.^{31,32} The prevalence of antibiotic resistance in any population is related to the proportion of the population that receives antibiotics, and also the total antibiotic exposure.³³⁻³⁵

An additional problem is the dramatic increase in the number of cases of colitis caused by *Clostridium difficile*. The prevalence of *C. difficile* infection is related to total antibiotic usage and, in particular, to the use of third generation cephalosporins.³⁶⁻³⁸ In epidemiological studies of *C. difficile* colitis, surgical antibiotic prophylaxis is the single most common indication for use of antibiotics.⁸ Although even single dose prophylaxis increases the risk of carriage of *C. difficile*,³⁹ in a case control study of patients all of whom received surgical prophylaxis *C. difficile* was more common in patients who received prophylaxis for >24 hours (56% vs. 17%).

Evidence level IIa

The consequences of *C. difficile* infections include increased morbidity and mortality and prolonged hospital stay, leading to an overall increase in healthcare costs. The estimated cost of treating a single episode of *C. difficile* in hospital is £4,000, largely due to prolongation of hospital stay.³⁸ Moreover, one study has shown a statistically significant increase in the frequency of bacteraemia and line infections in surgical patients who received prophylactic antibiotics for more than four days in comparison with those who received prophylaxis for one day or less.⁴⁰

- ☑ 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 4)
 - the consequences of prophylaxis for that patient (e.g. increased risk of colitis).

4 Indications for surgical antibiotic prophylaxis

4.1 INTRODUCTION

This section summarises the recommended indications for surgical antibiotic prophylaxis. The recommendations are based on the evidence for the clinical and cost-effectiveness of prophylactic antibiotics in reducing the incidence of SSI. However, the grading of the recommendations relates to the strength of evidence on **clinical effectiveness** alone (*see inside front cover*).

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 but there are no RCTs that prove that prophylaxis reduces the risk of mortality or long-term morbidity. However, prophylaxis is highly likely to reduce major morbidity, reduce hospital costs and may decrease overall consumption of antibiotics
- **Recommended but local policy makers may identify exceptions:** prophylaxis is recommended for all patients, but 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, 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 patients⁴⁵ that important treatment effects cannot be excluded.

A local policy that does not recommend prophylaxis for these operations can be justified on the basis that there is no conclusive evidence of effectiveness. However, local policy makers must be aware that their policy represents a minority of professional opinion.

- **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 section 4.2, which also lists the odds ratio for the risk of wound infection and numbers needed to treat (NNT), i.e. 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 Cook and Sackett.⁴¹

The odds ratio for risk of wound infection for patients receiving prophylaxis compared to patients receiving no prophylaxis is a useful estimate of clinical effectiveness. The odds ratio, together with the rate of wound infection for an operative procedure, is used to calculate the NNT using the following formula:

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

- *expected baseline risk = % of risk of wound infection in the hospital*
- *odds ratio = ratio of the odds of an event in the intervention group to the odds of an event in the control group. An odds ratio of one indicates no difference between comparison groups.*

Where possible the odds ratios and NNTs given in section 4.2 have been taken from published meta-analyses. However in some cases the guideline development group has taken data from pooled trials and combined it without formal meta-analysis (see annexes 5 and 6).

The NNT is just one part of the evidence required to estimate cost-effectiveness. Additional information is required about the clinical consequences of the outcome that was measured in the trial(s) used to calculate NNT. For example, 42 patients must be given prophylaxis to prevent one hip infection after total hip replacement, whereas only four patients need to receive prophylaxis to prevent one episode of infectious morbidity after vaginal hysterectomy (see section 4.2). However, infection of the hip joint results in major morbidity, almost certainly requiring revision arthroplasty.⁴² In contrast, febrile morbidity after vaginal hysterectomy is often not associated with any harmful consequences.⁴³

The economic implications of implementing surgical antibiotic prophylaxis must also be considered. For example, the estimated costs per wound infection in one UK hospital varied from £367 for hernia repair to £1,404 for colorectal surgery.²⁹ Section 6 considers how information on both clinical- and cost-effectiveness can be used to make an informed decision regarding the use of prophylactic antibiotics.

4.2 RECOMMENDED INDICATIONS FOR SURGICAL ANTIBIOTIC PROPHYLAXIS

Operation	Recommendation	Odds Ratio	NNT	Outcome	Evidence Level
CARDIOTHORACIC SURGERY					
Cardiac pacemaker insertion	A Antibiotic prophylaxis is recommended	0.26	37	Any infection	<i>Ia</i> ⁴⁴
Open heart surgery, including:					
▪ Coronary artery bypass grafting	B Antibiotic prophylaxis is recommended	0.20 ¹⁵⁰	14	Wound infection	<i>Ib</i> ⁴⁵⁻⁴⁹
▪ Prosthetic valve surgery					
Pulmonary resection	A Antibiotic prophylaxis is recommended	0.26	5	Surgical site infection	<i>Ib</i> ⁵⁰⁻⁵¹
ENT SURGERY					
Head and neck surgery - contaminated/ clean-contaminated	A Antibiotic prophylaxis is recommended	0.19	3	Wound infection	<i>Ia</i> ⁵²⁻⁵⁵
Ear surgery - clean	A Antibiotic prophylaxis is not recommended	There is no evidence of effectiveness from RCTs			<i>IV</i> ⁵⁷
Head and neck surgery - clean	C Antibiotic prophylaxis is not recommended	There is no evidence of effectiveness from RCTs			<i>IV</i> ⁵⁶
Nose or sinus surgery	C Antibiotic prophylaxis is not recommended	There is evidence of no effectiveness from RCTs			<i>Ib</i> ⁵⁸
Tonsillectomy	C Antibiotic prophylaxis is not recommended	There is no evidence of effectiveness of prophylaxis from RCTs. The cited trials are of treatment for seven days after tonsillectomy, not prophylaxis.			<i>IV</i> ^{15,59,60}

Operation	Recommendation		Odds Ratio	NNT	Outcome	Evidence Level
GENERAL SURGERY						
Colorectal surgery	A	Antibiotic prophylaxis is highly recommended	0.37	5	Infection	I _d ⁶¹
Appendicectomy	A	Antibiotic prophylaxis is recommended*	0.38	17	Mortality	I _a
Biliary surgery – open	A	Antibiotic prophylaxis is recommended*	0.63	13	Wound infection	I _b ⁶²⁻⁶⁴
Breast surgery	C	Antibiotic prophylaxis is recommended*	0.30	10	Wound infection	I _d ⁶⁵
Clean-contaminated procedures – where no direct evidence is available	C	Antibiotic prophylaxis is recommended*	One RCT showed a non-significant treatment effect. Subsequent inclusion of patients not randomised to the original study enhanced the treatment effect.			I _V ⁶⁶
Endoscopic gastrostomy	A	Antibiotic prophylaxis is recommended*	0.13	2	Peristomal and other infection	I _V ¹⁵
Gastroduodenal surgery	A	Antibiotic prophylaxis is recommended*	0.04	4	Wound infection	I _b ⁶⁷
Oesophageal surgery	C	Antibiotic prophylaxis is recommended*	Effectiveness is inferred from evidence about other clean-contaminated procedures			I _b ⁶⁸⁻⁷⁰
Small bowel surgery	C	Antibiotic prophylaxis is recommended*	Effectiveness is inferred from evidence about other clean-contaminated procedures			I _V ⁷¹
Laparoscopic or non-laparoscopic hernia repair with mesh	C	Antibiotic prophylaxis is recommended*	Effectiveness is inferred from evidence about other clean-contaminated procedures			I _V ⁷²
Laparoscopic or non-laparoscopic hernia surgery without a mesh	A	Antibiotic prophylaxis is not recommended	Effectiveness is inferred from evidence about other procedures with insertion of prosthetic devices			I _V ⁷⁹
Laparoscopic cholecystectomy	C	Antibiotic prophylaxis is not recommended	Pooled results from two RCTs show no statistically significant effect			I _b ⁷⁸
			There is no evidence of effectiveness from RCTs			I _{Ib} ⁷³⁻⁷⁷

* Local policy makers may identify exceptions

<i>Operation</i>	<i>Recommendation</i>	<i>Odds Ratio</i>	<i>NNT</i>	<i>Outcome</i>	<i>Evidence Level</i>
NEUROSURGERY					
Craniotomy	A Antibiotic prophylaxis is recommended	0.18	14	Wound infection	<i>Ia</i> ⁸⁰
CSF shunt	A Antibiotic prophylaxis is recommended	0.52	16	Wound & shunt infection	<i>Ia</i> ^{81,82}
		0.48	16	Shunt infection	
OBSTETRICS & GYNAECOLOGY					
Caesarean section	A Antibiotic prophylaxis is recommended*	0.35	17	Wound infection	<i>Ia</i> ^{83,84}
Hysterectomy – abdominal	A Antibiotic prophylaxis is recommended*	0.37	8	Wound infection	<i>Ia</i> ^{85,86}
Hysterectomy – vaginal	A Antibiotic prophylaxis is recommended*	0.11	4	Infectious morbidity/ pelvic infection	<i>Ib</i> ^{87,88}
Induced abortion	A Antibiotic prophylaxis is recommended*	0.58	25	Upper genital tract infection	<i>Ia</i> ⁸⁹
OPHTHALMOLOGY					
Cataract surgery	C Antibiotic prophylaxis is recommended*			Effectiveness is inferred from evidence about other procedures involving insertion of prosthetic devices	<i>IV</i> ^{90,91}

* Local policy makers may identify exceptions

Operation	Recommendation	Odds Ratio	NNT	Outcome	Evidence Level	
ORTHOPAEDIC SURGERY						
Total hip replacement†	A	Antibiotic prophylaxis is highly recommended	0.27	42	Hip infection	Ib ⁹²
Prosthetic knee joint replacement††	B	Antibiotic prophylaxis is highly recommended	Observational data supports effectiveness			IIc ⁹³
Closed fracture fixation	A	Antibiotic prophylaxis is recommended	0.42 ⁹⁶	58	Deep wound infection	Ia ^{96,97}
Hip fracture repair	A	Antibiotic prophylaxis is recommended	0.42 ⁹⁶	58	Deep wound infection	Ib ^{98,99}
Spinal surgery	A	Antibiotic prophylaxis is recommended	0.30	20	Wound infection††	Ib ^{94,95}
Insertion of prosthetic device† – any procedure where no direct evidence is available	C	Antibiotic prophylaxis is recommended*	Effectiveness is inferred from evidence about other procedures involving insertion of prosthetic devices			IV ¹⁵
Orthopaedic surgery without prosthetic device (elective)	C	Antibiotic prophylaxis is not recommended	There is no evidence of effectiveness from RCTs			IV ¹⁵
UROLOGY						
Transrectal prostate biopsy	A	Antibiotic prophylaxis is recommended	0.17	4	Bacteriuria	Ib ^{101,102}
Shock-wave lithotripsy	A	Antibiotic prophylaxis is recommended*	0.45	27	Urinary tract infection	Ia ¹⁰⁰
Transurethral resection of the prostate	A	Antibiotic prophylaxis is recommended*	0.42	7	Urinary tract infection	Ib ^{103,105}
Transurethral resection of bladder tumours	C	Antibiotic prophylaxis is not recommended	Robust RCTs have not been carried out in this area and therefore no evidence in favour of prophylaxis exists			IV ¹⁰⁶
VASCULAR SURGERY						
Lower limb amputation	A	Antibiotic prophylaxis is recommended	0.32	5	Wound infection	Ib ¹⁰⁷
Vascular surgery – abdominal and lower limb	A	Antibiotic prophylaxis is recommended	0.06	11	Wound infection	Ib ^{108,109}

* Local policy makers may identify exceptions.

† Regardless of use of antibiotic cement.

†† Evidence from two trials. Results from neither trial are statistically significant but the pooled results from these trials are significant.

5 Administration of intravenous prophylactic antibiotics

5.1 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.¹¹⁰

Evidence level IV

C The antibiotics selected for prophylaxis must cover the common pathogens.

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

A past history of a serious adverse event should preclude administration of a particular antibiotic (*see below for penicillin allergy*).

A comprehensive risk assessment should be part of the process of choosing the appropriate antibiotic.¹¹¹ This should include economic considerations, such as the acquisition costs of the drug and costs of administration and preparation (*see section 6*), set against consequences of failure of prophylaxis and the possible adverse events.

Prescribers need to be aware that infections that occur in patients who receive prophylaxis are usually caused by bacteria that remain sensitive to the prophylactic regimen. Implementation of prophylaxis should not be accompanied by radical changes in treatment policy because such changes may wipe out the benefits of prophylaxis. For example, changing to third generation cephalosporins for routine treatment of postoperative infection because of implementation of prophylaxis with first or second generation cephalosporins may lead to major drug-resistance problems.¹¹²

- Treatment policies should be based on local information about the epidemiology of drug-resistant bacteria. Implementation of a prophylaxis policy should not trigger an automatic change in treatment policy.

5.2 PENICILLIN ALLERGY

Reactions to penicillin may occur because of allergy to the parent compound or its metabolites.

In descending order of association the previous symptoms most allied with a subsequent immediate hypersensitivity reaction to penicillin are:¹¹³⁻¹¹⁵

- anaphylaxis
- urticaria
- rash.

Evidence level IIb

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

In patients allergic to penicillins, challenge tests can be used to demonstrate cross-reactions with cephalosporins¹¹⁶ and carbapenems.¹¹⁷ However, the frequency of these relationships and their clinical significance is uncertain.

Evidence level IIIb

Patients with a history of rash occurring more than 72 hours after administration of penicillin are probably not allergic to penicillin.

B Patients with a history of anaphylaxis or urticaria or rash occurring immediately after penicillin therapy are at increased risk of immediate hypersensitivity to penicillins and should not receive prophylaxis with a beta-lactam antibiotic.

- 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.

5.3 TIMING OF ADMINISTRATION

The period of risk for surgical site infection begins with the incision. The time taken for an antibiotic to reach an effective concentration in any particular tissue reflects its pharmacokinetic profile and the route of administration.¹¹⁸

Evidence level Ia

Administration of prophylaxis more than three hours after the start of the operation significantly reduces its effectiveness.¹¹⁹ For maximum effect, it should be given just before or just after the start of the operation.

A Prophylaxis should be started preoperatively in most circumstances, ideally within 30 minutes of the induction of anaesthesia.

However, there may be situations where overriding factors alter the normal timing of administration. For example, during a caesarean section prophylaxis should be delayed until the cord is clamped in order to prevent the drug reaching the neonate. When a tourniquet is to be applied (e.g. in orthopaedic surgery) the necessary tissue concentration must be achieved prior to its application. This probably occurs within 10 minutes of administration of an IV antibiotic injection.

5.4 DURATION OF PROPHYLAXIS

5.4.1 ADDITIONAL DOSES DURING THE OPERATION

Many of the drugs used in prophylaxis have relatively short half lives (1-2 hours in studies of normal volunteers). In such situations it may therefore seem logical to give an additional dose of prophylaxis during operations that last for more than 2-4 hours.¹²⁰ However, in comparison with normal volunteers, patients undergoing surgery have slower clearance of drugs from their blood.^{121,122} This is probably due to a combination of factors. For example, in comparison with normal volunteers, surgical patients are older (and therefore have poorer renal function) and have more co-morbidities. The limited data available show that drugs such as cefuroxime, which has a half life of 1-2 hours in normal volunteers have a half life of 2-4 hours in patients at the time of surgery, and that effective concentrations are maintained for at least five hours after the start of surgery.^{121,122}

The search strategy used in the development of this guideline (see annex 1) found only two clinical studies that explicitly compared a single dose preoperatively with a preoperative dose plus an additional intraoperative dose.^{123,124} One of these studies was a randomised trial that did not support the effectiveness of a second intraoperative dose.¹²³ In this study, a combination of ticarcillin and clavulanic acid (Timentin) was administered intravenously (3.1 g) at the commencement of operation to all patients, and this was repeated after two hours in those patients randomised to receive a second dose. The wound infection rate was 11% in those patients receiving a single dose, and 13% in the patients receiving two doses of Timentin.

The second study,¹²⁴ which had flaws, did support the use of second intraoperative doses of cefazolin when patients were still in the operating theatre three hours after the start of surgery. The odds ratio of wound infection was 0.21 (95% CI 0.04-0.98) in comparison with patients who only received a single, preoperative dose. However, there are important methodological flaws in this evidence. The data were collected ten years before the study was published, the method of allocation to treatment regimens is not stated, the study was not blinded and the definition of wound infection is not given.

In closed fracture fixation one study compared a single dose of cefamandol given 30 minutes preoperatively, with a five dose regimen (one dose 30 minutes preoperatively plus additional doses at two, eight, 14 and 24 hours postoperatively).¹²⁵ Although the multiple dose regimen was more effective, it is not clear whether this was due to the additional intraoperative dose or the additional postoperative doses. Moreover, any difference between the regimens may have been due to the fact that the preoperative dose was given too early and did not provide adequate intraoperative cover, therefore requiring an additional dose two hours after the start of the procedure.

A systematic review of prophylaxis for colorectal surgery failed to find evidence to support the superiority of long half life drugs over short half life drugs.¹⁹

In summary, the SIGN guideline development group did not find definitive evidence for or against additional *intraoperative* doses. The individual surgeon should be free to give an extra dose for prolonged operations or operations with major blood loss. However, there is insufficient evidence to make a general recommendation.

5.4.2 ADDITIONAL DOSES AFTER THE END OF THE OPERATION

In all operations the administration of additional doses *after* the end of surgery does not provide any additional prophylactic benefit.^{110,126-128} Individual studies claiming to support additional postoperative doses are methodologically flawed. For example, not blinding observers to treatment allocation and including culture of bacteria from a wound swab as an indication of wound infection.¹²⁹ This is specifically excluded from most definitions of wound infection, as the test does not distinguish between colonisation and infection.^{130,131} Moreover, patients who are continuing to receive antibiotics are clearly less likely to have bacteria grown from swabs than patients who are not receiving antibiotics.

The trial by Gatell *et al*¹²⁵ is frequently cited in support of additional postoperative doses for patients with closed fractures. However, the regimen also included an additional intraoperative dose (two hours after the start of the operation) and it is not clear what benefit, if any, the postoperative doses provided.

A large study of 2,651 hip replacements¹²⁸ found no difference in wound infection rate after either one or three doses of cefuroxime prophylaxis. Joint infection did occur less often in the three dose group (0.45% vs 0.83%) but the difference was not statistically significant (OR 0.54; 95% CI 0.20 to 1.48).

Evidence level Ib

Prophylaxis should be confined therefore to the perioperative period (i.e. administration immediately before or during the procedure). Postoperative doses of antibiotic for prophylaxis should not be given for any operation. Any decision to prolong prophylaxis beyond a single dose should be explicit and supported by an evidence base.

A Antibiotic prophylaxis should be administered immediately before or during a procedure.

5.5 ROUTE OF ADMINISTRATION

Intravenous administration of antibiotic prophylaxis immediately before or after induction of anaesthesia is the most reliable method for ensuring effective serum antibiotic concentrations at the time of surgery.

Serum concentrations after oral or intramuscular administration are determined in part by the rate of absorption, which varies between individuals. There is relatively little evidence about the effectiveness of orally or intramuscularly 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 antibiotic prophylaxis by the intravenous route is the only method that is supported by a substantial body of evidence.

Prophylactic antibiotics for surgical procedures should be administered intravenously.

5.6 DOSE SELECTION

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

The single dose of antibiotic for prophylactic use is, in most circumstances, the same as would be used therapeutically.

5.7 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.^{132,133}

*Evidence levels
IIa and IIb*

The precise effects of blood loss and fluid replacement are difficult to predict, depending on the timing and rate of loss and replacement.¹¹⁰ However, in adults the impact of intraoperative bleeding and fluid replacement on serum drug concentrations is usually negligible.^{134,135}

Evidence level IIIb

B An additional dose of prophylactic agent is not indicated in adults, unless there is blood loss of up to 1500 ml during surgery or haemodilution of up to 15 ml/kg.

In the event of major intraoperative blood loss (>1500 ml), additional doses of prophylactic antibiotic should be given after fluid replacement.

Fluid replacement bags should not be primed with prophylactic antibiotics because of the potential risk of contamination and calculation errors.

6 Economic evaluation of surgical 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.

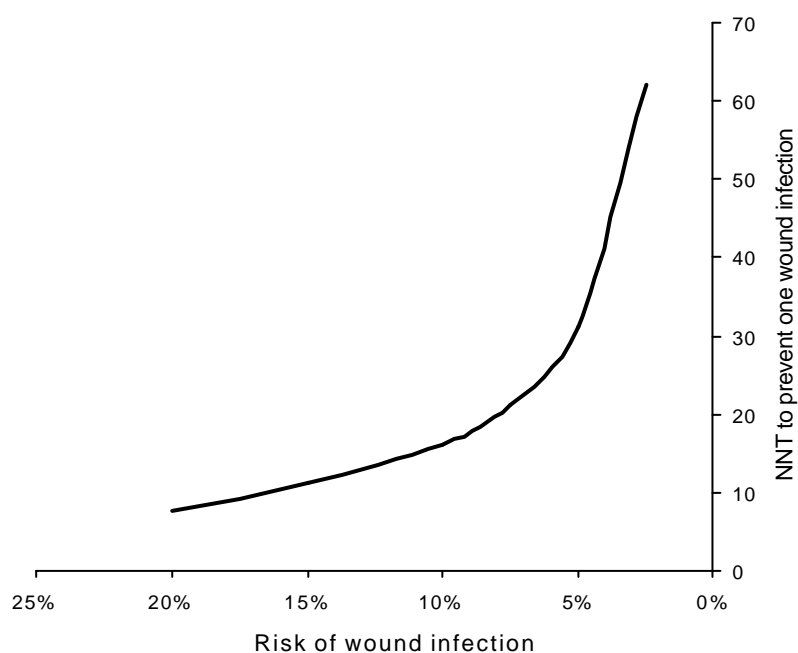
6.1 COST-EFFECTIVENESS OF ANTIBIOTIC PROPHYLAXIS

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 4.1, 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 that must receive prophylaxis in order to prevent one wound infection).⁴¹

The relationship between the baseline risk of wound infection and NNT is not linear. The NNT rise steeply with decreasing risk of baseline wound infection. Figure 1 shows the numbers needed to treat with antibiotic prophylaxis to prevent one wound infection in caesarean section surgery based on the results of a meta-analysis of randomised controlled clinical trials⁸³ which has recently been updated.⁸⁶ The odds ratio of wound infection with prophylaxis is 0.35.

Figure 1

NUMBERS NEEDED TO TREAT TO PREVENT ONE WOUND INFECTION WITH SURGICAL ANTIBIOTIC PROPHYLAXIS IN CAESAREAN SECTION SURGERY



From the NNT and the cost of administering prophylaxis it is easy to calculate the cost of preventing one wound infection (see section 6.3). If the cost of preventing a wound infection exceeds the cost of treating a wound infection then the decision about implementation of prophylaxis is a clinical one, dependent on the value of preventing the pain and suffering arising from wound infection.

Although the calculation of NNT is straightforward (see section 4.1), Table 4 estimates likely odds ratios for various baseline infection risks that can be generalised to most operations. The numbers in the body of the table are the NNTs for the corresponding odds ratios at that particular expected baseline risk.

Table 4

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

6.2 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.

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 is usually three doses/day for seven days, the total number of doses = 21.

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

Odds ratio of wound infection with prophylaxis versus no prophylaxis = 0.35 (see annex 5).

Baseline risk of wound infection without prophylaxis⁸³ = 9.7%.

From figure 1 at this baseline risk NNT = 16.5.

That is, 16.5 women must receive prophylaxis in order to prevent one wound infection.

Table 4 shows that the expected baseline risk at which NNT >21 for an odds ratio of 0.35 is between 5-7.5%.

If the baseline risk of wound infection after caesarean section in a hospital is <5% it would be reasonable to be concerned that giving prophylaxis routinely would increase antibiotic consumption. Conversely, if the baseline risk is >5% it would be reasonable to assume that giving prophylaxis would not increase 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 restricting prophylaxis to a single dose. Every additional prophylactic dose that is administered increases the baseline risk of wound infection that is required for prophylaxis to reduce overall antibiotic consumption.

In the example above, if a second prophylactic dose is administered after the operation and does not further reduce the risk of wound infection, then 40 doses are being administered to prevent one wound infection. As the NNT is the number of *patients* that must be treated, this remains at 20 with each patient now receiving two antibiotic doses.

This two dose regimen can only reduce overall antibiotic consumption if the number of patients treated to prevent one wound infection is 10 or lower, then the number of prophylactic doses (20) would be less than the number of doses needed to treat one wound infection. This would be the case if the baseline risk of wound infection was at least 15% (see Table 4).

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 4 can be used to calculate the number of patients that 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, if the odds ratio = 0.35 and the estimated baseline risk of wound infection = 9.7%, then the NNT = 16.5.

If prophylaxis costs £5 per patient then it costs £82.50 (£5 x 16.5) to prevent one wound infection.

This provides a threshold value, if the decision-maker believes that it is worth spending up to £82.50 to prevent a wound infection then prophylaxis should be implemented.

A cost per wound infection prevented of £82.50 is far less than £716, which is one published estimate of the cost of wound infection after caesarean section.^{29,136} However, this estimate is based on the cost of resources such as nursing time or length of hospital stay, and reducing wound infection rate may not result in the equivalent cash savings to the hospital.¹³⁷ Cost per wound infection varies greatly by operation type (*Table 5*). In general, infections complicating major surgical procedures have a much greater cost than infections complicating minor surgical procedures.

Table 5

ESTIMATED COST PER WOUND INFECTION BY SITE OF OPERATION

Procedure	Cost per wound infection (£)
Colorectal surgery	1,404
Vascular surgery with graft	1,085
Cholecystectomy	711
Malignant breast tumour	676
Oesophageal surgery	635
Groin hernia repair	367

Two additional points must be borne in mind when calculating the comparative costs of prophylaxis. Firstly, such calculations are highly sensitive to the cost of the antibiotics used for prophylaxis. The cost of a single dose of 1.2 g Co-amoxiclav is only £2.97¹³⁸ and even allowing for other costs such as drug preparation, administration and wastage, £5 for single dose prophylaxis is a realistic estimate.¹³⁹ However, the cost of some alternative agents is much higher (e.g. £9.65 for 2g cefotaxime or £30.00 for 1g imipenem).¹³⁸ Secondly, with very few exceptions, increasing the number of doses of prophylaxis adds to the cost without improving the effectiveness.

7 Implementation of the guideline

7.1 DEVELOPMENT OF LOCAL GUIDELINES

It is expected that this SIGN guideline will act as a framework for local development or modification after discussion with clinicians and management. The Trust or Area Quality & Clinical Effectiveness Groups should be involved in conjunction with the Drug & Therapeutics, Antibiotic and Protocol development committees. Responsibility for prophylaxis in each unit should be clearly assigned. This guideline should ideally be used in conjunction with local guidelines for the management of postoperative pyrexia. Guideline implementation should be supported by a programme of continuing education.

7.2 DRUG CHART DOCUMENTATION OF ANTIBIOTIC ADMINISTRATION

Introduction of special forms for ordering perioperative antimicrobial prophylaxis has been shown to reduce inappropriate prescribing from 64% to 21%.¹⁴⁰ Use of specific antibiotic order forms¹⁴⁰ has previously been shown to reduce inappropriate prescribing and was one of the recommendations of the IDSA.^{141,142} Prescribing antibiotic prophylaxis in the single dose section of drug prescription forms is also associated with a lower proportion of inappropriate additional doses.¹⁰

Evidence level III

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

7.3 CASE RECORD DOCUMENTATION AND MINIMUM DATA SET

All aspects of antibiotic prophylaxis should be recorded in the case notes and/or the drug prescription chart.^{140,143} Recommended means of facilitating this include the incorporation of a stamp or adhesive into the case records, including nursing checklists, or into integrated care pathways. As an alternative this information can be hand written in the records and/or the drug chart. The guideline development group accepts that routine collection of many details pertaining to the operative procedures or its complications are likely to prove unrealistic. The minimum data set that is required when administering antibiotic prophylaxis is summarised below. If prophylaxis is normally indicated, but not given, then the reasons for this should be clearly recorded in the case records.

Evidence level IV

C Recording the minimum data set in the case notes and drug prescription chart will facilitate audit of the appropriateness of surgical antibiotic prophylaxis.

Many types of outcome indicators have been suggested.¹⁴⁴ The commonest is surgical site infection rate, particularly wound infection rates.¹⁴⁴ Their measurement presents formidable problems due to lack of consensus about definitions. Additionally, there is a lack of accurate post-discharge surveillance as many patients have infections after they are discharged from hospital.

7.4 KEY POINTS AND CORE INDICATORS FOR AUDIT

7.4.1 CORE INDICATORS FOR AUDIT^{10,144-146}

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 dose of prophylaxis given within 30 minutes of the start of surgery?
- Was the prescription written in the “once-only” section of the drug prescription chart?
- Was the duration of prophylaxis greater than 24 hours?

Outcome measures:

- Surgical Site Infection (SSI) 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. difficile* 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.

7.4.2 MINIMUM DATA SET FOR SURGICAL ANTIBIOTIC PROPHYLAXIS

-
- Date
 - Operation performed
 - Justification for prophylaxis (e.g. evidence of high risk of SSI) if prophylaxis is given for an operation that is not one of the indications for routine prophylaxis
 - Time of antibiotic administration
 - Elective or emergency
 - Name, dose, route of antibiotic
 - Time of surgical incision
 - Number of doses given
 - Classification of operation (clean/clean-contaminated/ contaminated)
 - Previous adverse reactions to antibiotics?
 - Duration of operation
 - Second dose indicated?
 - Second dose given?
 - Name of anaesthetist
 - Name of surgeon
 - Designation of surgeon
-

Annex 1

DETAILS OF SYSTEMATIC REVIEW UNDERTAKEN FOR THE GUIDELINE

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 the SIGN Information Officer in collaboration with members of the guideline development group.

Searches were initially carried out on the Cochrane Library, Embase, Healthstar, and Medline from 1987 to 1998, and were updated during the course of development. In view of the volume of literature in this area, searches were initially restricted to existing guidelines, meta-analyses, and systematic reviews. Subsequently, searches for additional papers on audit of guideline effectiveness, and on the impact of haemodilution following intravenous administration of antibiotics were carried out. All search strategies were subject to independent review. Copies of the search strategies used are available from the SIGN Information Officer.

In the course of these searches it was noted that there is a high degree of inconsistency in the indexing of papers on antibiotic prophylaxis, with the terms *Antibiotic prophylaxis* or *Antibiotics/therapeutic use* apparently used interchangeably.

In addition to the initial search, members of the guideline development group searched the Medline database from 1960 to find the best evidence of the role of prophylactic antibiotics in surgical site infection prophylaxis. If a good meta-analysis was found this was used as the sole evidence. Failing this good quality randomised trials were sought. If there were one or two statistically sound randomised trials these are quoted as the sole evidence. Some of the references are old but these were used when they were judged to be "practice changing" papers. In the absence of good randomised trials, other published evidence (e.g. other trials, audits, expert opinion etc.) was used as a guide to prophylaxis. For a lot of procedures both common (e.g. varicose veins and thyroid surgery) and more specialised (e.g. urethroplasty, Nesbit's operation) no evidence exists either for or against prophylaxis. Here common practice and referral to first principles act as a guide.

All systematic reviews and reports of trials used as evidence were subjected to methodological evaluation using standard checklists.

Annex 2

CRITERIA FOR DEFINING A SURGICAL SITE INFECTION¹⁴⁷

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 is 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 (e.g. 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 histopathologic or radiologic examination
4. diagnosis of deep incisional SSI by a surgeon or attending physician.

Notes:

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

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 (e.g. 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 radiologic examination
4. diagnosis of an organ/space SSI by a surgeon or attending physician.

Annex 3

SITE-SPECIFIC CLASSIFICATIONS OF ORGAN/SPACE SURGICAL SITE INFECTION¹⁴⁷

- 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 (e.g. abscess of empyema)
- other male or female reproductive tract
- sinusitis
- spinal abscess without meningitis
- upper respiratory tract
- vaginal cuff

Annex 4

TABLE OF COMMON PATHOGENS

<i>SSI organism</i>	<i>Antibiotic susceptibility</i>
SURGICAL SITE INFECTION FOR A SKIN WOUND AT ANY SITE	
<i>Staphylococcus aureus</i>	– 90% remain susceptible to flucloxacillin, macrolides and clindamycin
<i>Beta-haemolytic streptococci (BHS)</i>	– 90% remain susceptible to penicillins, macrolides and clindamycin
ADDITIONAL PATHOGENS (to <i>S. aureus</i> and <i>BHS</i>) by site of infection	
Head and neck surgery	
<i>Oral anaerobes</i>	– 95% remain susceptible to metronidazole and co-amoxiclav. <i>Penicillin can no longer be relied upon.</i>
Operations below the waist	
<i>Anaerobes</i>	– 95% remain susceptible to metronidazole and co-amoxiclav. <i>Penicillin can no longer be relied upon.</i>
<i>E. coli</i> and other enterobacteriaceae	– Complex resistance problems. However, 90% of <i>E. coli</i> remain susceptible to second generation cephalosporins or beta-lactam drugs combined with a beta-lactamase inhibitor, or gentamicin.
Insertion of a prosthesis, graft or shunt	
<i>Coagulase Negative Staphylococci (CNS)</i> <i>Staphylococcus aureus</i>	– 90% of <i>S. aureus</i> remain susceptible to flucloxacillin, macrolides or clindamycin. Although two-thirds of CNS are methicillin-resistant, prophylaxis with beta-lactam antibiotics is still appropriate (<i>see below</i>).

MRSE, MRSA and glycopeptide prophylaxis

The increasing prevalence of Methicillin-resistant *S. aureus* (MRSA) raises the issue of glycopeptide prophylaxis against MRSA and Methicillin-resistant *S. epidermis* (MRSE) infections, usually when inserting large joint prostheses, vascular or cardiac grafts or shunts.

Clinical trials have failed to show an advantage for glycopeptides over beta-lactam drugs despite the high prevalence of MRSE.¹⁴⁸ It is conceivable that beta-lactam drugs remain effective for prevention of infections by MRSE or MRSA. In the absence of evidence of clinical benefit from glycopeptide prophylaxis the guideline group strongly supports recommendations against the use of glycopeptides in prophylaxis.^{148,149} The major reason for not recommending glycopeptides is fear that overuse of these drugs will increase the prevalence of Vancomycin-resistant enterococcus (VRE) and may lead to the development of Vancomycin-resistant *S. aureus*.

Annex 5

EFFICACY OF PROPHYLAXIS: NUMBERS NEEDED TO TREAT

DATA FROM PUBLISHED META-ANALYSES

The table lists odds ratios calculated from trials that demonstrated a statistically significant reduction in the incidence of wound infection following antibiotic prophylaxis. Individual units can estimate their own NNTs by substituting their unit's infection rates into the formula in section 4.1.

A worked example is given in section 6.

Operation	Outcome	No. of trials	Control infection rate	Odds Ratio	95% CI	NNT
Abortion (induced)	Upper genital tract infection	12 ⁸⁹	10%	0.58	0.47-0.71	25
Biliary surgery (open)	Wound infection	42 ⁶⁵	4%	0.30	0.23-0.38	10
Caesarean section	Wound infection	42 ⁸³	10%	0.35	0.28-0.44	17
Cardiac pacemaker	Any infection	7 ⁴⁴	4%	0.26	0.10-0.66	34
Cardiac surgery	Wound infection	3 ¹⁵⁰	9%	0.20	0.10-0.49	14
Closed fractures	Deep wound infection	6 ⁹⁶	3%	0.42	0.26-0.68	58
Colorectal surgery*	Infection	26 ²⁴	39%	0.37	0.30-0.45	5
	Mortality	17 ²⁴	10%	0.38	0.25-0.58	17
Craniotomy	Wound infection	8 ⁸⁰	9%	0.18	0.11-0.30	14
CSF Shunt	Wound & shunt infection	12 ⁸¹	15%	0.52	0.37-0.73	16
	Shunt infection	9 ⁸²	13%	0.48	0.31-0.73	16
Hysterectomy (abdominal)	Wound infection	25 ⁸⁶	21%	0.37	0.31-0.45	8
Shock wave lithotripsy	UTI	6 ¹⁰⁰	7%	0.45	0.22-0.93	27

Odds ratio

Odds ratio of infection if given prophylaxis

95% CI

Lower and upper 95% confidence interval of odds ratio

NNT

Numbers needed to treat with prophylaxis to prevent one infection at the infection rate observed in the control group

*This meta-analysis included studies in which antibiotic prophylaxis was given systemically (IV or IM injection or oral administration of well-absorbed drugs), by oral administration of non-absorbed drugs as part of the bowel preparation, topically (intraperitoneally) or by a combination of these methods. However, pooling of data from all trials that included systemic prophylaxis shows similar effectiveness in reduction of risk of SSI (18 trials, OR 0.28, 95% CI 0.21-0.36). In the 13 trials that only included systemic prophylaxis, the pooled odds ratio is slightly higher (0.39; 95% CI 0.29-0.52). However, the majority of these trials only included cover against aerobic bacteria (e.g. cephalothin alone) or only against anaerobic bacteria (e.g. metronidazole alone). The four trials with regimens that covered both aerobic and anaerobic organisms (e.g. gentamicin plus lincomycin) showed a marked reduction in risk of SSI with systemic prophylaxis alone (OR 0.15, 95% CI 0.06 to 0.37).

Annex 6

EFFICACY OF PROPHYLAXIS: NUMBERS NEEDED TO TREAT

DATA FROM SINGLE OR POOLED TRIALS

Data is from single trials or pooled trials that show a statistically significant reduction in risk of wound infection. Pooled trial data have been combined without formal meta-analysis (the supporting evidence table is available on the SIGN website: www.sign.ac.uk).

Operation	Outcome	No. of trials	Control infection rate	Odds Ratio	95% CI	NNT
Appendix	Wound infection	3 ⁶²⁻⁶⁴	26%	0.63	0.41-0.96	13
Endoscopic gastrostomy	Peristomal or other infection	1 ⁶⁷	65%	0.13	0.05-0.35	2
Gastroduodenal	Wound infection	6 ⁶⁸⁻⁷⁰	26%	0.04	0.01-0.14	4
Head & neck surgery (clean-contaminated/contaminated)	Wound infection	3 ⁵²	50%	0.19	0.10-0.35	3
Hysterectomy - vaginal	Infectious morbidity/ pelvic infection	3 ⁸⁶⁻⁸⁸	32%	0.11	0.06-0.21	4
Lower leg amputation	Wound infection	1 ¹⁰⁷	39%	0.32	0.15-0.69	5
Pulmonary	SSI	2 ^{50,51}	29%	0.26	0.14-0.46	5
Spinal	Wound infection	2 ^{94,95}	7%	0.30	0.09-0.97	28
Total hip replacement	Hip infection	1 ⁹²	3%	0.27	0.13-0.55	46
Transrectal prostate biopsy	Bacteriuria	2 ^{102,66}	30%	0.17	0.05-0.54	4
Transurethral resection of the prostate	UTI	2 ¹⁰³⁻¹⁰⁵	29%	0.42	0.30-0.58	7
Vascular	Wound infection	2 ^{108,109}	10%	0.06	0.02-0.27	11

Odds ratio Odds ratio of infection if given prophylaxis

95% CI Lower and upper 95% confidence interval of odds ratio

NNT Numbers needed to treat with prophylaxis to prevent one infection at the infection rate observed in the control group

References

- 1 US Department of Health and Human Services. Agency for Health Care Policy and Research. Acute Pain Management: operative or medical procedures and trauma. Rockville (MD): The Agency; 1993. Clinical Practice Guideline No.1. AHCPR Publication No.92-0023. p.107.
- 2 Emmerson AM, Enstone JE, Griffin M, Kelsey MC, Smyth ET. The Second National Prevalence Survey of infection in hospitals – overview of the results. *J Hosp Infect* 1996; 32: 175-90.
- 3 Tornqvist IO, Holm SE, Cars O. Pharmacodynamic effects of subinhibitory antibiotic concentrations. *Scand J Infect Dis* 1990; 74: 94-101.
- 4 Lorian V. Some effects of subinhibitory concentrations of antibiotics on bacteria. *Bull NY Acad Med* 1975; 51: 1046-55.
- 5 Cars O, Odenholt-Tornqvist I. The post-antibiotic sub-MIC effect in vitro and in vivo. *J Antimicrob Chemother* 1993; 31: 159-66.
- 6 Moss F, McNicol MW, McSwiggan DA, Miller DL. Survey of antibiotic prescribing in a district general hospital. I. Pattern of use. *Lancet* 1981; 2: 349-52.
- 7 Goldmann DA, Weinstein RA, Wenzel RP, Tablan OC, Duma RJ, Gaynes RP, et al. Strategies to Prevent and Control the Emergence and Spread of Antimicrobial-Resistant Microorganisms in Hospitals. A challenge to hospital leadership. *JAMA* 1996; 275: 234-40.
- 8 Jobe BA, Grasley A, Deveney KE, Deveney CW, Sheppard BC. *Clostridium difficile* colitis: an increasing hospital-acquired illness. *Am J Surg* 1995; 169: 480-3.
- 9 Gould IM, Jappy B. Trends in hospital antibiotic prescribing after introduction of an antibiotic policy. *J Antimicrob Chemother* 1996; 38: 895-904.
- 10 Davey P, Napier A, McMillan J, Ruta D. Audit of antibiotic prophylaxis for surgical patients in three hospital trusts in Tayside. *Health Bulletin* 1999; 57: 118-27.
- 11 Hospital antibiotic control measures in the UK. Working Party of the British Society for Antimicrobial Chemotherapy. *J Antimicrob Chemother* 1994; 34: 21-42.
- 12 Mangram AJ, Horan TC, Pearson ML, Christine Silver L, Jarvis WR. Guideline for prevention of surgical site infection. *Am J Infect Cont* 1999; 27: 97-132.
- 13 Cluzeau F, Littlejohns P, Grimshaw J, Feder G. Appraisal instrument for clinical guidelines. St George's Hospital Medical School, London, 1997.
- 14 Widdison AL, Pope NRJ, Brown EM. Survey of guidelines for antimicrobial prophylaxis in surgery. *J Hosp Infect* 1993; 25: 199-205.
- 15 Dellinger PE, Gross PA, Barrett TL, Krause PJ, Martone WJ, McGowan JE et al. Quality standard for antimicrobial prophylaxis in surgical procedures. *Clin Infect Dis* 1994; 18: 422-7.
- 16 Scottish Intercollegiate Guidelines Network (SIGN). SIGN Guidelines: An introduction to SIGN methodology for the development of evidence-based clinical guidelines. Edinburgh: SIGN, 1999 (SIGN publication no. 39).
- 17 Anonymous. Antibiotic prophylaxis of infective endocarditis: recommendations from the Endocarditis Working Party of the British Society for Antimicrobial Chemotherapy. *Lancet* 1990; 335: 88-9.
- 18 Simmons NA, Ball AP, Cawson RA, Eykyn SJ, Littler WA, McGowan DA et al. Antibiotic prophylaxis and infective endocarditis. *Lancet* 1992; 339: 1292-3.
- 19 Song F, Glenny AM. Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomised controlled trials. *Health Technol Assessment South Hampton NY* 1998; 2: 1-110.
- 20 Culver DH, Horan TC, Gaynes RP, Eykyn SJ, Littler WA, McGowan DA et al. Surgical wound infection rates by wound class, operative procedure and patient risk index. National Nosocomial Infections Surveillance System. *Am J Med* 1991; 91: 152-7.
- 21 Gristina AG, Costerton JW. Bacterial adherence and the glycocalyx and their role in musculoskeletal infection. *Orthop Clin North Am* 1984; 15: 517-35.
- 22 American Society of Anesthesiologists. New classification of physical status. *Anesthesiology* 1963; 24:111.
- 23 Haley RW, Culver DH, Morgan WM, White JW, Emori TG, Hooton TM. Identifying patients at high risk of surgical wound infection. A simple multivariate index of patient susceptibility and wound contamination. *Am J Epidemiol* 1985; 121: 206-15.
- 24 Baum ML, Anish DS, Chalmers TC, Sacks HS, Smith H, Fagerstrom RM. A survey of clinical trials of antibiotic prophylaxis in colon surgery: evidence against further use of no-treatment controls. *NEJM* 1981; 305: 795-9.
- 25 Lidwell OM. Air, antibiotics and sepsis in replacement joints. *J Hosp Infect* 1988; 11: 18-40.

- 26 McGowan JE. Cost and benefit in control of nosocomial infection: methods for analysis. *Rev Infect Dis* 1981; 3: 790-7.
- 27 Coello R, Glenister H, Fereres J, Bartlett C, Leigh D, Sedgwick J, et al. The cost of infection in surgical patients: a case control study. *J Hosp Infect* 1993; 25: 239-50.
- 28 Davies TW & Cottingham J. The cost of hospital infection in orthopaedic patients. *J Infect* 1979; 1: 329-38.
- 29 Lynch W, Malek M, Davey PG, Byrne DJ, Napier A. Costing wound infection in a Scottish hospital. *Pharmacoeconomics* 1992; 2: 163-70.
- 30 Davey PG, Duncan ID, Edward D, Scott AC. Cost-benefit analysis of cephadrine and mezlocillin prophylaxis for abdominal and vaginal hysterectomy. *Br J Obstet Gynaecol* 1988; 95: 1170-7.
- 31 Gold HS, Moellering RC. Antimicrobial drug resistance. *NEJM* 1996; 335: 1445-53.
- 32 American Society for Microbiology. Report of the ASM Task Force on antimicrobial resistance. Washington: The Society, 1994.
- 33 Austin DJ, Kakehashi M, Anderson RM. The transmission dynamics of antibiotic-resistant bacteria: the relationship between resistance in commensal organisms and antibiotic consumption. *Proc R Soc Lond B Biol Sci* 1997; 264: 1629-38.
- 34 Schwartz B, Bell DM, Hughes JM. Preventing the emergence of antimicrobial resistance. A call for action by clinicians, public health officials, and patients. *JAMA* 1997; 278: 944-5.
- 35 McCaig LF, Hughes JM. Trends in antimicrobial drug prescribing among office-based physicians in the United States. *JAMA* 1995; 273: 214-9.
- 36 Wilcox MH, Smyth ET. Incidence and impact of *Clostridium difficile* infection in the UK, 1993-1996. *J Hosp Infect* 1998; 39: 181-7.
- 37 Zadik PM, Moore AP. Antimicrobial associations of an outbreak of diarrhoea due to *Clostridium difficile*. *J Hosp Infect* 1998; 39: 189-93.
- 38 Wilcox MH, Cunliffe JG, Trundle C, Redpath C. Financial burden of hospital-acquired *Clostridium difficile* infection. *J Hosp Infect* 1996; 34: 23-30.
- 39 Privitera G, Scarpellini P, Ortisi G, Nicastro G, Nicolini R, de Lalla F. Prospective study of *Clostridium difficile* intestinal colonisation and disease following single dose antibiotic prophylaxis in surgery. *Antimicrob Agents Chemother* 1991; 35: 208-10.
- 40 Namias N, Harvill S, Ball S, McKenney MG, Salomone JP, Civetta JM. Cost and morbidity associated with antibiotic prophylaxis in the ICU. *J Am Coll Surg* 1999; 188: 225-30.
- 41 Cook RJ, Sackett DL. The number needed to treat: a clinically useful measure of treatment effect. *BMJ* 1995; 310: 452-4.
- 42 Berbari EF, Hanssen AD, Duffy MC, Steckelberg JM, Ilstrup DM, Harmsen WS, et al. Risk factors for prosthetic joint infection: case-control study. *Clin Infect Dis* 1998; 27: 1247-54.
- 43 Monif RG, Lowenkron JD. Temperature and fever in ob-gyn patients. In: *Obstetric and gynecologic infectious disease*, editor; G. Pastorek, New York Raven Press; 1994, 693-99.
- 44 Da Costa A, Kirkorian G, Cucherat M, Delahaye F, Chevalier P, Cerisier A, et al. Antibiotic prophylaxis for permanent pacemaker implantation: a meta-analysis. *Circulation* 1998; 97: 1796-801.
- 45 Fong IW, Baker CB, McKee DC. The value of prophylactic antibiotics in aorta-coronary bypass operations: a double-blind randomized trial. *J Thorac Cardiovasc Surg* 1979; 78: 908-13.
- 46 Austin TW, Coles JC, Burnett R, Goldbach M. Aortacoronary bypass procedures and sternotomy infections: a study of antistaphylococcal prophylaxis. *Can J Surg* 1980; 23: 483-5.
- 47 Penketh AR, Wansbrough-Jones MH, Wright E, Imrie F, Pepper JR, Parker DJ. Antibiotic prophylaxis for coronary artery bypass graft surgery. *Lancet* 1985; 1: 1500.
- 48 Amoury RA, Bowman FO Jr, Malm JR. Endocarditis associated with intracardiac prostheses. Diagnosis, management, and prophylaxis. *J Thorac Cardiovasc Surg* 1966; 51: 36-48.
- 49 Stein PD, Harken DE, Dexter L. The nature and prevention of prosthetic valve endocarditis. *Am Heart J* 1966; 71: 393-407.
- 50 Ilves R, Cooper JD, Todd TR, Pearson FG. Prospective, randomised, double-blind study using prophylactic cephalothin for major, elective, general thoracic operations. *J Thorac Cardiovasc Surg* 1981; 81: 813-7.
- 51 Aznar R, Mateu M, Miro JM, Gatell JM, Gimferrer JM, Aznar E, et al. Antibiotic prophylaxis in non-cardiac thoracic surgery: cefazolin versus placebo. *Eur J Cardiothorac Surg* 1991; 5: 515-8.
- 52 Velanovich V. A meta-analysis of prophylactic antibiotics in head and neck surgery. *Plast Reconstr Surg* 1991; 87: 429-34.
- 53 Dor P, Klastersky J. Prophylactic antibiotics in oral, pharyngeal and laryngeal surgery for cancer: (a double-blind study). *Laryngoscope* 1973; 83: 1992-8.

- 54 Becker GD, Parell GJ. Cefazolin prophylaxis in head and neck cancer surgery. *Ann Otol Rhinol Laryngol* 1979; 88: 183-6.
- 55 Johnson JT, Yu VL, Myers EN, Muder RR, Thearle PB, Diven WF. Efficacy of two third-generation cephalosporins in prophylaxis for head and neck surgery. *Arch Otolaryngol* 1984; 110: 224-7.
- 56 Johnson JT, Wagner RL. Infection following uncontaminated head and neck surgery. *Arch Otolaryngol Head Neck Surg* 1987; 113: 368-9.
- 57 Govaerts PJ, Raemaekers J, Verlinden A, Kalai M, Somers T, Offeciers FE. Use of antibiotic prophylaxis in ear surgery. *Laryngoscope* 1998; 108: 107-10.
- 58 Legent F, Arnould JF. Antibiotic prophylaxis in ORL surgery and oral medicine. [French]. *Ann Fr Anaesth Reanim* 1994; 13: 5100-9.
- 59 Grandis JR, Johnson JT, Vickers RM, Yu VL, Wagener MM, Wagner RL, et al. The efficacy of perioperative antibiotic therapy on recovery following tonsillectomy in adults: randomized double-blind placebo-controlled trial. *Otolaryngol Head Neck Surg* 1992; 106: 137-42.
- 60 Colreavy MP, Nanan D, Benamer M, Donnelly M, Blaney AW, O'Dwyer TP, et al. Antibiotic prophylaxis post-tonsillectomy: is it of benefit? *Int J Pediatr Otorhinolaryngol* 1999; 50: 15-22.
- 61 Baum ML, Anish DS, Chalmers TC, Sacks HS, Smith H Jr, Fagerstrom RM. A survey of clinical trials of antibiotic prophylaxis in colon surgery: evidence against further use of no-treatment controls. *NEJM* 1981; 305: 795-9.
- 62 Willis AT, Ferguson IR, Jones PH, Phillips KD, Tearle PV, Berry RB. Metronidazole in prevention and treatment of bacteroides infections after appendectomy. *BM J* 1976; 1: 318-21.
- 63 Winslow RE, Dean RE, Harley JW. Acute nonperforating appendicitis. Efficacy of brief antibiotic prophylaxis. *Arch Surg* 1983; 118: 651-5.
- 64 Donovan IA, Ellis D, Gatehouse D, Little G, Grimley R, Armistead S, et al. One-dose antibiotic prophylaxis against wound infection after appendectomy: a randomised trial of clindamycin, cefazolin sodium and a placebo. *Br J Surg* 1979; 66: 193-6.
- 65 Meijer WS, Schmitz PI, Jeekel J. Meta-analysis of randomised, controlled clinical trials of antibiotic prophylaxis in biliary tract surgery. *Br J Surg* 1990; 77: 283-90.
- 66 Platt R, Zucker JR, Zaleznik DF, Hopkins CC, Dellinger EP, Karchmer AW, et al. Perioperative antibiotic prophylaxis and wound infection following breast surgery. *J Antimicrob Chemother* 1993; 31: 43-8.
- 67 Preclik G, Grune S, Leser HG, Lebherz J, Heldwein W, Machka K, et al. Prospective, randomised, double blind trial of prophylaxis with single dose of co-amoxiclav before percutaneous endoscopic gastrostomy. *BMJ* 1999; 319: 881-4.
- 68 Polk HC Jr, Lopez-Mayor JF. Postoperative wound infection: a prospective study of determinant factors and prevention. *Surgery* 1969; 66: 97-103.
- 69 Evans C, Pollock AV. The reduction of surgical wound infections by prophylactic parenteral cephaloridine. A controlled clinical trial. *Br J Surg* 1973; 60: 434-7.
- 70 Lewis RT, Allan CM, Goodall RG, Lloyd-Smith WC, Marien B, Wiegand FM. Discriminate use of antibiotic prophylaxis in gastroduodenal surgery. *Am J Surg* 1979; 138: 640-3.
- 71 Bricard H, Deshayes JP, Sillard B, Lefrancois C, Delassus P, Lochu T, et al. Antibiotic prophylaxis in surgery of the esophagus. [Fre] *Ann Fr Anaesth Reanim* 1994; 13: 161-8.
- 72 Dellinger EP, Gross PA, Barrett TL, Krause PJ, Martone WJ, McGowan JE, et al. Quality standard for antimicrobial prophylaxis in surgical procedures. Infectious Diseases Society of America. *Clin Infect Dis* 1994; 18: 422-7.
- 73 Taylor EW, Byrne DJ, Leaper DJ, Karran SJ, Browne MK, Mitchell KJ. Antibiotic prophylaxis and open groin hernia repair. *World J Surg* 1997; 21: 811-4.
- 74 Frantzides CT, Sykes A. A reevaluation of antibiotic prophylaxis in laparoscopic cholecystectomy. *J Laparoendosc Surg* 1994; 4: 375-8.
- 75 Watkin DS, Wainwright AM, Thompson MH, Leaper DJ. Infection after laparoscopic cholecystectomy: are antibiotics really necessary? *Eur J Surg* 1995; 161: 509-11.
- 76 den Hoed PT, Boelhouwer RU, Veen HF, Hop WC, Bruining HA. Infections and bacteriological data after laparoscopic and open gallbladder surgery. *J Hosp Infect* 1998; 39: 27-37.
- 77 Garcia N, Kapur S, McClane J, Davis JM. Surgical infections and prophylactic antibiotics: 341 consecutive cases of gall bladder surgery in the era of laparoscopic surgery. *J Laparoendosc Adv Surg Tech A* 1997; 7: 157-62.
- 78 Platt R, Zaleznik DF, Hopkins CC, Dellinger EP, Karchmer AW, Bryan CS, et al. Perioperative antibiotic prophylaxis for herniorrhaphy and breast surgery. *NEJM* 1990; 322: 153-60.
- 79 Schwetling R, Barlehner E. Is there an indication for general perioperative antibiotic prophylaxis in laparoscopic plastic hernia repair with implantation of alloplastic tissue? [German] *Zentralbl Chir* 1998; 23: 193-5.
- 80 Barker FG 2nd. Efficacy of prophylactic antibiotics for craniotomy: a meta-analysis. *Neurosurgery* 1994; 35: 484-90.

- 81 Langley JM, LeBlanc JC, Drake J, Milner R. Efficacy of antimicrobial prophylaxis in placement of cerebrospinal fluid shunts: a meta analysis. *Clin Infect Dis* 1993; 17: 98-103.
- 82 Haines SJ, Walters BC. Antibiotic prophylaxis for cerebrospinal fluid shunts: a meta-analysis. *Neurosurgery* 1994; 34: 87-92.
- 83 Enkin M, Enkin E, Chalmers I, Hemminki E. Prophylactic antibiotics in association with caesarean section. In: Chalmers I, Enkin MW, Keirse MJNC (eds). *Effective care in pregnancy and childbirth*. Oxford: Oxford University Press, 1989. 1246-69.
- 84 Burrows RF. Review: antibiotic prophylaxis reduces infectious complications in caesarean delivery. *Evidence-Based Medicine* 1999; 4: 179.
- 85 Tanos V, Rojansky N. Prophylactic antibiotics in abdominal hysterectomy. *J Am Coll Surg* 1994; 179: 593-600.
- 86 Mittendorf R, Aronson MP, Berry RE, Williams MA, Kupelnick B, Klickstein A, et al. Avoiding serious infections associated with abdominal hysterectomy: a meta-analysis of antibiotic prophylaxis. *Am J Obstet Gynecol* 1993; 169: 1119-24.
- 87 Allen JL, Rampone JF, Wheelless CR. Use of a prophylactic antibiotic in elective major gynecologic operations. *Obstet Gynecol* 1972; 39: 218-24.
- 88 Ledger WJ, Sweet RL, Headington JT. Prophylactic cephaloridine in the prevention of postoperative pelvic infections in premenopausal women undergoing vaginal hysterectomy. *Am J Obstet Gynecol* 1973; 115: 766-74.
- 89 Sawaya GF, Grady D, Kerlikowske K, Grimes DA. Antibiotics at the time of induced abortion: the case for universal prophylaxis based on a meta-analysis. *Obstet Gynecol* 1996; 87: 884-90.
- 90 Morlet N, Gatus B, Coroneo M. Patterns of perioperative prophylaxis for cataract surgery: a survey of Australian ophthalmologists. *Aust N Z J Ophthalmol* 1998; 26: 5-12.
- 91 Liesegang TJ. Prophylactic antibiotics in cataract operations. *Mayo Clin Proc* 1997; 72: 149-59.
- 92 Hill C, Flamant R, Mazas F, Evrard J. Prophylactic cefazolin versus placebo in total hip replacement. Report of a multicentre double-blind randomised trial. *Lancet* 1981; 1: 795-6.
- 93 Lidwell OM, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D. Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement: a randomised study. *BM J* 1982; 285: 10-14.
- 94 Rubinstein E, Findler G, Amit P, Shaked I. Perioperative prophylactic cephalosporin in spinal surgery. A double-blind placebo-controlled trial. *J Bone Joint Surg Br* 1994; 76: 99-102.
- 95 Young RF, Lawner PM. Perioperative antibiotic prophylaxis for prevention of postoperative neurosurgical infections. A randomised clinical trial. *J Neurosurg* 1987; 66: 701-5.
- 96 Gillespie WJ, Walenkamp G. Antibiotic prophylaxis for surgery for proximal femoral and other closed long bone fractures (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2000. Oxford: Update Software.
- 97 Boxma H, Broekhuizen T, Patka P, Oosting H. Randomised controlled trial of single dose antibiotic prophylaxis in surgical treatment of closed fractures: the Dutch Trauma Trial. *Lancet* 1996; 347: 1133-7.
- 98 Burnett JW, Gustilo RB, Williams DN, Kind AC. Prophylactic antibiotics in hip fractures. A double-blind, prospective study. *J Bone Joint Surg* 1980; 62: 457-62.
- 99 Boyd RJ, Burke JF, Colton T. A double blind clinical trial of prophylactic antibiotics in hip fractures. *J Bone Joint Surg Am* 1973; 55: 1251-8.
- 100 Pearle MS, Roehrborn CG. Antimicrobial prophylaxis prior to shock wave lithotripsy in patients with sterile urine before treatment: a meta-analysis and cost-effectiveness analysis. *Urology* 1997; 49: 679-86.
- 101 Ruebush TK II, McConville JH, Calia FM. A double-blind study of trimethoprim-sulfamethoxazole prophylaxis in patients having transrectal needle biopsy of the prostate. *J Urol* 1979; 122: 492-4.
- 102 Crawford ED, Haynes AL Jr, Story MW, Borden TA. Prevention of urinary tract infection and sepsis following transrectal prostatic biopsy. *J Urol* 1982; 127: 449-51.
- 103 Taylor EW, Lindsay G. Antibiotic prophylaxis in transurethral resection of the prostate with reference to the influence of preoperative catheterisation. *J Hosp Infect* 1988; 12: 75-83.
- 104 Hargreave TB, Botto H, Rikken GH, Hindmarsh JR, McDermott TE, Mjølnerod OK, et al. European collaborative study of antibiotic prophylaxis for transurethral resection of the prostate. *Eur Urol* 1993; 23: 437-43.
- 105 Slavis SA, Miller JB, Golji H, Dunshee CJ. Comparison of single-dose antibiotic prophylaxis in uncomplicated transurethral resection of the prostate. *J Urol* 1992; 147: 1303-6.
- 106 Delavierre D, Huiban B, Fournier G, Le Gall G, Tande D, Mangin P. The value of antibiotic prophylaxis in transurethral resection of bladder tumours. Apropos of 61 cases. [Fre] *Prog Urol* 1993; 3: 577-82.
- 107 Sonne-Holm S, Boeckstyns M, Menck H, Sinding A, Leicht P, Dichmann O, et al. Prophylactic antibiotics in amputation of the lower extremity for ischemia. A placebo-controlled, randomized trial of cefoxitin. *J Bone Joint Surg* 1985; 67: 800-3.

- 108 Kaiser AB, Clayson KR, Mulherin JL Jr, Roach AC, Allen TR, Edwards WH, et al. Antibiotic prophylaxis in vascular surgery. *Ann Surg* 1978; 188: 283-9.
- 109 Pitt HA, Postier RG, MacGowan AW, Frank LW, Surmak AJ, Sitzman JV, et al. Prophylactic antibiotics in vascular surgery. Topical, systemic, or both? *Ann Surg* 1980; 192: 356-64.
- 110 Draft guideline for the prevention of surgical site infection, 1998 –CDC. Notice. *Fed Regist* 1998; 63: 33167-92.
- 111 McGowan JE. Cost and benefit of perioperative antimicrobial prophylaxis: methods for economic analysis. *Rev Infect Dis* 1991; 13: 879-89.
- 112 Ballow CH, Schentag JJ. Trends in antibiotic utilisation and bacterial resistance. Report of the National Nosocomial Resistance Surveillance Group. *Diagn Microbiol Infect Dis* 1992; 15: 37S-42S.
- 113 Adkinson NF Jr. Risk factors for drug allergy. *J Allergy Clin Immunol* 1984; 74: 567-72.
- 114 Penicillin allergy in childhood. *Lancet* 1989; 25: 420.
- 115 Idsoe O, Guthe T, Willcox RR, Weck AL de. Nature and extent of penicillin side-reactions, with particular reference to fatalities from anaphylactic shock. *Bull World Health Organ* 1968; 38: 159-88.
- 116 Sogn DD. Penicillin allergy. *J Allergy Clin Immunol* 1984; 74: 589-93.
- 117 Saxon A, Adelman DC, Patel A, Hajdu R, Calandra GB. Imipenem cross-reactivity with penicillin in humans. *J Allergy Clin Immunol* 1988; 82: 213-7.
- 118 Martin C. Antimicrobial prophylaxis in surgery: general concepts and clinical guidelines. French Study Group on Antimicrobial Prophylaxis in Surgery, French Society of Anesthesia and Intensive Care. *Infect Control Hosp Epidemiol* 1994; 15: 463-71.
- 119 Classen DC, Evans RS, Pestonik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *NEJM* 1992; 326: 281-6.
- 120 Page CP, Bohnen JM, Fletcher JR, McManus AT, Solomkin JS, Wittmann DH. Antimicrobial prophylaxis for surgical wounds. Guidelines for clinical care. *Arch Surg* 1993; 128: 79-88.
- 121 van Dijk-van Dam MS, Moll FL, de Letter JA, Langemeijer JJ, Kuks PF. The myth of the second prophylactic antibiotic dose in aortoiliac reconstructions. *Eur J Vasc Endovasc Surg*. 1996; 12: 428-30.
- 122 Vuorisalo S, Pokela R, Syrjala H. Is single-dose antibiotic prophylaxis sufficient for coronary artery bypass surgery? An analysis of peri- and postoperative serum cefuroxime and vancomycin levels. *J Hosp Infect* 1997; 37: 237-47.
- 123 Cuthbertson AM, McLeish AR, Penfold JC, Ross H. A comparison between single and double dose intravenous Timentin for the prophylaxis of wound infection in elective colorectal surgery. *Dis Colon Rectum* 1991; 34: 151-5.
- 124 Scher KS. Studies on the duration of antibiotic administration for surgical prophylaxis. *Am Surg* 1997; 63: 59-62.
- 125 Gatell JM, Garcia S, Lozano L, Soriano E, Ramon R, SanMiguel JG. Perioperative cefamandole prophylaxis against infections. *J Bone Joint Surg Am* 1987; 69:1189-93.
- 126 Culver DH, Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG, et al. Surgical wound infection rates by wound class, operative procedure, and patient risk index. National Nosocomial Infections Surveillance System. *Am J Med* 1991; 91: 152-7.
- 127 McDonald M, Grabsch E, Marshall C, Forbes A. Single- versus multiple-dose antimicrobial prophylaxis for major surgery: a systematic review. *Aust NZ J Surg* 1998; 68: 388-96.
- 128 Wymenga A, van Horn J, Theeuwes A, Muijtjens H, Slooff T. Cefuroxime for prevention of postoperative coxitis. One versus three doses tested in a randomized multicenter study of 2,651 arthroplasties. *Acta Orthop Scand* 1992; 63: 19-24.
- 129 Hall JC, Christiansen KJ, Goodman M, Lawrence-Brown M, Prendergast FJ, Rosenberg P, et al. Duration of antimicrobial prophylaxis in vascular surgery. *Am J Surg* 1998; 175: 87-90.
- 130 Steering Group of the Second National Prevalence Survey. National prevalence survey of hospital acquired infections: definitions. *J Hosp Infect* 1993; 24: 69-76.
- 131 Crowe MJ, Cooke EM. Review of case definitions for nosocomial infection - towards a consensus. Presentation by the Nosocomial Infection Surveillance Unit (NISU) to the Hospital Infection Liaison Group, subcommittee of the Federation of Infection Societies (FIS). *J Hosp Infect* 1998; 39: 3-11.
- 132 Levy M, Egersegi P, Strong A, Tessoro A, Spino M, Bannatyne R, et al. Pharmacokinetic analysis of cloxacillin loss in children undergoing major surgery with massive bleeding. *Antimicrob Agents Chemother* 1990; 34: 1150-3.
- 133 Wollinsky KH, Buchele M, Oethinger M, Kluger P, Mehrkens HH, Marre R, et al. Influence of hemodilution on cefuroxime levels and bacterial contamination of intra- and postoperative processed wound blood during hip replacement. *Beitr Infusionsther Transfusionsmed* 1996; 33: 191-5.
- 134 van Lindert AC, Giltaij AR, Derksen MD, Alsbach GP, Rozenberg-Araska M, Verhoef J. Single-dose prophylaxis with broad-spectrum penicillins (piperacillin and mezlocillin) in gynecologic oncological surgery, with observation on serum and tissue concentrations. *Eur J Obstet Gynecol Reprod Biol* 1990; 36: 137-45.

- 135 Sue D, Salazar TA, Turley K, Guglielmo BJ. Effect of surgical blood loss and volume replacement on antibiotic pharmacokinetics. *Ann Thorac Surg* 1989; 47: 857-9.
- 136 Mugford, M, Kingston, Chalmers I. Reducing the incidence of infection after caesarean section: implications of prophylaxis with antibiotics for hospital resources. *BMJ* 1989; 299: 1003-6.
- 137 Maynard, A. Is it worthwhile reducing hospital infection rates? In: Taylor EW Editor. *Infection in surgical practice*, Oxford: Oxford University Press 1992; 1: 119-22.
- 138 MIMS (Monthly Index of Medical Specialities), June 1999.
- 139 Davey P, Dodd T, Kerr S, Malek M. Audit of IV antibiotic administration. *Pharm J* 1999; 244: 793-6.
- 140 Au P, Salama S, Rotstein C. Implementation and evaluation of a preprinted perioperative antimicrobial prophylaxis order form in a teaching hospital. *Can J Infect Dis* 1998; 9: 157-66.
- 141 Soumerai SB, Avorn J, Taylor WC, Wessels M, Maher D., Hawley SL. Improving choice of prescribed antibiotics through concurrent reminders in an educational order form. *Med Care* 1993; 31: 552-8.
- 142 Marr JJ, Moffet HL, Kunin CM. Guidelines for improving the use of antimicrobial agents in hospitals: a statement by the Infectious Diseases Society of America. *J Infect Dis* 1988; 157: 869-76.
- 143 Girotti MJ, Fodoruk S, Irvine-Meek J, Rotstein OD. Antibiotic handbook and preprinted perioperative order forms for surgical antibiotic prophylaxis: do they work? *Can J Surg* 1990; 33: 385-8.
- 144 Goldmann DA, Weinstein RA, Wenzel RP, Tablan OC, Duma RJ, Gaynes RP, et al. Strategies to prevent and control the emergence and spread of antimicrobial resistant microorganisms in hospitals. A challenge to hospital leadership. *JAMA* 1996; 275: 234-40.
- 145 Martin C, Pourriat JL. Quality of perioperative antibiotic administration by French anaesthetists. *J Hosp Infect* 1998; 40: 47-53.
- 146 Dobranski S, Lawley DI, McDermott I, Selby M, Ausobsky JR. The impact of guidelines on peri-operative antibiotic administration. *J Clin Pharm Therap* 1991; 16: 19-24.
- 147 Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol* 1992; 13: 606-8.
- 148 Sanderson PJ. Prophylaxis in orthopaedic implant surgery - should we use a glycopeptide? *J Antimicrob Chemother* 1998; 41: 322-5.
- 149 Scottish Office Department of Health. *Hospital acquired infection – a framework for a national system of surveillance for the NHS in Scotland*. Edinburgh: Scottish Office, 1999.
- 150 Kreter B, Woods M. Antibiotic prophylaxis for cardiothoracic operations. Meta-analysis of thirty years of clinical trials. *J Thorac Cardiovasc Surg* 1992; 104: 590-9.

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