



**S I G N**

**Scottish  
Intercollegiate  
Guidelines  
Network**

# **Antibiotic Prophylaxis in Surgery**

Draft Guideline for discussion at ISPOR

DRAFT

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

### 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 Research 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

- |          |   |
|----------|---|
| <b>A</b> | <b>Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation.</b><br><i>(Evidence levels Ia, Ib)</i>                                   |
| <b>B</b> | <b>Requires the availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.</b><br><i>(Evidence levels IIa, IIb, III)</i>   |
| <b>C</b> | <b>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.</b><br><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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## ANTIBIOTIC PROPHYLAXIS IN SURGERY

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## ANTIBIOTIC PROPHYLAXIS IN SURGERY

# 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.

SIGN consents to the copying of this guideline for the purpose of producing local guidelines for use in Scotland.

### 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 2000 and will be reviewed in 2002 or sooner if new evidence becomes available. Any amendments in the interim period will be noted on the SIGN website. 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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## ANTIBIOTIC PROPHYLAXIS IN SURGERY

### Abbreviations

<b>ASA</b>	American Society of Anaesthesiologists
<b>NNT</b>	Numbers needed to treat
<b>RCT</b>	Randomised controlled trial
<b>SSI</b>	Surgical site infection
<b>UTI</b>	Urinary tract infection

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

# 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.<sup>1</sup>

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. Throughout this guideline the term surgical site infection (SSI) is used, unless the evidence relates specifically to surgical wound infection.

Prophylactic administration of antibiotics inhibits growth of contaminating bacteria<sup>2,3,4</sup> 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.<sup>5</sup> Administration of antibiotics also increases the prevalence of antibiotic resistant bacteria<sup>6</sup> and predisposes the patient to infection with organisms such as *Clostridium difficile*, the cause of antibiotic-associated colitis.<sup>7</sup>

### 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 immunocompetence.

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.<sup>8</sup> 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,<sup>9</sup> whereas a similar audit in Tayside found that only 12% continued prophylaxis for more than 24 hours.<sup>10</sup> 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.<sup>11</sup>

There have been a large number of studies of surgical prophylaxis to provide scientific evidence

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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.<sup>12</sup> The existing guidelines were reviewed by the SIGN guideline development group against the accepted criteria for appraisal of clinical guidelines.<sup>13</sup> 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.<sup>14</sup> 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 IDSA guideline<sup>15</sup> 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 therefore agreed 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.<sup>16</sup>

### 1.4 REMIT OF THE GUIDELINE

The remit of this guideline is confined to the administration of intravenous antibiotics to patients undergoing clean, clean-contaminated and some contaminated surgical procedures (*see definition in section 2.1.1*) in order to reduce the incidence of surgical site infection. As dirty operations and some contaminated procedures require antibiotic therapy of the established infection they are beyond the remit of this guideline.

It 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 & 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:

- 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 that is regularly updated.<sup>17,18</sup>
- Use of antiseptics or topical antibiotics (e.g. tetracycline lavage) for the prevention of wound

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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 bacterimia.
- Transplant surgery.

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# 2 Risk factors for surgical site infection

## 2.1 FACTORS AFFECTING THE INCIDENCE OF SURGICAL SITE INFECTION

### 2.1.1 CLASSIFICATION OF OPERATION

Operations are usually categorised into four classes (see Table 1) with an increasing incidence of bacterial contamination and subsequent incidence of postoperative infection:<sup>19</sup>

**Table 1:** Classification of operation

<b>Clean</b>	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.
<b>Clean-contaminated</b>	Operations in which the respiratory, alimentary or genitourinary tracts are entered but without significant spillage.
<b>Contaminated</b>	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 injuries operated on within four hours.
<b>Dirty</b>	Operations in the presence of pus, where there is a previously perforated hollow viscus, or, compound injuries more than four hours old.

The guideline applies to all elective operations in the clean, clean-contaminated or contaminated categories and to clean emergency operations (e.g. emergency repair of abdominal aortic aneurysm or open fixation of a closed fracture).

Antibiotic therapy for emergency clean-contaminated, contaminated or dirty operations is 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.<sup>20</sup> The implant has a detrimental effect on the patient's immunocompetence. 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.<sup>19</sup> In this study, operations that lasted longer than the 75th percentile for the procedure were classified as prolonged.

### 2.1.4 CO-MORBIDITIES

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The American Society of Anaesthesiologists (ASA) has devised a pre-operative risk score based on the presence of co-morbidities at the time of surgery (see Table 2).<sup>21</sup> 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.<sup>19</sup>

**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

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 comorbidity (as indicated by an ASA score > 2) and duration of operation (> 75<sup>th</sup> 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, in the following table, 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

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%

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

### 3 Benefits and risks of antibiotic prophylaxis

#### 3.1 BENEFITS OF PROPHYLAXIS

In many ways, the value of surgical antibiotic prophylaxis in terms of the incidence of SSI after elective surgery is related to the severity of the consequences of SSI. For example, in the presence of an anastomosis of the colon, prophylaxis reduces postoperative mortality.<sup>22</sup> In total hip replacement surgery prophylaxis reduces long term postoperative morbidity.<sup>23</sup> However, for most operations prophylaxis only decreases short term morbidity.

Evidence Level III

Surgical wound infection increases the length of hospital stay.<sup>24</sup> The additional length of stay is dependent on the type of surgery, for example, about three days for cholecystectomy or hysterectomy but 11-16 days for major orthopaedic procedures.<sup>25, 26, 27</sup> Prophylaxis therefore has the potential to shorten hospital stay. However, there is little direct evidence that it does so 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.<sup>28</sup>

#### 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.<sup>29,30</sup> 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.<sup>31,32,33</sup>

Evidence level IIa

An additional problem is the dramatic increase in the number of cases of colitis caused by *Clostridium difficile* in the UK from 1993-96. The prevalence of *C. difficile* infection is related to total antibiotic usage and, in particular, to the use of third generation cephalosporins.<sup>34 35, 36</sup> In epidemiological studies of *C. difficile* colitis, surgical antibiotic prophylaxis is the single most common indication for use of antibiotics.<sup>7</sup> Although even single dose prophylaxis increases the risk of carriage of *C. difficile*,<sup>37</sup> in a case control study of patients who all received surgical prophylaxis carriage of *C. difficile* was more common in patients who received prophylaxis for > 24 h (56% versus 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 £4000, largely due to prolongation of hospital stay.<sup>36</sup> Moreover, one study has shown a statistically significant increase in the frequency of bacteremia and line infections in surgical patients who received prophylactic antibiotics for more than 4 days in comparison with those who received prophylaxis for one day or less.<sup>38</sup>

- ☑ 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*)
  - the consequences of prophylaxis for the hospital (*e.g. increased cost*)
  - the consequences of prophylaxis for the environment (*e.g. increased antibiotic resistance*)

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

# 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*). The recommendations are presented in Table 4, 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.<sup>39</sup>

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. This, together with the rate of wound infection for an operative procedure, is used to calculate the NNT using the following formula:

---


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

*where expected baseline risk = % of risk of wound infection in the hospital*

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Where possible the odds ratios and NNTs given in Table 4 have been taken from published meta-analysis. However in some cases the guideline development group has taken data from pooled trials and combined it without formal meta-analysis. This is detailed in annex 2.

The economic implications of implementing surgical antibiotic prophylaxis must also be considered. 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 NOTES FOR USE WITH TABLE 4

1. Surgical antibiotic prophylaxis unequivocally reduces major morbidity, reduces hospital costs and is likely to decrease overall consumption of antibiotics
2. Surgical antibiotic 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
3. Although antibiotic prophylaxis is recommended for all patients, local policy makers may wish to identify exceptions, as prophylaxis may not reduce hospital costs and could increase consumption of antibiotics, especially if given to patients at low risk of infection. However, 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.
4. For some clean-contaminated procedures or procedures involving insertion of

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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 patients<sup>40</sup> 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, policy makers must be aware that their policy represents a minority of professional opinion.

5. Prophylaxis has not been proven to be clinically effective and as the consequences of infection are short-term morbidity, is likely to increase hospital antibiotic consumption for little clinical benefit.

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### 4.3 RECOMMENDED INDICATIONS FOR SURGICAL ANTIBIOTIC PROPHYLAXIS

**Table 4** Indications for surgical antibiotic prophylaxis

CARDIOTHORACIC SURGERY						
Operation	Recommended Indication	see note	Odds Ratio	NNT	Outcome	
Cardiac pacemaker insertion <sup>41</sup>	<b>A</b> Antibiotic prophylaxis is <u>recommended</u>	2	0.26	37	Any infection	<i>Evidence level Ia</i>
Open heart surgery, including:						
▪ Coronary artery bypass grafting, <sup>42,43,44</sup>	<b>A</b> Antibiotic prophylaxis is <u>recommended</u>	2	0.20 <sup>139</sup>	14	Wound infection	<i>Evidence level Ib</i>
▪ Prosthetic valve surgery <sup>45,46</sup>	<b>B</b> Antibiotic prophylaxis is <u>recommended</u>	2	0.20 <sup>139</sup>	14	Wound infection	<i>Evidence level IIa</i>
Pulmonary resection <sup>47,48</sup>	<b>A</b> Antibiotic prophylaxis is <u>recommended</u>	2	0.26	5	Surgical site infection	<i>Evidence level Ib</i>
ENT SURGERY						
Ear surgery - clean <sup>49,50,51</sup>	<b>C</b> Antibiotic prophylaxis is <u>not recommended</u>	5	<i>There is no evidence of effectiveness from RCTs</i>			<i>Evidence level IV</i>
Head and neck surgery - clean <sup>52</sup>	<b>B</b> Antibiotic prophylaxis is <u>not recommended</u>	5	<i>There is no evidence of effectiveness from RCTs</i>			<i>Evidence level IIb</i>
Head and neck surgery contaminated/ clean-contaminated <sup>53</sup>	<b>A</b> Antibiotic prophylaxis is <u>recommended</u>	2	0.19	3	Wound infection	<i>Evidence level Ia</i>

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

Nose or sinus surgery <sup>54</sup>	C	Antibiotic prophylaxis is <u>not recommended</u>	5	<i>There is no evidence of effectiveness from RCTs</i>	<i>Evidence level IV</i>
Tonsillectomy <sup>40</sup>	C	Antibiotic prophylaxis is <u>not recommended</u>	5	<i>There is no evidence of effectiveness from RCTs</i>	<i>Evidence level IV</i>

### GENERAL SURGERY

Operation		Recommended Indication	See note	Odds Ratio	NNT	Outcome	
Appendectomy <sup>55,56,57</sup>	A	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	3	0.63	13	Wound infection	<i>Evidence level Ib</i>
Biliary surgery - open <sup>58</sup>	A	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	3	0.30	10	Wound infection	<i>Evidence level Ia</i>
Breast surgery <sup>59</sup>	A	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	3				<i>Evidence level Ia</i>
Colorectal surgery <sup>60</sup>	A	Antibiotic prophylaxis is <u>highly recommended</u>	1	0.37	5	Infection	<i>Evidence level Ia</i>
				0.38	17	Mortality	<i>Evidence level Ia</i>
Endoscopic gastrectomy <sup>61</sup>	A	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	3	0.13	2	Peristomal and other infection	<i>Evidence level Ib</i>
Gastroduodenal surgery <sup>62,63,64</sup>	A	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	3	0.04	4	Wound infection	<i>Evidence level Ib</i>
Hernia surgery <sup>65,66</sup>	A	Antibiotic prophylaxis is <u>not recommended</u>	5	<i>Pooled results from 2 RCTs show no statistically significant effect</i>			<i>Evidence level Ib</i>
Laparoscopic cholecystectomy <sup>67,68,69,70</sup>	B	Antibiotic prophylaxis is <u>not recommended</u>	5	<i>There is no evidence of effectiveness from RCTs</i>			<i>Evidence level IIIb</i>
Laparoscopic hernia repair with mesh <sup>71,72</sup>	A	Antibiotic prophylaxis is <u>not recommended</u>	5				<i>Evidence level Ib</i>
Oesophageal surgery <sup>73</sup>	C	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	4	<i>Effectiveness is inferred from evidence about other clean-contaminated procedures</i>			<i>Evidence level IV</i>

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

Small bowel surgery <sup>74</sup>	C	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	4	<i>Effectiveness is inferred from evidence about other clean-contaminated procedures</i>	<i>Evidence level IV</i>
Clean-contaminated procedures –where no direct evidence is available <sup>40</sup>	C	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	4	<i>Effectiveness is inferred from evidence about other clean-contaminated procedures</i>	<i>Evidence level IV</i>

## NEUROSURGERY

Operation		Recommended Indication	see note	Odds Ratio	NNT	Outcome	
Craniotomy <sup>75</sup>	A	Antibiotic prophylaxis is <u>recommended</u>	2	0.18	14	Wound infection	<i>Evidence level Ia</i>
CSF shunt <sup>76,77</sup>	A	Antibiotic prophylaxis is <u>recommended</u>	2	0.52	16	Wound & shunt infection	<i>Evidence level Ia</i>
				0.48	16	Shunt infection	

## OBSTETRICS & GYNAECOLOGY

Caesarean section <sup>78</sup>	A	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	3	0.35	17	Wound infection	<i>Evidence level Ia</i>
Hysterectomy - abdominal <sup>79,80</sup>	A	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	3	0.37	8	Wound infection	<i>Evidence level Ia</i>
Hysterectomy - vaginal <sup>81,82</sup>	A	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	3	0.11	4	Infectious morbidity/ pelvic infection	<i>Evidence level Ib</i>
Induced abortion <sup>83</sup>	A	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	3	0.58	25	Upper genital tract infection	<i>Evidence level Ia</i>

## OPHTHALMOLOGY

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

Cataract surgery <sup>84,85</sup>	C	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	4	<i>Effectiveness is inferred from evidence about other procedures involving insertion of prosthetic devices</i>		<i>Evidence level IV</i>
<b>ORTHOPAEDIC SURGERY</b>						
<b>Operation</b>		<b>Recommended Indication</b>		<b>Odds Ratio</b>	<b>NNT</b>	<b>Outcome</b>
Closed fracture fixation <sup>86</sup>	A	Antibiotic prophylaxis is <u>recommended</u>	2	0.42 <sup>87</sup>	58	Deep wound infection
Fractured hip repair <sup>88,89</sup>	A	Antibiotic prophylaxis is <u>recommended</u>	2	0.42 <sup>87</sup>	58	Deep wound infection
Insertion of prosthetic device - <i>any procedure where no direct evidence is available</i> <sup>40</sup>	C	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	4	<i>Effectiveness is inferred from evidence about other procedures involving insertion of prosthetic devices</i>		<i>Evidence level IV</i>
Orthopaedic surgery without prosthetic device (elective) <sup>40</sup>	C	Antibiotic prophylaxis is <u>not recommended</u>	5	<i>There is no evidence of effectiveness from RCTs</i>		<i>Evidence level IV</i>
Prosthetic knee joint replacement. <sup>90</sup>	B	Antibiotic prophylaxis is <u>highly recommended</u>	1	<i>Observational data supports effectiveness</i>		<i>Evidence level IIa</i>
Spinal surgery <sup>91,92</sup>	A	Antibiotic prophylaxis is <u>recommended</u>	2	0.28	28	Wound infection
Total hip replacement <sup>93</sup>	A	Antibiotic prophylaxis is <u>highly recommended</u>	1	0.27	42	Hip infection

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

### UROLOGY

Operation		Recommended Indication		Odds Ratio	NNT	Outcome	
Shock-wave lithotripsy <sup>94</sup>	A	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	3	0.45	27	Urinary tract infection	<i>Evidence level Ia</i>
Trans-rectal prostate biopsy <sup>95,96</sup>	A	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	3	0.17	4	Bacteriuria	<i>Evidence level Ib</i>
Transurethral resection of bladder tumours <sup>97</sup>	C	Antibiotic prophylaxis is <u>not recommended</u>	5	<i>There is no evidence of effectiveness from RCTs</i>			<i>Evidence level IV</i>
Transurethral resection of the prostate <sup>98,99,100</sup>	A	Antibiotic prophylaxis is <u>recommended</u> but local policy makers may identify exceptions	3	0.42	7	Urinary tract infection	<i>Evidence level Ib</i>

### VASCULAR SURGERY

Lower limb amputation <sup>101</sup>	A	Antibiotic prophylaxis is <u>recommended</u>	2	0.32	5	Wound infection	<i>Evidence level Ib</i>
Vascular surgery - abdominal & lower limb <sup>102,103</sup>	A	Antibiotic prophylaxis is <u>recommended</u>	2	0.06	11	Wound infection	<i>Evidence level Ib</i>

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

# 5 The administration of 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 3*). Only these need to be covered by the antibiotic that is prescribed.<sup>104</sup>

*Evidence level Ia*

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.<sup>105</sup> 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

**A** The antibiotics selected for prophylaxis must cover the common pathogens.

## 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:<sup>106</sup>

- anaphylaxis
- urticaria
- rash

*Evidence level IIIb*

Other symptomatology shows 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 cephalosporins<sup>107</sup> and carbapenems.<sup>108</sup> However, the frequency of these relationships and their clinical significance is uncertain.

**B** Patients with a history of anaphylaxis, urticaria or rash 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.

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

### 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.<sup>109</sup>

Administration of prophylaxis more than three hours after the start of the operation significantly reduces its effectiveness.<sup>110</sup> For maximum effect, it should be given just before or just after the start of the operation.

*Evidence level Ia*

**A**

**In most circumstances, prophylaxis should be given pre-operatively, 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 drug reaching the neonate. When a tourniquet is to be applied the necessary tissue concentration must be achieved prior to its application rather than the time of incision.

Antibiotics should also be administered immediately after unexpected contamination of the tissues.

### 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.<sup>111</sup> However, in comparison with normal volunteers, patients undergoing surgery have slower clearance of drugs from their blood.<sup>112,113</sup> 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 has a half life of 2-4 hours in patients at the time of surgery, and that effective concentrations are maintained for at least 5 hours after the start of surgery.<sup>112,113</sup>

The search strategy used found only two clinical studies that explicitly compared a single dose pre-operatively with a pre-operative dose plus an additional intra-operative dose.<sup>114,115</sup> One randomised trial did not support the effectiveness of a second intra-operative dose.<sup>114</sup> In this study, Timentin, a combination of ticarcillin and clavulanic acid, was administered intravenously (3.1 g) at the commencement of operation to all patients, and this was repeated after 2 hours in those patients randomized 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<sup>115</sup> 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, pre-operative 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.

Furthermore, two systematic reviews have failed to find evidence to support the superiority of long half life drugs over short half life drugs.<sup>116,117</sup>

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

In short, the guideline development group did not find definitive evidence for or against additional intra-operative doses.

### 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.<sup>104,118,119</sup> 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.<sup>120</sup> This is specifically excluded from most definitions of wound infection, as the test does not distinguish between colonisation and infection.<sup>121</sup> 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.

*Evidence level Ib*

Prophylaxis should therefore be confined to the perioperative period (i.e. administration immediately before or during the procedure). Postoperative doses should not be given for any operations.

Any decision to prolong prophylaxis beyond a single dose should be explicit and supported by an evidence base.

**A** Prophylaxis should be confined to the perioperative period.

### 5.5 ROUTE OF ADMINISTRATION

Intravenous administration of 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 prophylaxis by the intravenous route is the only method that is supported by a substantial body of evidence.

Prophylactic antibiotics 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.

A single dose of antibiotic at the therapeutic concentration is sufficient for prophylaxis under most circumstances.

### 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.<sup>122,123</sup>

*Evidence level IIa & IIb*

The precise effects of blood loss and fluid replacement are difficult to predict, depending on the timing and rate of loss and replacement.<sup>104</sup> However, in adults the impact of intra-operative bleeding and fluid replacement on serum drug concentrations is usually negligible.<sup>124,125</sup>

*Evidence level IIb*

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

**B** In adults, blood loss of up to 1500 ml during surgery does not require an additional dose of prophylactic agent.

**B** In adults, haemodilution up to 15 ml/kg during surgery does not require an additional dose of prophylactic agent.

In the event of major intra-operative blood loss (> 1.5l), 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.



## ANTIBIOTIC PROPHYLAXIS IN SURGERY

# 6 Economic evaluation of surgical antibiotic prophylaxis

## 6.1 FRAMEWORK FOR ECONOMIC EVALUATION

The aims of this section are to:

1. Outline the cost considerations related to surgical antibiotic prophylaxis
2. Provide some “rules of thumb” that a decision-maker can use to estimate the likely cost-effectiveness of embarking upon a particular preventative.

## 6.2 COST-EFFECTIVENESS OF SURGICAL ANTIBIOTIC PROPHYLAXIS

There are very few prospective randomised trials of surgical prophylaxis that 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). This is the number of patients that must receive prophylaxis in order to prevent one wound infection.<sup>39</sup>

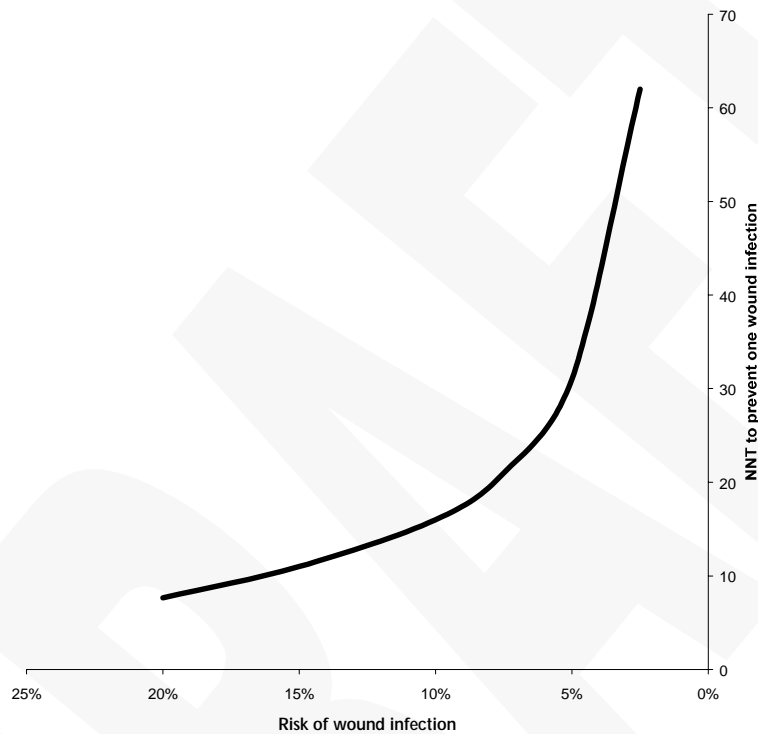
The relationship between the baseline risk of wound infection and NNT is not linear. The NNT rise steeply with decreasing risk of baseline wound infection (Figure 1).

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 5 estimates likely odds ratios for various baseline infection risks, that can be generalised to most operations.

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

**Figure 1:** Numbers Needed to Treat (NNT) to prevent one wound infection with surgical antibiotic prophylaxis in caesarean section surgery based on the results of a meta-analysis of randomised controlled clinical trials.<sup>78</sup> The odds ratio of wound infection with prophylaxis is 0.35. The graph shows how the NNT changes with expected baseline risk of infection. The method of calculation of NNT from baseline risk and odds ratio is given in Cook and Sackett.<sup>39</sup>



**Table 5:** Translating odds ratios to NNTs. The numbers in the body of the table are the NNTs for the corresponding odds ratios at that particular patient's expected baseline risk.

		NUMBERS NEEDED TO TREAT				
		Odds ratio				
Patient's expected baseline risk		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	

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

### 6.3 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.**

Focusing debate about prophylaxis on the likelihood of reducing overall antibiotic consumption highlights the importance of restricting prophylaxis to a single dose.

---

**Example A:** Calculating antibiotic consumption in relation to antibiotic prophylaxis following caesarean section.

For caesarean section the evidence supports restricting prophylaxis to a single dose of antibiotic when the umbilical cord is clamped.<sup>78</sup> There is no evidence that multiple doses of prophylaxis are more effective than single doses.

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

Baseline risk of wound infection without prophylaxis<sup>78</sup> = 9.7%

From figure 5.2 at this baseline risk NNT = 16.5

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

On an antibiotic treatment regimen of 3 doses/ day for 7 days, the total number of doses = 21

Table 5 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.

However, 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% (Table 5).



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

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

- **RULE 2: prophylaxis should definitely be given if it is likely to reduce overall hospital costs.**

There are limited data in the literature about the costs of wound infection for specific surgery types (Table 6). The major cost component of treating wound infection is increased length of stay.

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### Example B: Calculating the Relative Cost of Prophylaxis.

The cost of wound infection after caesarean section was £716 at 1988 prices.<sup>126 127</sup> A single dose of prophylaxis costing £5 would therefore reduce hospital costs provided that the NNT to prevent one wound infection is 143 (£716/ £5) or lower. Given that the odds ratio for risk of wound infection after caesarean section is 0.35<sup>78</sup> this is likely to occur even if the baseline risk of wound infection is as low as 1.0% (Table 5).



Use NNTs and the cost of prophylactic antibiotics to compare the cost of prophylaxis with the cost of treatment.

If prophylaxis does not appear cost-effective according to this decision rule then a hospital could justify withholding prophylaxis on the grounds that it is unlikely to reduce hospital costs.

---

### Example C: calculation of the cost per wound infection avoided.

Table 5 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,

odds ratio = 0.35

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.<sup>126</sup> However, this estimate is based on the cost of resources such as nursing time or length of hospital stay, and that reducing wound infection rate may not result in anything like the equivalent cash savings to the hospital.<sup>128</sup>

Such calculations are highly sensitive to the cost of the antibiotics used for prophylaxis. The cost of a single dose of 1.2g Co-amoxiclav is only £2.97<sup>129</sup> and even allowing for other costs such as drug preparation, administration and wastage, £5 for single dose prophylaxis is a conservative estimate.<sup>130</sup>

However, two points must be borne in mind when calculating the comparative costs of prophylaxis. Firstly, the cost of some alternative agents is much higher (e.g. £9.65 for 2G cefotaxime or £30.00 for 1g imipenem<sup>129</sup>). Secondly, with very few exceptions, increasing the number of doses of prophylaxis adds to the cost without improving the effectiveness.

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

### 6.4 IMPACT ON POLICIES FOR TREATMENT OF POSTOPERATIVE INFECTION

The antibiotics chosen for prophylaxis can be those used for the treatment of infection (*see section 5.1*).

- 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.

Prescribers need to be aware that radical changes in their treatment policy because of implementation of prophylaxis 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.<sup>131</sup>

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

**Table 6:** Comparing the cost of prophylaxis and treatment:

Treatment cost per wound infection and NNT at which cost of prophylaxis equals cost of treating one wound infection

	Treatment cost per wound infection*	NNT to prevent one wound infection (one dose costs £5)			
		Single dose		Two doses	
		NNT	£	NNT	£
Colorectal surgery	1404	281	1405	140	1400
Vascular surgery with graft	1085	217	1085	109	1090
Cholecystectomy	711	142	710	71	710
Malignant breast tumour	676	135	675	68	680
Oesophageal surgery	635	127	635	64	640
Groin hernia repair	367	73	365	34	340

\*1992 prices<sup>126</sup>



Calculate the cost per wound infection prevented by prophylaxis and make a decision about whether prophylaxis represents good value.

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

# 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%.<sup>132</sup> Use of specific antibiotic order forms<sup>132</sup> has previously been shown to reduce inappropriate prescribing and was one of the recommendations of the Infectious Diseases Society of America.<sup>133,134</sup> Prescribing antibiotic prophylaxis in the single dose section of drug prescription forms is also associated with a lower proportion of inappropriate additional doses.<sup>135</sup>

## 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.<sup>132,136</sup> 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 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.

## 7.4 KEY POINTS & CORE INDICATORS FOR AUDIT

The guideline development group accept that routine collection of many details pertaining to the operative procedures or its complications are likely to prove unrealistic. Here, the recommended standards for audit and core indicators identified have been previously validated and are thought by the guideline development group to be measurable and valuable.

Regular audit of surgical antibiotic prophylaxis should be implemented and could be a basis for comparing the process of delivering prophylaxis between different organisations for a common set of operations.

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

Many types of outcome indicators have been suggested.<sup>141</sup> The commonest is surgical site infection (SSI) rate, particularly wound infection rates.<sup>141</sup> 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.

*Evidence Level IV*

### CORE INDICATORS FOR AUDIT<sup>135,141-137-138</sup>

#### General

- Does the hospital have written guidelines that clearly identify the procedures that require prophylaxis and those that don't?
- Is there a written programme for dissemination, implementation, continuing education and audit with feedback, for the guideline?
- Are the guidelines easily available to all relevant personnel?
- The guidelines should state the appropriate antibiotics, dose, timing and duration.
- As additional doses are rarely necessary the risks and benefits of such doses must be substantiated in the protocol.

#### Specific

- Was prophylaxis given?
- Was the first dose of prophylaxis given within 30 minutes of the start of surgery?
- Was a second dose given if the operation lasted for longer than 2 hours?
- Was the prescription written in the "once-only" section of the drug prescription chart?
- Was the duration of prophylaxis greater than 24 hours?



The guideline development group recommends that process measures are linked to outcome and that process measures should be monitored.

### MINIMUM DATA SET (MDS) FOR SURGICAL ANTIBIOTIC PROPHYLAXIS

- Date
- Operation performed
- 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 surgeon
- Designation of surgeon

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

# 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.

Papers were only included if they adhered to recognisable methodological principles, including adequate sample size, a clearly identified hypothesis and measure of outcome, and accurate reporting of results. Whenever possible randomised trials have been discussed, but due to the paucity of sound randomised controlled trials work in this area, a number of clinical studies have also been included.

Searches were carried out on MEDLINE, EMBASE, SOCIAL SCIENCE CITATION INDEX, and CINAHL. Criteria for inclusion were studies (or reviews of studies) which evaluated sexual health promotion interventions aimed at behaviour change.

### LITERATURE SEARCH STRATEGY

The standard SIGN methodology was followed using searches of the Cochrane database, Medline, Healthstar and Embase using the keywords:

Evidence tables (available on the SIGN website) were prepared by searching 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 was 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.

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

### Annex 2

#### EFFICACY OF PROPHYLAXIS: NUMBERS NEEDED TO TREAT - DATA FROM PUBLISHED META-ANALYSES

The table below 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 below. A worked example is given in section 6.

Operation	Outcome	No. of trials	Control infection rate	Odds Ratio	95% CI	NNT
Abdominal hysterectomy	Wound infection	25 <sup>80</sup>	21%	0.37	0.31-0.45	8
Biliary surgery (open)	Wound infection	42 <sup>58</sup>	4%	0.30	0.23-0.38	10
Caesarean section	Wound infection	42 <sup>78</sup>	10%	0.35	0.28-0.44	17
Cardiac pacemaker	Any infection	7 <sup>41</sup>	4%	0.26	0.10-0.66	37
Cardiac surgery	Wound infection	3 <sup>139</sup>	9%	0.20	0.10-0.49	14
Closed fractures	Deep wound infection	6 <sup>87</sup>	3%	0.42	0.26-0.68	58
Colorectal surgery	Infection	26 <sup>22</sup>	39%	0.37	0.30-0.45	5
Colorectal surgery	Mortality	17 <sup>22</sup>	10%	0.38	0.25-0.58	17
Craniotomy	Wound infection	8 <sup>75</sup>	9%	0.18	0.11-0.30	14
CSF Shunt	Wound & shunt infection	12 <sup>76</sup>	15%	0.52	0.37-0.73	16
CSF Shunt	Shunt infection	9 <sup>77</sup>	13%	0.48	0.31-0.73	16
Induced abortion	Upper genital tract infection	12 <sup>83</sup>	10%	0.58	0.47-0.71	25
Shock wave lithotripsy	UTI	6 <sup>94</sup>	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					

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

\*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 4 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).

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

### 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 at the SIGN website)

Operation	Outcome	No. of trials	Control infection rate	Odds Ratio	95% CI	NNT
Appendix	Wound infection	3 <sup>55,56,57</sup>	26%	0.63	0.41-0.96	13
Endoscopic gastrostomy	Peristomal or other infection	1 <sup>61</sup>	65%	0.13	0.05-0.35	2
Gastroduodenal	Wound infection	6 <sup>62,63,64</sup>	26%	0.04	0.01-0.14	4
Head & neck surgery (clean-contaminated/contaminated)	Wound infection	3 <sup>53</sup>	50%	0.19	0.10-0.35	3
Hysterectomy - vaginal	Infectious morbidity/ pelvic infection	3 <sup>80,81,82</sup>	32%	0.11	0.06-0.21	4
Lower leg amputation	Wound infection	1 <sup>101</sup>	39%	0.32	0.15-0.69	5
Pulmonary	SSI	2 <sup>47,48</sup>	29%	0.26	0.14-0.46	5
Spinal	Wound infection	2 <sup>91,92</sup>	5%	0.28	0.12-0.65	28
Total hip Replacement	Hip infection	1 <sup>93</sup>	3%	0.27	0.13-0.55	42
Trans rectal prostate biopsy	Bacteriuria	2 <sup>96,59</sup>	30%	0.17	0.05-0.54	4
Trans urethral resection of the prostate	UTI	2 <sup>98,99,100</sup>	29%	0.42	0.30-0.58	7
Vascular	Wound infection	2 <sup>102,103</sup>	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					

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

### Annex 3

TABLE OF COMMON PATHOGENS

SSI ORGANISM	ANTIBIOTIC SUSCEPTIBILITY
<b>Surgical Site Infection</b>	
<i>Staphylococcus aureus</i>	90% remain susceptible to flucloxacillin, macrolides & clindamycin
<i>β haemolytic streptococci (BHS)</i>	90% remain susceptible to penicillins, macrolides & clindamycin
<b>Below the waist</b>	
<i>Anaerobes</i>	95% remain susceptible to metronidazole & co-amoxiclav. <i>Penicillin can no longer be relied upon.</i>
<i>Enterobacteriaceae (especially E. coli)</i>	Complex resistance problems. However, 90% of <i>E. coli</i> remain susceptible to second generation cephalosporins <i>or</i> penicillins combined with a beta lactamase inhibitor.
<i>Enterococci</i>	Vast majority remain susceptible to amoxicillin
<b>Insertion of a prosthesis, graft or shunt</b>	
<i>Coagulase negative Staphylococci (CNS)</i> <i>Staphylococcus aureus</i>	Approx. two thirds of CNS are methicillin resistant (MRSE, therefore resistant to all beta lactams).  The only reliably active agents are the glycopeptides and rifampicin. However resistance to teicoplanin and rifampicin is well documented.
<b>MRSE, MRSA &amp; Glycopeptide Prophylaxis</b>	
<p>The increasing prevalence of MRSA raises the issues of glycopeptide prophylaxis against MRSA and MRSE infections, usually when inserting large joint prosthesis, vascular or cardiac grafts or shunts.</p> <p>Guidelines urge restraint in the use of glycopeptides, fearing development of vancomycin resistant <i>S. aureus</i>. However it is acknowledged that it is appropriate to use glycopeptides for prophylaxis in some ("high risk") patients where there have been recent major problems with life-threatening postoperative MRSA infection. However, their use for prevention of MRSE infections in large joint prosthesis is not advocated.<sup>140</sup></p>	

## ANTIBIOTIC PROPHYLAXIS IN SURGERY

# Annex 4

### AUDITING THE GUIDELINE

#### STRATEGIES FOR SUCCESSFUL IMPLEMENTATION AND AUDIT<sup>141</sup>

An expert multidisciplinary group has recommended the following strategies to overcome any barriers to the implementation and audit of changes in surgical antibiotic prophylaxis.

- Specify process ownership for major steps in the system, e.g. by defining accountability for inappropriate antimicrobial prescribing practices, and build a cross-disciplinary team to improve the system, which should be surgeon-led.
- Identify local, regional and national guideline models.
- Develop guidelines that allow for individualised clinical decisions and variance from guidelines.

#### RECOMMENDED CORE INDICATORS<sup>141</sup>

This annex summarises core performance indicators that can be used to evaluate the impact of guidelines for surgical prophylaxis.

These can be used in prospective or retrospective audit.

##### A. Process Measures

- Number of educational activities related to prophylaxis in a specified period
- Percentage of surgeons/ anaesthetists attending educational activity
- Surgeons/ anaesthetists' assessment of the hospital's educational and administrative interventions
- Overall and clinical-indication-specific trends in antimicrobial usage, costs and resistance

##### B. Outcome Measures

- Surgical Site Infection (SSI) Rate = number of SSIs occurring postoperatively/ total number of postoperative 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.

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[Editorial note: References will be fully checked prior to publication]

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