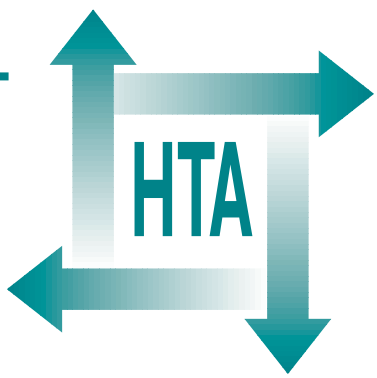
Health Technology Assessment 1998; Vol. 2: No. 7

Review

Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomised controlled trials

F Song
AM Glenny

Health Technology Assessment
NHS R&D HTA Programme



Standing Group on Health Technology

Chair: Professor Sir Miles Irving,
Professor of Surgery, University of Manchester, Hope Hospital, Salford †

Dr Sheila Adam,
Department of Health

Professor Martin Buxton,
Professor of Economics, Brunel University †

Professor Angela Coulter,
Director, King's Fund, London

Professor Anthony Culyer,
Deputy Vice-Chancellor, University of York

Dr Peter Doyle,
Executive Director, Zeneca Ltd,
ACOST Committee on Medical Research & Health

Professor John Farndon,
Professor of Surgery, University of Bristol †

Professor Charles Florey,
Department of Epidemiology & Public Health, Ninewells Hospital & Medical School, University of Dundee †

Professor John Gabbay,
Director, Wessex Institute for Health Research & Development †

Dr Tony Hope,
The Medical School, University of Oxford †

Professor Howard Glennester,
Professor of Social Science & Administration, London School of Economics & Political Science

Professor Sir John Grimley Evans,
Department of Geriatric Medicine, Radcliffe Infirmary, Oxford †

Mr John H James,
Chief Executive, Kensington, Chelsea & Westminster Health Authority

Professor Richard Lilford,
Regional Director, R&D, West Midlands †

Professor Michael Maisey,
Professor of Radiological Sciences, UMDS, London

Dr Jeremy Metters,
Deputy Chief Medical Officer, Department of Health †

Mrs Gloria Oates,
Chief Executive, Oldham NHS Trust

Dr George Poste,
Chief Science & Technology Officer, SmithKline Beecham †

Professor Michael Rawlins,
Wolfson Unit of Clinical Pharmacology, University of Newcastle-upon-Tyne

Professor Martin Roland,
Professor of General Practice, University of Manchester

Mr Hugh Ross,
Chief Executive, The United Bristol Healthcare NHS Trust †

Professor Ian Russell,
Department of Health, Sciences & Clinical Evaluation, University of York

Professor Trevor Sheldon,
Director, NHS Centre for Reviews & Dissemination, University of York †

Professor Mike Smith,
Director, The Research School of Medicine, University of Leeds †

Dr Charles Swan,
Consultant Gastroenterologist, North Staffordshire Royal Infirmary

Dr John Tripp,
Department of Child Health, Royal Devon & Exeter Healthcare NHS Trust †

Professor Tom Walley,
Department of Pharmacological Therapeutics, University of Liverpool †

Dr Julie Woodin,
Chief Executive, Nottingham Health Authority †

† Current members

HTA Commissioning Board

Chair: Professor Charles Florey, Department of Epidemiology & Public Health,
Ninewells Hospital & Medical School, University of Dundee †

Professor Ian Russell,
Department of Health, Sciences & Clinical Evaluation, University of York *

Dr Doug Altman,
Director, Institute of Health Sciences, Oxford †

Mr Peter Bower,
Independent Management Consultant, Newcastle-upon-Tyne †

Ms Christine Clark,
Hon. Research Pharmacist, Hope Hospital, Salford †

Professor David Cohen,
Professor of Health Economics, University of Glamorgan

Mr Barrie Dowdeswell,
Chief Executive, Royal Victoria Infirmary, Newcastle-upon-Tyne

Professor Martin Eccles,
Professor of Clinical Effectiveness, University of Newcastle-upon-Tyne †

Dr Mike Gill,
Brent & Harrow Health Authority †

Dr Jenny Hewison,
Senior Lecturer, Department of Psychology, University of Leeds †

Dr Michael Horlington,
Head of Corporate Licensing, Smith & Nephew Group Research Centre

Professor Sir Miles Irving
(Programme Director), Professor of Surgery, University of Manchester, Hope Hospital, Salford †

Professor Alison Kitson,
Director, Royal College of Nursing Institute †

Professor Martin Knapp,
Director, Personal Social Services Research Unit, London School of Economics & Political Science

Dr Donna Lamping,
London School of Hygiene & Tropical Medicine †

Professor Theresa Marteau,
Director, Psychology & Genetics Research Group, UMDS, London

Professor Alan Maynard,
Professor of Economics, University of York †

Professor Sally McIntyre,
MRC Medical Sociology Unit, Glasgow

Professor Jon Nicholl,
Director, Medical Care Research Unit, University of Sheffield †

Professor Gillian Parker,
Nuffield Professor of Community Care, University of Leicester †

Dr Tim Peters,
Department of Social Medicine, University of Bristol †

Professor David Sackett,
Centre for Evidence Based Medicine, Oxford

Professor Martin Severs,
Professor in Elderly Health Care, Portsmouth University †

Dr David Spiegelhalter,
MRC Biostatistics Unit, Institute of Public Health, Cambridge

Dr Ala Szczepura,
Director, Centre for Health Services Studies, University of Warwick †

Professor Graham Watt,
Department of General Practice, Woodside Health Centre, Glasgow †

Professor David Williams,
Department of Clinical Engineering, University of Liverpool

Dr Mark Williams,
Public Health Physician, Bristol

Dr Jeremy Wyatt,
Institute for Health Sciences, University College London †

* Previous Chair
† Current members

How to obtain copies of this and other HTA Programme reports.
An electronic version of this publication, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (http://www.hta.ac.uk). A fully searchable CD-ROM is also available (see below).

Printed copies of HTA monographs cost £20 each (post and packing free in the UK) to both public **and** private sector purchasers from our Despatch Agents.

Non-UK purchasers will have to pay a small fee for post and packing. For European countries the cost is £2 per monograph and for the rest of the world £3 per monograph.

You can order HTA monographs from our Despatch Agents:

– fax (with **credit card** or **official purchase order**)
– post (with **credit card** or **official purchase order** or **cheque**)
– phone during office hours (**credit card** only).

Additionally the HTA website allows you **either** to pay securely by credit card **or** to print out your order and then post or fax it.

Contact details are as follows:

HTA Despatch
c/o Direct Mail Works Ltd
4 Oakwood Business Centre
Downley, HAVANT PO9 2NP, UK

Email: orders@hta.ac.uk
Tel: 02392 492 000
Fax: 02392 478 555
Fax from outside the UK: +44 2392 478 555

NHS libraries can subscribe free of charge. Public libraries can subscribe at a very reduced cost of £100 for each volume (normally comprising 30–40 titles). The commercial subscription rate is £300 per volume. Please see our website for details. Subscriptions can only be purchased for the current or forthcoming volume.

Payment methods

Paying by cheque
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to *Direct Mail Works Ltd* and drawn on a bank with a UK address.

Paying by credit card
The following cards are accepted by phone, fax, post or via the website ordering pages: Delta, Eurocard, Mastercard, Solo, Switch and Visa. We advise against sending credit card details in a plain email.

Paying by official purchase order
You can post or fax these, but they must be from public bodies (i.e. NHS or universities) within the UK. We cannot at present accept purchase orders from commercial companies or from outside the UK.

How do I get a copy of *HTA on CD*?

Please use the form on the HTA website (www.hta.ac.uk/htacd.htm). Or contact Direct Mail Works (see contact details above) by email, post, fax or phone. *HTA on CD* is currently free of charge worldwide.

The website also provides information about the HTA Programme and lists the membership of the various committees.

Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomised controlled trials

F Song
AM Glenny

NHS Centre for Reviews and Dissemination
University of York
UK

Published May 1998

This report should be referenced as follows:

Song F, Glenny AM. Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomised controlled trials. *Health Technol Assessment* 1998;**2**(7).

Health Technology Assessment is indexed in *Index Medicus*/MEDLINE and *Excerpta Medica*/EMBASE. Copies of the Executive Summaries are available from the NCCHTA web site (see overleaf).

NHS R&D HTA Programme

The overall aim of the NHS R&D Health Technology Assessment (HTA) programme is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and work in the NHS. Research is undertaken in those areas where the evidence will lead to the greatest benefits to patients, either through improved patient outcomes or the most efficient use of NHS resources.

The Standing Group on Health Technology advises on national priorities for health technology assessment. Six advisory panels assist the Standing Group in identifying and prioritising projects. These priorities are then considered by the HTA Commissioning Board supported by the National Coordinating Centre for HTA (NCCHTA).

This report is one of a series covering acute care, diagnostics and imaging, methodology, pharmaceuticals, population screening, and primary and community care. It was identified as a priority by the Pharmaceutical Panel.

The views expressed in this publication are those of the authors and not necessarily those of the Standing Group, the Commissioning Board, the Panel members or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for the recommendations for policy contained herein. In particular, policy options in the area of screening will, in England, be considered by the National Screening Committee. This Committee, chaired by the Chief Medical Officer, will take into account the views expressed here, further available evidence and other relevant considerations.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

Series Editors: Andrew Stevens, Ruairidh Milne and Ken Stein
Assistant Editors: Jane Robertson and Jane Royle

The editors have tried to ensure the accuracy of this report but cannot accept responsibility for any errors or omissions. They would like to thank the referees for their constructive comments on the draft document.

ISSN 1366-5278

Published by Core Research, Alton, on behalf of the NCCHTA.
Printed on acid-free paper in the UK by The Basingstoke Press, Basingstoke.

Copies of this report can be obtained from:

The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 1703 595 639 Email: hta@soton.ac.uk
http://www.soton.ac.uk/~hta

Contents

List of abbreviations

CI	confidence interval
RCT	randomised controlled trial
SD	standard deviation*
SWI	surgical wound infection
UTI	urinary tract infection*
WI	wound infection*
i.v.	intravenous administration*
i.m.	intramuscular administration*
p.o.	oral administration*
b.d.	twice daily*
t.d.s	three-times daily*

* Used only in tables

Executive summary

Background

Wound infections are the most frequent nosocomial infections among surgical patients and are related to an increase in morbidity and mortality, a prolongation of hospital stay and an increase in the cost of medical care. Colorectal surgery is associated with a high risk of infection due to endogenous contamination by bacteria in the contents of the large bowel.

It is now generally accepted that antimicrobial prophylaxis is one of many important measures that should be taken to prevent postoperative wound infections. To achieve the most cost-effective use of antimicrobial prophylaxis, consideration of the choice, delivery and regimen of antimicrobial agents is necessary.

Objectives

This review evaluates the relative efficacy of antimicrobial prophylaxis in patients undergoing colorectal surgery where there is a high risk of surgical wound infection (SWI).

Methods

Data sources

Literature searches of Medline, Embase and the Cochrane Controlled Trials Register were conducted to identify randomised controlled trials (RCTs) published between 1984 and 1995, which investigated antimicrobial prophylaxis in the prevention of postoperative wound infection in patients who had undergone colorectal surgery. Bibliographies of reviews and all identified trials were examined to locate additional studies. A sample of key journals was also handsearched. All languages were considered.

Validity assessment and data extraction

The identified studies were assessed for both relevance and validity by one reviewer and checked by another. Data extraction was carried out by one reviewer using an electronic data extraction form. This process was again checked by a second reviewer. For articles containing insufficient detail, authors were contacted for clarification. Of all the studies assessed, 147 RCTs, including a total of 23,049 patients, met the review inclusion criteria.

The principal outcome assessed in the review was the incidence of SWI. Where possible, abdominal wound infections were recorded separately from perineal wound infections. Data on other postoperative infections and adverse events were also collected.

Data synthesis

Studies were grouped according to the antibiotic used, route of administration, and number of doses administered (i.e. single versus multiple doses). Where appropriate, formal meta-analysis and investigation of heterogeneity among trials were conducted.

Results

The quality of the RCTs has improved over the last 12 years, though there are still many methodological problems, including inappropriate method of patient allocation, lack of blinding during outcome assessment, and insufficient sample size. The criteria for inclusion and exclusion were described in 87% of the included trials. The exclusion criteria most frequently used were allergy to study drugs, preoperative use of other antibiotics, impaired renal or liver function, children or very old patients, pregnancy or lactation, and certain types of colorectal operations.

More than 70 different antibiotic regimens were tested in 147 trials. The overall rate of SWI across all the included trials of antimicrobials prophylaxis (excluding four non-antibiotic groups) was 11.1% (n = 22,927).

The results of this review confirm that the use of antimicrobial prophylaxis is generally effective for the prevention of SWIs in colorectal surgery. Some antimicrobial regimens appear to be less effective than others in this indication. For example, monotherapy with either metronidazole, doxycycline or piperacillin are inadequate for prophylactic treatment in colorectal surgery.

The review found that a single dose or short-term use of an antimicrobial agent is as efficacious as

long-term, postoperative use. Pooled results from 17 trials that compared a single-dose regimen with a multiple-dose regimen, showed no significant difference in the rate of SWI (odds ratio = 1.17; 95% confidence interval [CI]: 0.89, 1.54). There is a lack of convincing evidence concerning the importance of a second-dose regimen when surgical procedures are longer than 2 hours.

There is no convincing evidence to suggest that the second- and third-generation cephalosporins are more efficacious than the first-generation cephalosporins in this indication (6% versus 6.4%; odds ratio = 0.93; 95% CI: 0.46, 1.86).

Establishing the efficacy of different routes of administration of antibiotic prophylaxis was complicated by the use of different antibiotics or use of extra antibiotics. No additional benefit was observed in six trials that compared parenteral alone, with parenteral plus topical use of antibiotic prophylaxis. Several trials, showing extra benefit of oral antibiotics, used inadequate parenteral antibiotics such as metronidazole alone, or piperacillin alone. Oral or topical application of antibiotics in addition to the parenteral administration of appropriate antibiotics seem to be of limited value in most cases.

In general, the estimates of efficacy of many of the different regimens included are similar and it is very difficult, if not impossible, to identify the best one. However, the Type-II error or lack of statistical power cannot be ruled out as a potential reason for statistically non-significant findings in many small trials.

A total of 74 of the 134 trials published in English reported adverse events following antibiotic prophylaxis in colorectal surgery. Skin rash, diarrhoea, and nausea were commonly mentioned adverse events that may be attributable to the use of some antibiotic treatments. No serious toxicity or adverse events were reported except in one trial that reported postoperative bleeding in some patients treated with latamoxef.

The costs associated with SWI are high in terms of both antibiotic treatment and prolonged hospitalisation with some studies reporting an additional 12 days in hospital as a result of SWI. Three trials that included cost data in comparisons of monotherapy and combination therapy showed that monotherapy was as effective as the combination regimens but less expensive. The overall cost data available from the RCTs suggest that drug acquisition costs need to be viewed in terms of their efficacy, as a reduction in infection rates is associated with a shorter hospital stay, the 'hotel' costs of which account for the highest proportion of overall cost during treatment.

Conclusions

The use of antimicrobial prophylaxis is efficacious in the prevention of SWI in colorectal surgery. With the exception of a few inadequate regimens, there is no significant difference in the rate of SWI between many regimens. The use of a multiple-dose regimen may be unnecessary for the prevention of SWI, as single-dose regimens have been demonstrated to be as efficacious as multiple dosing and in addition, may be associated with less toxicity, fewer adverse events, less risk of developing bacterial resistance and lower costs. Similarly, no convincing evidence supports the idea that the new-generation cephalosporins are more efficacious than first-generation cephalosporins in preventing SWI in colorectal surgery.

Implications for policy

Two principles are important to follow when selecting an antimicrobial prophylactic regimen in colorectal surgery:

- antibiotics or antibiotic combinations should be active against both aerobic and anaerobic bacteria;
- the administration of antibiotics should be timed to ensure that the tissue concentration of antibiotics around the wound area is sufficiently high when bacterial contamination occurs.

Universal acceptance and use of a regimen should be avoided in order to minimise the development of antibiotic-resistant bacteria. Based on the research evidence, guidelines should be developed locally in order to achieve a more cost-effective use of antimicrobial prophylaxis in colorectal surgery.

Recommendations for research

Further studies of efficacy may be of little value and would require large numbers of patients in order to demonstrate a statistically significant difference. Future research should focus on the understanding of the practical use of antimicrobial prophylaxis in colorectal surgery in the UK and the cost-effectiveness of different regimens of antibiotic prophylaxis.

Chapter 1
Background

Wound infections are the most frequent nosocomial infections among surgical patients and are related to an increase in morbidity and mortality, a prolongation of hospital stay and an increase in the cost of medical care.[1,2]

Exogenous or endogenous contamination of the surgical wound by pathogenic organisms is one of the most important factors related to the risk of surgical wound infection (SWI), though it does not necessarily mean that a SWI will be inevitable.[3] According to the risk of bacterial contamination, surgical wounds have conventionally been classified as clean, clean-contaminated, contaminated, or dirty.[4] Colorectal surgery is associated with a high risk of infection due to endogenous contamination by bacteria in the contents of the large bowel. Postoperative wound infections have been shown to occur in about 40% of patients after colorectal surgery in whom antibiotic prophylaxis was not used.[5]

A review by Baum and co-workers[6] compared the wound infection and mortality rates of patients given antimicrobial prophylaxis for colorectal surgery with those of no-antibiotic controls. By pooling results from 26 randomised controlled trials (RCTs), it was found that the wound infection rate was significantly higher in the no-antibiotic control group with 36% of patients developing infections compared with 22% in the antibiotic prophylaxis groups. They also found that mortality was significantly reduced by using antibiotic prophylaxis (11.2% versus 4.5%, $p < 0.01$). It was concluded that the no-antibiotic control should not be used in further trials of colorectal surgery.[6]

It is now generally accepted that antimicrobial prophylaxis is one of many important measures that should be taken to prevent postoperative wound infections in contaminated or clean-contaminated surgery. Many different antimicrobial agents are available with different pharmacokinetic and pharmacodynamic features, spectra of activity, and toxicities. To achieve the most cost-effective use of antimicrobial prophylaxis, consideration of the choice, delivery and regimen of antimicrobial agents is necessary.[1,7,8] However, it is often argued that questions regarding the choice of antibiotics, and the timing and duration of treatment have yet to be answered satisfactorily.[9] Other important issues include the ease of administration and cost-effectiveness. The occurrence of antibiotic-resistant bacteria should also be considered when assessing the appropriate use of antimicrobial prophylaxis.

The main objective of this review, which was commissioned by the NHS HTA programme, is to evaluate the relative effectiveness of antimicrobial prophylaxis in patients undergoing colorectal surgery. Cost-effectiveness of antimicrobial prophylaxis is also summarised from the RCTs that examined this aspect of treatment. (It should be noted that the following agents are not available in the UK: cefmatazole, cefonicid, cefoperazone, cefotetan, cefotiam, cephalothin, chlorchinaldole, mezlocillin, latamoxef, ornidazole, sulbactam, and thymostimulin.)

Chapter 2
Methods

Inclusion criteria

This review includes RCTs, published between 1984 and 1995, that evaluate antimicrobial prophylaxis in the prevention of postoperative wound infection in patients who have undergone colorectal surgery. The year 1984 was chosen because activity in this field at this time included the introduction of many new antibiotics, changes in the clinical use of antibiotic prophylaxis, improvement in surgical procedures, possible emergence of antibiotic-resistant micro-organisms, and the large volume of literature on this topic.

Literature search strategy

A search of Medline from 1984, Embase/Embase Alert (1983–present) and the Cochrane Controlled Trials Register was conducted with the assistance of the NHS Centre for Reviews and Dissemination information services (appendix 1). The titles and abstracts were assessed and copies of relevant studies collected. The references of retrieved articles were checked to locate other relevant trials. Studies in all languages were considered for the evaluation, surgical wound outcome and study quality. For reasons of difficulty and cost of translation, studies published in non-English languages were not used in the discussion of adverse events, bacteriological test, and cost issues.

A sample of several key journals (*Acta Chirurgica Scandinavica, British Journal of Surgery, Journal of Antimicrobial Chemotherapy, Archives of Surgery, Annals of Surgery*) were handsearched in addition to the electronic database searches. No additional trials were located during handsearching.

Validity assessment

The relevance and validity of each study were assessed and data were extracted by one reviewer and checked by another. Data from individual studies were extracted using a pre-defined form (appendix 2) and managed using an Idealist database. When there was insufficient data on outcome of SWI in the article, authors were contacted for clarification (three authors were contacted, two replied). Indicators of study quality included method of randomisation, blind outcome assessment, written definition of SWI, withdrawals, and *a priori* calculation of sample size. True randomisation is defined as concealed patient allocation until the point of allocation.[10] According to examples listed in the *Cochrane Collaboration Handbook,*[10] the following methods were considered to be true randomisation:

- centralised or pharmacy-controlled randomisation
- pre-numbered or coded identical containers which are administered serially to participants
- on-site computer system combined with group assignments in a locked unreadable computer file that can be accessed only after entering characteristics of an enrolled subjects
- sequentially numbered, sealed, opaque envelopes.

Data extraction

The wound itself has the greatest risk of infection from endogenous bacterial contamination during surgical procedures.[11] In this review, therefore, the rate of SWI is used as the principal outcome measure to assess the relative effectiveness of antimicrobial prophylaxis in colorectal surgery. The definition and diagnosis of SWIs often vary in published studies. If possible, only abdominal wound infections are included because of their reliability. However, in some trials it was not clear whether perineal wound infections or other infections related to the surgical procedures were included. In these cases, the reported results are presented.

Data on other postoperative infections (systemic infections) were also collected from each trial. Remote infection (such as respiratory tract infections, urinary tract infections) may be important but the definition and diagnosis is more problematic. Anastomotic leakage is not considered in this review because it is mainly associated with the surgical technique used and complex patient characteristics. Other outcomes that are important include prolonged hospitalisation and increased cost of medical care. A data extraction sheet is detailed in appendix 2.

Mortality data were recorded where available, as mortality is a reliable and sensitive outcome

measure to compare the results of antibiotic prophylaxis with no-antibiotic controls in colorectal surgery.[6] However, when different regimens of antibiotic prophylaxis are compared, the mortality rate is too low for comparing relative efficacy.[12]

Data synthesis

The studies were grouped according to the antibiotic used. Where appropriate (e.g. when the same regimen of antibiotic prophylaxis was assessed in several trials), formal meta-analysis and investigation of heterogeneity among trials was conducted using MetaView in Cochrane Review Manager Software (RevMan, version 3.0 for Windows). The Mantel-Haenszel method was chosen for calculating overall odds ratios and the chi-squared method for testing heterogeneity between individual studies.

It is often inappropriate to pool results from trials quantitatively. For example, trials may compare an agent with other regimens in many different ways, such as alone or in combination with other agents. Therefore, results from individual studies are described in narrative form. To facilitate discussion, figures are used to present the results of SWI for antimicrobial prophylaxis regimens that have been assessed in four or more trials.

Chapter 3
Results

A total of 147 RCTs met the inclusion criteria for this review. Details of each trial, including the quality assessment, type of colorectal surgery, antibiotic prophylaxis used, clinical results, and conclusions are shown in appendix 3.[13–156] Among these RCTs, 134 were published in English and 13 in other languages. The trials were conducted in 25 different countries, mainly in Europe and North America. A quarter of the trials were carried out in the UK, 12% in the USA, 10% in Germany, 10% in Denmark, 6% in Italy, Sweden and Australia. The review included 24 trials of patients who underwent abdominal surgery, and from which the results for colorectal surgery could be separated from other procedures.

The overall rate of SWI with various regimens of prophylactic antimicrobial agents in colorectal surgery was 11.1% (2540/22,927) after excluding the four no-antibiotic arms. The rate of SWI was 10.6% in the 120 trials that included patients undergoing elective colorectal surgery only, and 13.4% in the 27 trials that included both elective and emergency colorectal surgery.

Quality of the studies

Table 1 summarises the results of the quality assessment of RCTs. The proportion of the trials that used truly concealed randomisation was 37% and the proportion of trials that assessed outcome blindly was 40%. The majority of the trials did not calculate the required sample size (84%) and many included fewer than 100 patients (39%). The withdrawals were not reported in 22% of the trials and follow-up period was not clear for 33% of the trials. The proportion of the trials that did not give a written definition of SWI was 21%.

When the studies were grouped according to the year of publication, it can be seen that the quality of trials has improved over the last 12 years (*Table 1*). The proportion of trials in which the method of randomisation was truly concealed

TABLE 1 *Summary of quality assessment of RCTs of antibiotic prophylaxis in colorectal surgery (1984–95)*

Year of publication	1984–87	1988–91	1992–95	All trials
True randomisation	30%	32.8%	65.2%	36.7%
Blinding assessment	44.4%	34.4%	43.5%	40.1%
A priori calculation of sample size	6.3%	19.7%	34.8%	16.3%
Definition of SWI	76.2%	80.3%	82.6%	78.9%
Follow-up, 28 days or longer	44.4%	62.3%	73.9%	56.5%
Withdrawal rate				
< 10%	28.6%	45.9%	34.8%	36.7%
Unsure	38.1%	13.1%	4.3%	22.4%
Sample size of the trials				
< 100	55.6%	34.4%	4.3%	38.8%
100–299	42.9%	52.4%	56.5%	49.0%
> 300	1.6%	13.1%	39.1%	12.2%
No. of centres in the trials				
Single centre	77.8%	70.5%	11.7%	64.4%
2–4 centres	11.1%	14.8%	15.0%	13.3%
5 centres or more	11.1%	14.8%	30.4%	15.7%
Total number of trials	**63**	**61**	**23**	**147**

was 30%, 33%, and 65%, respectively, for the three time periods, 1984–87, 1988–91, and 1992–95. Trials published between 1992 and 1995 were also of better quality in terms of *a priori* calculation of sample size, definition of SWI, appropriate follow-up period, and the reporting of withdrawals.

More multicentre studies have also been published more recently and, in addition, patient numbers have risen; the sample size was smaller than 100 in more than 50% of the trials published between 1984 and 1987 compared with only 4.3% of trials published since 1992.

Antibiotic prophylaxis versus no-antibiotic controls

The review identified four trials published since 1984 that compared patients receiving antibiotic prophylaxis for colorectal surgery with a control group not given antibiotics (*Table 2*).[53,56,137,150] The antibiotics used prophylactically in these four trials were gentamicin plus metronidazole,[53] metronidazole alone or metronidazole plus ampicillin,[56] mezlocillin plus oxacillin,[137] and cefoxitin.[150] The results from the individual studies showed consistently that the SWI rate was much lower in the antibiotic groups than that in the control groups (12.9% versus 40.2%; pooled odds ratio = 0.24; 95% CI: 0.13, 0.43).

Different antibiotics and surgical wound infections

Few regimens were directly compared, each comparison being evaluated by a limited number of trials, in which the sample size was often too small to have sufficient statistical power (appendix 4). Below, the results of SWI rates are discussed separately for each antibiotic agent that has been assessed in at least four trials.

Ampicillin

Ampicillin is a broad-spectrum penicillin and is active against certain Gram-positive and Gram-negative organisms. It may be inactivated by penicillinases produced by bacteria such as *Staphylococcus aureus* and *Escherichia coli*. When it is administered orally, less than half is absorbed.

Five trials compared ampicillin plus metronidazole with other regimens of prophylactic antibiotics in colorectal surgery (*Table 3*).[56,69,90,133,134] Two trials showed that ampicillin plus metronidazole was more effective than metronidazole alone in the prevention of SWI.[56,133] In the trial by Jensen and co-workers,[69] it was found that ampicillin plus metronidazole was associated with a significantly higher SWI rate than cefuroxime plus metronidazole in 39 patients who underwent emergency colorectal surgery, but there was no difference in 272 patients who underwent elective colorectal surgery. Two other trials did not find a difference between ampicillin plus metronidazole and ceftriaxone alone or cefoxitin alone.[90,134]

No statistically significant differences were found when ampicillin plus sulbactam was compared with gentamicin plus metronidazole[15] and cefoxitin.[41] The use of topical ampicillin in addition to oral antibiotics or in addition to intravenous cefotaxime was not found to have an additional benefit.[128,129]

Aztreonam

Aztreonam is a monocyclic beta-lactam antibiotic with an antibacterial spectrum limited to Gram-negative aerobic bacteria. Therefore, it is often combined with clindamycin (active against Gram-positive and anaerobic bacteria) in trials of antibiotic prophylaxis in colorectal surgery.

TABLE 2 *Antibiotic prophylaxis versus no-antibiotic control*

Study [reference]	Prophylaxis n/N	Control n/N	Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
Gomez-Alonso [53]	6/35	13/31		0.29 [0.09, 0.89]
Gottrup [56]	11/94	13/41		0.29 [0.11, 0.71]
Schiessel [137]	2/29	12/31		0.12 [0.02, 0.59]
Utley [150]	3/13	11/19		0.13 [0.04, 1.06]
Total (95% CI)	22/171	49/122		0.24 [0.13, 0.43]

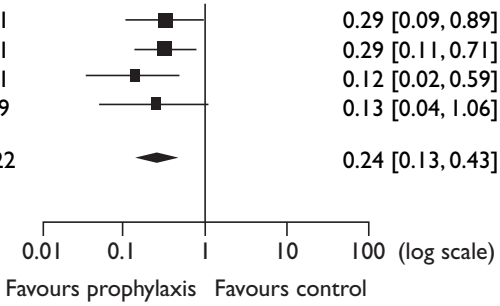
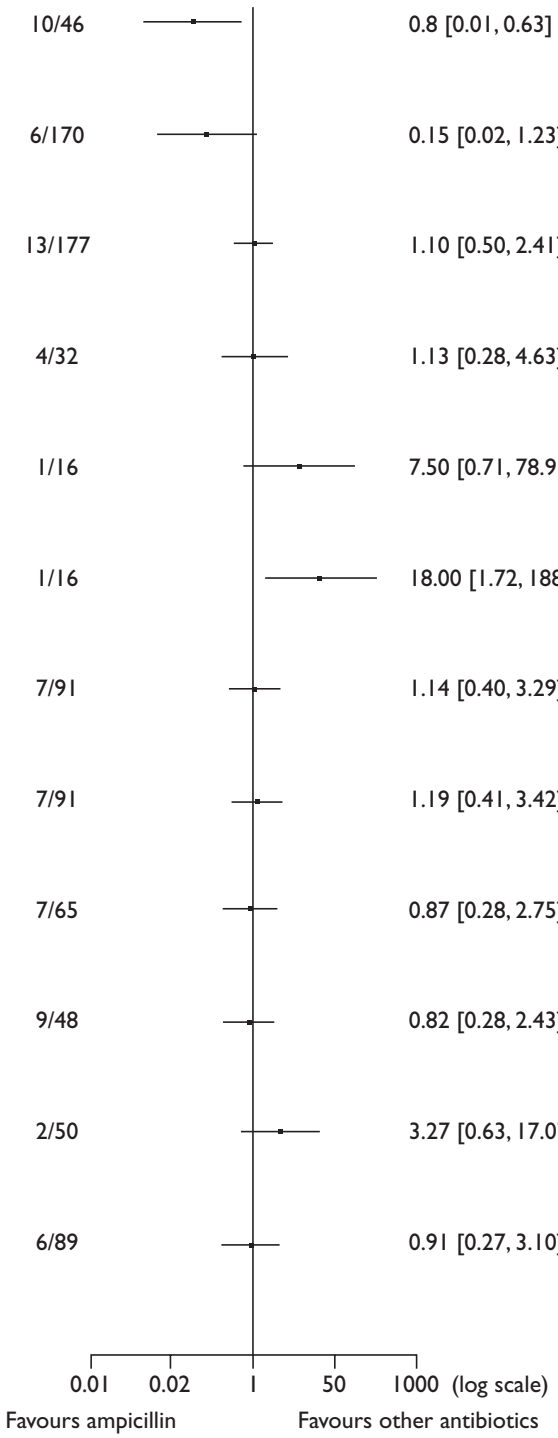


TABLE 3 *Ampicillin versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Ampicillin n/N	Other antibiotics n/N		
(Ampicillin + metronidazole) × 10 vs. metronidazole × 10 Gottrup [56]	1/48	10/46		0.8 [0.01, 0.63]
(Ampicillin + metronidazole) × 1 vs. (metronidazole × 1) Roland [133]	1/188	6/170		0.15 [0.02, 1.23]
(Ampicillin × 12) + (metronidazole × 9) vs. (cefoxitin × 3) Rorbaek-Madsen [134]	14/175	13/177		1.10 [0.50, 2.41]
(Ampicillin + metronidazole) × 1 vs. (ceftriaxone × 1) Luke [90]	5/36	4/32		1.13 [0.28, 4.63]
(Ampicillin + metronidazole) × 3 vs. (cefuroxime + metronidazole) × 1 Jensen [69]	4/12	1/16		7.50 [0.71, 78.91]
(Ampicillin + metronidazole) × 1 vs. (cefuroxime + metronidazole) × 1 Jensen [69]	6/11	1/16		18.00 [1.72, 188.09]
(Ampicillin + metronidazole) × 3 vs. (cefuroxime + metronidazole) × 1 Jensen [69]*	8/92	7/91		1.14 [0.40, 3.29]
(Ampicillin + metronidazole) × 1 vs. (cefuroxime + metronidazole) × 1 Jensen [69]*	8/89	7/91		1.19 [0.41, 3.42]
(Ampicillin + sulbactam) × 3 vs. (gentamicin + metronidazole) × 3 AhChong [15]	6/63	7/65		0.87 [0.28, 2.75]
(Ampicillin + sulbactam) × 4 vs. (cefoxitin × 4) De La Hunt [41]	7/44	9/48		0.82 [0.28, 2.43]
(Ampicillin + neomycin + erythromycin) × 3 vs. (cefotaxime × 3) Raahave [128]	6/50	2/50		3.27 [0.63, 17.07]
(Ampicillin × 1) + (cefotaxime × 3) vs. (cefotaxime × 3) Raahave [129]	5/81	6/89		0.91 [0.27, 3.10]



*Estimated number of SWI

Aztreonam plus metronidazole was a less efficacious regimen than cefotaxime plus metronidazole (32.4% versus 12.9%) for the prevention of SWIs in colorectal surgery.[106] The authors claimed that this was because aztreonam plus metronidazole provided good Gram-negative and anaerobic cover but little activity against Gram-positive bacteria.

Four trials compared aztreonam plus clindamycin with other antibiotics (*Table 4*).[25,50,109,132] Two very small trials compared aztreonam plus clindamycin with cefotetan[25] or ceftriaxone[50] and no significant differences were found. By pooling the results from two trials,[109,132] it was found that the rate of SWI in the aztreonam plus clindamycin group was significantly lower than that of the gentamicin plus clindamycin group (7.2% versus 13.6%, overall odds ratio = 0.51; 95% CI: 0.3, 0.87).

Clindamycin

Clindamycin is active against Gram-positive cocci, including penicillin-resistant staphylococci and also against many anaerobes, particularly *Bacteroides fragilis*, and is often combined with other antibiotics such as aztreonam or gentamicin. However, clindamycin is associated with an increased risk of pseudomembranous colitis which may be fatal. Clindamycin plus gentamicin was less effective than clindamycin plus aztreonam.[109,132] The difference was not statistically significant when clindamycin plus gentamicin were compared with cefoxitin, gentamicin plus lincomycin, or gentamicin plus metronidazole.[32,89]

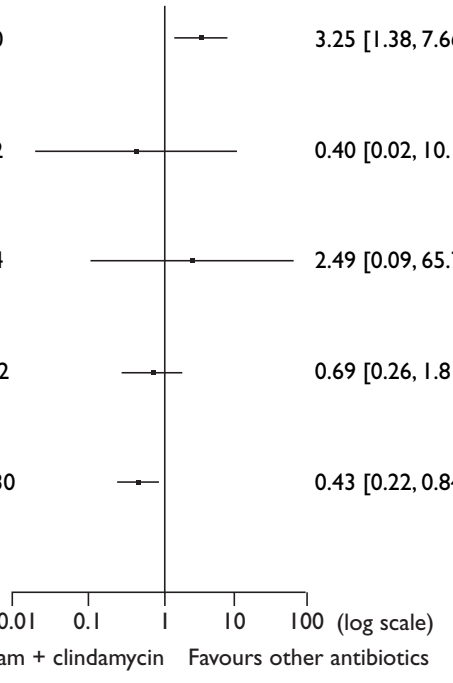
Cefotaxime

Cefotaxime is a 'third-generation' cephalosporin with great activity against Gram-negative bacteria.

Most trials showed no significant difference in SWI rate when cefotaxime alone was compared with other regimens *(Table 5)*, such as ticarcillin plus clavulanic acid[72] (Timentin®, SmithKline Beecham Pharmaceuticals, Welwyn, UK), cefoperazone,[70] penicillin plus streptomycin,[84] mezlocillin,[98] cefoxitin,[139] and oral neomycin plus erythromycin plus topical ampicillin.[128] Jones and co-workers[71] found that cefotaxime as a single dose (second dose if operation continued over 2 hours) was less effective than four doses of cephazolin or cefoxitin when all patients received intraluminal neomycin and erythromycin (14% versus 3%, $p = 0.057$).

TABLE 4 *Aztreonam versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Aztreonam + clindamycin n/N	Other antibiotics n/N		
(Aztreonam + metronidazole) × 3 vs. (cefotaxime + metronidazole) × 3 Morris [106]	23/71	9/70		3.25 [1.38, 7.66]
(Aztreonam + clindamycin) × 3 vs. (cefotetan × 3) Bellantone [25]	0/26	1/32		0.40 [0.02, 10.14]
(Aztreonam + clindamycin) × 5 vs. (ceftriaxone × 1) Franceshini [50]	1/18	0/14		2.49 [0.09, 65.76]
(Aztreonam + clindamycin) × 3 vs. (gentamicin + clindamycin) × 3 Rodolico [132]	8/66	12/72		0.69 [0.26, 1.81]
(Aztreonam + clindamycin) × 3 vs. gentamicin + clindamycin) × 3 Mozzillo [109]	13/224	29/230		0.43 [0.22, 0.84]



Five trials compared cefotaxime plus metronidazole with other regimens *(Table 5)*. It was found that a regimen of three doses of cefotaxime plus metronidazole was significantly more effective than aztreonam plus metronidazole.[106] Other trials did not find significant differences between cefotaxime plus metronidazole and other regimens such as co-amoxiclav,[82] cefoxitin,[81] ceftriaxone plus ornidazole,[49] and cefuroxime plus metronidazole.[135]

When cefotaxime plus metronidazole in a single dose was compared with multiple doses, no significant difference was found.[81,130] Hakansson and coworkers[59] showed that a single dose of cefotaxime plus metronidazole was significantly more effective than three doses of cefotaxime alone (6.6% versus 15.7%, $p = 0.0006$). In other trials, however, cefotaxime alone was as efficacious as cefotaxime plus metronidazole,[47] or plus topical ampicillin.[129]

Cefotetan

Cefotetan is a long-acting, broad-spectrum, third-generation cephalosporin.

Seven trials compared cefotetan alone with other regimens (*Table 6*).[19,25,64,68,107,117,118,140,149] No significant difference was observed when cefotetan alone was compared with cefoxitin,[68,117] gentamicin plus metronidazole,[149] co-amoxiclav,[19] cefuroxime plus metronidazole,[140] piperacillin,[64] or clindamycin plus aztreonam.[25] It was found that cefotetan alone was as effective as cefotetan plus metronidazole,[107] and cefotetan plus thymostimulin.[118] Greig and co-workers[57] found no extra benefit when cefotetan was used as a topical application in addition to intravenous gentamicin plus metronidazole.

Cefoxitin

Cefoxitin is a second-generation cephamycin that is active against bowel flora including *B. fragilis*.

There was no significant difference in SWI rate when cefoxitin alone was compared with other antibiotic regimens in 15 trials *(Table 7)*. Cefoxitin alone was at least as efficacious as cefoxitin plus oral neomycin (or tinidazole) and erythromycin.[37,120,141]

In addition to oral neomycin and erythromycin, three doses of cefoxitin, (2 g) seemed to be less efficacious compared with a single dose of cefmetazole (2 g) in the prevention of postoperative wound infection.[45,126] Cefoxitin plus oral neomycin and erythromycin was more efficacious than oral neomycin and erythromycin alone[138] and was of similar efficacy as oral neomycin and erythromycin plus cefonicid[46] or plus cephazolin.[71] Single-dose ceftriaxone appeared to be as efficacious as three doses of cefoxitin with or without metronidazole.[110]

Ceftriaxone

Ceftriaxone is a third-generation cephalosporin with a longer half-life than other cephalosporins.

The difference in the SWI rate was not significant when ceftriaxone alone was compared with aztreonam plus clindamycin,[50] ampicillin plus metronidazole,[90] cephazolin plus metronidazole,[91] cefoxitin,[110] or cefotiam plus gentamicin and metronidazole[155] (*Table 8*). Matikainen and Hiltunen[92] found that ceftriaxone plus tinidazole was more efficacious than netilmicin plus tinidazole. Ceftriaxone plus ornidazole was as efficacious as amikacin plus metronidazole.[147] Ceftriaxone plus metronidazole was as efficacious as ceftazidime plus metronidazole,[51] cefamandole plus metronidazole,[62] and co-amoxiclav,[113] and more efficacious than gentamicin plus metronidazole.[30] Two trials compared ceftriaxone plus metronidazole with oral neomycin plus erythromycin. In the trial by Weaver and coworkers,[152] ceftriaxone plus metronidazole was significantly more efficacious than oral neomycin plus erythro-mycin (9.7% versus 41.4%, $p = 0.005$). In the trial by Kling and Dahlgren[80] there were no abdominal wound infections and the rate of perineal wound infection was not significantly different between the two groups.

Cefuroxime

Cefuroxime is a second-generation cephalosporin, which are less susceptible than the earlier cephalosporins to inactivation by penicillinases.

In the RCTs reported in this review, cefuroxime was almost always combined with metronidazole (*Table 9*). Cefuroxime plus metronidazole was more efficacious than metronidazole alone,[35,39,63,101] piperacillin alone,[131] and co-amoxiclav.[116] Three trials compared cefuroxime plus metronidazole with mezlocillin alone.[33,44,143] A statistically significant difference was found in only one of these trials.[33] When the results of these three trials were pooled, the rate of SWI in the cefuroxime plus metronidazole group was significantly lower than that in the mezlocillin group (odds ratio = 0.55; 95% CI: 0.32, 0.93).

The results with cefuroxime plus metronidazole were not significantly different from those with ampicillin plus metronidazole,[69] cefoxitin,[38] netilmicin plus metronidazole,[63] imipenem,[75] latamoxef,[77] imipenem plus cilastatin,[115] cefotaxime plus metronidazole,[135] or cefotetan.[140] No significant difference was found in a small trial that compared a single dose of cefuroxime plus metronidazole with three

TABLE 5 *Cefotaxime versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Cefotaxime n/N	Other antibiotics n/N		
(Cefotaxime × 3) vs. (neomycin + erythromycin) × 3 + (ampicillin × 1) Raahave [128]	2/50	6/50		0.31 [0.06, 1.59]
(Cefotaxime × 1) vs. (cefoperazone × 1) Jones [70]	1/24	2/23		0.46 [0.04, 5.41]
(Cefotaxime × 1) vs. (mezlocillin × 1) Mendel [98]	3/52	2/48		1.41 [0.23, 8.81]
(Cefotaxime × 1) vs. (cefoxitin × 5) Shatney [139]	7/36	3/34		2.49 [0.59, 10.57]
(Cefotaxime × 1) vs. (cephazolin or cefoxitin) × 4 Jones [71]	4/29	2/71		5.52 [0.95, 32.02]
(Cefotaxime × 4) vs. (ticarcillin/clavulanic acid × 1) Jones [72]	1/8	0/11		4.60 [0.16, 128.55]
(Cefotaxime + metronidazole) × 3 vs. (aztreonam + metronidazole) × 3 Morris [106]	9/70	23/71		0.31 [0.13, 0.73]
(Cefotaxime × 4) + (metronidazole × 3) vs. (ceftriaxone + ornidazole) × 1 Fingerhut [49]	4/102	6/122		0.79 [0.22, 2.88]
(Cefotaxime + metronidazole) × 3 vs. (co-amoxiclav × 3) Kwok [82]	8/88	7/76		0.99 [0.34, 2.86]
(Cefotaxime + metronidazole) × 1 vs. (cefuroxime + metronidazole) × 3 Rowe-Jones [135]	33/454	32/453		1.03 [0.62, 1.71]
(Cefotaxime + metronidazole) × 1 vs. cefoxitin × 1 Kow [81]	7/84	10/73		0.57 [0.21, 1.59]
(Cefotaxime × 3) + (metronidazole × 1) vs. (cefoxitin × 3) Kow [81]	9/81	8/81		1.14 [0.42, 3.12]
(Cefotaxime × 3) + (metronidazole × 1) × 3 vs. (cefotaxime + metronidazole) × 1 Kow [81]	9/81	7/84		1.37 [0.49, 3.83]
[All: Metronidazole x 6] (Cefotaxime × 3) vs. (cefotaxime × 1) Rangabashyam [130]	1/17	2/17		0.47 [0.04, 5.72]
(Cefotaxime × 3) vs. (cefotaxime +metronidazole) × 1 Hakansson [59]	44/280	19/287		2.63 [1.49, 4.63]
(Cefotaxime × 3) vs. (cefotaxime × 3) + ampicillin Raahave [129]	6/89	5/81		1.10 [0.32, 3.75]
(Cefotaxime × 4) vs. (cefotaxime × 4) + metronidazole Favre [47]	4/74	10/143		0.76 [0.23, 2.51]
(Cefotaxime × 3) vs. (penicillin × 19) + (streptomycin × 9) Lauridsen [84]	0/52	1/48		0.30 [0.01, 7.58]
(Cefotaxime + metronidazole) × 10 + cefotaxime vs. (cefotaxime + metronidazole) × 10 Moesgaard [104]	2/21	4/19		0.39 [0.06, 2.45]

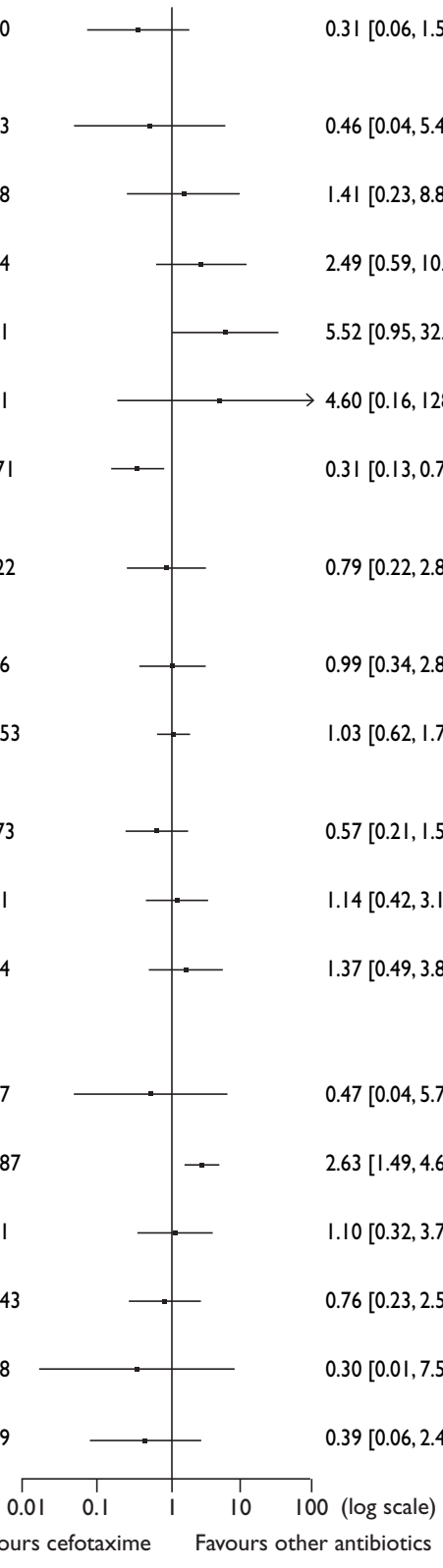
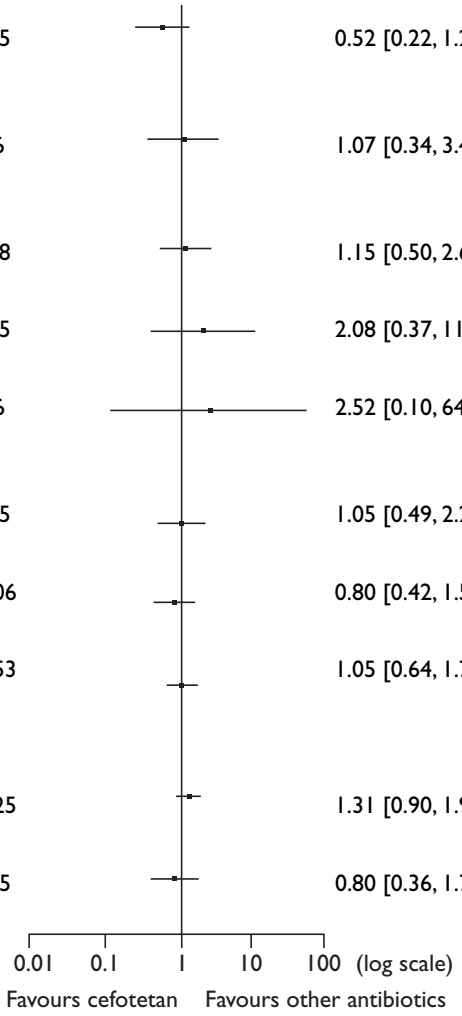


TABLE 6 *Cefotetan versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Cefotetan n/N	Other antibiotics n/N		
(Cefotetan × 2) vs. (gentamicin × 15) + metronidazole × 1 Tudor [149]	10/75	17/75		0.52 [0.22, 1.24]
(Cefotetan × 2) vs. (cefuroxime + metronidazole) × 3 Skipper [140]	10/68	5/36		1.07 [0.34, 3.41]
(Cefotetan × 1) vs. (piperacillin × 3) Hershman [64]	14/75	13/78		1.15 [0.50, 2.64]
(Cefotetan × 1) vs. (co-amoxiclav × 1) Arnaud [19]	4/103	2/105		2.08 [0.37, 11.62]
(Cefotetan × 3) vs. (clindamycin + aztreonam) × 3 Bellantone [25]	1/32	0/26		2.52 [0.10, 64.58]
(Cefotetan × 1) vs. (cefoxitin × 5) Jagelman [68]	25/164	11/75		1.05 [0.49, 2.26]
(Cefotetan × 1) vs. (cefoxitin × 4) Periti [117]	18/197	23/206		0.80 [0.42, 1.53]
(Cefotetan × 2) vs. (cefotetan × 2) + (metronidazole × 3) Morton [107]	39/278	34/253		1.05 [0.64, 1.72]
(Cefotetan × 1) vs. (cefotetan × 1) + (thymostimulin × 7) Periti [118]	72/434	56/425		1.31 [0.90, 1.91]
[All: Gentamicin + metronidazole] Cefotetan in saline lavage vs. saline only Greig [57]	15/64	18/65		0.80 [0.36, 1.77]



doses of the same antibiotics (10.5% versus 3.4%, $p = 0.554$).[14] Cefuroxime alone appeared to be less efficacious than cefuroxime plus metronidazole in a small trial but the difference was not statistically significant (9.4% versus 0%, $p = 0.24$).[38]

Co-amoxiclav

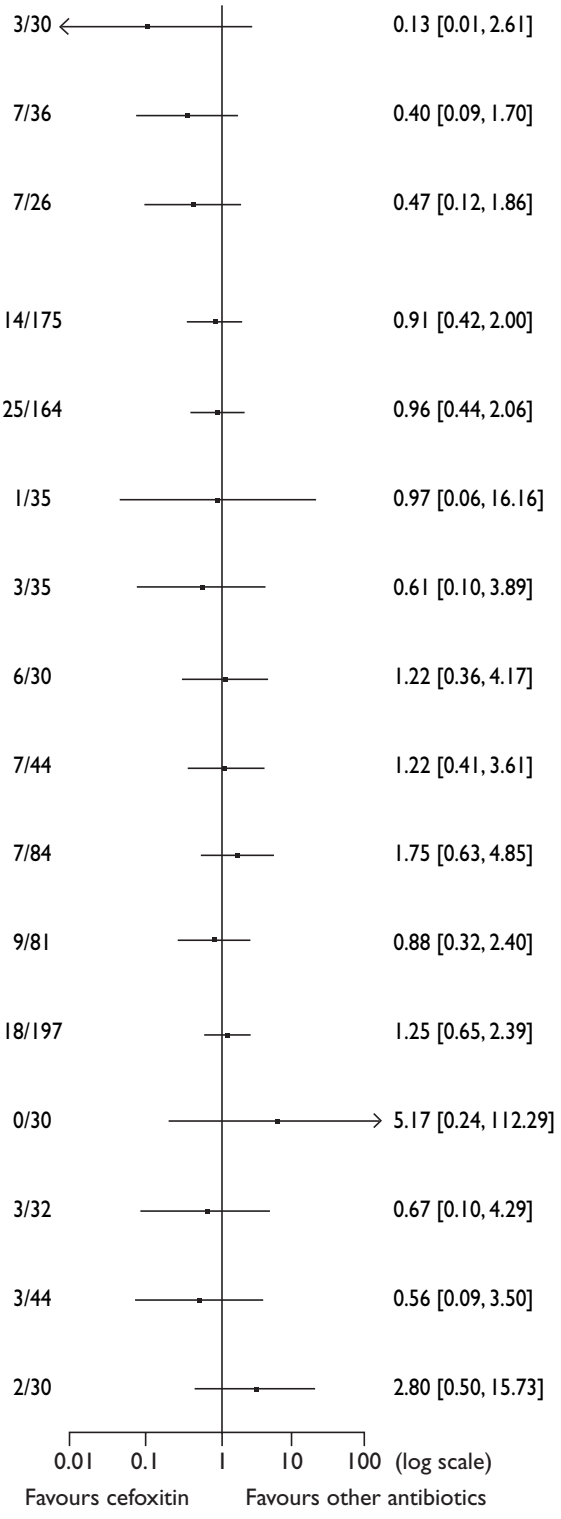
Co-amoxiclav (Augmentin®, SmithKline Beecham Pharmaceuticals, Welwyn, UK), is a combination of amoxycillin and clavulanic acid. Amoxycillin has a similar antibacterial spectrum to ampicillin but is better absorbed than ampicillin when given orally. Clavulanic acid is used to inactivate penicillinases. Therefore, it is believed that co-amoxiclav is active against penicillinase-producing bacteria that are resistant to amoxycillin.

Single or multiple doses of co-amoxiclav have been compared with other regimens of prophylactic antibiotics in eight trials of colorectal surgery *(Table 10)*. In one trial it was found that co-amoxiclav was significantly less efficacious than cefuroxime plus metronidazole ($p = 0.045$).[116] However, the significant difference observed in this trial was associated with a higher rate of re-operation for postoperative complications such as anastomotic leak or haematoma.

Seven trials did not find differences in the SWI rate between co-amoxiclav arms and other antibiotics such as cephradine plus metronidazole,[145] gentamicin plus metronidazole,[61] ceftriaxone plus metronidazole,[113] cefotaxime plus metronidazole,[82]

TABLE 7 *Cefoxitin versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Cefoxitin n/N	Other antibiotics n/N		
(Cefoxitin × 10) vs. (cephalothin × 18) Antonelli [17]	0/30	3/30		0.13 [0.01, 2.61]
(Cefoxitin × 5) vs. (cefotaxime × 1) Shatney [139]	3/34	7/36		0.40 [0.09, 1.70]
(Cefoxitin × 3) vs. (metronidazole + tobramycin) × 3 + (penicillin × 5) Perrott [119]	4/27	7/26		0.47 [0.12, 1.86]
(Cefoxitin × 3) vs. (ampicillin × 12) + (metronidazole × 9) Rorbaek-Madsen [134]	13/177	14/175		0.91 [0.42, 2.00]
(Cefoxitin × 5) vs. (cefotetan × 1) Jagelman [68]	11/75	25/164		0.96 [0.44, 2.06]
(Cefoxitin × 4) vs. (cephazolin × 4) Jones [71]	1/36	1/35		0.97 [0.06, 16.16]
(Cefoxitin × 2) vs. (gentamicin + clindamycin) × 3 Mosimann [108]	2/37	3/35		0.61 [0.10, 3.89]
(Cefoxitin × 3) vs. (gentamicin + clindamycin) × 2 Cainzos [32]	7/30	6/30		1.22 [0.36, 4.17]
(Cefoxitin × 4) vs. (ampicillin + sulbactam) × 4 De La Hunt [41]	9/48	7/44		1.22 [0.41, 3.61]
(Cefoxitin × 1) vs. (cefotaxime + metronidazole) × 1 Kow [81]	10/73	7/84		1.75 [0.63, 4.85]
(Cefoxitin × 3) vs. (cefotaxime × 3) + (metronidazole × 1) Kow [81]	8/81	9/81		0.88 [0.32, 2.40]
(Cefoxitin × 4) vs. (cefotetan × 1) Periti [117]	23/206	18/197		1.25 [0.65, 2.39]
(Cefoxitin × 1) vs. (cefuroxime + metronidazole) × 1 Corman [38]	2/31	0/30		5.17 [0.24, 112.29]
(Cefoxitin × 1) vs. (cefuroxime × 1) Corman [38]	2/31	3/32		0.67 [0.10, 4.29]
(Cefoxitin × 3) vs. (neomycin + erythromycin) × 3 Stellato [141]	2/51	3/44		0.56 [0.09, 3.50]
(Cefoxitin × 1) vs. (piperacillin × 1) Armengaud [18]	5/30	2/30		2.80 [0.50, 15.73]



continued

TABLE 7 contd *Cefoxitin versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Cefoxitin n/N	Other antibiotics n/N		
(Cefoxitin × 3) vs. (ampicillin + sulbactam) × 3 Menzel [99]	12/126	10/142		1.39 [0.58, 3.34]
(Cefoxitin × 3) vs. (piperacillin + metronidazole) × 3 Menzel [99]	12/126	12/137		1.10 [0.47, 2.54]
(Cefoxitin × 5) vs. (cefoxitin × 5) + (neomycin + erythromycin) × 3 Coppa [37]	15/141	9/169		2.12 [0.90, 5.00]
(Cefoxitin × 3) vs. (cefoxitin × 3) + (tinidazole × 1) + (neomycin × 3) Peruzzo [120]	0/39	4/41		0.11 [0.01, 2.03]
(Cefoxitin × 3) vs. (cefoxitin + neomycin + erythromycin) × 3 Stellato [141]	2/51	3/51		0.65 [0.10, 4.08]
(Cefoxitin × 3) vs. (ceftriaxone × 1) Nel [110]	3/45	6/45		0.46 [0.11, 1.98]
[All: (Neomycin + erythromycin)] (Cefoxitin × 3) vs. no additional antibiotics Stellato [141]	3/51	3/44		0.85 [0.16, 4.46]
[All: (Neomycin + erythromycin)] (Cefoxitin × 3) vs. no additional antibiotics Schoetz [138]	5/101	14/96		0.31 [0.11, 0.88]
[All: (Neomycin + erythromycin)] (Cefoxitin × 3) vs. (cefmetazole × 3) Plouffe [126]	2/12	0/28		13.57 [0.60, 306.66]
[All: (Neomycin + erythromycin) × 3] (Cefoxitin × 3) vs. (cefmetazole × 1) DiPiro [45]	4/32	1/63		8.86 [0.95, 82.89]
[All: (Neomycin + erythromycin) × 3] (Cefoxitin × 5) vs. (cefonicid × 1) Fabian [46]	1/17	2/23		0.66 [0.05, 7.89]
[All: (Neomycin + erythromycin) × 3] (Cefoxitin × 5) vs. (cephazolin × 4) Jones [71]	1/36	1/35		0.97 [0.06, 16.16]

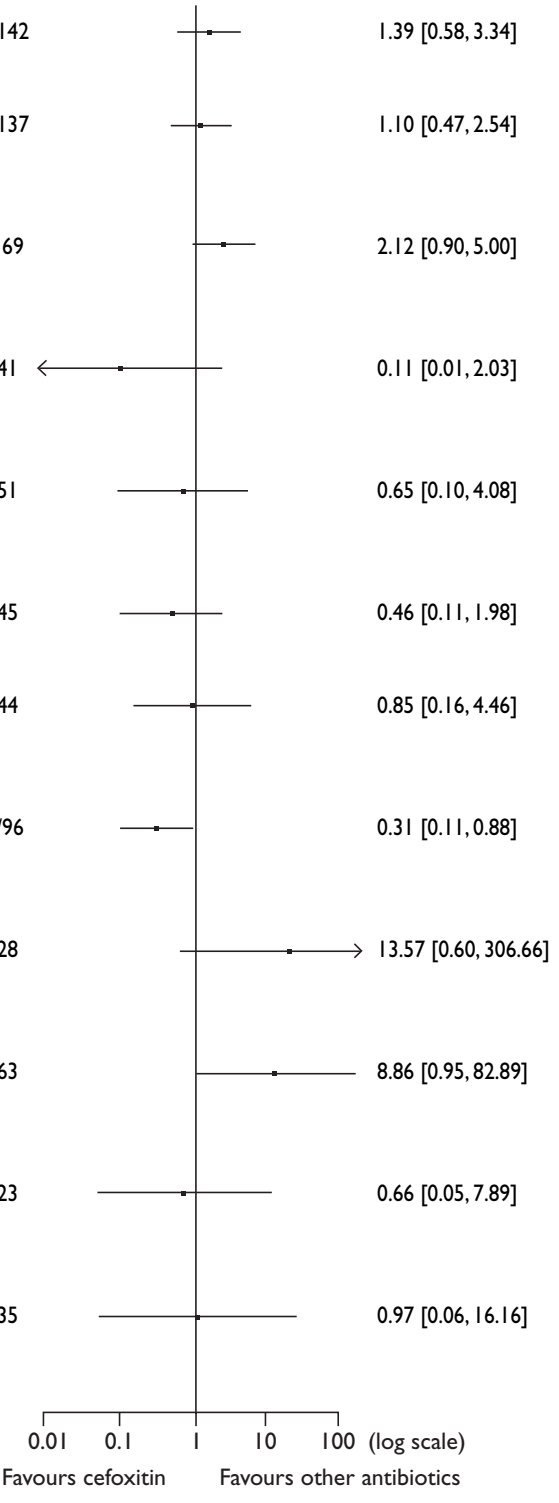


TABLE 8 *Ceftriaxone versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Ceftriaxone n/N	Other antibiotics n/N		
(Ceftriaxone × 1) vs. (aztreonam + clindamycin) × 5 Franceshini [50]	0/14	1/18		0.40 [0.02, 10.64]
(Ceftriaxone × 1) vs. (ampicillin + metronidazole) × 1 Luke [90]	4/32	5/36		0.89 [0.22, 3.63]
(Ceftriaxone + glycerol suppository) × 1 vs. (cephazolin × 1) + metronidazole suppository Lumley [91]	8/94	7/96		1.18 [0.41, 3.40]
(Ceftriaxone × 1) vs. (cefoxitin × 3) Nel [110]	6/45	3/45		2.15 [0.50, 9.21]
(Ceftriaxone + metronidazole) × 1 vs. (ceftazidime + metronidazole) × 4 Garcia [51]	1/30	2/30		0.48 [0.04, 5.63]
(Ceftriaxone + metronidazole) × 1 vs. (cefamandole + metronidazole) × 1 Hall [62]	4/56	6/75		0.88 [0.24, 3.30]
(Ceftriaxone + metronidazole) × 2 vs. (co-amoxiclav) × 2 Nyam [113]	4/100	4/100		1.00 [0.24, 4.11]
(Ceftriaxone + metronidazole) × 1 vs. (gentamicin + metronidazole) × 1 Burdon [30]	5/59	14/61		0.31 [0.10, 0.93]
(Ceftriaxone × 1) vs. (cefotiam + gentamicin + metronidazole) × 3 Wohlfart [155]	1/30	2/30		0.48 [0.04, 5.63]
(Ceftriaxone + tinidazole) × 1 vs. (netilmicin + tinidazole) × 1 Matikainen [92]	8/315	38/313		0.19 [0.09, 0.41]
(Ceftriaxone + ornidazole) × 3 vs. (amikacin × 5) + metronidazole × 7 Tsimoyiannis [147]	2/25	1/25		2.09 [0.18, 24.62]
(Ceftriaxone + metronidazole) × 1 vs. (neomycin + erythromycin) × 3 Kling [80]	2/27	1/27		2.08 [0.18, 24.41]
(Ceftriaxone + metronidazole) × 1 vs. (neomycin + erythromycin) × 3 Weaver [152]	3/31	12/29		0.15 [0.04, 0.62]

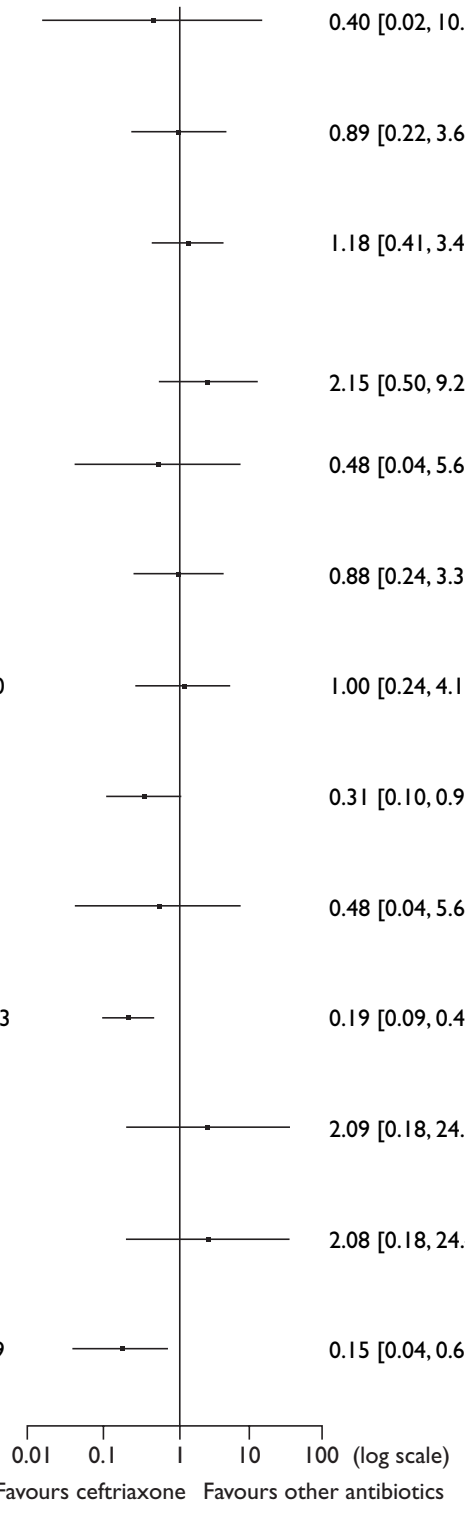
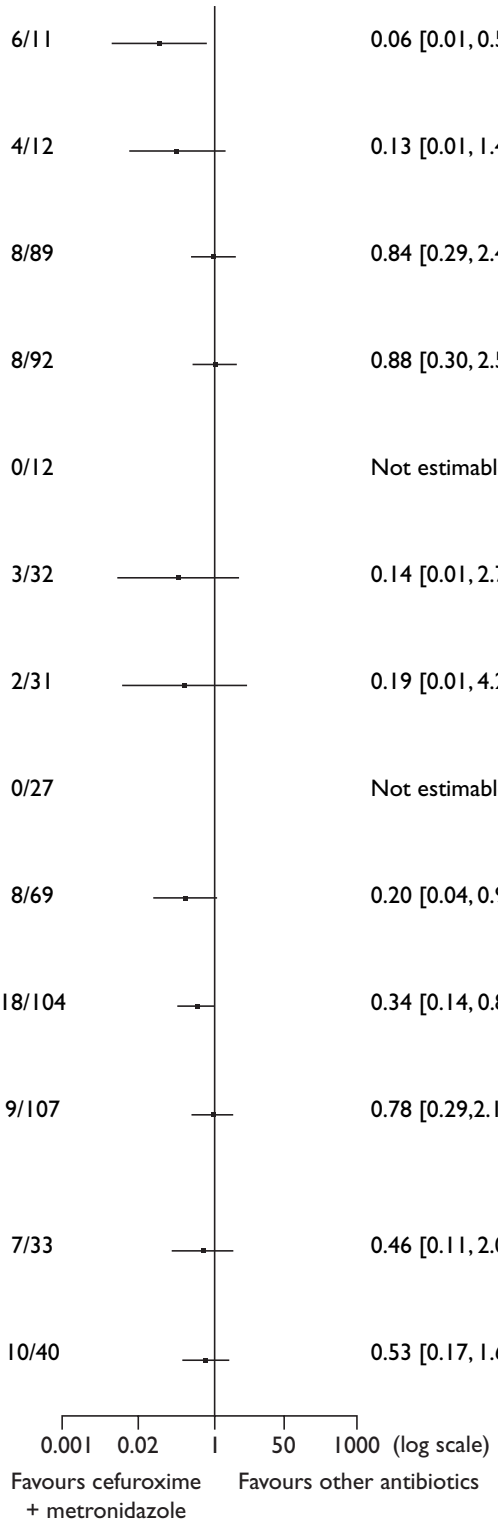


TABLE 9 *Cefuroxime plus metronidazole versus other antibiotics*

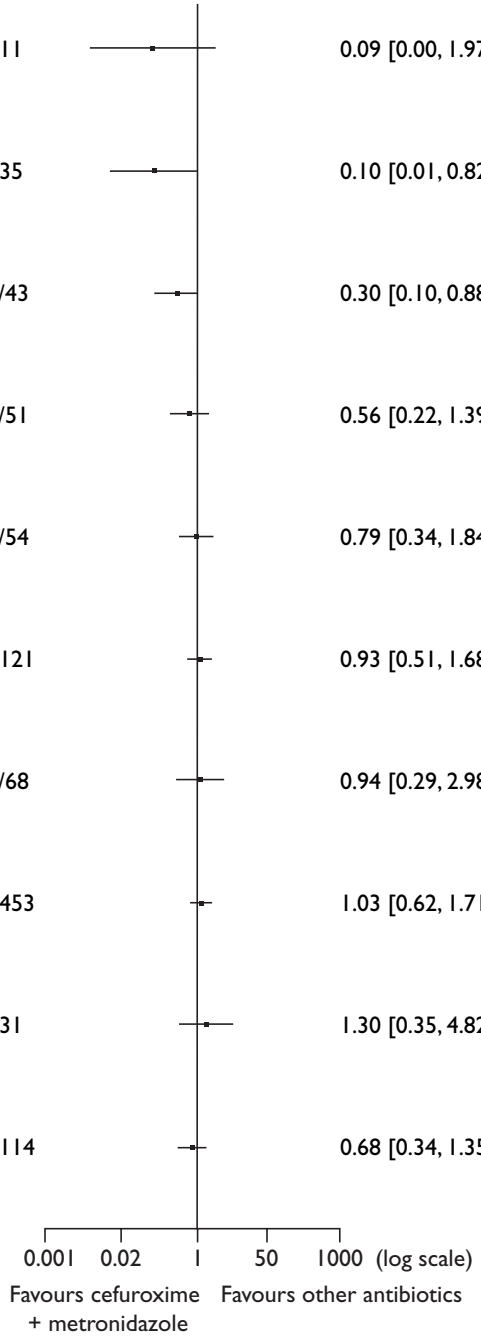
Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Cefuroxime + metronidazole n/N	Other antibiotics n/N		
(Cefuroxime + metronidazole) × 1 vs. (ampicillin + metronidazole) × 1 Jensen [69]	1/16	6/11		0.06 [0.01, 0.58]
(Cefuroxime + metronidazole) × 1 vs. (ampicillin + metronidazole) × 3 Jensen [69]	1/16	4/12		0.13 [0.01, 1.40]
(Cefuroxime + metronidazole) × 1 vs. (ampicillin + metronidazole) × 1 Jensen [69]	7/91	8/89		0.84 [0.29, 2.43]
(Cefuroxime + metronidazole) × 1 vs. (ampicillin + metronidazole) × 3 Jensen [69]	7/91	8/92		0.88 [0.30, 2.52]
(Cefuroxime + metronidazole) × 3 vs. (metronidazole + netilmicin) × 3 Haverkorn [63]	0/13	0/12		Not estimable
(Cefuroxime + metronidazole) × 1 vs. (cefuroxime × 1) Corman [38]	0/30	3/32		0.14 [0.01, 2.79]
(Cefuroxime + metronidazole) × 1 vs. (cefoxitin) × 1 Corman [38]	0/30	2/31		0.19 [0.01, 4.20]
(Cefuroxime + metronidazole) × 1 vs. cefoxitin × 4 Corman [38]	0/30	0/27		Not estimable
(Cefuroxime + metronidazole) × 3 vs. (co-amoxiclav × 3) Palmer [116]	2/79	8/69		0.20 [0.04, 0.97]
(Cefuroxime × 3) + (metronidazole × 4) vs. (piperacillin × 4) Reynolds [131]	8/119	18/104		0.34 [0.14, 0.83]
(Cefuroxime × 3) + (metronidazole × 4) vs. (piperacillin × 4) + (metronidazole × 6) + (neomycin × 8) Reynolds [131]	8/119	9/107		0.78 [0.29,2.11]
(Cefuroxime + metronidazole) × 1 vs. (metronidazole × 1) Mittermayer [101]	3/27	7/33		0.46 [0.11, 2.00]
(Cefuroxime + metronidazole) × 1 vs. (metronidazole × 1) Cunliffe [39]	6/40	10/40		0.53 [0.17, 1.63]



continued

TABLE 9 contd *Cefuroxime plus metronidazole versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Cefuroxime + metronidazole n/N	Other antibiotics n/N		
(Cefuroxime + metronidazole) × 3 vs. (metronidazole × 3) Haverkorn [65]	0/13	3/11		0.09 [0.00, 1.97]
(Cefuroxime × 6) + (metronidazole × 2) vs. (metronidazole × 2) Claesson [35]	1/36	8/35		0.10 [0.01, 0.82]
(Cefuroxime + metronidazole) × 10 vs. (mezlocillin × 7) Cann [33]	6/52	13/43		0.30 [0.10, 0.88]
(Cefuroxime + metronidazole) × 3 vs. (mezlocillin × 3) Diamond [44]	10/53	15/51		0.56 [0.22, 1.39]
(Cefuroxime + metronidazole) × 3 vs. (mezlocillin × 1) Stubbs [143]	14/56	16/54		0.79 [0.34, 1.84]
(Cefuroxime + metronidazole) × 1 vs. (latamoxef × 1) Kingston [77]	27/108	32/121		0.93 [0.51, 1.68]
(Cefuroxime + metronidazole) × 3 vs. (cefotetan × 2) Skipper [140]	5/36	10/68		0.94 [0.29, 2.98]
(Cefuroxime + metronidazole) × 3 vs. (cefotaxime + metronidazole) × 1 Rowe-Jones [135]	33/454	32/453		1.03 [0.62, 1.71]
(Cefuroxime + metronidazole) × 3 vs. (imipenem + cilastatin) × 1 Pacelli [115]	6/30	5/31		1.30 [0.35, 4.82]
(Cefuroxime + metronidazole) × 3 vs. (imipenem × 4) Karran [75]	17/122	22/114		0.68 [0.34, 1.35]

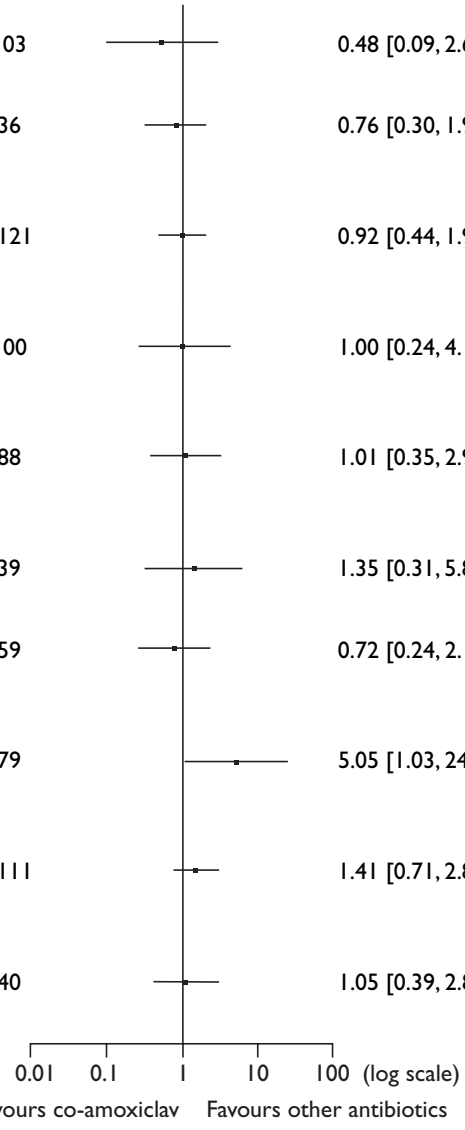


mezlocillin alone or plus metronidazole,[87,100] and cefotetan.[19]

Bates and co-workers[23] compared a single dose of co-amoxiclav with three doses of co-amoxiclav. The difference in the rate of SWI was not statistically significant (odds ratio = 1.41; 95% CI: 0.71, 2.82). There was no significant difference when topical use of co-amoxiclav was compared with parenteral use in the study by Pollock and co-workers,[127] in which the patients also received metronidazole.

TABLE 10 *Co-amoxiclav* versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Co-amoxiclav n/N	Other antibiotics n/N		
(Co-amoxiclav × 1) vs. (cefotetan × 1) Arnaud [19]	2/105	4/103		0.48 [0.09, 2.68]
(Co-amoxiclav × 3) vs. (cephradine + metronidazole) × 3 Tehan [145]	17/84	9/36		0.76 [0.30, 1.92]
(Co-amoxiclav × 2) vs. (gentamicin × 2) + (metronidazole × 1) Hall [61]	16/116	18/121		0.92 [0.44, 1.90]
(Co-amoxiclav × 2) vs. (ceftriaxone + metronidazole) × 2 Nyam [113]	4/100	4/100		1.00 [0.24, 4.11]
(Co-amoxiclav × 3) vs. (cefotaxime + metronidazole) × 3 Kwok [82]	7/76	8/88		1.01 [0.35, 2.94]
(Co-amoxiclav × 3) vs. (mezlocillin × 3) Menzies [100]	4/30	4/39		1.35 [0.31, 5.89]
(Co-amoxiclav × 1) vs. (mezlocillin + metronidazole) × 1 Lohde [87]	6/52	9/59		0.72 [0.24, 2.19]
(Co-amoxiclav × 3) vs. (cefuroxime + metronidazole) × 3 Palmer [116]	8/69	2/79		5.05 [1.03, 24.65]
(Co-amoxiclav × 1) vs. (co-amoxiclav × 3) Bates [23]	23/113	17/111		1.41 [0.71, 2.82]
(Co-amoxiclav + metronidazole) × 1 vs. (co-amoxiclav local injection + 1 metronidazole) × Pollock [127]	11/47	9/40		1.05 [0.39, 2.87]



* *Amoxycillin plus clavulanic acid*

Doxycycline

Doxycycline is a tetracycline antibiotic with a broad spectrum of activity. Doxycycline was assessed in eight trials for the prevention of SWIs after colorectal surgery *(Table 11)*.

Doxycycline alone was as efficacious as metronidazole plus netilmicin.[29] Doxycycline was as efficacious as metronidazole in one trial[13] but was less efficacious in another trial[78] in which the single dose of antibiotics was administered 3–4 hours before the operation.

Doxycycline alone was less efficacious than doxycycline plus metronidazole[26] or doxycycline plus tinidazole.[52] Doxycycline plus metronidazole appeared to be less efficacious than fosfomycin plus metronidazole ($p = 0.054$).[16] A large trial found that doxycycline added to tinidazole reduced the SWI rate significantly compared with tinidazole alone ($p = 0.017$).[112]

Gentamicin

Gentamicin is a broad-spectrum aminoglycoside. It is inactive against anaerobic bacteria and not absorbed from the gut.

Gentamicin alone was less efficacious in the prevention of SWI in colorectal surgery when compared with gentamicin plus ticarcillin.[42] Gentamicin was often combined with metronidazole, or clindamycin when used for the prevention of SWI in colorectal surgery *(Table 12)*. Gentamicin plus metronidazole was as efficacious as ampicillin plus sulbactam,[15] co-amoxiclav,[61] latamoxef,[94] cefotetan,[149] and metronidazole.[153] Gentamicin plus metronidazole was as efficacious as gentamicin plus lincomycin or gentamicin plus clindamycin.[89]

The rate of SWI in the group of gentamicin plus metronidazole was significantly higher than that of oral ciprofloxacin plus intravenous metronidazole,[93] aztreonam plus clindamycin,[109] and ceftriaxone plus metronidazole ($p < 0.05$).[30]

Two trials comparing gentamicin plus metronidazole with oral neomycin plus erythromycin on the day before surgery showed conflicting results. One trial found that the rate of SWI was higher in the group of gentamicin plus metronidazole compared with that of oral neomycin plus erythromycin, though the difference was not statistically significant ($p = 0.095$).[48] The other trial showed, however, that a single dose of gentamicin plus metronidazole was significantly more efficacious than oral neomycin plus erythromycin ($p = 0.03$).[83] It seems that these latter results were more reliable because of the superior study quality in terms of blind outcome measurement, longer follow-up, low withdrawal

TABLE 11 *Doxycycline versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Doxycycline n/N	Other antibiotics n/N		
(Doxycycline × 2) vs. (metronidazole × 8) Aberg [13]	16/76	21/81		0.76 [0.36, 1.60]
(Doxycycline × 1) vs. (metronidazole × 1) Kling [78]	12/67	2/52		5.45 [1.16, 25.58]
(Doxycycline × 6) vs. (netilmicin + metronidazole) × 3 Brolin [29]	5/50	4/50		1.28 [0.32, 5.07]
(Doxycycline + metronidazole) × 1 vs. (fosfomycin × 2) + (metronidazole × 1) Andaker [16]	16/258	7/259		2.38 [0.96, 5.89]
(Doxycycline + tinidazole) × 1 vs. (tinidazole × 1) Norwegian study [112]	4/132	14/135		0.27 [0.09, 0.84]
(Doxycycline × 1) vs. (doxycycline + metronidazole) × 1 Bergman [26]	12/126	2/135		7.00 [1.53, 31.93]
(Doxycycline × 1) vs. (doxycycline + tinidazole) × 1 Gerner [52]	10/107	3/116		3.88 [1.04, 14.51]
(Doxycycline × 1) vs. (doxycycline × 4) Goransson [54]	1/53	2/49		0.45 [0.04, 5.15]

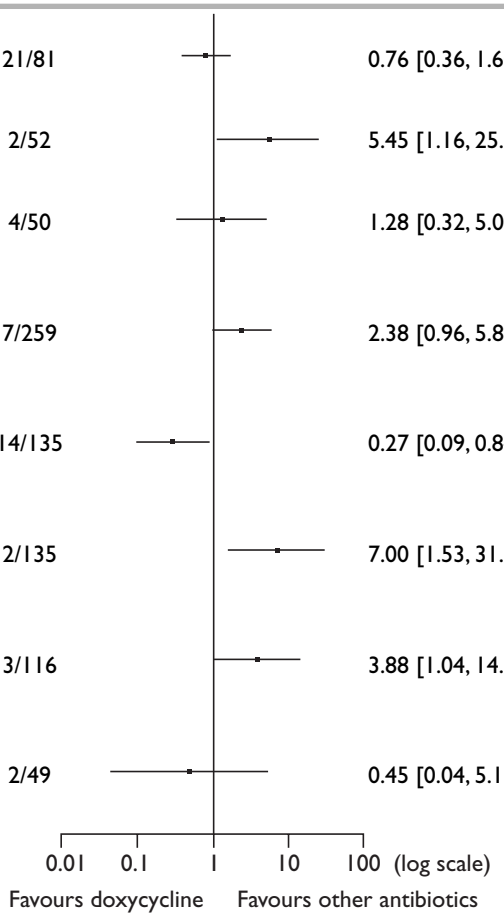
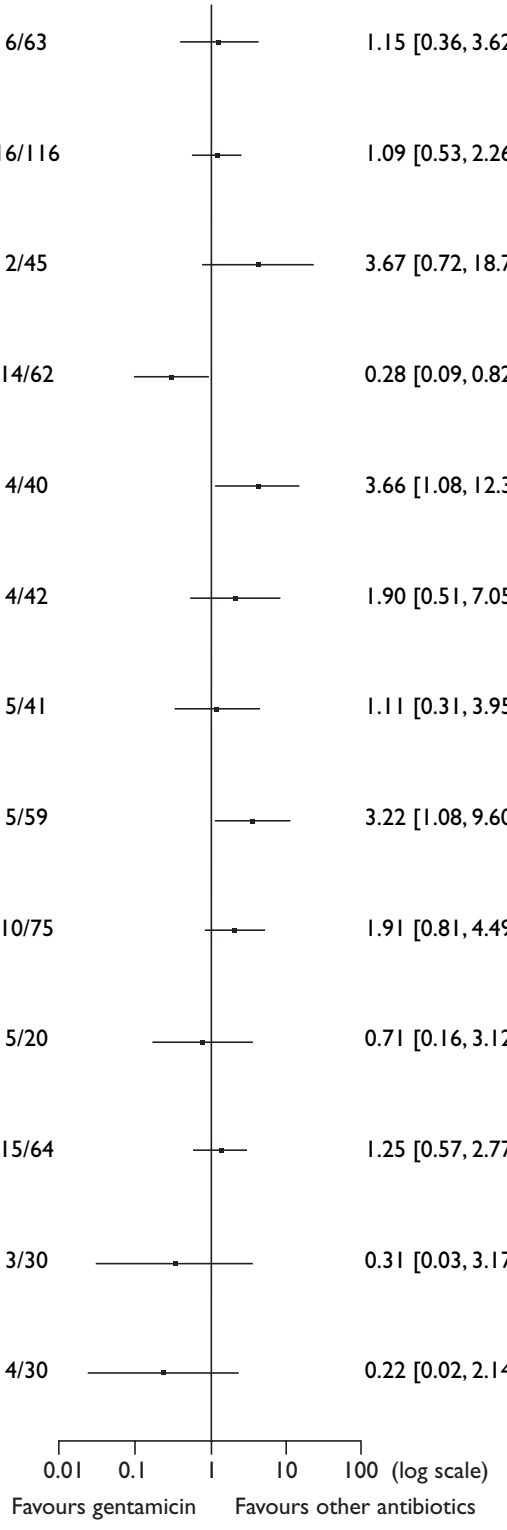


TABLE 12 *Gentamicin versus other antibiotics*

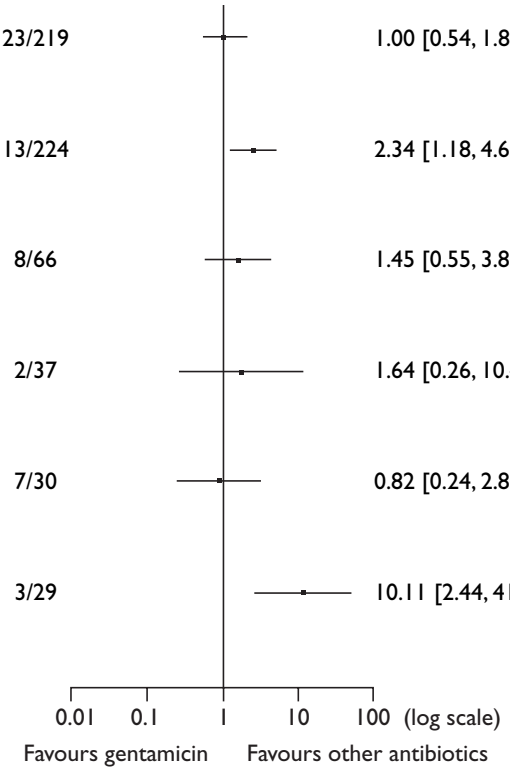
Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Gentamicin n/N	Other antibiotics n/N		
(Gentamicin + metronidazole) × 3 vs. (ampicillin + sulbactam) × 3 AhChong [15]	7/65	6/63		1.15 [0.36, 3.62]
(Gentamicin × 2) + (metronidazole × 1) vs. (co-amoxiclav × 2) Hall [61]	18/121	16/116		1.09 [0.53, 2.26]
(Gentamicin + metronidazole) × 3 vs. (neomycin + erythromycin) × 3 Figueras-Felip [48]	7/48	2/45		3.67 [0.72, 18.71]
(Gentamicin + metronidazole) × 1 vs. (neomycin + erythromycin) × 3 Lau [83]	5/67	14/62		0.28 [0.09, 0.82]
(Gentamicin + metronidazole) × 3 vs. (ciprofloxacin × 1) + (metronidazole × 3) McArdle [93]	13/45	4/40		3.66 [1.08, 12.36]
(Gentamicin + metronidazole) × 10 vs. (ciprofloxacin × 7) + (metronidazole × 10) McArdle [93]	7/42	4/42		1.90 [0.51, 7.05]
(Gentamicin + metronidazole) × 3 vs. (latamoxef × 3) McCulloch [94]	6/45	5/41		1.11 [0.31, 3.95]
(Gentamicin + metronidazole) × 1 vs. (ceftriaxone + metronidazole) × 1 Burdon [30]	14/61	5/59		3.22 [1.08, 9.60]
(Gentamicin × 15) + (metronidazole × 1) vs. (cefotetan × 2) Tudor [149]	17/75	10/75		1.91 [0.81, 4.49]
(Gentamicin + metronidazole) × 4 vs. (metronidazole × 4) Weidema [153]	4/21	5/20		0.71 [0.16, 3.12]
(Gentamicin + metronidazole) × 1 vs. (gentamicin + metronidazole + cefotetan) Greig [57]	18/65	15/64		1.25 [0.57, 2.77]
(Gentamicin + metronidazole) × 10 vs. (gentamicin + lincomycin) × 10 Lozano [89]	1/30	3/30		0.31 [0.03, 3.17]
(Gentamicin + metronidazole) × 10 vs. (gentamicin + clindamycin) × 10 Lozano [89]	1/30	4/30		0.22 [0.02, 2.14]



continued

TABLE 12 contd *Gentamicin versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Gentamicin n/N	Other antibiotics n/N		
(Gentamicin + metronidazole) × 2 vs. (gentamicin + metronidazole) × 7 Moesgaard [103]	22/209	23/219		1.00 [0.54, 1.86]
(Gentamicin + clindamycin) × 3 vs. (aztreonam + clindamycin) × 3 Mozzillo [109]	29/230	13/224		2.34 [1.18, 4.63]
(Gentamicin + clindamycin) × 3 vs. (aztreonam + clindamycin) × 3 Rodolico [132]	12/72	8/66		1.45 [0.55, 3.80]
(Gentamicin + clindamycin) × 3 vs. (cefoxitin × 2) Mosimann [108]	3/35	2/37		1.64 [0.26, 10.46]
(Gentamicin + clindamycin) × 2 vs. (cefoxitin × 3) Cainzos [32]	6/30	7/30		0.82 [0.24, 2.81]
(Gentamicin × 7) vs. (gentamicin + ticarcillin) × 7 Desaive [42]	14/26	3/29		10.11 [2.44, 41.93]



rate, and appropriate definition of SWI (see details in appendix 3).[48,83]

Metronidazole

Metronidazole is active against anaerobic bacteria. It seems that metronidazole alone was inadequate in the prevention of SWI in colorectal surgery when compared with other antibiotics *(Table 13)*. Metronidazole alone was significantly less efficacious than metronidazole plus ampicillin,[56] metronidazole plus doxycycline ($p = 0.056$),[133] metronidazole plus cefuroxime or netilmicin,[35,63] metronidazole plus fosfomycin,[86] cephazolin plus neomycin and erythromycin.[76] Six other trials did not find a significant difference between metronidazole alone and other antibiotics such as doxycycline alone,[13] oral neomycin plus erythromycin,[21] metronidazole plus nalidixic acid,[79] or gentamicin plus metronidazole.[153] Kling and co-workers[78] found that a single dose of metronidazole was significantly more efficacious than a single dose of doxycycline ($p = 0.02$).

Table 14 shows the results from trials that investigated the effect of adding metronidazole to other antibiotics. Three trials found significant benefit of additional metronidazole to neomycin,[67] doxycycline,[26] and cefotaxime.[59] The addition of metronidazole to cefuroxime was beneficial but not statistically significant in a small trial ($p = 0.24$).[38] No significant benefit was found when metronidazole was used in addition to cefotetan,[107] ceftriaxone,[91] latamoxef,[105] and ceftizoxime.[66]

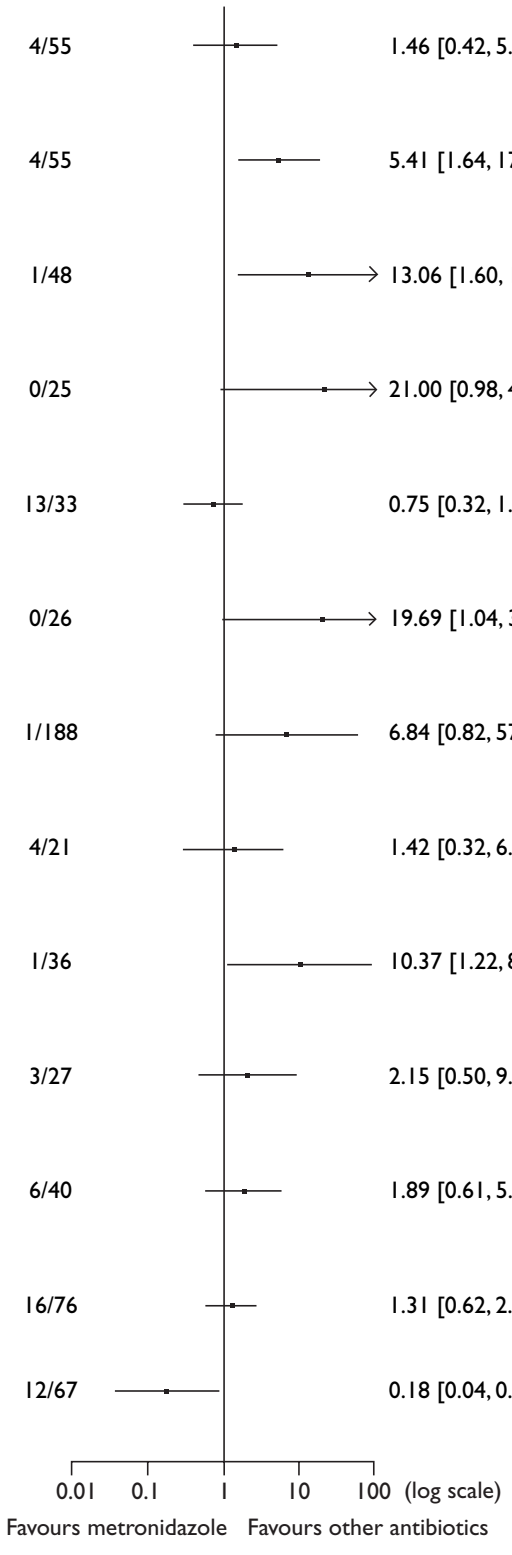
Mezlocillin

Mezlocillin is an acylureidopenicillin with *in vitro* activity against a wide range of Gram-positive and Gram-negative organisms, including anaerobes.

The efficacy of mezlocillin in preventing SWI was investigated in 11 trials *(Table 15)*. Three trials compared mezlocillin alone with cefuroxime plus metronidazole[33,44,143] and one found a significant difference in favour of cefuroxime plus metronidazole.[33] The rate of SWI in the mezlocillin group was not significantly different from that with

TABLE 13 *Metronidazole alone versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Metronidazole n/N	Other antibiotics n/N		
(Metronidazole × 3) vs. (neomycin + erythromycin) × 3 Auger [21]	8/78	4/55		1.46 [0.42, 5.10]
(Metronidazole × 3) vs. (cephazolin + neomycin + erythromycin) × 3 Khubchadani [76]	14/47	4/55		5.41 [1.64, 17.86]
(Metronidazole × 10) vs. (ampicillin + metronidazole) × 10 Gottrup [56]	10/46	1/48		13.06 [1.60, 106.72]
(Metronidazole × 3) vs. (netilmicin or cefuroxime + metronidazole) × 3 Haverkorn [63]	3/11	0/25		21.00 [0.98, 449.33]
(Metronidazole × 1) vs. (nalidixic acid + metronidazole) × 1 Kling [79]	23/70	13/33		0.75 [0.32, 1.78]
(Metronidazole × 4) vs. (fosfomycin + metronidazole) × 4 Lindhagen [86]	6/23	0/26		19.69 [1.04, 372.06]
(Metronidazole × 1) vs. (ampicillin or doxycycline + metronidazole) × 1 Roland [133]	6/170	1/188		6.84 [0.82, 57.42]
(Metronidazole × 4) vs. (gentamicin + metronidazole) × 4 Weidema [153]	5/20	4/21		1.42 [0.32, 6.27]
(Metronidazole × 2) vs. (cefuroxime × 6) + (metronidazole × 2) Claesson [35]	8/35	1/36		10.37 [1.22, 88.02]
(Metronidazole × 1) vs. (cefuroxime + metronidazole) × 1 Mittermayer [101]	7/33	3/27		2.15 [0.50, 9.29]
(Metronidazole × 1) vs. (cefuroxime + metronidazole) × 1 Cunliffe [39]	10/40	6/40		1.89 [0.61, 5.82]
(Metronidazole × 8) vs. (doxycycline × 3) Aberg [13]	21/81	16/76		1.31 [0.62, 2.76]
(Metronidazole × 1) vs. (doxycycline × 1) Kling [78]	2/52	12/67		0.18 [0.04, 0.86]



ticarcillin/clavulanic acid,[97] cefotaxime,[98] ceftizoxime,[98] latamoxef,[98] and co-amoxiclav.[100]

Latamoxef

Latamoxef (Moxalactam®, Shinogi, Japan), is a cephalosporin-like beta-lactam antibiotic with a broad spectrum of activity against gastrointestinal pathogens including strains of *Enterobacteriaceae* and *B. fragilis* that are resistant to older cephalosporins such as cephazolin.

Latamoxef alone was as efficacious as other antibiotic regimens in the prevention of SWI in colorectal surgery *(Table 16)*. The antibiotic regimens that were compared with latamoxef alone included ciprofloxacin plus metronidazole[55] cefuroxime plus metronidazole,[77] gentamicin plus metronidazole,[94] mezlocillin plus metronidazole,[98] co-amoxiclav,[123] cephazolin,[125] and cephazolin plus metronidazole.[146] Adding metronidazole to latamoxef was not found to be beneficial compared

TABLE 14 *Metronidazole as an additional antibiotic*

Regimen and study [reference]	Incidence of SWI: Additional metronidazole n/N	Incidence of SWI: Other antibiotics n/N	Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
(Doxycycline + metronidazole) × 1 vs. (doxycycline × 1) Bergman [26]	2/135	12/126		0.14 [0.03, 0.65]
(Cefuroxime + metronidazole) × 1 vs. cefuroxime × 1 Corman [38]	0/30	3/32		0.14 [0.01, 2.79]
(Cefotaxime + metronidazole) × 1 vs. (cefotaxime × 3) Hakansson [59]	19/287	44/280		0.38 [0.22, 0.67]
(Ceftizoxime × 2) + (metronidazole × 1) vs. (ceftizoxime × 2) Hosie [66]	7/89	9/85		0.72 [0.26, 2.03]
(Latamoxef × 2) + (metronidazole × 1) vs. (latamoxef × 2) Morris [105]	13/56	11/53		1.15 [0.47, 2.86]
(Cefotetan × 2) + (metronidazole × 3) vs. (cefotetan × 2) Morton [107]	34/253	39/278		0.95 [0.58, 1.56]
(Neomycin × 3) + (metronidazole × 3) vs. (neomycin × 3) Jagelman [67]	0/31	8/37		0.06 [0.00, 1.00]
(Ceftriaxone × 1) + (metronidazole suppository) vs. (ceftriaxone × 1) Lumley [91]	7/90	8/94		0.91 [0.31, 2.61]
(Cefotaxime × 4) + (metronidazole or ornidazole × 2) vs. (cefotaxime × 4) Favre [47]	5/72	4/74		1.31 [0.34, 5.07]

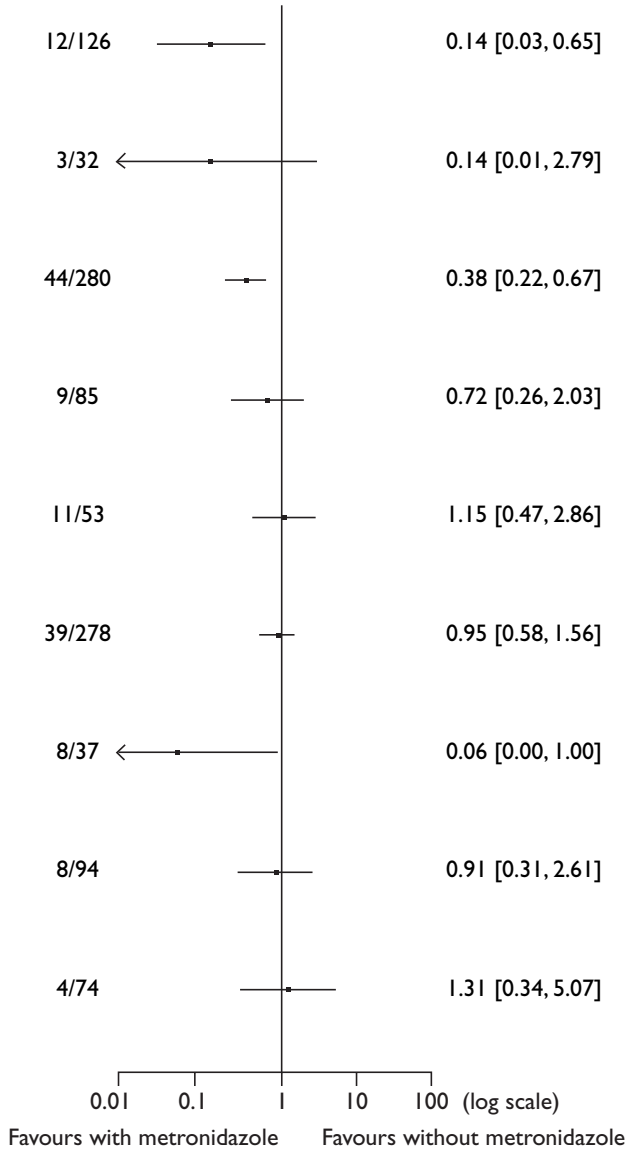
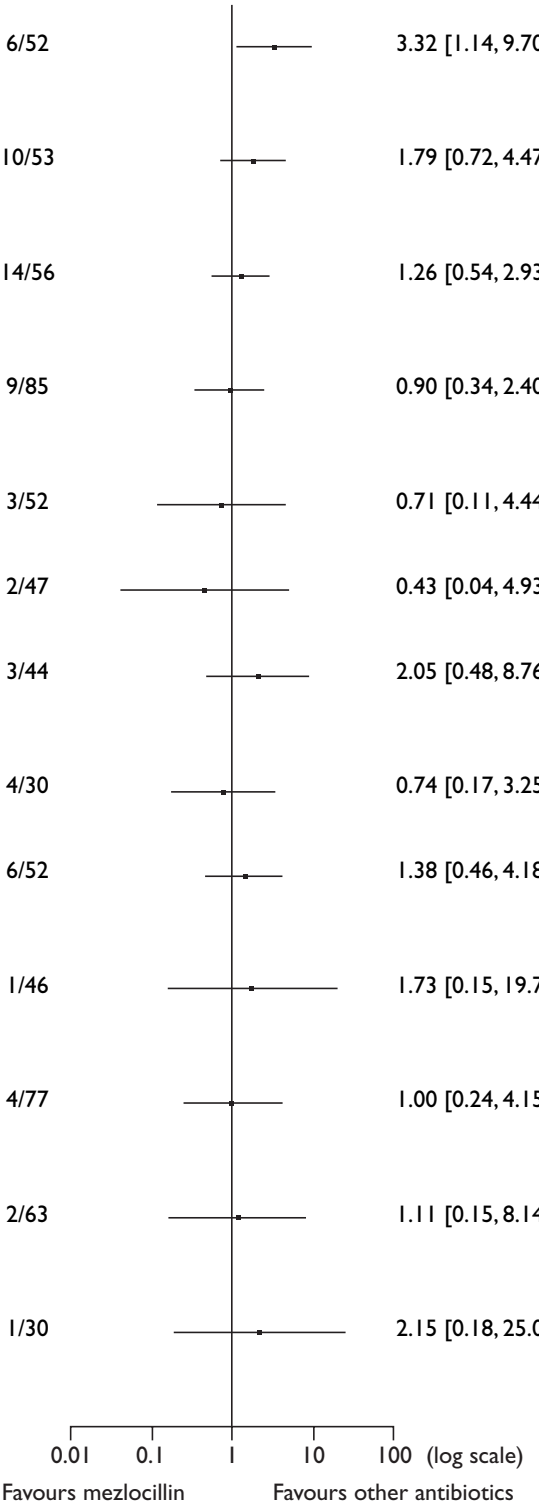


TABLE 15 *Mezlocillin versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Mezlocillin n/N	Other antibiotics n/N		
(Mezlocillin × 7) vs. (cefuroxime + metronidazole) × 10 Cann [33]	13/43	6/52		3.32 [1.14, 9.70]
(Mezlocillin × 3) vs. (cefuroxime + metronidazole) × 3 Diamond [44]	15/51	10/53		1.79 [0.72, 4.47]
(Mezlocillin × 1) vs. (cefuroxime + metronidazole) × 3 Stubbs [143]	16/54	14/56		1.26 [0.54, 2.93]
(Mezlocillin × 1) vs. (ticarcillin/clavulanic acid × 1) Melbourne study [97]	9/93	9/85		0.90 [0.34, 2.40]
(Mezlocillin × 1) vs. (cefotaxime × 1) Mendel [98]	2/48	3/52		0.71 [0.11, 4.44]
(Mezlocillin × 1) vs. (ceftizoxime × 1) Mendel [98]	1/53	2/47		0.43 [0.04, 4.93]
(Mezlocillin + metronidazole) × 1 vs. (mezlocillin + metronidazole) × 7 Bittner [27]	6/46	3/44		2.05 [0.48, 8.76]
(Mezlocillin × 3) vs. (co-amoxiclav × 3) Menzies [100]	4/39	4/30		0.74 [0.17, 3.25]
(Mezlocillin + metronidazole) × 1 vs. (co-amoxiclav × 1) Lohde [87]	9/59	6/52		1.38 [0.46, 4.18]
(Mezlocillin + metronidazole) × 1 vs. (mezlocillin + metronidazole) × 9 Mendel [98]	2/54	1/46		1.73 [0.15, 19.73]
(Mezlocillin + metronidazole) × 1 vs. (mezlocillin + metronidazole) × 3 Grundmann [58]	4/77	4/77		1.00 [0.24, 4.15]
(Mezlocillin + metronidazole) × 9 vs. (latamoxef × 1) Mendel [98]	2/57	2/63		1.11 [0.15, 8.14]
(Mezlocillin + oxacillin) × 3 vs. (neomycin + bacitracin + clindamycin) Schiessel [137]	2/29	1/30		2.15 [0.18, 25.07]



with latamoxef alone.[105] In a trial that included more than 100 patients in each treatment group, it was found that the single dose of latamoxef was as efficacious as multiple doses of latamoxef.[60] Latamoxef plus metronidazole suppository was more efficacious than oral tetracycline plus metronidazole suppository.[136]

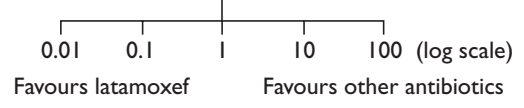
Neomycin plus erythromycin

Neomycin is an aminoglycoside, active against some Gram-positive and many Gram-negative organisms. It cannot be absorbed from the gut. Erythromycin has a similar but not identical antibacterial spectrum to that of penicillin, and it is active against anaerobic organisms. Neomycin plus erythromycin is often used orally (1 g of each) on the day before surgery (1 p.m., 2 p.m., and 11 p.m.). This regimen was compared with other antibiotic regimens in nine trials *(Table 17)*.

The overall rate of SWI was significantly higher in the oral neomycin plus erythromycin group than

TABLE 16 *Latamoxef versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Latamoxef n/N	Other antibiotics n/N		
(Latamoxef × 1) vs. (ciprofloxacin + metronidazole) × 1 Gortz [55]	1/57	4/54		0.22 [0.02, 2.06]
(Latamoxef × 3) vs. (neomycin + metronidazole) × 3 Hinchey [65]	5/64	3/67		1.81 [0.41, 7.09]
(Latamoxef × 1) vs. (cefuroxime + metronidazole) × 1 Kingston [77]	32/121	27/108		1.08 [0.60, 1.95]
(Latamoxef × 3) vs. (gentamicin + metronidazole) × 3 McCulloch [94]	5/41	6/45		0.90 [0.25, 3.22]
(Latamoxef × 1) vs. (mezlocillin + metronidazole) × 9 Mendel [98]	2/63	2/57		0.90 [0.12, 6.62]
[All: (Neomycin + metronidazole)] (Latamoxef × 1) vs. (co-amoxiclav × 1) Playforth [123]	10/36	15/56		1.05 [0.41, 2.69]
(Latamoxef × 3) vs. (cephazolin × 3) Plouffe [125]	1/26	1/24		0.92 [0.05, 15.58]
(Latamoxef × 3) vs. (cephazolin + metronidazole) × 3 Thomas [146]	3/60	5/60		0.58 [0.13, 2.54]
[All: Metronidazole] (Latamoxef × 1) vs. tetracycline Sauven [136]	6/39	15/43		0.34 [0.12, 0.99]
(Latamoxef × 1) vs. (latamoxef × 8) Hall [60]	12/119	10/126		1.30 [0.54, 3.13]
(Latamoxef × 2) vs. (latamoxef × 2) + metronidazole Morris [105]	11/53	13/56		0.87 [0.35, 2.15]



that in the group of neomycin plus erythromycin with additional antibiotics (overall odds ratio = 3.34; 95% CI: 1.66, 6.72).[83,121,138,141] Weaver and co-workers[152] found that oral neomycin plus erythromycin was significantly less efficacious than ceftriaxone plus metronidazole. In another trial, no abdominal wound infection was observed in patients receiving oral neomycin plus erythromycin or ceftriaxone plus metronidazole.[80]

The difference was not statistically significant when neomycin plus erythromycin was compared with metronidazole,[21] cefoxitin alone,[141] and erythromycin plus metronidazole.[85] Coppa and Eng[37] found that the rate of SWI was lower in patients receiving parenteral cefoxitin plus oral neomycin plus erythromycin compared with cefoxitin alone, but the difference was not statistically significant ($p > 0.1$).

Two trials compared oral neomycin plus erythromycin with gentamicin plus metronidazole.[48,83] One found that oral neomycin plus erythromycin was significantly less efficacious than gentamicin plus metronidazole ($p = 0.016$),[83] whereas the other found a non-significant benefit of neomycin plus erythromycin ($p = 0.10$).[48] The former results are likely to be more reliable, however, because of the superior quality of the study.

Netilmicin

Netilmicin is an aminoglycoside. It is used in serious Gram-negative infections that are resistant to gentamicin.

Matikainen and Hiltunen[92] found that netilmicin plus tinidazole was significantly less efficacious than ceftriaxone plus tinidazole (*Table 18*). There was no significant difference in the SWI rates when netilmicin plus metronidazole was compared with ticarcillin/clavulanic acid,[28] doxycycline,[29] cefuroxime plus metronidazole,[63] and piperacillin.[151]

Piperacillin

It has been suggested that piperacillin has a broad antibacterial spectrum covering both aerobic and anaerobic bacteria.[43] However, results of included trials *(Table 19)* showed that piperacillin alone was significantly less efficacious than piperacillin plus metronidazole, cefuroxime plus metronidazole,[131] and piperacillin plus oral ciprofloxacin.[144] There was no significant difference when piperacillin was compared with cefotetan,[64] piperacillin plus sulbactam,[142] or netilmicin plus metronidazole.[151]

Ticarcillin/clavulanic acid

Ticarcillin is active against *Pseudomonas aeruginosa*, certain other Gram-negative bacilli including *Proteus* spp. and *B. fragilis*. Clavulanic acid inactivates penicillinase produced by bacteria resistant to ticarcillin.

Ticarcillin/clavulanic acid (Timentin) was found to be as efficacious as metronidazole plus netilmicin,[28] cefotaxime,[72] and mezlocillin[97] *(Table 20)*. Ticarcillin/clavulanic acid was more efficacious than oral tinidazole.[96] A single dose of ticarcillin/clavulanic acid was found to be as efficacious as two doses.[40]

Tinidazole

Tinidazole is similar to metronidazole in activity but has a longer half-life and can therefore be given less frequently.

Tinidazole alone was significantly less efficacious than tinidazole plus doxycycline,[112] and less efficacious than ticarcillin[95] and ticarcillin/clavulanic acid[96] *(Table 21)*. Tinidazole plus doxycycline was significantly better than doxycycline alone.[52] Tinidazole plus ceftriaxone was significantly more efficacious than tinidazole plus netilmicin.[92]

Other antibiotics

Some agents were assessed in fewer than four trials and almost all of these agents have already been mentioned when they were compared with other agents that were more frequently tested.

A single dose of cefamandole plus metronidazole was as efficacious as a single dose of ceftriaxone plus metronidazole.[62] When parenteral cefamandole was added to oral neomycin plus erythromycin, no significant benefit was observed in a small trial.[121]

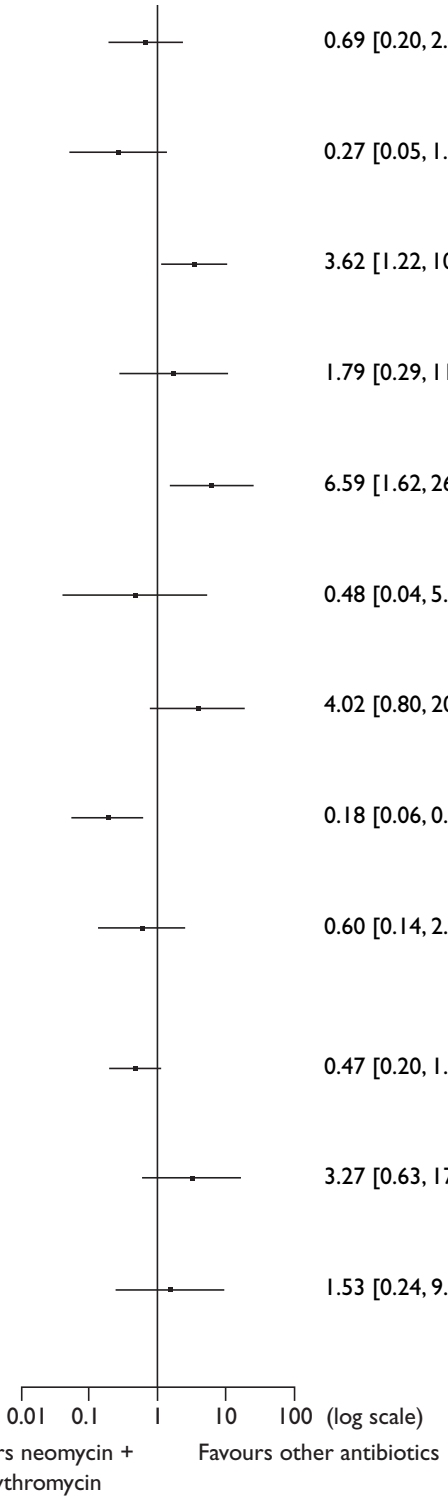
When all patients received oral neomycin plus erythromycin, additional parenteral cefmetazole was associated with a lower rate of SWI compared with additional cefoxitin but the difference was not statistically significant.[45,126]

Cefonicid in addition to oral neomycin plus erythromycin was as efficacious as cefoxitin used in combination with oral neomycin plus erythromycin.[46] Cefoperazone was as efficacious as cefotaxime.[70] Multiple doses of cefotiam plus gentamicin was of similar efficacy as a single dose of ceftriaxone.[155] The difference between cephalothin and cefoxitin was not statistically significant.[17] Cephradine plus metronidazole was as effective as co-amoxiclav.[145]

Three trials tested ciprofloxacin plus metronidazole. Ciprofloxacin plus metronidazole was as

TABLE 17 *Neomycin plus erythromycin*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Neomycin + erythromycin n/N	Other antibiotics n/N		
(Neomycin + erythromycin) × 3 vs. (metronidazole × 3) Auger [21]	4/55	8/78		0.69 [0.20, 2.40]
(Neomycin + erythromycin) × 3 vs. (gentamicin + metronidazole) × 3 Figueras-Felip [48]	2/45	7/48		0.27 [0.05, 1.39]
(Neomycin + erythromycin) × 3 vs. (gentamicin + metronidazole) × 1 Lau [83]	14/62	5/67		3.62 [1.22, 10.74]
(Neomycin + erythromycin) × 3 vs. (cefoxitin × 3) Stellato [141]	3/44	2/51		1.79 [0.29, 11.25]
(Neomycin + erythromycin) × 3 vs. (ceftriaxone + metronidazole) × 1 Weaver [152]	12/29	3/31		6.59 [1.62, 26.75]
(Neomycin + erythromycin) × 3 vs. (ceftriaxone + metronidazole) × 1 Kling [80]	1/27	2/27		0.48 [0.04, 5.64]
(Neomycin + erythromycin) × 3 vs. (erythromycin × 3) + (metronidazole × 6) Lewis [85]	7/61	2/64		4.02 [0.80, 20.17]
(Neomycin + erythromycin) × 3 + (cephazolin × 3) vs. (metronidazole × 3) Khubchandani [76]	4/55	14/47		0.18 [0.06, 0.61]
(Neomycin + erythromycin) × 3 + (gentamicin + metronidazole) × 1 vs. (gentamicin + metronidazole) × 1 Lau [83]	3/65	5/67		0.60 [0.14, 2.62]
(Neomycin + erythromycin) × 3 + (cefoxitin × 5) vs. (cefoxitin × 6) Coppa [37]	9/169	15/141		0.47 [0.20, 1.12]
(Neomycin + erythromycin) × 3 + (ampicillin × 1) vs. (cefotaxime × 3) Raahave [128]	6/50	2/50		3.27 [0.63, 17.07]
(Neomycin + erythromycin) × 3 + (cefoxitin × 3) vs. (cefoxitin × 3) Stellato [141]	3/51	2/51		1.53 [0.24, 9.57]



continued

TABLE 17 contd *Neomycin plus erythromycin*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Neomycin + erythromycin n/N	Other antibiotics n/N		
(Neomycin + erythromycin) × 3 vs. (neomycin + erythromycin) × 3 + (gentamicin + metronidazole) × 1 Lau [83]	14/62	3/65		6.03 [1.64, 22.18]
(Neomycin + erythromycin) × 3 vs. (neomycin + erythromycin) × 3 + (cefamandole × 4) Petrelli [121]	1/36	0/34		2.92 [0.11, 74.06]
(Neomycin + erythromycin) × 3 vs. (neomycin + erythromycin) × 3 + (cefoxitin × 3) Schoetz [138]	14/96	5/101		3.28 [1.13, 9.49]
(Neomycin + erythromycin) × 3 vs. (neomycin + erythromycin) × 3 + (cefoxitin × 3) Stellato [141]	3/44	3/51		1.17 [0.22, 6.12]

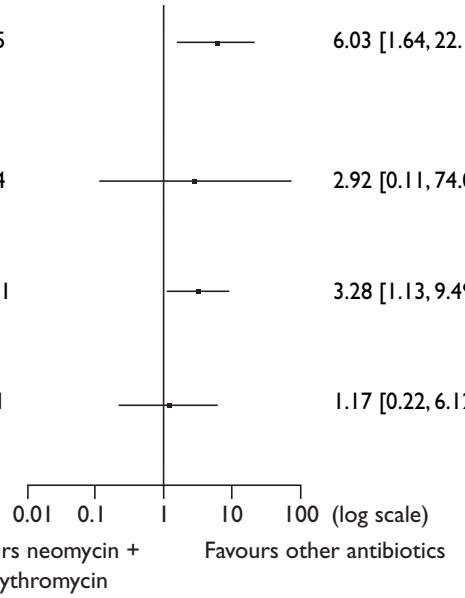


TABLE 18 *Netilmicin versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Netilmicin n/N	Other antibiotics n/N		
(Netilmicin + metronidazole) × 3 vs. (ticarcillin/clavulanic acid × 1) Blair [28]	5/46	3/46		1.75 [0.39, 7.79]
(Netilmicin + metronidazole) × 3 vs. (doxycycline × 6) Brolin [29]	4/50	5/50		0.78 [0.20, 3.10]
(Netilmicin + metronidazole) × 3 vs. (cefuroxime + metronidazole) × 3 Haverkorn [63]	0/12	0/13		Not estimable
(Netilmicin × 3) + (metronidazole × 2) vs. (piperacillin × 3) Walker [151]	13/105	17/108		0.76 [0.35, 1.65]
(Netilmicin or tobramycin + tinidazole) × 1 vs. (ceftriaxone + tinidazole) × 1 Matikainen [92]	38/313	8/315		5.30 [2.43, 11.56]

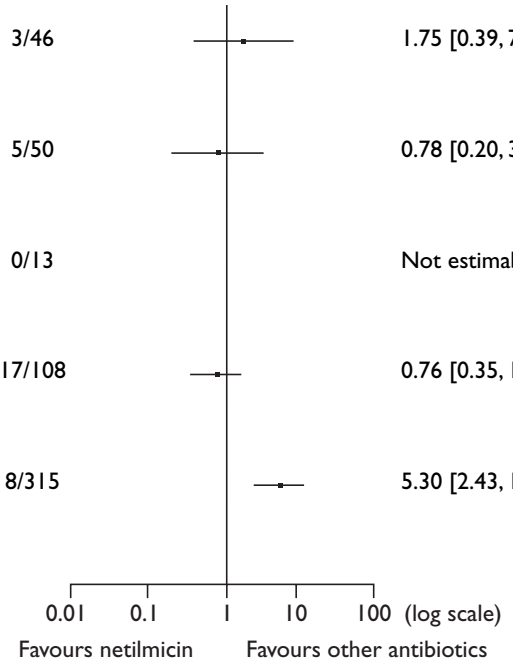


TABLE 19 *Piperacillin versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Piperacillin n/N	Other antibiotics n/N		
(Piperacillin × 3) vs. (cefotetan × 1) Hershman [64]	13/78	14/75		0.87 [0.38, 2.00]
(Piperacillin × 4) vs. (cefuroxime × 3) + (metronidazole × 4) Reynolds [131]	18/104	8/119		2.90 [1.21, 7.00]
(Piperacillin × 3) vs. (netilmicin × 3) + (metronidazole × 2) Walker [151]	17/108	13/105		1.32 [0.61, 2.88]
(Piperacillin × 4) vs. (piperacillin × 4) + (metronidazole × 6) + (neomycin × 8) Reynolds [131]	18/104	9/107		2.28 [0.97, 5.34]
(Piperacillin × 1) vs. (piperacillin + sulbactam) × 1 Stewart [142]	39/168	32/158		1.19 [0.70, 2.02]
(Piperacillin × 1) vs. (piperacillin × 1) + (ciprofloxacin × 2) Taylor [144]	39/168	18/159		2.37 [1.29, 4.35]
(Piperacillin × 1) vs. (cefoxitin × 1) Armengaud [18]	2/30	5/30		0.36 [0.06, 2.01]
(Piperacillin × 1) vs. (piperacillin × 4) Devecioglu [43]	3/25	2/25		1.57 [0.24, 10.30]

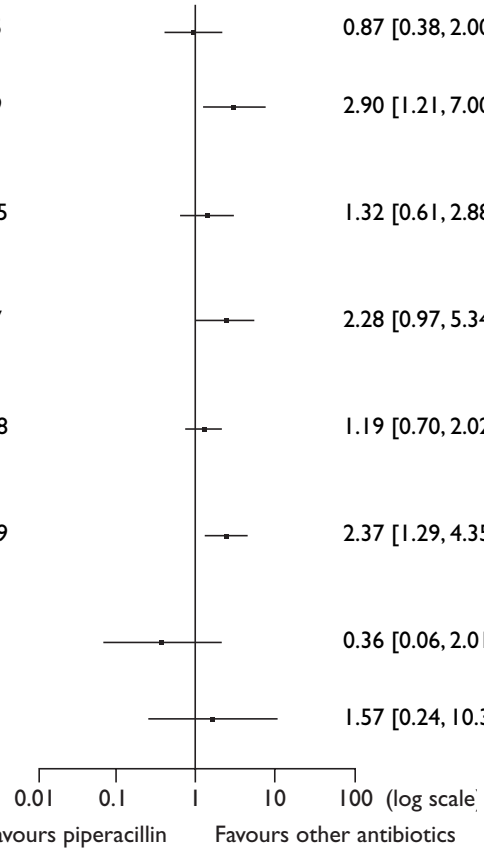


TABLE 20 *Ticarcillin/clavulanic acid*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Ticarcillin/ clavulanic acid n/N	Other antibiotics n/N		
(Ticarcillin/clavulanic acid × 1) vs. (netilmicin + metronidazole) × 3 Blair [28]	3/46	5/46		0.57 [0.13, 2.55]
(Ticarcillin/clavulanic acid × 1) vs. (cefotaxime × 4) Jones [72]	0/11	1/8		0.22 [0.01, 6.08]
(Ticarcillin/clavulanic acid × 1) vs. (mezlocillin × 1) Melbourne study [97]	9/85	9/93		1.11 [0.42, 2.93]
(Ticarcillin/clavulanic acid × 2) vs. (tinidazole × 1) Melbourne study [96]	2/83	12/84		0.15 [0.03, 0.68]

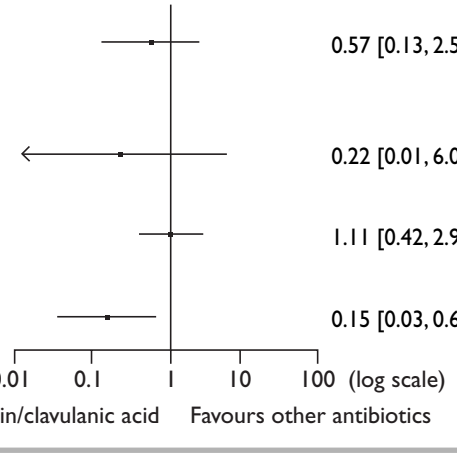
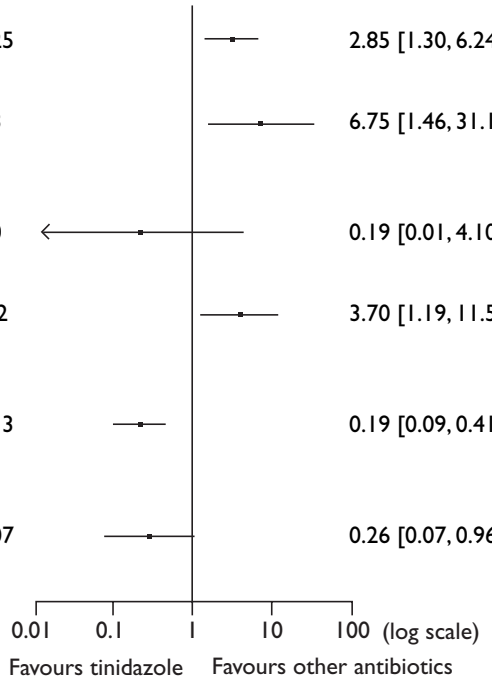


TABLE 21 *Tinidazole versus other antibiotics*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Tinidazole n/N	Other antibiotics n/N		
(Tinidazole × 1) vs. (ticarcillin × 2) Melbourne study [95]	24/121	10/125		2.85 [1.30, 6.24]
(Tinidazole × 1) vs. (ticarcillin/ clavulanic acid × 2) Melbourne study [96]	12/84	2/83		6.75 [1.46, 31.18]
(Tinidazole × 1) vs. (metronidazole × 10) Athanasiadis [20]	0/50	2/50		0.19 [0.01, 4.10]
(Tinidazole × 1) vs. (tinidazole + doxycycline) × 1 Norwegian study [112]	14/135	4/132		3.70 [1.19, 11.56]
(Tinidazole + ceftriaxone) × 1 vs. (tinidazole + netilmicin or tobramycin) × 1 Matikainen [92]	8/315	38/313		0.19 [0.09, 0.41]
(Tinidazole + doxycycline) × 1 vs. (doxycycline × 1) Gerner [52]	3/116	10/107		0.26 [0.07, 0.96]



efficacious as latamoxef,[55] cephazolin plus metronidazole,[114] and gentamicin plus metronidazole.[93]

The difference was not significant when fosfomycin plus metronidazole was compared with doxycycline plus metronidazole[16] or ampicillin plus metronidazole plus bacitracin plus neomycin.[111] Fosfomycin plus metronidazole was significantly more efficacious than metronidazole alone ($p = 0.007$).[86]

Imipenem plus cilastatin was as efficacious as cefuroxime plus metronidazole.[115] Imipenem alone was associated with a higher rate of SWI compared with cefuroxime plus metronidazole, though the difference was not statistically significant ($p = 0.27$).[75]

No statistically significant difference was found when penicillin plus streptomycin or penicillin plus metronidazole and tobramycin were compared with cefotaxime[84] or cefoxitin.[119]

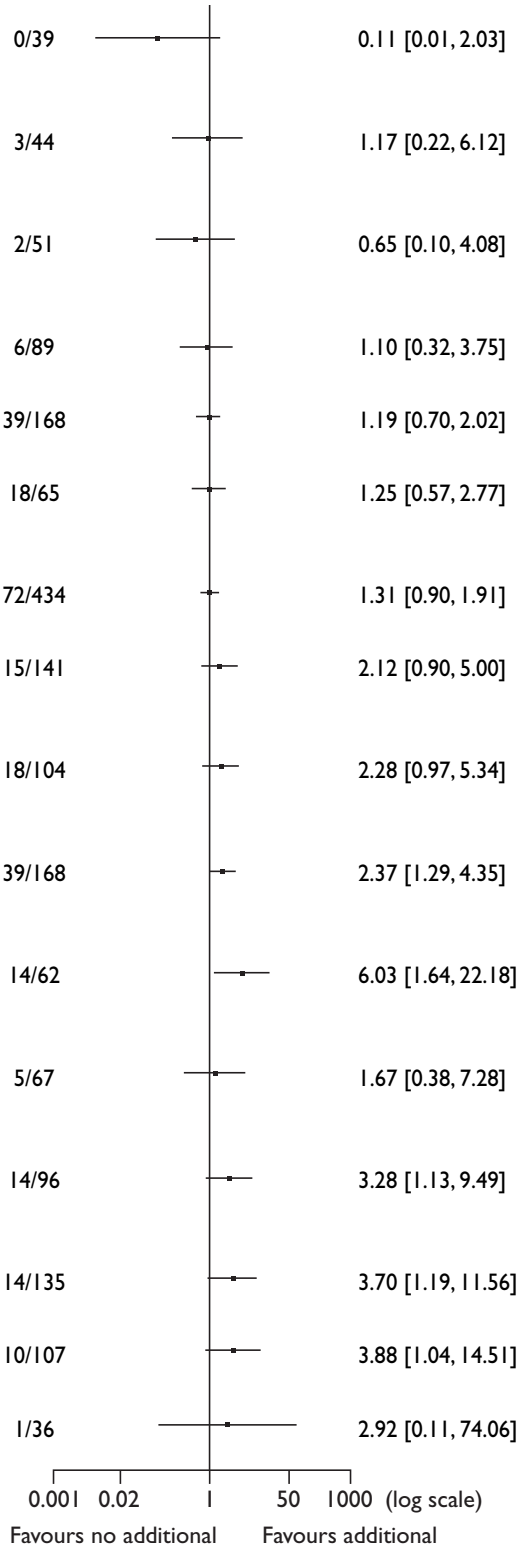
Additional antibiotics

Table 22 shows the results of trials that compared a regimen with the same regimen plus other antibiotic agents (excluding trials that have been included in *Tables 13* and *14*). It appears that piperacillin alone was less efficacious than piperacillin plus oral ciprofloxacin,[144] or plus oral neomycin and metronidazole.[131] Doxycycline alone was less effective than doxycycline plus metronidazole,[26] or tinidazole.[52] Tinidazole alone was less efficacious than tinidazole plus doxycycline.[112]

Oral neomycin plus erythromycin was similarly efficacious with or without the addition of cefoxitin.[141] Cefotaxime alone was as efficacious as cefotaxime plus topical ampicillin.[129] The addition of metronidazole to cefotaxime was found to be beneficial[59] (*Table 14*). Cefoxitin alone was as effective as cefoxitin plus oral neomycin and erythromycin.[37,141] However, in a small trial cefoxitin alone was more effective than cefoxitin plus oral tinidazole, though the difference was not significant ($p = 0.12$).[120] The outcome was not significantly improved when additional antibiotics were added to cefotetan,[107] ceftriaxone,[91] ceftizoxime,[66] gentamicin plus metronidazole,[57] and latamoxef.[105]

TABLE 22 *Additional antibiotics*[*]

Regimen and study [reference]	Incidence of SWI: Additional antibiotics n/N	Incidence of SWI: No additional antibiotics n/N	Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
(Cefoxitin × 3) vs. (cefoxitin × 3) + (tinidazole × 1) + (neomycin × 3) Peruzzo [120]	4/41	0/39		0.11 [0.01, 2.03]
(Neomycin + erythromycin) × 3 vs. (neomycin + erythromycin + cefotaxime) × 3 Stellato [141]	3/51	3/44		1.17 [0.22, 6.12]
(Cefoxitin × 3) vs. (cefoxitin + neomycin + erythromycin) × 3 Stellato [141]	3/51	2/51		0.65 [0.10, 4.08]
(Cefotaxime × 3) vs. (cefotaxime × 3) + (ampicillin × 1) Raahave [129]	5/81	6/89		1.10 [0.32, 3.75]
(Piperacillin × 1) vs. (piperacillin + sulbactam) × 1 Stewart [142]	32/158	39/168		1.19 [0.70, 2.02]
(Gentamicin + metronidazole) × 1 vs. (gentamicin + metronidazole + cefotetan) Greig [57]	15/64	18/65		1.25 [0.57, 2.77]
(Cefotetan × 1) vs. (cefotetan × 1) + (thymostimulin × 7) Periti [118]	56/425	72/434		1.31 [0.90, 1.91]
(Cefoxitin × 5) vs. (cefoxitin × 5) + (neomycin + erythromycin) × 3 Coppa [37]	9/169	15/141		2.12 [0.90, 5.00]
(Piperacillin × 4) vs. (piperacillin × 4) + (metronidazole × 6) + (neomycin × 8) Reynolds [131]	9/107	18/104		2.28 [0.97, 5.34]
(Piperacillin × 1) vs. (piperacillin × 1) + (ciprofloxacin × 2) Taylor [144]	18/159	39/168		2.37 [1.29, 4.35]
(Neomycin + erythromycin) × 3 vs. (metronidazole + gentamicin) × 1 + (neomycin + erythromycin) × 3 Lau [83]	3/65	14/62		6.03 [1.64, 22.18]
(Metronidazole + gentamicin) × 1 vs. (metronidazole + gentamicin) × 1 + (neomycin + erythromycin) × 3 Lau [83]	3/65	5/67		1.67 [0.38, 7.28]
(Neomycin + erythromycin) × 3 vs. (neomycin + erythromycin + cefoxitin) × 3 Schoetz [138]	5/101	14/96		3.28 [1.13, 9.49]
(Tinidazole × 1) vs. (tinidazole + doxycycline) × 1 Norwegian study [112]	4/132	14/135		3.70 [1.19, 11.56]
(Doxycycline × 1) vs. (doxycycline + tinidazole) × 1 Gerner [52]	3/116	10/107		3.88 [1.04, 14.51]
(Neomycin + erythromycin) × 3 vs. (neomycin + erythromycin) × 3 + (cefamandole × 4) Petrelli [121]	0/34	1/36		2.92 [0.11, 74.06]



[*] *Excluding metronidazole*

Single-dose versus multiple-dose regimens

Seventeen trials compared a single-dose regimen with a multiple-dose regimen (two or more doses) using the same antibiotic or the same combination of antibiotics *(Table 23)*. None of these trials found a significant difference in postoperative SWI between single-dose and multiple-dose regimens. The antibiotics that were investigated in these trials were cefoxitin,[38,81] cefuroxime plus metronidazole,[14] metronidazole,[34] ampicillin plus metronidazole,[69,74] co-amoxiclav,[23] latamoxef,[60] mezlocillin plus metronidazole,[27,58,98] ticarcillin/clavulanic acid,[40] cefotaxime plus metronidazole,[81] gentamicin plus ornidazole,[154] piperacillin plus tinidazole,[148] doxycycline,[54] and cefotaxime.[88] When the results from these 17 trials were pooled, there was no significant difference between the single- and multiple-dose groups (10.6% versus 9.7%; odds ratio = 1.17; 95% CI: 0.89, 1.54).

Timing and duration of treatment

The duration of operation and the half-life of an antibiotic may be related to the effectiveness of a single dose or short-term use of antibiotic prophylaxis. It was claimed that an extended duration of operation is associated with a higher rate of SWI.[157] Several trials that compared a single dose with multiple doses reported the duration of operation. The average duration of operation was 92 minutes in the trial by Carr and co-workers,[34] 135 minutes in Cuthbertson's trial[40] and 116 minutes (range: 20–270) in Wenzel's trial.[154] In the trial by Jensen and co-workers, the proportion of patients whose operation lasted longer than 180 minutes was 29%.[69] It was also found that the rate of SWI was similar in patients whose operations lasted less than 3 hours and in those whose operations were longer than 3 hours' duration.[69]

Other outcomes

The results of deep wound infections, remote infections (such as urinary tract infection, respiratory tract infection) and mortality, if reported, are also presented in appendix 3. However, these results have not been reported consistently across trials and therefore their reliability may suffer from the potential reporting and detection bias.

Mortality

The rate of total mortality ranged from 0% to 16.4% according to the results reported in 42 trials.

The rate of total mortality ranged from 0% to 16.4% according to the results reported in 42 trials. This gives an average death rate of 4.1%. However, this is likely to be an overestimation of the average death rate for all patients undergoing colorectal surgery because of reporting bias (i.e. trials that involve deaths are more likely to report mortality data than those in which no deaths occur).

With the exception of two trials,[91,156] no significant difference was found in the number of deaths between different antibiotic groups. Both elective and emergency colorectal surgery were included in the trial by Lumley and co-workers.[91] There were five deaths in the cephazolin group and no deaths in the two ceftriaxone groups. However, more patients underwent emergency operations in the cephazolin group (12% versus 5%) and there were also more surgical wounds that were classified as contaminated or dirty (31% versus 21%) in this group. In addition, all five deaths were infection related but not because of wound infection. Zuber and co-workers[156] recorded five deaths in the cephazolin group (n = 50) and no deaths in the cephazolin plus ornidazole group (n = 50). (This paper was in German and details related to cause of death were not explored.)

Intraabdominal abscess

Results of intraabdominal abscesses were available from 46 trials. The average rate of intraabdominal abscess in these 46 trials was about 3% and no statistically significant difference was observed between the different antibiotic groups.

Respiratory and urinary tract infection

The average rate of reported respiratory infection after colorectal surgery was 5.4%, according to 37 trials. Among these, several found significant differences between the antibiotic groups.[16,55,91,93,106,118]

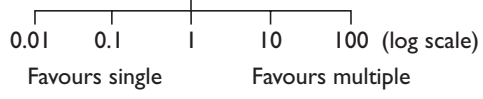
Thirty-nine trials reported the results of urinary tract infection after colorectal surgery. The average rate was 9.9% and seven of these trials found statistically significant differences.[27,78,80,91,96,98,115]

Adverse events

Among 134 trials that were published in English, 74 (55%) measured and reported results of adverse events after antibiotic prophylaxis in colorectal surgery. This proportion was 58%, 56% and 45% during 1984–87, 1988–91 and 1992–95, respectively. Patients with a history of drug allergy were not included in the trials. Skin rash, diarrhoea, and nausea were commonly reported adverse events that may be attributable to the antibiotic agents used.

TABLE 23 *Single versus multiple doses of antibiotic*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Single n/N	Other antibiotics n/N		
(Cefoxitin × 1) vs. (cefoxitin × 3) Kow [81]	10/73	8/81		1.45 [0.54, 3.89]
(Cefoxitin × 1) vs. (cefoxitin × 4) Corman [38]	2/31	0/27		4.66 [0.21, 101.47]
(Cefotaxime × 1) vs. (cefotaxime × 3) Lohr [88]	4/30	3/30		1.38 [0.28, 6.80]
(Co-amoxiclav × 1) vs. (co-amoxiclav × 3) Bates [23]	23/113	17/111		1.41 [0.71, 2.82]
(Ticarcillin/clavulanic acid × 1) vs. (ticarcillin/clavulanic acid × 2) Cuthbertson [40]	16/146	17/132		0.83 [0.40, 1.72]
(Latamoxef × 1) vs. (latamoxef × 8) Hall [60]	12/119	10/126		1.30 [0.54, 3.13]
(Ampicillin + metronidazole) × 1 vs. (ampicillin + metronidazole) × 3 Jensen [69]	6/11	4/12		2.40 [0.44, 12.98]
(Ampicillin + metronidazole) × 1 vs. (ampicillin + metronidazole) × 3 Jensen [69]	8/89	8/92		1.04 [0.37, 2.89]
(Ampicillin + metronidazole) × 1 vs. (ampicillin + metronidazole) × 4 Juul [74]	9/149	8/145		1.10 [0.41, 2.94]
(Cefotaxime + metronidazole) × 1 vs. (cefotaxime + metronidazole) × 3 Kow [81]	7/84	9/81		0.73 [0.26, 2.05]
(Mezlocillin + metronidazole) × 1 vs. (mezlocillin + metronidazole) × 3 Grundmann [58]	4/77	4/77		1.00 [0.24, 4.15]
(Mezlocillin + metronidazole) × 1 vs. (mezlocillin + metronidazole) × 7 Bittner [27]	6/46	3/44		2.05 [0.48, 8.76]
(Mezlocillin + metronidazole) × 1 vs. (mezlocillin + metronidazole) × 9 Mendel [98]	2/54	1/46		1.73 [0.15, 19.73]
(Cefuroxime + metronidazole) × 1 vs. (cefuroxime + metronidazole) × 3 Aberg [14]	2/19	1/29		3.29 [0.28, 39.14]
(Metronidazole × 1) vs. (metronidazole × 2–4) Carr [34]	7/22	11/68		2.42 [0.80, 7.30]
(Doxycycline × 1) vs. (doxycycline × 4) Goransson [54]	1/53	2/49		0.45 [0.04, 5.15]
(Gentamicin + ornidazole) × 1 vs. (gentamicin + ornidazole) × 4 Wenzel [154]	6/30	10/30		0.50 [0.15, 1.62]
(Piperacillin + tinidazole) × 1 vs. (piperacillin × 4) + (tinidazole × 3) Tuchmann [148]	4/61	5/63		0.81 [0.21, 3.19]



No serious toxicity or adverse events were reported except in the trial by Morris and co-workers.[105] Morris observed postoperative bleeding in 12 of the 97 patients treated with latamoxef. The trial was discontinued, and the investigators concluded that even short-term treatment with latamoxef could not be advised.[105] These results were not confirmed, however, by other trials that compared latamoxef with tetracycline,[136] cephazolin,[125] cephazolin plus metronidazole,[146] co-amoxiclav,[123] gentamicin plus metronidazole,[94] cefuroxime plus metronidazole,[77] and ciprofloxacin,[55] where no excessive bleeding was observed.

Cost and cost-effectiveness

Among the trials reviewed, 18 included some quantitative cost information. The proportion of trials that reported quantitative cost information was 10% for those published during 1984–91, and 26% for trials published during 1992–95. The cost information reported in these trials should be interpreted with caution because of small sample sizes, incomplete measures of cost and benefit, and data from many different countries in different years. (Equivalent costs in £ sterling are calculated from the average exchange rate for the year of publication, according to the financial statistics from the Office for National Statistics.) Only three UK studies reported cost information.[116,123,144]

Cost of surgical wound infection

A study has reported that superficial SWI prolonged hospital stay by an average of 12.6 days.[158] Another study estimated that on average the hospital stay was 12 days longer for patients with wound infection or suture line leak, and the treatment cost increased by about US $2000 (£1120).[55] A study in Scotland found that the median cost to the hospital of a wound infection after colorectal surgery in 1990 was £978 (95% CI: £484.04–£1521.22), including £858 hotel costs, £83.02 dressing costs, and £37.02 drug costs.[174] In another Scottish study, Taylor and co-workers[144] estimated that the financial consequence was £1000–1300 for each infected patient (according to an estimate of 8.8 more days of hospital stay for each patient with SWI, and the cost of £120–150 for each hospital bed per day).

In a study where more than 300 patients were included and more than 24 patients developed postoperative wound infection, it was estimated that each wound infection cost about US $8400 (£4720) per patient, while the total cost of parenteral antibiotic use for the entire study was about US $14,880 (£8361).[37]

Monotherapy

Three trials compared the efficacy and cost of monotherapy with combination therapy. One trial concluded that the monotherapy regimen (ampicillin/sulbactam, HK $10.11 [£0.85]) was cheaper than the combination of cephalosporins and metronidazole in Hong Kong.[15] Another found that the efficacy of co-amoxiclav was comparable with cefotaxime plus metronidazole, while monotherapy of co-amoxiclav (three doses) was cheaper, simpler and easier to administer than cefotaxime plus metronidazole (three doses) (US $14.70 versus US $25.80 [£9.79 versus £17.18]).[82] A third trial concluded that monotherapy with co-amoxiclav was effective and cheaper than the combination of cefuroxime plus metronidazole (£8.10 versus £24.91) in abdominal surgery.[116] However, this conclusion was based on the results of all patients with abdominal surgery. When only colorectal surgery was considered, the SWI was significantly higher in the co-amoxiclav group than in the cefuroxime plus metronidazole group (11.6% versus 2.5%), and therefore the reduction in comparative efficacy will have a direct effect on cost-effectiveness data.

Single dose or short-term use

Costs of single dose or short-term use were compared with those of multiple doses or long-term use of antimicrobial prophylaxis in four trials. Jones and Wojeski[71] concluded that over US $200,000 (£122,000) could be saved in their hospital if single-dose cefotaxime prophylaxis was used rather than multiple-dose cephazolin or cefoxitin. Becker and Alexander[24] compared cefoxitin for 5 days with cefoxitin for 16 hours. The cost of the two regimens was US $586 and US $66 (£328 and £37), respectively, and no SWI was reported in either group. Corman and co-workers[38] compared single-dose cefuroxime plus metronidazole with single-dose cefuroxime alone, four-dose cefoxitin, and single-dose cefoxitin. There were no SWIs in the cefuroxime plus metronidazole group or the four-dose cefoxitin group. It was reported that the costs of these two regimens were US $30 and US $68 (£20 and £45), respectively. Single-dose cefoxitin or single-dose cefotaxime plus metronidazole were compared with a three-dose regimen of the same antibiotics by Kow and co-workers.[81] They concluded that the single-dose regimen was associated with significant cost savings, particularly if the combination of cefotaxime plus metronidazole was used.

Less expensive drugs

The rates of SWI after two regimens of prophylactic latamoxef plus metronidazole and co-amoxiclav

plus metronidazole have been found to be comparable, but the cost of co-amoxiclav (£2.62 for 1.2 g) was lower than that of latamoxef (£6.11 for 1 g).[123] The cost of ceftriaxone was higher than cefamandole (AUS $22.78 versus AUS $8.22 per dose [£10.04 versus £3.62]), but they resulted in similar SWI rates.[62] In a trial in which amikacin plus metronidazole started just before surgery for 48 hours (seven doses) was compared with ceftriaxone plus ornidazole (three doses) for 48 hours, the efficacies and costs were similar.[147]

More efficacious regimens

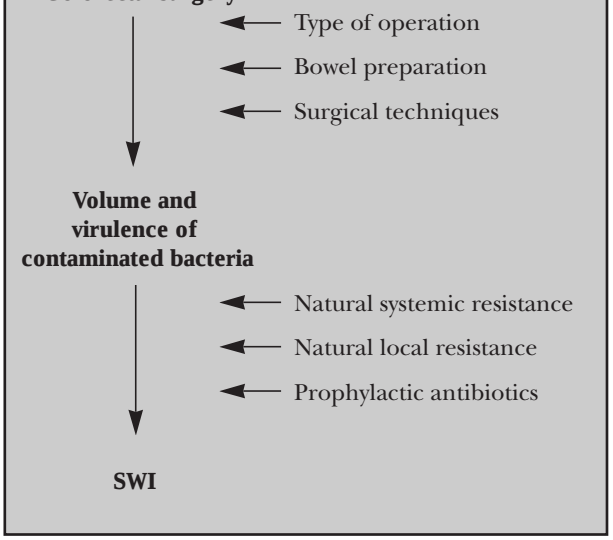
Gomez-Alonso and co-workers[53] found that, compared with a control group, prophylactic gentamicin plus metronidazole resulted in a lower SWI rate and saved US $406 (£304) per patient. Two trials observed that more expensive regimens may be associated with a lower total cost of treatment because of improved efficacy. One trial compared ten doses of gentamicin plus lincomycin (US $24.7, £19.04), gentamicin plus clindamycin (US $51.6, £39.77) and gentamicin plus metronidazole (US $117.7, £90.71).[89] Although gentamicin plus metronidazole was the most expensive regimen, it was associated with the lowest postoperative wound infection rate and the lowest total hospital cost (US $1587.7, £1223.57), compared with gentamicin plus lincomycin (US $1629.7, £1255.93) and gentamicin plus clindamycin (US $1611.6, £1241.99). A study in Scotland compared piperacillin alone (one dose) with piperacillin (one dose) plus oral ciprofloxacin (two doses).[144] Higher SWI rates in the piperacillin group (23.2% versus 11.3%) resulted in patients remaining in hospital on average 2.7 days more than patients in the combination group. The addition of oral ciprofloxacin reduced the overall cost of hospital treatment.[144]

Chapter 4
Discussion

Risk factors

The occurrence of SWI depends on two necessary conditions: contamination of the wound by pathogenic bacteria, and a defective host resistance to infection.[159] All factors associated with bacterial contamination and patient's resistance will also be associated with the risk of SWI (see Box).

Determinants of SWI in colorectal surgery



Colorectal surgery is classified as clean-contaminated or contaminated, depending on the type of operation. For example, the risk of contamination may be higher for rectal resections (abdominal–perineal operations) than other types of colorectal surgery.[160] Measures should be taken to reduce the exogenous and endogenous contamination of the surgical wound by pathogenic bacteria. Because a large volume of bacterial flora is contained in the large bowel, mechanical cleansing is often used to reduce the contents of the colon before the operation. Seventy-eight per cent of included trials (105 of 134 trials published in English) stated that preoperative bowel preparations was carried out, though this does not necessarily mean that mechanical cleansing was not performed in the remaining 29 trials.

It is clear that mechanical cleansing alone is insufficient in preventing bacterial contamination of the wound because it is very difficult (if not impossible) for this to be complete. Patient's natural resistance (systemic and local) is essential to prevent contaminated wounds becoming infected. The risk of SWI increases if patient's resistance is compromised because of, for example, radiotherapy, corticotherapy, chemotherapy, previous transplantation, diabetes, old age, obesity or weight loss.[7] In addition, patient's local resistance may be impaired because of ischaemia at the operation site.[159]

National Nosocomial Infection Surveillance (NNIS) is a risk index that can be used to estimate the risk of developing SWI.[157] It includes three risk factors:

- a patient having an American Society of Anesthesiologists (ASA) preoperative assessment score of 3, 4, or 5; (the ASA score is a measure of patient's general condition; it ranges from 1, when a patient is normally healthy, to 5, when a patient is very likely to die within 24 hours)
- an operation classified as either contaminated or dirty-infected
- an operation of more than $T^{75\%}$ hours' duration, where $T^{75\%}$ depends on the operative procedure being performed. $T^{75\%}$ is 3 hours in colon surgery because the 75th percentile of the distribution for duration of colon surgery was found to be 3 hours.

For patients undergoing surgery of the colon, it was found that the rate of SWI was 3.2%, 8.5%, 16.1%, and 22.2% for those with 0, 1, 2, and 3 risk factors, respectively.[157] Therefore, patients who undergo colorectal surgery may have different underlying risks of postoperative wound infection because of differences in patient characteristics, diagnoses, and level of complexity of the operations.

As wound contamination by pathogenic bacteria is often inevitable and host resistance is often defective, the use of antibiotic prophylaxis becomes important in preventing infection following colorectal surgery. In 1981, Baum and co-workers[6] concluded that no-antibiotic controls should not be considered in further trials of colorectal surgery. However, three trials that included no-antibiotic controls were published in 1984 and one in 1985.[53,56,137,150] In these four trials, the SWI rate

ranged from 32% to 58% in the no-antibiotic groups, considerably higher than that in the antibiotic prophylaxis groups *(Table 2)*.

In the trials included in this review, some factors were identified as being associated with an increased risk of SWI following colorectal surgery, such as duration of operation, obesity, the presence of drains, left-sided colonic resection, and inflammatory bowel disease. Two trials reported that the surgeon's experience might be a significant predictor of postoperative wound infection.[40,97] Perioperative blood transfusion was also found to be associated with an increased risk of SWI in two trials.[69,142] However, a reliable analysis of risk factors is impossible because potential risk factors were inconsistently measured and findings might have been selectively reported in the trials.

Methodological limitations of the studies

Evans and Pollock[161] used a score system to assess the quality of published RCTs (1979–86) of antibacterial prophylaxis in colorectal surgery. The score system included design and conduct, analysis, and presentation. They found that only 23% of the trials reached a score of more than 70 (maximum score 100). The most frequent error in design was a faulty method of randomisation (36%). They also observed that 80% (45/56) of the papers did not report the fate of withdrawals. In 32 'negative' trials only two considered the Type-II error. They found no evidence of improvement in the quality standard of these reports over the 7 years.[161]

In the present review, internal validity was the main concern. The quality of included studies was assessed using a checklist which includes study components such as design and analysis. An overall score is not calculated because different scales may result in important difference in quality assessment and none has been developed with sufficient rigour.[162]

Patient allocation

Empirical evidence has shown that an inappropriate method of patient allocation is related to biased estimation of relative efficacy of healthcare interventions.[163,164] In order to avoid the selection bias, patients should be allocated to each group randomly and the procedure should be concealed until allocation (true randomisation).[11] The appropriateness of the method of randomisation used was judged to be uncertain in about 63% of the included trials. Though many trials reported no significant difference in patients' characteristics and operation procedures between intervention groups, the potential selection bias is still possible when the patient assignment is not appropriate.

Follow-up and withdrawals

Incisional SWI is defined as an infection that occurs at an incision site within 30 days of surgery.[165] A considerable number of SWIs may be detected after discharge from the hospital.[166] Patients were usually followed up for 4 weeks or longer in many trials. In some trials, only infections occurring during hospital stay were recorded. About 30% of the trials did not report the duration of follow-up. The observed variation in the rate of SWI may be partially due to the different length of follow-up between the trials.

Patients may withdraw or be excluded from evaluation after randomisation for various reasons, for example, protocol violation, cancellation of scheduled surgery, or death within 48 hours of surgery. The withdrawal rate ranged from 0% to 42% in those trials that reported the number of withdrawals. About 23% of the trials did not record withdrawals. If withdrawals from the trial are non-random, and there are systematic differences between the groups, the different groups in a trial may no longer be comparable and attrition bias may be introduced. Intention-to-treat analysis is a method of including all participants in an analysis according to their initially assigned intervention group, regardless of whether or not they are withdrawn, fully comply with treatment, or cross over and receive the alternative treatment. However, the clinical outcome of participants who withdrew was not available for many trials. In the present review, the rate of SWI was calculated by using number of patients for whom SWI outcomes were evaluated.

Definition of surgical wound infection

A written definition of SWI was available in 79% of the included trials. SWI can be classified differently, for example, primary versus secondary, superficial versus deep, minor versus major, and early versus late. The SWI was defined in most cases as "the presence of purulent discharge" in the surgical wound, with or without positive bacteriological evidence. Swelling and reddening at the wound site and temperature exceeding 38 °C were also included as criteria for SWI.[13,38] If possible, we used abdominal wound infection as a principal outcome measure to compare efficacy of antibiotic prophylaxis. However, in some trials, it was not clear whether the wound infection included perineal wound infection or deep intraabdominal infections. As the main concern is the internal

validity, the differences in the definition of SWI across trials may have little impact on the evaluation of relative efficacy within trials. However, detection bias may occur when the diagnosis criteria are less objective, such as swelling or reddening of surgical wound. In the diagnosis of SWI, blind assessment of the outcome is a method to avoid detection bias. Only 40% of the included trials assessed outcome blindly.

Magnitude of relative efficacy and sample size

The majority of included trials compared different regimens of antibiotic prophylaxis. The difference in the mortality rate is generally expected to be very small. Therefore, SWI is used as the principal outcome measure in the review. Even when SWI is measured as the main outcome, the difference between comparison groups is still small, or moderate in most cases. A meta-analysis concluded that "comparisons of new therapies with standard therapies will become prohibitively expensive because of the large number of patients required".[6] Thus, it is not surprising to find that about 80% of the trials that compared different regimens did not find a statistically significant difference between groups.

When no significant difference was found, it may be because both regimens being compared were similarly effective. However, another reason for non-significant findings may be the low power due to inadequate sample size, particularly when the difference between antibiotics is small or moderate. Suppose the rate of SWI can be lowered by a regimen of antibiotic prophylaxis from 10% to 5%, to detect such a difference at the 5% significance level and 80% power, more than 400 patients are required in each group.[167] Such a large number of patients was unusual in the trials included. Eighty-two per cent of the trials had not undertaken an *a priori* calculation of required sample size. It is encouraging that the sample sizes of studies published more recently (1992–95) are larger than studies published previously (1984–87). The number of patients included in each group was on average 51, 77 and 124 for the trials published during 1984–87, 1988–91, and 1992–95, respectively.

The increase in the number of patients in the clinical trials does not correspond with an increase in the number of trials that found significant difference. The proportion of trials finding significant difference in SWI was 20.6%, 18.0%, and 17.4% for trials published during 1984–87, 1988–91, and 1992–95, respectively. This may also be because inadequate antibiotic regimens were tested more frequently in the earlier trials but were excluded from recent trials.

Inadequate direct comparison

More than 70 different regimens of antibiotic prophylaxis were compared in 147 trials (excluding different doses or duration of treatment or antibiotic combinations). Only a limited number of regimens were compared directly and each comparison was evaluated by a limited number of trials, in which the sample size was often too small to have sufficient statistical power (see appendix 4). The quantitative pooling of results from individual studies was not appropriate in most cases because of the diverse regimens used.

Publication and related bias

The majority of the included trials reported results which showed no statistically significant difference between the groups. Therefore, the risk that treatment effects have been over-estimated due to publication bias seems to be remote. It is not clear whether bias exists due to unrepresentative inclusion of non-English language publications.

Generalisability of results from included trials

It may not be possible to generalise the results from RCTs if the trials' participants were different from patients seen in the ordinary practice. The criteria for inclusion and exclusion were described in 87% of the trials reviewed here. The exclusion criteria most frequently used were allergy to study drugs, preoperative use of other antibiotics, impaired renal or liver function, children or very old patients, pregnancy or lactation, and certain types of colorectal operations. Lack of informed consent may be an important reason for exclusion but only a few trials stated this explicitly.[60,62,67,84] Data reported in the trials were insufficient for a reliable comparison between trial participants and patients who were excluded.

Timing and duration

According to the definition of prophylaxis, antimicrobial agents should be administered before the onset of SWI. Once the infection occurs antibiotic administration should be considered as therapeutic, rather than prophylactic, for wound infection. Bartlett and Burton[12] classified the timing of the antibiotic treatment into three categories:

- **preoperative** regimens, in which antibiotics are given before the day of surgery

- **perioperative** regimens, in which antibiotics are given before or during the surgical procedure
- **postoperative** regimens, in which antibiotics are given after surgery.

A different approach was used by Classen and co-workers[168] to define the timing of prophylactic administration of antibiotics. It was defined as:

- **early**, if prophylactic antibiotics were administered 2–24 hours before the surgical incision
- **preoperative**, if administered 2 hours before the incision
- **perioperative**, if administered within 3 hours after the incision
- **postoperative**, if administered 3–24 hours after the incision.

In order to be effective against postoperative wound infection, it is crucial that the concentration of antibiotics in the tissue surrounding the surgical wound should be sufficient at the time of bacterial contamination. Therefore, prophylactic antibiotics should be administered 2 hours before surgery.[168] However, it is not clear for how long antibiotics should be given after the operation. In some trials, antibiotic prophylaxis was used for several days after the operation. It has been argued that antibiotic prophylaxis should only be used as short-term treatment, in order to reduce toxicity, costs and the possibility of developing bacteria resistance.[169]

Seventeen trials compared a single-dose regimen with a multiple-dose regimen. None of these trials found a significant difference in postoperative SWI rate between the two regimens. Because the single dose of antibiotics is as efficacious as a multiple-dose regimen, the use of single dose or short-term antibiotics (e.g. less than 24 hours) is justified in the prevention of SWI in colorectal surgery.

Several trials reported the duration of operation. These trials did not provide any convincing evidence of the relation between the efficacy of single-dose regimens and the duration of operation. However, it has been recommended that a second dose is needed if the operation is over 2 hours' duration, particularly if the half-life of the antibiotic is short.[1,4,5,7] Due to a lack of convincing evidence, clinicians need to consider other factors such as perioperative blood loss to decide whether a second-dose regimen is required.

When an antibiotic is administered more than a day before the operation, the tissue concentration of the antibiotic agent may not be adequate during the operation. For example, oral neomycin plus erythromycin is given from 9–20 hours before the operation. The main aim is to reduce the risk of bacterial contamination of the surgical wound by reducing the bacteria in the large bowel prior to surgery. Some trials showed that oral neomycin and erythromycin on the day before the surgery is effective at reducing SWI, but may not be sufficient on its own. Further lowering of the rate of SWI may be achieved by adding parenteral antibiotics immediately before surgery.[83,138]

Inadequate antibiotic regimens

Some regimens appear to be poor at preventing SWI in colorectal surgery because of inadequate antimicrobial coverage, or inappropriate timing and dosing. Due to the divergent (polymicrobial) nature of the micro-organisms that are potentially responsible for infection following colorectal surgery, the antibiotics used should be of broad-spectrum activity and active against both aerobic and anaerobic bacteria. Metronidazole is active against anaerobic bacteria but inadequate against aerobic bacteria and should therefore be combined with other antibiotics. The following regimens were also shown to be inadequate in some trials: neomycin alone,[67] gentamicin alone,[42] doxycycline alone,[26,52] cefotaxime alone,[59] tinidazole alone,[95,96,112] and piperacillin alone.[131,144]

In the overview by Baum and co-workers,[6] the SWI rate after colorectal surgery in patients who received antibiotic prophylaxis was, on average, 22% in 26 trials published between 1965 and 1980. In another review by Bartlett and Burton,[12] the overall rate of SWI in colorectal surgery with antibiotic prophylaxis was 18% according to 23 trials published between 1960 and 1980. In our review, the overall rate of SWI in antibiotic groups was 11%, which is lower than rates reported previously. This difference may be due to different definitions of SWI, different methods of bowel preparation in trials, variation in patient selection, different length of follow-up, or different intensity of surveillance. It may also be due to a more effective or appropriate use of antibiotic prophylaxis in trials published more recently.

In Baum's review, the antibiotics that were used included metronidazole, gentamicin, cephalothin, doxycycline, and neomycin plus erythromycin.[6] In Bartlett and Burton's review, the trials used a wider range of antibiotics including neomycin, kanamycin, erythromycin, penicillin, gentamicin, cephalothin, doxycycline, metronidazole, tinidazole,

tetracycline, ampicillin, bacitracin, chlorchinaldole, clindamycin, and cefamandole.[12] According to the results from recently published trials, other regimens may be more effective than monotherapy with metronidazole, gentamicin, and doxycycline, and the combination of neomycin plus erythromycin (*Tables 11–13* and *17*). Significant advances in therapy since 1975 have resulted in a more effective range of antibiotic regimens in the prevention of SWIs.[170]

There is no obvious difference, however, in the rate of SWI when the RCTs included in this review are grouped according to the year of publication. The overall rate of SWI was 11% (6195 patients), 12% (10,297 patients), and 11% (6262 patients) for trials published during 1984–87, 1988–91, and 1992–95, respectively.

Additional antibiotics

Many trials tested whether combination therapy was more effective than monotherapy. For example, metronidazole alone was found to be less efficacious than a combination of metronidazole with other antibiotics (such as cefuroxime, fosfomycin, and ampicillin) *(Table 13)*. Similarly, the efficacy of some agents could be improved by the addition of metronidazole *(Table 14)*.

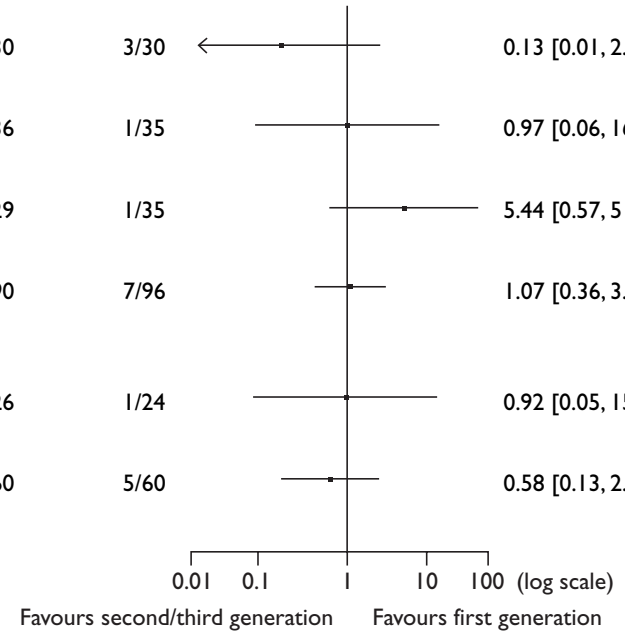
In summary, it appears that additional antibiotics were beneficial when they were added to piperacillin, doxycycline, tinidazole, and metronidazole, but no additional benefit was observed when antibiotics were added to cefoxitin, cefotetan, ceftriaxone, ceftizoxime, latamoxef, and gentamicin plus metronidazole.

New-generation cephalosporins

There is no consistent evidence to suggest that the new-generation cephalosporins are more effective than old-generation cephalosporins in the prevention of SWI in colorectal surgery. Six trials compared a first-generation cephalosporin with a second- or third-generation cephalosporin and the differences in rates of SWI between groups were not statistically significant *(Table 24)*. Similarly, pooling results from these six trials to increase the power did not show a statistically significant difference between the new-generation and the first-generation cephalosporins (overall rate of SWI: 6.0% versus 6.4%; odds ratio = 0.93; 95% CI: 0.46, 1.86).

TABLE 24 *Second- and third-generation cephalosporins versus first-generation cephalosporins*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Second/third generation n/N	First generation n/N		
(Cefoxitin × 11) vs. (cephalothin × 18) Antonelli [17]	0/30	3/30		0.13 [0.01, 2.61]
(Cefoxitin × 5) vs. (cephazolin × 4) Jones [71]	1/36	1/35		0.97 [0.06, 16.16]
(Cefotaxime × 1) vs. (cephazolin × 4) Jones [71]	4/29	1/35		5.44 [0.57, 51.68]
[All: Metronidazole suppository] (Ceftriaxone × 1) vs. (cephazolin × 1) Lumley [91]	7/90	7/96		1.07 [0.36, 3.19]
(Latamoxef × 3) vs. (cephazolin × 3) Plouffe [125]	1/26	1/24		0.92 [0.05, 15.58]
(Latamoxef × 3) vs. (cephazolin + metronidazole) × 3 Thomas [146]	3/60	5/60		0.58 [0.13, 2.54]



Route of administration

Prophylactic antibiotics can be administered in three ways.[12]

- **Oral administration** antibiotics are given by mouth, rectum, colostomy, or nasogastric tube.
- **Parenteral route** antibiotics are administered subcutaneously, intramuscularly, or intravenously.
- **Topical administration** antibiotics are applied directly to the surgical wound at the time of operation.

The intravenous route is the most reliable method of achieving a rapid increase in plasma level and tissue concentration of the antibiotic, because the intramuscular route may be limited by pharmacokinetic features of a drug and the absorption of antibiotics by oral route may be unreliable.[7]

No trial compared different routes of the same antibiotic. No extra benefit was observed in six trials that compared parenteral alone with parenteral plus topical use of antibiotic prophylaxis *(Table 25)*. However, the regimens that included oral antibiotics were associated with a lower rate of SWI in nine out of 12 trials, though the difference was statistically significant in only three trials. Some of these trials used inadequate parenteral antibiotics such as metronidazole alone or piperacillin alone. In general, oral or topical application of antibiotics in addition to the parenteral administration of appropriate antibiotics seem to be of limited value.

In the USA, the most commonly used oral regimen is a combination of neomycin and erythromycin on the day before operation.[160] However, this regimen alone was less efficacious than intravenous regimens of ceftriaxone plus metronidazole,[152] additional cefamandole,[121] additional cefoxitin,[138] and gentamicin plus metronidazole.[83]

Adverse events with antibiotic prophylaxis

Consideration of toxicity profiles and adverse events is important when selecting prophylactic antimicrobial agents. Reports of adverse events appear to have declined over the years and consequently, it seems that concern about adverse events associated with antimicrobial prophylaxis may also have diminished. However, skin rash, diarrhoea, and nausea are still commonly reported and may be attributable to the use of some antibiotic agents.

Bacteriology and antibiotic resistance

Most trials reported results of bacteriological testing (110/134). Bacteria isolated from infected wounds in colorectal surgery were often a mixture of aerobic and anaerobic organisms, among which *E. coli* and *B. fragilis* were most common. *S. aureus* was also frequently isolated. The type of bacteria isolated from surgical wounds might be altered after use of antibiotic prophylaxis. For example, bacteria isolated from wound infections were predominantly aerobic bacteria when prophylactic metronidazole had been administered.[35] One trial found that anaerobes were isolated from only one of 15 wound infections in the metronidazole group but from three of six wound infections in patients receiving cephozolin plus oral neomycin plus erythromycin.[76]

A regimen of antibiotic prophylaxis in surgery may become ineffective if antibiotic-resistant bacteria develop. The type and extent of antibiotic resistance may vary from country to country and within a country.[171] Evidence has shown that increased usage of antibiotics might be related to a rise in the prevalence of resistant bacteria and *vice versa*.[172] It was suggested that the development of antibiotic-resistant bacteria may be reduced if hospital infections could be prevented and if the use of antibiotics could be reduced.[172]

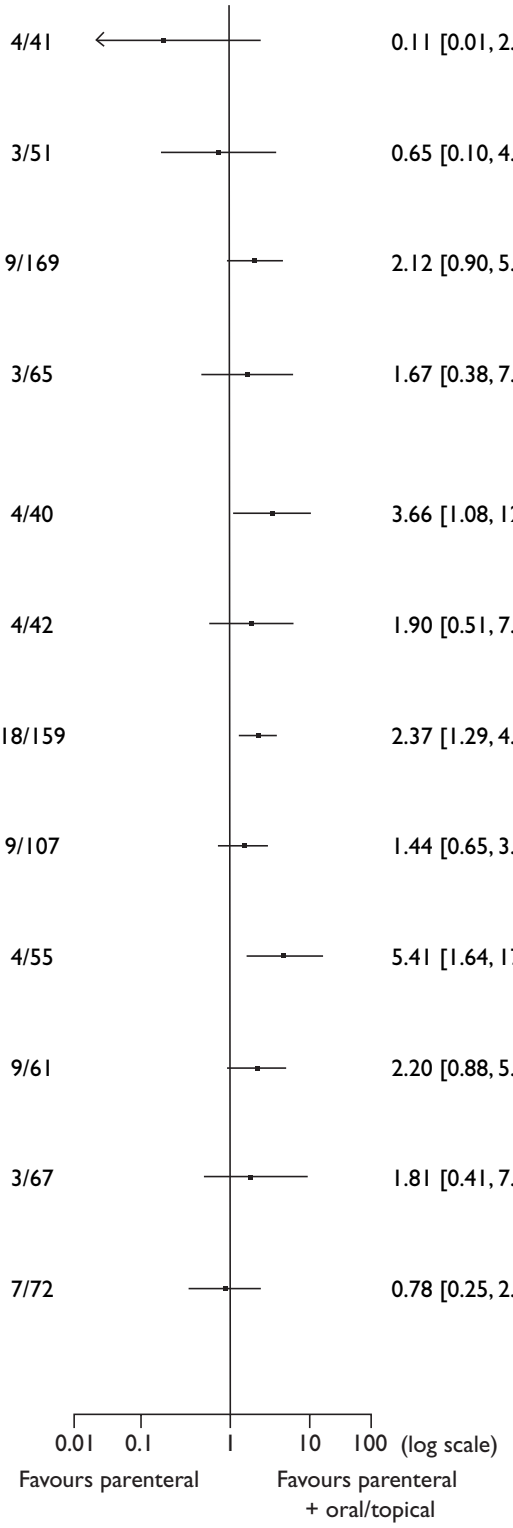
By preventing postoperative wound infection, a single dose or short-term antibiotic prophylaxis can reduce the need for long-term antibiotic therapy and therefore may contribute to reducing selection of antibiotic-resistant bacteria. To be effective in preventing SWIs, prophylactic antibiotics should be selected according to the local presence and prevalence of antibiotic-resistant bacteria.[172] For these reasons, the search for the ideal prophylactic regimen must be a continuous process and universal acceptance and use of a regimen should be avoided.[173]

Cost and cost-effectiveness

Both costs and benefits of antimicrobial prophylaxis in surgery may be direct or indirect, and a number of components may be included.[2] Costs of antibiotic prophylaxis include costs of antibiotic drugs, equipment, and staff time. These may be offset to some extent by reductions in the length of the hospital stay. Although this report has not attempted a systematic review of the cost-effectiveness of antimicrobial prophylaxis in

TABLE 25 *Route of administration: parenteral versus parenteral plus oral or topical*

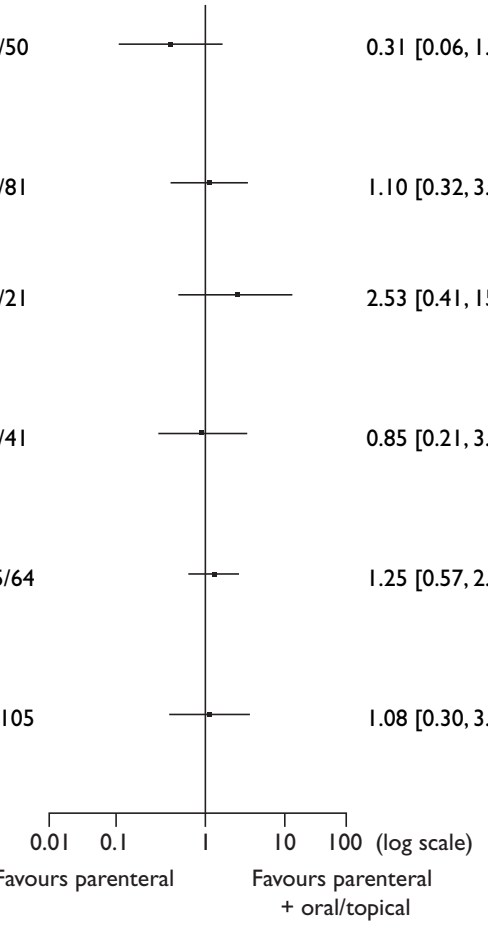
Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Parenteral only n/N	Parenteral plus oral/topical n/N		
(Cefoxitin × 3) vs. (cefoxitin × 3) + (tinidazole × 1) + (metronidazole oral × 3) Peruzzo [120]	0/39	4/41		0.11 [0.01, 2.03]
(Cefoxitin × 3) vs. (cefoxitin × 3) + (neomycin + erythromycin oral) × 3 Stellato [141]	2/51	3/51		0.65 [0.10, 4.08]
(Cefoxitin × 5) vs. (cefoxitin × 5) + (neomycin + erythromycin oral) × 3 Coppa [37]	15/141	9/169		2.12 [0.90, 5.00]
(Gentamicin + metronidazole) × 1 vs. (gentamicin + metronidazole) × 1 + (neomycin + erythromycin oral) × 3 Lau [83]	5/67	3/65		1.67 [0.38, 7.28]
(Gentamicin + metronidazole) × 3 vs. (metronidazole × 3) + (ciprofloxacin oral) McArdle [93]	13/45	4/40		3.66 [1.08, 12.36]
(Gentamicin + metronidazole) × 10 vs. (metronidazole × 10) + (ciprofloxacin oral × 1) McArdle [93]	7/42	4/42		1.90 [0.51, 7.05]
(Piperacillin × 1) vs. (piperacillin × 1) + (ciprofloxacin oral × 2) Taylor [144]	39/168	18/159		2.37 [1.29, 4.35]
(Piperacillin × 4) vs. (piperacillin × 4) + (metronidazole × 6) + (neomycin oral × 8) Reynolds [131]	26/223	9/107		1.44 [0.65, 3.18]
(Metronidazole × 3) vs. (cephazolin + neomycin + erythromycin oral) × 3 Khubchandani [76]	14/47	4/55		5.41 [1.64, 17.86]
(Metronidazole × 1) vs. (metronidazole × 1) + (metronidazole × 3) + (neomycin oral × 4) Playforth [124]	16/58	9/61		2.20 [0.88, 5.48]
(Latamoxef × 3) vs. (metronidazole × 3) + (neomycin oral × 3) Hinchey [65]	5/64	3/67		1.81 [0.41, 7.90]
(Fosfomycin + metronidazole) × 1 vs. (ampicillin × 1) + (metronidazole + bacitracin + neomycin) × 6 Nohr [111]	6/77	7/72		0.78 [0.25, 2.46]



continued

TABLE 25 contd *Route of administration: parenteral versus parenteral plus oral or topical*

Regimen and study [reference]	Incidence of SWI		Odds ratio (95% CI fixed)	Odds ratio [95% CI fixed]
	Parenteral only n/N	Parenteral plus oral/topical n/N		
(Cefotaxime × 3) vs. (neomycin + erythromycin oral) × 3 + (ampicillin topical × 1) Raahave [128]	2/50	6/50		0.31 [0.06, 1.59]
(Cefotaxime × 3) vs. (cefotaxime × 3) + (ampicillin topical × 1) Raahave [129]	6/89	5/81		1.10 [0.32, 3.75]
(Cefotaxime + metronidazole) × 10 + (cefotaxime + metronidazole) × 10 + (cefotaxime topical × 1) Moesgaard [104]	4/19	2/21		2.53 [0.41, 15.75]
(Gentamicin + metronidazole) × 7 vs. (gentamicin + metronidazole) × 7 + (gentamicin + metronidazole) topical Moesgaard [102]	4/38	5/41		0.85 [0.21, 3.42]
(Gentamicin + metronidazole) × 1 vs. (gentamicin + metronidazole) + cefotetan topical Greig [57]	18/65	15/64		1.25 [0.57, 2.77]
(Ampicillin + metronidazole) × 9 vs. (ampicillin + metronidazole) × 9 + ampicillin topical Juul [73]	5/98	5/105		1.08 [0.30, 3.83]



colorectal surgery, some general issues about cost-effectiveness of antibiotic prophylaxis are discussed, as well as cost information that was reported in some RCTs.

Cost of surgical wound infection

The risk of postoperative wound infection is high (> 50%) in colorectal surgery if antimicrobial prophylaxis is not employed, and SWI is associated with a prolonged hospitalisation and costly antibiotic treatment.

Relative cost-effectiveness

The costs associated with SWI are high, in terms of both antibiotic treatment and prolonged hospitalisation. Two studies showed that patients with SWIs remained in hospital for approximately 12 days longer than those patients without infections,[55,158] and another study calculated that wound infection following colorectal surgery was £978 in 1990.[174] These are clearly all costs that could be reduced or avoided with an appropriate prophylactic regimen.

The relative cost-effectiveness of different regimens need to be compared to decide which regimen should be selected in the prevention of SWI in colorectal surgery. A cost-effectiveness ratio is determined by the net cost and the effect of a healthcare intervention.[175] The net cost of a regimen depends not only on the cost of a regimen (including the cost of drug purchase, preparation and administration of the drug) but also the savings associated with the use of antibiotic prophylaxis, such as a reduction in hospital stay. When there is no difference in the efficacy and safety of prophylactic antibiotics, the cost and ease of use become criteria for the selection of regimens.[173,176]

It is possible to reduce the cost of antibiotic prophylaxis without adversely affecting SWI rate.[177–181] For example, where appropriate:

- a single dose or short-term regimen (less than 24 hours after surgery) can be adopted instead of inappropriate long-term use of antibiotics
- more effective and less costly drugs can be used instead of expensive drugs
- monotherapy can be used instead of combination therapy.

Antibiotic prophylaxis in surgical practice

Evidence from hospital surveys suggests that inappropriate use of antimicrobial prophylaxis in surgery is common in many countries. In seven Malaysian hospitals, the use of surgical antibiotic prophylaxis was investigated and it was found that it was often prescribed for an unnecessarily long period.[182] A Spanish study (n = 714) showed that prophylaxis was given for a mean of 8.4 days, and that the first choice antibiotic was selected in only 20% of the cases.[183] A survey on antibiotic prophylaxis in 889 surgical departments in German hospitals found that inappropriate antibiotics were selected 70.5% of the time, and that the duration of prophylaxis was not optimal in 57.1% of cases.[184]

In a District General Hospital in England, Dobrzanski and co-workers[179] identified the major problems associated with the use of antimicrobial prophylaxis in abdominal and arterial surgery. These included no antibiotics at induction (35%), questionable antibiotics at induction (22%), questionable postoperative antibiotics (25%), and unnecessarily long postoperative treatment courses (70%). The investigators developed the surgical antibiotic prophylaxis guidelines.[179] According to these guidelines, one perioperative and two postoperative doses of cefotaxime (1 g) plus metronidazole (500 mg) should be intravenously administered, in addition to oral neomycin (1 g) plus metronidazole (400 mg) for bowel preparation on the day before abdominal surgery. The antibiotic regimen recommended in these guidelines may not be optimal; for example, a single dose may be enough in many patients. However, by introducing the guidelines, the use of surgical antibiotic prophylaxis became more appropriate and the cost of antibiotic prophylaxis per surgical patient was reduced from £38.13 to £16.93. The rate of SWI was not followed in this study.[179]

In an audit of surgical prophylaxis in three Hospital Trusts in Tayside, Scotland, it was found that approximately 28% of patients undergoing colorectal surgery received antibiotic prophylaxis for more than 24 hours.[185] Against the standard recommended by the three hospitals, a second dose of antibiotic prophylaxis was seldom given for operations lasting more than 2 hours.

Janknegt and co-workers[186] studied 33 guidelines for antibiotic prophylaxis in surgery used in 89 Dutch hospitals. Since 1991, more guidelines have recommended the use of single-dose prophylaxis in colorectal surgery compared with before this date (50% versus 8%). The antibiotics recommended generally are active against anaerobic and aerobic bacteria. The most commonly recommended regimens for colorectal surgery include co-amoxiclav (8% before 1991 versus 25% since 1991), cefuroxime plus metronidazole (25% versus 25%), and gentamicin plus metronidazole (33% versus 20%).[186]

Oral neomycin plus erythromycin on the day before or 9–20 hours prior to surgery were often recommended by authors in North America.[4,5,8] Results from trials that compared this regimen alone with other regimens were inconsistent. Oral neomycin plus erythromycin were found to be significantly less efficacious than parenteral ceftriaxone plus metronidazole,[152] gentamicin plus metronidazole,[83] or with additional cefoxitin.[138]

In the British National Formulary (BNF No. 34, September 1997), a single dose of gentamicin plus metronidazole or cefuroxime plus metronidazole are recommended for preventing infection in colorectal surgery. A survey of guidelines for antimicrobial prophylaxis in surgery in 392 hospitals in the UK found that formal guidelines were available in 47% of the 160 hospitals that responded.[187] Recommended regimens for colorectal surgery included co-amoxiclav (6%), second-generation cephalosporin (2%), metronidazole alone (4%), aminoglycoside plus metronidazole (19%), first-generation cephalosporin plus metronidazole (15%), second-generation cephalosporin plus metronidazole (42%), and other antibiotics (12%). It was claimed that 94% of these regimens included antibiotics with activity against both aerobic and anaerobic bacteria.[187]

In a recent survey of antibiotic policies, Bloxham sent a total of 172 letters to consultant microbiologists in hospitals in the UK.[188] Recommendations on antibiotic prophylaxis in colorectal surgery was available in 49 of the 68 antibiotic policies

returned. Cefuroxime plus metronidazole was the most frequently recommended (28 policies) as the first choice. Co-amoxiclav was recommended in seven hospital antibiotic policies and gentamicin plus metronidazole in five policies. Other antibiotics recommended for antimicrobial prophylaxis in colorectal surgery included cephradine and cefotaxime plus metronidazole.

Chapter 5
Conclusions

Antibiotic prophylaxis is effective in the prevention of SWI in colorectal surgery. It appears that some regimens may be inadequate, such as metronidazole alone, and piperacillin alone compared with other regimens. The efficacy of many different regimens may be similar and it is very difficult to identify the most effective. There is no convincing evidence to suggest that the new-generation cephalosporins are more efficacious than first-generation cephalosporins in the prevention of SWI in colorectal surgery.

A single dose or short-term use (less than 24 hours after operation) is as efficacious as long-term postoperative use of antibiotic prophylaxis, and may be associated with less toxicity, fewer adverse events, a reduced risk of developing bacterial resistance, and lower overall costs.

Implications for policy

Two principles are important to follow when selecting an appropriate regimen.

- Antibiotics or antibiotic combinations should be active against both aerobic and anaerobic bacteria.
- The administration of antibiotics should be timed to ensure that the tissue concentration of antibiotics around the wound area is sufficiently high when bacterial contamination occurs.

In addition, universal acceptance and use of a regimen should be prevented in order to minimise the development of antibiotic-resistant bacteria. Based on available research evidence, guidelines should be developed locally in order to achieve more cost-effective use of antimicrobial prophylaxis in colorectal surgery.

Recommendations for research

The review of RCTs presented here has highlighted some important aspects of investigation and of antibiotic use. The quality of the included trials has improved over the last 12 years, though there still appear to be many methodological problems such as inappropriate methods of patient allocation, lack of blinding during assessment of outcomes, and insufficient sample sizes.

Further studies of efficacy may be of little value and would require large numbers of patients in order to demonstrate a statistically significant difference between regimens. Future research should focus on the understanding of the practical use of antimicrobial prophylaxis in colorectal surgery in the UK and the cost-effectiveness of the different regimens.

Acknowledgements

This review was commissioned by the NHS R&D HTA programme. The authors would like to thank Julie Glanville and Janette Boynton for assisting with the search and location of the literature. We are most grateful to Professor R Freeman, Professor DJ Leaper, Mr EW Taylor, Professor RJC Steele, Dr PG Davey and Professor CS McArdle for their helpful comments on the review protocol and draft report, and Professor MRB Keighley, Mr P McCulloch, and Professor A Pollock for responding to our inquiries about their studies. The report also benefited greatly from the HTA referees' comments. We would like to thank Professor Trevor Sheldon for his supervision and support during the review.

References

1. Dellinger EP, 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.
2. McGowan JE. Cost and benefit of perioperative antimicrobial prophylaxis: methods for economic anaysis. *Rev Infect Dis* 1991;**13**:879–89.
3. McDonald P, Finlay-Jones J. Microbial evolution of surgical infection. In: Watts JM, McDonald P, O'Brien PE, Marshall VR, Finlay-Jones J, editors. Infection in surgery: basic and clinical aspects. Edinburgh: Churchill Livingstone, 1981:3–9.
4. Waddell TK, Rotstein OD. Antimicrobial prophylaxis in surgery. *CMAJ* 1994;**151**:925–31.
5. Ludwig KA, Carlson MA, Condon RE. Prophylactic antibiotics in surgery. *Annu Rev Med* 1993;**44**:385–93.
6. Baum ML, Anish DS, Chambers 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. *New Engl J Med* 1981;**305**:795–9.
7. Martin C. Antimicrobial prophylaxis in surgery: general concepts and clinical guidelines. *Infect Control Hosp Epidemiol* 1994;**15**:463–71.
8. Page CP, Bohnen JM, Fletcher R, McManus AT, Solomkin JS, Wittman DH. Antimicrobial prophylaxis for surgical wounds. *Arch Surg* 1993;**128**:79–88.
9. Gorbach SL, Condon RE, Conte JE, Kaiser AB, Ledger WJ, Nichols RL. Evaluation of new anti-infective drugs for surgical prophylaxis. *Clin Infect Dis* 1992;**15**:S313–38.
10. Mulrow CD, Oxman AD. Cochrane Collaboration Handbook. [Update 9 December 1996]. Available in The Cochrane Library [database on disk and CD-ROM]. The Cochrane Collaboration; Issue 1. Oxford: Update Software, 1997.
11. Pollock A. Surgical infection. London: Edward Arnold Ltd., 1987.
12. Bartlett SP, Burton RC. Effects of prophylactic antibiotics on wound infection after elective colon and rectal surgery. *Am J Surg* 1983;**145**:300–9.
13. Aberg C, Olin B, Oresland T, Lundholm C, Bernander S, Stromberg A, *et al.* Comparison of metronidazole with doxycycline prophylaxis in elective colorectal surgery. *Acta Chir Scand* 1984;**150**:79–83.
14. Aberg C, Thore M. Single versus triple dose antimicrobial prophylaxis in elective abdominal surgery and the impact on bacterial ecology. *J Hosp Infect* 1991;**18**:149–54.
15. AhChong K, Yip AWC, Lee FCW, Chiu KM. Comparison of prophylactic ampicillin/sulbactam with gentamicin and metronidazole in elective colorectal surgery: a randomized clinical study. *J Hosp Infect* 1994;**27**:149–54.
16. Andaker L, Burman LG, Eklund A, Graffner H, Hansson J, Hellberg R, *et al.* Fosfomycin/metronidazole compared with doxycycline/metronidazole for the prophylaxis of infection after elective colorectal surgery. *Eur J Surg* 1992;**158**:181–5.
17. Antonelli W, Borgani A, Machella C, Morri F, Parrino A, Poloni M, *et al.* Comparison of two systematic antibiotics for the prevention of complications in elective colorectal surgery. *Ital J Surg Sci* 1985;**15**:225–58.
18. Armengaud F, Jobard J, Bernard E, Cordero C, Mouiel J, Sicard D, *et al.* Single dose antibiotic prophylaxis in colorectal surgery: cefoxitin versus piperacillin [French]. *Presse Med* 1986;**15**:2351–2.
19. Arnaud JP, Bellissant E, Boissel P, Carlet J, Chastang C, LaFaix C, *et al.* Single-dose amoxycillin-clavulanic acid versus cefotetan for prophylaxis in elective colorectal surgery: a multicentre prospective, randomized study. *J Hosp Infect* 1992;**22**:23–32.
20. Athanasiadis VS, Khulgatz C, Hanel E. Peri-operative antibiotikapropylaxw in der kolon – und rektumchirurgie [German]. *Zentralbl Chir* 1985;**110**:532–8.
21. Auger P, Legros G, Girard R, Laverdiere M, Bergeron M, Bourgouin J, *et al.* Intravenous metronidazole V's oral erythromycin base plus neomycin in the prevention of infection following elective colorectal surgery. *Curr Ther Res* 1987;**42**:922–31.
22. Bates T, Crathern BC, Bradley SP, Zlotnik RD, Crouch C, James RDG, *et al.* Timing of prophylactic antibiotics in abdominal surgery: trial of a pre-operative versus an intraoperative first dose. *Br J Surg* 1989;**76**:52–6.
23. Bates T, Roberts JV, Smith K, German KA. A randomised trial of one versus three doses of Augmentin as wound prophylaxis in at-risk abdominal surgery. *Postgrad Med J* 1992;**68**:811–16.
24. Becker JM, Alexander DP. Colectomy, mucosal proctectomy and ileal pouch-anal anastomosis: a prospective trial of optimal antibiotic management. *Ann Surg* 1991;**213**:242–47.

25. Bellantone R, Pacelli F, Sofo L, Doglietto GB, Bossola M, Ratto C, *et al.* Systematic preoperative prophylaxis in elective oncological colorectal surgery: cefotetan versus clindamicin plus aztreonam. *Drugs Exp Clin Res* 1988;**XIV**:763–6.

26. Bergman L, Solhaug JH. Single-dose chemoprophylaxis in elective colorectal surgery: a comparison between doxycycline plus metronidazole and doxycycline. *Ann Surg* 1987;**205**:77–81.

27. Bittner R, Butters M, Rampf W, Kapfer X. Duration of antibiotic prophylaxis in colorectal surgery – one-shot dose vs short-term prophylaxis [German]. *Langenbecks Arch Chir* 1989;**374**:272–9.

28. Blair JE, McLeod RS, Cohen Z, Devlin HR. Ticarcillin/clavulanic acid (Timetin) compared to metronidazole/netilmicin in preventing postoperative infection after elective colorectal surgery. *Can J Surg* 1987;**30**:120–3.

29. Brolin J, Lahnborg G, Ljung A, Rietz KA. A comparison between netilmicin with metronidazole and doxycycline as prophylaxis in elective colorectal surgery. *Ann Chir Gynaecol* 1986;**75**:219–24.

30. Burdon DW, Keighley MRB. Ceftriaxone and metronidazole as single-dose prophylaxis in colorectal surgery. *S Afr Med J* 1987;(**suppl**):15–18.

31. Cai CJ. Clinical study of prophylactic use of gentamicin and metronidazole in the surgery of colorectal carcinoma [Chinese]. *Chinese J Surg* 1992;**30**:237–40.

32. Cainzos M, Potel J, Puente JL. Short-term antibiotic prophylaxis in colorectal surgery: a comparative study of gentamicin plus clindamycin vs cefoxitin. *Acta Therapeutica* 1986;**12**:399–412.

33. Cann KJ, Watkins RM, George C, Rayne-James J, Crawfurd E, Rogers TR. A trial of mezlocillin versus cefuroxime with or without metronidazole for the prevention of wound sepsis after biliary and gastrointestinal surgery. *J Hosp Infect* 1988;**12**:207–14.

34. Carr ND, Hobbiss J, Cade D, Schofield PF. Metronidazole in the prevention of wound sepsis after elective colorectal surgery. *J R Coll Surg Edinb* 1984;**29**:139–42.

35. Claesson BEB, Filipsson S, Holmlund DEW, Matzsch TW, Wahlby L. Selective cefuroxime prophylaxis following colorectal surgery based on intra-operative dipslide culture. *Br J Surg* 1986;**73**:953–7.

36. Colizza S, Fazio D, Addari A, Grande R, Cucchiara G. Short-term prophylaxis with cefuroxime in colorectal surgery for cancer. *J Surg Oncol* 1987;**35**:266–8.

37. Coppa GF, Eng K. Factors involved in antibiotic selection in elective colon and rectal surgery. *Surgery* 1988;**104**:853–8.

38. Corman ML, Robertson WG, Lewis TH, Odenheimer DB, Zegarra P, Prager ED. A controlled clinical trial: cefuroxime, metronidazole and cefoxitin as prophylactic therapy for colorectal surgery. *Complications in Surgery* 1993;**20**:37–40.

39. Cuncliffe WJ, Carr N, Schofield PF. Prophylactic metronidazole with and without cefuroxime in elective colorectal surgery. *J R Coll Surg Edinb* 1985;**30**:123–5.

40. Cuthbertson AM, McLeish AR, Penfold JCB, 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.

41. De La Hunt MN, Karran SJ. Sulbactam/ampicillin compared with cefoxitin for chemoprophylaxis in elective colorectal surgery. *Dis Colon Rectum* 1986;**29**:157–9.

42. Desaive C. Utilisation de la ticarcilline et/ou de la gentamicine dans la propylaxie de l'infection en chirurgie recto-colique: etude randomisee [French]. *Acta Therapeutica* 1985;**11**:405–15.

43. Devecioglu S, Tuylu Y, Zissis NP. Piperacillin prophylaxis in colorectal surgery. A randomized comparative evaluation of two dosage schedules. *Saudi Medical Journal* 1990;**11**:385–8.

44. Diamond T, Mulholland CK, Hanna WA, Parks TG. A prospective randomized trial to compare triple dose mezlocillin with triple dose cefuroxime plus metronidazole as prophylaxis in colorectal surgery. *J Hosp Infect* 1988;**12**:215–19.

45. DiPiro JT, Welage LS, Levine BA, Wing PE, Stanfield JA, Gaskill HV, *et al.* Single-dose cefmetazole versus multiple dose cefoxitin for prophylaxis in abdominal surgery. *J Antimicrob Chemother* 1989;**23**:71—7.

46. Fabian TC, Mangiante EC, Boldreghini SJ. Prophylactic antibiotics for elective colorectal surgery or operation for obstruction of the small bowel: a comparison of cefonicid and cefoxitin. *Rev Infect Dis* 1984;**6**:S896–S900.

47. Favre JP, Bouchet Y, Clotteau JE, Hypousteguy L, Marchal G, Mercier R, *et al.* Prophylactic use of cefotaxime in colonic and rectal surgery. *J Antimicrob Chemother* 1984;**14**:247–53.

48. Figueras-Felip J, Basilio-Bonet E, Lara-Eisman F, Fava-Bargallo P, Isamat-Baro E, Rosell-Abaurrea F. Oral is superior to systematic to systematic antibiotic prophylaxis in operations upon the colon and rectum. *Surg Gynecol Obstetr* 1984;**158**:359–62.

49. Fingerhut A, Hay J-M, and the French Association for Surgical Research. Single-dose ceftriaxone, ornidazole and povidone-iodine enema in elective left colectomy. *Arch Surg* 1993;**128**:228–32.

50. Franceshini FD, Mastio A, Manzoli D, Mancini P, Rubbo G, Crescioli R. Short-term antimicrobial prophylaxis in colorectal surgery: ceftriaxone vs aztreonam-clindamicin association in randomized studies [Italian]. *Chirurgia* 1989;**XLII**:229.

51. Garcia JP, Pedroso JC. Ceftriaxone single dose versus ceftazidime multiple doses in the prophylaxis if infection in colorectal surgery. *Eur Surg Res* 1989;**2**:14–18.

52. Gerner T, Nygaard K, Kaaresen R, Mjoerud J, Larsen S, *et al.* Antibiotic prophylaxis in colorectal surgery. *Acta Chir Scand* 1989;**155**:121–4.

53. Gomez-Alonso A, Lozano F, Perez A, Almazan A, Abdel-Lah A, Cuadrado F. Systematic prophylaxis with gentamicin-metronidazole in appendicectomy and colorectal surgery: a prospective controlled clinical study. *Int Surg* 1984;**69**:17–20.

54. Goransson G, Nilsson-Ehle I, Olsson S-A, Petersson BG, Bengmark S. Single versus multiple dose doxycycline prophylaxis in elective colorectal surgery. *Acta Chir Scand* 1984;**150**:245–9.

55. Gortz G, Boese-Landgraf J, Hopfenmuller W, Rodloff A, Kotwas J. Ciprofloxacin as single-dose antibiotic prophylaxis in colorectal surgery. *Diagn Microbiol Infect Dis* 1990;**13**:181–5.

56. Gottrup F, Diederich P, Sorensen K, Nielson SV, Ornsholt J, Brandsborg O. Prophylaxis with whole gut irrigation and antimicrobials in colorectal surgery: a prospective, randomised double-blind clinical trial. *Am J Surg* 1985;**149**:317–22.

57. Greig J, Morran C, Gunn R, Mason B, Sleigh D, McArdle C. Wound sepsis after colorectal surgery: the effect of cefotetan lavage. *Chemioterapion* 1987;**6**:595–6.

58. Grundmann R, Burkardt F, Scholl H, Koelschbach D. One versus three doses of metronidazole/mezlocillin for antibiotic prophylaxis in colon surgery. *Chemioterapia* 1987;**6**:604–5.

59. Hakansson T, Raahave D, Hansen OH, Pedersen T. Effectiveness of single dose prophylaxis with cefotaxime and metronidazole compared with three doses of cefotaxime alone in elective colorectal surgery. *Eur J Surg* 1993;**159**:177–80.

60. Hall JC, Watts JM, O'Brien P, Turnbridge J, McDonald P. Single-dose antibiotic prophylaxis in contaminated abdominal surgery. *Arch Surg* 1989;**124**:224–47.

61. Hall C, Curran F, Burdon DW, Keighley MRB. A randomized trial to compare amoxycillin/clavulanate with metronidazole plus gentamicin in prophylaxis in elective colorectal surgery. *J Antimicrob Chemother* 1989;**24**:195–202.

62. Hall JC, Hall JL, Christiansen K. A comparison of the roles of cefamandole and ceftriaxone in abdominal surgery. *Arch Surg* 1991;**126**:512–16.

63. Haverkorn MJ. Peroperative systematic prophylaxis in colorectal surgery. *Drugs Exp Clin Res* 1985;**X1**:111–14.

64. Hershman MJ, Swift RI, Reilly DT, Logan WA, Sackier JM, Gompertz H, *et al.* Prospective comparative study of cefotetan with piperacillin for prophylaxis against infection in elective colorectal surgery. *J R Coll Surg Edinb* 1990;**35**:29–32.

65. Hinchey EJ, Richards GK, Lewis R, Echave V, Biron JS, Weissglass I. Moxalactam as single-agent prophylaxis in the prevention of wound infection following colon surgery. *Surgery* 1987;**101**:15–19.

66. Hosie KB, Fielding JWL, Alexander-Williams J, Temple JG, Keighley MRB. Ceftizoxime alone or in combination with metronidazole as prophylaxis in elective colorectal surgery. *Drug Invest* 1992;**4**:13–16.

67. Jagelman DG, Fazio VW, Lavery IC, Weakley FL. A prospective, randomised, double-blind study of 10% mannitol mechanical bowel preparation combined with oral neomycin and short-term, perioperative, intravenous Flagyl as prophylaxis in elective colorectal resections. *Surgery* 1985;**98**:861–5.

68. Jagelman DJ, Fabian TC, Nichols RL, Stone HH, Wilson SE, Zellner SR. Single-dose cefotetan versus multiple-dose cefoxitin as prophylaxis in colorectal surgery. *Am J Surg* 1988;**155**:71–6.

69. Jensen LS, Anderson A, Fristrup SC, Holme JB, Hvid HM, Kraglund K, *et al.* Comparison of one dose versus three doses of prophylactic antibiotics and the influence of blood transfusion, on infectious complications in acute and elective colorectal surgery. *Br J Surg* 1990;**77**:513–18.

70. Jones RN, Wojeski WV. Single-dose cephalosporin prophylaxis of 929 surgical procedures in a prepaid group practice: a prospective, randomised comparison of cefoperazone and cefotaxime. *Diagn Microbiol Infect Dis* 1987;**6**:323–34.

71. Jones RN, Wojeski W, Bakke J, Porter C, Searles M. Antibiotic prophylaxis of 1036 patients undergoing elective surgical procedures: a prospective randomized comparative trial of cephazolin, cefoxitin and cefotaxime in a prepaid medical practice. *Am J Surg* 1987;**153**:341–6.

72. Jones RN, Wojeski WV. Single-dose surgical prophylaxis using ticarcillin/clavulanic acid (Timentin): a prospective, randomised comparison with cefotaxime. *Diagn Microbiol Infect Dis* 1987;**7**:219–23.

73. Juul P, Merrild U, Kronborg O. Topical ampicillin in addition to a systematic antibiotic prophylaxis in elective colorectal surgery: a prospective randomised study. *Dis Colon Rectum* 1985;**28**:804–6.

74. Juul P, Klaaborg KE. Single or multiple doses of metronidazole and ampicillin in elective colorectal surgery: a randomised trial. *Dis Colon Rectum* 1987;**30**:526–8.

75. Karran SJ, Sutton G, Gartell P, Karran SE, Finnis D, Blenkinsop J. Imipenem prophylaxis in elective colorectal surgery. *Br J Surg* 1993;**80**:1196–8.

76. Khubchandani IT, Karamchandani MC, Sheets JA, Stasik JJ, Rosen L, Riether RD. Metronidazole versus erythromycin, neomycin and cefazolin in prophylaxis for colonic surgery. *Dis Colon Rectum* 1989;**32**:17–20.

77. Kingston RD, Kiff RS, Duthie JS, Walsh S, Spicer A, Jeacock J. Comparison of two prophylactic single-dose intravenous antibiotic regimens in the treatment of patients undergoing elective colorectal surgery in a district general hospital. *J R Coll Surg Edinb* 1989;**34**:208–11.

78. Kling PA, Homlund D, Burman L. Single-dose intravenous metronidazole v. doxycycline prophylaxis in colorectal surgery. *Acta Chir Scand* 1985;**151**:163–8.

79. Kling P-A, Burman LG. Failure of single-dose metronidazole prophylaxis in colorectal surgery. *Acta Chir Scand* 1988;**154**:305–9.

80. Kling P-A, Dahlgren S. Oral prophylaxis with neomycin and erythromycin in colorectal surgery. *Arch Surg* 1989;**124**:705–7.

81. Kow L, Toouli J, Brookman J, McDonald PJ. Comparison of cefotaxime plus metronidazole versus cefoxitin for prevention of wound infection after abdominal surgery. *World J Surg* 1995;**19**:680–6.

82. Kwok. Amoxycillin and clavulanic acid versus cefotaxime and metronidazole as antibiotic prophylaxis in elective colorectal resectional surgery. *Chemotherapy* 1993;**39**:135–9.

83. Lau WY, Chu KW, Poon GP, Ho K. Prophylactic antibiotics in elective colorectal surgery. *Br J Surg* 1988;**75**:782–5.

84. Lauridsen F, Bjoernsen K, Nielsen SAD, Hansen OH. Short-term prophylaxis with cefotaxime in colorectal surgery: a prospective, randomized trial. *Dis Colon Rectum* 1988;**31**:25–7.

85. Lewis RT, Goodall RG, Marien B, Lloyd-Smith W, Park M, Wiegand FM. Is neomycin necessary for bowel preparation in surgery of the colon? Oral neomycin plus erythromycin versus erythromycin-metronidazole. *Can J Surg* 1989;**32**:265–70.

86. Lindhagen J, Andaker L, Hojer H. Comparison of systematic prophylaxis with metronidazole/placebo and metronidazole/fosfomycin in colorectal surgery. *Acta Chir Scand* 1984;**150**:317–23.

87. Lohde E, Scholz L, Gemperle A, Langmark H, Hopfenmuller W, Abri O, *et al.* Comparative analysis of mezlocillin/metronidazole and amoxicillin/clavulanic acid as 'one-shot' antibiotic prophylaxis in colorectal surgery [German]. *Zentralbl Chir* 1992;**117**:325–30.

88. Lohr J, Wagner PK, Rothmund M. Perioperative antibioticaprophylaxe (Einmal-oder Mehrfachgabe) bei elektiven colorectalen eingriffen [German]. *Chirurg* 1984;**55**:512–14.

89. Lozano F, Alonso AG, Almazan A, Garcia JG, Cuadrado F, Moran MR. A comparison of three different prophylactic parenteral antibiotic regimens of colorectal surgery: a prospective study. *Int Surgery* 1985;**70**:227–31.

90. Luke M, Iversen J, Sondergaard J, Kvist E, Lund P, Andersen F, *et al.* Ceftriaxone versus ampicillin and metronidazole as prophylaxis against infections after clean-contaminated abdominal surgery. *Eur J Surg* 1991;**157**:45–9.

91. Lumley JW, Siu SK, Pillay SP, Stitz R, Kemp RJ, Faoagali J, *et al.* Single dose ceftriaxone as prophylaxis for sepsis in colorectal surgery. *Aust N Z J Surg* 1992;**62**:292–6.

92. Matikainen M, Hiltunen KM. Parenteral single dose ceftriaxone with tinidazole versus aminoglycoside with tinidazole in colorectal surgery: a prospective single-blind randomized multicentre study. *Int J Colorect Dis* 1993;**8**:148–50.

93. McArdle CS, Moran CG, Pettit L, Gemmell CG, Sleigh JD, Tillotson GS. Value of oral antibiotic prophylaxis in colorectal surgery. *Br J Surg* 1995;**82**:1046–8.

94. McCulloch PG, Blamey SL, Finlay IG, Baird A, Sleigh D, Gardner E, *et al.* A prospective comparison of gentamicin and metronidazole and moxalactam in the prevention of septic complications associated with elective operations of the colon and rectum. *Surg Gynecol Obstet* 1986;**162**:521–4.

95. University of Melbourne Colorectal Group. Clinical trial of prophylaxis of wound sepsis in elective colorectal surgery comparing ticarcillin with tinidazole. *Aust N Z J Surg* 1986;**56**:209–13.

96. University of Melbourne Colorectal Group. Systematic Timentin is superior to oral tinidazole for antibiotic prophylaxis in elective colorectal surgery. *Dis Colon Rectum* 1987;**30**:786–9.

97. University of Melbourne Colorectal Group. A comparison of single-dose systematic Timentin with mezlocillin for prophylaxis of wound infection in elective colorectal surgery. *Dis Colon Rectum* 1989;**32**:940–3.

98. Mendel V, Jung D, Heymann H. Single-shot antibiotic prophylaxis in colon surgery. *Chemioterapia* 1987;**6**:597–600.

99. Menzel J, Bauer J, Pritzbuer E, Klempa I. Peripherative anwendung von ampicillin/sulbactam, cefoxitin und piperacillin/metronidazol in der elektiven colon- und rectumchirurgie [German]. *Chirurg* 1993;**64**:649–52.

100. Menzies D, Gilbert JM, Shepherd MJ, Rogers TR. A comparison between amoxycillin/clavulanate and mezlocillin in abdominal surgical prophylaxis. *J Antimicrob Chemother* 1989;**24**:203–8.

101. Mittermayer H, Gross C, Brucke P. Single dose cefuroxime/metronidazole versus metronidazole alone in elective colorectal surgery. *Am Surg* 1984;**50**:418–23.

102. Moesgaard F, Nielsen ML. Failure of topically applied antibiotics, added to systematic prophylaxis, to reduce perineal wound infection in abdomino-perineal excision of the rectum. *Acta Chir Scand* 1988;**154**:589–92.

103. Moesgaard F, Lykkegaard-Nielsen M. Preoperative cell-meditated immunity and duration of antibiotic prophylaxis in relation to postoperative infectious complications. *Acta Chir Scand* 1989;**155**:281–6.

104. Moesgaard F, Nielsen ML, Hjortrup A, Kjersgaard P, Sorensen C, Larsen PN, *et al.* Intraincisional antibiotic in addition to systematic antibiotic treatment fails to reduce wound infection rates in contaminated abdominal surgery. *Dis Colon Rectum* 1989;**32**:36–8.

105. Morris DL, Fabricius PJ, Ambrose NS, Scammell B, Burdon DW, Keighley MRB. *et al.* A high incidence of bleeding is observed in a trial to determine whether addition of metronidazole is needed with latamoxef for prophylaxis in colorectal surgery. *J Hosp Infect* 1984;**5**:398–408.

106. Morris DL, Wilson SR, Pain J, Edwardson KF, Jones J, Strachan C, *et al.* A comparison of aztreonam/metronidazole and cefotaxime/metronidazole in elective colorectal surgery: antimicrobial prophylaxis must include Gram-positive cover. *J Antimicrob Chemother* 1990;**25**:673–8.

107. Morton AL, Taylor EW, Lindsay G, Wells GR. A multicenter study to compare cefotetan alone with cefotetan and metronidazole as prophylaxis against infection in elective colorectal operations. *Surg Gynecol Obstet* 1989;**169**:41–5.

108. Mosimann F, Chamero J. Preventive preoperative antibiotic therapy in elective colon surgery. A controlled prospective randomized study. *Schweiz Med Wochenschr* 1987;**117**:570–3.

109. Mozzillo N, Dionigi R, Ventriglia L. Multicenter study of aztreonam in the prophylaxis of colorectal, gynecologic and urologic surgery. *Azttre: New Dev Curr Perspect Chemother* 1989;**35**:58–71.

110. Nel CJC. Ceftriaxone as prophylaxis for elective abdominal and colorectal surgery. *S Afr J Surg* 1989;(**suppl**):6.

111. Nohr M, Andersen JC, Juul-Jensen KE. Prophylactic single-dose fosfomycin and metronidazole compared with neomycin, bacitracin, metronidazole and ampicillin in elective colorectal operations. *Acta Chir Scand* 1990;**156**:223–30.

112. The Norwegian Study Group for Colorectal Surgery. Should antimicrobial prophylaxis in colorectal surgery include agents effective against both anaerobic and aerobic microorganisms? A double-blind, multicenter study. *Surgery* 1985;**97**:402–7.

113. Nyam DCNK, Yeo M, Cheong D, Goth HS. Antibiotic prophylaxis in colorectal surgery: a randomised, double-blind, controlled trial of amoxycillin-clavulanic acid versus ceftriaxone and metronidazole. *Asian J Surg* 1995;**18**:227–30.

114. Offer C, Weuta H, Bodner E. Efficacy of preoperative with ciprofloxacin or cefazolin in colorectal surgery. *Infection* 1988;**16**:46–7.

115. Pacelli F, Brisinda G, Bellantone R, Doglietto GB, Crucitti F. Single dose imipenem-cilastatin compared with three doses of cefuroxime and metronidazole as prophylaxis in elective colorectal surgery: a prospective randomized study. *J Chemother* 1991;**3**:372–5.

116. Palmer BV, Mannur KR, Ross WB. An observer blind trial of co-amoxiclav versus cefuroxime plus metronidazole in the prevention of postoperative wound infection after general surgery. *J Hosp Infect* 1994;**26**:287–92.

117. Periti P, Mazzei T, Tonelli F. Single-dose cefotetan versus multiple-dose cefoxitin antimicrobial prophylaxis in colorectal surgery: results of a prospective, multicenter, randomised study. *Dis Colon Rectum* 1989;**32**:121–7.

118. Periti P, Tonelli F, Mazzei T, Ficari F, and the Italian Study Group on Antimicrobial Prophylaxis in Abdominal Surgery. Antimicrobial chemo-immunoprophylaxis in colorectal surgery with cefotetan and thymostimulin: prospective controlled multicenter study. *J Chemother* 1993;**5**:37–42.

119. Perrott CAV, Hinder RA, Cassel R, Koornhof HJ, Naude G, Kleinman M, *et al.* Prophylactic antimicrobials in elective colorectal and biliary surgery. *S Afr Med J* 1985;**68**:387–91.

120. Peruzzo L, Savio S, Lalla FD. Systematic versus systematic plus oral chemoprophylaxis in elective colorectal surgery. *Chemioterapia* 1987;**6**:601–2.

121. Petrelli NJ, Conte CC, Herrera L, Stulc J, O'Neill P. A prospective trial of preoperative prophylactic cefamandole in elective colorectal surgery for malignancy. *Dis Colon Rectum* 1988;**31**:427–9.

122. Petropoulos P, Dietrich PY, Ammann J, Ayer G, Buchmann P, Martinoli S. Prophylaxie antibiotique par dose unique pour la chirurgie colo-rectale elective [French]. *Helv Chir Acta* 1985;**52**:703–6.

123. Playforth MJ, Smith GMR, Evans M, Pollock AV. Single-dose intravenous antibiotics for the prophylaxis of abdominal surgical wound infection: a trial of amoxycillin/clavulanate against latamoxef. *Surg Res Comm* 1987;**1**:173–80.

124. Playforth MJ, Smith GMR, Evans M, Pollock AV. Antimicrobial bowel preparation: oral, parenteral or both? *Dis Colon Rectum* 1988;**31**:90–3.

125. Plouffe JF, Perkins RL, Fass RJ, Carey LC, Macynski ME. *et al.* Comparison of the effectiveness of moxalactam and cefazolin in the prevention of infection in patients undergoing abdominal operations. *Diagn Microbiol Infect Dis* 1985;**3**:25–31.

126. Plouffe JF. Cefmetazole versus cefoxitin in prevention of infections after abdominal surgery. *J Antimicrob Chemother* 1989;**23**:85–8.

127. Pollock AV, Evans M, Smith GMR. Preincisional intraparietal Augmentin in abdominal operations. *Ann R Coll Surg Engl* 1989;**71**:97–100.

128. Raahave D, Hesselfeldt P, Pedersen TB. Cefotaxime i.v. versus oral neomycin-erythromycin for prophylaxis of infections after colorectal operations. *World J Surg* 1988;**12**:369–73.

129. Raahave D, Hesselfeldt P, Pedersen T, Zachariassen A, Kann D, Hansen OH. No effect of topical ampicillin prophylaxis in elective operations of the colon or rectum. *Surg Gynecol Obstet* 1989;**168**:112–14.

130. Rangabashyam N, Rathnasami A. Prophylaxis of infection following colorectal surgery. *Infection* 1991;**19**:459–61.

131. Reynolds JR, Jones JA, Evans DF, Hardcastle JD. Do preoperative oral antibiotics influence sepsis rates following elective colorectal surgery in patients receiving perioperative intravenous prophylaxis? *Surg Res Comm* 1989;**7**:71–7.

132. Rodolico G, Puelo S, Blandono G, Russello D, Amoedo C, Latteri F, *et al.* Colorectal surgery: short-term prophylaxis with clindamycin plus aztreonam or gentamicin. *Rev Infect Dis* 1991;**13**:612–15.

133. Roland M. Prophylactic regimens in colorectal surgery: an open, randomised, consecutive trial on metronidazole used alone or in combination with ampicillin or doxycycline. *World J Surg* 1986;**10**:1003–8.

134. Rorbaek-Madsen M, Toftgaard C, Graversen HP, Kristiansen JD, Lauesen N, Randberg FA, *et al.* Cefoxitin for one day versus ampicillin and metronidazole for three days in elective colorectal surgery. *Dis Colon Rectum* 1988;**31**:774–7.

135. Rowe-Jones DC, Peel ALG, Kingston RD, Shaw JFL, Teasdale C, Cole DS. Single dose cefotaxime plus metronidazole versus three dose cefuroxime plus metronidazole as prophylaxis against wound infection in colorectal surgery: multicentre prospective randomised study. *BMJ* 1990;**300**:18–22.

136. Sauven P, Playforth MJ, Smith GMR, Evans M, Pollock AV. Single-dose antibiotic prophylaxis of abdominal surgical wound infection: a trial of preoperative latamoxef against preoperative tetracycline lavage. *J R Soc Med* 1986;**79**:137–41.

137. Schiessel R, Huk I, Wunderlich M, Rotter M, Wewalka G, Schemper M. Postoperative infections in colonic surgery after enteral bacitracin-neomycin-clindamycin or parenteral mezlocillin-oxacillin prophylaxis. *J Hosp Infect* 1984;**5**:289–97.

138. Schoetz DJ, Roberts PL, Murray JJ, Coller JA, Veidenheimer MC. Addition of parenteral cefoxitin to regimen of oral antibiotics for elective colorectal operations. *Ann Surg* 1990;**212**:209–12.

139. Shatney CH. Antibiotic prophylaxis in elective gastro-intestinal tract surgery: a comparison of single-dose pre-operative cefotaxime and multiple-dose cefoxitin. *J Antimicrob Chemother* 1984;**14**:241–5.

140. Skipper D, Karran SJ. A randomized prospective study to compare cefotetan with cefuroxime plus metronidazole as prophylaxis in elective colorectal surgery. *J Hosp Infect* 1992;**21**:72–7.

141. Stellato TA, Danziger LH, Gordon N, Hau T, Hull CC, Zollinger RM, *et al.* Antibiotics in elective colon surgery. *Am Surg* 1990;**56**:251–4.

142. Stewart M, Taylor EW, Lindsay G, and the West of Scotland Surgical Infection Study Group. Infection after colorectal surgery: a randomised trial of prophylaxis with piperacillin versus sulbactam/piperacillin. *J Hosp Infect* 1995;**29**:135–42.

143. Stubbs RS, Griggs NJ, Kelleher JP, Dickinson IK, Moat N, Rimmer DMD. Single dose mezlocillin versus three dose cefuroxime plus metronidazole for the prophylaxis of wound infection after large bowel surgery. *J Hosp Infect* 1987;**9**:285–90.

144. Taylor EW, Lindsay G, and the West of Scotland Surgical Infection Study Group. Selective decontamination of the colon before elective colorectal surgery. *World J Surg* 1994;**18**:926–32.

145. Tehan S, Whittaker J. A multi-centre double-blind prospective study comparing the efficacy and tolerance of Augmentin with the combination of cephradine plus metronidazole as surgical prophylaxis. *Surg Res Comm* 1989;**6**:97–105.

146. Thomas WEG, Cooper MJ, Holt A, Reeves D. Latamoxef: single agent prophylaxis in colorectal surgery. *J Antimicrob Chemother* 1985;**16**:121–8.

147. Tsimoyiannis EC, Paizis JB, Kabbani K, Lekkas ET, Floras GA, Boulis SA. Short-term antibiotic prophylaxis in elective colorectal surgery. *Chemotherapy* 1991;**91**:66–9.

148. Tuchmann V, Breyer S, Ganzinger U. Antibiotic prophylaxis in colorectal surgery, short-term vs one-shot prophylaxis – a multicentre study [German]. *Fortchr Med* 1988;**106**:537–60.

149. Tudor RG, Haynes I, Youngs DJ, Burdon DW, Keighley MRB. Comparison of short-term antibiotic cover with a third-generation cephalosporin against conventional five-day therapy using metronidazole with an aminoglycoside in emergency and complicated colorectal surgery. *Dis Colon Rectum* 1988;**31**:28–32.

150. Utley RJ, Macbeth WAAG. Preoperative cefoxitin: a double-blind prospective study in the prevention of wound infection. *J R Coll Surg Edinb* 1984;**29**:143–6.

151. Walker AJ, Taylor EW, Lindsay G, Dewar EP, and the West of Scotland Surgical Infection Study Group. A multicentre study to compare piperacillin with the combination of netilmicin and metronidazole for prophylaxis in elective colorectal surgery undertaken in district general hospitals. *J Hosp Infect* 1988;**11**:340–8.

152. Weaver M, Burdon DW, Youngs DJ, Keighley MRB. Oral neomycin and erythromycin compared with single-dose systematic metronidazole and ceftriaxone prophylaxis in elective colorectal surgery. *Am J Surg* 1986;**15**:437–41.

153. Weidema WF, Van den Boogaard AEJM, Wesdorp RIC, Van Boven CPA, Greep JM. 24-Hour systematic prophylaxis with gentamicin and metronidazole, or metronidazole alone, in elective colorectal surgery after mechanical bowel preparation with mannitol and whole gut irrigation. *Acta Chir Belg* 1985;**85**:349–53.

154. Wenzel M, Heinrich M, Schmidt C. Peri-operative infection prophylaxis with ornidazole and gentamicin in elective colonic surgery. *Pharmatherapeutica* 1985;**4**:351–5.

155. Wohlfahrt R, Siedek M. Perioperative infection prophylaxis in colon surgery. *Chemioterapia* 1987;**6**:603–5.

156. Zuber M, Durig M, Neff U, Laffer U. Antibiotic prophylaxis in colorectal surgery: cefazolin-ornidazole versus cefazolin-placebo [German]. *Helv Chir Acta* 1989;**56**:211–15.

157. 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. *Am J Med* 1991;**91**:152S–157S.

158. Vegas AA, Jodra VM, Garcia ML. Nosocomial infection in surgery wards: a controlled study of increased duration of hospital stays and direct cost of hospitalisation. *Eur J Epidemiol* 1993;**9**:504–10.

159. Burke J. Current perspective of surgical infection. In: Watts JM, McDonaldson PJ, O'Brien PE, Marshall VR, Finlay-Jones JJ, editors. Infection in surgery: basic and clinical aspects. Edinburgh: Churchill Livingstone, 1981:14–26.

160. Gorbach SL. Antimicrobial prophylaxis for appendectomy and colorectal surgery. *Rev Infect Dis* 1991;**13**:S815–S819.

161. Evans M, Pollock AV. The inadequacy of published random control trials of antibacterial prophylaxis in colorectal surgery. *Dis Colon Rectum* 1987;**30**:743–6.

162. Moher D, Jadad AR, Tugwell R. Assessing the quality of randomised controlled trials. *Int J Technol Assess Health Care* 1996;**12**:195–208.

163. Chalmers TC, Celano P, Sacks HS, Smith H. Bias in treatment assignment in controlled clinical trials. *New Engl J Med* 1983;**309**:1358–61.

164. Schulz KF, Chalmers I, Hayes RJ, Altman D. Empirical evidence of bias. *JAMA* 1995;**273**:408–12.

165. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections. *Am J Infect Control* 1988;**16**:128–40.

166. Hyryla MLJ, Sintonen H. The use of the health services in the management of wound infection. *J Hosp Infect* 1994;**26**:1–14.

167. Altman DG. Practical statistics for medical research. London: Chapman and Hall, 1991:455–60.

168. Classen DC, Evans S, Pestotnik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical wound infection. *New Engl J Med* 1992;**326**:281–6.

169. Danielsen S, Midtvedt T, Giercksky KE. Preventive antibiotics in elective colorectal surgery. *Nord Med* 1989;**104**:247–55.

170. Nichols RL. Surgical infections: prevention and treatment. *Am J Surg* 1996;**172**:68–74.

171. Gold HS, Moellering RC. Antimicrobial drug resistance. *New Engl J Med* 1996;**335**:1445–54.

172. Office of Technology Assessment. Impact of antibiotic-resistant bacteria. OTA-H-629. Washington DC: US Government Printing Office, 1995.

173. Norrby SR. Cost effective prophylaxis of surgical infections. *Pharmacoeconomics* 1996;**10**:129–39.

174. Davey P, Lynch B, Malek M, Byrne D, Thomas P. Cost-effectiveness of single dose cefotaxime plus metronidazole compared with three doses each of cefuroxime plus metronidazole for the prevention of wound infection after colorectal surgery. *J Antimicrob Chemother* 1992;**30**:855–64.

175. Eisenberg J. Clinical economics. A guide to the economic analysis of clinical practices. *JAMA* 1989;**262**:2879–86.

176. Fry DE. Antibiotics in surgery. An overview. *Am J Surg* 1988;**155**:11–15.

177. Scalley RD, Irwin AD, Poduska PJ, Wolff AJ, Cochran RS. Surgical antibiotic prophylaxis, patient morbidity, and cost reduction: a three year study. *Drug Intell Clin Pharm* 1987;**21**:648–52.

178. Scher KS, Bernstein JM, Arenstein GL, Sorensen C. Reducing the cost of surgical prophylaxis. *Am J Surg* 1990;**56**:32–5.

179. Dobrzanski S, Lawley DI, McDermott I, Selby M, Ausobsky JR. The impact of guidelines on peri-operative antibiotic administration. *J Clin Pharm Ther* 1991;**16**:19–24.

180. Evans RS, Pestotnik SL, Burke JP, Gardner RM, Larsen RA, Classen DC. Reducing the duration of prophylactic antibiotic use through computer monitoring of surgical patients. *Drug Intell Clin Pharm* 1990;**24**:351–4.

181. Davey PG, Vacani P, Parker SE, Malek MM. Assessing cost effectiveness of antimicrobial treatment: monotherapy compared with combination therapy. *Eur J Surg* 1994;**573**:67–72.

182. Lim VK, Cheong YM, Suleiman AB. The use of surgical antibiotic prophylaxis in seven Malaysian hospitals. *Southeast Asian J Trop Med Public Health* 1994;**25**:698–701.

183. Delgadillo L, Ramirez R, Cebrecos J, Arnau JM, Laporte JR. The use of antibiotics in surgical prophylaxis. The characteristics and consequences. *Med Clin (Barc)* 1993;**100**:404–6.

184. Kappstein I, Daschner FD. Use of perioperative antibiotic prophylaxis in selected surgical procedures – results of a survey in 889 surgical departments in German hospitals. *Infection* 1991;**19**:391–4.

185. Davey P, Napier A, Barrie H, Dodd T, McMillan J, Ruta D. Audit of surgical prophylaxis in three hospital trusts in Tayside. 1997, unpublished.

186. Janknegt R, Wijnands WJA, Stobberingh E. Antimicrobial prophylaxis in bowel surgery in The Netherlands. *Eur J Clin Microbial Infect* 1994;**13**:596–600.

187. Widdison AL, Pope NRJ, Brown EM. Survey of guidelines for antimicrobial prophylaxis in surgery. *J Hosp Infect* 1993;**25**:199–205.

188. Bloxham CA. Towards evidence-based antibiotic prescribing: a national survey of antibiotic policies [dissertation]. Durham: University of Durham; 1996.

Appendix 1

Medline search strategies

Set	Search
001	Surgical Wound Infection/
002	Postoperative Complications/dt,ec,pc,su
003	exp preoperative care/
004	exp intraoperative care/
005	Premedication/
006	premedication.tw.
007	or/2-6
008	Bacterial Infections/dt,ec,pc,su
009	Infection/dt,ec,pc,su
010	Sepsis/dt,ec,pc,su
011	(bacteri$ adj2 infect$).tw.
012	(wound$ adj2 infect$).tw.
013	(wound$ adj2 contamin$).tw.
014	sepsis.tw.
015	or/8-14
016	exp Anti-Infective Agents/
017	Antibiotics/tu
018	antibiotic$.tw.
019	antimicro$.tw.
020	(antimicro$ adj3 prophyla$).tw.
021	(anti$ adj2 infect$).tw.
022	or/16-21
023	15 or 22
024	7 and 23
025	1 and 22
026	24 or 25
027	randomized controlled trial.pt.
028	(randomized controlled trial$ or randomised controlled trial
029	random allocation/
030	double-blind method/
031	(single adj blind adj method).tw.
032	or/27-31
033	clinical trial.pt.
034	exp clinical trials/
035	(clinical$ adj5 trial$).tw.
036	((singl$ or doubl$ or trebl$ or tripl$) adj5 (blind$ or mask$))
037	placebos/
038	(placebo$ or random$).tw.
039	research design/
040	or/33-39
041	comparative study/
042	exp evaluation studies/
043	follow-up studies/
044	prospective studies/
045	(control$ or prospectiv$ or volunteer$).tw.
046	or/41-45
047	32 or 40 or 46
048	26 and 47
049	(animal not (human and animal)).sh.
050	exp HIV Infections/
051	bone marrow transplantation/
052	or/49-51
053	48 not 52
054	[exp surgery, digestive system (non mesh)/]
055	exp digestive system/su
056	abdomen/su
057	"colon and rectal surgery (specialty)"/
058	anastomosis, surgical/
059	appendectomy.tw.
060	cholecystectomy.tw.
061	choledochostomy.tw.
062	portoenterostomy.tw.
063	sphincterotomy.tw.
064	colectomy.tw.
065	protocolectomy.tw.
066	enterostomy.tw.
067	cecostomy.tw.
068	colostomy.tw.
069	duodenostomy.tw.
070	ileostomy.tw.
071	jejunostomy.tw.
072	esophagectomy.tw.
073	esophagoplasty.tw.
074	esophagostomy.tw.
075	gastrectomy.tw.
076	gastroenterostomy.tw.
077	hepatectomy.tw.
078	fundoplication.tw.
079	peritoneovenous shunt$.tw.
080	(transplant$ and (liver or pancreas)).tw.
081	or/54-80
082	surg$.tw.
083	(digesti$ adj2 system$).tw.
084	biliary$.tw.
085	bilio$.tw.
086	(colon$ or rectum$ or rectal$ or cecum$).tw.
087	gastric$.tw.
088	gastro$.tw.
089	jejunoileal.tw.
090	esophag$.tw.
091	pancrea$.tw.
092	anastomosis$.tw.
093	intestin$.tw.
094	abdomen$.tw.
095	oesophageal$.tw.
096	(stomach$ or liver$).tw.

097 or/83-96
098 82 and 97
099 81 or 98
100 53 and 99
101 100

Appendix 2

Data extraction sheet and field definitions

Field	Data to be entered
Reviewers	Initials of reviewer carrying out data extraction, plus those of reviewer checking
Refs	First author's surname, publication year, e.g. Ahmed, 1987
Copies	State how the article was located, e.g. name the database, handsearching. If an article is to have more than one record, only the first record should list the method of location, for any further records enter Repeat.
Author	All authors
Title	Article title
Journal	Full journal title
PYear	Publication year
Volume	Journal volume
Chapter	Chapter
Page	Page numbers
Place_of_publication	Type of publication (journal article, book, unpublished)
Country	Country of origin
Aim_of_study	Enter the author's aim of the study
Surgical_procedure	Enter colorectal, appendicectomy or biliary
Surgery	Give further details of the procedures used, e.g. elective, emergency
Bowel_prep	Description of bowel preparation procedure
Duration_of _operation	Enter the average (preferably mean) length of operation in minutes
Study_design	Describe the method of randomisation, outcome measurement, etc.
Randomisation	Code for truly randomised (TR), pseudo randomised (PR) or not stated (NS)
Blinding_assessor	Was the person measuring the outcome blind to the antibiotic used? Enter Yes, No or Unsure
Inclusion_exclusion	Enter the inclusion and exclusion criteria used for entering subjects to the trial
Interventions	Give a clear description of the regimens used in each group
Purpose	State the purpose, e.g. single vs. multiple dose same antibiotic, different doses different antibiotics, same doses different antibiotics, different doses extra antibiotics other description

Antibiotic_A **Antibiotic_B** **Antibiotic_C** **Antibiotic_D**	State only the names of the antibiotic used in each regimen, e.g. ampicillin + sulbactam; gentamicin + metronizadole
Dose_A **Dose_B** **Dose_C** **Dose_D**	State the dosage used for each treatment group, e.g. 100 mg × 5; 1.5 g × 1 + 750 mg × 2; (1.5 mg/kg + 500 mg) × 3
Time_A **Time_B** **Time_C** **Time_D**	Enter preop, periop or postop
Route_A **Route_B** **Route_C** **Route_D**	Enter the route of administration, e.g. i.v., p.o.
Duration_A **Duration_B** **Duration_C** **Duration_D**	Enter the duration of administration in hours
Number_A **Number_B** **Number_C** **Number_D**	State the number of patients evaluated for SWI in each treatment group
Blood_tissue_conc	Give details of any blood and tissue concentrations reported
Definition_SWI	Enter the authors definition of SWI
Other_outcomes	Enter other outcomes measured and their definitions if stated
Dur_of_follow-up	Enter duration of follow-up postoperatively in days
Age	Enter the average age of all the subjects undergoing surgery (colorectal, biliary or appendicectomy)
Sex	Enter total male to female (M/F) ratio for the subjects
Underlying_disease	Give details on the underlying diseases of the subjects as a whole
Other_char	Give details of any other characteristics reported
Comparable	State whether the groups were comparable or not

SWI_A **SWI_B** **SWI_C** **SWI_D**	Give the total number of patients with SWIs
***p*_value**	Enter *p*-value if available
Adverse_events	Describe adverse events for each treatment group
Other_results	Give results of other outcomes measured including different subgroups of SWIs and other infections, hospital stay, mortality. Enter total number of patients with any infection.
Withdrawal_rate	Give the numbers withdrawing after randomisation
Withdrawals	Give reasons and group for withdrawals
Cost	State whether cost was discussed in the article, Yes or No
Cost_effect	Give details of costs reported (costs of drugs, or cost implications, e.g. nursing workload, hospital stay)
Conclusion_au	State author's conclusions
Review_comments	Enter any comments on the trial design, statistics used, etc.
Extra1	
Extra2	

If a paper examines more than one type of surgery, the data should be extracted for colorectal only. If relevant data are not available for a particular field enter NA. If, however, a field is not applicable for an article mark it with '~'.

Appendix 3

RCTs of antimicrobial prophylaxis in colorectal surgery (1984–95)

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Aberg, 1984[13] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 10–15 days. Withdrawal: 21%. 2-centres.	Elective colorectal surgery. Cancer patients: 84%. Age: 66. SWI: Swelling and reddening with temperature > 38 °C and no other known cause; or purulent secretion from the wound; or serous secretion yielding pathogenic bacteria on culture.	**Group A:** Metronidazole, 1 g intravenous administration (i.v.) given over 40 min at premedication. A postoperative dose of 500 mg was given in the evening and thereafter the patients received 500 mg every 8 h for 2 days. **Group B:** Doxycycline, 200 mg i.v. at premedication and 100 mg given in the morning of the first 2 postoperative days.	**SWI: 21/81 vs. 16/76.** Mild infection: 21/81 vs. 11/76. Severe infection, purulent lesion: 18/81 vs. 11/76. Suspected abscess: 2/81 vs. 0/76. Abscess: 1/81 vs. 5/76. Bacteraemia: 2/81 vs. 0/76. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Doxycycline was significantly more effective in preventing complications in general, but metronidazole gave better protection against anaerobes.
Aberg, 1991[14] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 4%.* 1-centre.	Elective abdominal surgery.* Cancer patients: NA. Age: NA. SWI: Discharge of pus.	**Group A:** Cefuroxime, 1.5 g i.v. at skin incision and metronidazole, 500 mg i.v. at anaesthesia, with repeated doses of both antibiotics after 8 h and 16 h. **Group B:** Cefuroxime, 1.5 g i.v. at skin incision, plus metronidazole, 500 mg at start of anaesthesia.	**SWI: 1/29 vs. 2/19.** Deep surgical sepsis: 4/29 vs. 2/19. [Adverse event result: NA. Cost information: NA.] **Conclusion:** No significant differences in infection rates were seen in patients undergoing jejunal, ileal or colorectal operation who received either triple- or single-dose cefuroxime plus metronidazole.
AhChong, 1994[15] Randomisation: True. Blind outcome assessment: No. Follow-up: 42 days. Withdrawal: 10%. 1-centre.	Elective colorectal surgery. Cancer patients: 93%. Age: 63 (22–92). SWI: Presence of pus or purulent discharge in the wound, or marked cellulitis or serous discharge with positive bacteriological culture.	**Group A:** Ampicillin plus sulbactam, 1.5 g i.v. preoperatively, followed by two postoperative doses of 750 mg every 8 h. **Group B:** Gentamicin, 1.5 mg/kg body weight plus metronidazole, 500 mg i.v. before the operation, and two postoperative doses every 8 h.	**SWI: 6/63 vs. 7/65.** No intraabdominal abscess in either group. Median hospital stay: 12 vs. 11 days. [Adverse event result: Yes. Cost information: Yes.] **Conclusion:** Prophylactic ampicillin/sulbactam is effective in reducing the risk of wound infection (WI) following colorectal surgery.
Andaker, 1992[16] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 28 days. Withdrawal: 7.5%. 8-centres.	Elective colorectal surgery. Cancer patients: NA. Age: 67 (standard deviation [SD] 14). SWI: Purulent discharge.	**Group A:** Fosfomycin, 8 g plus metronidazole, 1 g i.v. given half an hour before skin incision, and a further 8 g of fosfomycin 8 h later. **Group B:** Doxycycline, 400 mg plus metronidazole, 1 g i.v. half an hour before the skin incision, and placebo 8 h later.	Abdominal WI: 7/259 vs. 16/258. Deep WI: 3/259 vs. 4/258. Septicaemia: 6/259 vs. 3/258. Pneumonia: 13/259 vs. 5/258. Urinary tract infection (UTI): 25/259 vs. 27/258. Death: 5/259 vs. 5/258. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Fosfomycin plus metronidazole is as well tolerated and effective as the combination of doxycycline plus metronidazole in the prevention of infective complications after elective colorectal surgery.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Antonelli, 1985[17] Randomisation: True. Blind outcome assessment: No. Follow-up: 42 days. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: NA. Age: 66 (SD 12). SWI: Purulent discharge or dehiscence.	**Group A:** Cefoxitin, 2 g i.v. 30 min preoperatively, and intraoperatively (operation over 2 h) and then every 8 h for 72 h. **Group B:** Cephalothin, 2 g i.v. 2 h preoperatively, 2 g during surgery, and every 6 h postoperatively for 4 days.	**Overall SWI: 2/40 vs. 9/37.** Abdominal WI: 0/30 vs. 3/30. Perineal WI: 1/6 vs. 2/4. Peritonitis: 0 vs. 2. Septicaemia: 0 vs. 0. Anastomotic leak: 0 vs. 1. Dehiscence: 0 vs. 2. Fistula: 1 vs. 1. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Cefoxitin used during the perioperative and postoperative period is a well-tolerated, simple and effective method of reducing postoperative sepsis.
Armengaud, 1986[18] (French) Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 21 days. Withdrawal: 0%.	Emergency or elective colorectal surgery. Cancer patients: NA from translation. Age: 65. SWI: Not defined.	**Group A:** Cefoxitin, 2 g i.v. (time not stated). **Group B:** Piperacillin, 4 g i.v. (time not stated).	**SWI: 5/30 vs. 2/30** (p = 0.42). [Adverse event result: Yes. Cost information: NA from translation] **Conclusion:** The two antibiotics have equivalent prophylactic effectiveness in colorectal surgery.
Arnaud, 1992[19] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 6%. 19-centres.	Elective colorectal surgery. Cancer patients: 73%. Age: 66 (SD 12). SWI: Primary infections subclassified as minor infections in cases of stitch abscess or wound abscess, and major infections in the case of intraperitoneal abscess, peritonitis, bacteraemia, or septicaemia of intestinal origin.	**Group A:** Amoxycillin/clavulanic acid, 2 g/200 mg as a single 30-min infusion at induction of anaesthesia. If operation lasted over 4 h, a perioperative top-up dose (2 g/200 mg) was given during the 3 h after incision. **Group B:** Cefotetan, 2 g as a single 30-min infusion on the induction of anaesthesia. No further dose when operation lasted over 4 h.	Surgical wound cellulitis: 0/105 vs. 1/103. Surgical wound abscess: 2/105 vs. 4/103. Intraabdominal abscess: 6/105 vs. 3/103. Peritonitis: 1/105 vs. 1/103. Septicaemia: 1/105 vs. 2/103. Bacteraemia: 1/105 vs. 1/103. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Co-amoxiclav and cefotetan have very similar efficacy when used for the prevention of postoperative infection in elective colorectal surgery.
Athanasiadis, 1985[20] (German) Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 6-12 days. Withdrawal: 1%. 1-centre.	Colorectal surgery. Cancer patients: NA from translation. Age: 21–86. SWI: Secondary healing or abscess in the area of the wound, or fever.	**Group A:** Tinidazole, 160 mg i.v. 80 min prior to operation, during anaesthesia. **Group B:** Metronidazole, 500 mg i.v. 2 h preoperatively and then every 8 h over the next 3 days.	**SWI: 0/50 vs. 2/50.** Perineal WI: 1/50 vs. 4/50. [Adverse event result: Yes. Cost information: NA from translation.] **Conclusion:** Prophylactic treatment with tinidazole as a preoperative high and single dose is important for preventing postoperative infection in patients undergoing bowel surgery.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Auger, 1987[21] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 14%. 3-centre.	Elective colorectal surgery. Cancer patients: 76%. Age: 62. SWI: Possibly infected (wound inflamed without discharge or draining culture positive serous discharge); definitely infected (presence of a purulent discharge).	**Group A:** Metronidazole, 1 g i.v. prior to the operation, with two further doses of 500 mg being administered at 8 h and 16 h after the first dose. **Group B:** Erythromycin base, 1 g plus neomycin sulphate, 1 g p.o. at 1 p.m., 2 p.m. and 11 p.m. on the day before operation.	Definite WI: 8/78 vs. 4/55. Possible WI: 5/78 vs. 3/55. Bacteraemia: 3/78 vs. 3/55. UTI: 8/78 vs. 5/55. Chest infection: 4/78 vs. 3/55. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** The parenteral metronidazole, 2 g in divided doses on the day of operation represents a satisfactory and cost-effective alternative to the administration of oral neomycin plus erythromycin for the prevention of postoperative infections in elective operation of the colon.
Bates, 1989[22] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 24%.* 1-centre.	Emergency and elective abdominal surgery. Cancer patients: NA. Age: 54.* SWI: Discharge of pus.	**Group A:** Metronidazole, 500 mg i.v. plus cephazolin, 1 g i.v. intraoperatively, and 6 h and 12 h later. **Group B:** Metronidazole, 500 mg i.v. plus cephazolin, 1 g i.v. preoperatively, and 6 h and 12 h later.	**SWI: 25/116 vs. 24/101.** [Adverse event result: NA. Cost information: NA.] **Conclusion:** This study failed to show any advantage to starting antibiotics preoperatively.
Bates, 1992[23] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 9.5%.* 1-centre.	At risk abdominal surgery.* Cancer patients: NA. Age: 55 (SD 21.7). SWI: Discharge of pus.	**Group A:** Amoxycillin/clavulanic acid (co-amoxiclav), 250 mg/125 mg i.v. at induction of anaesthesia. **Group B:** Amoxycillin/clavulanic acid (co-amoxiclav), 250 mg/125 mg i.v. at induction of anaesthesia, and at 8 h and 16 h later.	**SWI: 23/113 vs. 17/111.** [Adverse event result: NA. Cost information: NA.] **Conclusion:** One dose of a suitable i.v. antibiotic is at least as effective at preventing SWI as multiple doses. However, there may be a risk of overwhelming systemic sepsis in very elderly patients having emergency surgery.
Becker, 1991[24] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 56 days. Withdrawal: 2.5%. 1-centre.	Elective colorectal surgery. Cancer patients: 0%. Age: 33. SWI: Purulent drainage, regardless of culture results or if non-purulent material contained pathogenic bacteria.	**Both groups:** Oral neomycin, 1 g plus erythromycin, 1 g on preoperative day. Cefoxitin, 2 g i.v. before operation and at 6 h and 12 h after the initial dose. **Group A:** Cefoxitin, 1 g i.v. every 6 h for 5 days, beginning 6 h after the fixed postoperative dose. **Group B:** Placebo.	WI: 0/18 vs. 0/22. Intraabdominal infection: 0/18 vs. 0/22. Febrile after postoperative day 2: 5/18 vs. 9/22. Elevated white blood cells 2* preoperative 9/18 vs. 4/22. Elevated creatinine or blood urea nitrogen: 1/18 vs. 0/22. Mean hospital stay: 8.4 vs. 8.7. [Adverse event result: Yes. Cost information: Yes.] **Conclusion:** The overall and antibiotic-related complication rates were similar in both groups, though the incidence of late postoperative ileal pouchitis was significantly greater in patients who received a prolonged postoperative course of intravenous antibiotics.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Bellantone, 1988[25] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 11%. 1-centre.	Elective colorectal surgery. Cancer patients: NA. Age: 65. SWI: Purulent discharge with or without culture of pathogenic micro-organism.	**Group A:** Cefotetan, 2 g i.v. at the time of anaesthesia and two further doses every 12 h. **Group B:** Clindamycin, 600 mg i.v. plus aztreonam, 1 g i.v. at induction of anaesthesia, two further doses every 8 h.	**SWI: 1/32 vs. 0/26.** Subphrenic abscess: 1/32 vs. 0/26. UTI: 0/32 vs. 1/26. Respiratory tract infection: 0/32 vs. 2/26. Postoperative hospital stay: 14.7 vs. 16.2 days. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Cefotetan appears to be as effective as clindamycin plus aztreonam in prophylaxis against infection in elective colorectal surgery.
Bergman, 1987[26] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 1 month. Withdrawal: 14%. 2-centres.	Elective colorectal surgery. Cancer patients: 62%. Age: 62. SWI: Discharge and positive culture.	**Group A:** Doxycycline, 400 mg plus metronidazole, 1.5 g i.v. 0.2–6 h preoperatively. **Group B:** Doxycycline, 400 mg plus placebo.	Superficial WI: 2/135 vs. 12/126. Deep WI: 2/135 vs. 4/126. Septicaemia: 0/135 vs. 4/126. Total septic complications: 4/135 vs. 20/126. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Single-dose administration of a long-acting, broad-spectrum antibiotic, with an effect mainly on aerobes, in combination with an effective antianaerobic agent, lowers the postoperative septic rate in elective colorectal surgery. The combination of doxycycline plus metronidazole is also easy to administer, relatively cheap, and does not cause major adverse events.
Bittner, 1989[27] (German) Randomisation: Not clear. Blind outcome assessment: No. Follow-up: > 30 days. Withdrawal: 0%. 1-centre.	Elective colorectal surgery. Cancer patients: NA from translation. Age: NA SWI: Differentiation was made between superficial infections with little secretion and those with abscess or peritonitis.	**Group A:** Mezlocillin, 4 g plus metronidazole, 500 mg i.v. 20–30 min preoperatively. **Group B:** Mezlocillin, 4 g plus metronidazole, 500 mg i.v. preoperatively, and repeated every 8 h for 2 days.	**SWI: 6/46 vs. 3/44.** UTI: 40.9% vs. 18.6%. [Adverse event result/cost information: NA from translation.] **Conclusion:** The one-shot dose of the antibiotic combination of mezlocillin plus metronidazole for the prophylaxis against wound infections is equivalent to the short-term dose of 48 h.
Blair, 1987[28] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 14 days. Withdrawal: 7%. 1-centre.	Elective colorectal surgery. Cancer patients: 34%. Age: 43 (15–86). SWI: Purulent discharge from the surgical wound or peritoneal cavity.	**Group A:** Ticarcillin/clavulanic acid (Timentin), 3 g/100 mg i.v. infused at induction of anaesthesia. **Group B:** Metronidazole, 500 mg plus netilmicin, 80 mg i.v. infused within 15 min of induction of anaesthesia, then at 8 h and 16 h later.	**SWI: 3/46 vs. 5/46.** Intraabdominal abscess: 1/46 vs. 0/46. UTI: 1/46 vs. 5/46. Fever unknown aetiology: 1/46 vs. 1/46. Anastomotic dehiscence: 1/46 vs. 1/46. Small bowel obstruction: 1/46 vs. 2/46. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Timentin and metronidazole plus netilmicin are equally effective in preventing septic complications after elective colorectal surgery.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Brolin, 1986[29] Randomisation: True. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 10%. 1-centre.	Elective colorectal surgery. Cancer patients: 58%. Age: 67 (18–86). SWI: Pus present in the wound or if a micro-biological culture was positive from a wound which opened spontaneously or was opened by a surgeon when an infection was suspected.	**Group A:** Metronidazole, 500 mg plus netilmicin, 100 mg i.v. on induction of anaesthesia and 8 h and 16 h later. **Group B:** Doxycycline, 200 mg i.v. 4 h preoperatively and then 100 mg daily for 5 days.	**SWI: 4/50 vs. 5/50.** Remote infections: 3/50 vs. 3/50. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** A combination of netilmicin plus metronidazole administered for 1 day reduces the incidence of postoperative WI in colorectal operation at least as well as doxycycline prophylaxis administered for 5 days.
Burdon, 1987[30] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 21–28 days. Withdrawal: 2.5%. 1-centre	Emergency and elective colorectal surgery. Cancer patients: NA. Age: NA. SWI: Wound sepsis was graded as minor or major. Major wound sepsis was defined as the discharge of pus from a wound opening at least 2 cm in length with fever and anorexia.	**Group A:** Ceftriaxone, 2 g plus metronidazole, 1.5 g i.v. at start of operation. **Group B:** Gentamicin, 120 mg plus metronidazole, 1.5 g i.v. at start of operation.	**SWI: 5/59 vs. 14/61.** Abscess: 4/59 vs. 4/61. Patients with sepsis: 8/59 vs. 14/61. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Abdominal wound sepsis occurred in 8.5% of patients in the ceftriaxone group compared with 23% in the gentamicin group ($p < 0.05$). Ceftriaxone results in high serum and tissue levels throughout the entire period of potential wound contamination because of its long half-life.
Cai, 1992[31] (Chinese) Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 0%. 1-centre	Elective radical resection of colorectal cancer. Cancer patients: 100%. Age: 55 (SD 13). SWI: Not defined.	**Group A:** Gentamicin, 80 mg plus metronidazole, 400 mg oral administration (p.o.) every 8 h for 2 days before operation. **Group B:** Gentamicin, 80 mg plus metronidazole, 400 mg p.o. every 8 h for 2 days before the operation, and followed by gentamicin, 80 mg plus metronidazole, 500 mg i.v. at induction of anaesthesia and at 6 h and 12 h later.	**SWI: 0/8 vs. 0/8.** [Adverse event result: NA. Cost information: NA]. **Conclusion:** Effective metronidazole concentrations were found in serum and tissue in both groups but gentamicin was detected only in Group B from intraoperative tissue specimens and blood samples. The short-term preoperative oral medication combined with perioperative i.v. gentamicin and metronidazole prophylaxis appears to be rational.
Cainzos, 1986[32] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 28 days. Withdrawal: 0%. 1-centre.	Elective colorectal surgery. Cancer patients: 72%. Age: 55 (19–82). SWI: Not defined.	**Group A:** Gentamicin, 80 mg plus clindamycin, 600 mg intramuscular administration (i.m.), 1 h preoperatively and 8 h later. **Group B:** Cefoxitin, 2 g i.v. prior to skin incision, then 2 h and 6 h after the first dose.	Abdominal WI: 6/30 vs. 7/30. Perineal WI: 3/6 vs. 10/12. Intraabdominal abscess: 2/30 vs. 2/30. Faecal fistula: 0/30 vs. 1/30. Septicaemia: 0/30 vs. 0/30. Death: 0/30 vs. 0/30. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Cefoxitin had a similar infection rate to that of the combination of gentamicin plus clindamycin, but short-term antibiotic prophylaxis with systemic antibiotics alone has inadequate efficacy.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Cann, 1988[33] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 7%.* 1-centre.	Emergency and elective abdominal surgery. Cancer patients: NA. Age: NA. SWI: Primary – the first discharge from a dry sutured wound being pus; secondary – discharging serum, bile or intestinal contents subsequently becoming contaminated with micro-organisms.	**Group A:** Mezlocillin, 5 g at induction of anaesthesia, plus mezlocillin 2 g every 8 h for 48 h. **Group B:** Cefuroxime, 750 mg plus metronidazole, 500 mg at induction of anaesthesia, and then every 8 h for 72 h.	**SWI: 13/43 vs. 6/52.** Primary major WI: 5/43 vs. 2/52. Primary minor WI: 8/43 vs. 3/52. Secondary major WI: 0/43 vs. 0/52. Secondary minor WI: 0/43 vs. 1/52. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Mezlocillin may be an effective sole prophylactic agent in appendicectomy but not in colorectal surgery. The possible reasons for failure to adequately prevent infection, following colorectal surgery, are discussed.
Carr, 1984[34] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 52 days. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 77%. Age: 65. SWI: Purulent discharge from the main suture line even if culture was negative.	**Group A:** Metronidazole, 500 mg i.v. preoperatively, plus placebo. **Group B:** Metronidazole, 500 mg i.v. preoperatively and at 8 h postoperatively, plus placebo. **Group C:** Metronidazole, 500 mg i.v. preoperatively, and at 8 h and 16 h postoperatively, plus placebo. **Group D:** Metronidazole, 500 mg i.v. preoperatively, and at 8 h, 16 h and 24 h postoperatively.	Abdominal WI: 7/22 vs. 2/21 vs. 4/24 vs. 5/23. Perineal WI: 1/3 vs. 2/6 vs. 2/3 vs. 3/4. Anastomotic dehiscence: 1/22 vs. 3/21 vs. 1/24 vs. 1/23. Deaths: 0/22 vs. 3/21 vs. 2/24 vs. 3/23. Hospital stay mean (SD): 18(7) vs. 21(14) vs. 19(9) vs. 19(15). [Adverse event result: NA. Cost information: NA.] **Conclusion:** Although the number of patients in the present study is the results indicate that the addition of postoperative doses of i.v. small, metronidazole does not reduce the rate of wound sepsis achieved by a single preoperative dose of this antimicrobial agent.
Claesson, 1986[35] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 28 days. Withdrawal: 1%. 1-centre.	Elective colorectal surgery. Cancer patients: 65%. Age: 63 (20–86). SWI: Discharge of pus. Classified as early when found within 10 days after the operation, and otherwise as late. Only primary wound sepsis was recorded.	**All patients:** Metronidazole, 1 g i.v. at induction of anaesthesia and 12 h postoperatively. **Group A:** Additional antibiotic of cefuroxime, 1.5 g i.v. every 8 h for 2 days. **Group B:** No additional antibiotics.	**SWI: 1/36 vs. 8/35.** Deep surgical infections: 2/36 vs. 6/35. Total patients with postoperative infection: 3/36 vs. 14/35. [Adverse event result: NA. Cost information: NA.] **Conclusion:** This study supports the concept that, although metronidazole almost invariably copes with the potential anaerobic pathogens in colonic surgery, this agent should be combined with an antiaerobic drug.
Colizza, 1987[36] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: NA. 1-centre.	Elective surgery. Cancer patients: 88.5%. Age: median 62. SWI: Not defined.	**Group A:** Cefuroxime, 750 mg i.m. preoperatively, 750 mg liquid over the fascia before skin closure, and 750 mg i.v. at the end of the operation, repeated four times every 6 h. **Group B:** Cefuroxime, 750 mg i.v. at the end of the operation, repeated six times every 6 h.	Wound sepsis: 3/26 vs. 6/26. Other sepsis (peritoneal, urinary, pulmonary): 9/26 vs. 3/26. Operative mortality: 2/26 vs. 1/26. [Adverse event result: Yes. Cost imformation: NA] **Conclusion:** Group A treatment produced better control of wound sepsis than Group B, but Group B treatment seemed to afford better protection from other infectious complications.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Coppa, 1988[37] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 0%. 1-centre.	Elective colorectal surgery. Cancer patients: 82%. Age: 63 (21–94). SWI: Suppurated and had positive cultures.	**Group A:** Cefoxitin, 1–2 g i.v. at induction of anaesthesia, intraoperatively, and every 6 h for the first postoperative day. **Group B:** Cefoxitin, as in Group A, plus neomycin, 8 g/day p.o. plus erythromycin base, 4 g/day p.o. in divided doses for 24 h preoperatively.	**SWI:15/141 vs. 9/169.** WI by type of surgery: Rectal resection: 14/62 vs. 7/61; intraperitoneal surgery: 1/79 vs. 2/108. Days of hospitalisation: without infection 132; with infection 27.2 ($p < 0.05$). [Adverse event result: NA. Cost information: Yes.] **Conclusion:** Postoperative WI is associated with length of operation and location of colon resection and can be significantly lowered by a combination of oral and parenteral antibiotics.
Corman, 1993[38] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 12%. 1-centre.	Elective colorectal surgery. Cancer patients: 53%. Age: 66. SWI: An unsatisfactory response was defined in terms of patients with evidence of wound or systemic infections, including chills, sweating, temperature > 38 °C, or purulent drainage, swelling, or erythema at the incision site.	Oral erythromycin plus neomycin were administered the day before surgery. **Group A:** Cefuroxime, 1.5 g plus metronidazole, 500 mg 30–60 min prior to incision. **Group B:** Cefuroxime, 1.5 g 30–60 min prior to incision. **Group C:** Cefoxitin, 2 g 30–60 min prior to incision and every 6 h for three additional doses. **Group D:** Cefoxitin, 2 g 30–60 min prior to incision.	**SWI: 0/30 vs. 3/32 vs. 0/27 vs. 2/31.** Death: 0/30 vs. 2/32 vs. 0/27 vs. 2/31. [Adverse event result: NA. Cost information: Yes.] **Conclusion:** The single-dose combination regimen is as effective in the prevention of postoperative infections associated with colorectal operation as standard therapy with multiple-dose cefoxitin.
Cunliffe, 1985[39] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 10 days. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 67%. Age: 61. SWI: Purulent discharge from the main suture line irrespective of negative bacteriological culture.	**Group A:** Metronidazole, 500 mg i.v. plus cefuroxime, 1.5 g i.v. preoperatively. **Group B:** Metronidazole, 500 mg i.v. preoperatively.	**SWI: 6/40 vs. 10/40.** Deaths: 1/40 vs. 3/40. Hospital stay (SD): 17(8) vs. 19(11). [Adverse event result: NA. Cost information: NA.] **Conclusion:** This study was terminated with 40 patients in each group with no significant difference demonstrated between the two groups. If the trend had persisted, the number of patients required to achieve statistical significance would be in the order of 250–300. It may be that each surgeon should make the decision for antibiotic prophylaxis based on his own experience within the bacteriological environment in their hospital.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Cuthbertson, 1991[40] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 17%. 1-centre.	Elective colorectal surgery. Cancer patients: 82%. Age: 63. SWI: Purulent discharge from the suture line or a non-purulent discharge that contained pathogenic bacteria. Minor WI – localised inflammation with only a serous discharge.	**Group A:** Ticarcillin/clavulanic acid (Timentin), 3.1 g i.v. commenced before skin incision and given over 30 min. **Group B:** Ticarcillin/clavulanic acid (Timentin), 3.1 g i.v. before skin incision and a second dose 2 h after start of operation.	All WI: 16/146 vs. 17/132 (excluding minor WI: 11/146 vs. 13/132). Minor WI only: 6/146 vs. 10/132. Septicaemia: 4/146 vs. 5/132. Intraabdominal abscess: 8/146 vs. 10/132. Perineal WI: 4/9 vs. 4/9. UTI: 24/146 vs. 24/132. Deaths: 4/146 vs. 5/132. [Adverse event result: NA. Cost information: NA.] **Conclusion:** A single dose of intravenous Timentin was as effective as two doses for prophylaxis against surgical infection.
De La Hunt, 1986[41] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 12%. 2-centres.	Elective colorectal surgery. Cancer patients: 72%. Age: 66. SWI: Major wound sepsis – discharge of pus from the wound; minor – non-purulent, bacteriologically positive wound discharge which did not significantly alter management or prolong hospital stay.	**Group A:** Sulbactam, 1 g plus ampicillin, 1 g i.v. four doses every 6 h, commencing at induction of anaesthesia. **Group B:** Cefoxitin, 2 g i.v. four doses, every 6 h, commencing at induction of anaesthesia.	**SWI: 7/44 vs. 9/48.** Major WI: 3/44 vs. 4/48. Minor WI: 4/44 vs. 5/48. Intraabdominal: 2/44 vs. 0/48. Respiratory tract infection: 3/44 vs. 4/48. UTI: 14/44 vs. 16/48. Anastomotic leak/fistula: 2/44 vs. 7/48. Deaths: 1/44 vs. 3/48. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Sulbactam combined with ampicillin was effective in reducing risk from postoperative septic complications.
Desaive, 1985[42] (French) Randomisation: True. Blind outcome assessment: Yes. Follow-up: NA. Withdrawal: 15%. 1-centre.	Emergency and elective colorectal surgery. Cancer patients: NA from translation. Age: 60. SWI: NA from translation.	**Group A:** Gentamicin, 80 mg i.v. at anaesthesia and then t.d.s for 48 h. **Group B:** Gentamicin, 80 mg plus ticarcillin, 5 g i.v. 1 h preoperatively and then t.d.s. for 48 h.	**SWI: 14/26 vs. 3/29** ($p < 0.001$, Fisher's exact test). Minor SWI: 7/26 vs. 2/29. Major SWI: 7/26 vs. 1/29. Perineal WI: 2 vs. 2. Intraperitoneal I: 3 vs. 1. Septicaemia: 1/26 vs. 1/29. Deaths: 5/26 vs. 4/29. [Adverse event result: Yes. Cost information: NA from translation.] **Conclusion:** The combination of gentamicin plus ticarcillin is recommended in emergency or as a complement to oral antibiotics in elective colorectal surgery.
Devecioglu, 1990[43] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 28 days. Withdrawal: NA. 1-centre.	Emergency and elective colorectal surgery. Cancer patients: 70%. Age: 45 (20–81). SWI: Not defined. (Infection at the operative site was determined by clinical evidence, culture results and febrile morbidity [> 38 °C > 24 h].)	**Group A:** Piperacillin, 2 g at the induction of anaesthesia then perioperatively, and every 6 h for two more doses. **Group B:** Piperacillin, 2 g at induction of anaesthesia and perioperatively.	**SWI:2/25 vs. 3/25.** Intraabdominal infection: 1/25 vs. 1/25. UTI: 1/25 vs. 2/25. Pneumonia: 0/25 vs. 1/25. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Patients receiving the four-dose schedule showed a lower incidence of local and remote infection rates, compared with the two-dose piperacillin group.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Diamond, 1988[44] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 42 days. Withdrawal: 7%. 1-centre.	Emergency and elective colorectal surgery. Cancer patients: 70%. Age: 60 (18–92). SWI: Minor – swelling with purulent or bacteriologically positive discharge but no constitutional upset; severe – pus discharged, the patient suffered constitutional symptoms and discharge from hospital was delayed.	**Group A:** Mezlocillin, 5 g at induction of anaesthesia, then 2 g at 8 h and 16 h postoperatively. **Group B:** Cefuroxime, 1.5 g plus metronidazole, 500 mg at induction of anaesthesia, then cefuroxime, 750 mg plus metronidazole, 500 mg at 8 h and 16 h postoperatively.	**SWI:15/51 vs. 10/53.** Severe WI: 5/51 vs. 4/10. Minor WI: 10/51 vs. 6/53. Septicaemia: 2/51 vs. 0/53. Chest infection: 8% vs. 5%. UTI: 27% vs. 25%. [Adverse event result: NA. Cost information: NA.] **Conclusion:** There was no significant difference in antibiotic prophylaxis with mezlocillin monotherapy, compared with combination therapy of cefuroxime plus metronidazole.
DiPiro, 1989[45] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 28 days. Withdrawal: 21%.* 3-centres.	Elective abdominal surgery. Cancer patients: 41%. Age: 54.* SWI: Drained purulent material spontaneously or as a result of incision. If wound drainage was serous it was considered infected if organisms were isolated on culture. A deep space infection was considered to have occurred if there was evidence of intraabdominal abscess or peritonitis.	All colorectal patients: Neomycin, 1 g plus erythromycin, 1 g p.o. at 19 h, 18 h, and 9 h preoperatively. Patients received an additional dose of study drug if operation exceeded 2–4 h. **Group A:** Cefmetazole, 2 g i.v. preoperatively. **Group B:** Cefoxitin, 2 g i.v. preoperatively, and then every 6 h for two doses.	**SWI:1/63 vs. 4/32** (p = 0.042). [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Administration of single-dose cefmetazole is as effective as a standard three-dose regimen of cefoxitin for the prevention of SWIs following abdominal operations.
Fabian, 1984[46] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: NA. Withdrawal: 14%. 1-centre.	Elective colorectal surgery. Cancer patients: 50%. Age: 50 (19–81). SWI: The discharge of pus.	All patients: Neomycin, 1 g plus erythromycin base, 1 g p.o. three times on the day before operation. **Group A:** Cefonicid, 1 g i.v. 0.5–1 h preoperatively and placebo every 6 h thereafter for no more than 24 h. **Group B:** Cefoxitin, 2 g i.v. 0.5–1 h preoperatively and 2 g every 6 h thereafter for no more than 24 h.	**SWI: 2/23 vs. 1/17.** One intraabdominal abscess, no anastomotic dehiscence and no deaths. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Cefonicid offers the advantages associated with the administration of a single daily dose, among which are reduction of pharmacy costs (the final consideration of overall cost can only be addressed when cefonicid enters the market place) and the freeing of nursing hours for patient care.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Favre, 1984[47] Randomisation: True. Blind outcome assessment: No. Follow-up: mean 20 days. Withdrawal: NA. 8-centres.	Elective colorectal surgery. Cancer patients: 73%. Age: 65. SWI: Estimated by combining local wound abscess with abdominal wall discharge. Major as intraabdominal abscess, peritonitis, septicaemia or death related with infection. Minor as local (wound abscess, fistula, purulent discharge at drain site) or extraabdominal (urinary or pulmonary infection, lymphangitis, unexplained fever).	**Group A:** Cefotaxime, 1 g i.v., at premedication, and 1 g with the abdomen open but before any visceral procedure, two more 1 g doses every 4 h. If the operation lasted for more than 3 h an additional injection of 1 g was given 3 h after the second injection. **Group B:** Cefotaxime, as in Group A, plus metronidazole or ornidazole, 1 g i.v. in two injections (500 mg at premedication and 500 mg with the final injection of cefotaxime). **Group C:** Metronidazole, 750 mg/day p.o. for 3 days before operation, plus cefotaxime, as in Group A.	Infection complications, major: 6/74 vs. 4/72 vs. 4/71; minor: 21/74 vs. 23/72 vs. 18/71. Local: 8/74 vs. 11/72 vs. 7/71. Wound abscess: 2/74 vs. 2/72 vs. 5/71. Abdominal wall discharge: 2/74 vs. 3/72 vs. 0/73. Perineal discharge: 3/74 vs. 2/72 vs. 0/71. Antibiotic treatment: 20/74 vs. 19/72 vs. 16/71. Mean hospitalisation (days): 21 vs. 20 vs. 21. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Cefotaxime alone 4 g intraoperatively is useful for the prevention of SWIs during rectal and colonic surgery. The incidence of postoperative sepsis is not changed, when cefotaxime is used in combination with imidazole derivatives.
Figueras-Felip, 1984[48] Randomisation: True. Blind outcome assessment: No. Follow-up: > 7 days. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 78%. Age: 70. SWI: Classified as no signs of sepsis; erythema, swelling or excessive pain or tenderness in wound not opened; wound opened, no pus; and pus visible in wound.	**Group A:** Neomycin, 1 g plus erythromycin, 1 g p.o. 2 h before mannitol (bowel preparation 22 hours before operation), and at 18 h and 10 h preoperatively. **Group B:** Metronidazole, 500 mg plus gentamicin, 80 mg i.v. 2 h preoperatively, and 8 h and 16 h after the first dose.	Erythema, swelling or excessive pain or tenderness in wound not opened: 1/45 vs. 0/48. Wound opened, no pus: 1/45 vs. 6/48. Pus visible in wound: 2/45 vs. 7/48. Pus visible in perineal wound: 7/12 vs. 8/12. Deaths: 1/45 vs. 4/48. [Adverse event result: NA. Cost information: NA.] **Conclusion:** The greater efficacy observed with neomycin plus erythromycin is probably an addition of two effects – the decrease in the colon flora and the adequate serum levels of antibiotics during the operation.
Fingerhut, 1993[49] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 15%. 20-centres.	Elective colorectal surgery. Cancer patients: 74%. Age: 65 (SD 12). SWI: Discharge of pus or inflammation or serous discharge. Peritonitis, anastomotic leakage – diagnosed by fistulography, or found at reoperation or autopsy.	**Group A:** Cefotaxime sodium, 1 g (four injections, total 4 g), plus metronidazole, 500 mg (three injections, total 1.5 g) i.v. for 24 h starting at induction of anaesthesia. **Group B:** Ceftriaxone sodium, 1 g plus ornidazole, 1 g i.v. at induction of anaesthesia.	Wound abscess: 4/102 vs. 6/122. Anastomotic leakage: 4/102 vs. 4/122. Peritonitis: 3/102 vs. 5/122. Deaths: 4/102 vs. 1/122. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Single-dose ceftriaxone plus ornidazole combined with povidone/iodine enemas is an effective regimen against infective complications in elective left colonic operation for carcinoma or diverticular disease. Single-dose antibiotic prophylaxis reduced costs and work for the nursing staff.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Franceshini, 1989[50] (Italian) Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 0%. 1-centre.	Elective colorectal surgery. Cancer patients: NA from translation. Age: NA SWI: Suppuration of wounds, dehiscence of anastomosis, fever > 38 °C beyond 6 days postoperative.	**Group A:** Ceftriaxone, 1 g before anaesthetic. **Group B:** Clindamycin, 0.6 g plus aztreonam, 1 g in the morning and evening before operation, and at anaesthesia and at 8 h and 16 h after first dose.	**SWI: 0/14 vs. 1/18.** [Adverse event result/cost information: NA from translation.] **Conclusion:** There are no significant differences between the two regimens.
Garcia, 1989[51] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: NA. 1-centre.	Elective colorectal. Cancer patients: 50%. Age: 65 (14–89). SWI: Not defined.	**Group A:** Ceftriaxone, 2 g plus metronidazole, 500 mg i.v. at 30 min prior to induction of anaesthesia. **Group B:** Ceftazidime, 2 g plus metronidazole, 500 mg i.v. 30 min prior to induction of anaesthesia, and every 8 h for 24 h.	**SWI: 1/30 vs. 2/30.** Perineal infection: 0 vs. 2. Intraperitoneal: 1 vs. 1 UTI: 1/30 vs. 2/30. Respiratory tract infection: 1/30 vs. 2/30. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Single-dose ceftriaxone plus metronidazole seems to be the ideal combination in the prophylaxis of infection in colorectal operation because it has a long half-life that provides concentrations exceeding the minimum inhibitory concentration for 14–24 h.
Gerner, 1989[52] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 6%. 2-centres.	Elective colorectal surgery. Cancer patients: 74%. Age: 68 (16–89). SWI: Purulent discharge, or fluid discharge yielding positive bacteriological culture.	**Group A:** Doxycycline, 400 mg plus tinidazole, 1.6 g i.v. infusion over 2 h shortly before operation. **Group B:** Doxycycline, 400 mg plus placebo.	**SWI: 3/116 vs. 10/107.** Perineal wound: 2 vs. 7. Intraabdominal abscess: 3 vs. 4. Total infected patients: 8 vs. 20. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Single-dose doxycycline in combination with a nitroamidazole compound lowered the postoperative septic complication rate in colorectal operation more than doxycycline monotherapy. The difference was most marked among the patients who underwent rectal surgery.
Gomez-Alonso, 1984[53] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 21–29 days. Withdrawal: NA. 1-centre.	Emergency and elective appendicectomy and colorectal surgery. Cancer patients: 79%. Age: 61. SWI: Not defined.	**Group A:** Control group did not receive any antibiotics. **Group B:** Gentamicin, 80 mg i.m. plus metronidazole, 500 mg i.v. 2 h preoperatively, then every 8 h for 72 h.	**SWI:13/31 vs. 6/35.** Deaths: 2/31 vs. 1/35. Intraabdominal abscess: 2/31 vs. 0/35. [Adverse event result: NA. Cost information: Yes.] **Conclusion:** The results show the greater effectiveness of the combination gentamicin plus metronidazole compared with the control group with no antibiotics.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Goransson, 1984[54] Randomisation: True. Blind outcome assessment: No. Follow-up: < 30 days. Withdrawal: 12%. 1-centre.	Elective colorectal surgery. Cancer patients: 86%. Age: NA. SWI: Pus or fluid emptied spontaneously or after incision from the wound, or pus recovered from the abdomen at laparotomy, or anastomotic leakage.	**Group A:** Doxycycline, 0.4 g in 1 litre of saline as an infusion completed 2 h preoperatively. **Group B:** Doxycycline, 0.2 g preoperatively as for Group A, then doxycycline, 0.1 g i.v. for 3 days postoperatively.	**SWI: 1/53 vs. 2/49.** Deep abscess: 0/53 vs. 2/49. Anastomotic leakage: 4/53 vs. 1/49. Total number of infections: 5/53 vs. 5/49. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** A single dose of doxycycline preoperatively results in an acceptable rate of postoperative infections, with the associated advantages of one-dose treatment compared with four-dose treatment from practical and economical standpoints.
Gortz, 1990[55] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: NA. Withdrawal: 7.5%. 1-centre.	Elective colorectal surgery. Cancer patients: 70%. Age: NA. SWI: Not defined. (The assessment was based on the clinical appearance; demonstration of pathogens was not required.)	**Group A:** Latamoxef (Moxalactam), 2 g i.v. at induction of anaesthesia. **Group B:** Ciprofloxacin, 200 mg i.v. at induction of anaesthesia plus metronidazole, 500 mg i.v. 2 h preoperatively.	SWI: 1/57 vs. 4/54. UTI: 3/57 vs. 3/54. Pneumonia: 5/57 vs. 1/54. Deaths: 4/57 vs. 1/54. [Adverse event result: Yes. Cost information: Yes.] **Conclusion:** Economic reasons justify the single application of ciprofloxacin, 200 mg or latamoxef, 2 g as perioperative prophylaxis.
Gottrup, 1985[56] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: NA. Withdrawal: 8%. Multi-centre.	Elective colorectal surgery. Cancer patients: 90%. Age: NA. SWI: Superficial accumulation of pus requiring surgical drainage.	**Group A:** Whole gut irrigation alone. **Group B:** Whole gut irrigation plus metronidazole, 500 mg i.v. 30 min preoperatively, then every 8 h for 3 days. **Group C:** Whole gut irrigation plus ampicillin, 1 g plus metronidazole, 500 mg i.v. 30 min preoperatively, then every 8 h for 3 days.	Abdominal WI: 13/41 vs. 10/46 vs. 1/48. Intraabdominal abscess: 5/41 vs. 4/46 vs. 1/48. Perineal WI: 2 vs. 2 vs. 3. Anastomotic leakage: 5/41 vs. 2/46 vs. 2/48. Pneumonia: 3/41 vs. 4/46 vs. 1/48. UTI: 1/41 vs. 1/46 vs. 1/48. Deaths due to infection: 1/41 vs. 1/46 vs. 1/48. Deaths from noninfectious causes within 4 days: 2/41 vs. 0/46 vs. 0/48. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Whole gut irrigation is a rapid, well-tolerated and easily performed method of preoperative bowel preparation in elective colorectal operation if combined with systemic antimicrobial prophylaxis consisting of antimicrobial agents effective against anaerobic and aerobic organisms.
Greig, 1987[57] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: NA. 1-centre.	Emergency and elective colorectal surgery. Cancer patients: NA. Age: NA. SWI: Discharge of pus from the wound.	All patients: Gentamicin, 120 mg plus metronidazole, 500 mg i.v., on induction of anaesthesia. **Group A:** 1 litre of saline lavage. **Group B:** 1 litre of saline containing cefotetan, 1 g at the end of the operative procedure.	**SWI: 18/65 vs. 15/64.** [Adverse event result: NA. Cost information: NA.] **Conclusion:** The results show that cefotetan lavage confers no benefit compared with saline lavage in preventing wound sepsis in patients undergoing colorectal surgery.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Grundmann, 1987[58] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: NA. Age: 59. SWI: Not defined.	**Group A:** Metronidazole, 500 mg plus mezlocillin, 5 g preoperatively. **Group B:** Three times the same combination of antibiotics, at premedication, 1.5 h after skin incision and 6 h later.	**SWI: 4/77 vs. 4/77.** Intraabdominal abscesses: 2.6% vs. 1.3%. Peritonitis: 2.6% vs. 2.6%. Pneumonia: 2.6% vs. 2.6%. Deaths: 2.6% vs. 5.2%. [Adverse event result: NA. Cost information: NA.] **Conclusion:** A single perioperative dose of mezlocillin plus metronidazole is sufficient to reduce the rate of WIs after colon resection. However, there are circumstances where multiple treatment is justified, including long operations and all patients with insufficient preoperative bowel preparation.
Hakansson, 1993[59] Randomisation: True. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 14%. 2-centres.	Elective colorectal surgery. Cancer patients: 71%. Age: 70 (20–97). SWI: Discharge of pus from the wound. Anastomosic leakage – air or faeces discharged through a drain or fistula. Intraabdominal abscess – collection of pus detected by either ultrasound-guided aspiration or spontaneous discharge of pus directly from the peritoneum.	**Group A:** Cefotaxime, 2 g i.v. at induction of anaesthesia, and 3 h and 9 h later. **Group B:** Cefotaxime, 2 g plus metronidazole, 1.5 g i.v. at induction of anaesthesia.	WI: 44/280 vs. 19/287. Anastomotic leakage: 22/241 vs. 8/239. Intraabdominal abscess: 7 vs. 7. Wound dehiscence: 3 vs. 5. [Adverse event result: NA. Cost information: NA.] **Conclusion:** One dose of cefotaxime and metronidazole is active against a wide range of organisms and resulted in significantly fewer wound infections than three doses of cefotaxime alone. It is active against a wide range of aerobes and anaerobes, and has few undesirable effects, as well as being easily administrated and at reasonable cost.
Hall, 1989[60] Randomisation: True. Blind outcome assessment: No. Follow-up: 35 days. Withdrawal: 0.7%.* 2-centres.	Emergency and elective abdominal surgery. Cancer patients: NA. Age: NA. SWI: Purulent wound discharge or a serous wound discharge with culture of pathogenic organisms. A WI was classified as major if it resulted in an extension of the hospital stay or required dressings at home for more than 7 days.	**Group A:** Latamoxef (Moxalactam), 1 g i.v. at induction of anaesthesia. **Group B:** Latamoxef, 1 g i.v. at induction of anaesthesia, then every 6 h for a further seven doses.	**SWI: 12/119 vs. 10/126.** SWI-elective: 11/102 vs. 6/105. SWI-emergency: 1/17 vs. 4/21. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** A single dose of latamoxef is as effective as a 48-hour course when attempting to prevent infection after contaminated abdominal surgery.
Hall, 1989[61] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: > 30 days. Withdrawal: 10%. 1-centre.	Elective colorectal surgery. Cancer patients: 37%. Age: 57 (18–92). SWI: Pus in a surgical wound with or without constitutional disturbance such as fever, dehiscence, foul smell or prolonged hospital stay.	**Group A:** Amoxycillin/clavulanic acid, 1 g/200 mg (co-amoxiclav, 1.2 g) immediately before operation, and 2 h later. **Group B:** Gentamicin, 120 mg immediately before operation and 2 h later, plus one preoperative dose of metronidazole, 1.5 g.	Abdominal WI: 16/116 vs. 18/121. Perineal WI: 13/48 vs. 8/44. An abscess: 15/182 vs. 10/177. Septicaemia: 2/182 vs. 2/177. Patients with infected site: 41/182 vs. 32/177. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Our previous studies have demonstrated that cephalosporins alone, without metronidazole provide insufficient protection against the obligate anaerobes. It may also be true for amoxycillin/clavulanic acid.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Hall, 1991[62] Randomisation: True. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 4%.* 1-centre.	Elective abdominal operation (laparotomy).* Cancer patients: NA. Age: 56 (14–98).* SWI: Purulent or serous wound discharge with culture of pathogenic organisms.	**Group A:** Ceftriaxone, 1 g plus metronidazole, 500 mg i.v. after induction of anaesthesia. **Group B:** Cefamandole, 1 g plus metronidazole, 500 mg i.v. after induction of anaesthesia.	**SWI:4/56 vs. 6/75.** [Adverse event result: Yes. Cost information: Yes.] **Conclusion:** Single-dose prophylaxis with 1 g of cefamandole naftate and sodium carbonate was relatively inexpensive and provided a cost saving of 64%. When treatment was required, a 23% cost saving was associated with the use of a once-daily dose of 1 g of ceftriaxone sodium.
Haverkorn, 1985[63] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: > 10 days. Withdrawal: 28%. Multi-centre.	Elective colorectal surgery. Cancer patients: NA. Age: NA. SWI: Not defined.	All patients: Started treatment after the induction of anaesthesia, then at 8 h and 16 h later. **Group A:** Metronidazole, 500 mg i.v. followed immediately by netilmicin, 100 mg i.v. three doses. **Group B:** Metronidazole, 500 mg i.v. followed immediately by cefuroxime, 1.5 g i.v. three doses. **Group C:** Metronidazole, 500 mg i.v. followed immediately by saline i.v. three doses.	**SWI: 0/12 vs. 0/13 vs. 3/11.** Local infectious complications: 1/12 vs. 0/13 vs. 4/11. Distant infectious complication: 2/12 vs. 1/13 vs. 4/11. [Adverse event result: NA. Cost information: NA.] **Conclusion:** A short course of preoperative systemic prophylaxis with metronidazole plus netilmicin or cefuroxime, without the use of oral non-absorbable antimicrobials, gave acceptable results in the centres studied.
Hershman, 1990[64] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 42 days. Withdrawal: 9%. 2-centre.	Elective colorectal surgery. Cancer patients: 77%. Age: 61 (SD 17). SWI: Presence of an abscess or discharging pus from the wound. This definition excluded erythema or serous discharge.	**Group A:** Cefotetan, 2 g i.v. at induction of anaesthesia. **Group B:** Piperacillin, 2 g i.v. three doses commencing at induction of anaesthesia.	Abdominal WI: 14/75 vs. 13/78. Perineal WI: 4 vs. 2. Drain site infection: 2/75 vs. 3/78. Intraabdominal infection: 4/74 vs. 5/78. Chest infection: 12/75 vs. 15/78. UTI: 11/75 vs. 9/78. Other infections: 0/75 vs. 1/78. Septic deaths: 1/75 vs. 2/78. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Single-dose antibiotic prophylaxis is as effective as multiple-dose regimens. Cefotetan appears to be a well-tolerated and effective antibiotic treatment.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Hinchey, 1987[65] Randomisation: True. Blind outcome assessment: Yes. Follow-up: > 21 days. Withdrawal: 4%. 3-centres.	Elective colorectal surgery. Cancer patients: NA. Age: 67. SWI: Inflammation and induration with the discharge of pus, irrespective of culture results.	**Group A:** Latamoxef (Moxalactam), 2 g i.v. 1 h preoperatively and at 4 h and 8 h after the first dose. **Group B:** Neomycin, 1 g orally t.d.s. on the day before operation plus metronidazole, 1 g i.v. 1 h preoperatively followed by 500 mg at 8 h and 16 h after the first dose.	Abdominal WI: 5/64 vs. 3/67. Perineal WI: 0/64 vs. 1/67. UTI: 7/64 vs. 8/67. Pneumonia: 0/64 vs. 2/67. Anastomotic leak: 1/64 vs. 1/67. [Adverse event result: NA. Cost information: NA.] **Conclusion:** A single agent systemic antibiotic (latamoxef) when used prophylactically in patients undergoing colon operation was associated with a WI rate comparable to that achieved by a combination of oral neomycin plus intravenous metronidazole. The data obtained demonstrated that the reduced infection rate was not the result of a reduction in the bacterial content of the colon alone but due to the prophylactic agents used for elective colon surgery.
Hosie, 1992[66] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 42 days. Withdrawal: 13%. 1-centre.	Elective colorectal surgery. Cancer patients: NA. Age: 59 (16–96). SWI: Discharged pus. Minor – superficial pus in the incision; major – wound dehiscence, or associated with intraabdominal or pelvic abscess and/or systemic disturbance.	**Group A:** Ceftizoxime, 2 g plus metronidazole, 500 mg i.v. infusion at induction of anaesthesia. **Group B:** Ceftizoxime, 2 g plus placebo i.v. infusion at induction of anaesthesia. Both groups received a second dose of ceftizoxime 2 h later.	WI: 7/89 vs. 9/85. UTI: 8/89 vs. 7/85. Chest infection: 7/89 vs. 4/85. Pyrexia: 3/89 vs. 5/85. Hospital stay: 12/89 vs. 11/85 days. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Intravenous ceftizoxime offers effective prophylaxis in colorectal operation and may be used without metronidazole.
Jagelman, 1985[67] Randomisation: True. Blind outcome assessment: No. Follow-up: 28 days. Withdrawal: 22%. 1-centre.	Elective colorectal surgery. Cancer patients: 43%. Age: 50 (14–89). SWI: Passage or isolation of pus with a positive culture in the postoperative follow-up period.	Both groups received oral neomycin 1 g every 3 h with a total of 3 g given to all patients. **Group A:** Metronidazole, 15 mg/kg (≈ 1 g) i.v. 1 h preoperatively, then 7.5 mg/kg (≈ 0.5 g) 6 h and 12 h later. **Group B:** Placebo three times as for Group A.	Septic complication: 0/31 vs. 8/37. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** One-day mechanical bowel preparation with 10% mannitol combined with oral neomycin and short-term, perioperative, intravenous metronidazole is a well-tolerated, effective, and inexpensive method for reducing the septic complications of elective colorectal resections.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Jagelman, 1988[68] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 17%. 6-centres.	Elective colorectal surgery. Cancer patients: 32%. Age: NA. SWI: 0 – no erythema or discharge; 1 – cellulitis with or without minimal purulent exudate; 2 – cellutlitis with moderate purulent exudate; and 3 – infection throughout wound or intraabdominal abscess.	**Group A:** Cefotetan, 2 g i.v. 30–60 min before initial incision. **Group B:** Cefoxitin, 2 g i.v. 30–60 min before initial incision, then 2 g every 6 h for no more than 24 h postoperatvely.	WI, wound grade 0: 139/164 vs. 63/75; wound grade 1: 17 vs. 10; wound grade 2: 5 vs. 1; wound grade 3: 3 vs. 0. Major WI: 14 vs. 6. Minor WI: 9 vs. 2. Intraabdominal abscess: 2 vs. 0. Peritoneal infection: 1 vs. 0. Stitch abscess: 2 vs. 0. UTI: 4 vs. 2. Pneumonia: 1 vs. 1. Febrile morbidity: 2 vs. 0. Atelectasis: 1 vs. 1. Length of hospital stay: 9.6 vs. 9.2 days. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** A single preoperative dose of cefotetan, 2 g was as well-tolerated and effective as multiple doses of cefoxitin in the reduction of postoperative WIs after colorectal surgery.
Jensen, 1990[69] Randomisation: True. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 8%. 4-centres.	Emergency and elective colorectal surgery. Cancer patients: 77%. Age: 65 (18–90). SWI: Accumulation of pus, either with spontaneous discharge or requiring surgical drainage.	**Group A:** Cefuroxime, 3 g plus metronidazole, 1.5 g i.v. after induction of anaesthesia. **Group B:** Ampicillin, 3 g plus metronidazole, 1.5 g i.v. after induction of anaesthesia. **Group C:** Ampicillin, 1 g plus metronidazole, 500 mg i.v. after induction of anaesthesia and 8 h and 16 h later.	Emergency patients: SW 1/16 vs. 6/11 vs. 4/12. Elective patients: SWI 7/91 vs. 8/89 vs. 8/92. (Note: for elective patients, SWI was estimated according to authors' statement that no difference between groups) [Adverse event result: Yes. Cost information: NA.] **Conclusion:** One single preoperative dose of antibiotic prophylaxis in acute and elective colorectal operation is sufficient. The likelihood of developing infectious complications after colorectal operation is related to the use of blood transfusion.
Jones, 1987[70] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 13%.* 1-centre.	Elective surgical procedures requiring prophylactic antibiotics (abdominal, obstetrics/gynaecology, orthopaedic). Cancer patients: NA. Age: 52 (18–92).* SWI: Presence of purulent material drained from the surgical incision or the peritoneal cavity, regardless of bacteriological or laboratory investigation.	**Group A:** Cefoperazone, 1 g as a slow i.v. bolus injection after induction of anaesthesia. **Group B:** Cefotaxime 1 g as slow i.v. bolus injection after induction of anaesthesia. An additional 1 g was administered intraoperatively if the procedure lasted longer than two drug serum half-lives or approximately 2 h.	**SWI: 2/23 vs. 1/24.** [Adverse event result: Yes. Cost information: Yes.] **Conclusion:** Cefoperazone can also be used as a single-dose prophylactic antibiotic for nearly all elective surgical procedures, though its application as a single dose for colorectal operation is uncertain.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in yeras) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Jones, 1987[71] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 33%.* 2-centres.	Elective surgical procedures requiring prophylactic antibiotics (abdominal, obstetrics/gynaecology, orthopaedic). Cancer patients: NA. Age: 54 (18–96).* SWI: Presence of purulent material drained from the surgical incision or the peritoneal cavity, regardless of bacteriological or laboratory investigation.	Intraluminal antimicrobials such as neomycin or erythromycin were used in all colorectal operations. **Group A:** Cephazolin, 1 g i.v. on arrival in the operating room, and 1 g every 8 h for 24 h. **Group B:** Cefoxitin, 2 g i.v. on arrival in the operating room, and 2 g every 6 h for 24 h. **Group C:** Cefotaxime, 1 g i.v. on arrival in the operating room. If operation lasted longer than 2 h, one additional dose of 1 g was administered intraoperatively for patients receiving cephazolin or cefotaxime.	**SWI: 1/35 vs. 1/36 vs. 4/29** (A + B vs. C, $p = 0.057$). [Adverse event result: Yes. Cost information: Yes.] **Conclusion:** A single-dose prophylactic cephalosporin can be used for all indicated surgical procedures in our practice with the exception of colorectal resections.
Jones, 1987[72] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 12%.* 1-centre.	Elective surgical procedures requiring prophylactic antibiotics (abdominal, obstetrics/gynaecology, orthopaedic). Cancer patients: NA. Age: 51 (18–92).* SWI: Purulence at the wound site.	**Group A:** Ticarcillin/clavulanic acid (Timentin), 3.1 g i.v. slow bolus injection upon induction of anaesthesia. **Group B:** Cefotaxime, 1 g i.v. at induction of anaesthesia, then three further doses postoperatively.	**SWI:0/11 vs. 1/8.** [Adverse event result: Yes. Cost information: Yes.] **Conclusion:** The beta-lactam inhibitor combination reported herein should be considered along with other newer beta-lactamases for use as a cost-effective, single-dose surgical prophylactic agent on a wide variety of operative procedures.
Juul, 1985[73] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 3–6 months. Withdrawal: 7%. 1-centre.	Elective colorectal surgery. Cancer patients: 83%. Age: 69. SWI: Deep WI defined as accumulation of pus requiring surgical drainage.	All patients: Ampicillin, 1 g plus metronidazole, 500 mg i.v. t.d.s. from induction of anaesthesia for at least 3 days. **Group A:** Subcutaneous and subfascial application of 1 g of ampicillin in 10 ml of saline in each of the surgical wounds. **Group B:** No further prophylactic antibiotic treatment.	Deep WI: 5/105 vs. 5/98. Dehiscence: 7/105 vs. 4/98. Hernia: 10/105 vs. 3/98. Deaths (without infection): 12/105 vs. 8/98. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Topical ampicillin should be omitted in elective colorectal operation when a perioperative systemic prophylaxis with ampicillin and metronidazole is used.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Juul, 1987[74] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 5%. 1-centre.	Elective colorectal surgery. Cancer patients: 68%. Age: 65. SWI: Accumulation of pus either with spontaneous discharge or requiring surgical drainage.	All patients: Metronidazole, 1.5 g plus ampicillin, 3 g i.v. during induction of anaesthesia and operation. **Group A:** Received no further antibiotic treatment. **Group B:** Metronidazole, 500 mg plus ampicillin 1 g i.v. t.d.s. for the second and third postoperative days.	Deep WI: 9/149 vs. 8/145. Wound dehiscence: 4/149 vs. 3/145. Anastomotic leakage: 4/149 vs. 5/145. Intraabdominal abscess: 1/149 vs. 2/145. Septicaemia: 1/149 vs. 0/145. Pneumonia: 16/149 vs. 8/145. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Single preoperative dose of metronidazole and ampicillin is at least as effective as a 3-day course for reducing septic complications following elective colorectal surgery.
Karran, 1993[75] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 42–56 days. Withdrawal: 15%. 1-centre.	Elective colorectal surgery. Cancer patients: 77%. Age: 68. SWI: If purulent discharge from the wound occurred, a positive bacteriological culture was obtained, or a deep abscess developed at the site of operation.	**Group A:** Imipenem, 1 g i.v. at induction of anaesthesia with a further dose 3 h after operation. **Group B:** Imipenen, 1 g i.v. at induction of anaesthesia and 3 h postoperatively, then a further two doses (500 mg) at 8 h and 16 h. **Group C:** Cefuroxime, 1.5 g plus metronidazole, 500 mg i.v. at induction of anaesthesia, then further doses of cefuroxime, 0.75 g plus metronidazole, 500 mg at 8 h and 16 h postoperatively.	Abdominal WI: 23/113 vs. 22/114 vs. 17/122. Perineal WI: 7/113 vs. 3/114 vs. 6/122. Intrapelvic abscess: 2/113 vs. 2/114 vs. 4/122. Intraabdominal abscess: 2/113 vs. 1/114 vs. 3/122. Discharging drain: 8/113 vs. 8/114 vs. 10/122. Peritonitis: 0/113 vs. 1/114 vs. 1/122. Septicaemia: 2/113 vs. 2/114 vs. 6/122. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Both regimens of imipenem provided equivalent protection to that afforded by the triple-dose therapy of cefuroxime plus metronidazole. There were no obvious differences between the two imipenem regimens in the proportion of patients developing a postoperative infection, type of infection or duration of hospital stay, thus supporting the use of a short-course prophylaxis in non-contaminated patients undergoing elective colorectal surgery.
Khubchandani, 1989[76] Randomisation: True. Blind outcome assessment: No. Follow-up: 7 days. Withdrawal: 34%. 1-centre.	Elective and non-obstructive colon surgery. Cancer patients: NA. Age: NA. SWI: Exhibited redness, induration, or discharge of pus.	**Group A:** Neomycin, 1 g plus erythromycin, 1 g p.o. at 1 p.m. 2 p.m. and 11 p.m. the day before operation, plus cephazolin, 1 g i.v. 1 h preoperatively. and at 6 h and 12 h postoperatively. **Group B:** Metronidazole, 1 g i.v. 1 h preoperatively, and 500 mg i.v. at 6 h and 12 h postoperatively.	**SWI: 4/55 vs. 14/47.** Wound cellulitis: 1/55 vs. 1/47. Anastomotic leak: 1/55 vs. 1/47. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Single-dose antibiotic prophylaxis with metronidazole is not effective in reducing WIs. A combination of drugs directed against both aerobes and anaerobes in required to effectively reduce the infection rate to acceptable range.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Kingston, 1989[77] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 6 weeks. Withdrawal: 5%. 1-centre.	Elective colorectal surgery. Cancer patients: 63%. Age: 65 (SD 13.5). SWI: Purulent discharge. A major infection was a discharge associated with pain and/or pyrexia and positive bacteriology.	**Group A:** Latamoxef (Moxalactam), 1 g i.v. at induction of anaesthesia. **Group B:** Cefuroxime, 1 g plus metronidazole, 500 mg i.v. at induction of anaesthesia.	**SWI:32/121 vs. 27/108.** Minor WI: 26/121 vs. 19/108. Major WI: 6/121 vs. 8/108. Deaths: 9/121 vs. 12/108. Hospital stay (median) 13 vs. 15 days. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Both current regimens evaluated are simple, well tolerated, require no nursing time and are effective prophylactics against major WI in over 96% of cases.
Kling, 1985[78] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: > 28 days. Withdrawal: 11%. 1-centre.	Elective and emergency surgery. Cancer patients: 50%. Age: mean 59. SWI: Visible pus.	**Group A:** Metronidazole, 1 g i.v. over 30 min, 3–4 h preoperatively. **Group B:** Doxycycline, 0.2 g i.v. over 30 min, 3–4 h preoperatively. (Note: Nine patients in each group received antibiotics for prolonged periods.)	Superficial WI: for all patients 2/52 vs. 12/67; for elective operation 2/50 vs. 11/64. Deaths: 3/52 vs. 2/67. Anastomotic dehiscence: 0/52 vs. 1/67. Pneumonia: 1/52 vs. 0/67. UTI: 4/52 vs. 0/67. [Adverse event result: Yes. Cost information: NA]. **Conclusion:** The prophylactic effect of a single intravenous dose (1 g) of metronidazole was better than that of a standard intravenous loading dose (0.2 g) of doxycycline.
Kling, 1988[79] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 42 days. Withdrawal: 14%. 1-centre.	Elective colorectal. Cancer patients: 57%. Age: 62 (21–95). SWI: Discharge of pus either spontaneously or by debridement.	**Group A:** Metronidazole, 1 g i.v. at induction of anaesthesia. **Group B:** Metronidazole, 3 g i.v. at induction of anaesthesia. **Group C:** Metronidazole, 1 g plus nalidixic acid, 3 g slow infusion, at induction of anaesthesia.	**SWI: 14/39 vs. 9/31 vs. 13/33.** UTI: 7/39 vs. 3/31 vs. 2/33. Chest infection: 1/39 vs. 1/31 vs. 1/33. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Addition of nalidixic acid to metronidazole reduced neither the incidence of Gram-negative aerobic infection nor the total surgical infection rate. A 3 g dose of metronidazole was not superior to a 1 g dose of metronidazole.
Kling, 1989[80] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 14%. 1-centre.	Elective surgery. Cancer patients: 100%. Age: Mean 67 (44–81). SWI: The discharge of pus.	**Group A:** Neomycin sulfate, 1 g plus erythromycin base, 1 g p.o. at 1 p.m., 2 p.m. and 11 p.m. on the day before operation. **Group B:** Metronidazole, 1.5 g plus ceftriaxone, 2 g i.v. at induction of anesthesia.	Perineal WI: 1/27 vs. 2/27. No septicemia. UTI: 5/27 vs. 0/27. [Adverse event result: NA. Cost information: NA] **Conclusion:** No signficant difference was observed between regimens. Better and larger trials are needed to determine the efficacy of antimicrobial prophylaxis.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Kow, 1995[81] Randomisation: True. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 32%.* 2-centres.	Emergency and elective abdominal surgery.* Cancer patients: NA. Age: 54 (15–93). SWI: Presence of purulent discharge from the wound or a serous discharge with a positive culture of pathogenic organisms.	**Group A:** Cefoxitin, 2 g i.v. at induction of anaesthesia. **Group B:** Cefotaxime, 1 g plus metronidazole, 500 mg at induction of anaesthesia. **Group C:** Cefoxitin, 2 g at induction of anaesthesia then at 6 h and 12 h postoperatively. **Group D:** Cefotaxime, 1 g plus metronidazole, 500 mg at induction of anaesthesia followed by two more doses of cefotaxime at 6 h and 12 h postoperatively.	Elective colorectal surgery: WI: 8/65 vs. 5/71 vs. 8/70 vs. 7/67. Emergency colorectal surgery: WI: 2/8 vs. 2/13 vs. 0/11 vs. 2/14. [Adverse event result: Yes. Cost information: Yes.] **Conclusion:** A single dose of cefotaxime plus metronidazole administered preoperatively is effective in reducing postoperative infection and is as good as other commonly used regimens. Further improvements in reducing infective complications may require changes in surgical technique and other measures to reduce the potential bacterial contamination.
Kwok, 1993[82] Randomisation: True. Blind outcome assessment: Yes. Follow-up: > 28. Withdrawal: 7%. 1-centre.	Elective colorectal surgery. Cancer patients: 94%. Age: 61 (25–94). SWI: Pus discharge from the surgical wound or pus accumulation in the wound that required drainage. Serous discharge with positive bacteriological culture and marked cellulitis that warranted systemic antibiotic treatment were also taken as definite infection.	**Group A:** Co-amoxiclav, 1.2 g i.v. on call to the operating theatre, and two more doses postoperatively every 8 h. **Group B:** Cefotaxime, 500 mg plus metronidazole, 500 mg as an i.v. infusion over 15 min on call to the operating theatre, and two more doses postoperatively every 8 h.	WI only: 6/76 vs. 7/88. Deep infection only: 1/76 vs. 1/88. Wound and deep infection: 1/76 vs. 1/88. [Adverse event result: NA. Cost information: Yes.] **Conclusion:** Both co-amoxiclav and the combination of cefotaxime plus metronidazole offer the same degree of protection against postoperative infection. The use of co-amoxiclav is recommended because of its easier use and lower cost.
Lau, 1988[83] Randomisation: True. Blind outcome assessment: Yes. Follow-up: > 30 days. Withdrawal: 4%. 1-centre.	Elective colorectal surgery. Cancer patients: 100%. Age: 64 (SD 14). SWI: Purulent discharge. Wounds with serous discharge which gave positive bacteriological cultures and wounds with serous discharge after the patients had returned home so that cultures could not be taken were also included in the infected group.	**Group A:** Neomycin, 1 g plus erythromycin, 1 g p.o. at 1 p.m., 2 p.m., and 11 p.m. on the day before operation. **Group B:** Metronidazole, 500 mg plus gentamicin, 2 mg/kg body weight i.v. over half an hour before operation. **Group C:** Both p.o. and i.v. antibiotics as in Group A and Group B.	Abdominal WI, major: 13/62 vs. 4/67 vs. 3/65; minor: 1/62 vs. 1/67 vs. 0/65. Perineal WI, major: 4/62 vs. 2/67 vs. 2/65; minor: 0/62 vs. 0/67 vs. 1/65. Intraperitoneal abscess: 3/62 vs. 2/67 vs. 2/65. Patients with complications: 17/62 vs. 8/67 vs. 8/65. Hospital stay (mean): 14 vs. 12 vs. 12 days. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** There is no additional advantage of combining oral and systemic antibiotics. We recommend systemic metronidazole and gentamicin to be used with mechanical bowel preparation in elective colorectal surgery.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Lauridsen, 1988[84] Randomisation: True. Blind outcome assessment: Yes. Follow-up: NA. Withdrawal: 9%. 1-centre.	Elective colorectal surgery. Cancer patients: 82%. Age: 73 (44–91). SWI: Superficial accumulation of pus requiring surgical drainage.	**Group A:** Penicillin, 2 ml, IU, i.m. plus streptomycin, 500 mg i.m. in the evening before surgery, then penicillin t.d.s. for 6 days and streptomycin twice daily (b.d.) for 4 days. **Group B:** Cefotaxime, 2 g i.v. at the induction of anaesthesia and at 3 h and 6 h later. If the wound was heavily contaminated, metronidazole was given t.d.s. for 3 days in both groups.	WI: 1/48 vs. 0/52. Wound rupture: 1/48 vs. 1/52. Anastomosis: 4/48 vs. 4/52. Additional metronidazole: 11/48 vs. 8/52. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Short-term prophylaxis with cefotaxime is as effective as long-term prophylaxis with penicillin plus streptomycin.
Lewis, 1989[85] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 5%. 1-centre.	Elective colorectal surgery. Cancer patients: 69%. Age: 68. SWI: Pus drained from the wound; a sample of the discharge was then obtained for culture.	**Group A:** Erythromycin base, 1 g plus neomycin sulfate, 1 g p.o. at 1 p.m., 2 p.m. and 11 p.m. on the day before operation. **Group B:** Erythromycin base, as in Group A, plus metronidazole, 750 mg p.o. t.d.s. for 2 days before operation.	**SWI: 7/61 vs. 2/64.** Anastomotic leak: 1/61 vs. 2/64. Intraabdominal abscess: 0/61 vs. 1/64. Bloodstream infection: 1/61 vs. 0/64. Total sepsis: 7/61 vs. 3/64. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Oral neomycin is not necessary for antibiotic preparation of the colon when adequate prophylaxis against anaerobic bacteria is provided.
Lindhagen, 1984[86] Randomisation: True. Blind outcome assessment: Yes. Follow-up: > 28 days. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 84%. Age: NA. SWI: Discharge of pus, classified as major if the patient was ill and as minor when symptoms were only trivial and local.	Prophylactic treatment began 1–1.5 h before operation. All patients: metronidazole, 500 mg i.v. infused over 20 min. After operation it was repeated three times every 8 h. **Group A:** 5.5% glucose solution, 100 ml was given immediately after each metronidazole infusion. **Group B:** Fosfomycin, 2 g in 100 ml 5.5% glucose was given i.v. after each of the four metronidazole doses.	Abdominal WI: 6/23 vs. 0/26 (p = 0.007, Fisher's exact test). Perineal WI: 2/23 vs. 0/26. Intraabdominal abscess: 1/23 vs. 0/26. Patients with septic complications: 8/23 vs. 0/26. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Monoprophylaxis with systemic metronidazole is inadequate in preventing aerobic septic complications after elective colorectal surgery, but short-term combined prophylactic therapy with systemic metronidazole plus fosfomycin is an efficacious regimen.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Lohde, 1992[87] (German) Randomisation: True. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 31%.	Colorectal surgery. Cancer patients: NA from translation. Age: NA. SWI: Not defined.	**Group A:** Mezlocillin, 5 g plus metronidazole, 500 mg one short i.v. during anaesthesia. **Group B:** Amoxycillin/clavulanic acid, 2 g/0.2 g one short i.v. during anaesthesia.	**SWI: 9/59 vs. 6/52.** [Adverse event result/cost information: NA from translation.] **Conclusion:** This study is not able to prove a significant difference between the two groups.
Lohr, 1984[88] (German) Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: NA from translation. Age: 62. SWI: Not defined.	**Group A:** Cefotaxime, 3 g i.v. with anaesthesia. **Group B:** Cefotaxime, 3 g i.v. with anaesthesia, and 2 g 8 h and 16 h later.	**SWI: 4/30 vs. 3/30.** Perineal WI: 1/30 vs. 1/30. UTI: 10/30 vs. 7/30. [Adverse event result/cost information: NA from translation.] **Conclusion:** Single-dose prophylaxis is as efficient as multiple dose application to reduce postoperative infections in elective colorectal surgery.
Lozano, 1985[89] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 28 days. Withdrawal: NA. 1-centre.	Emergency and elective colorectal surgery. Cancer patients: 82%. Age: 60. SWI: A positive culture of any discharge from the wound.	**Group A:** Gentamicin, 80 mg plus lincomycin, 600 mg i.m. 2 h preoperatively, and every 8 h postoperatively for 3 days. **Group B:** Gentamicin, 80 mg plus clindamycin, 600 mg i.m. 2 h preoperatively, and every 8 h postoperatively for 3 days. **Group C:** Gentamicin, 80 mg plus metronidazole, 500 mg 2 h preoperatively, and every 8 h postoperatively for 3 days.	Abdominal WI: 3/30 vs. 4/30 vs. 1/30. Perineal WI: 1/4 vs. 0/2 vs. 2/3. Intraabdominal abscess: 0/30 vs. 1/30 vs. 0/30. Sepsis: None. Pneumonia: None. Patients with infection: 4/30 vs. 5/30 vs. 3/30. Anastomotic fistulas: 1/17 vs. 2/15 vs. 0/14. [Adverse event result: Yes. Cost information: Yes.] **Conclusion:** Although not statistically significant the present study showed the combination, gentamicin plus metronidazole (Group C) to have both clinical and socioeconomic advantages, compared with the other combinations and this superiority was associated with metronidazole and its effectiveness against anaerobic bacteria.
Luke, 1991[90] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 28 days. Withdrawal: 7%.* 1-centre.	Emergency and elective abdominal surgery* (clean-contaminated laparotomy). Cancer patients: NA. Age: 51 (1–96). SWI: Cicatricial infection, rupture or cleavage of the skin with discharge of pus.	**Group A:** Ceftriaxone, 1 g i.v. at induction of anaesthesia. **Group B:** Ampicillin, 2 g plus metronidazole, 1.5 g i.v. at induction of anaesthesia.	Elective colon surgery: Wound related infection: 4/32 vs. 5/36. Acute colon surgery: Wound related infection: 1/6 vs. 1/5. [Adverse event result: NA. Cost information: Yes.] **Conclusion:** Ceftriaxone seems to be more efficient than ampicillin plus metronidazole as prophylaxis against incisional WI (1.4% vs. 4.5%, $p < 0.05$, for all patients*), but should preferably by supplemented with an antianaerobic agent to prevent deep WIs. (For patients undergoing colorectal surgery, no difference was observed in SWIs between the ceftriaxone and the ampicillin plus metronidazole group.)

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Lumley, 1992[91] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 30. Withdrawal: 0%. 1-centre.	Emergency and elective colorectal surgery. Cancer patients: 50%. Age: 56. SWI: Presence of erythema accompanied by deep or superficial pus.	**Group A:** Ceftriaxone, 2 g i.v. plus metronidazole 1 g suppository on call to operating theatre. **Group B:** Ceftriaxone, 2 g i.v. plus glycerol suppository on call to theatre. **Group C:** Cephazolin, 1 g i.v. plus metronidazole, 1 g suppository on call to theatre.	WI: 7/90 vs. 8/94 vs. 7/96. Respiratory tract infection: 4/90 vs. 1/94 vs. 9/96. UTI: 4/90 vs. 5/94 vs. 14/96. Deaths: 0/90 vs. 0/94 vs. 5/96. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Ceftriaxone is as effective as cephazolin and metronidazole in preventing WIs following colorectal surgery. The study also demonstrated a reduced rate of postoperative urinary and respiratory tract infections in those patients who received ceftriaxone in comparison with cephazolin.
Matikainen, 1993[92] Randomisation: True. Blind outcome assessment: Yes. Follow-up: Mean 28 days. Withdrawal: 21%. 7-centres.	Elective colorectal surgery. Cancer patients: 65%. Age: 63 (15–92). SWI: Suppuration of the wound or positive bacterial culture of the wound.	**Group A:** Ceftriaxone, 2 g plus tinidazole, 500 mg i.v. at induction of anaesthesia. **Group B:** Netilmicin, 150 mg or tobramycin, 80 mg (aminoglycosides) plus tinidazole, 500 mg i.v. during induction of anaesthesia.	WI: 8/315 vs. 38/313. Other infection: 24/315 vs. 33/313. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Single-dose ceftriaxone was shown to be significantly more efficient in reducing WI rate in elective colorectal operation compared with the aminoglycosides when both were combined with tinidazole.
McArdle, 1995[93] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 28 days. Withdrawal: 4%. 1-centre.	Emergency and elective colorectal surgery. Cancer patients: 43%. Age: 62. SWI: Presence of pus either discharging spontaneously or requiring drainage. Major wound sepsis – the discharge of pus with constitutional disturbance; minor wound sepsis – patients with cellulitis and a positive wound culture.	**Group A:** Gentamicin, 120 mg plus metronidazole, 500 mg i.v. at induction of anaesthesia. Further doses of gentamicin, 80 mg and metronidazole, 500 mg at 8 h and 16 h postoperatively. **Group B:** Ciprofloxacin, 1 g p.o. 1 h preoperatively plus metronidazole, 500 mg i.v. at induction of anaesthesia. Further doses of metronidazole, 500 mg i.v. at 8 h and 16 h postoperatively. **Group C:** Gentamicin, 120 mg plus metronidazole, 500 mg i.v. at induction of anaesthesia. Further doses of gentamicin, 80 mg t.d.s. and metronidazole, 500 mg t.d.s. for 3 days. **Group D:** Ciprofloxacin, 1 g p.o. 1 h preoperatively plus metronidazole, 500 mg i.v. at the induction of anaesthesia. Then p.o. ciprofloxacin, 750 mg p.o. b.d. and metronidazole, 500 mg i.v. t.d.s. for 3 days.	Total WI: 13/45 vs. 4/40 vs. 7/42 vs. 4/42. Major WI: 4/45 vs. 2/40 vs. 3/42 vs. 0/42; minor WI: 9/45 vs. 2/40 vs. 4/42 vs. 4/42. Chest infection: 12/45 vs. 2/40 vs. 8/42 vs. 3/42. UTI: 2/45 vs. 1/40 vs. 1/42 vs. 2/42. Deaths: 3/45 vs. 1/40 vs. 2/42 vs. 1/42. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Oral ciprofloxacin for prophylaxis may offer advantages in efficacy and ease of administration compared with parenteral antibiotics.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
McCulloch, 1986[94] Randomisation: True. Blind outcome assessment: Yes. Follow-up: NA. Withdrawal: 8%. 1-centre.	Elective colorectal surgery. Cancer patients: 67%. Age: 60. SWI: Discharge of pus, either spontaneously or on expression from the wound.	**Group A:** Metronidazole, 500 mg plus gentamicin, 120 mg i.v. at induction of anaesthesia, and at 8 h and 16 h after operation. **Group B:** Latamoxef (Moxalactam), 1 g i.v. at induction of anaesthesia, and at 8 h and 16 h after surgery. Dosages were reduced by one-third in patients who were more than 80 years old and in those weighing less than 50 kg.	WI: 6/45 vs. 5/41. Intraabdominal abscess: 1/45 vs. 1/41. Fistula: 1/45 vs. 3/41. Septicaemia: 2/45 vs. 1/41. Chest infection: 6/45 vs. 7/41. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Latamoxef is as effective as conventional two-drug antibiotic combinations in preventing septic complications after colorectal operations.
Melbourne study, 1986[95] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 15%. 7-centres.	Elective colorectal surgery. Cancer patients: NA. Age: 66. SWI: Presence of pus or recovery of bacteria of pathogenic potential from a wound exudate.	**Group A:** Ticarcillin, 3 g i.v. before skin incision, and at 2 h after the first dose. **Group B:** Tinidazole, 2 g p.o. at 10 p.m. on the night before operation.	**SWI: 10/125 vs. 24/121.** Mortality: 1.5% vs. 9.2%. Anastomotic leakage: 8.6% vs. 7.3%. Intraabdominal abscess: 3.8% vs. 1.5%. Postoperative antibiotics: 8.6% vs. 22%. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** The WI rate was 8% in those patients receiving ticarcillin prophylaxis and 20% in those receiving tinidazole ($p < 0.05$). The mortality was 1.5% and 9.2% ($p < 0.05$), respectively.
Melbourne study, 1987[96] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 13%. 7-centres.	Elective colorectal surgery. Cancer patients: NA. Age: 64. SWI: Purulent discharge that contained pathogenic bacteria.	**Group A:** Ticarcillin/clavulanic acid (Timentin), 3.1 g i.v. before skin incision and 2 h later. **Group B:** Tinidazole, 2 g p.o. at 10 p.m. on the night before the operation.	Abdominal WI: 2/83 vs. 12/84. Perineal WI: 2/6 vs. 1/8. Intraabdominal abscess: 0/87 vs. 4/90. Septicaemia: 0/87 vs. 3/90. UTI: 11/87 vs. 23/90. Death within 30 days: 3/87 vs. 8/90. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Because of the statistically significant increase in postoperative WI in patients receiving tinidazole prophylaxis alone, it is no longer ethical to deny patients undergoing elective colorectal operation antibiotic prophylaxis effective against both aerobic and anaerobic bowel flora.
Melbourne study, 1989[97] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 15%. 7-centres.	Elective colorectal surgery. Cancer patients: 81%. Age: 65. SWI: Purulent discharge from the suture line or non-purulent discharge that contained pathogenic bacteria.	**Group A:** Ticarcillin/clavulanic acid (Timentin), 3.1 g i.v. before skin incision and completed after 30 min. **Group B:** Mezlocillin, 2 g i.v. before skin incision and completed after 30 min.	**SWI:9/85 vs. 9/93.** Anastomotic breakdown: 2/73 vs. 4/80. [Adverse event result: NA. Cost information: NA.] **Conclusion:** There were no clinical or statistically significant differences between the two regimens. A controlled trial comparing single-dose with double-dose Timentin prophylaxis is necessary to determine whether there is an advantage of prolonged prophylaxis when this agent is used.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Mendel, 1987[98] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: NA. Age: 63. SWI: Not defined.	**Group A:** Ceftizoxime, 2 g. **Group B:** Mezlocillin, 5 g.	Minor WI: 0/47 vs. 1/53; Serious WI: 0/47 vs. 1/53; Pulmonary infection: 4/47 vs. 2/53; UTI: 7/47 vs. 1/53. Mortality: 0/47 vs. 0/53; Relaparotomy: 1/47 vs. 0/53; Anastomotic leak: 0/47 vs. 1/53. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Single prophylactic dose is as efficient as multiple applications. However, a mechanical bowel preparation is likely to succeed only if the mechanical bowel preparation and the surgical technique are of a high standard.
Mendel, 1987[98] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: NA. Age: 63. SWI: Not defined.	**Group A:** Mezlocillin, 5 g plus metronidazole, 500 mg. **Group B:** Mezlocillin, 5 g plus metronidazole, 500 mg t.d.s. for 3 days.	Minor WI: 0/54 vs. 0/46; Serious WI: 2/54 vs. 1/46; Pulmonary infection: 1/54 vs. 0/46; UTI: 9/54 vs. 7/46. Mortality: 0/54 vs. 0/46; Relaparotomy: 3/54 vs. 1/46; Anastomotic leak: none. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Single prophylactic dose is as efficient as multiple applications. However, a mechanical bowel preparation is likely to succeed only if the mechanical bowel preparation and the surgical technique are of a high standard.
Mendel, 1987[98] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: NA. Age: 63. SWI: Not defined.	**Group A:** Cefotaxime, 2 g. **Group B:** Mezlocillin, 5 g.	Minor WI: 0/52 vs. 1/48; Serious WI: 3/52 vs. 2/48; Pulmonary infection: 1/52 vs. 2/48; UTI: 6/52 vs. 5/48; Relaparotomy: 2/52 vs. 0/48; Anastomotic leak: 1/52 vs. 0/48. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Single prophylactic dose is as efficient as multiple applications. However, a mechanical bowel preparation is likely to succeed only if the mechanical bowel preparation and the surgical technique are of a high standard.
Mendel, 1987[98] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: NA. Age: 63. SWI: Not defined.	**Group A:** Latamoxef, 2 g. **Group B:** Mezlocillin, 5 g plus metronidazole, 500 mg t.d.s. for 3 days.	Minor WI: 0/63 vs. 1/57. Serious WI: 2/63 vs. 2/57. Pulmonary infection: 3/63 vs. 2/57. UTI: 9/63 vs. 8/57. Relaparotomy: 0/63 vs. 1/57. Anastomotic leak: 0/63 vs. 1/57. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Single prophylactic dose is as efficient as multiple applications. However, a mechanical bowel preparation is likely to succeed only if the mechanical bowel preparation and the surgical technique are of a high standard.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Menzel, 1993[99] (German) Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 4%.	Elective colorectal surgery. Cancer patients: NA from the translation. Age: NA. SWI: Definition set out by Centre for Disease Control (details NA).	**Group A:** Ampicillin, 2 g plus sulbactam, 1 g i.v. on anaesthesia, and a further two doses every 6–8 h. **Group B:** Cefoxitin, 2 g i.v. on anaesthesia, and a further two doses every 6–8 h. **Group C:** Piperacillin, 4 g plus metronidazole, 500 mg on anaesthesia, and a further two doses every 6–8 h.	**SWI: 10/142 vs. 12/126 vs. 12/137.** [Adverse event result/cost information: NA from translation.] **Conclusion:** All three treatment regimens have equal efficacy.
Menzies, 1989[100] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 14%.* 2-centres.	Emergency and elective abdominal surgery. Cancer patients: NA. Age: 67 (18–88).* SWI: WI, no infection; stitch infection; superficial infection; deep infection.	**Group A:** Co-amoxiclav, 1.2 g at induction of anaesthesia, and 8 h and 16 h postoperatively. **Group B:** Mezlocillin, 5 g at induction of anaesthesia, and 8 h and 16 h postoperatively.	**SWI: 4/30 vs. 4/39.** [Adverse event result: Yes. Cost information: NA.] **Conclusion:** The efficacy of co-amoxiclav is comparable with that of mezlocillin, though the appearance of several deep WIs caused by organisms sensitive to co-amoxiclav, despite its prophylactic administration, is cause for concern.
Mittermayer, 1984[101] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 21 days. Withdrawal: 9%. 1-centre.	Elective colorectal surgery. Cancer patients: 68%. Age: 59. SWI: Purulent discharge only. Moderate – pus with constitutional upset (fever > 37.4 °C and/or leucocytosis); severe – requiring active surgical interventions.	Drugs were administered as a single dose at the induction of anaesthesia. Metronidazole was infused over 20 min and cefuroxime was given as an i.v. injection. **Group A:** Cefuroxime, 1.5 g plus metronidazole, 500 mg. **Group B:** Metronidazole, 500 mg.	All WI: 3/27 vs. 7/33. Primary WI: 1/27 vs. 6/33. Secondary WI: 2/27 vs. 1/33. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Single-dose antibiotic prophylaxis is effective in reducing primary WIs in elective colorectal surgery. An appropriate antibiotic regimen must be directed against both aerobic and anaerobic organisms. The use of cefuroxime plus metronidazole in combination can be considered to be an appropriate regimen effective in the prevention of postoperative infection.
Moesgaard, 1988[102] Randomisation: True. Blind outcome assessment: No. Follow-up: 90 days. Withdrawal: 17%. 1-centre.	Elective colorectal surgery. Cancer patients: 63%. Age: 58 (17–83). SWI: Presence of pus, either discharging spontaneously or requiring drainage.	All patients: Metronidazole, 500 mg plus gentamicin, 80 mg at induction of anaesthesia, then every 8 h for 2 days. **Group A:** Local injection of 80 ml metronidazole (500 mg/100 ml) and 2 ml gentamicin (80 mg/ml) into the muscular and subcutaneous layer of the perineal wound, during and after closure of that wound. **Group B:** No locally injected antibiotics.	Abdominal WI: 5/41 vs. 4/38. Perineal WI: 19/41 vs. 18/38. Intraabdominal abscess: 1/41 vs. 1/41. Septicaemia: 2/41 vs. 0/41. Death from septic: 1/41 vs. 0/41. [Adverse event result: NA. Cost information: NA.] **Conclusion:** The risk of perineal WI cannot be further reduced by topical use of antibiotics if optimal systemic antibiotic prophylaxis is given.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Moesgaard, 1989[103] Randomisation: True. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 9%.* 1-centre.	Elective abdominal surgery. Cancer patients: 47%. Age: 63 (18–86). SWI: Presence of pus, either discharging spontaneously or requiring drainage.	**Group A:** Gentamicin, 80 mg plus metronidazole, 500 mg i.v. at start of operation and 6 h later. **Group B:** Gentamicin, 80 mg plus metronidazole, 500 mg i.v. at start of operation and every 8 h for 2 days.	**SWI: 22/209 vs. 23/219.** Intraabdominal abscess: 6/209 vs. 8/219. Septicaemia: 10/209 vs. 9/219. Death: 10/209 vs. 9/219. [Adverse event result: NA. Cost information: NA.] **Conclusion:** There is no significant difference in septic complications or mortality rates following short-term vs. long-term prophylaxis.
Moesgaard, 1989[104] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 2%.* 3-centres.	Elective abdominal surgery. Cancer patients: 28%. Age: 57 (13–95). SWI: Accumulation of pus, draining spontaneously or after opening the wound.	All patients: Cefotaxime, 2 g i.v. plus metronidazole, 500 mg i.v. pre- or intraoperatively, then every 8 h for 3 days. **Group A:** Cefotaxime, 2 g applied topically to the subcutaneous layer at the time of wound closure. **Group B:** No intraincisional antibiotic.	**SWI: 2/21 vs. 4/19.** [Adverse event result: NA. Cost information: NA.] **Conclusion:** Intraincisional antibiotics as an addition to systemic administration do not reduce WI rates in contaminated abdominal surgery.
Morris, 1984[105] Randomisation: True. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 7%. 1-centre.	Elective colorectal surgery. Cancer patients: NA. Age: NA. SWI: Major – fever, purulent discharge from the wound with erythema and necrotic slough; minor – no surrounding erythema, slough or constitutional disturbance.	All patients: Latamoxef sodium, 2 g i.v. at the start of the operation and repeated 4 h after first dose. **Group A:** No additional antibiotics. **Group B:** Metronidazole, either 500 mg or 1.5 g, in single or divided doses.	N: 53 vs. 56. Abdominal WI: 11/53 vs. 13/56. Minor WI: 6/53 vs. 12/56. Major: 5/53 vs. 1/56. Sepsis at drain site: 1/53 vs. 0/56. Sepsis at colostomy site: 1/53 vs. 0/56. Perineal sepsis: 7/16 vs. 5/15. Major: 6/16 vs. 4/15. Minor: 1/16 vs. 1/15. Abscess: 0/53 vs. 2/56. Septicaemia: 0/53 vs. 1/56. Anastomotic dehiscence: 4/24 vs. 6/25. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Sepsis rates with latamoxef alone are the same as when it is combined with metronidazole in elective colorectal surgery. However due to treatment-related bleeding, even short-term latamoxef can no longer be advised in colorectal surgery.
Morris, 1990[106] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 8%. 3-centres.	Elective colorectal surgery. Cancer patients: NA. Age: NA. SWI: 1 – the discharge of pus; 2 – the presence of a serous discharge with the isolation of pathogenic bacteria from the culture; 3 – abnormal erythema and induration requiring drainage and antibiotic therapy.	**Group A:** Aztreonam, 1 g i.v. plus metronidazole, 500 mg i.v. at induction of anaesthesia followed by two more doses every 8 h. **Group B:** Cefotaxime, 1 g plus metronidazole, 500 mg i.v. at induction of anaesthesia followed by two more doses every 8 h.	SWI: 23/71 vs. 9/70. Intraabdominal abscess: 6/71 vs. 1/70. Anastomotic leak: 6/71 vs. 1/70. Drain infection: 8/71 vs. 6/70. Chest infection: 17/71 vs. 6/70. UTI: 17/71 vs. 11/70. Deaths: 5/71 vs. 6/70. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Any antibacterial combination chosen for prophylaxis in colorectal operation must include adequate cover against Gram-positive organisms.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Morton, 1989[107] Randomisation: True. Blind outcome assessment: No. Follow-up: 42 days. Withdrawal: 14%. 8-centres.	Elective colorectal surgery. Cancer patients: NA. Age: 64. SWI: Discharge of pus from the wound, wound dehiscence or the discharge of serous fluid from which organisms were isolated on bacterial culture. Operation-related infection was defined as wound, intraabdominal or pelvic sepsis, septicaemia or any infection specifically related to the colorectal operation.	**Group A:** Cefotetan, 2 g i.v. at induction of anaesthesia and at 12 h postoperatively. **Group B:** Cefotetan, 2 g at induction of anaesthesia and at 12 h postoperatively plus metronidazole, 500 mg by slow i.v. infusion at induction of anaesthesia and at 8 h and 16 h postoperatively.	**SWI: 39/278 vs. 34/253.** Wound dehiscence: 7/278 vs. 12/253. Septicaemia: 3/278 vs. 3/253. Intraabdominal sepsis: 7/278 vs. 3/253. Deaths: 8/278 vs. 3/253. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Cefotetan given alone is as effective as the combination of cefotetan plus metronidazole for prophylaxis against operation-related infection in elective colorectal operations.
Mosimann, 1987[108] (French) Randomisation: True. Blind outcome assessment: No. Follow-up: > 28 days. Withdrawal: 9%. 1-centre.	Elective colonic surgery. Cancer patients: 50%. Age (mean): 66.2. SWI: Not defined.	**Group A:** Cefoxitin, 2 g i.v. 0.5–1 h before incision, repeated 2 h later. **Group B:** Clindamycin, 600 mg plus gentamicin, 80 mg i.v. 1 h before operation, repeated 8 h and 16 h later.	Abdominal SWI: 2/37 vs. 3/35. Anastomic failure: 1/37 vs. 1/35. Fistule: 1/37 vs. 1/35. Intraabdominal abscess: 0/37 vs. 0/35. [Adverse event result: Yes. Cost information: NA from translation]. **Conclusion:** This small sample trial showed that prophylaxis with cefoxitin alone appears to be as effective as double-drug prophylaxis with clindamycin plus gentamicin.
Mozzillo, 1989[109] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 39–46 days. Withdrawal: 8%. 26-centres.	Elective colorectal surgery. Cancer patients: 87%. Age: 62 (21–91). SWI: Discharge of pus; serous discharge with a positive culture or erythema and/or induration requiring antibiotic therapy.	**Group A:** Aztreonam, 1 g plus clindamycin, 900 mg at induction of anaesthesia, and 8 h and 16 h later. **Group B:** Gentamicin, 80 mg plus clindamycin 900 mg at induction of anaesthesia and 8 h and 16 h later.	Abdominal WI: 13/224 vs. 29/230. Perineal WI: 10/28 vs. 22/45. Intraabdominal abscess: 6/224 vs. 8/230. Fever: 83/224 vs. 91/230. Antibiotic therapy: 36/224 vs. 43/230. Postoperative stay: 15 vs. 16 days. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** The prophylactic use of aztreonam (when combined with clindamycin) reduces significantly the incidence of postoperative infections in colorectal surgery.
Nel, 1989[110] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective abdominal surgery. Cancer patients: NA. Age: 49. SWI: Not defined.	**Group A:** Ceftriaxone, 1 g. **Group B:** Cefoxitin, 4–6 g three doses with or without metronidazole.	**SWI: 6/45 vs. 3/45.** UTI: 1/45 vs. 2/45. Chest infection: 1/45 vs. 1/45. Intraabdominal abscess 1/45 vs. 2/45. Death-septic: 0/45 vs. 4/45. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** A single low dose of ceftriaxone was as effective in surgical prophylaxis as our conventional method of three doses of cefoxitin.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Nohr, 1990[111] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 28 days. Withdrawal: 13%. 1-centre.	Elective colorectal surgery. Cancer patients: 78%. Age: 66 (56–74). SWI: Presence of pus in the wound that either discharged spontaneously or required drainage. Perineal wounds were included in the assessment.	All patients: Placebo was used in both groups, starting 2 days before the operation. **Group A:** Bacitracin, 250 mg plus neomycin, 250 mg p.o. t.d.s. for 2 days before operation, plus metronidazole, 500 mg p.o. three times on the day before operation, plus ampicillin, 1 g i.v. 1 h preoperatively. **Group B:** Fosfomycin, 8 g plus metronidazole, 1 g infusion 1 h before operation.	**SWI: 7/72 vs. 6/77.** Deep infection: 3/72 vs. 3/77. Septicaemia: 1/72 vs. 2/77. Pneumonia: 2/72 vs. 2/77. UTI: 7/72 vs. 5/77. Deaths: 5/72 vs. 2/77. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Both regimens are effective in preventing infections after elective colorectal surgery. Fosfomycin plus metronidazole is easy to administer as a single-dose infusion at induction of anaesthesia.
Norwegian study, 1985[112] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 5%. 10-centres.	Elective colorectal surgery. Cancer patients: 87%. Age: 65. SWI: Presence of pus or discharge resulting in a positive bacteriological culture. Perineal sepsis was defined as discharge of pus from the perineal wound or drain channel.	All drugs were administered i.v. within 2 h preoperatively. **Group A:** Tinidazole, 1600 mg plus doxycycline, 400 mg. **Group B:** Tinidazole 1600 mg plus placebo (vitamin solution).	WI: 4/132 vs. 14/135. Perineal abscess: 1/132 vs. 7/135. Intraabdominal abscess: 0/132 vs. 3/135. Anastomosis dehiscence: 0/132 vs. 3/135. Septicaemia: 0/132 vs. 2/135. Pneumonia: 4/132 vs. 9/135. UTI: 7/132 vs. 12/135. Wound dehiscence: 1/132 vs. 3/135. Lung embolism: 2/132 vs. 0/135. Deaths: 2/132 vs. 4/135. Duration of hospital stay: 11.3 vs. 15.4. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** A single preoperative dose of antimicrobial agents effective against both anaerobic and aerobic bowel organisms seems to be the preferred prophylaxis for patients undergoing colorectal surgery.
Nyam, 1995[113] Randomisation: True. Blind outcome assessment: Yes. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 91%. Age: 62 (23–93). SWI: Abscess or wound discharging pus.	**Group A:** Amoxycillin/clavulanic acid, 1 g/200 mg (1.2 g co-amoxiclav) at induction of anesthesia, and at 8 h postoperatively. **Group B:** Ceftriaxone, 1 g plus metronidazole, 500 mg at induction of anaesthesia, and at 12 h postoperatively.	WI: 4/100 vs. 4/100. Chest infection: 1/100 vs. 2/100. UTI: 0/100 vs. 1/100. Anastomotic leak: 0/100 vs. 1/100. Intraabdominal abscess: none. Death: none. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Co-amoxiclav is as effective as ceftriaxone plus metronidazole. Being a single antibiotic regimen, it reduced the cost in terms of pharmacy and nursing time.
Offer, 1988[114] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 1.4%. 1-centre.	Colorectal surgery. Cancer patients: 81%. Age: NA. SWI: Not defined.	The first dose was given with the start of anaesthesia. Both groups received metronidazole, 500 mg i.v. every 8 h for 24 h. **Group A:** Ciprofloxacin, 200 mg i.v. two doses every 12 h. **Group B:** Cephazolin, 2 g i.v. b.d. for 3 days.	**SWI: 2/34 vs. 3/36.** [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Both regimens can be recommended for perioperative use to prevent bacterial infections, ciprofloxacin having the advantage of low dose (2×200 mg) and short duration of treatment (1 day).

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Pacelli, 1991[115] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 0%. 1-centre.	Elective colorectal surgery. Cancer patients: 100%. Age: 67 (34–88). SWI: Purulent discharge with or without culture of pathogenic microorganism.	**Group A:** Imipenem plus cilastatin, 1 g at anaesthesia. **Group B:** Cefuroxime, 1.5 g i.v. plus metronidazole, 500 mg i.v. at induction of anaesthesia two further doses every 8 h.	**SWI: 5/30 vs. 6.** UTI: 0/30 vs. 4/30. Intraabdominal abscess: 1/30 vs. 1/30. Anastomotic leakage: 1/30 vs. 1/30. Hospital stay: 13.6 vs. 15.7 days. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** A single intravenous dose of imipenem plus cilastatin appears to be as effective as three doses of cefuroxime plus metronidazole for the prevention of infection in elective colorectal surgery.
Palmer, 1994[116] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 21–35 days. Withdrawal: 11%.* 1-centre.	Emergency and elective abdominal surgery. Cancer patients: NA. Age: 53 (12–96). SWI: Erythema, discharge or dehiscence.	**Group A:** Co-amoxiclav (Augmentin), 1.2 g i.v. at induction of anaesthesia, and 2 h and 8 h later. **Group B:** Cefuroxime, 1.5 g plus metronidazole, 500 mg i.v. at induction of anaesthesia, then cefuroxime, 750 mg plus metronidazole, 500 mg i.v. at 8 h and 16 h after initial dose.	**SWI: 8/69 vs. 2/79.** [Adverse event result: Yes. Cost information: Yes.] **Conclusion:** This study demonstrates that co-amoxiclav is an effective prophylactic antibiotic for abdominal operation and that potential savings may be made with its use in the field of general operation without sacrificing quality of care.
Periti, 1989[117] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 11%. > 10-centres.	Elective colorectal surgery. Cancer patients: 86%. Age: 63 (13–85). SWI: Drained purulent or serous material.	**Group A:** Cefoxitin, 1 g i.v. at the start of operation and 3 h, 6 h, and 12 h after first dose. **Group B:** Cefotetan, 2 g i.v. at start of operation.	Abdominal WI: 23/206 vs. 18/197. Perineal WI: 5/13 vs. 2/10. Intraabdominal abscess: 1/206 vs. 0/197. Anastomotic dehiscence: 5/206 vs. 2/197. Postoperative diarrhoea: 22/206 vs. 19/197. Febrile morbidity: 53/206 vs. 39/197. Deaths: 4/206 vs. 4/197. Postoperative stay (Mean days): 15 vs. 16. [Adverse event result: NA. Cost information: NA.] **Conclusion:** It is sufficient for prophylactic purposes for an antimicrobial agent to cover the critical moment of bacterial colonisation during the operative procedure. A single dose of a drug having a half-life longer than the duration of operation would be of value for this type of prophylaxis.
Periti, 1993[118] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 11%. 19-centres.	Elective colorectal surgery. Cancer patients: 87%. Age: 64 (SD 13). SWI: Not defined. (Criteria defining failure of the chemoprophylaxis: fever > 38 °C [excluding the first 24 h] on at least two occasions with an interval of not less than 6 h; SWI, and infection in other sites [abdominal abscess, bronchopneumonia, etc.]. Bacteriuria > 100,000 CFU/ml; the need of administering antimicrobial chemotherapy after completion of chemoprophylaxis in the absence of above criteria.)	**Group A:** Cefotetan, 2 g rapid i.v. at induction of anaesthesia, plus thymostimulin, 70 mg i.m. for 7 days starting 48 h preoperatively. **Group B:** Cefotetan, 2 g rapid i.v. at induction of anaesthesia.	N: 425 vs. 434. Total abdominal WI: 56/425 vs. 72/434. Abdominal wound serous: 34/425 vs. 45/434. Abdominal wound purulent: 22/425 vs. 27/434. Perineal WI: 6/425 vs. 6/434. Abdominal abscess: 5/425 vs. 15/434. Peritonitis: 7/425 vs. 9/434. Total infected patients: 63/425 vs. 67/434. Respiratory tract infection: 8/425 vs. 20/434. UTI: 58/425 vs. 58/434. Thrombophlebitis: 2/425 vs. 0/434. Septicaemia: 1/425 vs. 3/434. Hospital stay: 15 vs. 15 days. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Pro-host immunotherapy with thymostimulin administered intraoperatively for 7 days can potentiate the efficacy of antimicrobial chemoprophylaxis in colorectal surgery.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Perrott, 1985[119] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 28 days. Withdrawal: 5%.* 1-centre?	Elective colorectal and biliary surgery. Cancer patients: NA. Age: 64. SWI: Showing abnormal reddening and swelling out of proportion to the expected, or if frank suppuration occurred.	**Group A:** Metronidazole, 500 mg plus tobramycin, 80 mg at start of operation, then at 8 h and 16 h later, plus penicillin, 2 milliunits at start of operation followed by a further four doses, one every 4 h. **Group B:** Cefoxitin, 2 g at start of operation and two more doses, one every 6 h.	WI: 7/26 vs. 4/27. Patients with sepsis: 10/26 vs. 6/27. [Adverse event result: NA. Cost information: NA.] **Conclusion:** The single agent, cefoxitin, is as effective in prophylaxis in colorectal and biliary operation as a combination of penicillin, an aminoglycoside and metronidazole. The cost and ease of administering the single agent are advantages which make it preferable for prophylactic use in colorectal and biliary surgery.
Peruzzo, 1987[120] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 39%. Age: 67 (47–87). SWI: Drainage of serous-purulent material, with or without culture of pathogen micro-organisms from a discharging abdominal wound.	**Group A:** Cefoxitin, as i.v. bolus 0.5 h preoperatively and then 6 h and 12 h postoperatively. **Group B:** Cefoxitin, (same doses and timing as in Group A) plus tinidazole, 2 g p.o. 2 h preoperatively plus neomycin 1 g p.o. 19 h, 18 h and 9 h preoperatively.	WI: 0/39 vs. 4/41 ($p = 0.12$, Fisher's exact test). Chest infection: 2/39 vs. 0/41. UTI: 2/39 vs. 4/41. Febrile morbidity: 13/39 vs. 13/41. Diarrhoea: 1/39 vs. 3/41. Postop hospital stay: 11.5 (9–22) vs. 11.0 (9–18). [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Concomitant use of parenteral and oral combination in elective colorectal operation is no more effective than the single systemic haemoprophylaxis with cefoxitin.
Petrelli, 1988[121] Randomisation: Quasi. Blind outcome assessment: No. Follow-up: 90 days. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 100%. Age: 59. SWI: Discharge of pus.	All patients underwent a 3-day mechanical bowel preparation and received erythromycin base, 1 g plus neomycin, 1 g p.o. at 1 p.m., 2 p.m., and 11 p.m. on the day before operation. **Group A:** Cefamandole, 1 g i.v. 1 h preoperatively, then every 6 h for a total of four doses. **Group B:** No i.v. antibiotics.	**SWI: 0/34 vs. 1/36.** UTI: 6/34 vs. 3/36. [Adverse event result: NA. Cost information: NA.] **Conclusion:** The addition of perioperative intravenous cefamandole to a good mechanical bowel preparation with oral antibiotics provides no further benefit in decreasing WIs following resection of colorectal neoplasias in this small group of patients.
Petropoulos, 1985[122] (French) Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 0%. 5-centres.	Elective colorectal surgery. Cancer patients: NA from translation. Age: 67. SWI: Not defined.	**Group A:** Cefotaxime, 2 g i.v. at induction of anaesthesia. **Group B:** Cefotaxime, 2 g plus ornidazole, 500 mg at induction of anaesthesia, and two further doses of cefotaxime 8 h and 16 h later plus a further dose of ornidazole 12 h later.	**SWI: 4/80 vs. 3/80.** Anastomotic leaks: 2/80 vs. 3/80. [Adverse event result: Yes. Cost information: NA from translation] **Conclusion:** A single dose of ceftriaxone provides adequate prophylactic antibiotic cover in elective colorectal surgery.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Playforth, 1987[123] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 1%.* 1-centre.	Emergency and elective abdominal surgery. Cancer patients: NA. Age: NA. SWI: Discharge of pus. Major infections caused constitutional disturbances including pyrexia and delayed patients' discharge from hospital. Minor infections did neither. Serous and haemoserous discharges were not counted as infections.	All colorectal patients: Either 24-h p.o. neomycin plus metronidazole, or single suppository of metronidazole, 1 g approx. 2 h preoperatively. **Group A:** Latamoxef, 1 g in 20 ml of solution as single i.v. injection at induction of anaesthesia. **Group B:** Co-amoxiclav, 1.2 g in 20 ml of solution as single i.v. injection at induction of anaesthesia.	Ileocolorectal using metronidazole: **SWI: 10/36 vs. 15/56.** Ileocolorectal (emergency), no metronidazole: SWI: 0/9 vs. 7/18. [Adverse event result: Yes. Cost information: Yes.] **Conclusion:** A single preoperative dose of co-amoxiclav is as effective as one of latamoxef for the prophylaxis of infective complications in abdominal surgery. Continued speculation about the possibility that cephalosporins can cause bleeding complications may encourage the use of co-amoxiclav for this indication.
Playforth, 1988[124] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 74%. Age: 20–89. SWI: Major – causing pyrexia and delaying patient's discharge from hospital; or minor.	All patients: a single preoperative or intraoperative dose of an antibiotic effective against faecal aerobic bacteria. **Group A:** Metronidazole, i.v. at premedication. **Group B:** Neomycin, 1 g p.o. every 6 h plus metronidazole, 200 mg every 8 h, for 24 h, plus parenteral preoperative dose of metronidazole, 1 g rectal or 500 mg i.v.	**SWI: 16/58 vs. 9/61.** Minor WI: 11/58 vs. 8/61. Major WI: 5/58 vs. 1/61. Anastomotic leak/abs: 4/58 vs. 7/61. Deaths: 5/58 vs. 6/61. [Adverse event result: NA. Cost information: NA.] **Conclusion:** It is advisable not only to ensure adequate tissue levels of antimicrobials but also to reduce the risk of endogenous bacterial infection by partially decontaminating the bowel in colorectal operations.
Plouffe, 1985[125] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: NA. Withdrawal: 20%.* 1-centre.	Elective abdominal surgery. Cancer patients: NA. Age: NA. SWI: Purulent discharge and isolated pathogen.	**Group A:** Cephazolin, 1 g i.v. on call to the operating theatre and twice postoperatively every 6 h. **Group B:** Latamoxef (Moxalactam), 1 g i.v on call to the operating theatre and twice postoperatively every 6 h.	**SWI: 1/24 vs. 1/26.** [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Latamoxef is no more effective than cephazolin in preventing postoperative infections in this study population.
Plouffe, 1989[126] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 31%.* 1-centre.	Elective abdominal surgery. Cancer patients: NA. Age: 52.* SWI: Not defined.	Patients undergoing colorectal operation also received oral antibiotic bowel preparation. **Group A:** Cefmetazole, 2 g preoperatively, and two doses every 8 h. **Group B:** Cefoxitin, 2 g preoperatively, and two doses every 6 h.	**SWI: 0/28 vs. 2/12.** [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Both regimens are well tolerated and provide effective perioperative prophylaxis for elective intraabdominal surgery. The only differences noted were in colon operation where three patients in the cefoxitin group had infections, two of which were minor WIs.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Pollock, 1989[127] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 30 days. Withdrawal: 0%. 1-centre.	Elective abdominal surgery. Cancer patients: NA. Age: NA. SWI: Discharge of pus. Major – causing fever and delaying the patient's discharge from hospital); minor – requiring dressings only; late – all these were minor and occurred after patients had left hospital.	**Group A:** Amoxycillin/clavulanic acid 1 g/200 mg (co-amoxiclav, 1.2 g) i.v. at induction of anaesthesia. **Group B:** Co-amoxiclav, 1.2 g injected subcutaneously along the line of the proposed abdominal incision, using a spinal needle. Metronidazole was used in the majority of colorectal patients.	SWI: with metronidazole: 11/47 vs. 9/40; without metronidazole: 6/15 vs. 3/20. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** The incidence of WI was considerably lower in the group given the antibiotic into the abdominal wall (8.4% vs. 15.9%, $p = 0.005$). Preincisional intraparietal injection is more effective than intravenous injection of co-amoxiclav for the prophylaxis of SWI. (This conclusion was based on the results of all surgical procedures.)
Raahave, 1988[128] Randomisation: True. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 9%. 1-centre.	Elective colorectal surgery. Cancer patients: 81%. Age: 73 (39–90). SWI: Obvious collection of pus, which drained spontaneously or on incision.	**Group A:** Cefotaxime, 2 g i.v. at induction of anaesthesia, and at 6 h and 12 h after first dose. **Group B:** Neomycin, 1 g plus erythromycin, 1 g three times on the day before operation, plus ampicillin, 2 g powered in the wound at closure.	**SWI: 2/50 vs. 6/50.** Wound dehiscence: 2/50 vs. 2/50. Anastomotic leak: 5/50 vs. 2/50. Intraabdominal abscess: 1/50 vs. 1/50. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** A three-dose intravenous course with cefotaxime is comparable to neomycin plus erythromycin orally in preventing postoperative infective complications.
Raahave, 1989[129] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 12%. 2-centres.	Elective colorectal surgery. Cancer patients: 84%. Age: 71. SWI: Collection of pus, draining either spontaneously or at the site of incision.	**Group A:** Cefotaxime, 2 g i.v. at induction of anaesthesia, and at 6 h and 12 h later. **Group B:** Cefotaxime, 2 g i.v. at induction of anaesthesia, and at 6 h and 12 h later, plus ampicillin, 2 g powdered in the wound subfascially and subcutaneously during closure.	**SWI: 6/89 vs. 5/81.** Wound dehiscence: 1/89 vs. 2/81. Intraabdominal abscess: 2/89 vs. 3/81. Anastomoses: 71/89 vs. 66/81. Anastomotic leakage: 6 (8.5%) vs. 3 (4.5%). [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Topical ampicillin could not lower the WI rate further when a 12-h systemic antibiotic cover was used.
Rangabashyam, 1991[130] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 21% 1-centre.	Elective colorectal surgery. Cancer patients: 85%. Age: 53 (15–80). SWI: Not defined.	All patients: Metronidazole, 500 mg b.d. for 3 days, with the first dose administered immediately prior to operation. **Group A:** Cefotaxime, 1 g 1 h preoperatively. **Group B:** Cefotaxime, 1 g 1 h preoperatively and 8 h and 16 h postoperatively.	**SWI: 2/17 vs. 1/17.** [Adverse event result: NA. Cost information: NA.] **Conclusion:** Prophylactic cefotaxime and metronidazole are effective in reducing the incidence of septic complications following colorectal surgery. Nevertheless, a study with a larger number of patients is needed to reach a definitive conclusion.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Reynolds, 1989[131] Randomisation: True. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 16%. 1-centre.	Elective colorectal surgery. Cancer patients: 75%. Age: 67 (20–89). SWI: Presence of pus of purulent fluid in the wound appearing spontaneously or upon incision.	**Group A:** Metronidazole, 400 mg every 8 h plus neomycin, 1 g p.o. every 6 h for 48 h prior to operation with the last dose given 8 h and 12 h preoperatively, respectively, plus piperacillin, 2 g i.v. at induction of anaesthesia followed by three further doses every 8 h. **Group B:** Piperacillin, 2 g i.v. at induction of anaesthesia and three further doses every 8 h. **Group C:** Metronidazole, 500 mg plus cefuroxime, 1.5 g at induction of anaesthesia followed by three further doses of metronidazole and two doses of cefuroxime, 750 mg.	Abdominal WI: 9/107 vs. 18/104 vs. 8/119. Perineal WI: 7/16 vs. 8/18 vs. 5/18. Chest infection: 6/107 vs. 7/104 vs. 9/119. [Adverse event result: NA. Cost information: NA.] **Conclusion:** The efficacy of piperacillin can be improved by preoperative oral antibiotic therapy. Excellent results were obtained with the combination of cefuroxime plus metronidazole and it remains to be seen whether these results with combination therapy could be improved by the addition of preoperative oral antibiotic prophylaxis.
Rodolico, 1991[132] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 84%. Age: 64 (SD 8). SWI: Purulent discharge from the surgical wound or a serous discharge with a positive microbiological culture.	**Group A:** Clindamycin, 0.6 g plus aztreonam, 1 g i.v. 30 min preoperatively, and 8 h and 16 h postoperatively. **Group B:** Clindamycin, 0.6 g plus gentamicin, 80 mg i.v. 30 min preoperatively and 8 h and 16 h postoperatively.	**SWI: 8/66 vs. 12/72.** [Adverse event result: NA. Cost information: NA.] **Conclusion:** Aztreonam plus clindamycin appears to be a valid alternative to gentamicin plus clindamycin for the prophylaxis of infections following colorectal surgery.
Roland, 1986[133] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 15 days. Withdrawal: 15%. 17-centres.	Elective colorectal surgery. Cancer patients: NA. Age: 95% > 51. SWI: Inflammation of the wound, a serous or purulent discharge, and a positive culture of a pathogen from the discharge.	Different antimicrobial agents were administered simultaneously but as separate infusions, approximately 1 h preoperatively. **Group A:** Metronidazole, 1.5 g i.v.. **Group B:** Metronidazole, 1.5 g i.v. plus ampicillin, 6.0 g i.v. plus doxycycline, 400 mg i.v.	**SWI: 6/170 vs. 1/188.** Intraperitoneal infection: 6 vs. 2. Perineal infection: 8 vs. 2. WI plus septicaemia: 1 vs. 0. WI plus perineal infection: 0 vs. 1. Chest infection: 3/170 vs. 3/188. UTI: 8/170 vs. 4/188. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** A single preoperative intravenous infusion of metronidazole in combination with ampicillin or doxycycline is a simple and effective prophylactic regimen in colorectal surgery. Although no difference was found between ampicillin and doxycycline in this investigation, ampicillin is the preferred choice due to the increasing selection of tetracycline-resistant bacteria.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Rorbaek-Madsen, 1988[134] Randomisation: True. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 11%. 6-centres.	Elective colorectal surgery. Cancer patients: 76%. Age: 68. SWI: Abscess or discharge of pus.	**Group A:** Cefoxitin, 2 g i.v. 15 min preoperatively, and at 4 h and 10 h after the first dose. **Group B:** Ampicillin, 1 g plus metronidazole, 500 mg i.v. 15 min preoperatively and every 6 h (ampicillin) and 8 h (metronidazole) for a total of 72 h.	Wound sepsis: 13/177 vs. 14/175. Patients with septic complications: 20/177 vs. 25/175. Perineal WI: 2/23 vs. 5/33. Intraabdominal abscess: 1/177 vs. 2/175. Peritonitis: 1/177 vs. 3/175. Septicaemia: 4/177 vs. 4/175. UTI: 14/177 vs. 18/175. Pneumonia: 17/177 vs. 19/175. Deaths: 6/177 vs. 12/175. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Short-term prophylactic treatment with cefoxitin is at least as efficient as 3-day treatment with ampicillin plus metronidazole in the prevention of postoperative septic complications after elective colorectal surgery.
Rowe-Jones, 1990[135] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 4-8 weeks. Withdrawal: 11%. 14-centres.	Emergency and elective colorectal surgery. Cancer patients: 66%. Age: 68 (16–92). SWI: Abdominal incision discharged pus.	**Group A:** Cefotaxime, 1 g plus metronidazole, 500 mg i.v. infusion after induction of anaesthesia and 5–10 min before opening of peritoneum. **Group B:** Cefuroxime, 1.5 g plus metronidazole, 500 mg i.v. infusion after induction of anaesthesia and before peritoneal opening, and two further i.v. doses of cefuroxime, 750 mg plus metronidazole, 500 mg at 8 h and 16 h postoperatively.	**SWI: 32/453 vs. 33/454.** Overall incidence of complications: 130/470 vs. 150/471. Deaths: 26/470 vs. 31/471. Death due to sepsis (usually pneumonia): 3/470 vs. 4/471. UTI: 30/470 vs. 45/471. Total infections other than SWI (abscess, septicaemia, chest, urinary tract): 71/470 vs. 91/471. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** A single preoperative dose of cefotaxime plus metronidazole is as efficacious as a three-dose regimen of cefuroxime plus metronidazole in preventing WI after colorectal operation and has practical advantages in eliminating the need for postoperative antibiotics.
Sauven, 1986[136] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 28 days. Withdrawal: 21%.* 1-centre.	Emergency and elective abdominal surgery. Cancer patients: NA. Age: 63 (12–95).* SWI: Discharge of pus.	For elective ileocolorectal operations, patients were given preoperative metronidazole suppositories, with or without oral neomycin. **Group A:** Latamoxef, 1 g i.v. at induction of anaesthesia. **Group B:** Peritoneal and parietal irrigation with one litre of saline containing 1 g tetracycline at the conclusion of the operation.	Ileocolorectal not perforated. SWI: 6/39 vs. 15/43. Ileocolorectal perforated SWI: 3/7 vs. 4/8. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** A single dose of latamoxef at induction of anaesthesia provides better prophylaxis against abdominal WI than peritoneal and parietal tetracycline lavage.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Schiessel, 1984[137] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 28 days. Withdrawal: 18%. 1-centre.	Elective colorectal surgery. Cancer patients: 90%. Age: 63. SWI: Inflammation of the wound with discharge of pus occurring within 4 weeks from surgery. By definition, suppuration of the stab wound was not considered to be a WI.	**Group A:** No antibiotics. **Group B:** Intraluminal antibiotics; neomycin, 1 g/l plus bacitracin, 50,000 IU/l plus clindamycin, 900 mg/l were added to the last 3 litres of the irrigation fluid. **Group C:** Parenteral antibiotics; mezlocillin, 4 g plus oxacillin, 2 g i.v. on induction of anaesthesia then at 8 h and 16 h postoperatively.	**SWI: 12/31 vs. 1/30 vs. 2/29.** Fistulae: 1/31 vs. 1/30 vs. 3/30. Pneumonia: 3/31 vs. 1/30 vs. 0/29. Intraabdominal abscess: 1/31 vs. 1/30 vs. 0/30. Peritonitis: 2/31 vs. 0/30 vs. 0/29. UTI: 2/31 vs. 3/30 vs. 1/29. Deaths: 2/31 vs. 0/30 vs. 0/29. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Perioperative administration of antibiotics dramatically and significantly reduces the incidence of WIs following colorectal surgery, regardless of the route of administration – intraluminally or intravenously.
Schoetz, 1990[138] Randomisation: True. Blind outcome assessment: Yes. Follow-up: 120 days. Withdrawal: 12%. 1-centre.	Elective colorectal surgery. Cancer patients: 46%. Age: 55 (18–96). SWI: Purulent wound drainage; the exudate either spontaneously drained or was expressed after removal of skin staples over a clinically suspect area of the wound.	**Group A:** Neomycin, 1 g plus erythromycin base, 1 g p.o. at 1 p.m., 2 p.m.and 11 p.m. on the day before the operation. **Group B:** Neomycin, 1 g plus erythromycin base, 1 g p.o. at 1 p.m., 2 p.m. and 11 p.m. on the day before the operation, and cefoxitin, 2 g i.v. within 60 min before incision, 6 h and 12 h thereafter.	**SWI: 14/96 vs. 5/101.** Anastomotic leakage: 4/96 vs. 3/101. Intraabdominal abscess: 3/96 vs. 2/101. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** The addition of perioperative parenteral cefoxitin greatly reduced the incidence of WIs in patients undergoing elective colorectal operations who had been prepared with mechanical bowel cleansing and oral antimicrobial agents.
Shatney, 1984[139] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 14%.* 5-centres.	Elective abdominal surgery. Cancer patients: NA. Age: 44 (18–75). SWI: If the incision or peritoneal cavity drained purulent material, it was considered infected, regardless of bacteriological or laboratory testing.	**Group A:** Cefotaxime, 1 g i.v. or i.m. 30–90min preoperatively. **Group B:** Cefoxitin, 2 g i.v. or i.m. 30–90min preoperatively and every 6 h for no more than 24 h postoperatively.	**SWI: 7/36 vs. 3/34.** [Adverse event result: Yes. Cost information: NA.] **Conclusion:** The effectiveness of a single-dose antibiotic regimen for surgical prophylaxis is important, both for its potential to reduce the emergence of resistant strains and for its contribution to cost savings without compromising the quality of patient care.
Skipper, 1992[140] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 30 days. Withdrawal: 17%. 1-centre.	Elective colorectal surgery. Cancer patients: NA. Age: NA. SWI: 1 – no infection; 2 – erythema; 3 – purulent or bacteriologically positive discharge; or 4 – severe WI with or without dehiscence.	**Group A:** Cefotetan, 2 g at induction of anaesthesia and at 12 h postoperatively. **Group B:** Cefuroxime, 1.5 g plus metronidazole, 500 mg at induction of anaesthesia, and cefuroxime, 750 mg plus metronidazole, 500 mg at 8 h and 16 h postoperatively.	Total WI (grade 3 and 4): 10/68 vs. 5/36. Death: 7/68 vs. 3/36. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Cefotetan is as effective as a combination of cefuroxime plus metronidazole when used as prophylaxis in elective colorectal surgery. The advantages of cefotetan are that it is a single agent given in two doses, whereas cefuroxime plus metronidazole are two agents given in three doses each.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Stellato, 1990[141] Randomisation: True. Blind outcome assessment: Yes. Follow-up: NA. Withdrawal: 14%. 1-centre.	Elective colorectal surgery. Cancer patients: 84%. Age: 68 (16–91). SWI: Wound with visible pus or with a positive culture.	**Group A:** Neomycin, 1 g plus erythromycin base, 1 g p.o. at 1 p.m., 2 p.m. and and 11 p.m. on the day prior to operation for patients whose operation was scheduled at 8 a.m. Plus i.v. placebo. **Group B:** Cefoxitin, 1 g i.v. at induction of anaesthesia and at 6 h and 12 h following the first dose. Plus p.o. placebo. **Group C:** Both p.o. and i.v. antibiotics.	**SWI: 3/44 vs. 2/51 vs. 3/51.** Abscess/peritonitis: 1/44 vs. 5/51 vs. 1/51. Anastomotic major: 1/44 vs. 2/51 vs. 0/51. Leak minor: 0/44 vs. 1/51 vs. 1/51. Septicaemia: 1/44 vs. 2/51 vs. 0/51. Death: 0/44 vs. 2/51 vs. 0/51. [Adverse event result: NA. Cost information: NA.] **Conclusion:** No advantage could be identified in the combination of oral and intravenous antibiotics in elective colorectal surgery.
Stewart, 1995[142] Randomisation: True. Blind outcome assessment: No. Follow-up: 42 days. Withdrawal: 12%. 13-centres.	Elective colorectal surgery. Cancer patients: 80%. Age: 67 (SD 13). SWI: WI, intraabdominal infection or septicaemia occurring within 42 days of operation were considered to be evidence of failure of antibiotic prophylaxis. These diagnoses were made on clinical criteria with microbiological confirmation whenever possible.	**Group A:** Piperacillin, 4 g i.v. as single bolus dose at induction of anaesthesia. **Group B:** Piperacillin, 4 g plus sulbactam, 2 g i.v. as bolus dose at induction of anaesthesia.	WI alone: 30/168 vs. 27/158. Intraabdominal abscess alone: 5/168 vs. 1/158. Septicaemia alone: 10/168 vs. 3/158. Wound plus intraabdominal abscess: 5/168 vs. 1/158. WI plus septicaemia: 3/168 vs. 4/158. Intraabdominal abscess plus septicaemia: 1/168 vs. 0/158. WI plus septicaemia plus intraabscess: 1/168 vs. 0/158. Total infections: 55/168 vs. 36/158. Deaths within 42 days: 8 vs. 9. (Group A was the same as in Taylor, 1994) [Adverse event result: NA. Cost information: NA.] **Conclusion:** Sulbactam improves the efficacy of piperacillin as prophylaxis in elective colorectal operation but does little to protect against staphylococcal WI.
Stubbs, 1987[143] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 5%. 1-centre.	Elective colorectal surgery. Cancer patients: 67%. Age: 66 (26–87). SWI: Failure of primary healing in any portion of the wound or when there was wound discharge.	**Group A:** Mezlocillin, 5.0 g i.v. at start of operation. **Group B:** Cefuroxime, 1.5 g plus metronidazole, 500 mg i.v. at start of operation, followed by two doses of cefuroxime, 750 mg plus metronidazole, 500 mg i.v. 8 h and 16 h later.	**SWI: 16/54 vs. 14/56.** [Adverse event result: NA. Cost information: NA.] **Conclusion:** A single dose of mezlocillin is as effective for the prophylaxis of WI after large bowel operation as the commonly used regimen of three doses of cefuroxime plus metronidazole.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Taylor, 1994[144] Randomisation: True. Blind outcome assessment: No. Follow-up: 42 days. Withdrawal: 14%. 13-centres.	Elective colorectal surgery. Cancer patients: 79%. Age: 67 (SD 13). SWI: Not defined. (Diagnosis based on clinical criteria with microbiological confirmation whenever it was available.)	All patients: Single dose of piperacillin, 4 g i.v. at induction of anaesthesia. **Group A:** Ciprofloxacin, 500 mg b.d. p.o. on the day before operation. **Group B:** No oral antibiotic.	WI alone: 17/159 vs. 30/168. Intraabdominal abscess alone: 2/159 vs. 5/168. Septicaemia alone: 3/158 vs. 10/168. WI plus intraabdominal abscess: 0/159 vs. 5/168. Wound plus septicaemia: 1/159 vs. 3/168. Intraabdominal abscess plus septicaemia: 0/159 vs. 1/168. WI plus septicaemia plus intraabdominal abscess: 0/159 vs. 1/168. Total patients with infective morbidity: 23/159 vs. 55/168. Death within 42 days: 7/189 vs. 13/192. (Group B was the same as in Stewart, 1995) [Adverse event result: NA. Cost information: Yes.] **Conclusion:** The administration of ciprofloxacin, 500 mg twice daily with the preoperative cathartic significantly reduces the incidence of infection after elective colorectal operations and should form part of the preoperative preparations for such operations.
Tehan, 1989[145] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 28 days. Withdrawal: 16%.* 13-centres.	Elective general or gynaecological surgery. Cancer patients: NA. Age: 51.* SWI: 1 – moderate or severe erythema (in one centre, mild erythema was classed as WI); 2 – purulent discharge; 3 – serous discharge from which an organism was isolated; 4 – serous discharge associated with either erythema or other factors indicative of infection e.g. pyrexia.	First dose was given at induction of anaesthesia, and then 8 h and 16 h after the first dose. **Group A:** Co-amoxiclav, 1.2 g i.v. plus placebo suppository. **Group B:** Cephradine, 1 g i.v. plus metronidazole, 1 g suppository.	**SWI: 17/84 vs. 9/36.** [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Co-amoxiclav has been shown to be comparable to the regimen of cephradine plus metronidazole as prophylaxis for a wide range of surgical procedures. Co-amoxiclav offers the convenience of administration of a single agent, unlike the combination regimen.
Thomas, 1985[146] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 42 days. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 75%. Age: 64 (32–92). SWI: Not defined.	**Group A:** Latamoxef, 1 g i.v. at induction of anaesthesia, and at 6 h and 12 h postoperatively. **Group B:** Cephazolin, 1 g plus metronidazole, 500 mg i.v. at induction of anaesthesia, and at 6 h and 12 h postoperatively.	**SWI: 3/60 vs. 5/60.** Intraabdominal abscess: 2 vs. 5. Anastomotic leak: 1/49 vs. 3/52. Additional postoperative antibiotics: 4 vs. 12. Additional postoperative complications: 7 vs. 21. Deaths within 30 days: 1 vs. 5. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** The intravenous administration of latamoxef at induction of anaesthesia provides good serum and tissue levels during colorectal operations. It is at least as effective as a combination of cephazolin plus metronidazole in preventing septic complications.

* *Indicates data for all surgical procedures included in a trial (i.e where data for elective colorectal operation cannot be separated out from other procedures)*
NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Tsimoyiannis, 1991[147] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 80%. Age: 61 (SD 15). SWI: Obvious collection of pus, which drained spontaneously or on incision	**Group A:** Metronidazole, 500 mg plus amikacin, 500 mg i.v. 2 h preoperatively and every 8 h (metronidazole) or every 12 h (amikacin) for 2 days postoperatively. **Group B:** Ornidazole, 1 g plus ceftriaxone, 2 g i.v. 2 h preoperatively and every 24 h postoperatively for 2 days.	Wound with visible pus: 1/25 vs. 2/25. Anastomotic leakage: 1/25 vs. 0/25. Pulmonary embolism: 0/25 vs. 1/25. Deep vein thrombosis: 0/25 vs. 1/25. [Adverse event result: Yes. Cost information: Yes.] **Conclusion:** The antibiotic cover in elective colorectal operation with ornidazole plus ceftriaxone, both administered preoperatively and per 24 h for 2 days postoperatively, provides clinical results that do not differ significantly from a classic antibiotic cover with metronidazole plus amikacin. The short-term ornidazole plus ceftriaxone antibiotic prophylaxis constitutes an effective, inexpensive therapy free from adverse events for patients undergoing elective colorectal surgery.
Tuchmann, 1988[148] (German) Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 0%.	Elective colorectal surgery. Cancer patients: NA from translation. Age: 41% > 71 years. SWI: Not defined.	**Group A:** Piperacillin, 4 g plus tinidazole, 0.8 g i.v. before operation. **Group B:** Piperacillin, 4 g plus tinidazole, 0.8 g i.v. before operation, and every 8 h (piperacillin) and every 12 h (tinidazole) for 24 h postoperatively.	SWI: 4/61 vs. 5/63. Overall postoperative infection: 23% vs. 19%. [Adverse event result/cost information: NA from translation.] **Conclusion:** Both prophylactic antibiotic schemes were comparably effective. Intestinal lavage could decrease the infection rate further.
Tudor, 1988[149] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: 28 days. Withdrawal: 1.3%. 1-centre.	Emergency and complicated colorectal surgery. Cancer patients: 0.0%. Age: NA. SWI: Pus in the incision. Major – associated with constitutional disturbance and dehiscence: minor – no serious morbidity and no prolongation in hospital stay.	**Group A:** Cefotetan, 2–3 g two doses. **Group B:** Metronidazole, 1.5 g i.v. infusion at start of operation plus gentamicin (weight in kg × 5/3 mg) every 8 h for 5 days.	Abdominal WI: 10/75 vs. 17/75. Pus in incision: 3/75 vs. 8/75. Open-wound sepsis: 4/75 vs. 5/75. Perineal WI: 3/6 vs. 4/9. Intraabdominal abscess: 8/75 vs. 7/75. Anastomotic dehiscence: 4/75 vs. 3/75. Superficial wound dehiscence: 2/75 vs. 0/75. Purulent discharge from drain: 0/75 vs. 1/75. Stomal sepsis: 2/75 vs. 2/75. Chest/upper respiratory tract infection: 3/75 vs. 5/75. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Cefotetan was a useful drug in colorectal surgery, but should be used in combination with vitamin K in malnourished patients. Its activity against *Bacteroides* spp. is rather disappointing *in vivo* and it might be wise to combine cefotetan with a nitroimidazole.
Utley, 1984[150] Randomisation: Not clear. Blind outcome assessment: Yes. Follow-up: 42 days. Withdrawal: NA. 1-centre.	Colorectal operation. Cancer patients: NA. Age: 64. SWI: Moderate – superficial inflammation of wound with purulent discharge; severe – infection: deep purulent infection with an obvious inflammatory reaction and pus.	**Group A:** Cefoxitin, 6 g given as three 2 g i.v. doses, the first before skin incision. **Group B:** Placebo.	**SWI: 3/13 vs. 11/19** (p = 0.055, Fisher's exact test). [Adverse event result: NA. Cost information: NA.] **Conclusion:** Preoperative cefoxitin has resulted in a significant reduction in WIs in this study and appears to be an effective broad-spectrum antibiotic for prophylactic use in general surgical procedures.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Walker, 1988[151] Randomisation: True. Blind outcome assessment: No. Follow-up: NA. Withdrawal: 11%. 7-centres.	Elective colorectal surgery. Cancer patients: 70%. Age: 64 (23–89). SWI: Discharge of frank pus from the wound, wound dehiscence, or the discharge of serous fluid from which organisms were isolated on bacteriological culture. WIs were considered major when they threatened life, required further surgical intervention or delayed discharge from hospital.	**Group A:** Piperacillin, 2 g i.v. at induction of anaesthesia, and at 8 h and 16 h postoperatively. **Group B:** Netilmicin, 120 mg i.v. at induction of anaesthesia and at 8 h and 16 h postoperatively, plus metronidazole, 500 mg i.v. infusion at induction of anaesthesia and at 12 h postoperatively.	Abdominal WI: 17/108 vs. 13/105. Major: 3/108 vs. 1/105. Minor: 14/108 vs. 12/105. Perineal WI: 1 vs. 5. Subphrenic abscess: 1/108 vs. 0/105. Pelvic abscess: 3/108 vs. 0/105. Peritonitis plus septicaemia: 1/108 vs. 0/105. Chest infection: 5/108 vs. 8/105. UTI: 13/108 vs. 7/105. [Adverse event result: NA. Cost information: NA.] **Conclusion:** The incidence of infection was similar in the two groups. The bacteriological findings suggest that the addition of a beta-lactamase inhibitor to piperacillin would render it more effective, not only in reducing the incidence of staphylococcal WIs but also improving its activity against Enterobacteriaceae.
Weaver, 1986[152] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 70%. Age: NA. SWI: Discharge of pus. Major infection was defined as purulent discharge associated with: fever; foul-smelling discharge; dehiscence; a hospital stay greater then 14 days; or leukocytosis (more than 20,000 cells/mm^3).	**Group A:** Neomycin sulfate, 1 g plus erythromycin base, 1 g p.o. at 1 p.m., 2 p.m. and 11 p.m. on the day before the operation. **Group B:** Ceftriaxone, 2 g plus metronidazole, 1.5 g slow i.v. infusion at the start of the operation.	Abdominal WI, major: 11/29 vs. 2/31, minor: 1/29 vs. 1/31. Perineal WI: 4 vs. 0. Abscess: 1/29 vs. 0/31. Septicaemia: 2/29 vs. 0/39. Total number with sepsis: 14/29 vs. 3/31. Total number with major sepsis: 13/29 vs. 2/31. [Adverse event result: NA. Cost information: NA.] **Conclusion:** Single-dose systemic prophylaxis with appropriate antibiotics is superior to oral neomycin and erythromycin. It is more effective to use a single-dose, long-acting antimicrobial agents that provide high serum concentrations during the postoperative period without disturbing the normal microflora of the colon.
Weidema, 1985[153] Randomisation: True. Blind outcome assessment: No. Follow-up: 28 days. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: NA. Age: 59 (SD 14). SWI: Presence of pus in the wound.	**Group A:** Gentamicin, 80 mg plus metronidazole, 500 mg i.v. starting at premedication, and then every 8 h for 24 h. **Group B:** Metronidazole, 500 mg i.v. every 8 h for 24 h, starting at premedication.	Superficial WI: 4/21 vs. 5/20. Intraabdominal abscess: 1/21 vs. 0/20. Symptomatic anastomotic dehiscence: 1/21 vs. 0/20. [Adverse event result: NA. Cost information: NA.] **Conclusion:** From this small study it cannot be concluded that the administration of gentamicin in the antibiotic prophylaxis before elective colorectal operation can be omitted.
Wenzel, 1985[154] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: 62%. Age: 70 (45–84). SWI: Oedematous and/or red wound with a purulent secretion.	**Group A:** Ornidazole, 1 g i.v. plus gentamicin, 80 mg i.v. 45 mins preoperatively. **Group B:** Ornidazole plus gentamicin as for Group A, followed by three further doses of ornidazole, 500 mg every 12 h and three doses of gentamicin, 80 mg every 8 h.	**SWI: 6/30 vs. 10/30.** Fever: 6/30 vs. 4/30. Intraabdominal abscess: 2/30 vs. 2/30. Anastomosis insufficiency: 1/30 vs. 5/30. Peritonitis: 1/30 vs. 3/30. UTI: 6/30 vs. 7/30. Respiratory tract infection: 1/30 vs. 1/30. Sepsis: 1/30 vs. 0/30. Deaths: 0/30 vs. 1/30. [Adverse event result: Yes. Cost information: NA.] **Conclusion:** No significant differences were found in the results. All the infectious complications which occurred postoperatively were due to bacterial contamination by aerobic pathogens.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

continued

continued

Study and quality	Surgery and definition of SWI	Antibiotic regimens	Results (Group A vs. Group B vs. Group C vs. Group D) Authors' conclusions
Wohlfart, 1987[155] Randomisation: Not clear. Blind outcome assessment: No. Follow-up: NA. Withdrawal: NA. 1-centre.	Elective colorectal surgery. Cancer patients: NA. Age: 63. SWI: Not defined.	**Group A:** Ceftriaxone, 2 g short i.v. infusion. **Group B:** Cefotiam, 1 g three doses, gentamicin, 80 mg two doses, plus metronidazole, 500 mg two doses.	**SWI: 1/30 vs. 2/30.** [Adverse event result: Yes. Cost information: NA.] **Conclusion:** Ceftriaxone proved its efficiency in infection prophylaxis for colon operation in comparison with a potent combination dose of cefotiam, gentamicin, and metronidazole. There was no difference in the clinical response between the two antibiotic regimens, but ceftriaxone has the considerable practical advantages of a once-daily dosage.
Zuber, 1989[156] (German) Randomisation: True. Blind outcome assessment: Yes. Follow-up: NA. Withdrawal: 5%. 1-centre.	Elective colorectal surgery. Cancer patients: NA from translation. Age: 68. SWI: Presence of pus or abscess.	**Group A:** Cephazolin, 2 g plus ornidazole, 1 g i.v. on anaesthesia. **Group B:** Cephazolin, 2 g i.v. on anaesthesia.	SWI: 4/50 vs. 10/50 ($p = 0.28$). Hospitalisation days: 16.7 vs. 20.3 ($p < 0.05$). 5 deaths in group B. [Adverse event result: Yes. Cost information: NA from translation.] **Conclusion:** Combination of cephazolin plus ornidazole shows better results when compared with cephazolin alone in reducing SWI rates. However, the difference was not statistically significant.

NA = not available or not applicable

Note: The age (in years) presented in the table is a rough calculation, across all groups in any one trial, based on the available data

Appendix 4

Number of comparisons between antibiotics in included trials

Number of comparisons between antibiotics in included trials

	Ampicillin + metronidazole	Aztreonam + clindamycin	Cephazolin + metronidazole	Cefotaxime + metronidazole	Cefotaxime	Cefotetan	Cefoxitin + neomycin + erythromycin	Cefoxitin	Ceftriaxone + metronidazole	Ceftriaxone	Cefuroxime + metronidazole	Ciprofloxacin + metronidazole	Co-amoxiclav	Doxycycline	Gentamicin + clindamycin	Gentamicin + metronidazole	Metronidazole	Mezlocillin + metronidazole	Mezlocillin	Latamoxef	Neomycin + erythromycin	Netilmicin + metronidazole	Piperacillin	Ticarcillin/clavulanic acid	Tinidazole	Control	All others
Ampicillin + metronidazole	2							1	1	1	1						2									1	
Aztreonam + clindamycin						1				1					2												
Cephazolin + metronidazole			1				1		1	1		1								1							
Cefotaxime + metronidazole				3	2			2			1		1														2
Cefotaxime				2	1			1											1					1			4
Cefotetan		1						2			1		1			1							1				2
Cefoxitin + neomycin + erythromycin			1					2													2						3
Cefoxitin	1			2	1	2	2			1					2						1		1			1	8
Ceftriaxone + metronidazole	1		1										1			1					2						2
Ceftriaxone	1	1	1					1																			1
Cefuroxime + metronidazole	1			1		1					1		1				4		3	1		1	1				5
Ciprofloxacin + metronidazole			1									1				2				1							
Co-amoxiclav				1		1			1		1		1			1		1	1								1
Doxycycline														1			2					1					2
Gentamicin + clindamycin		2						2								1											
Gentamicin + metronidazole						1			1			2	1		1	1	1			1	2						1	3
Metronidazole	2										4			2		1	1				1					1	1	5
Mezlocillin + metronidazole													1					3		1								
Mezlocillin					1						3		1												1			1
Latamoxef			1								1	1				1		1		1								4
Neomycin + erythromycin							2	1	2							2	1											2
Netilmicin + metronidazole											1			1									1	1				
Piperacillin						1		1			1											1	1					3
Ticarcillin/clavulanic acid					1														1			1		1	1			
Tinidazole																	1							1				2
Control	1							1								1	1											1
All others				2	4	2	3	8	2	1	5		1	2		3	5		1	4	2		3		2	1		

HTA panel membership

This report was identified as a priority by the Pharmaceutical Panel.

Acute Sector Panel

Chair: Professor John Farndon, University of Bristol †

Professor Senga Bond, University of Newcastle-upon-Tyne †

Professor Ian Cameron, Southeast Thames Regional Health Authority

Ms Lynne Clemence, Mid-Kent Health Care Trust †

Professor Francis Creed, University of Manchester †

Professor Cam Donaldson, University of Aberdeen

Mr John Dunning, Papworth Hospital, Cambridge †

Professor Richard Ellis, St James's University Hospital, Leeds

Mr Leonard Fenwick, Freeman Group of Hospitals, Newcastle-upon-Tyne †

Dr David Field, Leicester Royal Infirmary †

Ms Grace Gibbs, West Middlesex University Hospital NHS Trust †

Dr Neville Goodman, Southmead Hospital Services Trust, Bristol †

Mr Ian Hammond, Bedford & Shires Health & Care NHS Trust

Professor Adrian Harris, Churchill Hospital, Oxford

Professor Robert Hawkins, University of Bristol †

Dr Chris McCall, General Practitioner, Dorset †

Professor Alan McGregor, St Thomas's Hospital, London

Mrs Wilma MacPherson, St Thomas's & Guy's Hospitals, London

Professor Jon Nicoll, University of Sheffield †

Professor John Norman, University of Southampton

Dr John Pounsford, Frenchay Hospital, Bristol †

Professor Gordon Stirrat, St Michael's Hospital, Bristol

Professor Michael Sheppard, Queen Elizabeth Hospital, Birmingham †

Dr William Tarnow-Mordi, University of Dundee

Professor Kenneth Taylor, Hammersmith Hospital, London

Diagnostics and Imaging Panel

Chair: Professor Mike Smith, University of Leeds †

Professor Michael Maisey, Guy's & St Thomas's Hospitals, London *

Professor Andrew Adam, UMDS, London †

Dr Pat Cooke, RDRD, Trent Regional Health Authority

Ms Julia Davison, St Bartholomew's Hospital, London †

Professor Adrian Dixon, University of Cambridge †

Professor MA Ferguson-Smith, University of Cambridge †

Dr Mansel Hacney, University of Manchester

Professor Sean Hilton, St George's Hospital Medical School, London

Mr John Hutton, MEDTAP International Inc., London †

Professor Donald Jeffries, St Bartholomew's Hospital, London †

Dr Andrew Moore, Editor, *Bandolier* †

Professor Chris Price, London Hospital Medical School †

Dr Ian Reynolds, Nottingham Health Authority

Professor Colin Roberts, University of Wales College of Medicine †

Miss Annette Sergeant, Chase Farm Hospital, Enfield

Professor John Stuart, University of Birmingham

Dr Ala Szczepura, University of Warwick †

Mr Stephen Thornton, Cambridge & Huntingdon Health Commission

Dr Gillian Vivian, Royal Cornwall Hospitals Trust †

Dr Jo Walsworth-Bell, South Staffordshire Health Authority †

Dr Greg Warner, General Practitioner, Hampshire †

Methodology Panel

Chair: Professor Martin Buxton, Brunel University †

Professor Anthony Culyer, University of York *

Dr Doug Altman, Institute of Health Sciences, Oxford †

Professor Michael Baum, Royal Marsden Hospital

Professor Nick Black, London School of Hygiene & Tropical Medicine †

Professor Ann Bowling, University College London Medical School †

Dr Rory Collins, University of Oxford

Professor George Davey-Smith, University of Bristol

Dr Vikki Entwistle, University of Aberdeen †

Professor Ray Fitzpatrick, University of Oxford †

Professor Stephen Frankel, University of Bristol

Dr Stephen Harrison, University of Leeds

Mr Philip Hewitson, Leeds FHSA

Professor Richard Lilford, Regional Director, R&D, West Midlands †

Mr Nick Mays, King's Fund, London †

Professor Ian Russell, University of York †

Professor David Sackett, Centre for Evidence Based Medicine, Oxford †

Dr Maurice Slevin, St Bartholomew's Hospital, London

Dr David Spiegelhalter, Institute of Public Health, Cambridge †

Professor Charles Warlow, Western General Hospital, Edinburgh †

* Previous Chair
† Current members

continued

continued

Pharmaceutical Panel

Chair: Professor Tom Walley, University of Liverpool †

Professor Michael Rawlins, University of Newcastle-upon-Tyne*

Dr Colin Bradley, University of Birmingham

Professor Alasdair Breckenridge, RDRD, Northwest Regional Health Authority

Ms Christine Clark, Hope Hospital, Salford †

Mrs Julie Dent, Ealing, Hammersmith & Hounslow Health Authority, London

Mr Barrie Dowdeswell, Royal Victoria Infirmary, Newcastle-upon-Tyne

Dr Desmond Fitzgerald, Mere, Bucklow Hill, Cheshire

Dr Alistair Gray, Health Economics Research Unit, University of Oxford †

Professor Keith Gull, University of Manchester

Dr Keith Jones, Medicines Control Agency

Professor Trevor Jones, ABPI, London †

Ms Sally Knight, Lister Hospital, Stevenage †

Dr Andrew Mortimore, Southampton & SW Hants Health Authority †

Mr Nigel Offen, Essex Rivers Healthcare, Colchester †

Dr John Posnett, University of York

Mrs Marianne Rigge, The College of Health, London †

Mr Simon Robbins, Camden & Islington Health Authority, London †

Dr Frances Rotblat, Medicines Control Agency †

Mrs Katrina Simister, Liverpool Health Authority †

Dr Ross Taylor, University of Aberdeen †

Dr Tim van Zwanenberg, Northern Regional Health Authority

Dr Kent Woods, RDRD, Trent RO, Sheffield †

Population Screening Panel

Chair: Professor Sir John Grimley Evans, Radcliffe Infirmary, Oxford †

Dr Sheila Adam, Department of Health*

Ms Stella Burnside, Altnagelvin Hospitals Trust, Londonderry †

Dr Carol Dezateux, Institute of Child Health, London †

Dr Anne Dixon Brown, NHS Executive, Anglia & Oxford †

Professor Dian Donnai, St Mary's Hospital, Manchester †

Dr Tom Fahey, University of Bristol †

Mrs Gillian Fletcher, National Childbirth Trust †

Professor George Freeman, Charing Cross & Westminster Medical School, London

Dr Mike Gill, Brent & Harrow Health Authority †

Dr JA Muir Gray, RDRD, Anglia & Oxford RO †

Dr Ann Ludbrook, University of Aberdeen †

Professor Alexander Markham, St James's University Hospital, Leeds †

Professor Theresa Marteau, UMDS, London

Dr Ann McPherson, General Practitioner, Oxford †

Professor Catherine Peckham, Institute of Child Health, London

Dr Connie Smith, Parkside NHS Trust, London

Dr Sarah Stewart-Brown, University of Oxford †

Ms Polly Toynbee, Journalist †

Professor Nick Wald, University of London †

Professor Ciaran Woodman, Centre for Cancer Epidemiology, Manchester

Primary and Community Care Panel

Chair: Dr John Tripp, Royal Devon & Exeter Healthcare NHS Trust †

Professor Angela Coulter, King's Fund, London *

Professor Martin Roland, University of Manchester *

Dr Simon Allison, University of Nottingham

Mr Kevin Barton, East London & City Health Authority †

Professor John Bond, University of Newcastle-upon-Tyne †

Ms Judith Brodie, Age Concern, London †

Dr Nicky Cullum, University of York †

Professor Shah Ebrahim, Royal Free Hospital, London

Mr Andrew Farmer, Institute of Health Sciences, Oxford †

Ms Cathy Gritzner, The Patients' Association †

Professor Andrew Haines, RDRD, North Thames Regional Health Authority

Dr Nicholas Hicks, Oxfordshire Health Authority †

Professor Richard Hobbs, University of Birmingham †

Professor Allen Hutchinson, University of Sheffield †

Mr Edward Jones, Rochdale FHSA

Professor Roger Jones, UMDS, London

Mr Lionel Joyce, Chief Executive, Newcastle City Health NHS Trust

Professor Martin Knapp, London School of Economics & Political Science

Professor Karen Luker, University of Liverpool

Professor David Mant, NHS Executive South & West †

Dr Fiona Moss, North Thames British Postgraduate Medical Federation †

Professor Dianne Newham, King's College London

Professor Gillian Parker, University of Leicester †

Dr Robert Peveler, University of Southampton †

Dr Mary Renfrew, University of Oxford

Ms Hilary Scott, Tower Hamlets Healthcare NHS Trust, London †

* Previous Chair
† Current members

Health Technology Assessment 1998; Vol. 2: No. 7

Copies of this report can be obtained from:

The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 1703 595 639 Email: hta@soton.ac.uk
http://www.soton.ac.uk/~hta

ISSN 1366-5278