Health Technology Assessment 2011; Vol. 15: No. 30
ISSN 1366-5278

Identification of risk factors by systematic review and development of risk-adjusted models for surgical site infection

C Gibbons, J Bruce, J Carpenter, AP Wilson, J Wilson, A Pearson, DL Lamping, ZH Krukowski and BC Reeves

September 2011
10.3310/hta15300

Health Technology Assessment
NIHR HTA programme
www.hta.ac.uk

How to obtain copies of this and other HTA programme reports

An electronic version of this title, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (www.hta.ac.uk). A fully searchable DVD is also available (see below).

Printed copies of HTA journal series issues 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 issue and for the rest of the world £3 per issue.

How to order:

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

Additionally the HTA website allows you to either print out your order or download a blank order form.

Contact details are as follows:

Synergie UK (HTA Department)
Digital House, The Loddon Centre
Wade Road
Basingstoke
Hants RG24 8QW

Email: orders@hta.ac.uk

Tel: 0845 812 4000 – ask for 'HTA Payment Services' (out-of-hours answer-phone service)

Fax: 0845 812 4001 – put 'HTA Order' on the fax header

Payment methods

Paying by cheque
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to *University of Southampton* and drawn on a bank with a UK address.

Paying by credit card
You can order using your credit card by phone, fax or post.

Subscriptions

NHS libraries can subscribe free of charge. Public libraries can subscribe at a reduced cost of £100 for each volume (normally comprising 40–50 titles). The commercial subscription rate is £400 per volume (addresses within the UK) and £600 per volume (addresses outside the UK). Please see our website for details. Subscriptions can be purchased only for the current or forthcoming volume.

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

Please use the form on the HTA website (www.hta.ac.uk/htacd/index.shtml). *HTA on DVD* is currently free of charge worldwide.

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

Identification of risk factors by systematic review and development of risk-adjusted models for surgical site infection

C Gibbons,[1] J Bruce,[2] J Carpenter,[1] AP Wilson,[3] J Wilson,[4] A Pearson,[5] DL Lamping,[1†] ZH Krukowski[6] and BC Reeves[7*]

[1]London School of Hygiene and Tropical Medicine, London, UK
[2]University of Aberdeen, Aberdeen, UK
[3]University College London, London, UK
[4]Imperial College Healthcare NHS Trust, London, UK
[5]Health Protection Agency, London, UK
[6]Aberdeen Royal Infirmary, Aberdeen, UK
[7]University of Bristol, Bristol, UK

*Corresponding author
†In memoriam

Declared competing interests of authors: Barnaby C Reeves was awarded a grant by the National Institute for Health Research to carry out this research. The grant was awarded to the London School of Hygiene and Tropical Medicine (Barnaby C Reeves' employer until 2005). James Carpenter has consultancy and grants. A Peter Wilson has consultancy (Roche, drug safety monitoring board) and a grant with the Department of Health (trial of cleaning on hospital wards).

Published September 2011
DOI: 10.3310/hta15300

This report should be referenced as follows:

Gibbons C, Bruce J, Carpenter J, Wilson AP, Wilson J, Pearson A, *et al*. Identification of risk factors by systematic review and development of risk-adjusted models for surgical site infection. *Health Technol Assess* 2011;**15**(30).

Health Technology Assessment is indexed and abstracted in *Index Medicus*/MEDLINE, *Excerpta Medica*/EMBASE, *Science Citation Index Expanded* (*SciSearch*) and *Current Contents*/Clinical Medicine.

NIHR Health Technology Assessment programme

The Health Technology Assessment (HTA) programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The research findings from the HTA programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

The HTA programme is needs led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, from the public and consumer groups and from professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA programme then commissions the research by competitive tender.

Second, the HTA programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Third, through its Technology Assessment Report (TAR) call-off contract, the HTA programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer reviewed by a number of independent expert referees before publication in the widely read journal series *Health Technology Assessment*.

Criteria for inclusion in the HTA journal series

Reports are published in the HTA journal series if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

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.

The research reported in this issue of the journal was commissioned by the National Coordinating Centre for Research Methodology (NCCRM), and was formally transferred to the HTA programme in April 2007 under the newly established NIHR Methodology Panel. The HTA programme project number is 06/90/19. The contractual start date was in April 2003. The draft report began editorial review in October 2010 and was accepted for publication in March 2011. The commissioning brief was devised by the NCCRM who specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA programme or the Department of Health.

ISSN 1366-5278 (Print)
ISSN 2046-4924 (Online)
ISSN 2046-4932 (DVD)

Published by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk), on behalf of NETSCC, HTA.
Printed on acid-free paper in the UK by the Charlesworth Group. MR

Abstract

Identification of risk factors by systematic review and development of risk-adjusted models for surgical site infection

C Gibbons,[1] J Bruce,[2] J Carpenter,[1] AP Wilson,[3] J Wilson,[4] A Pearson,[5] DL Lamping,[1†] ZH Krukowski[6] and BC Reeves[7*]

[1]London School of Hygiene and Tropical Medicine, London, UK
[2]University of Aberdeen, Aberdeen, UK
[3]University College London, London, UK
[4]Imperial College Healthcare NHS Trust, London, UK
[5]Health Protection Agency, London, UK
[6]Aberdeen Royal Infirmary, Aberdeen, UK
[7]University of Bristol, Bristol, UK

*Corresponding author
[†]In memoriam

Background: Surgical site infections (SSIs) are complications of surgery that cause significant postoperative morbidity. SSI has been proposed as a potential indicator of the quality of care in the context of clinical governance and monitoring of the performance of NHS organisations against targets.
Objectives: We aimed to address a number of objectives. Firstly, identify risk factors for SSI, criteria for stratifying surgical procedures and evidence about the importance of postdischarge surveillance (PDS). Secondly, test the importance of risk factors for SSI in surveillance databases and investigate interactions between risk factors. Thirdly, investigate and validate different definitions of SSI. Lastly, develop models for making risk-adjusted comparisons between hospitals.
Data sources: A single hospital surveillance database was used to address objectives 2 and 3 and the UK Surgical Site Infection Surveillance Service database to address objective 4.
Study design: There were four elements to the research: (1) systematic reviews of risk factors for SSI (two reviewers assessed titles and abstracts of studies identified by the search strategy and the quality of studies was assessed using the Newcastle Ottawa Scale); (2) assessment of agreement between four SSI definitions; (3) validation of definitions of SSI, quantifying their ability to predict clinical outcomes; and (4) development of operation-specific risk models for SSI, with hospitals fitted as random effects.
Results: Reviews of SSI risk factors other than established SSI risk indices identified other risk; some were operation specific, but others applied to multiple operations. The factor most commonly identified was duration of preoperative hospital stay. The review of PDS for SSI confirmed the need for PDS if SSIs are to be compared meaningfully over time within an institution. There was wide variation in SSI rate (SSI%) using different definitions. Over twice as many wounds were classified as infected by one definition only as were classified as infected by both. Different SSI definitions also classified different wounds as being infected. The two most established SSI definitions had broadly similar ability to predict the

chosen clinical outcomes. This finding is paradoxical given the poor agreement between definitions. Elements of each definition not common to both may be important in predicting clinical outcomes or outcomes may depend on only a subset of elements which are common to both. Risk factors fitted in multivariable models and their effects, including age and gender, varied by surgical procedure. Operative duration was an important risk factor for all operations, except for hip replacement. Wound class was included least often because some wound classes were not applicable to all operations or were combined because of small numbers. The American Association of Anesthesiologists class was a consistent risk factor for most operations.

Conclusions: The research literature does not allow surgery-specific or generic risk factors to be defined. SSI definitions varied between surveillance programmes and potentially between hospitals. Different definitions do not have good agreement, but the definitions have similar ability to predict outcomes influenced by SSI. Associations between components of the National Nosocomial Infections Surveillance risk index and odds of SSI varied for different surgical procedures. There was no evidence for effect modification by hospital. Estimates of SSI% should be disseminated within institutions to inform infection control. Estimates of SSI% across institutions or countries should be interpreted cautiously and should not be assumed to reflect quality of medical care. Future research should focus on developing an SSI definition that has satisfactory psychometric properties, that can be applied in everyday clinical settings, includes PDS and is formulated to detect SSIs that are important to patients or health services.

Funding: The National Institute for Health Research Technology Assessment programme.

Contents

List of abbreviations

ASA	American Society of Anesthesiologists
ASEPSIS	Additional treatment, the presence of Serous discharge, Erythema, Purulent exudate, and Separation of the deep tissues, the Isolation of bacteria and the duration of inpatient Stay
CABG	coronary artery bypass graft
CDC	Centers for Disease Control and Prevention
CI	confidence interval
HR	hazard ratio
HTA	health technology assessment
IGLS	iterative generalised least squares
IQR	interquartile range
LOS	length of stay
MeSH	medical subject heading
MQL	marginal quasi-likelihood
NIHR	National Institute for Health Research
NINSS	Nosocomial Infection National Surveillance Scheme
NNIS	National Nosocomial Infections Surveillance
NOS	Newcastle Ottawa Scale
NRC	National Research Council
OR	odds ratio
PAB	prescription of antibiotics in hospital or after discharge
PDS	postdischarge surveillance
PLOS	protracted length of hospital stay
Pneg	number of negative predictions
Ppos	number of positive predictions
PQL	penalised quasi-likelihood
PWH	patient-reported problem with wound healing
RCT	randomised controlled trial
ROC	receiver operating characteristic
RR	rate ratio
SENIC	Study of the Efficacy of Nosocomial Infection Control
SSI	surgical site infection
SSI%	surgical site infection rate
SSISS	Surgical Site Infection Surveillance Service
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
UCLH	University College London Hospitals
WBC	white blood cell
WRTX	wound retreatment in hospital or after discharge

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

Executive summary

Background to the research

Surgical site infections (SSIs) are complications of surgery that cause significant postoperative morbidity. They are costly to health services and inconvenient, painful and potentially fatal to affected patients. Rates of SSI have been observed to vary widely by hospital and may be influenced by surgical management and other aspects of the quality of health care. SSI rate (SSI%) has been proposed as a potential indicator of the quality of care in the context of clinical governance and monitoring of the performance of NHS organisations against targets.

The risk of developing an SSI is likely to be influenced by the characteristics of patients, of operations and postoperative care. Therefore, the use of SSI as a performance indicator requires hospital-specific rates to be risk adjusted. This research sought to identify important risk factors for SSI in defined contexts, whether surgery specific or generic, and investigate the feasibility of risk-adjusting SSI%.

Aim and objectives of the research

The aim of the proposed research was to investigate methods for the risk adjustment of rates of SSI. We proposed to address the following specific objectives.

1. To identify risk factors for SSI, criteria for the stratification of surgical procedures and evidence about the importance of postdischarge surveillance (PDS) from systematic reviews of the literature.
2. To test whether or not 'short-listed' variables from the literature are risk factors in available SSI surveillance databases. To identify in univariable analyses other potential risk factors from available databases and to investigate interactions between risk factors.
3. To develop models for making risk-adjusted comparisons between hospitals.
4. To investigate modifications of the definition of SSI used by the Centers for Disease Control and Prevention (CDC) and the impact of modified definitions on the importance (use for prediction) of risk factors identified.

How the research was conducted

Reviews of the literature

Four systematic reviews of the literature were carried out. These reviews sought to identify:

1. surgery-specific risk factors for SSI following joint replacement
2. surgery-specific risk factors for SSI following large bowel surgery
3. generic risk factors (relevant to many surgical procedures) for SSI that are not included in existing SSI risk indices
4. risk factors for SSIs detected by following up patients after discharge.

Systematic searches were conducted on two biomedical databases, MEDLINE and EMBASE (1966–2004 and 1980–2004, respectively). Search strategies consisted of medical subject headings and free-text terms relating to surgical infection (surgical wound infection/SSI/postoperative

infection), risk adjustment (risk assessment/factor/adjustment/stratification/modelling) and, where appropriate, the surgical area being reviewed or terms describing PDS. The review also used literature identified by a previous systematic review.

Agreement between definitions of surgical site infection

This part of the research used data collected by SSI surveillance of cardiac, thoracic, orthopaedic, general, obstetric, gynaecological, urological, maxillofacial, plastic and vascular surgical specialties in one UK hospital. The data, for 5804 surgical wounds in 4773 patients, allowed four SSI definitions to be applied: (1) ASEPSIS (Additional treatment, the presence of Serous discharge, Erythema, Purulent exudate, and Separation of the deep tissues, the Isolation of bacteria and the duration of inpatient Stay); (2) 1992 definition of the CDC; (3) a modified version of the 1992 CDC definition used for SSI surveillance in England; and (4) a definition based on pus. Patients were contacted by post or telephone 1–2 months after their operations to complete a PDS questionnaire designed to detect SSIs arising after discharge from hospital. SSIs identified by different definitions were tabulated and agreement between definitions was quantified.

Validation of definitions of surgical site infection

This part of the research used an updated version of the above data set from the same UK hospital, describing 11,124 wounds in 8691 patients. We constructed a set of clinical outcomes that wound infection would be expected to influence or cause: (1) clinical actions that were likely to reflect both mild (prescription of antibiotic) and severe infection (wound retreated); (2) patients' views about whether or not there was a problem with the healing of their wounds; and (3) length of hospital stay, reflecting health service resource use. Modifications were made to SSI definitions to try to ensure that they were independent of the outcomes. We then developed logistic regression models to quantify the ability of alternative SSI definitions to predict the outcomes.

Surgical site infection risk modelling

This part of the research used data submitted to the UK Surgical Site Infection Surveillance Service [at the time, the Nosocomial Infection National Surveillance Scheme (NINSS)]. Hospitals taking part carried out surveillance of one or more of 12 categories of surgical procedure, e.g. large bowel surgery, coronary artery bypass graft (CABG) or hip replacement. In order for data to be included, there was a requirement for a hospital to carry out surveillance for at least 3 consecutive months. Hospitals submitted data about key risk factors for SSI [including the National Nosocomial Infections Surveillance (NNIS) risk index, demographic information about patients, and characteristics of the operation and wound] and information about SSIs that developed during the hospital stay. Univariable logistic regression analyses were initially carried out on the entire data set of 113,824 operations, stratifying by surgical procedure and then for each procedure separately. Multivariable risk models, with hospitals fitted as random effects, were then developed for each procedure. Effect modification of risk factors by hospital was investigated in multilevel models.

Research findings

Reviews of the literature

The literature reviewed was found to be mainly of poor methodological quality, preventing quantitative summaries of the risk conferred by specific risk factors. The reviews of surgery-specific risk factors, other than those which make up the established risk indices, identified other factors associated with increasing risk of SSI. This has also been suggested for operations other than those which we reviewed. Some risk factors are unequivocally surgery specific, but

others may apply to a range of procedures. The factor most commonly identified by the review of generic risk factors was duration of preoperative stay in hospital. The review of SSIs detected by PDS demonstrated that a significant proportion of SSIs develop after discharge and that the need to include PDS is an important consideration for procedures where the length of hospital stay is short or likely to vary over time or between institutions.

Agreement between definitions of surgical site infection

There was wide variation in the frequency of SSI identified using different definitions. Using existing CDC and ASEPSIS definitions of SSI (most and least sensitive definitions), over twice as many wounds were classified as infected by one definition only as were classified as infected by both. Different SSI definitions also classified different wounds as being infected, although some wounds were classified as infected by all definitions.

Validation of definitions of surgical site infection

Both ASEPSIS and CDC SSI definitions had a broadly similar ability to predict the chosen clinical outcomes; areas under receiver operating characteristic curves ranged from 0.75 to 0.88, except for prediction of prolonged hospital stay (0.64). These findings are paradoxical given the poor agreement between definitions in classifying individual wounds. There may be elements of each definition that are important in identifying the outcomes but which are not common to both, or the ability to predict the outcomes may depend on only a subset of features that are common to both. These possibilities suggest that there is an opportunity to produce a better definition by combining the elements from different definitions or by dropping redundant ones.

Surgical site infection risk modelling

Univariable models highlighted that components of existing risk indices should be modelled separately and that there was effect modification of risk factors by surgical procedure. The risk factors included in best-fit multivariable models varied by surgical procedure, as did the effects of risk factors included in the models. This conclusion applies to components of existing risk indices as well as to other factors considered in the analyses. Of the components in established risk indices, operative duration appeared to be an important risk factor for all operations, except for hip replacement. Wound class was included least often because some wound classes were not applicable to some surgical procedures or were combined because of small numbers. The American Association of Anesthesiologists class was a consistent risk factor for most surgery categories (except open reduction of fractures); its effect was uncertain for limb amputation and vascular surgery because of the small sample sizes available.

Age and gender were included in all models. The odds of SSI clearly increased with age for four surgery categories (CABG, hip and knee prostheses and open reduction of fracture), but not for four other surgery categories (large and small bowel, limb amputation and vascular surgery). The results were most varied for gender. Women had lower odds of SSI for knee prosthesis and open reduction of fracture, higher odds of SSI for CABG and similar odds of SSI for small and large bowel surgery, hip prosthesis and limb amputation. Preoperative duration of stay, an additional generic risk factor identified by the reviews, was associated with an increase in the risk of SSI for the four surgery categories with the largest number of data (hip and knee prosthesis, CABG and large bowel surgery).

Conclusions

The research literature does not allow a set of surgery-specific or generic risk factors to be defined. We believe that there is a need for high-quality research to develop a revised SSI definition that has satisfactory psychometric properties and which can be applied in everyday

clinical settings and to the surveillance for SSI after discharge from hospital. Research to identify risk factors for SSI needs to be carried out to higher methodological standards, primarily by following established epidemiological principles.

Surgical site infection definitions vary between surveillance programmes and, because they are complex and difficult to apply, potentially between hospitals within programmes. Definitions that are different, some in apparently only minor ways, do not have good agreement. The most widely established definitions have a similar ability to predict outcomes influenced by SSI.

In surgery-specific multivariable risk-adjusted models, associations between components of the NNIS risk index and the odds of SSI varied both quantitatively and qualitatively for different surgical procedures; this finding also applied to other risk factors investigated. There was no evidence for effect modification of risk factors by hospital.

Surveillance programmes are important to inform clinical governance and the management of infection control over time. Performance estimates (data quality and SSI%) based on consistent surveillance methods for institutions and groupings within institutions should be disseminated locally for this purpose. Comparisons of performance estimates (SSI%) for institutions or countries should be regarded with caution; nevertheless, comparisons against a benchmark may prompt institutions to make changes to infection control practices that are associated with improved performance. Judgements about the quality of medical care provided by hospitals should not be based on these statistics alone by agencies responsibility for auditing performance. National surveillance systems should comply with a set of features designed to ensure their quality.

Future research should focus on devloping an SSI definition that has satisfactory psychometric properties, that can be applied in everyday clinical settings, includes PDS and is formulated to detect SSIs that are important to patients or health services.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Chapter 1

Introduction to the research

Background

Wound infections (referred to subsequently as surgical site infections; SSIs) are relatively frequent complications of surgery that cause significant postoperative morbidity. They are costly to health services and inconvenient, painful and potentially fatal to affected patients.[1–9] There have been several initiatives in the UK to monitor and to control SSIs. The UK Department of Health established working groups to draw up guidance for hospitals to reduce the occurrence of SSIs.[4] The UK National Institute for Health Research (NIHR) commissioned research about methods for measuring and monitoring SSI rates (SSI%).[9] Hospital-acquired infection (which includes SSIs) was the subject of a report by the UK National Audit Office.[10]

Rates of SSI have been observed to vary widely by hospital and it is believed that rates are, to a greater or lesser extent, influenced by surgical management and other aspects of the quality of health care. Variation in health-care indicators led the UK government to promote clinical governance and monitoring of the performance of UK NHS organisations against targets[11,12] and SSI% has been proposed as a potential indicator of the quality of care, in the context of clinical governance and performance monitoring in the NHS.[13] Surveillance of SSIs arising after orthopaedic surgery became mandatory in England from 1 April 2004.[14,15] Although the performance indicators set out in *The NHS plan: a progress report* in 2001[16] were criticised, and subsequently modified, the UK Care Quality Commission continues to have responsibility for monitoring the performance of NHS organisations against specified targets.[17]

The commissioned research described in this report emerged from both research evidence and health policy.[9,17] The commissioning brief identified the following goals of the research:

1. To develop 'a set of models for risk-adjusting wound infection outcomes, so as to enable meaningful *comparisons* between units or surgeons, and over time, within broadly similar procedures for broadly similar underlying conditions'.
2. To develop 'an integrated model which aims at setting *absolute standards* for wound infection rates in different procedures/underlying conditions, in the presence of different risk factors'. [It is customary to describe the frequency of SSI as a 'rate' and we adopt this convention in this report. However, it is important to note that SSI%s are conventionally calculated as risks, i.e. the number of infected wounds/patients divided by the total number of wounds/patients recorded. We abbreviate this to SSI% in this report.]

Risk-adjusting rates of surgical site infection

Risk factors

Stratifying surgical procedures by 'risk' is a key issue for the performance monitoring in SSI surveillance programmes. The NIHR review[9] identified three main risk indices, namely the National Research Council (NRC),[18] the Study of the Efficacy of Nosocomial Infection Control (SENIC)[19] and the National Nosocomial Infections Surveillance (NNIS) indices.[7,20] Bacterial contamination during operations contribute to the risk of SSI and all three of these

indices include the four-class NRC wound classification system (class I, clean; class II, clean–contaminated; class III, contaminated; class IV, dirty). Duration of operation is also common to the last two systems, although the NNIS index[7,20] uses a procedure-specific cut-off criterion rather than an absolute cut-off.[19] The SENIC and NNIS indices also include a measure of the 'host resistance', i.e. three or more different diagnoses[19] or American Society of Anesthesiologists (ASA) class.[20]

The NIHR review found that the NNIS index, developed by the Centers for Disease Control and Prevention (CDC) for NNIS in the USA, is the most widely used method of risk adjustment.[9] It is designed to be used only within clinically similar operation types, reflecting a consensus that comparisons of surgical infection rates can only be useful within clinically similar contexts ('procedure groups'). Stratification by NNIS risk index has been adopted by many national surveillance programmes.[3,21,22] Bruce *et al.* concluded that, although it has been criticised for not including other potential risk factors, it is the best available method for stratification of SSI%s, thereby achieving a degree of risk adjustment.[9] However, they also commented that the NNIS index has yet to be fully validated in the UK patient and hospital setting, although UK and US data have been compared with respect to the risk conferred by the duration of operation.[23]

A number of points about risk stratification emerged from a workshop held prior to the commissioning of this research:

- The specific type of surgery, e.g. implantation of a prosthetic device, may also contribute to the risk of SSI.
- Different risk scoring systems may be more or less suitable in different contexts and for different procedures.
- Existing data suggest that a gradient in SSI%s with increasing risk index scores may be a reflection of poor quality, e.g. duration of operation is partly under the control of the surgeon and may vary across centres. This possibility could be investigated by exploring effect modification of risk factors by hospitals.
- A generic risk index does not adequately characterise all the factors that contribute to the risk of SSI. Careful consideration needs to be given both to the identification of risk factors and to whether or not comparisons between centres should take account of particular risk factors.

As pointed out by the research brief:

> 'Some care is required when devising or using risk indices.
>
> - "As knowledge of how to prevent infections in particular circumstances grows, individuals who would previously have been at high risk might no longer be so. For instance, one could speculate (NB without any evidence) that appropriate anti-microbial prophylaxis might essentially remove the importance of length of operation as a risk factor. Note that, if this were the case, careful analysis of relevant databases might suggest that length of operation was an important risk factor in some centres (those not giving appropriate prophylaxis), and not in others. Detailed examination of heterogeneity, and time trends is thus clearly important for setting *absolute* standards, though not necessary for making valid *comparisons*."
> - "Where the aim is to compare centres or surgeons, one might also question the appropriateness of 'adjusting' for variables under 'surgical control' (i.e. variables that are themselves, in part, 'outcomes' on the pathway to infection) rather than purely a priori infection risks. For instance, length of operation, and 'wound class' come into this category. Thus (to play devil's advocate), using the NNIS, a low-risk operation

which through poor technique results in 'gross spillage from the gastrointestinal tract', and thus takes a long time, will be judged against difficult operations in which contamination and long operating times are inevitable, while heroic, fast, skilful surgery which manages to avoid contamination will be judged against straightforward, routine, low-risk operations." '

The aetiology of SSIs in different procedures and settings may vary. If so, the completeness of ascertainment of SSIs may affect the risk factors identified and their empirical weights in risk-adjustment models. Ascertainment is likely to vary most depending on whether or not postdischarge surveillance (PDS) has been carried out. If only infections detected in hospital are included, up to 72% of all SSIs may be missed depending on the duration of postoperative stay. The proposed research will estimate the effect of including PDS on the identification of risk factors.

Requirement of systems for risk adjustment and target setting

A system for establishing valid targets for SSI%s, and making meaningful comparisons of SSI%s between hospitals, requires:

1. a high and consistent level of ascertainment across hospitals
2. adequate characterisation of important risk factors
3. a statistical model to weight risk factors appropriately in order to take account of differences in case-mix between hospitals.

Describing the extent to which existing databases achieve these requirements is a key objective of the proposed research.

A final note of caution concerns bias in data collection. Publication of centre-specific performance measures may create pressures to bias data collection to improve outcomes and data about risk factors. Susceptibility to bias should be a further consideration when choosing the data items required for statistical models that aim to adjust comparisons between centres for varying case-mix.

Databases considered

This research aimed to use databases containing data from wound infection surveillance that were already available (*Table 1*).

We investigated the scope of these different databases. The Scottish and Northern Irish surveillance programmes were at an earlier stage of development and we considered that they would introduce additional heterogeneity to the risk modelling aspects of the project. The

TABLE 1 Summary of SSI surveillance databases

Database	Availability	Use in this project
NINSS	Anonymised data set obtained	Used in risk modelling
UCLH	Anonymised data set obtained	Used in SSI definition study
Scottish PHLS surveillance	Not obtained	
Northern Irish PHLS surveillance	Not obtained	
Inverclyde groin hernia repair	Not obtained. Groin hernia operations only	

NINSS, Nosocomial Infection National Surveillance Scheme; PHLS, Public Health Laboratory Service; UCLH, University College London Hospitals.

Inverclyde groin hernia data were felt unlikely to add to the other databases and would also have introduced heterogeneity. Therefore, we chose to carry out our proposed research on two databases, namely the surveillance databases from (1) the University College London Hospitals (UCLH) and (2) the UK Nosocomial Infection National Surveillance Scheme (NINSS) in England. In 2005, NINSS was renamed the Surgical Site Infection Surveillance Service (SSISS); we have maintained the NINSS abbreviation through this report as this was the name of the surveillance programme during the period covered by the data set that was analysed.

These two databases complemented one another. The UCLH database was the most comprehensive and included information about procedures not covered by the NINSS database. However, it only covered one institution. In contrast, the NINSS database covered many hospitals but contained less information about each procedure.

Research aims and objectives

The aim of the proposed research was to investigate methods for the risk adjustment of rates of surgical wound infection. We proposed to address the following specific objectives.

- Identify risk factors for SSI, criteria for the stratification of surgical procedures and evidence about the importance of PDS from systematic reviews of the literature.
- Test whether or not 'short-listed' variables from the literature are risk factors in available SSI surveillance databases, to identify in univariable analyses other potential risk factors from available databases and to investigate interactions between risk factors.
- Develop models for making risk-adjusted comparisons between hospitals.
- Investigate modifications of the definition of SSI used by the CDC and the impact of modified definitions on the importance (use for prediction) of risk factors identified.

Appendix 1 describes the prespecified aims and objectives and the proposed methods of the research in detail, including an extension of the project to address the objective of investigating the validity of SSI definitions.

Chapter 2

Systematic reviews of literature

Introduction to systematic reviews

Review research questions

The original proposal identified three review areas relevant to the project:

1. potential risk factors
2. evidence relating to stratification by procedure type
3. evidence about how the inclusion of infections identified after hospital discharge may require modification of systems for risk adjustment.

Following preliminary discussions among the research team, these review areas were restructured as follows:

- potential operation-specific risk factors, including stratification by subprocedures
- potential generic risk factors
- evidence about how the inclusion of infections identified after hospital discharge may require modification of systems for risk adjustment.

Review research questions

The content of the reviews given in this report are outlined in *Table 2*.

Potential operation specific risk factors, including stratification by subprocedures

At the outset, we planned to identify risk factors and extract associated information about unadjusted and adjusted risk estimates, confidence intervals (CIs), etc. Lists of risk factors, with examples of their effects from particular papers judged to be of higher quality, would illustrate whether or not documentation of generic risk factors is likely to be sufficient to control for case-mix. We intended to carry out reviews for all of the main operation types.

It quickly became clear that it would not be possible to review risk factors for so many operation types. We reduced the number of operations we aimed to review to two: (1) hip or knee

TABLE 2 Systematic reviews conducted

Review topic proposed	Systematic reviews carried out
Operation-specific SSI risk factors, including stratification by subprocedures	Limit to: ■ joint replacement ■ large bowel surgery Provide a quantitative summary (but not necessarily a quantitative synthesis) of risk factors identified and quality assessment of eligible papers
Generic SSI risk factors	Provide a quantitative summary (but not necessarily a quantitative synthesis) of risk factors identified and quality assessment of eligible papers.
Differences in risk factors for in-hospital and PDS	Review carried out as described in the original protocol

replacement and (2) large bowel surgery. These operations were chosen because they represent high-volume operations in which infection can be catastrophic, with (in the case of bowel surgery) wounds of varying cleanliness.

Potential generic risk factors

This review aimed to identify additional generic risk factors for SSI not included in existing risk adjustment indices. As for surgery-specific risk factors, failure to consider other important generic risk factors would undermine the validity of existing systems for risk adjustment. We also sought to identify risk adjustment indices or systems other than SENIC and NNIS.

Risk factors for surgical site infections identified after hospital discharge

The NIHR Health Technology Assessment (HTA) programme review identified the importance of PDS of wound infection for complete ascertainment of the true rates of SSI following surgery, with rates potentially doubling with inclusion of SSIs detected by PDS.[9] The influence of operational factors, such as the average length of stay (LOS), on the proportion of SSIs detected in hospital illustrates why comparisons of the rate of SSIs detected in hospital could be misleading. Any decision to include infections detected by PDS raises the question of whether or not existing risk indices, developed in the context of SSI surveillance in hospital,[18–20] are applicable to infections detected by PDS. Hence, we sought to review research studies that investigated whether or not risk factors for infections identified by PDS are similar to risk factors for infections identified by SSI surveillance in hospital.

The risk factors contributing to existing risk indices all characterise either the patient or the operation at the time of surgery, on the assumption that most SSIs arise as a result of exposures in the operating theatre and the physiological capacity of patients to combat these exposures. Factors related to the postoperative period may play a part in whether or not a patient develops an SSI, e.g. if a wound drain is present postoperatively providing a route of microbial access to the deep wound tissues or if there are delays in healing of the superficial incision. As PDS identifies SSIs that, on average, become apparent later than SSIs detected in hospital, it is possible that they may arise from exposures that occur after leaving the operating theatre. Relevant exposures may be reflected in different risk factors than those considered for SSI surveillance in hospital.

Systematic review methods

Searches for eligible literature

Systematic searches were conducted on two major biomedical databases, MEDLINE and EMBASE (1966–2004 and 1980–2004, respectively).

Pilot searches were conducted early in 2004 to identify a sensitive but specific search. The final search strategies were conducted in June (hip and knee replacement, bowel surgery), July (generic risk factors) and August 2004 (PDS; see *Appendix 2*).

Surgery-specific risk factors

The final search strategy for surgery-specific risk factors consisted of medical subject headings (MeSH) and free-text terms relating to surgical infection (surgical wound infection/SSI/postoperative infection), risk adjustment (risk assessment/factor/adjustment/stratification/modelling) and the surgical area being reviewed.

- Hip or knee replacement: hip prosthesis, knee prosthesis, joint prosthesis, arthroplasty, knee replacement, etc.

- Large bowel surgery: colorectal surgery, colectomy, colon surgery, proctocolectomy, restorative proctocolectomy, hemicolectomy, colostomy, etc.

Boolean operators were used to combine terms. A decision was made at the outset not to apply study design terms to increase the search sensitivity.

Inclusion criteria were determined prior to independent abstract appraisal by two independent assessors. Studies were eligible for full assessment if abstracts showed that:

- SSI was recorded as an outcome
- the operative procedures studied included one or more of the procedures being reviewed
- risk assessment was mentioned
- the paper was in English.

Full papers were obtained and appraised for all eligible abstracts. A paper was excluded at this stage if:

- duplicate data were presented
- no relevant data were presented
- outcomes were grouped in a way that prevented reporting of risk factors for SSIs, e.g. by combining all hospital-acquired infections
- the paper described a randomised controlled trial (RCT) of alternative antibiotic prophylaxis regimens (which have been reviewed elsewhere[5,24,25]).

Generic risk factors for surgical site infection

The final search strategy for generic risk factors consisted of MeSH and free-text terms relating to surgical infection (surgical wound infection/surgical site infection/postoperative infection), risk adjustment (risk assessment/factor/adjustment/stratification/modelling) and existing generic risk indices (SENIC/NNIS). The last group were included to try to ensure that studies identified took into account such risk indices when estimating the effects of additional generic risk factors.

Risk factors for surgical site infections identified by postdischarge surveillance

The final search strategy for risk factors for SSIs detected by PDS consisted of MeSH and free-text terms relating to surgical infection (surgical wound infection/surgical site infection/postoperative infection), risk adjustment (risk assessment/factor/adjustment/stratification/modelling) and PDS (postdischarge surveillance/population surveillance patient discharge/follow-up/post discharge). This review also used literature on PDS already identified by one of the authors (JB).

Quality assessment

We aimed to assess methodological quality and the risk of bias in primary studies that we included in each review, as this is a recommended part of the process of systematic reviewing.[26] This assessment is conducted to exclude less rigorous studies, to weight studies in meta-analysis or to perform sensitivity analyses of assumptions or results from meta-analyses. Although there are many check-lists for the assessment of randomised and epidemiological studies, there is no gold-standard tool for assessment of methodological quality in non-randomised and observational studies.[27] We chose to carry out the assessment using the Newcastle Ottawa Scale (NOS),[28] one of the six most suitable instruments identified by a systematic review for assessing the quality of non-randomised studies.[27]

We intended that two assessors should carry out the assessment. The NOS assigns 'stars' to studies that meet specified quality criteria for cohort (25 questions) and case–control studies

(22 questions). Criteria are grouped into three main categories, assigned a maximum 'value' of four, two or three stars, respectively. For cohort studies, these categories are (1) selection of intervention/exposed and control/unexposed cohorts; (2) comparability of cohorts; and (3) adequacy of outcome assessment. For case–control studies, the categories are (1) selection of cases and controls; (2) comparability of cases and controls; and (3) adequacy of assessment of exposure/intervention.[28] At the outset, we intended to report inter-rater agreement between two independent assessors. In the event, experience using the NOS for the hip and knee replacement review (see *Potential surgery-specific risk factors for hip and knee replacement*) led us to discontinue the assessment.

Data extraction, synthesis and analysis

References were downloaded using Reference Manager software (Thomson Reuters, CA, USA). Data were extracted into Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) spreadsheets to allow quantitative estimates of effect [odds ratios (OR), rate ratios (RR) or hazard ratios (HR)] to be calculated, if appropriate. Quantitative data were extracted from publications and estimates calculated by the reviewers whenever possible (if not reported by the original researchers).

Risk factors were categorised as related to the patient, operation or postoperative care. Typical patient factors were patient comorbidities. Operative factors included variables such as operation duration and competing aspects of operative technique, e.g. type of prosthesis for joint replacement, coronary artery bypass graft (CABG) with one or two internal mammary arteries. Substratification of operations was also considered an operative factor, e.g. CABG with or without cardiopulmonary bypass. Postoperative factors included, for example, the presence of wound drains and postoperative LOS.

The distinction between patient, operative or postoperative factors can be blurred, certainly in so far as these categories are attributed to the patient, the surgeon/operation and subsequent care. For example, a long preoperative stay in hospital may arise because a patient's condition needs to be optimised prior to surgery or because of hospital-specific practices or unnecessary delays. As pointed out above (see *Chapter 1, Risk factors*), operation duration or wound class may be determined primarily *either* by the generic operation required (and, hence, might be more correctly regarded as patient factors) *or* by the operating technique of an individual surgeon or the surgical strategy adopted. The level of stratification by operative procedure documented in surveillance databases is unlikely to have sufficient detail or accuracy to distinguish between these reasons for 'long' operative duration or wound class.

Results

Potential surgery-specific risk factors for hip and knee replacement

Review-specific eligibility issues

Revision-only surgeries were excluded, although papers with combined primary and revision procedures were included in the review (assuming that revisions would constitute a very small proportion of the total).

Long-term 'deep' infections requiring revision of a joint replacement was the focus of several studies, with infections being detected over 1 year after surgery. These studies were included in the review. However, infections that occur at this distance in time after surgery are difficult to attribute to exposure during the index operation.

Literature identified

The bibliographic searches identified 169 abstracts that were independently assessed for eligibility. A total of 38 papers were fully critically appraised, 23 (61%) of which were rejected leaving 15 papers (*Figure 1*).[29–43] Fourteen papers were scored for risk of bias/methodological quality using NOS.[27–36,38–43] The 15th paper was a systematic review and a meta-analysis.[37]

Quality assessment

The NOS first requires reviewers to classify studies as cohort or case–control designs, as this decision dictates the items that reviewers use to assess studies. The two reviewers found it very difficult to assign and then agree the designs used by researchers for included studies, as most studies were reports of retrospective analyses of routinely collected data in surveillance databases. The patients documented in such databases usually constitute a representative 'cohort' over time. However, when analysing the data, researchers typically divided the cohort according to whether or not a patient experienced the outcome of an SSI, then investigated multiple predictors of SSI.

Of the 15 included papers,[29–43] 12 were finally classified as case–control studies,[29–36,38,39,42,43] two as cohort studies[40,41] and one as a systematic review with meta-analysis.[37] Although reported as using a cohort design, nine studies that compared the prevalence of risk factors among people who did and did not develop SSI were 'categorised' by reviewers as case–control studies for NOS scoring (see above). Typically, these studies reported analyses of surveillance databases, from which groups of 'infected' and 'uninfected' patients were identified; analyses then sought to identify risk factors associated with SSI, presenting tables of risk factor prevalence in the two groups. The analyses were uniformly carried out using multivariable logistic regression and SSI 'rates' were calculated and reported as probabilities without considering time at risk. These features of the

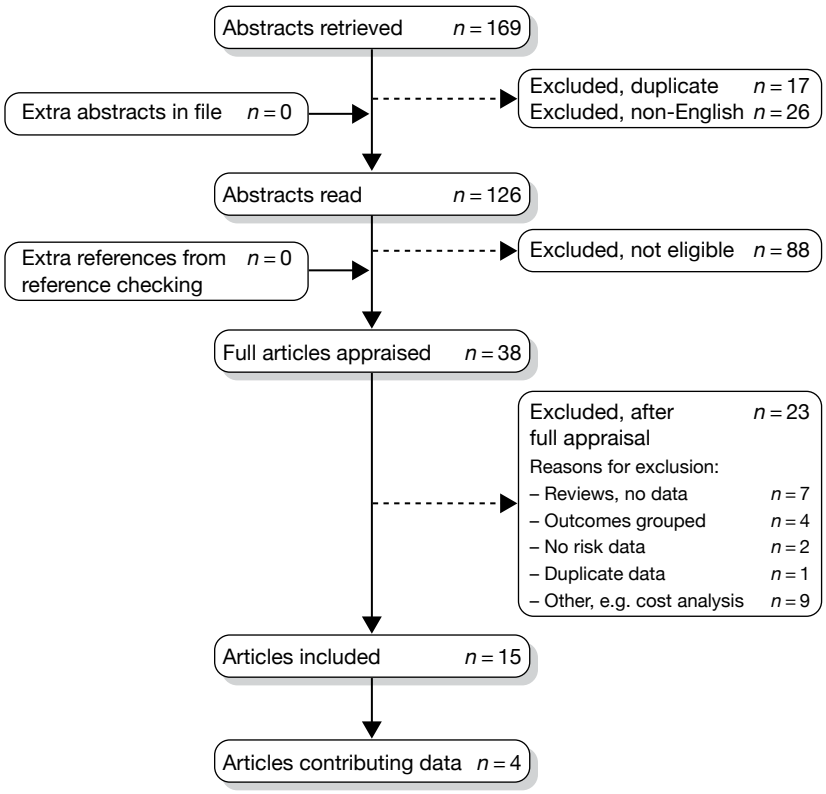


FIGURE 1 Flow diagram of literature identified and appraised for hip and knee replacement review.

analysis are indicative of a nested case–control study, albeit using an entire cohort.[44] Therefore, although the reviewers acknowledged that the process of surveillance, i.e. data collection, was often prospective, they decided that the analyses should be classified as case–control studies. One of the two cohort studies investigated risk factors for deep infection and analysed time to revision of the prosthesis using survival techniques.[40] The second explicitly hypothesised and investigated a difference in outcome between morbidly obese patients and the remainder, albeit without considering time at risk.[41]

The NOS star ratings by the two reviewers for the selection, comparability and outcome/exposure assessment categories for the 14 primary studies are shown in *Table 3*.

Table 3 suggests that agreement was good. However, there were often disagreements for items within the three dimensions. Moreover, without prior resolution of the choice of study design, the ratings could not have been compared at all for several studies, because different items would have been rated by the two reviewers.

Only four papers achieved high-quality scores for selection of cases and controls (three stars), comparability (two stars) and exposure (three stars).[31,32,34,35] These four studies had large samples ranging from 243 to 47,500 patients. One other study was judged to have poor comparability, but otherwise was high quality and reported data for a moderately large sample size.[39] Remaining studies provided weak evidence about risk factors, having poor methodological quality or small sample sizes.

The reviewers were not satisfied that the NOS provided an appropriate measure of quality for the purposes of the study. Instead, they set four criteria for the reporting of risk factor estimates:

1. multivariable analysis of potential risk factors or an RCT of a 'risk factor' that was randomised

TABLE 3 The NOS quality scores for hip and knee replacement studies included in the review

		Reviewer 1/reviewer 2		
Study	**Study design**	**Selection (max. 4 stars)**	**Comparability (max. 2 stars)**	**Outcome (max. 3 stars)**
Arjona *et al.*[29]	Case–control	3/3	0/0	3/3
Bengtson and Knutson[30]	Case–control	3/3	0/0	2/2
Berbari *et al.*[31]	Case–control	3/4	2/2	3/3
Brandt *et al.*[32]	Case–control	3/4	2/2	3/3
de Boer *et al.*[33]	Case–control	3/4	1/1	3/3
de Boer *et al.*[34]	Case–control	3/4	2/2	3/3
Gordon *et al.*[35]	Case–control	3/3	2/2	3/3
Lazzarini *et al.*[36]	Case–control	3/3	0/0	3/3
Rosencher *et al.*[38]	Case–control	3/3	0/0	3/3
Saleh *et al.*[39]	Case–control	4/4	0/0	3/3
Surin *et al.*[40]	Cohort	4/4	0/0	3/3
Winiarsky *et al.*[41]	Cohort	3/4	0/0	2/2
Yong *et al.*[42]	Case–control	2/2	0/0	2/2
Wilson *et al.*[43]	Case–control	3/3	0/0	2/3

Max., maximum.
Note: one other paper reviewed was a systematic review and meta-analysis.[37]

2. sufficient SSIs observed to justify multivariable analysis (on the basis of the rule-of-thumb that there should be ≥ 10 events per predictor included in the model);[45] one of the four studies with maximum NOS scores did not meet this criterion as it reported 20 SSIs in 243 patients and fitted multiple risk factors in a logistic regression model[35]
3. inclusion of NNIS or SENIC risk indices or components of these indices in a multivariable analysis or an RCT (see 1), as the reviews were interested in identifying operation-specific risk factors that are important after adjusting for generic risk factors
4. effect estimates for putative surgery-specific risk factors adjusted for SENIC or NNIS risk indices or, separately, duration of procedure, wound contamination class and ASA class, or an RCT (see 1).

Risk factors identified

A total of 30 different risk factors were extracted from the 15 included papers.[29–43] Risk factors reported in more than one (eligible) study are listed in *Table 4*; the table is restricted to risk factors reported by multiple studies because of the risk of selective reporting of significant risk factors and chance findings in single papers. Risk factors are not distinguished by hip and knee replacement as some studies analysed data for both and the risk factors considered did not appear to differ for the two procedures. The most commonly investigated factors included age, gender, obesity, diabetes, duration of surgery, diagnosis or indication for surgery, antibiotic prophylaxis (correct administration) and wound drainage.

Studies differed with respect to the categorisation or inclusion of risk factors, differences in study population (hip/knee), method of measurement of outcome (superficial/deep SSI) and adjustment for covariates. Although papers sometimes reported data from multivariable analyses, it was not always possible to determine precisely which risk factors had been considered or included in regression models.

Four papers satisfied the quality criteria (see *Quality Assessment*) set by the reviewers.[31,32,34,39] Two of these papers had very large sample sizes; for example, Berbari *et al.*[31] analysed data for > 26,000 procedures and Brandt *et al.*[32] almost 50,000 hip replacements. In total, the four papers provided infection data on 108,577 patients undergoing joint replacement. Estimates of the independent risk factors from these papers, adjusted either for the NNIS index or for components of this index, are shown in *Table 5*. No quantitative synthesis was carried out because of the heterogeneity between studies.

TABLE 4 The risk factors for SSIs after hip and knee replacement reported by more than one paper

Patient	Operative	Postoperative
Osteoarthritis or rheumatoid arthritis	Duration of surgery	Wound drainage/drains
Diabetes or use of insulin	Wound class	LOS > 30 days; duration of admission
Obesity	More than one intervention/surgery	Bladder catheter
Increasing age	Preoperative LOS	Other HAIs
Gender	Blood transfusion	
Diagnosis/aetiology/indication for surgery	Type of prosthesis	
Antibiotic prophylaxis (correct/incorrect)	Use of steroids preoperatively	
Previous surgery		
Acute vs elective surgery		
ASA class		
Pressure sores/ulcers		

HAIs, hospital-acquired infections.

TABLE 5 The main study characteristics and ORs for risk factors identified from the 'best' studies of hip and knee replacement

Study characteristic/ risk factor	Study					
	Berbari *et al.*[31]	Brandt *et al.*[32]	Brandt *et al.*[32]	de Boer *et al.*[34]	de Boer *et al.*[34]	Saleh *et al.*[39]
Study characteristic						
Study population	Hip and knee replacement	Hip replacement	Knee replacement	Hip replacement	Knee replacement	Hip and knee replacement
Size of study population	26,505	47,347	15,630	12,588	4202	2305
SSI definition	Based on microbiology	CDC	CDC	CDC	CDC	CDC
Overall SSI% (%)	1.8	2.0	1.1	3.4	2.2	2.0[a]
Superficial (%)				2.6	1.4	1.4
Deep (%)				0.8	0.8	0.8
Sample size for analysis	924 (462 + 462)	47,347	15,630	5339	1744	97 (33 + 64)[a]
Risk factor (95% CI)						
ASA > 2	NNIS in model[b]	1.9 ($p < 0.05$[c])	Not significant	Not reported[d]	Not reported	Not significant[a]
Wound class dirty or contaminated	NNIS in model[b]	2.6 ($p < 0.05$[c])	3.4 ($p < 0.05$[c])	10.8 (1.7 to 67.8)	Not reported	Not considered[a]
Operation time > 75th percentile	NNIS in model[b]	1.4 ($p < 0.05$[c])	1.9 ($p < 0.05$[c])	1.2 (0.9 to 1.8)	10.0 (1.3 to 77)	Not significant[a]
NNIS 1 vs NNIS 0	1.7 (1.2 to 2.3)	NNIS components in model[e]	Not considered	Not considered	Not considered	Not significant[a]
NNIS 2 vs NNIS 0	3.9 (2.0 to 7.5)	NNIS components in model[e]	Not considered	Not considered	Not considered	Not significant[a]
NNIS 3 vs NNIS 0	Not applicable	NNIS components in model[e]	Not considered	Not considered	Not considered	Not significant[a]
Male gender	Not considered	1.2 ($p < 0.05$[c])	Not significant	Not reported	Not reported	Not considered[a]
Age > 75th percentile	Not considered	1.9 ($p < 0.05$[c])	Not significant	Not reported	Not reported	Not significant[a]
PDS	Not considered	Not considered	Not considered	1.9 (1.0 to 1.9)	3.6 (1.4 to 9.4)	Not considered[a]
SSI not involving prosthesis	35.9 (8.3 to 154.0)	Not considered	Not considered	Not considered	Not considered	Not considered[a]
Malignancy	3.1 (1.3 to 7.2)	Not considered	Not considered	Not considered	Not considered	Not considered[a]
Prior joint replacement	2.0 (1.4 to 3.0)	Not considered	Not considered	Not considered	Not considered	Not considered[a]
Haematoma	Not considered	Not considered	Not considered	Not considered	Not considered	11.8 (3.0 to 46.0)[a]
Per day of drainage	Not considered	Not considered	Not considered	Not considered	Not considered	1.3 (1.1 to 1.6)[a]

a Thirty-three patients developed a superficial SSI. Seven of these 33 patients subsequently developed a deep SSI. A further 12 patients developed a deep SSI with no superficial SSI recorded. The multivariable analysis was carried out for superficial SSI cases and 64 controls.
b The NNIS index was included in the model, but the components of the NNIS index were not considered separately.
c CIs were not reported, but authors stated that these factors were independently statistically significant.
d ASA grade was considered, but was not reported. The effect of duration of preoperative stay was reported separately for ASA classes 1 and 2, and ASA classes 3, 4 and 5, implying that there was an interaction of ASA class and duration of preoperative stay. However, the effect of duration of preoperative stay (> 2 days or not) was not significant for either ASA stratum.
e The NNIS index only was considered in a separate model. Tabulated estimates were from a model that deliberately included components of the NNIS index separately.

A systematic review with meta-analysis of an intervention (closed-suction drainage) reported no effect of this intervention on SSI%s after hip or knee replacement (RR 0.73, 95% CI 0.47 to 1.14).[37]

Potential surgery-specific risk factors for large bowel surgery

Review-specific eligibility issues

Studies that reported data for groups of mixed operations, e.g. studies that included both large and small bowel operations, were excluded. Studies reporting only stoma closure operations were also excluded.

Because of the nature of large bowel surgery, deep infections can arise from anastomotic leaks, as well as from exposures during the index operation. In practice, researchers did not attempt to distinguish competing causes of SSIs.

Literature identified

The bibliographic searches identified 82 abstracts that were independently assessed for eligibility. A total of 51 papers were fully appraised, 29 (57%) of which were rejected (*Figure 2*). Of the remaining 22 papers,[20,32,46–65] relevant data were reported by 13.[20,32,47–49,53,56–59,62–64] Two papers reported different analyses of the same data set.[63,64]

Quality assessment

The two reviewers classified studies by design and carried out methodological quality assessment by applying the four criteria described in *Quality assessment* (for the reasons described above for the hip and knee replacement review, see *Risk factors identified*). Of the 13 papers reporting relevant data, only four met these quality criteria.[32,47,49,59]

Risk factors identified

A total of 21 different risk factors were extracted from the 13 included papers.[20,32,47–49,53,56–59,62–64] Risk factors reported in more than one (eligible) study are listed in *Table 6*, categorised as patient, operative or postoperative factors. The most commonly investigated factors included age, gender,

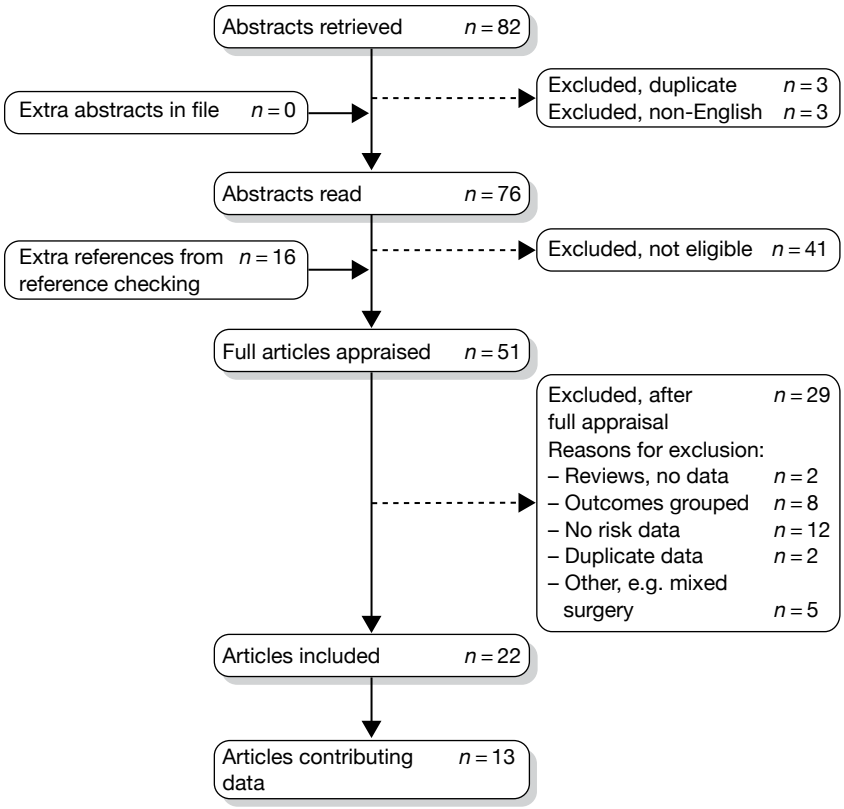


FIGURE 2 Flow diagram of literature identified and appraised for large bowel surgery review.

TABLE 6 The risk factors for SSI after colon surgery reported by >1 of the 15 included studies

Patient	Operative	Postoperative
ASA class	Duration of surgery	Wound drainage/drains
Diabetes or use of insulin[a]	Wound class	
Increasing age	More than one intervention/surgery	
Arab ethnicity[b]	Blood transfusion	
	Creation of ostomy/stoma	

a These factors were reported in pairs of papers by the same research teams.[63,64]
b These factors were reported in pairs of papers by the same research teams.[56,57]

obesity, diabetes, duration of surgery, diagnosis or indication for surgery, antibiotic prophylaxis (correct administration) and wound drainage.

As in the review of hip and knee replacement, studies differed with respect to the categorisation or inclusion of risk factors, differences in study population (different large bowel procedures), method of measurement of outcome and adjustment for covariates. Although papers sometimes reported data from multivariable analyses, it was not always possible to determine precisely which risk factors had been considered or included in regression models. Estimates of independent risk factors from the four papers that were judged to have better methodological quality, adjusted either for the NNIS index or for components of this index, are shown in *Table 7*.

Potential generic risk factors

The literature search for this review generated a very large number of citations (*Figure 3*) and the project had insufficient resources to double-review all of the abstracts. Both reviewers independently appraised two batches of 100 abstracts and compared their choices of papers to obtain in full. Agreement was reasonable (4/200 discrepancies), but not formally quantified because of the paucity of citations selected to be obtained in full (one reviewer selected 23 citations and the other 27 citations). One reviewer read the remaining citations, selecting for further review if in doubt, generating 222 abstracts. These 222 abstracts were reviewed by both reviewers and a sample of 46 papers was identified for full review.

The same methodological quality criteria were applied as for the reviews of surgery-specific risk factors. We also excluded studies of the NNIS describing the development of the SENIC or NNIS risk indices, reports of other national surveillance programmes that did not consider additional risk factors and studies within single surgical specialties. The 16 papers included described patient populations for selected specialties, one or more hospitals, or from national surveillance programmes (*Table 8*) over a period of > 20 years.[32,66–80] We describe the findings of these studies in a purely qualitative manner because of the varied way in which they were reported in the primary studies and heterogeneity between the studies.

Operation duration, wound contamination class and ASA class are already well documented as generic risk factors by NNIS and are reflected in the SENIC and NNIS risk indices. Therefore, these risk factors are omitted from *Table 8*. The most commonly reported additional generic risk factor was duration of preoperative stay in hospital (in six studies[67,72,73,75,78,80]), with all studies across a variety of surgical settings finding that increasing duration of preoperative stay was associated with an increasing risk of SSI.

TABLE 7 The main study characteristics and ORs for risk factors identified from the 'best' studies of large bowel surgery

Study characteristic/ risk factor	Study			
	Brandt *et al.*[32]	Chang *et al.*[47]	Ford *et al.*[49]	Tang *et al.*[59]
Study characteristic				
Study population	Colon surgery	Colorectal surgery	Colorectal surgery	Colon surgery
Size of study population	14,393	1349	839	2809
SSI definition	CDC	Pus or culture positive	Pus or culture positive	CDC
Overall SSI% (%)	6.3		8.8	4.7
Superficial (%)		15.3		2.9
Deep (%)		1.3 (sepsis)		1.2
Organ space (%)				1.8
Sample size for analysis	14,393	1349	839	2809
Risk factor (95% CI)				
ASA 2 vs 1[a]		NNIS in model[b]	Not significant	1.7 (1.1 to 2.5)
ASA > 2	1.5 ($p < 0.05$[a])	NNIS in model[b]	Not significant	
Wound class dirty vs contaminated	1.6 ($p < 0.05$[a])	NNIS in model[b]	Not significant	2.8 (1.3 to 5.7)
Operation time > 75th percentile	1.6 ($p < 0.05$[a])	NNIS in model[b]	Not significant	2.6 (1.4 to 4.8)[c]
Male gender	1.2 ($p < 0.05$[a])	Not significant	Not significant	1.5 (1.0 to 2.2)
Blood transfusion vs 0 units	Not considered	1.1 (1.0 to 1.5): any	3.4 ($p < 0.05$)[d]	
1–3 units				2.0 (1.1 to 3.3)
> 3 units				6.2 (4.2 to 10.2)
Anastomotic leak	Not considered	4.3 (2.1 to 9.1)	Not significant	Results reported by anastomotic leak; SSI risk higher if leak present
Use of drain	Not considered	1.6 (1.0 to 2.6)	3.1 ($p < 0.05$)[d]	1.6 (1.0 to 2.5)
Creation of ostomy/stoma	Not considered	Not considered	2.4 ($p < 0.05$)[d]	2.1 (1.3 to 3.6)

a CIs were not reported, but authors stated that these factors were independently statistically significant.
b Multivariable analysis credited with adjusting for NNIS components separately, although it was not clear that ASA class was included.
c ORs reported only for incisional SSIs (includes superficial and deep); the effect for all SSIs was not reported.
d Dose–response effect of packed red blood cells given during or after surgery was reported, but not quantified. CIs were not reported, but authors stated that these factors were independently statistically significant.

Weight was identified as an additional generic risk factor by four studies.[66,74,76,79] Three reported that obesity increased the risk of SSI.[66,76,79] However, the fourth reported that weight loss in the 6 months prior to surgery increased the risk of SSI.[74] Both findings seem plausible, perhaps in different patient populations, although one of the three papers reporting that obesity increased the risk of SSI% was based on a population of patients having surgery to treat cancer.[66]

A range of other additional risk factors was identified in fewer studies. Smoking was commented on by researchers in three papers, but in two this was expressly to state that smoking was not associated with SSI;[68,74] these studies had larger sample sizes than the one study that reported smoking to be associated with an increased risk of SSI.[79] Other risk factors reported in more than one study were heavy alcohol consumption, diabetes and multiple interventions.

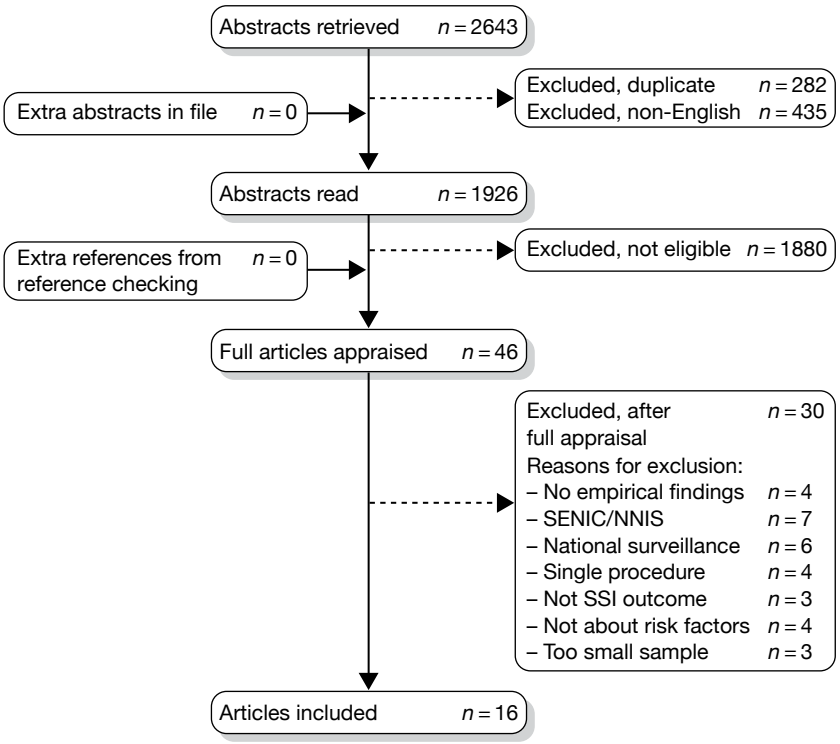


FIGURE 3 Flow diagram showing citations and papers considered for the review of generic risk factors for SSI.

Two methodological considerations may explain some of the inconsistency between the findings. First, SSI surveillance is likely to have been heterogeneous between studies, e.g. including PDS or not; PDS increases the number of SSIs detected and SSIs detected by PDS may be associated with different risk factors (see *Risk factors for surgical site infections identified by postdischarge surveillance*). A second reason could be the selective reporting of risk factors, analogous to outcome reporting bias.[81] The studies uniformly reported analyses of observational databases that may not have had a priori analysis plans; subjective judgements often have to be made by analysts when fitting multivariable models which may be biased by prior beliefs or the statistical significance of findings. Databases also afford the opportunity for reanalysis, using the same data set or one covering a slightly different (potentially overlapping) observation period, giving rise to duplicate or 'salami' publications. The reviewers were aware of multiple publications from particular institutions presenting different findings, in which the relationships between successive papers were not carefully described.

Risk factors for surgical site infections identified by postdischarge surveillance

The same methodological quality criteria were applied as for the reviews of surgery-specific risk factors, except that reviewers were sometimes uncertain if SENIC or NNIS risk indices, or their components, had been adjusted for. As with the previous review of generic risk factors, the 10 papers included described patient populations for selected specialties, one or more hospitals or from national surveillance programmes (*Table 9*), over a period of > 20 years.[78,82–90] It should be noted that two research teams/institutions published five of the 10 papers, one from Spain[83–85] and one from Israel.[88,89]

TABLE 8 Potential generic risk factors excluding NNIS or SENIC risk indices and their component variables

Risk factor	Study population	Sample size	Comment	Reference
Duration of preoperative hospital stay	Orthopaedic and general surgery	4340	Longer duration of stay associated with increasing risk of SSI	Bremmelgaard *et al.*[67]
	National surveillance; varied surgical procedures	18,063	Longer duration of stay associated with increasing risk of SSI; magnitude of association depended on surgical procedure	Geubbels *et al.*[72]
	Trauma surgery	5320	Longer duration of stay associated with increasing risk of SSI	Herruzo-Cabrera *et al.*[73]
	Orthopaedic and general surgery	1452	Longer duration of stay associated with increasing risk of SSI	Moro *et al.*[75]
	General surgery; only wounds classified as clean	1964	Longer duration of stay associated with increasing risk of SSI	Reid *et al.*[78]
	National surveillance; varied surgical procedures	16,799	Longer duration of stay associated with increasing risk of SSI	Ronveaux *et al.*[80]
Weight	Varied surgical procedures to treat cancer	1280	Obesity associated with increasing risk of SSI	Barber *et al.*[66]
	Non-cardiac surgical procedures	5031	Weight loss in 6 months prior to surgery associated with increasing risk of SSI	Malone *et al.*[74]
	General, vascular and thoracic surgery; only wounds classified as clean	2262	Obesity associated with increasing risk of SSI	Moro *et al.*[76]
	Varied surgical procedures	2202	Obesity associated with increasing risk of SSI	Reilly[79]
Smoking	General surgery	2989	Smoking not associated with risk of SSI	Delgado-Rodriguez *et al.*[68]
	Non-cardiac surgical procedures	5031	Smoking not associated with risk of SSI	Malone *et al.*[74]
	Varied surgical procedures	2202	Smoking associated with increased risk of SSI	Reilly[79]
Alcohol	General surgery	1505	Heavy alcohol consumption associated with increased risk of SSI	Delgado-Rodriguez *et al.*[69]
	General surgery; only wounds classified as clean	1964	Alcohol misuse associated with increased risk of SSI	Rantala *et al.*[77]
Diabetes	Orthopaedic, general and vascular surgery; only wounds classified as clean	9108	Diabetes associated with increased risk of SSI	Ehrenkranz[70]
	Non-cardiac surgical procedures	5031	Diabetes associated with increased risk of SSI	Malone *et al.*[74]
Multiple interventions/ operations	Trauma surgery	5620	More than one intervention associated with increasing risk of SSI	Fernandez *et al.*[71]
	Orthopaedic surgery; general surgery	1452	More than one operation associated with increasing risk of SSI	Moro *et al.*[75]
Drains	Orthopaedic surgery; general surgery	1452	Presence of open drain after surgery associated with increased risk of SSI	Moro *et al.*[76]
Remote infection	Orthopaedic, general and vascular surgery; only wounds classified as clean	9108	Remote infection associated with increasing risk of SSI	Ehrenkranz[70]
Immunodeficiency	Trauma surgery	5620	Immunodeficiency associated with increasing risk of SSI	Fernandez *et al.*[71]
Malignancy	Varied surgical procedures	2202	Malignancy associated with increased risk of SSI	Reilly[79]
Emergency procedure	National surveillance; varied surgical procedures	16,799	Emergency procedure associated with increased risk of SSI	Ronveaux *et al.*[80]
Use of endoscope	National surveillance; varied surgical procedures	214,271	Use of endoscope associated with a reduced risk of SSI	Brandt *et al.*[32]

TABLE 9 The main study characteristics, frequencies and risk factors for in-hospital and PDS SSI%s in studies reporting risk factors for SSI by PDS

Study population	In-hospital SSI	PDS SSI%[a]	*p* (PDS SSI%)[b]	Reference
General surgery; only wounds classified as clean	In-hospital SSI%: 4.5% (86/1898) Increasing operative duration, ASA class, age and preoperative stay associated with increasing risk of SSI	PDS SSI%: 8.1% (n=153; 98% follow-up) None of the risk factors for in-hospital SSI were associated with PDS SSI	0.64	Reid *et al.*[78]
CABG surgery	In-hospital SSI%: 1.9% (25/1324) NNIS risk index associated with increasing risk of SSI	PDS SSI%: 4.8% (n=63; 96% follow-up) NNIS risk index associated with increasing risk of PDS SSI, but less strongly	0.72	Avato and Lai[82]
General surgery	In-hospital SSI%: 8.2% (123/1506) Increasing operative duration, wound class, ASA class, age, male gender, BMI associated with increasing risk of SSI	PDS SSI%: 6.8% (n=103; 96% follow-up) Increasing age, BMI associated with an increasing risk of PDS SSI Antibiotic prophylaxis associated with a decreasing risk of PDS SSI	0.46	Delgado-Rodriguez *et al.*[83]
General surgery	In-hospital SSI%: 7.3% (81/1104) NNIS risk index, age, male gender, diabetes, antibiotic prophylaxis associated with increasing risk of SSI	PDS SSI%: 2.1% (n= 23; 70% follow-up) No risk factors identified by multivariable logistic regression	0.22	Lecuona *et al.*[84]
General surgery	In-hospital SSI%: 9.0% (134/1483) NNIS risk index, malignancy, surgeon's baseline risk associated with increasing risk of SSI	PDS SSI%: 1.4% (n=21) No risk factors identified by multivariable logistic regression	0.14	Medina-Cuadros *et al.*[85]
General surgery	In-hospital SSI%: 7.9% (50/630) Increasing operative duration, postoperative hospital stay, wound class, ASA class, emergency associated with increasing risk of SSI	PDS SSI%: 22.2% (n=140; 64% follow-up) Increasing operative duration, postoperative hospital stay associated with an increasing risk of PDS SSI[c]	0.74	[d]Oliveira and Carvalho[86]
Varied, non-obstetric, surgical procedures	In-hospital SSI%: not reported Increasing operative duration, chronic disease, congestive heart failure associated with increasing risk of SSI	PDS SSI%: 1.9% (n=89/4571) Increasing operative duration associated with increasing risk of SSI; PDS SSI cases tended to have even longer operative duration than in-hospital SSI cases		[d]Perencevich *et al.*[87]
Hernia surgery	In-hospital SSI%: 1.7% (47/2846) Increasing operative duration, age, male gender, use of drain, recurrent hernia chronic disease associated with increasing risk of SSI	PDS SSI%: 1.7% (n=48; 88% follow-up) Treated wounds and ventral hernias associated with an increased risk of PDS SSI	0.51	[e]Simchen *et al.*[88,89]
General, thoracic and trauma surgery	In-hospital SSI%: 5.8% (952/16,543) Increasing operative duration, wound class, obesity and alcoholism associated with increasing risk of SSI	PDS SSI%: 3.1% (n=516; 90% follow-up) Clean operations, short operative duration, short postoperative LOS, obesity and non-alcoholism associated with an increasing risk of PDS SSI	0.35	Weigelt *et al.*[90]

BMI, body mass index.
a PDS SSI% calculated with respect to original denominator, where available.
b *p* (PDS SSI) = PDS SSI%/(in-hospital SSI% + PDS SSI%)
c PDS carried out only until 8 days after surgery.
d Not multivariable analysis.
e Data relate to operations in the 1980s when postoperative LOS was about 6 days.

The SSI% detected in-hospital and by PDS varied considerably across studies. More importantly, the proportion of all SSIs detected by PDS also varied considerably (from 0.14 to 0.74). Variation in the definition of SSI, differences in the way PDS was carried out (e.g. interval after surgery) and SSIs arising during readmission were classified may explain some of the variation, as well as the differing study populations. (The proportion of all SSIs arising after discharge might be expected to be influenced by the usual length of postoperative stay.) Nevertheless, it appears that, in most surgical populations, a substantial proportion of SSIs arise after discharge from hospital.

Not all studies reported the magnitude of associations in multivariable analyses. Risk factors detected in hospital and by PDS were mainly investigated by characterising and comparing the distribution of potential risk factors among three groups: patients with SSIs detected in hospital, patients with SSIs detected by PDS and patients who did not develop an SSI. Authors commented descriptively about the patterns of risk factors in these groups. Therefore, we also describe the findings of the studies in a qualitative manner.

The findings of each paper are described in *Table 9*, but are difficult to summarise. The risk factors for SSIs identified in hospital were unremarkable. Some of the risk factors for SSIs detected by PDS were also familiar, e.g. the NNIS risk index,[82] increasing operative duration[86,87] and age.[83] However, almost all authors remarked on the fact that the patients in whom SSIs were detected by PDS were different to those in whom SSIs were detected in hospital, for example:[89]

> 'Risk factors for both in-hospital and postdischarge infections seemed to be influenced by; (a) the selective nature of discharge, (b) the differential effect some risk factors had on either early or late infections. On any given day, patients selected by the clinical team to remain in hospital were more 'at risk' for infection than those who left. As a result, they had a better chance of being diagnosed as infected during hospitalization. By contrast, those who were discharged home were perceived as low risk for complications. Subsequent infections in these patients occurred either due to factors 'causing' late infections, therefore, unappreciated at the time of discharge, or unknown risk factors. More study risk factors were associated with in-hospital than with postdischarge infections, especially those associated with 'early' infections.'

This observation is borne out by other, sometimes contradictory, risk factors that were identified, e.g. clean operations and short operative duration.[89] SSIs detected by PDS also tended to be less severe.

Patients who stay in hospital longer have a greater chance of an infection acquired during an operation becoming manifest and being detected in hospital. Finally, as described by authors of the studies reviewed, patients discharged from hospital earlier represent a selected sample, perhaps patients with 'clean' wounds, who are younger and have less comorbidity. In these circumstances, empirical findings become difficult to interpret. The aetiology and severity of SSIs detected by PDS may be different but the existing evidence cannot inform this question.

Summary of findings

The reviews highlighted that the literature is heterogeneous and not of a high methodological quality. These features precluded any attempt to synthesise findings quantitatively.

The reviews of hip and knee replacement and large bowel surgery suggested that risk factors other than those that make up the NNIS risk index are associated with increasing risk of SSI. This has also been suggested for other operations, e.g. obesity and the use of bilateral internal mammary arteries for CABG.[91,92] Some of the risk factors identified in these reviews were also found in the review of additional generic risk factors. Some risk factors, e.g. creation of ostomy in bowel surgery or the use of bilateral mammary arteries in CABG (potentially, representing a stratification of CABG surgery), will be unequivocally surgery specific but others, e.g. the use of drains, may apply to a range of procedures, albeit not with equal magnitude.

As described above, risk factors identified in the review of generic risk factors overlapped to some degree with the surgery-specific reviews. However, the factor most commonly reported, namely duration of preoperative stay in hospital, was identified in the latter set of reviews; this risk factor may be a proxy marker, e.g. for severity of underlying illness or previous recent surgery or hospital admission.

It is of note that variation in the detail of a surgical procedure was not identified. This is perhaps not surprising as coding of surgical complexity may not support analysis at this level of detail, particularly in national surveillance programmes. However, as already described, some risk factors, such as operative duration or wound class, may arise either from the characteristics of a patient (e.g. individual differences in anatomy) or from the operation (e.g. technical skill of the surgeon), making these variables, and SSI% estimates adjusted for these variables, difficult to interpret.

The review of SSIs detected by PDS demonstrated the importance of SSIs arising after discharge and the need to include PDS if SSIs are to be compared meaningfully over time within an institution (because LOS and discharge behaviour may change) or between institutions. The review also highlighted the difficulty of investigating the question of whether or not risk factors for SSIs arising after discharge differ from risk factors for SSIs detected in hospital. Without an answer to this question, it is not possible to be confident that all factors relevant to risk adjustment of SSI% are collected.

Chapter 3

Definitions of surgical site infection

Agreement of alternative surgical site infection definitions

Introduction

The UK Department of Health has given little guidance on the definition of SSI used for surveillance in England, namely the NINSS version of the SSI definition set out by the CDC in 1992.[93] There has been little or no critical evaluation of either the original or modified CDC definitions. Choosing an appropriate definition and ensuring that the definition is applied consistently are necessary conditions for the observed percentage of wounds classified as infected at any time during follow-up (SSI%) to be valid across hospitals.

Designers of the systems of national surveillance must judge available definitions by their ability to identify infections that matter most to patients and to health services (see *Validation of surgical site infection definitions*). In addition, the practicability of collecting the information for SSI definitions is important as laborious or complex definitions are less likely to be implemented consistently across hospitals. To investigate their robustness, we used data from UCLH to compare agreement between four definitions of SSI applied to the same series of surgical wounds, namely:

1. the CDC 1992 definition[93]
2. the NINSS modification of the CDC definition[94]
3. the presence of pus[18] and
4. the ASEPSIS (Additional treatment, the presence of Serous discharge, Erythema, Purulent exudate, and Separation of the deep tissues, the Isolation of bacteria and the duration of inpatient Stay) scale.[95]

We also compared SSI% based on (1) the 1992 CDC definition and (2) the modified NINSS definition, to investigate the contribution of the two subjective CDC criteria to the overall SSI% and the potential effect of variation between hospitals in data collection methods. The findings reported in this section have already been published.[96]

Defining a surgical site infection

The NIHR review[9] identified five nationally proposed definitions. Many studies used one or another of these definitions, but over half used various non-standardised combinations of components from these definitions or new components. From the review, it was clear that CDC definitions,[97] more recently the 1992 definition,[93] have been most widely adopted, especially for hospital-based monitoring. The 1992 modification stressed that wound infections should be described as 'surgical site infections' to distinguish surgical wound infections from other infected wounds, e.g. burns.[93] The 1992 CDC definition is based on the presence of purulent drainage, the ability to culture organisms from an aseptic tissue sample from the wound or organ/space, local pain, tenderness, swelling, redness or heat, spontaneous wound separation or deliberate opening of the wound by a surgeon, presence of an abscess or other evidence from direct examination of a

deep infection or organ/space, other evidence of an organ/space infection, diagnosis by a surgeon or attending physician.

The NIHR review[9] recommended that surveillance programmes should use the 1992 CDC definition.[93] However, the 1992 CDC definition is not without critics. Inevitably, CDC definitions have considerable authority, but this does not necessarily mean that the definition is optimal. Anecdotally, surveillance teams have reported that the CDC definition can be difficult to apply, raising concern about its reproducibility. At a workshop held before this project was commissioned, some clinicians also expressed concern that the CDC definition is too microbiological and that SSIs detected using the definition may not reflect SSIs that are of most concern, from the point of view of both threats to the patient and additional resource use in the health service. The consequences of different classes of infections may vary considerably. Some infections can be catastrophic (fatal or permanent disability) and others relatively minor (extra NHS resource use, cost and inconvenience to patients, but no long-term consequences). There may, therefore, be a need to prioritise surveillance and investigation of some types of SSI, but more information is needed on the impact and costs of different types of SSIs in a range of surgical procedures. There is certainly a need for consensus between microbiologists, surgeons and other interested parties about an appropriate working definition of SSI.

Data collection and analysis

Data source: University College London Hospital, surgical site infection surveillance

Since May 2000, surgical wound surveillance has been conducted at UCLH. Ethical approval was not deemed necessary as the surveillance was part of the hospital audit programme. Cardiac, thoracic, orthopaedic, general (including small and large bowel operations), obstetric, gynaecological, urological, maxillofacial, plastic and vascular surgical specialties participated up to July 2003, each for at least 6 months a year. Only patients staying in hospital for at least two nights were included. Information was collected on all patients and on their surgical wounds, allowing the ASEPSIS, CDC (both the 1992 version and NINSS modification) and pus-only definitions to be applied.

The 1992 CDC definition requires the observation of 16 wound/patient characteristics in order to classify SSI and has two subjective criteria, namely (1) surgeon's diagnosis of infection and (2) micro-organisms able to be cultured from a wound.[93] The US NNIS programme has recommended that the latter criterion should be based only on positive cultures of fluid and tissue rather than on wound swabs, but this interpretation may not be generally applied.[9] The English NINSS modified the CDC definition to (1) require that pus cells be present for the positive wound culture criterion to be satisfied and (2) exclude surgeon's diagnosis alone as a sufficient criterion for a superficial SSI, unless at least two clinical signs of inflammation at the incision are also present.[94] Others have relied on a definition of SSI that simply uses the presence or absence of pus; this has the advantage of simplicity, but is likely to miss many SSIs captured by other definitions.[18] ASEPSIS is a quantitative scoring method which provides a numerical score related to the severity of the wound infection using objective criteria based on wound appearance and the clinical consequences of the infection.[95] This requires observation of four wound characteristics, i.e. serous discharge, erythema, purulent exudate and separation of the deep tissues. Each of these four characteristics is scored on a 6-point scale according to the proportion of the wound that is affected: 0 = 0%, 1 = 1–20%, 2 = 21–40%, 3 = 41–60%, 4 = 61–80% and 5 = 81–100%. Isolation of bacteria and the duration of inpatient stay contribute additional points.

During the period of surveillance, patients were assessed every 2–3 days by surveillance staff using direct observation, case note review and questioning of the nurses caring for the patient. Patients were contacted by post or by telephone 1–2 months after their operations to complete a

PDS questionnaire designed to ascertain late infections (*Table 10*). Thus, patients were followed up either until their wounds had healed without infection, or until an infection was detected, although the precise duration of follow-up varied from patient to patient depending on LOS in hospital or when they were telephoned to ascertain late infections. Each wound was classified as infected or not and we refer to the proportion of wounds classified as infected at any time during follow-up as 'SSI percentage' (SSI%), despite the fact that infections occurred at varying time intervals after surgery.

Information collected was entered into an Access database (Microsoft Corporation, Redmond, WA, USA). Microbiological results, demographic and some operative information came directly by linking wound records with other computer databases. Quarterly reports of SSI% were given to surgeons sorted by clinical team, specialty, ward and degree of contamination.

Preparation of data for analysis

The relational Access database was exported to Stata v8.2 (StataCorp LP, College Station, TX, USA), with each observation representing one wound. A description of the procedure used to collapse the relational data and extract the required SSI definitions from available measurements can be found in the *Appendix 3*.

Statistical analysis

Counts and percentages presented refer to wounds unless otherwise indicated. CIs for proportions were adjusted for clustering on patient using the robust variance estimators 'svy' commands available in Stata. Agreement was summarised with a kappa statistic and the statistics 'Ppos' (number of positive predictions) and 'Pneg' (number of negative predictions), which give the proportional agreement of ASEPSIS and CDC respectively for SSI-positive and SSI-negative diagnoses. These statistics were calculated as:

$$\text{Ppos} = (2 \times \text{agreed SSI present}) / [(2 \times \text{agreed SSI present}) + (\text{SSI present by definition 1}) + (\text{SSI present by definition 2})]$$

$$\text{Pneg} = (2 \times \text{agreed SSI absent}) / [(2 \times \text{agreed SSI absent}) + (\text{SSI absent by definition 1}) + (\text{SSI absent by definition 2})]$$

Confidence intervals for the agreement statistics were adjusted for clustering on patient by bootstrap methods; bias-corrected intervals are reported. Adjustment for acceleration of the

TABLE 10 Postdischarge surveillance questionnaire

Questionnaire item	Response
Have the wounds healed without any problems at all?	Yes ❑ No ❑
If 'yes' please ignore the following questions. If 'no' please answer the following:	
1. Has the wound been red?	Yes ❑ No ❑
2. Has the wound discharged clear yellow fluid?	Yes ❑ No ❑
3. Has the wound discharged pus?	Yes ❑ No ❑
4. Has the wound broken open?	Yes ❑ No ❑
5. Have you been given antibiotics for wound infection?	Yes ❑ No ❑
6. Has a district nurse had to dress the wound?	Yes ❑ No ❑
7. Has a doctor opened/drained an abscess?	Yes ❑ No ❑
8. Have you been admitted to hospital elsewhere?	Yes ❑ No ❑
9. Has the wound been opened and cleaned under general anaesthetic in hospital?	Yes ❑ No ❑

bootstrapped statistics was not performed because it was inappropriate for Ppos and Pneg and made very little difference to CIs for the kappa statistics.

For purposes of comparison, ASEPSIS scores above 20 were classified as infected. ASEPSIS scores between 10 and 20 ('disturbance of healing') are known to describe some SSIs, but most reflect wound breakdown owing to causes other than infection.[98] Moderate-to-severe infections score over 30 points. The CDC definition also describes the severity of infection by classifying infections as 'none', 'superficial', 'deep' or 'organ space'. Organ space infections were not initially distinguished from deep infections at the start of surveillance and, as the former were rare, we combined these categories for analysis. Both CDC and ASEPSIS definitions purport to describe the importance of an infection with respect to the morbidity of the patient and the likely clinical consequences.

Results

A total of 5804 surgical wounds in 4773 patients were assessed during 5028 separate hospital admissions between May 2000 and July 2003, representing all surgical specialties in the hospital (*Table 11*). The median age was 53.5 years [interquartile range (IQR) 37.5–69.6 years] and 2281 (47.8%) of patients were female. The median hospital stay was 8 days (IQR 6–14 days) and duration of operation 111 minutes (IQR 62–180 minutes).

The overall SSI% differed substantially for different definitions: 19.2% (18.1–20.4%) for CDC, 14.6% (13.6–15.6%) for the NINSS-modified version of CDC, 12.3% (11.4–13.2%) for pus alone and 6.8% (6.1–7.5%) for ASEPSIS score > 20. The overall level of agreement in SSI% reported by the ASEPSIS and CDC systems is shown in *Table 12*. When superficial infections were included as SSIs (*Table 12a*), 13% (778) of all observed wounds received conflicting diagnoses and 6% were classified as infected by both definitions. If they were excluded (*Table 12b*), ASEPSIS and CDC definitions produced approximately the same overall SSI% (6.8% and 7.0%, respectively,) but there were then about twice as many conflicting infection diagnoses ($n = 371$) as there were concordant ones ($n = 215$).

Wounds with pus were automatically diagnosed as SSIs by the CDC, NINSS and pus alone definitions, but only 40% (283/714) had ASEPSIS scores > 20 (*Figure 5*). For these wounds, the CDC scale also consistently diagnosed greater infection severity relative to ASEPSIS. Most wounds with pus were classified by ASEPSIS as having a 'disturbance of healing' (39%, 280/714) or as healing satisfactorily (21%, 151/714). Of these 151 wounds, 26% were classified as deep infections by the CDC definition.

TABLE 11 Characteristics of the study population ($n = 4473$)

Patient characteristic	*n*	%[a]
Age, years (mean, 95% CI)	53.5	53.0 to 54.1
Female	2281	47.8
Hospital stay, days (median, IQR)	8	6–14
Duration of operation, minutes (median, IQR)	111	62–180
Cardiothoracic surgery	1703	29.3
Orthopaedic surgery	1103	19.0
Urology	957	16.5
Obstetrics/gynaecology	632	10.9
General surgery	564	9.7
Other	845	14.6

a Median and IQRs are given for characteristics measured on continuous scales.

TABLE 12a Comparison of crude SSI% reported by CDC and ASEPSIS – superficial or deep/organ space infections considered to be SSI for CDC definition[a]

	CDC (superficial, deep/organ space infections)		
ASEPSIS	**Uninfected (%) [95% CI]**	**Infected (%) [95% CI]**	**Total (%) [95% CI]**
Uninfected (ASEPSIS ≤ 20)	4660 (80.3)	750 (12.9)	5410 (93.2) [92.5 to 93.9]
Infected (ASEPSIS > 20)	28 (0.5)	366 (6.3)	394 (6.8) [6.1 to 7.5]
Total	4688 (80.8) [79.6 to 81.9]	1116 (19.2) [18.1 to 20.4]	5804 (100)

a Agreement statistics: (a) kappa 0.43 (95% CI 0.40 to 0.46); Ppos 0.48 (95% CI 0.45 to 0.52); Pneg 0.92 (95% CI 0.92 to 0.93); (b) kappa 0.50 (95% CI 0.46 to 0.55); Ppos 0.54 (95% CI 0.49 to 0.58); Pneg 0.97 (95% CI 0.96 to 0.97).
Values are frequencies of wounds (and percentages) (95% CIs for marginal percentages, adjusted for multiple wounds in the same patients).

TABLE 12b Comparison of crude SSI% reported by CDC and ASEPSIS – only deep/organ space infections considered to be SSI for CDC definition[a]

	CDC (deep/organ space infections))		
ASEPSIS	**Uninfected (%) [95% CI]**	**Infected (%) [95% CI]**	**Total (%) [95% CI]**
Uninfected (ASEPSIS ≤ 20)	5218 (89.9)	192 (3.3)	5410 (93.2) [92.5 to 93.9]
Infected (ASEPSIS > 20)	179 (3.1)	215 (3.7)	394 (6.8) [6.1 to 7.5]
Total	5397 (93.0) [92.3 to 93.7]	407 (7.0) [6.3 to 7.7]	5804 (100)

a Agreement statistics: (a) kappa 0.43 (95% CI 0.40 to 0.46); Ppos 0.48 (95% CI 0.45 to 0.52); Pneg 0.92 (95% CI 0.92 to 0.93); (b) kappa 0.50 (95% CI 0.46 to 0.55); Ppos 0.54 (95% CI 0.49 to 0.58); Pneg 0.97 (95% CI 0.96 to 0.97).
Values are frequencies of wounds (and percentages) (95% CIs for marginal percentages, adjusted for multiple wounds in the same patients).

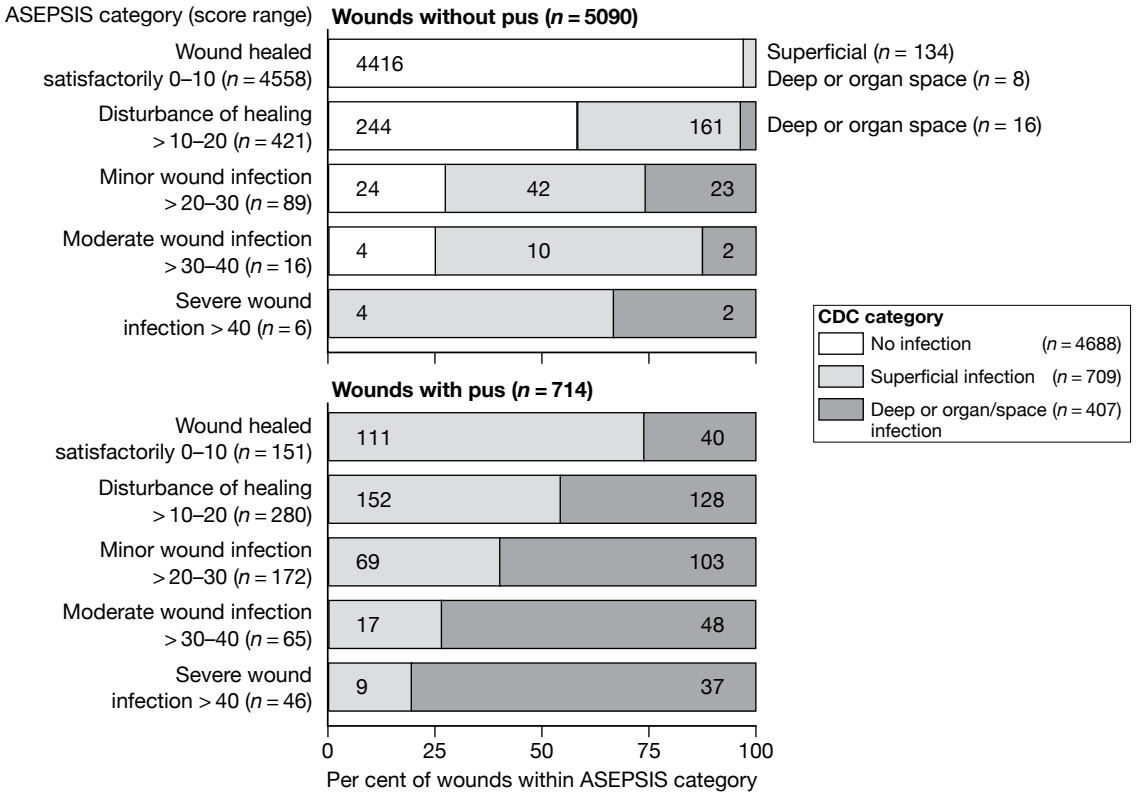


FIGURE 5 Comparison of wound diagnosis by ASEPSIS and CDC definitions, for wounds with and without pus.

In wounds without pus, the relationship between the ASEPSIS and CDC scales was less consistent. For example, 43% (177/412) of wounds classified only as 'disturbance of healing' by ASEPSIS were classified as infected by the CDC definition, with 3.9% (16/412) classified as deep infections. Conversely, four of the six wounds classified as 'severe wound infections' by ASEPSIS were classified as superficial by the CDC definition.

Figure 6 compares the classification of all wounds by the original CDC scale and its modified version as used by NINSS. Each category of SSI demonstrates unique discrepancies between the two definitions. As an example, over 30% of wounds defined as superficially infected by CDC were classified as not infected by NINSS (229/709). In the CDC superficial infection category, 94% (222/237) of the observed discrepancy is attributable to the NINSS modification of the CDC criterion related to positive bacterial cultures. In the CDC deep infection category, the discrepancy observed is owing to the exclusion of SSIs based solely on surgeon's diagnosis.

Discussion

There is a wide variation in the apparent SSI% using different definitions. Using existing CDC and ASEPSIS definitions of SSI (most and least sensitive definitions), over twice as many wounds are classified as infected by one definition only ($n = 778$) as are classified as infected by both ($n = 366$).

Some assumptions were made in the application of definitions (see *Appendix 3*), but these are unlikely to explain the extent of the discrepancies observed. For the CDC definition, 'surgeon's diagnosis' was commonly attributed from a decision to start a specific antibiotic or to provide surgical treatment. For example, opening of a wound under general anaesthetic for drainage of pus was taken to indicate deep infection. In other studies, differences in results between CDC and other surveillance methods have been associated with a lack of follow-up, use of positive culture results or clinical criteria.[99] Although this study was conducted in a single group of hospitals, data came from multiple sites, many surgical specialties and a large number of surgeons, so that the majority of the relevant sources of variation are represented. Nevertheless, the surveillance programme was consistent across sites, and methods of data collection, training of infection control practitioners and application of criteria for observing wound characteristics will not have varied to the same extent as surveillance programmes implemented across organisations.

Both CDC and ASEPSIS definitions describe the severity of the wound infection. Although CDC describes only three categories, none, superficial or deep/organ space (four if organ space infections are considered as a separate category), ASEPSIS has scores of up to 50 or more. For wounds with pus, CDC tends to rate wounds as being more severely infected than ASEPSIS. For wounds without pus, CDC still tends to rate wounds as being more severely infected than ASEPSIS; however, some wounds classified as moderately (31–40 points) and severely (>40 points) infected by ASEPSIS are classified as not infected, or only superficially infected, by CDC.

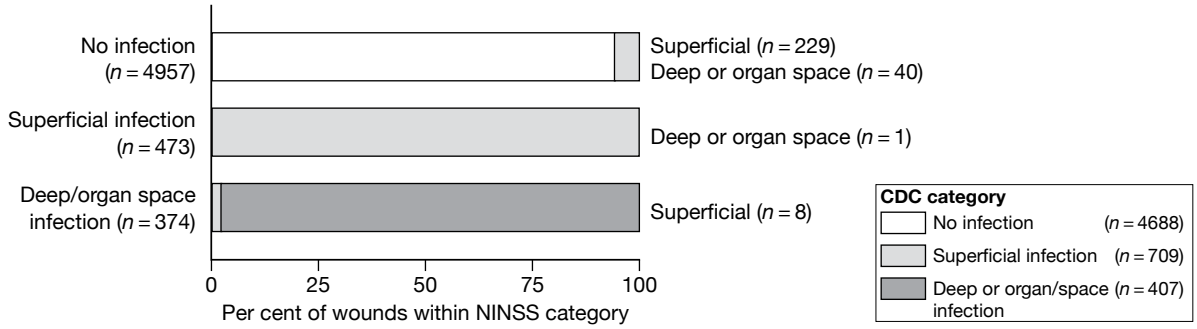


FIGURE 6 Comparison of wound diagnosis by CDC and NINSS definition, for wounds with and without pus.

The criteria used for CDC use some subjective criteria. The English NINSS modified the CDC definition following advice from a multidicplinary expert group to make it less subjective and more applicable in a UK hospital setting.[94] In contrast, the equivalent Scottish surveillance system adopted the original CDC definition, albeit allowing surveillance practitioners as well clinicians to diagnose SSI.[9]

The absence of a clear pattern to the type of wounds classified as infected by CDC but as not infected by NINSS indicates that small changes made to the CDC definition or even its interpretation, as practised by NINSS and others, causes substantial variation in the apparent SSI%. Although the CDC definition has been adopted in many countries to allow international comparison, this finding suggests that the CDC definition is open to variation in interpretation, especially with regard to superficial SSI. Some criteria need clarification if the CDC definition is to be applied consistently.

Validation of surgical site infection definitions

Introduction

In the preceding section (see *Agreement of alternative surgical site infection definitions*), we compared different SSI definitions and found poor concordance between them. To some extent, discrepant classifications could be explained as the consequence of alternative definitions adopting varying cut-off criteria for classification along a 'severity of infection' continuum. For example, the CDC definition tended to classify SSIs as being more severe than ASEPSIS. The concept of a continuum of infection severity implies that there should be an optimal severity cut-off for classifying wounds as being infected or not. Not all discrepancies could be explained on the basis of varying infection severity criteria for classification. These other discrepancies could be owing to chance, but some appeared to be systematic and to reflect differing interpretations of clinical signs by the classification algorithms which form the basis of alternative SSI definitions.

Investigating the optimal cut-off empirically requires an independent, gold standard method for classifying wounds as infected or not. Such a definition needs to capture all infections considered to be 'important' by patients, clinicians and NHS managers (e.g. taking into account the consequences of infection in the management and financing of scarce resources). The gold standard method could take into account information not necessarily available when applying SSI definitions in practice, e.g. longer-term outcome. If such a definition could be agreed, the ability of alternative SSIs to predict this independent definition of infection could be studied.

Current SSI definitions are based on information about clinical wound characteristics as well as information about a patient's management and infection control. This makes their validation against an *independent* gold standard difficult. One way of tackling this problem is to adopt a psychometric approach, i.e. investigating the construct validity of alternative SSI definitions.[100] This approach involves, first, choosing a range of generic health outcomes (relevant to patients, clinicians and NHS managers) that infection would be expected to influence and then investigating the extent to which alternative SSI definitions are able to predict these outcomes.

We were able to identify outcomes of this kind from the UCLH surveillance data set, namely:

1. protracted length of hospital stay (PLOS)
2. prescription of antibiotics in hospital or after discharge (PAB)
3. wound retreatment in hospital or after discharge (WRTX)
4. patient-reported problem with wound healing (PWH).

Therefore, our specific objective was to compare the extent to which different CDC and APSEPSIS definitions were able to predict these four outcomes. We did not investigate the other two definitions studied with respect to agreement because (1) we did not anticipate major differences between the CDC and modified CDC definitions and (2) we considered that the pus definition was not credible given the disagreement between CDC and ASEPSIS definitions (see *Agreement of alternative surgical site infection definitions*).

Data collection and analysis

Data source: University College London Hospital, surgical site infection surveillance

We again used data from the UCLH SSI surveillance programme to address this objective. These data included information from PDS, as carried out at UCLH (see *Data collection and analysis*). Before carrying out any analyses, we obtained an updated UCLH surveillance data set containing data for a total 11,124 wounds from 9450 operations in 8691 patients. The surgical wounds arose from operations carried out between 22 October 2000 and 12 February 2004.

Preparation of data for analysis

The majority of patients (8069, 92.8%) were observed for only one operation and one wound. In the 622 patients with multiple wounds, we kept only the primary wounds from the patients' first operations for analysis, giving 8691 wounds in 8691 patients. We subsequently excluded 594 wounds that had incomplete or erroneous data for one or more of the four outcomes being investigated, or for important confounding factors. The final data set analysed, therefore, included a total of 8097 wounds in 8097 patients.

For stratification by operation (see *Statistical analysis* below), we used surgical categories as recorded in the UCLH surveillance (*Table 13*) instead of the categories of surgical procedure reported by the NINSS.[21] We took this decision because the NINSS operation categories only cover a proportion of the operations monitored at UCLH.

Generic health outcomes

We used the surveillance information to construct a set of 'generic' outcomes that wound infection would be expected to influence or cause (*Table 14*). These outcomes included clinical actions that were likely to reflect both mild (prescription of antibiotic) and severe infection (wound retreated); patients' views about whether or not there was a problem with the healing of their wounds; and length of hospital stay, reflecting health service resource use (albeit only hospital resources).

Length of stay

Length of stay varied in its distribution by year and operation category (see *Table 13*). Therefore, we created a variable to designate 'protracted LOS', defined as calendar year- and operation-specific LOS in excess of the 85th centile.

Prescription of antibiotics

Prescription of antibiotics was identified from surveillance data collected in hospital or from reports by patients that they had been prescribed antibiotics for a wound infection (item 5, PDS questionnaire; see *Table 10*).

Wound retreatment

Wound retreatment was identified from surveillance data collected in hospital or from reports by patients of wound opening/abscess drainage by a doctor, or opening and cleaning under general anaesthetic in hospital (items 7 and 9, PDS questionnaire; see *Table 10*).

TABLE 13 Median (IQR) lengths of stay by operation category and calendar year

			LOS: median (IQR)				
Operation category	***n***	**%**	**2000**	**2001**	**2002**	**2003**	**2004**
Cardiothoracic	2292	28.3	7 (6)	6 (4)	7 (4)	7 (4)	7 (5)
Maxillofacial surgery	148	1.8	4 (9)	6 (13)	3 (7)	2 (4)	4 (9)
Neurosurgery	816	10.1		3 (6)	6 (7)	6 (7)	6 (7)
Obstetrics and gynaecology	1276	15.8	4 (2)	4 (2)	4 (3)	3 (3)	4 (2)
Orthopaedic	2007	24.8	8 (10)	8 (9)	6 (9)	6 (6)	6 (6)
Plastic	260	3.2	7 (6)	12 (13)	4 (5)	4 (7)	5 (7)
Urology/nephrology	1122	13.9	5 (6)	5 (5)	4 (6)	4 (4)	7 (9)
Vascular	176	2.2	14 (11)	6 (8)	6 (10)	5 (10)	6 (9)
Total	8097	100.0	7 (8)	6 (6)	6 (6)	6 (6)	6 (6)

TABLE 14 Binary outcome measures and corresponding modified SSI definitions used for analyses

Outcome	**Modification(s) applied to SSI definitions**
Length of hospital stay > 85th centile (calculated by year and operation category)	Remove contribution of all PDS information to CDC and ASEPSIS, as well as 'LOS > 14 days' criterion (ASEPSIS only)
Antibiotics prescribed in hospital or after discharge	Remove PDS information about antibiotics from ASEPSIS score (worth 5 points) and from CDC classification ('surgeon diagnosis' criterion)
Wound retreated in hospital or after discharge	Remove retreatment contribution to ASEPSIS score (maximum possible of 15 points) and from CDC classification ('surgeon diagnosis' criterion)
Patient reported problem with wound healing	None
Patient reported problem with wound healing or no problem reported with wound healing, but prescribed antibiotics in hospital	None (prescription of antibiotics in hospital does not contribute to UCLH application of ASEPSIS and CDC SSI definitions)

Patient reported problem with wound healing

Any 'no' response to the stem question of PDS questionnaire (see *Table 10*) was assumed to indicate a problem with wound healing. However, because of potential ambiguity among respondents about whether or not this question referred only to the period after discharge, or to the entire postoperative period including the time in hospital, we defined this outcome in two ways. First, we created a binary response based solely on responses to the stem question from the PDS questionnaire. We classified a wound as having had a problem healing whenever a respondent answered 'no' to the stem question (i.e. inferring, yes, there was a problem). Second, we created a binary response that was classified as 'yes' *either* when the response to stem question was 'no' *or* when antibiotics were prescribed in hospital (using data from wound infection surveillance in hospital). Analyses for both versions of this outcome are reported below.

Modifications to surgical site infection definitions

Some of the information used to generate our selected outcome variables is used at UCLH and elsewhere to apply CDC and ASEPSIS definitions. For example, a protracted LOS (> 14 days) adds 10 points to ASEPSIS score; wound retreatment under anaesthetic is used to infer 'surgeon's SSI diagnosis' for the CDC classification and contributes additional points to the ASEPSIS score. If we had used the SSI definitions described in *Agreement of alternative surgical site infection definitions* without modification, this would have created dependencies between predictors and outcomes. In other words, there would have been one-to-one correspondence between SSI definition and outcome for patients with positive infection signs shared by predictor and outcome. This would have 'credited' a particular definition with predicting an outcome when, to

some degree, the predictive performance arose simply because of the way in which the outcome was defined.

In order to avoid this problem, we modified the SSI definitions for each analysis, excluding any contribution of the outcome to the SSI score/classification. *Table 14* describes how each definition was modified. The modifications to ASEPSIS scores frequently cut down the score by 10 points or more, resulting in a less dispersed distribution; using the original cut-points, the upper two categories for the modified ASEPSIS scores consistently had < 0.5% in each. Therefore, we recalculated the categorical form of this score to create more evenly spaced categories, keeping the number of categories constant (*Table 15*).

Statistical analysis

We developed logistic regression models to quantify the ability of alternative SSI definitions to predict the outcomes. The CDC definition was modelled using indicator variables to code three categories of infection: no infection, superficial infection and deep/organ space infection. The ASEPSIS definition was modelled separately both as a continuous variable and as a categorical variable, using indicator variables (with categories as described in *Table 15*). We also classified ASEPSIS into fewer categories to investigate how this affected prediction and, for outcomes based on patients' reports of problems with wound healing where no modification to the ASEPSIS scores was required, both original and revised cut-off criteria. In our models using continuous ASEPSIS scores, we also included a squared ASEPSIS score to allow for non-linear associations between ASEPSIS score and outcome. All models were adjusted for operation type (see *Table 13*).

From each logistic model, we obtained the receiver operating characteristic (ROC) curve and estimated the area under the curve (a summary of goodness-of-fit) for CDC and ASEPSIS definitions. As in the case of our comparison of CDC and ASEPSIS definitions, the statistics here are for descriptive purposes. We have deliberately not included inferential statistics such as *p*-values or CIs for differences in ROC area because their statistical significance would be difficult to interpret or apply directly to other settings.

TABLE 15 Distribution of wounds in original and modified ASEPSIS severity categories – number (%) of wounds

ASEPSIS cut-off points	All ASEPSIS		Without all PDS items		Without antibiotic items		Without retreatment items	
	n	%	*n*	%	*n*	%	*n*	%
Original cut-off points								
0–10	6819	84.2	7565	93.4	7264	89.7	7022	86.7
11–20	817	10.1	418	5.2	624	7.7	802	9.9
21–30	325	4.0	79	1.0	162	2.0	218	2.7
31–40	80	1.0	8	0.1	8	0.1	15	0.2
>40	56	0.7	27	0.3	39	0.5	40	0.5
Modified cut-off points								
0	4118	50.9	4686	57.9	4250	52.5	4203	51.9
1–5	1971	24.3	2193	27.1	2186	27.0	1973	24.4
6–10	730	9.0	674	8.3	804	9.9	824	10.2
11–15	498	6.2	324	4.0	423	5.2	548	6.8
>15	780	9.6	220	2.7	434	5.4	549	6.8

Results

Areas under the curve for ROC curves for each outcome are summarised in *Table 16*. The ROC curves for continuous and categorical ASEPSIS and categorical CDC SSI definitions are shown in *Figures 7–11*, adjusted for operation category.

Results follow one of two patterns:

1. CDC and ASEPSIS definitions perform similarly, with a modest overall degree of prediction. This pattern was observed for PLOS and PAB.
2. ASEPSIS performs better than CDC, and the overall degree of prediction is good for ASEPSIS (areas under the curve > 0.8). This pattern was observed for WRTX and both outcomes based on PWH (with or without inclusion of information about PAB). Both SSI definitions predicted the outcome of a PWH alone better than when this outcome was combined with PAB.

Models in which ASEPSIS scores were fitted continuously did not predict outcome better than models in which ASEPSIS scores were fitted categorically, using the five revised categories. For the two outcomes based on PWH, it did not make any difference whether or not the original or revised ASEPSIS categories were used. Also for these outcomes, when we classified ASEPSIS scores into three categories (the same number as for the CDC definition) based on the revised cut-off points (i.e. 0–5, 6–15 and > 15), ROC areas were as large as for five categories; when we classified ASEPSIS scores into three categories based on the original cut-off points (0–20, 21–40 and > 40), ROC areas were intermediate between ASEPSIS and CDC areas. For LOS, prescription of antibiotics and wound retreatment outcomes, ROC areas for ASEPSIS scores classified into three categories (based on the revised cut-off points, i.e. 0–5, 6–15 and > 15) were equally good as five categories for revised cut-off points (i.e. 0–5, 6–15 and > 15).

TABLE 16 Comparison of areas under the curve (asymptotic 95% CIs) for ASEPSIS and CDC SSI definitions, adjusted for operation category

	ROC area under the curve (95% CI)		
Outcome	**ASEPSIS score**	**ASEPSIS category**	**CDC**
LOS	0.64 (0.62 to 0.66)	0.65 (0.63 to 0.67)	0.65 (0.62 to 0.66)
Antibiotics	0.75 (0.73 to 0.76)	0.75 (0.73 to 0.76)	0.74 (0.73 to 0.76)
Retreatment	0.85 (0.84 to 0.87)	0.85 (0.83 to 0.86)	0.79 (0.77 to 0.80)
Patient-reported wound healing problem	0.88 (0.87 to 0.89)	0.87 (0.86 to 0.88)	0.76 (0.75 to 0.77)
Patient-reported wound healing problem or antibiotics given in hospital	0.80 (0.79 to 0.81)	0.80 (0.79 to 0.81)	0.74 (0.73 to 0.75)

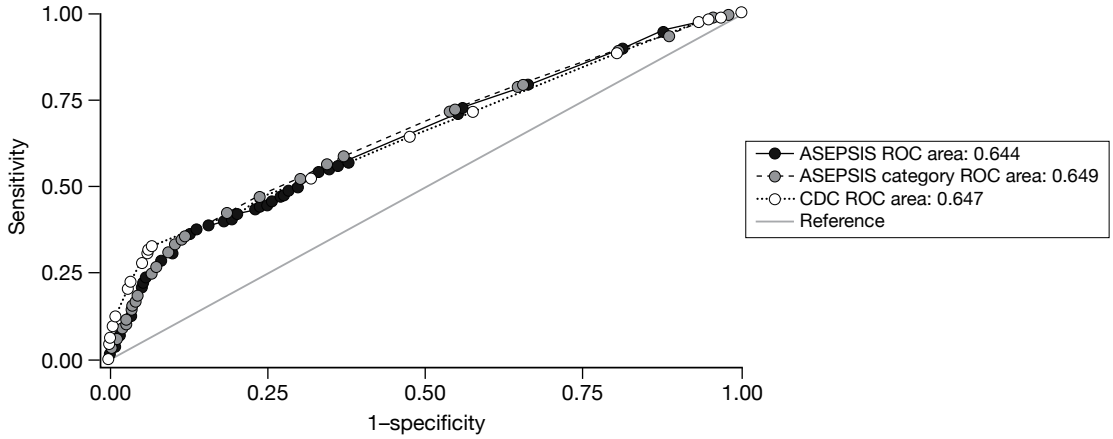


FIGURE 7 Receiver operating characteristic curves for continuous and categorical ASEPSIS and categorical CDC SSI definitions for 'PLOS'. ROC curves for CDC models show multiple data points because of the inclusion of operation category in the model.

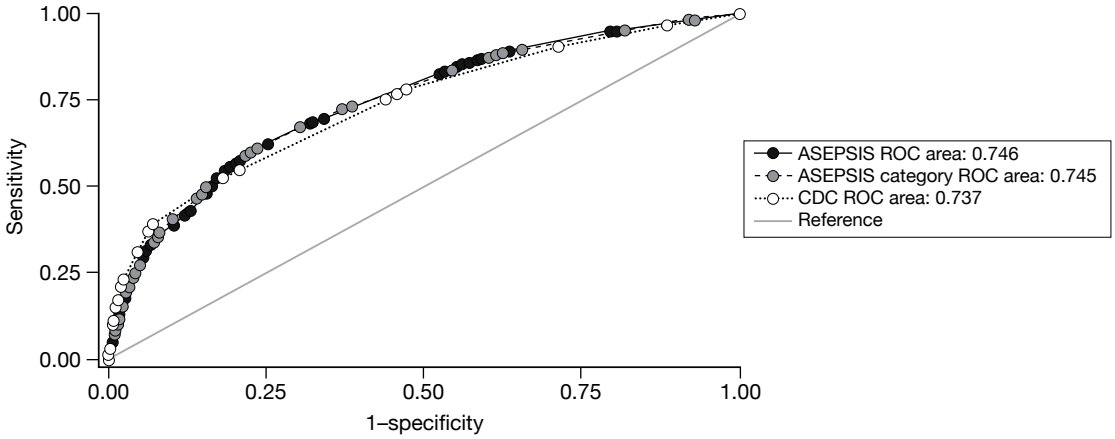


FIGURE 8 Receiver operating characteristic curves for continuous and categorical ASEPSIS and categorical CDC SSI definitions for 'PAB'. ROC curves for CDC models show multiple data points because of the inclusion of operation category in the model.

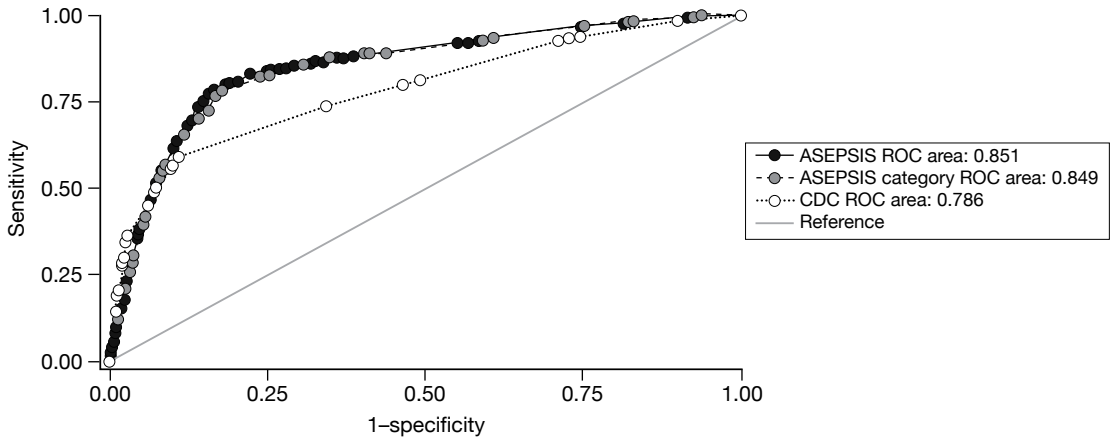


FIGURE 9 Receiver operating characteristic curves for continuous and categorical ASEPSIS and categorical CDC SSI definitions for 'WRTX'. ROC curves for CDC models show multiple data points because of the inclusion of operation category in the model.

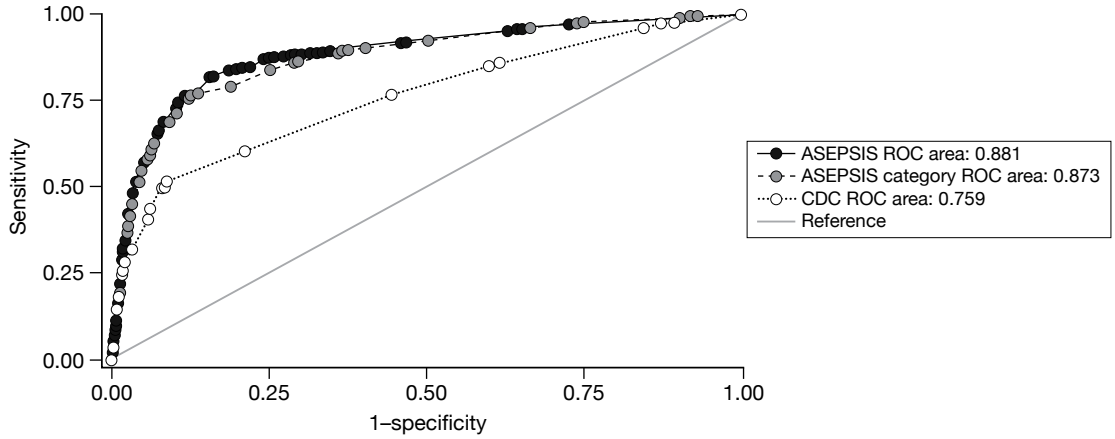


FIGURE 10 Receiver operating characteristic curves for continuous and categorical ASEPSIS scores and categorical CDC SSI definitions for 'PWH' ROC curves for CDC models show multiple data points because of the inclusion of operation category in the model.

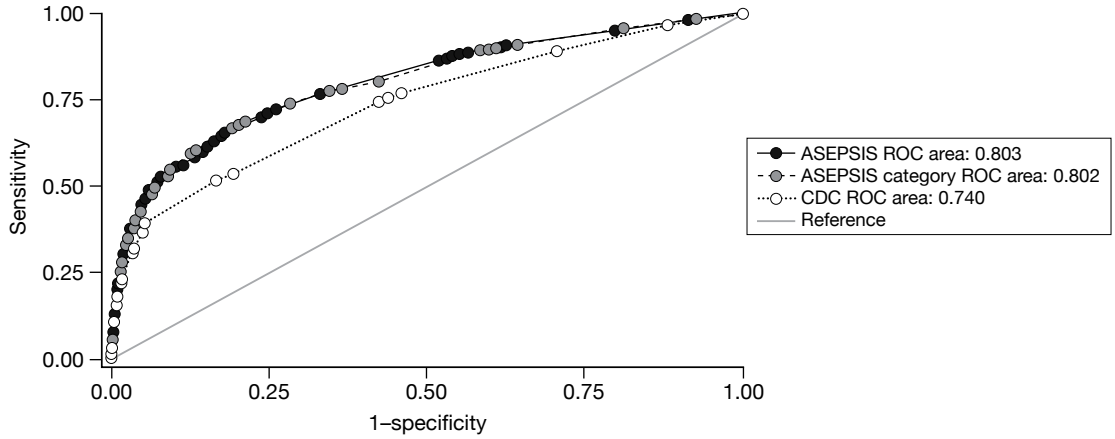


FIGURE 11 Receiver operating characteristic curves for continuous and categorical ASEPSIS and categorical CDC SSI definitions for 'PWH *or* PAB in hospital' ROC curves for CDC models show multiple data points because of the inclusion of operation category in the model.

Discussion

The ASEPSIS and CDC SSI definitions both show reasonable ability to predict the generic outcomes we formulated (ROC areas ranging from about 0.65 for PLOS to about 0.80 for WRTX and PWH). The ability to predict PWH is important as this outcome is completely independent of the SSI definitions. It also reflects patients' perceptions of whether or not their wounds healed satisfactorily, although not their views about the importance to them of any problems with wound healing that they experienced.

It is not surprising that prediction is imperfect. Misclassifications arise from two sources:

1. limitations of the definitions
2. limitations of the outcomes.

Limitations of the definitions

Both CDC and ASEPSIS are based on particular clinical signs or microbiological results that do not necessarily have a one-to-one correspondence with SSI. For example, it seems clear from

the stratified analysis of wounds, with or without any pus, that a wound with some pus is not necessarily infected from a clinical perspective (i.e. may not increase stay or cause other change in clinical management); conversely wounds without obvious pus may still be infected. The same is true for the signs of erythema and serous discharge which are 'scored' for ASEPSIS, although one would expect the additive nature of ASEPSIS, combined with the use of a threshold score to denote SSI, to be less affected by this limitation than the CDC categorical definition.

Limitations of the outcomes

There are important limitations of each of the generic outcomes that we formulated, some of which arose from intrinsic limitations of the outcome and some from limitations in the data available to us. However, we are not aware of reasons why these limitations should affect ASEPSIS and CDC definitions differentially.

Surgical site infection has been observed to be strongly associated with LOS in previous studies[1] but, to some degree, this association could be explained by confounding, e.g. patients likely to stay longer may be more likely to have an SSI detected. Causation is very difficult to prove, although clinicians report that they delay patients' discharge because of infection. Discharge can be delayed by other factors unrelated to SSI, e.g. the availability of an appropriate discharge destination. Patients discharged early may develop SSIs after discharge, so these SSIs have no opportunity to influence LOS. For the analyses reported, we tried to exclude SSIs detected after discharge by revising the SSI definitions (see *Table 14*).

We obtained information about prescription of antibiotics from in-hospital surveillance of wounds and from patients. Staff carrying out in-hospital surveillance are instructed to record use of antibiotics only when they are prescribed for SSI, but this may not have been the case in all instances of antibiotic use. If antibiotic use was recorded sometimes when antibiotics were prescribed routinely, rather than in response to signs of infection or for a systemic (respiratory/urinary) infection that was not an SSI, this will have weakened the ability of SSI definitions to predict this outcome. A similar problem may have arisen for PDS data, despite the wording of the item about the use of antibiotics (see *Table 10*); some patients may not have been aware of why they were given antibiotics.

With respect to PWH, patients were not always clear whether or not the PDS questionnaire referred only to the time since discharge or to their time in hospital as well. Patients may also have been unaware of infections in hospital. We tried to overcome this limitation by creating alternative formulations of this outcome with and without the inclusion of a supporting clinical variable (antibiotics); SSI definitions predicted the simple formulation better. PWH may also have been misclassified for a small minority of patients with more than one wound, as the problem identified by the patient could relate to a wound that was not included.

The WRTX outcome has the advantage that it is less likely to be misclassified than the other outcomes. However, it has the disadvantage that it is likely only to relate to the most serious SSIs. Almost twice as many patients reported having a problem with wound healing (1412, 17.4%) as were classified as having had a wound retreated (782, 9.7%). It is probable that many clinically important SSIs do not require retreatment but nevertheless cause discomfort and inconvenience to patients and, for those SSIs detected in hospital, increase the cost to health services of surgical admissions.

We believe that these limitations are reflected in our findings. For example, the predictive ability of SSI definitions was poorer for LOS and use of antibiotics than for the other outcomes.

Interpretation of the findings

Much of the information used in applying the SSI definitions and in deriving the generic outcomes was collected after discharge, i.e. through systematic PDS. We regard this as an important strength of the UCLH surveillance programme. The exception was the LOS outcome, which SSI definitions were least able to predict. Therefore, our findings are unlikely to be replicable using data from other routine surveillance programmes, as most do not include PDS.

We suspect that the distinction between the two patterns of results is because of the influence of information from PDS. PDS at UCLH was designed in the context of the ASEPSIS rather than the CDC definition and, therefore, integration of these items into the ASEPSIS score may have characterised infections after discharge better than their integration into the CDC algorithms for classifying infection site/severity. Although we were able to revise SSI definitions for most outcomes to take into account the fact that the outcome contributed to the definition, we could not do this for PWH. The PDS stem question did not contribute directly to ASEPSIS or CDC definitions but, when problems were reported, the subsequent PDS items did. These items, and the extent to which they contributed to the ASEPSIS score, were chosen in the context of the development of the ASEPSIS score.

We considered carefully whether or not to adjust for other potential confounding factors in the models, in addition to surgical category. We decided not to do so for two reasons. First, we were worried about the danger of overadjusting as potential confounding factors are likely to influence outcome partly by virtue of being a risk factor for infection and partly directly. Second, we could not identify reasons why residual confounding should be differential by SSI definition. Residual confounding is likely to mean that the models are somewhat optimistic about the ability of SSI definitions to predict the generic outcomes.

ASEPSIS may be considered to have an inherent advantage over the CDC classification in terms of its ability to predict outcome, because it yields a continuous score compared with the four categories of the CDC definition. Interestingly, classifying ASEPSIS scores into five or even three categories did not markedly affect the ability of ASEPSIS to predict outcome.

We have not reported the total number of misclassifications, Ppos or Pneg for the different models because these depend critically on the cut-off chosen for dichotomous classification. The trade-off between sensitivity and specificity for the different cut-offs is represented by the ROC curves in *Figures 7* to *11*. An advantage of ASEPSIS is that the cut-point for classifying a wound as infected can be varied and optimal cut-off chosen empirically on the basis of the frequency of 'false' positive and negatives, their consequences and costs.

Overview of findings of surgical site infection definitions

The analyses reported in this chapter were carried out with the aim of informing the choice of the most suitable SSI definition for surveillance from the options that have been proposed, most of which are in use in one surveillance programme or another. The detailed consideration of different SSI definitions highlighted that none of them have been psychometrically evaluated, as would be the case, for example, for a patient-reported measure of health outcome. The only evaluation that has been carried out relates to the reliability of the measurements from which the ASEPSIS scale and SSI definition are calculated. However, the method of data collection for the ASEPSIS scale has since been modified. This represents a serious evidence gap, as all three commonly used definitions (CDC, NINSS and ASEPSIS) require infection control practitioners to observe wounds and make subjective assessments.

Our findings indicate that different SSI definitions classify different wounds as being infected, although some wounds are classified as infected by all definitions. The lack of agreement between the two definitions, CDC and ASEPSIS, should be a concern, particularly in the context of comparisons of SSI%s between surveillance programmes that use different definitions.

There appears to be a paradox in that both ASEPSIS and CDC definitions had broadly similar abilities to predict the generic outcomes, despite the poor agreement in classifying individual wounds. This implies either that there may be features of each definition that are important in identifying the outcomes we chose but which are not common to both, or that the ability to predict the outcomes depends only on a subset of features used by each definition which are common to both. Both possibilities suggest that there is an opportunity to produce a better definition, by combining the important predictive items from different definitions or by dropping redundant items (see *Chapter 5, Research recommendations*).

Whatever definition is chosen, there is the underlying problem of choosing the sensitivity of the definition (e.g. ASEPSIS cut-off or inclusion/exclusion of wounds classified as superficially infected by the CDC definition). Choosing an optimal cut-off is extremely difficult, as illustrated by the ROC curves for the generic outcomes. A definition that is too sensitive will give rise to high estimates of absolute SSI% that may cause public alarm. Moreover, if overall rates are influenced primarily by minor infections of relatively little consequence to patients and health services, the use of such a definition could mask important changes over time or differences between institutions. Conversely, a definition that lacks sensitivity would not identify some SSIs that might be avoidable and which have important consequences; a lack of sensitivity could also obscure important changes over time or differences between institutions. Preliminary analysis of outcomes for ASEPSIS suggests that minor infections may be important to health services.[98] Some wounds classified in the 'disturbance of healing' category (11–20 points) can delay hospital discharge by 1–2 days, a significant cost pressure if they are frequent.

Chapter 4

Surgical site infection risk modelling (National Nosocomial Infection Surveillance Scheme data)

National Nosocomial Infection Surveillance Scheme

The NINSS was established in 1996. The aim of the scheme is to provide information to help to identify, and reduce, the incidence of avoidable hospital-acquired infection including SSI. NINSS requires participating hospitals to implement a standard protocol for data collection and to submit data for collation centrally. Reports are fed back, allowing hospitals to view their own SSI%s against those for other hospitals.[14,21]

At the outset, participation in NINSS was both voluntary and confidential. In 2003, the Chief Medical Officer announced that reporting of SSIs following orthopaedic surgery was to become mandatory from 1 April 2004. There was a steady increase over time in the number of hospitals participating over the period covered by the data that were analysed (*Figure 12*).[14]

Hospitals taking part in the SSI module can choose to carry out surveillance of one or more of 12 categories of clinically similar procedures, e.g. large bowel surgery, CABG procedures, hip prostheses, etc. In order for data to be included for reporting, there is a requirement for a hospital to carry out surveillance for at least 3 consecutive months. However, surveillance in a hospital does not have to be continuous, e.g. a hospital could opt to collect data for the same 3 months in consecutive years.

Hospitals collect data to characterise key risk factors for infection and information about SSIs that develop during the hospital stay for all patients who undergo an operation included in the categories chosen for surveillance. NINSS has observed that the proportion of 'infected operations' varies considerably between hospitals, as shown in *Figure 13*.

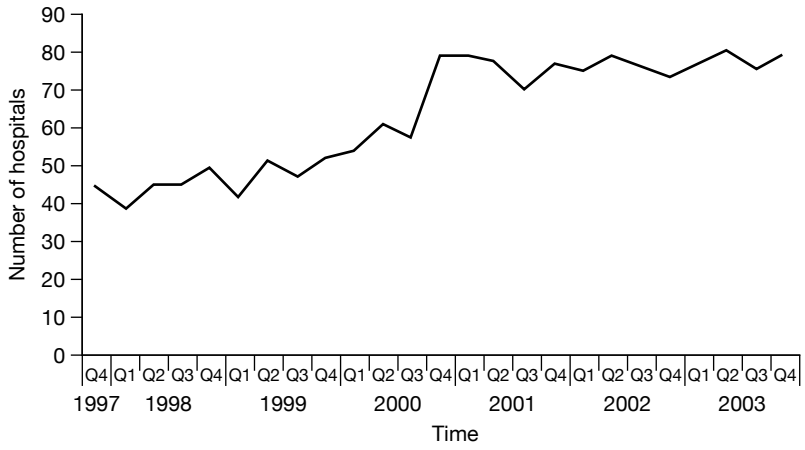


FIGURE 12 Hospital participation in the NINSS from October 1997 to December 2003.

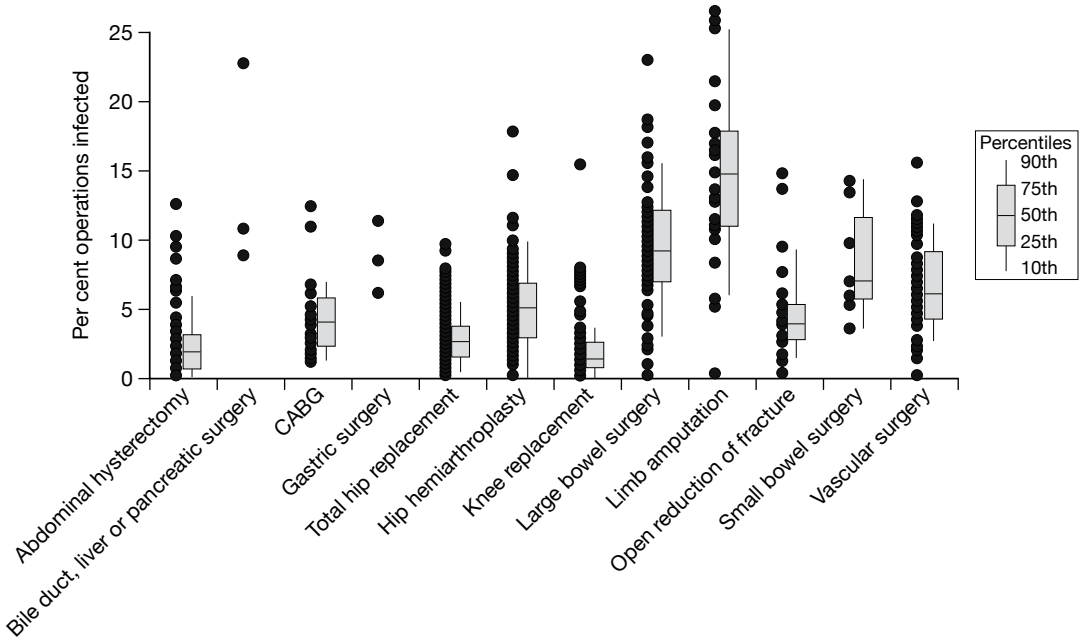


FIGURE 13 Distribution of the incidence of SSI by category of surgical procedure in the NINSS, October 1997 to December 2003.[10] Reproduced with permission from the National Audit Office.

Data management prior to analysis

Introduction

National Nosocomial Infection Surveillance Scheme data for 113,824 operations observed between 10 September 1997 and 31 December 2002 were used in the risk modelling analyses. Data were supplied in their native Microsoft Access format, and were imported into Stata v9 statistical software for data management and analysis. This section describes properties of the NINSS database that were relevant for the risk modelling analysis.

Observations and their correspondence with records in the data set

The NINSS data collection protocol gives instructions for some advanced methods to record multiple or related observations, i.e. multiple infections in a single patient.

ID numbers

The NINSS database allocates a unique ID number to identify each operation. More than one SSI can be allocated to an incision, although this is uncommon.

Operations

For most of the data set, one record represents one *operation*. An *operation* is defined as a single patient visit to the operating theatre, in which one or multiple surgical procedures are performed through a single incision. If more than one type of procedure is carried out through one incision during one operation, any subsequent SSI is assigned to the procedure most likely to be responsible.

The exception is for CABG procedures (e.g. sternal wound to provide access to the heart and leg or arm wound to harvest the saphenous vein or radial artery for grafting) where a single record for the procedure would be created, but SSI are allocated to the sternal or donor incision.

For most operations there is a single incision and procedure undertaken. For each, there is set of risk factors such as 'NNIS risk index', 'wound classification' and 'duration of operation'. For CABG operations, because some operations involve both a sternal and donor site incision, the 'wound classification' stored against an operation should be considered to reflect the averaged wound classification of all wounds incurred in the operation. However, the above aggregation does not apply to SSI (see *Multiple surgical site infection*).

Only operations involving a period of ≥ 24 hours between admission and discharge were included in the surveillance. A reoperation within 72 hours was included in the classification of the original procedures. A reoperation through the same incision after 72 hours would be considered as a new procedure (provided it was eligible for inclusion in the surveillance) and the surveillance on the original procedure would then be discontinued; if an SSI developed subsequently, it would be allocated to the second procedure.

As the system is based on the follow-up of a specific operation for SSI, multiple operations separated in time on the same patient cannot be linked or clustered. In addition, data are not captured on extended operations through the same incision if these are not procedures included in the surveillance. However, other procedures carried out are recorded as 'multiple procedures through the same incision', e.g. a valve replacement performed through the same sternal incision as a CABG operation.

Multiple surgical site infections

Some operation records were associated with more than one SSI. These were identified by linkages in the database. In validated 'SSI sets', we included in the analysis only the SSI which was observed first. The first observation is determined by the dssi (date SSI detected) variable.

Variables available for analysis

Box 1 summarises the variables that were included in the data set. Height and weight were not included in the analysis because collection of these data was optional for contributing hospitals and data were available for only about 50% of records. Antibiotic prophylaxis was also not included; this was given for the majority of operations and, therefore, was not discriminatory as a risk factor.

Data cleaning

Actions are summarised in *Table 17*. Further specialised data cleaning was undertaken when building risk models for some categories of surgery (see each surgery-specific sections of the results and *Appendix 4* for further details). A small number of operations were assigned an ASA class of 5. These were excluded from risk modelling for all surgery categories except for CABG, because they were considered most likely to represent coding errors as it was judged unlikely that patients in ASA class 5 would have the operations.

Results of univariable analyses of risk factors

Introduction

The tabulations in this section are generated from the NINSS database after cleaning (see *Data management prior to analysis*). In each table, frequencies and SSI%s, together with ORs and 95% CIs, are presented by levels of one risk factor. Results are stratified by category of surgical procedure and, where applicable, results for the entire data set at the bottom of each table.

BOX 1 Variables in NINSS data set

Variable

Diagnostic/system variables

Hospital code – unique integer starting at 0

Surgeon code – unique within hospital code

Time period – code representing year/quarter of observation

Reason for discontinuation of surveillance

Category of surgical procedure, defined by NINSS

Potential risk factors

Length of preoperative stay (days); continuous in original data set, categorised during data management (categories vary by surgery type)

Age at admission; continuous in original data, categorised during data management (constant categories by surgery type, but some categories not used for some surgery types)

Gender

Weight (kilograms)

Height (centimetres)

Duration of operation (minutes); continuous in original data, categorised during data management (categories vary by surgery type)

Operation duration > 75th percentile for surgery category (yes/no); derived variable used to generate NNIS risk index

Emergency surgery (yes/no)

Surgery due to trauma (yes/no)

Implant installed during procedure (yes/no)

Multiple surgical procedures performed through the same incision (yes/no)

Antibiotic prophylaxis administered (yes/no)

Wound classification, defined as ‘clean’, ‘clean-contaminated’, ‘contaminated’, ‘dirty’

Wound classification ‘contaminated’ or ‘dirty’ (yes/no, i.e. ‘clean’ or ‘clean-contaminated’); derived variable used to generate NNIS risk index

ASA class (five categories, 1–5, describing preoperative ‘illness severity’/morbidity/comorbidity)

ASA class ≥ 3 (yes/no, i.e. ASA class < 3); derived variable used to generate NNIS risk index

NNIS risk index (four categories, 0–3); derived variable

Year of observation

Outcome variables

SSI observed (yes/no)

Time from operation to SSI detection (days)

Time between SSI detection and discharge from hospital

Length of postoperative stay (days); stays of ‘0 days’ assumed to be half-days

TABLE 17 Summary of data cleaning

Data cleaning operation	Records removed	Records remaining
Initial number of records imported		113,824
Males categorised under abdominal hysterectomy	2	113,822
Excess records of SSI from individuals ('>1 SSI' sets)	113	113,709
Wounds with blank SSI field	16	113,693
Children <18 years of age	545	113,148
Subjects with blank 'time to SSI' information[a]	80	113,068
Final number of records for analysis		113,068

a Blank 'time to SSI' information did not necessarily imply that a SSI had been observed; the information was missing rather than not applicable. Further specialised data cleaning/preparation was undertaken when building risk models for some categories of surgery. See each subheading for further details.

Risk factors which were measured continuously

Risk factors which were measured as continuous variables (preoperative stay, operation duration, age) have been converted to categories in these summaries. The distribution of 'continuous' risk factors varied substantially between categories of surgical procedure, so it was necessary to assign categories within each surgery type. The exception is age, for which specific age bands were predefined, although they were not all populated for every procedure.

Odds ratios

All ORs come from unadjusted, univariable logistic regression on SSI. Frequencies and SSI%s are given for missing data, but the missing category was not included in these logistic regressions. Categories with no SSI events are also excluded from the logistic regression.

Odds ratios are presented relative to a 'reference' category which is denoted by OR = [1.00].

Results

Table 18 gives summaries of the numbers of records in different categories of surgical procedure, the distribution of LOS and, among records classified as SSIs, the time from surgery to identification of the SSI ('time to SSI'). It is important to point out that, despite the large number of records in the data set, the numbers in some categories of surgical procedure were small. The overall SSI% in the data set was 4.5%. ORs for surgical categories of surgical procedure varied considerably (reference category hip prosthesis, OR = 1.00, SSI% 3.5%), from 0.6 (knee prosthesis, SSI% 2.1%) to ≥ 3 (for small and large bowel surgery, bile liver and pancreatic surgery, gastric surgery and limb amputation; SSI%s of about ≥ 10%).

Table 19 shows the numbers of records classified in different SSI categories by category of surgical procedure. Overall, the SSI% for superficial, deep and organ/space categories were 3.2%, 0.9% and 0.4%. This ratio across SSI categories was generally reflected across categories of surgical procedures, although procedures with a high overall SSI% tended to have a higher proportion of SSIs classified as organ/space (limb amputation being an exception).

Tables 20–25 show results of univariable analyses for the NNIS risk index, each of the components of the NNIS risk index (operation duration/wound class/ASA class), age and gender.

TABLE 18 Number of observations, SSIs, LOS and time to SSI by surgery category

Category of surgical procedure	SSI cases (*n*)	OR (95% CI)	LOS [median (min–max)]		Time to SSI [median (min–max)]
			SSI non-cases	SSI cases	SSI cases
Abdominal hysterectomy	271 (9119)	0.84 (0.73 to 0.95)	5 (0–35)	8 (2–35)	6 (0–122)
Bile duct, liver, pancreatic surgery	21 (188)	3.44 (2.18 to 5.43)	11 (1–31)	19 (6–31)	12 (4–25)
Cholecystectomy	5 (117)	1.22 (0.5 to 2.99)	6 (2–41)	17 (8–26)	7 (5–11)
CABG	745 (15,384)	1.39 (1.27 to 1.52)	7 (0–121)	17 (3–113)	9 (0–69)
Gastric surgery	32 (221)	4.63 (3.17 to 6.75)	12 (0–33)	21 (2–30)	9 (1–34)
Hip replacement	1526 (43,226)	1.00 [Ref]	10 (0–129)	21 (0–123)	10 (0–123)
Knee replacement	476 (22,585)	0.59 (0.53 to 0.65)	9 (0–130)	18 (0–121)	10 (0–149)
Large bowel surgery	921 (9514)	2.93 (2.69 to 3.19)	11 (0–55)	21 (0–60)	9 (0–60)
Limb amputation	240 (1528)	5.09 (4.4 to 5.9)	15 (0–35)	28 (1–34)	11 (0–37)
Open reduction of fractures	230 (4593)	1.44 (1.25 to 1.66)	10 (0–125)	28 (1–92)	12 (0–123)
Small bowel surgery	106 (1091)	2.94 (2.39 to 3.62)	11 (0–35)	19.5 (0–34)	8 (0–76)
Vascular surgery	491 (5502)	2.68 (2.41 to 2.98)	8 (0–121)	19 (1–121)	10 (0–61)
Main effect [χ^2 (*p*-value)]	1564 ($p<0.0001$)				
	SSI cases (n)	***SSI% (95% CI)***			
All surgery types	5064 (113,068)	0.045 (0.044 to 0.046)	9 (0–130)	19 (0–123)	9 (0–149)

TABLE 19 Number of SSIs classified in different SSI categories by surgery category

Category of surgical procedure	Superficial infection			Deep infection			Organ/space infection			Missing
	No. of infections	% of total	% of all SSIs	No. of infections	% of total	% of all SSIs	No. of infections	% of total	% of all SSIs	
Abdominal hysterectomy	209	2.3	77.1	37	0.4	13.7	23	0.3	8.5	2
Bile duct, liver, pancreatic surgery	11	5.9	52.4	4	2.1	19.1	6	3.2	28.6	0
Cholecystectomy	4	3.4	80.0	0	0.0	0.0	1	0.9	20.0	0
CABG	514	3.3	69.0	181	1.2	24.3	45	0.3	6.0	5
Gastric surgery	19	8.6	59.4	8	3.6	25.0	4	1.8	12.5	1
Hip replacement	1096	2.5	71.8	299	0.7	19.6	127	0.3	8.3	4
Knee replacement	358	1.6	75.2	75	0.3	15.8	40	0.2	8.4	3
Large bowel surgery	553	5.8	60.0	226	2.4	24.5	134	1.4	14.6	8
Limb amputation	170	11.1	70.8	65	4.3	27.1	4	0.3	1.7	1
Open reduction of fractures	190	4.1	82.6	28	0.6	12.2	12	0.3	5.2	0
Small bowel surgery	63	5.8	59.4	30	2.7	28.3	9	0.8	8.5	4
Vascular surgery	408	7.4	83.1	66	1.2	13.4	15	0.3	3.1	2
All surgery types	3595	3.2	71.0	1019	0.9	20.1	420	0.4	8.3	30

TABLE 20 Number of SSIs in categories of NNIS risk index, with univariable OR estimates, by surgery category

Category of surgical procedure	Categories of NNIS risk index				Missing	Main effect χ^2 (*p*-value)
	0	1	2	3		
Abdominal hysterectomy (*n* = 9119)						
SSI cases (*n*)	167 (6229)	43 (918)	8 (91)	1 (4)	52 (1877)	19.6 ($p<0.01$)
OR (95% CI)	(1.00)	1.78 (1.27 to 2.51)	3.50 (1.67 to 7.35)	12.10 (1.25 to 116.93)		
Bile duct, liver, pancreatic surgery (*n* = 188)						
SSI cases (*n*)	8 (64)	8 (60)	1 (12)		4 (52)	0.25 ($p=0.88$)
OR (95% CI)	(1.00)	1.08 (0.38 to 3.08)	0.64 (0.07 to 5.61)			
Cholecystectomy (*n* = 117)						
SSI cases (*n*)	0 (31)	0 (26)	2 (13)	2 (9)	1 (38)	6.35 ($p=0.04$)
OR (95% CI)						
CABG (*n*=15,384)						
SSI cases (*n*)	6 (495)	507 (11,613)	54 (674)		178 (2602)	33.6 ($p<0.01$)
OR (95% CI)	0.27 (0.12 to 0.60)	(1.00)	1.91 (1.42 to 2.55)			
Gastric surgery (*n* = 221)						
SSI cases (*n*)	2 (42)	11 (85)	9 (40)	1 3)	9 (51)	6.70 ($p=0.08$)
OR (95% CI)	0.34 (0.07 to 1.59)	(1.00)	1.95 (0.74 to 5.18)	3.36 (0.28 to 40.27)		
Hip replacement (*n* = 43,226)						
SSI cases (*n*)	520 (19,894)	608 (13,369)	97 (1660)	4 (52)	29 7(8251)	114 ($p<0.01$)
OR (95% CI)	(1.00)	1.78 (1.58 to 2.00)	2.31 (1.85 to 2.89)	3.10 (1.12 to 8.64)		
Knee replacement (*n* = 22,585)						
SSI cases (*n*)	220 (11,669)	133 (5308)	28 (715)	2 (9)	93 (4884)	21.8 ($p<0.01$)
OR (95% CI])	(1.00)	1.34 [(1.08 to 1.66)	2.12 (1.42 to 3.17)	14.87 (3.07 to 71.98)		

continued

TABLE 20 Number of SSIs in categories of NNIS risk index, with univariable OR estimates, by surgery category *(continued)*

	Categories of NNIS risk index					
Category of surgical procedure	**0**	**1**	**2**	**3**	**Missing**	**Main effect χ^2 (*p*-value)**
Large bowel surgery (*n*=9514)						
SSI cases (*n*)	175 (3100)	325 (3167)	202 (1205)	34 (140)	185 (1902)	149 ($p<0.01$)
OR (95% CI)	0.52 (0.43 to 0.63)	(1.00)	1.76 (1.46 to 2.13)	2.80 (1.87 to 4.20)		
Limb amputation (*n*=1528)						
SSI cases (*n*)	16 (162)	85 (538)	65 (368)	17 (87)	57 (373)	6.61 ($p=0.09$)
OR (95% CI)	0.58 (0.33 to 1.03)	(1.00)	1.14 (0.80 to 1.63)	1.29 (0.73 to 2.31)		
Open reduction of fractures (*n*=4593)						
SSI cases (*n*)	68 (1771)	87 (1635)	25 (268)	3 (29)	47 (890)	15.6 ($p<0.01$)
OR (95% CI)	(1.00)	1.41 (1.02 to 1.95)	2.58 (1.60 to 4.15)	2.89 (0.85 to 9.78)		
Small bowel surgery (*n*=1091)						
SSI cases (*n*)	19 (217)	25 (375)	28 (173)	3 (26)	31 (300)	11.7 ($p=0.01$)
OR (95% CI)	1.34 (0.72 to 2.50)	(1.00)	2.70 (1.52 to 4.79)	1.83 (0.51 to 6.50)		
Vascular surgery (*n*=5502)						
SSI cases (*n*)	43 (967)	187 (2384)	171 (1084)	9 (21)	81 (1046)	101 ($p<0.01$)
OR (95% CI)	0.55 (0.39 to 0.77)	(1.00)	2.20 (1.76 to 2.75)	8.81 (3.67 to 21.18)		
All surgery types (*n*=113,068)						Interaction: 58.3 ($p<0.01$)

DOI: 10.3310/hta15300

TABLE 21 Number of SSIs in categories of operation duration, with univariable OR estimates, by surgery category

Category of surgical procedure	Categories of operation duration					Missing	Main effect χ^2 (*p*-value)
	1	2	3	4	5		
Abdominal hysterectomy (*n* = 9119)	**≤45 minutes**	**46–60 minutes**	**61–90 minutes**	**91–120 minutes**	**>120 minutes**		
SSI cases (*n*)	33 (1590)	60 (2291)	88 (3101)	49 (1305)	35 (691)	6 (141)	17.43 (*p* = 0.00)
OR (95% CI)	1.0 [Ref]	1.27 (0.83 to 1.95)	1.38 (0.92 to 2.07)	1.84 (1.18 to 2.88)	2.52 (1.55 to 4.09)		
Bile duct, liver, pancreatic surgery (*n* = 188)	**≤90 minutes**	**91–120 minutes**	**121–180 minutes**	**181–240 minutes**	**>240 minutes**		
SSI cases (*n*)	1 (22)	2 (14)	3 (40)	10 (70)	5 (42)	0 (0)	1.64 (*p* = 0.80)
OR (95% CI)	1.0 [Ref]	3.50 (0.29 to 42.8)	1.70 (0.17 to 17.4)	3.50 (0.42 to 29.0)	2.84 (0.31 to 25.9)		
Cholecystectomy (*n* = 117)		**≤120 minutes**	**121–180 minutes**	**181–240 minutes**	**>240 minutes**		
SSI cases (*n*)		1 (79)	2 (20)	1 (14)	0 (2)	1 (2)	1.63 (*p* = 0.44)
OR (95% CI)		1.0 [Ref]	8.67 (0.74 to 100)	6.00 (0.35 to 102)	0.0		
CABG (*n* = 15,384)		**≤120 minutes**	**121–150 minutes**	**151– 240 minutes**	**>240 minutes**		
SSI cases (*n*)		28 (1060)	71 (2165)	418 (8937)	226 (3104)	2 (118)	61.58 (*p* = 0.00)
OR (95% CI)		1.0 [Ref]	1.25 (0.80 to 1.95)	1.81 (1.23 to 2.67)	2.89 (1.94 to 4.31)		
Gastric surgery (*n* = 221)	**≤90 minutes**	**91–120 minutes**	**121–180 minutes**	**181–240 minutes**	**>240 minutes**		
SSI cases (*n*)	9 (70)	3 (19)	4 (39)	8 (54)	7 (38)	1 (1)	1.64 (*p* = 0.80)
OR (95% CI)	1.0 [Ref]	1.27 (0.31 to 5.25)	0.77 (0.22 to 2.70)	1.18 (0.42 to 3.29)	1.53 (0.52 to 4.50)		
Hip replacement (*n* = 43,226)	**≤60 minutes**	**61–90 minutes**	**91–120 minutes**	**>121 minutes**			
SSI cases (*n*)	457 (10,598)	441 (13,769)	298 (10,268)	279 (7483)		51 (1108)	35.66 (*p* = 0.00)
OR (95% CI)	1.0 [Ref]	0.73 (0.64 to 0.84)	0.66 (0.57 to 0.77)	0.86 (0.74 to 1.00)			
Knee replacement (*n* = 22,585)	**≤60 minutes**	**61–90 minutes**	**91–120 minutes**	**>121 minutes**			
SSI cases (*n*)	57 (3313)	150 (8810)	155 (6492)	93 (3370)		21 (600)	18.60 (*p* = 0.00)
OR (95% CI)	1.0 [Ref]	0.99 (0.73 to 1.35)	1.40 (1.03 to 1.90)	1.62 (1.16 to 2.26)			

continued

TABLE 21 Number of SSIs in categories of operation duration, with univariable OR estimates, by surgery category *(continued)*

Category of surgical procedure	Categories of operation duration					Missing	Main effect χ^2 (*p*-value)
	1	2	3	4	5		
Large bowel surgery (*n* = 9514)		**≥ 120 minutes**	**121–150 minutes**	**151–240 minutes**	**> 241 minutes**		
SSI cases (*n*)		332 (4267)	176 (1735)	305 (2770)	76 (528)	27 (172)	36.26 ($p < 0.01$)
OR (95% CI)		1.0 [Ref]	1.34 (1.10 to 1.62)	1.47 (1.25 to 1.73)	1.99 (1.53 to 2.60)		
Limb amputation (*n* = 1528)	**≤ 30 minutes**	**30–60 minutes**	**61–90 minutes**	**≥ 91 minutes**			
SSI cases (*n*)	50 (355)	89 (537)	51 (338)	40 (228)		10 (70)	1.68 ($p = 0.64$)
OR (95% CI)	1.0 [Ref]	1.21 (0.83 to 1.76)	1.08 (0.71 to 1.65)	1.30 (0.82 to 2.04)			
Open reduction of fractures (*n* = 4593)	**≤ 60 minutes**	**61–90 minutes**	**91–120 minutes**	**≥ 121 minutes**			
SSI cases (*n*)	75 (1743)	62 (1232)	46 (761)	42 (787)		5 (70)	3.69 ($p = 0.30$)
OR (95% CI)	1.0 [Ref]	1.18 (0.83 to 1.66)	1.43 (0.98 to 2.09)	1.25 (0.85 to 1.85)			
Small bowel surgery (*n* = 1091)	**≤ 120 minutes**	**121–150 minutes**	**151–240 minutes**	**≥ 241 minutes**			
SSI cases (*n*)	59 (640)	16 (127)	22 (245)	7 (56)		2 (23)	1.91 ($p = 0.59$)
OR (95% CI)	1.0 [Ref]	1.42 (0.79 to 2.56)	0.97 (0.58 to 1.62)	1.41 (0.61 to 3.25)			
Vascular surgery (*n* = 5502)	**≤ 90 minutes**	**91–120 minutes**	**121–180 minutes**	**181–240 minutes**	**≥ 241 minutes**		
SSI cases (*n*)	40 (822)	57 (889)	125 (1765)	113 (1100)	145 (813)	11 (113)	100.72 ($p < 0.01$)
OR (95% CI)	1.0 [Ref]	1.34 (0.88 to 2.03)	1.49 (1.03 to 2.15)	2.24 (1.54 to 3.25)	4.24 (2.95 to 6.11)		
All surgery types (*n* = 113,068)							Interaction: 279.59 ($p < 0.01$)

DOI: 10.3310/hta15300

TABLE 22 Number of SSIs in categories of wound class, with univariable OR estimates, by surgery category

Category of surgical procedure	Categories of wound class				Missing	Main effect χ^2 (*p*-value)
	Clean	Clean/contaminated	Contaminated	Dirty		
		Clean or clean/contaminated				
Abdominal hysterectomy (*n* = 9119)						
SSI cases (*n*)		264 (9044)	5 (31)	1 (7)	1 (37)	11.08 ($p < 0.01$)
OR (95% CI)		1.0 [Ref]	6.40 (2.44 to 16.79)	5.54 (0.66 to 46.21)		
		Clean or clean/contaminated				
Bile duct, liver, pancreatic surgery (*n* = 188)						
SSI cases (*n*)		20 (175)	1 (6)	0 (4)	0 (3)	0.14 ($p = 0.71$)
OR (95% CI)		1.0 [Ref]	1.55 (0.17 to 13.95)			
		Clean or clean/contaminated				
Cholecystectomy (*n* = 117)						
SSI cases (*n*)		1 (95)	1 (9)	3 (10)	0 (3)	11.45 ($p < 0.01$)
OR (95% CI)		1.0 [Ref]	11.75 (0.67 to 206.1)	40.29 (3.69 to 439.6)		
CABG (*n* = 15,384)						
SSI cases (*n*)	721 (15,073)	15 (232)	1 (3)	0 (2)	8 (74)	3.73 ($p = 0.15$)
OR (95% CI)	1.0 [Ref]	1.38 (0.81 to 2.33)	9.95 (0.90 to 109.89)			
		Clean or clean/contaminated				
Gastric surgery (*n* = 221)						
SSI cases (*n*)		25 (190)	5 (21)	2 (6)	0 (4)	2.88 ($p = 0.24$)
OR (95% CI)		1.0 [Ref]	2.06 (0.69 to 6.13)	3.30 (0.57 to 18.97)		
		Clean or clean/contaminated				
Hip replacement (*n* = 43,226)						
SSI cases (*n*)		1483 (42,704)	11 (153)	16 (122)	16 (247)	24.86 ($p < 0.01$)
OR (95% CI)		1.0 [Ref]	2.15 (1.16 to 3.99)	4.20 (2.47 to 7.12)		

continued

TABLE 22 Number of SSIs in categories of wound class, with univariable OR estimates, by surgery category *(continued)*

Category of surgical procedure	Categories of wound class				Missing	Main effect χ^2 (*p*-value)
	Clean	Clean/contaminated	Contaminated	Dirty		
	Clean or clean/contaminated					
Knee replacement (*n*=22,585)						
SSI cases (*n*)		461 (22,270)	1 (75)	7 (55)	7 (185)	14.53 ($p<0.01$)
OR (95% CI)		1.0 [Ref]	0.64 (0.09 to 4.61)	6.90 (3.11 to 15.33)		
	Clean or clean/contaminated					
Large bowel surgery (*n*=9514)						
SSI cases (*n*)		593 (7256)	181 (1513)	125 (502)	17 (198)	125.32 ($p<0.01$)
OR (95% CI)		1.0 [Ref]	1.53 (1.28 to 1.82)	3.73 (2.99 to 4.64)		
Limb amputation (*n*=1528)						
SSI cases (*n*)	98 (805)	54 (314)	40 (201)	43 (172)	5(36)	20.96 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	1.50 (1.04 to 2.15)	1.79 (1.19 to 2.69)	2.40 (1.60 to 3.60)		
Open reduction of fractures (*n*=4593)						
SSI cases (*n*)	198 (4111)	6 (151)	13 (159)	12 (142)	1(30)	6.48 ($p=0.09$)
OR (95% CI)	1.0 [Ref]	0.82 (0.36 to 1.87)	1.76 (0.98 to 3.16)	1.82 (0.99 to 3.35)		
	Clean or clean/contaminated					
Small bowel surgery (*n*=1091)						
SSI cases (*n*)		62 (683)	43 (393)		1 (15)	0.97 ($p=0.32$)
OR (95% CI)			1.23 (0.82 to 1.86)			
	Clean/contaminated or contaminated					
Vascular surgery (*n*=5502)						
SSI cases (*n*)	453 (5345)		15 (37)	13 (36)	10 (84)	48.01 ($p<0.01$)
OR (95% CI)	1.0 [Ref]		7.36 (3.79 to 14.29)	6.10 (3.07 to 12.13)		
All surgery types (*n*=113,068)						Interaction: 57.51 ($p<0.01$)

TABLE 23 Number of SSIs in categories of ASA class, with univariable OR estimates, by surgery category

Category of surgical procedure	Categories of ASA class					Missing	Main effect χ^2 (*p*-value)
	1	2	3	4	5		
Abdominal hysterectomy (*n* = 9119)							
SSI cases (*n*)	91 (4327)	100 (2501)	30 (485)	4 (26)	0 (3)	46 (1777)	41.09 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	1.94 (1.45 to 2.59)	3.07 (2.01 to 4.69)	8.46 (2.86 to 25.1)			
Bile duct, liver, pancreatic surgery (*n* = 188)							
SSI cases (*n*) (classes 1–2)	12 (87)		4 (42)	1 (8)		4 (51)	0.49 ($p=0.78$)
OR (95% CI) (classes 1–2)	1.0 [Ref]		0.66 (0.20 to 2.18)	0.89 (0.10 to 7.92)			
Cholecystectomy (*n* = 117)							
SSI cases (*n*) (classes 1–2)	2 (49)		2 (20)	1 (9)	0 (2)	0 (37)	1.15 ($p=0.56$)
OR (95% CI) (classes 1–2)	1.0 [Ref]		2.61 (0.34 to 20.0)	2.94 (0.24 to 36.3)			
CABG (*n* = 15,384)							
SSI cases (*n*) (classes 1–2)	8 (509)		481 (11,382)	73 (907)	14 (81)	169 (2505)	55.59 ($p<0.00$)
OR (95% CI) (classes 1–2)	1.0 [Ref]		2.76 (1.37 to 5.59)	5.48 (2.62 to 11.5)	13.1 (5.29 to 32.5)		
Gastric surgery (*n* = 221)							
SSI cases (*n*) (classes 1–2)	10 (90)		7 (60)	6 (21)	1 (1)	8 (49)	3.90 ($p=0.14$)
OR (95% CI) (classes 1–2)	1.0 [Ref]		1.06 (0.38 to 2.95)	3.20 (1.01 to 10.1)			
Hip replacement (*n* = 43,226)							
SSI cases (*n*) (classes 4–5)	104 (6514)	595 (18,580)	481(9412)	92 (1309)		254 (7411)	193.03 ($p<0.00$)
OR (95% CI) (classes 4–5)	1.0 [Ref]	2.04 (1.65 to 2.52)	3.32 (2.68 to 4.11)	4.66 (3.50 to 6.21)			
Knee replacement (*n* = 22,585)							
SSI cases (*n*) (classes 4–5)	53 (2838)	233 (11,275)	105 (3901)	8 (160)		77 (4411)	10.89 ($p=0.01$)
OR (95% CI) (classes 4–5)	1.0 [Ref]	1.11 (0.82 to 1.50)	1.45 (1.04 to 2.03)	2.7 7 (1.29 to 5.92)			

continued

TABLE 23 Number of SSIs in categories of ASA class, with univariable OR estimates, by surgery category *(continued)*

Category of surgical procedure	Categories of ASA class					Missing	Main effect χ^2 (*p*-value)
	1	2	3	4	5		
Large bowel surgery (*n*=9514)							
SSI cases (*n*) (classes 4–5)	70 (1239)	314 (3828)	268 (2240)	101 (489)		163 (1673)	101.00 ($p<0.01$)
OR (95% CI) (classes 4–5)	1.0 [Ref]	1.49 (1.14 to 1.95)	2.27 (1.73 to 2.98)	4.35 (3.14 to 6.02)			
Limb amputation (*n*=1528)							
SSI cases (*n*) (classes 4–5)	8 (93)	43 (288)	114 (619)	27 (205)		48 (323)	8.54 ($p=0.04$)
OR (95% CI) (classes 4–5)	1.0 [Ref]	1.86 (0.84 to 4.13)	2.40 (1.13 to 5.09)	1.61 (0.70 to 3.70)			
Open reduction of fractures (*n*=4593)							
SSI cases (*n*)	33 (1154)	63 (1284)	71 (1085)	15 (232)	5 (17)	43 (821)	29.62 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	1.75 (1.14 to 2.69)	2.38 (1.56 to 3.63)	2.35 (1.25 to 4.40)	14.2 (4.72 to 42.5)		
Small bowel surgery (*n*=1091)							
SSI cases (*n*) (classes 4–5)	5 (149)	30 (308)	30 (242)	13 (109)		28 (283)	11.38 ($p<0.01$)
OR (95% CI) (classes 4–5)	1.0 [Ref]	3.11 (1.18 to 8.18)	4.08 (1.54 to 10.8)	3.90 (1.35 to 11.29)			
Vascular surgery (*n*=5502)							
SSI cases (*n*) (classes 4–5)	13 (214)	86 (1302)	235 (2295)	86 (733)		71 (958)	22.43 ($p<0.01$)
OR (95% CI) (classes 4–5)	1.0 [Ref]	1.09 (0.60 to 2.00)	1.76 (0.99 to 3.14)	2.06 (1.12 to 3.76)			
All surgery types (*n*=113,068)							Interaction: 64.23 ($p<0.01$)

DOI: 10.3310/hta15300

TABLE 24 Number of SSIs in categories of age, with univariable OR estimates, by surgery category

Surgical procedure	Categories of age						Missing	Main effect χ^2 (p-value)
Abdominal hysterectomy (n=9119)	**≤34 years**	**35–49 years**	**50–59 years**	**60–69 years**	**70–79 years**	**≥80 years**		
SSI cases (n)	22 (741)	107 (4913)	62 (1870)	37 (830)	30 (488)	10 (160)	3 (117)	35.77 (p=0.00)
OR (95% CI)	1.0 [Ref]	0.73 (0.46 to 1.16)	1.12 (0.68 to 1.84)	1.52 (0.89 to 2.61)	2.14 (1.22 to 3.76)	2.18 (1.01 to 4.70)		
Bile duct, liver, pancreatic surgery (n=188)								
SSI cases (n)	2 (13)	3 (26)	2 (40)	7 (55)	6 (40)	1 (5)	0 (9)	6.50 (p=0.16)
OR (95% CI)	1.0 [Ref]	0.72 (0.10 to 4.93)	0.29 (0.04 to 2.30)	0.80 (0.15 to 4.40)	0.97 (0.17 to 5.52)	1.38 (0.10 to 19.60)		
Cholecystectomy (n=117)		**≤49 years**	**50–59 years**	**60–69 years**	**70–79 years**	**≥80 years**		
SSI cases (n)		1 (36)	0 (25)	1 (18)	3 (25)	0 (9)	0 (4)	5.79 (p=0.06)
OR (95% CI)		1.0 [Ref]	0.0	2.06 (0.12 to 35.00)	4.77 (0.47 to 48.80)	0.0		
CABG (n=15,384)		**≤49 years**	**50-59 years**	**60–69 years**	**70–79 years**	**≥80 years**		
SSI cases (n)		18 (980)	130 (3386)	278 (5783)	266 (4436)	40 (547)	13 (252)	51.14 (p<0.01)
OR (95% CI)		1.0 [Ref]	2.13 (1.30 to 3.51)	2.70 (1.67 to 4.37)	3.41 (2.10 to 5.52)	4.22 (2.39 to 7.43)		
Gastric surgery (n=221)		**≤49 years**	**50–59 years**	**60–69 years**	**70–79 years**	**≥80 years**		
SSI cases (n)		2 (27)	4 (32)	9 (61)	8 (56)	4 (35)	5 (10)	0.76 (p=0.68)
OR (95% CI)		1.0 [Ref]	1.79 (0.30 to 10.60)	2.16 (0.43 to 10.80)	2.08 (0.41 to 10.60)	1.61 (0.27 to 9.54)		
Hip replacement (n=43,226)		**≤49 years**	**50–59 years**	**60–69 years**	**70–79 years**	**≥80 years**		
SSI cases (n)		27 (1850)	95 (4461)	245 (9947)	516 (13,748)	588 (12,104)	55 (1116)	154.71 (p<0.01)
OR (95% CI)		1.0 [Ref]	1.47 (0.95 to 2.26)	1.71 (1.14 to 2.55)	2.63 (1.78 to 3.89)	3.45 (2.34 to 5.09)		

continued

TABLE 24 Number of SSIs in categories of age, with univariable OR estimates, by surgery category *(continued)*

Surgical procedure	Categories of age						Missing	Main effect χ^2 (*p*-value)
Knee replacement (*n*=22,585)		**≤49 years**	**50–59 years**	**60–69 years**	**70–79 years**	**≥80 years**		
SSI cases (*n*)		9 (437)	31 (2140)	130 (6609)	185 (9502)	106 (3466)	15 (431)	20.20 ($p<0.01$)
OR (95% CI)		1.0 [Ref]	0.70 (0.33 to 1.48)	0.95 (0.48 to 1.89)	0.94 (0.48 to 1.86)	1.50 (0.75 to 2.98)		
Large bowel surgery (*n*=9514)	**≤34 years**	**35–49 years**	**50–59 years**	**60–69 years**	**70–79 years**	**≥80 years**		
SSI cases (*n*)	31 (378)	69 (806)	122 (1272)	211 (2216)	331 (2944)	127 (1622)	25 (231)	16.87 ($p=0.00$)
OR (95% CI)	1.0 [Ref]	1.05 (0.67 to 1.63)	1.19 (0.79 to 1.79)	1.18 (0.79 to 1.75)	1.42 (0.97 to 2.08)	0.95 (0.63 to 1.43)		
Limb amputation (*n*=1528)	**≤34 years**	**35–59 years**		**60–69 years**	**70–79 years**	**≥80 years**		
SSI cases (*n*)	3 (45)	40 (262)		42 (340)	119 (732)		36 (149)	5.81 ($p=0.12$)
OR (95% CI)	1.0 [Ref]	2.52 (0.75 to 8.53)		1.97 (0.59 to 6.65)	2.72 (0.83 to 8.91)			
Open reduction of fractures (*n*=4593)								
SSI cases (*n*)	17 (641)	23 (527)	14 (405)	15 (462)	47 (828)	109 (1637)	5 (93)	24.43 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	1.68 (0.89–3.17)	1.31 (0.64–2.70)	1.23 (0.61–2.49)	2.21 (1.26–3.88)	2.62 (1.56–4.40)		
Small bowel surgery (*n*=1091)								
SSI cases (*n*)	8 (109)	23 (200)	22 (155)	20 (216)	17 (207)	12 (149)	4 (55)	5.68 ($p=0.34$)
OR (95% CI)	1.0 [Ref]	1.64 (0.71–3.80)	2.09 (0.89–4.88)	1.29 (0.55–3.03)	1.13 (0.47–2.71)	1.11 (0.44–2.81)		
Vascular surgery (*n*=5502)			**≤59 years**	**60–69 years**	**70–79 years**	**≥80 years**		
SSI cases (*n*)			67 (715)	110 (1378)	193 (1975)	99 (806)	22 (137)	7.74 ($p=0.05$)
OR (95% CI)			1.0 [Ref]	0.85 (0.62 to 1.69)	1.04 (0.78 to 1.39)	1.31 (0.95 to 1.82)		
All surgery types (*n*=113,068)								Interaction: 136.25 ($p<0.01$)

TABLE 25 Number of SSIs in males and females, with univariable OR estimates for females, by surgery category

	Gender			
Category of surgical procedure	**Male**	**Female**	**Missing**	**Main effect χ^2 (*p*-value)**
Abdominal hysterectomy (*n* = 9119)				
SSI cases (*n*)		271 (9119)		
OR (95% CI)				
Bile duct, liver, pancreatic surgery (*n* = 188)				
SSI cases (*n*)	9 (101)	12 (86)	0 (1)	1.18 ($p = 0.28$)
OR (95% CI)	1.0 [Ref]	1.66 (0.66 to 4.15)		
Cholecystectomy (*n* = 117)				
SSI cases (*n*)	4 (42)	1 (75)		4.27 ($p = 0.04$)
OR (95% CI)	1.0 [Ref]	0.13 (0.01 to 1.19)		
CABG (*n* = 15,384)				
SSI cases (*n*)	554 (12,292)	190 (3050)	1 (42)	14.79 ($p < 0.00$)
OR (95% CI)	1.0 [Ref]	1.41 (1.19 to 1.67)		
Gastric surgery (*n* = 221)				
SSI cases (*n*)	19 (126)	13 (94)	0 (1)	0.07 ($p = 0.79$)
OR (95% CI)	1.0 [Ref]	0.90 (0.42 to 1.94)		
Hip replacement (*n* = 43,226)				
SSI cases (*n*)	492 (14,587)	1030 (28,438)	4 (201)	1.77 ($p = 0.18$)
OR (95% CI)	1.0 [Ref]	1.08 (0.97 to 1.20)		
Knee replacement (*n* = 22,585)				
SSI cases (*n*)	229 (9277)	246 (13,212)	1 (96)	9.57 ($p < 0.00$)
OR (95% CI)	1.0 [Ref]	0.75 (0.62 to 0.90)		
Large bowel surgery (*n* = 9514)				
SSI cases (*n*)	489 (4821)	423 (4604)	4 (44)	2.46 ($p = 0.12$)
OR (95% CI)	1.0 [Ref]	0.90 (0.78 to 1.03)		
Limb amputation (*n* = 1528)				
SSI cases (*n*)	156 (984)	83 (533)	1 (11)	0.02 ($p = 0.89$)
OR (95% CI)	1.0 [Ref]	0.98 (0.73 to 1.31)		
Open reduction of fractures (*n* = 4593)				
SSI cases (*n*)	77 (1648)	152 (2922)	1 (23)	0.63 ($p = 0.43$)
OR (95% CI)	1.0 [Ref]	1.12 (0.85 to 1.48)		
Small bowel surgery (*n* = 1091)				
SSI cases (*n*)	51 (581)	55 (502)	0 (8)	1.44 ($p = 0.23$)
OR (95% CI)	1.0 [Ref]	1.28 (0.86 to 1.91)		
Vascular surgery (*n* = 5502)				
SSI cases (*n*)	334 (3878)	156 (1602)	1 (22)	1.74 ($p = 0.19$)
OR (95% CI)	1.0 [Ref]	1.14 (0.94 to 1.40)		
All surgery types (*n* = 113,068)				Interaction: 36.41 ($p < 0.00$)

(*Appendix 5* contains tables showing the results of univariable analyses for other risk factors.) OR estimates are tabulated for different categories of each risk factor, by category of surgical procedure. Tests of the statistical significance are reported for varying category within each risk factor, and for the interaction of the categorised risk factor with category of surgical procedure. These tables demonstrate several important points:

1. For the NNIS index and its components, there are very strong interactions between the index and category of surgical procedure.
2. This is also true for most risk factors which are not included in the index, e.g. age and gender.
3. The increase in odds of an SSI conferred by each factor, estimated by the OR, varies considerably for different risk factors (hence, the interaction of risk factor and category of surgical procedure).
4. Some risk factors are not appropriate for some categories of surgical procedure.

Conclusion

The univariable analyses demonstrate differences in risk factor effects by category of surgical procedure. Importantly, statistically significant effect modification (quantified by the interaction of risk factor and category of surgical procedure) by category of surgical procedure is observed for nearly every risk factor. Therefore, it is justified to focus on developing surgery-specific risk models rather than a global model.

The need to include interaction terms in a global model, make such a model difficult to interpret and to apply. Surgery-specific models, although more time-consuming to develop and to apply, will give the most robust and interpretable picture of SSI risk.

Methods for multivariable and multilevel risk modelling

Introduction

Based on the conclusions from the univariable analyses, we undertook to build 'best-fitting' multivariable logistic models for SSIs for each category of surgical procedure for which the numbers of observations were sufficient (*Table 26*).

TABLE 26 Categories of surgical procedure used and omitted from multivariable risk modelling analyses

Category as recorded in NINSS	Used/omitted	*n*
Abdominal hysterectomy	Used	9119
Cholecystectomy	Omitted	117
CABG	Used	15,384
Gastric surgery	Omitted	221
Small bowel surgery	Used	1091
Bile duct, liver, pancreatic surgery	Omitted	188
Hip replacement	Used	43,226
Knee replacement	Used	22,585
Large bowel surgery	Used	9514
Limb amputation	Used	1528
Open reduction of fracture of long bones	Used	4593
Vascular surgery	Used	5502
Total		113,068

Consultation on risk factors and data management

In developing the multivariable models, our selection of risk factors was guided by advice from people with experience of particular categories of surgical procedure, either through clinical expertise, ongoing work for the NINSS or analyses of other procedure specific databases, before employing any tests of statistical significance. We contacted clinicians and surgeons for their comments, as well as the NINSS data custodians who gave valuable accounts of their experience with the risk factors in NINSS.

Data management for multivariable modelling

Preparation of the data for multivariable and multilevel risk modelling raised data management issues not encountered during univariable analyses. These concerns applied to all surgery categories and are outlined below.

National Nosocomial Infections Surveillance risk index

The NNIS risk index is a score from 0 to 3, calculated from data for three risk factors, i.e. wound class, operation duration and ASA class. Each of these three variables is dichotomised and the values are then added together to give a score that ranges from 0 to 3.

A set of diagnostic analyses were undertaken to determine whether or not alternative combinations of the constituent variables of the NNIS risk index could give a better model for SSI risk than the index itself. The analyses were done for large bowel surgery, a category of surgery for which all three constituents of NNIS risk index are known to vary.

The findings from these analyses (see *Appendix 6*) supported the decision to model the constituent variables of the NNIS risk score in detail, rather than using the score itself.

Contribution to surveillance by hospitals

Hospitals varied with respect to their contribution of data to NINSS over time as the surveillance programme allowed them to undertake surveillance for 3-month periods without requiring them to collect the data continuously. Many hospitals started surveillance some time after the programme first commenced and contributed data to NINSS periodically. This means that care needed to be taken in multivariable modelling when interpreting the effects of the 'year' risk factor. Although we considered that it should be included as a controlling variable, we were wary of potential inconsistency in categories of surgery where the total number of hospitals contributing data was small (e.g. CABG data came from only 20 hospitals).

Method for developing surgery-specific multivariable risk models

Prior to undertaking model-building for each surgery category, a protocol was developed to ensure a consistent approach.

Risk factors measured continuously

As with the univariable analyses, continuous variables were coded as categories most appropriate to each surgery type.

Variables inappropriate to category of surgery, or variables requiring recoding

Risk factors were recoded (as for univariable analyses) if they had small SSI frequencies in certain categories, or were omitted from modelling altogether if they are not appropriate. Examples are gender (omitted from the model for abdominal hysterectomy) and ASA score (lowest two categories aggregated for the model for CABG).

Categories with missing data

Where a categorical risk factor was missing on a larger number of observations (with sufficient SSI cases), the missing group was experimentally modelled in a logistic model containing all 'eligible' risk factors. If inclusion of this missing category in the logistic model satisfied the following two conditions, it was allowed to remain in the model until the final stage:

1. Missing category was significantly different in SSI risk to the most prevalent category.
2. Inclusion of the missing category altered the ORs for other risk factors in the model to a substantial degree. This decision was a judgement made primarily on the standard errors of the ORs.

In practice, missing ASA score was the only category modelled.

Observations with missing continuous data were discarded from all surgery categories as they were relatively few in number.

Final models

Final models were constructed through assessment of the variables not already excluded (*Box 2*). All the variables which made a statistically significant change to the fit of the model (log likelihood) or which were important or potential confounders (namely age, gender and year) were included.

Steps in the modelling procedure

Step 1 involved developing 'best-fit' logistic models. These were the starting point for examining hospital-based differences using multilevel modelling. These models were fitted by maximum likelihood, and a robust standard error (at the cluster, i.e. hospital level) was calculated and used to estimate *p*-values and CIs.

Step 2 was the primary multilevel modelling analysis. The best-fit model for each surgery category was refitted as a two-level variance components (random intercepts) model in Stata

BOX 2 Potential risk factors considered in multivariable modelling

- Length of preoperative stay
- Duration of operation
- Wound contamination classification
- ASA class
- NNIS risk index
- Age at admission
- Gender (yes/no)
- Emergency surgery (yes/no)
- Surgery due to trauma (yes/no)
- Implant installed during procedure (yes/no)
- Multiple surgical procedures performed through the same incision (yes/no)
- Antibiotic prophylaxis administered (yes/no)
- Year of observation

v9.0. All patient-level risk factors remain in the model, but the constant (intercept) term modelled hospital-based differences in log-odds of SSI, given the covariates in the model, as a random factor. Variance components models were fitted using the function 'xtlogit' in Stata, which uses quadrature to evaluate the integral in the likelihood function. In addition, models were fitted in MLwiN (version 1.2), in order to form rank plots of between hospital differences in the log-odds of SSI, after adjustment for covariates. In MLwiN, estimation used a second-order penalised quasi-likelihood (PQL) iterative generalised least squares (IGLS) approximation, following initial estimates obtained using a first-order maximum marginal quasi-likelihood (MQL) IGLS approximation.

In the following results section (see *Risk modelling results by category of surgical procedure*), these random effects and 'best-fit' models are shown side by side to show the effect on estimates and CIs of including the hospital-level term. Likelihood ratio tests are shown for the improvement in fit when including the random intercept term. As the variance of the random intercept term is bounded by 0, the reference distribution is:

$$\frac{1}{2}\chi_1^2$$

For each model, rank plots of hospital-level residuals (and associated 95% CIs) about the overall intercept are also provided. These show, after adjustment for covariates in the model, between-hospital variation in the log-odds of SSI. After adjustment for covariates, the overall intercept (on the odds scale) is the constant term at the bottom of the corresponding table.

Step 3 investigated effect modification by hospital.

Additionally, using MLwiN, we explored each risk factor in turn to see if its effect varied randomly across hospitals. Specifically, starting from the variance components model (i.e. 'best-fit' model plus allowance for random, hospital-based variation), the effect estimate for each risk factor was allowed to vary randomly between hospitals. A risk factor was often represented by several variables in the model, e.g. multiple indicator variables to code risk factor categories. Owing to the limited sample sizes in some hospitals, we analysed each indicator variable separately in these 'effect modification' investigations. It was not possible to fit all the models under this investigation using second-order PQL approximation (IGLS). Both the number of operations and the number of hospitals contributing data for an operation type varied by operation type. Therefore, the power of these analyses to detect effect modification varied by operation. Most analyses had limited power to detect moderate levels of effect modification.

Risk modelling results by category of surgical procedure

Coronary artery bypass graft

The American Association of Anesthesiologists classes 1 and 2 were combined when developing models for CABG. Missing ASA classes were modelled to prevent the loss of approximately 3000 records contributed by a hospital, which did not routinely recode the score. Almost all CABG procedures were classified as clean; therefore, wound class was not entered in the models.

Odds ratios and CIs for risk factor estimates from fixed- and random-effects risk-adjusted models for CABG are shown in *Table 27*. With respect to components of the NNIS risk index, the odds of SSI varied by ASA class and operation duration. The odds of SSI after CABG increased with

TABLE 27 Fixed- and random-effects multivariable models for CABG

	Fixed-effects model (sandwich estimate of standard errors at the hospital level)		Random-effects model (variance components)	
Number of observations	14,969		Number of observations	14,969
Wald χ^2 (df 18)			Hospitals	20
Probability > χ^2				
Log likelihood	–2783.7		Log likelihood	–2763.5
Area under ROC curve	0.672		Likelihood ratio test for random intercepts	40.4, $p = 1.035e^{-10}$
Risk factor	**OR**	**95% CI**	**OR**	**95% CI**
Operation duration (minutes)				
≤120	1.000	[Ref]		
121–150	1.296	0.860 to 1.953	1.272	0.797 to 2.031
151–240	1.950	1.354 to 2.810	2.017	1.332 to 3.055
>240	3.166	1.976 to 5.071	3.451	2.246 to 5.301
Preoperative stay duration (no. of nights)				
0	1.000	[Ref]		
1	0.858	0.594 to 1.240	0.774	0.514 to 1.166
2–7	1.147	0.783 to 1.679	1.056	0.682 to 1.635
>7	1.635	1.117 to 2.393	1.523	0.964 to 2.405
Age (years)				
<50	1.000	[Ref]		
50–59	2.070	1.350 to 3.175	2.016	1.221 to 3.328
60–69	2.499	1.528 to 4.088	2.398	1.477 to 3.894
70–79	2.937	1.788 to 4.824	2.730	1.677 to 4.443
≥80	3.013	1.779 to 5.104	2.727	1.530 to 4.860
Gender				
Male	1.000	[Ref]		
Female	1.289	1.077 to 1.544	1.296	1.085 to 1.547
ASA score				
1 or 2	1.000	[Ref]		
3	2.082	1.024 to 4.233	2.021	0.991 to 4.120
4	3.665	1.610 to 8.341	3.702	1.742 to 7.866
5	8.958	1.411 to 56.88	7.960	3.152 to 0.104
<missing>	3.312	1.485 to 7.385	2.091	0.987 to 4.432
Year				
1997	1.000	[Ref]		
1998	0.995	0.644 to 1.537	0.993	0.607 to 1.622
1999	1.454	0.974 to 2.169	1.940	1.162 to 3.239
2000	1.501	1.144 to 1.969	2.005	1.214 to 3.311
2001	1.296	0.888 to 1.893	1.871	1.120 to 3.125
2002	1.865	1.436 to 2.422	2.493	1.555 to 3.997
<constant>	0.003	0.001 to 0.008	0.003	0.0008 to 0.0078

df, degrees of freedom.

increasing operation duration and ASA class (i.e. across categories that were modelled). Other risk factors in the model were age, gender, length of preoperative stay and calendar year.

Statistically significant variation in the (log)-odds of SSI was observed overall between hospitals, after adjustment for covariates. On assessment of the hospital-based residuals, however, it was apparent that just three or four hospitals out of the 20 contributing data were responsible for the statistical significance of this estimate, with the majority of hospitals having similar starting odds after adjustment for covariates (*Figure 14*). Some effect modification was modelled, but none of the variances or covariances estimated exceeded the size of their standard errors and consequently none was statistically significant.

Large bowel surgery

Clean and clean/contaminated wound classifications were combined when developing models for large bowel surgery. Wounds from patients with ASA scores of 5 were excluded.

Odds ratios and CIs for risk factor estimates from fixed- and random-effects risk-adjusted models for large bowel procedures are shown in *Table 28*. With respect to components of the NNIS risk index, the odds of SSI varied by all ASA class and operation duration, but not by wound contamination. This lack of a statistically significant effect of wound contamination may have arisen because categories were combined to fit the models (there were very few clean wounds), because of the omission of patients with ASA class 5 or because of associations between factors included in the model.

Other risk factors in the model were age, gender, length of preoperative stay and calendar year. Patients with no overnight preoperative stay had the highest odds of SSI (reference category), probably because these represent emergency patients (explaining why emergency operation was not included in the model). There was no clear effect of age across age categories, but women appeared to have a slightly reduced odds of SSI.

Statistically significant variation in the (log)-odds of SSI was observed overall between hospitals, after adjustment for covariates. However, from assessment of the hospital-based residuals, it was apparent that just four or five hospitals out of the 59 contributing data were responsible for the statistical significance of this estimate. The majority of hospitals had a similar 'risk' (i.e. log-odds) of an SSI after adjustment for covariates (*Figure 15*). Some effect modification was modelled,

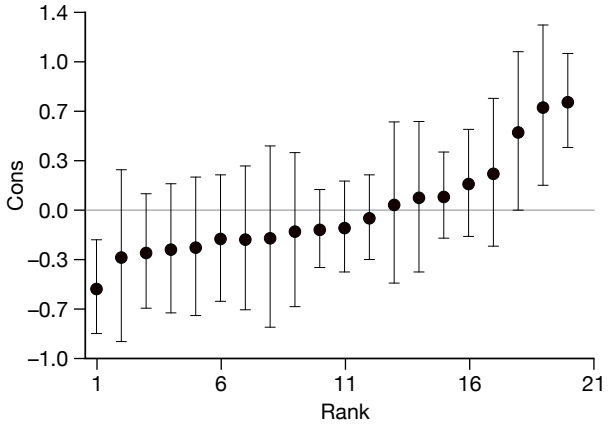


FIGURE 14 Multilevel model for CABG: variation in estimated log-odds by hospital. Rank plot of hospital level residuals (±2 standard errors) on the log-odds scale. After adjusting for the variables shown in the corresponding table, the points are the estimated difference between the log-odds of SSI in each hospital and the overall log-odds of SSI shown as the (log)-constant term in *Table 27*.

TABLE 28 Fixed- and random-effects multivariable models for large bowel surgery

	Fixed-effects model (sandwich estimate of standard errors at the hospital level)		Random-effects model (variance components)	
Number of observations	7297		Number of observations	7297
Wald χ^2 (df 20)	173.3		Hospitals	59
Probability $>\chi^2$	0.0001			
Log likelihood	–2229.0		Log likelihood	–2208.8
Area under ROC curve	0.663		Likelihood ratio test for random intercepts	40.4, $p = 1.035e^{-10}$
Risk factor	**OR**	**95% CI**	**OR**	**95% CI**
Operation duration (minutes)				
≤120	1.000	[Ref]		
121–150	1.350	1.000 to 1.822	1.428	1.140 to 1.789
151–240	1.605	1.272 to 2.025	1.778	1.464 to 2.160
>240	2.035	1.447 to 2.863	2.455	1.772 to 3.403
Preoperative stay duration (no. of nights)				
0	1.000	[Ref]		
1	0.633	0.464 to 0.864	0.618	0.471 to 0.812
2–7	0.656	0.503 to 0.854	0.661	0.496 to 0.882
>7	0.967	0.692 to 1.352	0.957	0.691 to 1.325
Age (years)				
≤34	1.000	[Ref]		
35–49	1.250	0.759 to 2.058	1.223	0.726 to 2.058
50–59	1.320	0.845 to 2.061	1.288	0.788 to 2.105
60–69	1.204	0.793 to 1.829	1.160	0.722 to 1.864
70–79	1.248	0.805 to 1.934	1.199	0.751 to 1.913
≥80	0.738	0.431 to 1.265	0.715	0.434 to 1.179
Gender				
Male	1.000	[Ref]		
Female	0.900	0.746 to 1.086	0.891	0.759 to 1.047
ASA score				
1	1.000	[Ref]		
2	1.446	1.110 to 1.883	1.459	1.105 to 1.926
3	2.305	1.610 to 3.298	2.301	1.716 to 3.087
4	4.262	2.782 to 6.528	4.271	2.975 to 6.130
Year				
1997	1.000	[Ref]		
1998	0.771	0.435 to 1.364	0.776	0.457 to 1.318
1999	0.886	0.487 to 1.611	0.913	0.518 to 1.608
2000	0.843	0.471 to 1.508	0.833	0.480 to 1.443
2001	0.676	0.409 to 1.120	0.691	0.398 to 1.202
2002	0.692	0.410 to 1.167	0.679	0.386 to 1.197
<constant>	0.080	0.041 to 0.155	0.073	0.034 to 0.155

df, degrees of freedom.

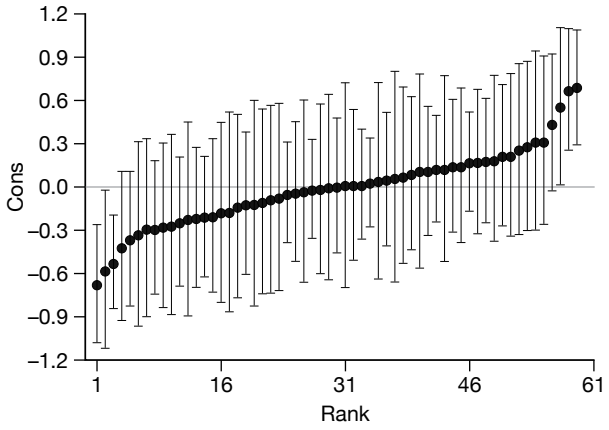


FIGURE 15 Multilevel model for large bowel surgery: variation in estimated log-odds by hospital. Rank plot of hospital-level residuals (± 2 standard errors) on the log-odds scale. After adjusting for the variables shown in the corresponding table, the points are the estimated difference between the log-odds of SSI in each hospital, and the overall log-odds of SSI shown as the (log)-constant term in *Table 28*.

but none of the estimated variances or covariances exceeded the size of its standard error and consequently none was statistically significant.

Abdominal hysterectomy

Clean and clean/contaminated wound classifications were combined when developing models for abdominal hysterectomy (almost all wounds were classified as clean/contaminated). Wounds from patients with ASA scores of 5 were excluded.

Odds ratios and CIs for risk factor estimates from fixed- and random-effects risk-adjusted models for abdominal hysterectomies are shown in *Table 29*. With respect to components of the NNIS risk index, the odds of SSI increased with increasing ASA class and operation duration. Wound contamination was not included in the model, presumably because this was essentially constant.

Other risk factors in the model were length of preoperative stay, age and calendar year. The effect of preoperative stay was unclear, probably because almost all patients had no or only one night preoperative stay. The youngest patients (the reference category) had the highest odds of SSI (apart from the oldest category), perhaps because these represent a selected group not adequately characterised by other risk factors available for analysis; for patients aged ≥ 35 years, the odds of SSI appeared to increase steadily with increasing age.

Statistically significant variation in the log-odds of SSI was observed overall between hospitals, after adjustment for covariates. On assessment of the hospital-based residuals, seven or eight of the 73 hospitals contributing data were largely responsible for the statistical significance of this estimate (*Figure 16*). In the multilevel model, there was no effect modification.

TABLE 29 Fixed- and random-effects multivariable models for abdominal hysterectomy

	Fixed-effects model		Random-effects model (variance components)	
Number of observations	7154		Number of observations	7154
Wald χ^2 (df 19)	113.5		Hospitals	73
Probability > χ^2	0.0001			
Log likelihood	–934.811		Log likelihood	–917.4
Area under ROC curve	0.681		Likelihood ratio test for random intercepts	34.82, $p = 1.81e^{-9}$
Risk factor	**OR**	**95% CI**	**OR**	**95% CI**
Operation duration (minutes)				
≤ 44	1.000	[Ref]		
45–59	1.220	0.825 to 1.805	1.254	0.778 to 2.019
60–89	1.204	0.788 to 1.839	1.254	0.792 to 1.985
90–119	1.609	0.964 to 2.685	1.843	1.107 to 3.069
> 120	1.684	0.958 to 2.960	2.291	1.284 to 4.087
Preoperative stay duration (no. of nights)				
0	1.000	[Ref]		
1	1.000	0.640 to 1.561	0.998	0.698 to 1.426
2–7	0.841	0.360 to 1.962	1.010	0.517 to 1.973
> 7	1.654	0.655 to 4.173	1.684	0.617 to 4.595
Age (years)				
≤ 34	1.000	[Ref]		
35–49	0.578	0.365 to 0.915	0.635	0.382 to 1.055
50–59	0.895	0.580 to 1.380	1.005	0.585 to 1.728
60–69	0.808	0.448 to 1.457	0.919	0.491 to 1.717
70–79	1.160	0.645 to 2.086	1.210	0.632 to 2.317
≥ 80	1.073	0.486 to 2.369	1.216	0.493 to 2.999
ASA score				
1	1.000	[Ref]		
2	1.748	1.330 to 2.297	1.881	1.366 to 2.589
3	2.483	1.539 to 4.005	2.763	1.683 to 4.538
4	7.922	2.795 to 22.456	9.289	2.827 to 30.524
Year				
1997	1.000	[Ref]		
1998	2.050	0.620 to 6.778	2.408	0.624 to 9.293
1999	5.082	1.359 to 19.005	5.263	1.414 to 19.592
2000	3.177	0.875 to 11.533	3.388	0.895 to 12.821
2001	3.319	0.942 to 11.696	3.202	0.847 to 12.109
2002	2.286	0.653 to 8.005	2.837	0.724 to 11.108
<constant>	0.008	0.002 to 0.029	0.005	0.001 to 0.020

df, degrees of freedom.

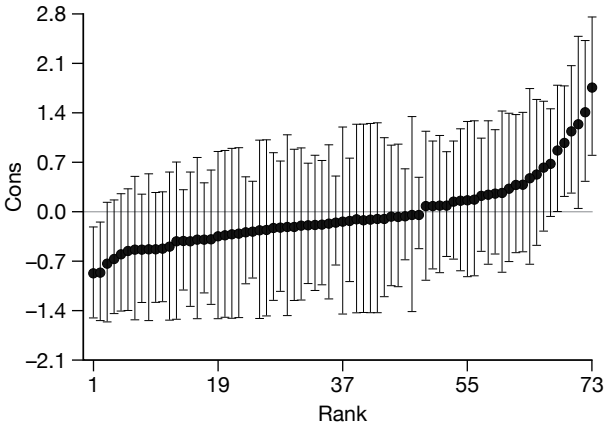


FIGURE 16 Multilevel model for abdominal hysterectomy: variation in estimated log-odds by hospital. Rank plot of hospital-level residuals (±2 standard errors) on the log-odds scale. After adjusting for the variables shown in the corresponding table, the points are the estimated difference between the log-odds of SSI in each hospital, and the overall log-odds of SSI shown as the (log)-constant term in *Table 29*.

Hip replacement

Clean and clean/contaminated wound classifications were combined when developing models for hip replacement. Almost all operations were classified as clean. A small number of operations were classified as contaminated or dirty. Wounds from patients with ASA scores of 5 were excluded.

Odds ratios and CIs for risk factor estimates from fixed and random effects risk-adjusted models for hip replacement are shown in *Table 30*. With respect to components of the NNIS risk index, the odds of SSI varied by operation duration, ASA class and wound class. The odds of SSI clearly increased with increasing ASA class. However, only operations classed as dirty had significantly increased odds of SSI. The effect of operation duration was not consistent across categories, possibly because the operations with the shortest duration (< 60 minutes; not uncommon for a hip replacement) perhaps represent a selected group not adequately characterised by other risk factors available for analysis.

Other risk factors in the model were length of preoperative stay, age, gender and calendar year. The odds of SSI increased with increasing age and longer durations of preoperative stay but did not vary by gender. Wounds from patients with ASA scores of 5 were excluded.

Statistically significant variation in the log-odds of SSI was observed overall between hospitals, after adjustment for covariates. About 15 hospitals out of the 127 hospitals contributing data were responsible for the statistical significance of this estimate (*Figure 17*). In the multilevel model, there was no effect modification.

TABLE 30 Fixed- and random-effects multivariable models for hip replacement

	Fixed-effects model (sandwich estimate of standard errors at the hospital level)		Random-effects model (variance components)	
Number of observations	30,481		Number of observations	30,481
Wald χ^2 (df 20)	328.8		Hospitals	127
Probability > χ^2	0.0001			
Log likelihood	–4559.0		Log likelihood	–4506.8
Area under ROC curve	0.640		Likelihood ratio test for random intercepts	104.4, $p = 8.3e^{-25}$
Risk factor	**OR**	**95% CI**	**OR**	**95% CI**
Operation duration (minutes)				
≤ 60	1.000	[Ref]		
61–90	0.867	0.733 to 1.025	0.861	0.730 to 1.017
91–120	0.948	0.775 to 1.159	0.924	0.767 to 1.113
> 120	1.216	0.962 to 1.537	1.195	0.983 to 1.453
Preoperative stay duration (no. of nights)				
0	1.000	[Ref]		
1	0.973	0.778 to 1.216	0.977	0.780 to 1.224
2–7	1.308	1.038 to 1.649	1.249	0.968 to 1.611
> 7	1.696	1.253 to 2.296	1.664	1.174 to 2.360
Age (years)				
≤ 49	1.000	[Ref]		
50–59	1.478	0.804 to 2.719	1.446	0.866 to 2.413
60–69	1.514	0.833 to 2.752	1.453	0.898 to 2.351
70–79	2.136	1.173 to 3.891	2.012	1.255 to 3.226
≥ 80	2.280	1.215 to 4.275	2.120	1.316 to 3.417
Gender				
Male	1.000	[Ref]		
Female	1.003	0.873 to 1.152	0.991	0.867 to 1.134
Wound classification				
Clean/contaminated	1.000	[Ref]		
Contaminated	1.068	0.299 to 3.816	1.463	0.627 to 3.417
Dirty	3.397	1.305 to 8.842	3.397	1.683 to 6.856
ASA score				
1	1.000	[Ref]		
2	1.730	1.306 to 2.294	1.628	1.281 to 2.068
3	2.452	1.801 to 3.338	2.252	1.749 to 2.900
4	3.303	2.299 to 4.747	3.148	2.255 to 4.393
Year				
1998	1.000	[Ref]		
1999	1.113	0.666 to 1.861	1.032	0.699 to 1.523
2000	0.915	0.585 to 1.430	0.861	0.585 to 1.267
2001	1.111	0.719 to 1.718	0.966	0.658 to 1.418
2002	0.914	0.585 to 1.427	0.800	0.546 to 1.172
<constant>	0.010	0.004 to 0.023	0.012	0.006 to 0.023

df, degrees of freedom.

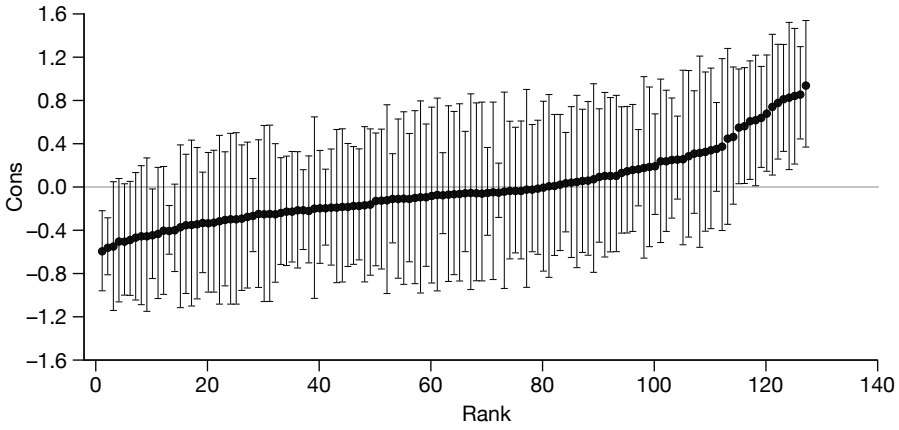


FIGURE 17 Multilevel model for hip replacement: variation in estimated log-odds by hospital. Rank plot of hospital-level residuals (±2 standard errors) on the log-odds scale. After adjusting for the variables shown in the corresponding table, the points are the estimated difference between the log-odds of SSI in each hospital, and the overall log-odds of SSI shown as the (log)-constant term in *Table 30*.

Knee replacement

Clean and clean/contaminated wound classifications were combined when developing models for knee replacement. Almost all operations were classified as clean. A small number of operations were classified as dirty but almost none as clean/contaminated or contaminated. Wounds from patients with ASA scores of 5 were excluded.

Odds ratios and CIs for risk factor estimates from fixed and random effects risk-adjusted models for hip replacement are shown in *Table 31*. With respect to components of the NNIS risk index, the odds of SSI clearly increased with increasing operation duration and ASA class. Wound class was not included in the final model.

Other risk factors in the model were length of preoperative stay, age, gender and calendar year. The odds of SSI increased with increasing age and longer durations of preoperative stay. Surprisingly, in view of the finding above for hip replacement, the odds of SSI were significantly lower for women than for men.

Statistically significant variation in the log-odds of SSI was observed overall between hospitals, after adjustment for covariates. About 9 of the 115 hospitals contributing data were responsible for the statistical significance of this estimate (*Figure 18*). In the multilevel model, there was no effect modification.

TABLE 31 Fixed- and random-effects multivariable models for knee replacement

	Fixed-effects model (sandwich estimate of standard errors at the hospital level)		Random-effects model (variance components)	
Number of observations	17,734		Number of observations	17,734
Wald χ^2 (df 19)	88.0		Hospitals	115
Probability > χ^2	0.0001			
Log likelihood	–1756.4		Log likelihood	–1731.3
Area under ROC curve	0.632		Likelihood ratio test for random intercepts	50.2, $p = 6.9e^{-13}$
Risk factor	**OR**	**95% CI**	**OR**	**95% CI**
Operation duration (minutes)				
≤60	1.000	[Ref]		
61–90	1.012	0.740 to 1.385	1.077	0.756 to 1.534
91–120	1.443	1.018 to 2.045	1.500	1.047 to 2.149
>120	1.536	1.015 to 2.324	1.650	1.107 to 2.459
Preoperative stay duration (no. of nights)				
0	1.000	[Ref]		
1	1.150	0.660 to 2.006	1.198	0.746 to 1.926
2–7	1.675	0.869 to 3.229	1.796	0.971 to 3.322
>7	3.345	1.525 to 7.339	3.586	1.602 to 8.028
Age (years)				
≤49	1.000	[Ref]		
50–59	0.687	0.333 to 1.417	0.659	0.290 to 1.493
60–69	0.924	0.475 to 1.799	0.886	0.423 to 1.854
70–79	0.960	0.492 to 1.875	0.904	0.435 to 1.879
≥80	1.521	0.748 to 3.091	1.426	0.674 to 3.015
Gender				
Male	1.000	[Ref]		
Female	0.677	0.548 to 0.838	0.673	0.546 to 0.830
ASA score				
1	1.000	[Ref]		
2	1.084	0.815 to 1.442	1.054	0.765 to 1.453
3	1.300	0.904 to 1.871	1.279	0.891 to 1.836
4	2.357	1.094 to 5.078	2.213	1.004 to 4.875
Year				
1997	1.000	[Ref]		
1998	0.715	0.311 to 1.648	0.815	0.385 to 1.725
1999	1.249	0.705 to 2.212	1.514	0.748 to 3.063
2000	0.844	0.512 to 1.390	1.165	0.580 to 2.340
2001	1.033	0.619 to 1.726	1.152	0.587 to 2.262
2002	0.692	0.419 to 1.143	0.730	0.372 to 1.434
<constant>	0.019	0.007 to 0.050	0.016	0.005 to 0.048

df, degrees of freedom.

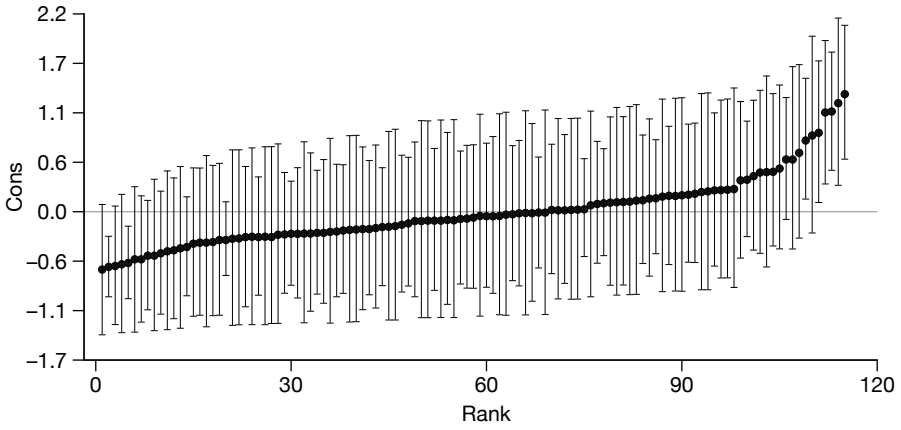


FIGURE 18 Multilevel model for knee replacement: variation in estimated log-odds by hospital. Rank plot of hospital-level residuals (±2 standard errors) on the log-odds scale. After adjusting for the variables shown in the corresponding table, the points are the estimated difference between the log-odds of SSI in each hospital, and the overall log-odds of SSI shown as the (log)-constant term in *Table 31*.

Limb amputation

Wounds from patients with ASA scores of 5 were excluded.

Odds ratios and CIs for risk factor estimates from fixed- and random-effects risk-adjusted models for hip replacement are shown in *Table 32*. With respect to components of the NNIS risk index, the odds of SSI appeared to increase with operation duration, wound contamination and ASA class. However, the small sample size meant that these effects were estimated imprecisely.

Other risk factors in the model were length of preoperative stay, age and calendar year. The effects of preoperative stay and age did not show consistent trends across categories.

There was some statistically significant variation in the log-odds of SSI between hospitals, after adjustment for covariates. However, 2 of the 37 hospitals contributing data were largely responsible for the statistical significance of this estimate (*Figure 19*). In the multilevel model, there was no effect modification.

TABLE 32 Fixed- and random-effects multivariable models for limb amputation

	Fixed-effects model (sandwich estimate of standard errors at the hospital level)		Random-effects model (variance components)	
Number of observations	1021		Number of observations	1021
Wald χ^2 (df 22)	163.9		Hospitals	37
Probability > χ^2	0.0001			
Log likelihood	–410.0		Log likelihood	–406.3
Area under ROC curve	0.644		Likelihood ratio test for random intercepts	7.4, $p = 0.0033$
Risk factor	**OR**	**95% CI**	**OR**	**95% CI**
Operation duration (minutes)				
≤ 30	1.000	[Ref]		
31–60	1.173	0.746 to 1.845	1.216	0.732 to 2.019
61–90	1.168	0.710 to 1.922	1.153	0.658 to 2.019
≥ 90	1.476	0.922 to 2.363	1.455	0.791 to 2.674
Preoperative stay duration (no. of nights)				
0	1.000	[Ref]		
1	0.649	0.329 to 1.279	0.681	0.317 to 1.465
2–7	1.133	0.579 to 2.216	1.125	0.559 to 2.264
> 7	1.197	0.724 to 1.979	1.212	0.602 to 2.442
Age (years)				
≤ 34	1.000	[Ref]		
35–49	1.820	0.587 to 5.647	1.575	0.379 to 6.544
50–59	1.905	0.563 to 6.448	1.719	0.428 to 6.904
60–69	1.171	0.381 to 3.601	0.981	0.251 to 3.838
70–79	1.801	0.546 to 5.938	1.491	0.389 to 5.712
≥ 80	1.313	0.402 to 4.289	1.045	0.262 to 4.158
Wound classification				
Clean	1.000	[Ref]		
Clean/ contaminated	1.198	0.758 to 1.892	1.164	0.711 to 1.905
Contaminated	1.235	0.812 to 1.877	1.419	0.786 to 2.564
Dirty	1.979	1.226 to 3.196	2.367	1.325 to 4.231
ASA score				
1	1.000	[Ref]		
2	1.531	0.573 to 4.088	1.643	0.633 to 4.260
3	1.977	0.720 to 5.428	2.345	0.880 to 6.250
4	1.156	0.378 to 3.539	1.411	0.477 to 4.175
Year				
1997	1.000	[Ref]		
1998	0.823	0.197 to 3.431	0.589	0.166 to 2.093
1999	0.723	0.139 to 3.767	0.616	0.161 to 2.354
2000	0.659	0.170 to 2.552	0.564	0.157 to 2.028
2001	0.948	0.249 to 3.617	0.726	0.203 to 2.589
2002	0.820	0.293 to 2.296	0.637	0.174 to 2.328
<constant>	0.061	0.014 to 0.260	0.064	0.011 to 0.392

df, degrees of freedom.

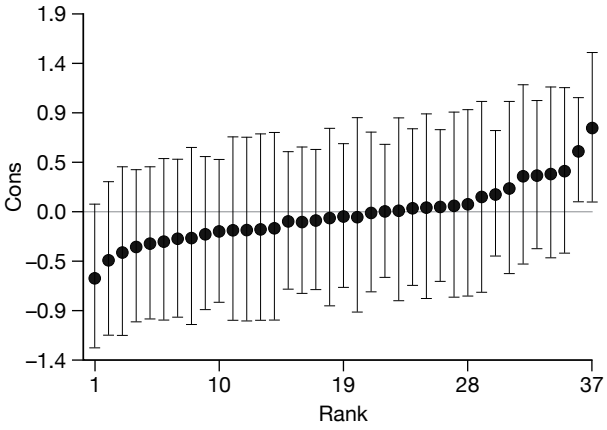


FIGURE 19 Multilevel model for limb amputation: variation in estimated log-odds by hospital. Rank plot of hospital-level residuals (±2 standard errors) on the log-odds scale. After adjusting for the variables shown in the corresponding table, the points are the estimated difference between the log-odds of SSI in each hospital, and the overall log-odds of SSI shown as the (log)-constant term in *Table 32*.

Open reduction of fracture

Wounds from patients with ASA scores of 5 were excluded.

Odds ratios and CIs for risk factor estimates from fixed- and random-effects risk-adjusted models for hip replacement are shown in *Table 33*. With respect to components of the NNIS risk index, the odds of SSI clearly increased with operation duration, but wound contamination and ASA class were not included in the final model.

The other risk factors in the model were length of preoperative stay, age, gender and calendar year. The odds of SSI increased with increasing duration of preoperative stay and was substantially lower in women than in men.

There was statistically significant variation in the log-odds of SSI between hospitals, after adjustment for covariates, but this was principally owing to only 3 of the 27 hospitals contributing data (*Figure 20*). There was no effect modification in the multilevel model.

TABLE 33 Fixed- and random-effects multivariable models for open reduction of fracture

	Fixed-effects model (sandwich estimate of standard errors at the hospital level)		Random-effects model (variance components)	
Number of observations	3602		Number of observations	3602
Wald χ^2 (df 13)	195.9		Hospitals	27
Probability $>\chi^2$	0.0001			
Log likelihood	–674.1		Log likelihood	–667.7
Area under ROC curve	0.663		Likelihood ratio test for random intercepts	12.8, $p=0.00017$
Risk factor	**OR**	**95% CI**	**OR**	**95% CI**
Operation duration (minutes)				
≤60	1.000	[Ref]		
61–90	1.351	1.021 to 1.787	1.377	0.905 to 2.095
91–120	1.878	1.184 to 2.979	2.114	1.329 to 3.363
>120	1.765	1.216 to 2.564	2.037	1.253 to 3.314
Age (years)				
≤34	1.000	[Ref]		
35–49	1.745	0.791 to 3.851	1.792	0.865 to 3.712
50–59	1.415	0.657 to 3.045	1.504	0.650 to 3.480
60–69	1.862	0.551 to 6.298	1.967	0.894 to 4.328
70–79	3.336	1.464 to 7.598	3.493	1.807 to 6.750
≥80	4.173	1.892 to 9.203	4.412	2.337 to 8.331
Gender				
Male	1.000	[Ref]		
Female	0.595	0.402 to 0.883	0.573	0.402 to 0.817
Year				
1997	1.000	[Ref]		
1998	1.139	0.467 to 2.781	1.232	0.386 to 3.933
1999	2.131	1.007 to 4.508	2.175	0.732 to 6.464
2000	2.890	1.176 to 7.104	2.718	0.987 to 7.483
2001	1.832	0.890 to 3.773	1.770	0.656 to 4.777
2002	1.448	0.655 to 3.202	1.424	0.530 to 3.825
<constant>	0.011	0.003 to 0.035	0.010	0.003 to 0.030

df, degrees of freedom.

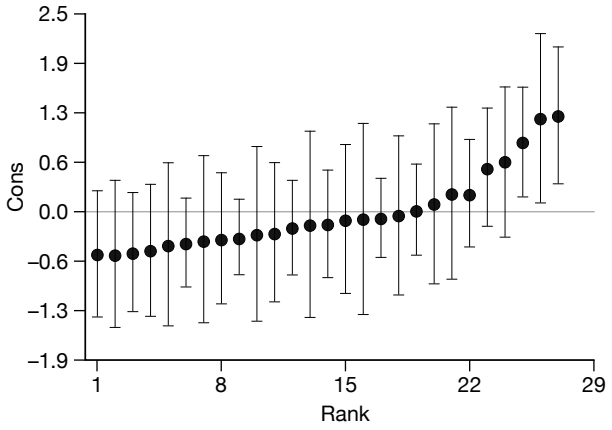


FIGURE 20 Multilevel model for open reduction of fracture: variation in estimated log-odds by hospital. Rank plot of hospital-level residuals (±2 standard errors) on the log-odds scale. After adjusting for the variables shown in the corresponding table, the points are the estimated difference between the log-odds of SSI in each hospital, and the overall log-odds of SSI shown as the (log)-constant term in *Table 33*.

Vascular surgery

Clean/contaminated and contaminated wound classifications were combined when developing models for vascular surgery. Almost all operations were classified as clean, with a few operations in the combined and dirty categories. Wounds from patients with ASA scores of 5 were excluded.

Odds ratios and CIs for risk factor estimates from fixed- and random-effects risk-adjusted models for vascular surgery are shown in *Table 34*. With respect to components of the NNIS risk index, the odds of SSI clearly increased with operation duration and wound contamination. The odds of SSI also increased across ASA class, but the estimates were imprecise.

Other risk factors in the model were length of preoperative stay, age, gender and calendar year. The odds of SSI increased with increasing duration of preoperative stay, but there was no clear effect of age or gender.

There was some statistically significant variation in the log-odds of SSI between hospitals, after adjustment for covariates. This was principally because of only 2 of the 44 hospitals contributed data (*Figure 21*). There was no effect modification in the multilevel model.

TABLE 34 Fixed- and random-effects multivariable models for vascular surgery

	Fixed-effects model (sandwich estimate of standard errors at the hospital level)		Random-effects model (variance components)	
Number of observations	4241		Number of observations	4241
Wald χ^2 (df 21)	246.7		Hospitals	44
Probability > χ^2	0.0001			
Log likelihood	–1188.7		Log likelihood	–1177.2
Area under ROC curve	0.691		Likelihood ratio test for random intercepts	23.0, $p = 8.1e^{-7}$
Risk factor	**OR**	**95% CI**	**OR**	**95% CI**
Operation duration (minutes)				
≤ 90	1.000	[Ref]		
91–120	1.306	0.883 to 1.933	1.302	0.802 to 2.114
121–180	1.469	1.083 to 1.993	1.445	0.939 to 2.224
181–240	2.301	1.647 to 3.214	2.231	1.434 to 3.469
> 240	3.966	2.652 to 5.932	3.982	2.572 to 6.167
Preoperative stay duration (no. of nights)				
0	1.000	[Ref]		
1	0.752	0.544 to 1.039	0.749	0.531 to 1.056
2–7	1.122	0.775 to 1.625	1.214	0.844 to 1.746
> 7	1.746	1.341 to 2.274	1.859	1.256 to 2.753
Age (years)				
≤ 59	1.000	[Ref]		
60–69	0.742	0.460 to 1.195	0.738	0.515 to 1.058
70–79	0.810	0.529 to 1.240	0.802	0.574 to 1.120
≥ 80	1.012	0.523 to 1.959	0.993	0.679 to 1.453
Gender				
Male	1.000	[Ref]		
Female	1.187	0.975 to 1.446	1.190	0.933 to 1.517
Wound classification				
Clean/contaminated	1.000	[Ref]		
Contaminated	6.200	2.662 to 14.442	6.042	2.579 to 14.156
Dirty	4.777	2.025 to 11.268	5.194	2.139 to 12.614
ASA score				
1	1.000	[Ref]		
2	1.206	0.471 to 3.092	1.256	0.633 to 2.491
3	1.605	0.678 to 3.801	1.645	0.843 to 3.210
4	1.812	0.841 to 3.902	1.877	0.929 to 3.792
Year				
1997	1.000	[Ref]		
1998	1.009	0.366 to 2.779	1.127	0.490 to 2.593
1999	1.048	0.474 to 2.318	1.254	0.552 to 2.848
2000	1.218	0.472 to 3.147	1.178	0.535 to 2.591
2001	0.994	0.371 to 2.665	0.984	0.439 to 2.208
2002	1.218	0.402 to 3.693	0.958	0.435 to 2.111
<constant>	0.034	0.008 to 0.136	0.029	0.010 to 0.087

df, degrees of freedom.

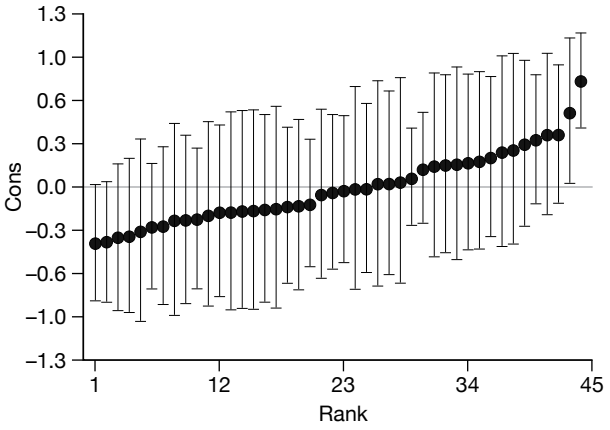


FIGURE 21 Multilevel model for vascular surgery: variation in estimated log-odds by hospital. Rank plot of hospital-level residuals (± 2 standard errors) on the log-odds scale. After adjusting for the variables shown in the corresponding table, the points are the estimated difference between the log-odds of SSI in each hospital, and the overall log-odds of SSI shown as the (log)-constant term in *Table 34*.

Small bowel surgery

Clean and clean/contaminated wound categories, and contaminated and dirty categories, were combined for models for small bowel surgery. Almost all operations were classified as clean or clean/contaminated, with a few operations in the combined and dirty categories. Wounds from patients with ASA scores of 5 were excluded.

Odds ratios and CIs for risk factor estimates from fixed- and random-effects risk-adjusted models for hip replacement are shown in *Table 35*. With respect to components of the NNIS risk index, the odds of SSI clearly increased with increasing ASA class and contaminated or dirty wound class. The odds of SSI was high for operations with the longest duration (> 240 minutes), but there was no consistent trend across categories.

Other risk factors in the model were length of preoperative stay, age, gender and calendar year. The odds of SSI appeared to increase with increasing duration of preoperative stay, but there were no clear effects of age or gender, possibly because of the small sample size.

There was some statistically significant variation in the log-odds of SSI between hospitals, after adjustment for covariates. However, this was principally because only 1 of the 19 hospitals contributed data, and this hospital appeared to have outlying odds (*Figure 22*). Effect modification could not be tested in the multilevel model because of the small sample size.

Summary of findings

In surgery-specific multivariable risk-adjusted models, associations between components of the NNIS risk index and the odds of SSI varied both quantitatively and qualitatively for different surgical procedures. This finding also applied to other risk factors that were investigated, i.e. age, gender and duration of preoperative stay. In the final random-effect models, statistically significant variation in the (log)-odds of SSI, after adjustment for covariates, was observed between hospitals for all surgery categories. There was no convincing evidence from multilevel models for effect modification of risk factors by hospital, although data to estimate these effects were sometimes limited.

Table 36 summarises the findings from the surgery-specific risk models to illustrate that the effects of risk factors vary across surgery categories. This conclusion applies to components of the NNIS index (although to a lesser extent), as well as to other factors considered in the analyses.

TABLE 35 Fixed- and random-effects multivariable models for small bowel surgery

	Fixed-effects model (sandwich estimate of standard errors at the hospital level)		Random-effects model (variance components)	
Number of observations	744		Number of observations	744
Wald χ^2 (df 17)			Hospitals	19
Probability > χ^2				
Log likelihood	–221.6		Log likelihood	–219.1
Area under ROC curve	0.684		Likelihood ratio test for random intercepts	5.0, $p = 0.013$
Risk factor	**OR**	**95% CI**	**OR**	**95% CI**
Operation duration (minutes)				
≤120	1.000	[Ref]		
121–150	0.921	0.261to 3.252	0.989	0.439 to 2.230
151–240	0.733	0.505 to 1.064	0.747	0.380 to 1.469
≥241	1.727	0.747 to 3.992	1.262	0.474 to 3.359
Preoperative stay duration (no. of nights)				
0	1.000	[Ref]		
1	1.138	0.618 to 2.096	1.049	0.469 to 2.346
2–7	1.441	0.563 to 3.686	1.379	0.567 to 3.353
>7	2.191	0.972 to 4.943	1.967	0.810 to 4.775
Age (years)				
≤34	1.000	[Ref]		
35–49	1.608	0.875 to 2.954	1.790	0.603 to 5.309
50–59	1.611	0.871 to 2.978	1.786	0.577 to 5.529
60–69	0.991	0.243 to 4.033	1.155	0.379 to 3.520
70–79	0.901	0.387 to 2.094	0.948	0.308 to 2.920
≤80	0.673	0.178 to 2.544	0.714	0.206 to 2.476
Gender				
Male	1.000	[Ref]		
Female	1.390	0.934 to 2.066	1.415	0.845 to 2.368
Wound classification				
Clean/contaminated	1.000	[Ref]		
Contaminated/dirty	1.523	0.787 to 2.947	1.520	0.883 to 2.618
ASA score				
1	1.000	[Ref]		
2	3.133	0.921 to 10.657	2.877	1.032 to 8.024
3	4.176	1.375 to 12.684	3.656	1.259 to 10.614
4	4.250	2.964 to 6.093	3.998	1.213 to 13.175
Year				
1997	1.000	[Ref]		
1998	0.359	0.156 to 0.830	0.294	0.054 to 1.615
1999	0.891	0.365 to 2.173	0.604	0.125 to 2.915
2000	1.283	0.612 to 2.690	0.692	0.151 to 3.159
2001	0.838	0.311 to 2.258	0.655	0.168 to 2.561
2002	0.805	0.266 to 2.443	0.528	0.129 to 2.161
<constant>	0.021	0.002 to 0.194	0.025	0.004 to 0.156

df, degrees of freedom.

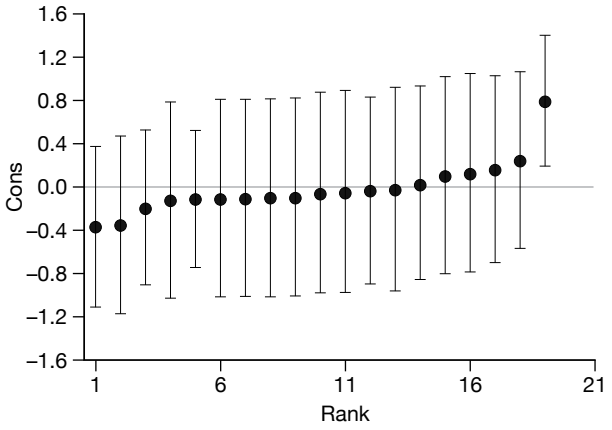


FIGURE 22 Multilevel model for small bowel surgery: variation in estimated log-odds by hospital. Rank plot of hospital-level residuals (±2 standard errors) on the log-odds scale. After adjusting for the variables shown in the corresponding table, the points are the estimated difference between the log-odds of SSI in each hospital, and the overall log-odds of SSI shown as the (log)-constant term in *Table 35*.

TABLE 36 Qualitative summary of the effects of risk factors from multivariable models across different operations

Operation	Operation duration	Wound class	ASA class	Preoperative stay	Age	Gender
CABG	⇑	n/a	⇑	⇑	⇑	⇑
Large bowel surgery	⇑	n/a	⇑	⇑	⇔	↓
Abdominal hysterectomy	⇑	n/a	⇑	⇔	↑	n/a
Limb amputation	↑	↑	↑	⇔	⇔	n/a
Open reduction of fracture	⇑	n/a	n/a	n/a	⇑	⇓
Hip prosthesis	⇔	⇑	⇑	⇑	⇑	⇔
Knee prosthesis	⇑	n/a	⇑	⇑	⇑	⇓
Vascular surgery	⇑	⇑	↑	⇑	⇔	⇔
Small bowel surgery	↑	↑	⇑	↑	⇔	⇔

⇑, (↑) odds of SSI definitely (possibly) increases as risk factor increases or with female gender; ⇓, (↓) odds of SSI definitely (possibly) decreases as risk factor increases or with female gender; ⇔, risk factor included in the final model, but no trend observed in odds of SSI across categories of risk factor or with gender; n/a, risk factor not included in the final model for the surgery category, because it was not applicable (e.g. male gender for hysterectomy), or it did not improve the fit of the model or because the risk factor was constant for (almost) all operations and could not be modelled.

Of the NNIS components, operation duration appeared to be an important risk factor for all operations except for hip prosthesis. The result for hip prosthesis cannot be attributed to poor precision; this surgery category had the largest sample size and had an intermediate risk of SSI. A further analysis of risk factors has been reported elsewhere.[101] Wound class was included least often, but this was because some wound classes were not applicable to some surgical procedures or were combined because of small numbers. ASA class appeared to be a consistent risk factor for all surgery categories, although not for open reduction of fractures, and its effect was uncertain for limb amputation and vascular surgery because of the small sample sizes available.

Age and gender were included in all the models. The odds of SSI clearly increased with age for four surgery categories (CABG, hip and knee prostheses and open reduction of fracture), but not for four other surgery categories (large and small bowel, limb amputation and vascular surgery). The results were most varied for gender. Women had lower odds of SSI for knee prosthesis and open reduction of fracture, higher odds of SSI for CABG and similar odds of SSI for small

and large bowel surgery, hip prosthesis and limb amputation. Preoperative duration of stay, an additional generic risk factor identified by the reviews, was associated with an increase in the risk of SSI for the four surgery categories with the largest number of data (hip and knee prosthesis, CABG and large bowel surgery).

Chapter 5

Discussion and conclusions

Summary of findings

The reviews of the literature (see *Chapter 2, Summary of findings*) concluded that there are potentially important procedure-specific and generic risk factors not included in existing indices for risk-adjusting SSI data. The distinction between procedure-specific and generic risk factors is not dichotomous; some risk factors are important for some but not all procedures, whereas some risk factors may apply to only one procedure. Potential additional risk factors are not always 'captured' by national or institution-wide surveillance systems.

The independent influences of additional risk factors have not been well researched. Analyses may not have taken account of the organisational hierarchy in data sets and risk factors achieving statistical significance are likely to have been selectively reported. Both of these issues would lead to spurious identification of additional risk factors. However, duration of preoperative stay in a hospital was consistently reported as an additional risk factor associated with increasing risk of SSI, but the magnitude of this risk and its independence from other risk factors, e.g. procedure and components of the NNIS risk index, could not be established from the literature. Our own risk-adjusted models (see *Chapter 4, Risk modelling results by category of surgical procedure*) also highlighted the importance of duration of preoperative stay as an independent risk factor.

The use of relatively simple risk adjustment methods for national surveillance programmes means that the associations between additional risk factors and NNIS risk factors have not been well studied by researchers. The literature suggested that the risk conferred by particular factors varies by surgical procedure, an observation supported by our own analyses to develop risk-adjusted models (see *Chapter 4, Results of univariable analyses of risk factors*). The important implication is that procedure-specific risk-adjusted models are needed; stratification of analyses of data for multiple procedures by surgery type does not achieve this.

The literature demonstrated substantial variation in SSI%. There are many sources of such variation other than chance and genuine differences in the risk of SSI. Our research has shown how varying definitions of SSI, even small ones, can lead to substantially different estimates of SSI% (see *Chapter 3, Agreement of alternative surgical site infections*). Public health and infection control practitioners in our research team highlighted that established SSI definitions include subjective elements and have been modified to facilitate their implementation. 'Standards' adopted by a surveillance programme (e.g. about a definition or methods of data collection) may be applied differently across institutions, generating variable SSI ascertainment and a health policy focus on 'hospital league tables' of SSI% may create an incentive to bias the collection of risk factors[102] or to use methods that detect fewer SSIs. The inclusion or not of PDS in a surveillance protocol and, if included, varying completeness of follow-up are other sources of variation given that a substantial proportion of SSIs appear to occur after discharge (see *Chapter 2, Risk factors for surgical site infections identified by postdischarge surveillance*).

We were unable to identify a preferred SSI definition (see *Chapter 3, Validation of surgical site infections definitions*) and noted that existing definitions have focused almost exclusively on

clinical and microbiological criteria. Although two established SSI definitions do not agree well (see *Chapter 3, Agreement of alternative surgical site infection definitions*), they predict likely outcomes of SSI to a similar and modest extent. The ASEPSIS wound scoring approach explicitly acknowledges the underlying continuum of infection. This is an important attribute of infection to bear in mind when researching which infections are important – to patients and health services, as well as to surgeons and microbiologists.

Developing risk-adjusted models showed the importance of fitting components of the NNIS risk index separately, as well as effect modification of these components by procedure (see *Chapter 4, Results of univariable analyses of risk factors* and *Chapter 4, Risk modelling results by category of surgical procedure*). Little effect modification of risk factors by hospital was observed, although we had limited power to test for such effects (see *Chapter 4, Risk modelling results by category of surgical procedure*). Without continuous surveillance of specified procedures, even data sets from national surveillance may be too small to quantify the importance of risk factors for procedures carried out less frequently (see *Chapter 4, Risk modelling results by category of surgical procedure*). There needs to be clarity about whether or not surveillance should be carried out at the level of an incision, a procedure (potentially requiring multiple incisions) or a patient; this hierarchy, including surgeon and hospital, should be respected in analyses.

Limitations

Systematic reviews

We are not confident that the reviews were as 'thorough' as is recommended for reviews of effectiveness because of the difficulties of specifying literature searches.[103] This may not have introduced bias; however, as it quickly became apparent that quality of literature would not justify formal meta-analysis, it has been suggested that when reviewing observational studies, very thorough searching may paradoxically introduce bias.[104] Although we aimed to identify systematically potential risk factors, we did not need to identify all literature that reported evidence about each potential risk factor. Also, we expected the most important literature about SSIs to be published in journals indexed by MEDLINE and EMBASE. In view of the suspected high risk of selective reporting, a more thorough search might have led to identification of many spurious risk factors.

The reviews are now considerably out of date. The importance of this limitation is unknown. However, following the above argument, it is likely to be serious only if there has been a major improvement in the methodological quality of relevant literature in recent years, or dramatic changes in surgical practice creating new risk factors or making ones we identified redundant. We think that the former is unlikely. The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) initiative is unlikely to have achieved dramatic improvements since its publication in 2008 and its recommendations are primarily about the reporting of observational research.[105,106] Surgical readers will be able to decide whether or not important recent risk factors have been missed.

Agreement between and validation of surgical site infection definitions

The main limitation of these analyses was the assumptions required when processing the available data to derive the definitions of interest. These assumptions were developed with advice from authors who had responsibility for and many years' experience of the data sets that were used.

Risk modelling

The main limitations of these analyses were again the consequence of the available data. For example, data were not collected for some potential risk factors or data were missing for other

potential risk factors where data capture was optional. The inability to model all levels of the data hierarchy may have led to the standard errors of estimates being underestimated. However, the main findings are not based primarily on statistical inferences.

Implications of findings

Surveillance systems that monitor SSI% and provide feedback to clinicians have been demonstrated to contribute to quality improvement and are acknowledged to be an important and effective component of local infection prevention and control programmes.[6] In this context, comparisons of SSI% statistics over time provide valuable feedback to surgical teams or specialties within institutions, providing that SSI surveillance and the methods to derive the statistics are constant during the period of surveillance. Local knowledge of circumstances can be used to interpret changes that are observed.

However, we believe that it is premature to use SSI% as a performance indicator to compare surgeons, hospitals or countries with a view to drawing statistical inferences about relative performance.[107] Without a means to interpret absolute rates, publication of SSI% comparing nations must be interpreted with caution because perceived differences in SSI% may be explained by variations in the way that infections are defined, the way data are collected, the availability of data on risk factors for SSIs and methods of risk adjustment and the risk factors considered. Judgements about the quality of medical care provided by hospitals should not be based on these statistics alone by agencies with responsibility for auditing performance. Adjustment for confounding by case-mix will always be incomplete.[104] In the context of data that are necessarily observational, the extent the resulting bias cannot be quantified. Incomplete confounding also contributes non-statistical uncertainty, causing CIs around estimates to be underestimated; this is most marked with large data sets.[27]

Attribution of risk factors as under the control of the institution or not is another important consideration for those who advocate making institutional comparisons. Presumably, the aim of such comparisons is to 'name and shame' those with high risk-adjusted rates and, preferably, to applaud those with low risk-adjusted rates and to learn from their institutional practices. In this context, risk-adjusted models should only adjust for factors that are not under the control of the institution, i.e. intrinsic risks that patients bring to the operations. Alternatively, risk adjustment could be carried out in two steps to try to explain variation in SSI% attributable to institutions or not. The inability to categorise two of the best-established risk factors for SSI (operative duration and wound class, and possibly others) in this way precludes this level of interpretation of observed SSI variation (see *Chapter 2, Summary of findings*).

Our research suggests that national surveillance programmes should include the following features.

- A clear definition of SSI that is practicable in all settings participating in surveillance without modification and standard methods of surveillance, e.g. with respect to training of staff carrying out surveillance and applying components of the definition.
- PDS (also using a standard method) to take into account decreasing lengths of stay over time and different discharge policies between hospitals, with a requirement that a target level of follow-up be achieved.
- Standard set of risk factors in the required data set.
- Application of a predefined risk adjustment model, which should be subject to periodic revision; at the time of any revision, statistics using both the current and revised model should be disseminated.

- Standards for data quality and a policy about exclusion of hospitals not meeting the standards from the statistics.

Research recommendations

Our research recommendations arise from limitations in the literature reviewed and data available for analysis.

The CDC definition is widely used by national surveillance programmes, but is vulnerable to variation in interpretation and is perceived by some as complex to apply. There are currently few data on the long-term impact of SSIs, particularly as many infections develop after discharge from hospital. Improvements to the definition of SSI may be possible to achieve a more reliable measure of significant adverse outcome.

We believe there is a need for high-quality research to develop an SSI definition that:

- has satisfactory performance as a psychometric instrument[100]
- can be applied in everyday clinical settings without compromising its performance and consistency as a measuring instrument
- can be applied to surveillance for SSIs after discharge from hospital within a specified minimum period
- is formulated to detect SSIs that are important to patients or health services.

The 1992 CDC definition and ASEPSIS have substantial overlap, but also differ with respect to their component items. Items covered by these definitions should provide a starting point, although it is likely that they will need to be supplemented by additional items. The reproducibility of wound assessments within and between observers needs to be investigated.

Our third point is critically important because, otherwise, national surveillance may merely be describing variations in compliance of local surveillance with a standard protocol. Proxy measures, e.g. aspects of data quality, may highlight hospitals that are struggling to comply with a surveillance protocol; however, the 'perverse incentive' created by dissemination of hospital-specific SSI% to under-record SSIs may give rise to more subtle deviations from protocol, i.e. 'gaming', and this may be justification to carry out qualitative research at a sample of hospitals to describe how surveillance is actually carried out.

Existing surveillance data sets often do not include data on potential risk factors of interest and more comprehensive data sets available for one hospital have limited applicability. Therefore, neither offers a definitive opportunity to carry out the high-quality primary research on risk factors that the reviews identified as being necessary. This is a 'chicken-and-egg' problem; one cannot specify a minimum data set for surveillance without high-quality research on relevant risk factors, but one cannot identify the key risk factors without large amounts of representative data. One way to resolve this impasse would to identify a shortlist of key risk factors for sentinel procedures by clinical consensus and then expand national surveillance to include those for which there is the strongest consensus. (Ideally, national surveillance would allow the required data set to vary to some degree by procedure.) Analyses of postulated risk factors would be carried out once sufficient data and events had accrued and decisions made whether or not to drop redundant ones or substitute new candidates.

Analyses of large observational data sets are at risk of a number of biases. These can be minimised by the following steps:

1. prespecifying quality criteria for inclusion of data, e.g. the proportion of missing or follow-up data allowed
2. prespecified methods for data management of missing data or follow-up
3. predefined exposure and outcomes of interest and analysis plan
4. methods of statistical analysis that respect the data hierarchy
5. full reporting of results for all prespecified comparisons.

Conclusions

The research literature does not allow a set of surgery-specific or generic risk factors to be defined. Research to identify risk factors for SSI needs to be carried out to higher methodological standards.

Surgical site infection definitions vary between surveillance programmes and, because they are complex and difficult to apply, potentially between hospitals within programmes. Definitions that are different, some in apparently only minor ways, do not have good agreement but have similar ability to predict outcomes influenced by SSI.

In surgery-specific multivariable risk-adjusted models, associations between components of the NNIS risk index and the odds of SSI varied both quantitatively and qualitatively for different surgical procedures; this finding also applied to other risk factors investigated. There was no evidence for effect modification of risk factors by hospital.

Our findings suggest that performance estimates (data quality and SSI%) for institutions and groupings within institutions should be disseminated locally to inform clinical governance and the management of infection control. The findings also indicate that performance estimates (SSI%) for institutions or countries should be regarded with caution. Judgements about the quality of medical care provided by hospitals should not be based on these statistics alone by agencies with responsibility for auditing performance. National surveillance systems should comply with a set of features designed to ensure their quality.

Acknowledgements

Contributions of authors

Carl Gibbons was employed as a research fellow on the project. He was a member of the project's steering group. He managed the data in both of the databases investigated, carried out most of the statistical analyses reported and, with the other authors, interpreted the findings. He wrote the first draft of the report.

Julie Bruce was a co-applicant on the grant awarded for the project and a member of the project's steering group. She had been the systematic reviewer on an earlier HTA systematic review on the measurement and monitoring of surgical adverse events. She was employed part-time as a research fellow and worked on the systematic reviews. She developed the search strategies, carried out initial filtering of the citations identified, appraised and extracted from the papers that were included in the reviews and drafted the reports of the systematic reviews.

James Carpenter was a co-applicant on the grant awarded for the project and a member of the project's steering group. He was employed part-time as the principal statistician with expertise in multilevel modelling. He devised the analysis plan to develop risk-adjusted models for SSI and supervised all analyses.

A Peter Wilson was a co-applicant on the grant awarded for the project and a member of the project's steering group. He is a consultant microbiologist and designed and implemented the SSI surveillance programme at UCLH. He had expert knowledge of the data from the programme, which were analysed to investigate agreement between SSI definitions and their validity.

Jennie Wilson was a co-applicant on the grant awarded for the project and a member of the project's steering group. During the project, she was a nurse consultant and programme leader for SSI surveillance at the Health Protection Agency. She had expert knowledge of the data from the NINSS programme which were analysed to develop risk-adjusted models for SSI.

Andrew Pearson was a co-applicant on the grant awarded for the project and a member of the project's steering group. He is a consultant in microbiology and epidemiology at the Health Protection Agency and led the implementation of NINSS SSI surveillance programme in England. He had expert knowledge of the data from the NINSS programme which were analysed to develop risk-adjusted models for SSI.

Donna Lamping (in memoriam) was a co-applicant on the grant awarded for the project and a member of the project's steering group. She was a professor of psychology with expertise on developing an evaluating the psychometric attributes of measures of health. She contributed to analysis plan for the analyses relating to agreement between SSI definitions and their validity and the development of risk-adjusted models for SSI and their interpretation.

Zygmunt H Krukowski was a co-applicant on the grant awarded for the project and a member of the project's steering group. He is a consultant general surgeon and had been a member of the research team for the earlier HTA systematic review on the measurement and monitoring of surgical adverse events. He contributed surgical expertise.

Barnaby C Reeves was the lead applicant on the grant awarded for the project and had overall responsibility for the project and chaired the project's steering group. He appraised the literature with Julie Bruce and worked closely with the other authors on the analyses relating to agreement between SSI definitions and their validity and the development of risk-adjusted models for SSI. He wrote the final draft of this report.

Publication

Wilson APR, Gibbons C, Reeves BC, Hodgson B, Liu M, Plummer D, *et al*. Surgical wound infection as a performance indicator: agreement of common definitions of wound infection in 4773 patients. *BMJ* 2004;**329**:720.

References

1. Plowman R, Graves N, Griffin M, Roberts JA, Swan AV, Cookson B, *et al. The socio-economic burden of hospital acquired infection*. London: Public Health Laboratory Service; 1999.
2. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Control* 1999;**27**:97–132.
3. Anonymous. National Nosocomial Infections Surveillance (NNIS) system report, data summary from January 1992-June 2001, issued August 2001. *Am J Infect Control* 2001;**29**:404–21.
4. Pratt RJ, Pellowe C, Loveday HP, Robinson N, Smith GW, Barrett S, *et al.* The epic project: developing national evidence-based guidelines for preventing healthcare associated infections. Phase I: guidelines for preventing hospital-acquired infections. London: Department of Health. *J Hosp Infect* 2001;**47**:S3–82.
5. Scottish Intercollegiate Guideline Network. *Guideline 104: antibiotic prophylaxis in surgery. A national clinical guideline*. Edinburgh: Scottish Intercollegiate Guideline Network; 2008.
6. Gaynes R, Richards C, Edwards J, Emori TG, Horan T, Alonso-Echanove J, *et al. CDC. Feeding back surveillance data to prevent hospital-acquired infections.* 2011. URL: www.cdc.gov/ncidod/eid/vol7no2/gaynes.htm (accessed 27 February 2011).
7. Gaynes RP. Surgical-site infections and the NNIS SSI risk index: room for improvement. *Infect Control Hosp Epidemiol* 2000;**21**:184–5.
8. Gaynes RP. Surgical-site infections (SSI) and the NNIS basic SSI risk index. Part II: room for improvement. *Infect Control Hosp Epidemiol* 2001;**22**:266–7.
9. Bruce J, Russell EM, Mollison J, Krukowski ZH. The measurement and monitoring of surgical adverse events. *Health Technol Assess* 2001;**5**(22).
10. National Audit Office. *Improving patient care by reducing the risk of hospital acquired infection: a progress report*. London: National Audit Office; 2004.
11. Department of Health. *A first class service: quality in the new NHS. HSC* 1998/113. Norwich: Her Majesty's Stationery Office; 1998.
12. Department of Health. *Clinical governance in the new NHS*. London: Department of Health, HSC; 1999.
13. Department of Health. Indicator 23003. In: *NHS performance indicators: a consultation*. London: Department of Health, 2001.
14. Anonymous. Surgical site infection surveillance in England. *CDR* 2004;**14**:13.
15. Health Protection Agency. *Fourth report of the mandatory surveillance of surgical site infection in orthopaedic surgery. April 2004 to March 2008*. 2008. URL: www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1227774003450 (accessed 27 February 2011).
16. NHS Modernisation Board. *The NHS plan: a progress report*. The NHS modernisation board's annual report 2000–2001. Chapter 11: The future. 2001: 60–3.
17. Healthcare Commission. *Assessing existing and new national targets*. URL: http://ratings2006.healthcarecommission.org.uk (accessed 27 February 2011).

18. Cruse PJ, Foord R. The epidemiology of wound infection. A 10-year prospective study of 62,939 wounds. *Surg Clin North Am* 1980;**60**:27–40.

19. Haley RW. Nosocomial infections in surgical patients: developing valid measures of intrinsic patient risk. *Am J Med* 1991;**91**:145S–51S.

20. Gaynes RP, Culver DH, Horan TC, Edwards JR, Richards C, Tolson JS. Surgical site infection (SSI) rates in the United States, 1992–1998: the National Nosocomial Infections Surveillance System basic SSI risk index. *Clin Infect Dis* 2001;**33**:S69–77.

21. NINSS Partnership. *Surveillance of surgical site infection in English hospitals* 1997–2002. London: Health Protection Agency; 2003.

22. Brandt C, Hansen S, Sohr D, Daschner F, Rüden H, Gastmeier P. Finding a method for optimizing risk adjustment when comparing surgical-site infection rates. *Infect Control Hosp Epidemiol* 2004;**25**:313–18.

23. Leong G, Wilson J, Charlett A. Duration of operation as a risk factor for surgical site infection: comparison of English and US data. *J Hosp Infect* 2006;**63**:255–62.

24. National Institute for Health and Clinical Excellence (NICE). Clinical guideline CG74. *Surgical site infection. Prevention and treatment of surgical site infection*. London: NICE; 2008.

25. Sanchez-Manuel FJ, Lozano-García J, Seco-Gil JL. Antibiotic prophylaxis for hernia repair. *Cochrane Database Syst Rev* 2007;**3**:CD003769.

26. Higgins JPT, Altman DG on behalf of the Cochrane Statistical Methods Group and the Cochrane Bias Methods Group. Assessing the risk of bias in included studies. In Higgins JPT, Green S, editors. *Cochrane handbook for systematic reviews of interventions version 5.0.1*. 2008. URL: www.cochrane.org/training/cochrane-handbook (accessed 27 February 2011).

27. Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F, *et al.* Evaluating non-randomised intervention studies. *Health Technol Assess* 2003;**7**(27).

28. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, *et al.* The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. URL: www.ohri.ca/programs/clinical_epidemiology/oxford.htm (accessed 27 February 2011).

29. Arjona MF, Gómez-Sancha F, Ibarra FP, Cabrera RH. Risk infection factors in the total hip replacement. *Eur J Epidemiol* 1997;**13**:443–6.

30. Bengtson S, Knutson K. The infected knee arthroplasty. A 6-year follow-up of 357 cases. *Acta Orthop Scand* 1991;**62**:301–11.

31. Berbari EF, Hanssen AD, Duffy MC, Steckelberg JM, Ilstrup DM, Harmsen WS, *et al.* Risk factors for prosthetic joint infection: case–control study. *Clin Infect Dis* 1998;**27**:1247–54.

32. Brandt C, Hansen S, Sohr D, Daschner F, Rüden H, Gastmeier P. Finding a method for optimizing risk adjustment when comparing surgical-site infection rates. *Infect Control Hosp Epidemiol* 2004;**25**:313–18.

33. de Boer AS, Mintjes-de Groot AJ, Severijnen AJ, van den Berg JM, van Pelt W. Risk assessment for surgical-site infections in orthopedic patients. *Infect Contr Hosp Epidemiol* 1999;**20**:402–7.

34. de Boer AS, Geubbels EL, Wille J, Mintjes-de Groot AJ. Risk assessment for surgical site infections following total hip and total knee prostheses. *J Chemother* 2001;**13**:42–7.

35. Gordon SM, Culver DH, Simmons BP, Jarvis WR. Risk factors for wound infections after total knee arthroplasty. *Am J Epidemiol* 1990;**131**:905–16.

36. Lazzarini L, Pellizzer G, Stecca C, Viola R, de Lalla F. Postoperative infections following total knee replacement: an epidemiological study. *J Chemother* 2001;**13**:182–7.

37. Parker MJ, Roberts CP, Hay D. Closed suction drainage for hip and knee arthroplasty: a meta-analysis. *J Bone Joint Surg Am* 2004;**86**:1146–52.

38. Rosencher N, Kerkkamp HEM, Macheras G, Munuera LM, Menichella G, Barton DM, *et al.* Orthopedic surgery transfusion hemoglobin European overview (OSTHEO) study: blood management in elective knee and hip arthroplasty in Europe. *Transfusion* 2003;**43**:459–69.

39. Saleh K, Olson M, Resig S, Bershadsky B, Kuskowski M, Gioe T, *et al.* Predictors of wound infection in hip and knee joint replacement: results from a 20 year surveillance program. *J Orthop Res* 2002;**20**:506–15.

40. Surin VV, Sundholm K, Backman L. Infection after total hip replacement. With special reference to a discharge from the wound. *J Bone Joint Surg Br* 1983;**65**:412–18.

41. Winiarsky R, Barth P, Lotke P. Total knee arthroplasty in morbidly obese patients. *J Bone Joint Surg Am* 1998;**80**:1770–4.

42. Yong KS, Kareem BA, Ruslan GN, Harwant S. Risk factors for infection in total hip replacement surgery at Hospital Kuala Lumpur. *Med J Malaysia* 2001;**56**:57–60.

43. Wilson MG, Kelley K, Thornhill TS. Infection as a complication of total knee-replacement arthroplasty. Risk factors and treatment in sixty-seven cases. *J Bone Joint Surg Am* 1990;**72**:878–83.

44. Last JM, Spasoff RA, Harris SS. *A dictionary of epidemiology*. 4th edn. New York, NY: Oxford University Press; 2000.

45. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 2006;**49**:1373–9.

46. Busch ORC, Hop WCJ, Marquet RL, Jeekel J, Houbiers JGA, Van de Watering LMG, *et al.* Autologous blood and infections after colorectal surgery. *Lancet* 1994;**343**:668.

47. Chang H, Hall GA, Geerts WH, Greenwood C, McLeod RS, Sher GD. Allogeneic red blood cell transfusion is an independent risk factor for the development of postoperative bacterial infection. *Vox Sang* 2000;**78**:13–18.

48. Claesson BE, Holmlund DEW. Predictors of intraoperative bacterial contamination and postoperative infection in elective colorectal surgery. *J Hosp Infect* 1998;**11**:127–35.

49. Ford CD, VanMoorleghem G, Menlove RL. Blood transfusions and postoperative wound infection. *Surgery* 1993;**113**:603–7.

50. Hackam DJ, Rotstein OD. Stoma closure and wound infection: an evaluation of risk factors. *Can J Surg* 1995;**38**:144–8.

51. Jensen LS, Kissmeyer-Nielsen P, Wolff B, Qvist N. Randomised comparison of leucocyte-depleted vs. buffy coat-poor blood transfusion and complications after colorectal surgery. *Lancet* 1996;**348**:841–5.

52. Lewis RT. Oral vs. systemic antibiotic prophlayxis in elective colon surgery: an RCT and meta-analysis. *Can J Surg* 2002;**45**:173–80.

53. McLaws M-L, Taylor PC. The Hospital Infection Standardised Surveillance (HISS) programme: analysis of a two-year pilot. *J Hosp Infect* 2003;**53**:259–67.

54. Miransky J, Ruo L, Nicoletta S, Eagan J, Sepkowitz K, Margetson N, *et al.* Impact of a surgeon-trained observer on accuracy of colorectal surgical site infection rates. *Dis Colon Rectum* 2001;**44**:1100–5.

55. Platell C, Hall JC. The role of wound infection as a clinical indicator after colorectal surgery. *J Qual Clin Pract* 1997;**17**:203–7.

56. Simchen E, Shapiro JM, Michel J, Sacks T. Multivariate analysis of determinants of postoperative wound infection: a possible basis for intervention. *Rev Infect Dis* 1981;**3**:678–82.

57. Simchen E, Shapiro M, Sacks TG, Michel J, Durst A, Eyal Z. Determinants of wound infection after colon surgery. *Ann Surg* 1984;**199**:260–5.

58. Smith RL, Bohl JK, McElearney ST, Friel CM, Barclay MM, Sawyer RG, *et al.* Wound infection after elective colorectal resection. *Ann Surg* 2004;**239**:599–605.

59. Tang R, Hong HC, Yung LW, Chung RC, Chen J-S, Hsu K-C, *et al.* Risk factors for surgical site infection after elective resection of the colon and rectum: a single-center prospective study of 2,809 consecutive patients. *Ann Surg* 2001;**234**:181–9.

60. Titlestad IL, Ebbesen LS, Ainsworth AP, Lillevang ST, Qvist N, Georgsen J. Leukocyte-depletion of blood components does not significantly reduce the risk of infectious complications. Results of a double-blinded, randomized study. *Int J Colorectal Dis* 2001;**16**:147–53.

61. Torchia MG,.Danzinger RG. Perioperative blood transfusion and albumin administration are independent risk factors for the development of postoperative infections after colorectal surgery. *Can J Surg* 2000;**43**; 212–16.

62. Vamvakas EC, Carven JH, Hibberd PL. Blood transfusion and infection after colorectal cancer surgery. *Transfusion* 1996;**36**:1000–8.

63. Zelenitsky SA, Silverman RE, Duckworth H, Harding GKM. A prospective, randomized, double-blind study of single high dose versus multiple standard dose gentamicin both in combination with metronidazole for colorectal surgical prophylaxis. *J Hosp Infect* 2000;**46**:135–40.

64. Zelenitsky SA, Ariano RE, Harding GKM, Silverman RE. Antibiotic pharmacodynamics in surgical prophylaxis: an association between intraoperative antibiotic concentrations and efficacy. *Antimicrob Agents Chemother* 2002;**46**:3026–30.

65. Zmora O, Mahajna A, Bar-Zakai B, Rosin D, Hershko D, Shabtai M, *et al.* Colon and rectal surgery without mechanical bowel preparation: a randomized prospective trial. *Ann Surg* 2003;**237**:363–7.

66. Barber GR, Miransky J, Brown AE, Coit DG, Lewis FM, Thaler HT, *et al.* Direct observations of surgical wound infections at a comprehensive cancer center. *Arch Surg* 1995;**130**:1042–7.

67. Bremmelgaard A, Raahave D, Beier-Holgersen R, Pedersen JV, Andersen S, Sorensen AI. Computer-aided surveillance of surgical infections and identification of risk factors. *J Hosp Infect* 1989;**13**:1–18.

68. Delgado-Rodriguez M, Medina-Cuadros M, Martinez-Gallego G, Gomez-Ortega A, Mariscal-Ortiz M, Palma-Perez S, *et al.* A prospective study of tobacco smoking as a predictor of complications in general surgery. *Infect Control Hosp Epidemiol* 2003;**24**:37–43.

69. Delgado-Rodriguez M, Mariscal-Ortiz M, Gomez-Ortega A, Martinez-Gallego G, Palma-Perez S, Sillero-Arenas M, *et al.* Alcohol consumption and the risk of nosocomial infection in general surgery. *Br J Surg* 2003;**90**:1287–93.

70. Ehrenkranz NJ. Surgical wound infection occurrence in clean operations; risk stratification for interhospital comparisons. *Am J Med* 1981;**70**:909–14.

71. Fernandez AM, Herruzo CR, Gomez-Sancha F, Calero RJ. Four year study of the risk factors of surgical wound infection in 5260 traumatological patients. *Minerva Medica* 1996;**87**:189–94.

72. Geubbels EL, Mintjes-de Groot AJ, van den Berg JM, de Boer AS. An operating surveillance system of surgical-site infections in The Netherlands: results of the PREZIES national surveillance network. Preventie van Ziekenhuisinfecties door Surveillance. *Infect Control Hosp Epidemiol* 2000;**21**:311–18.

73. Herruzo-Cabrera R, Lopez-Gimenez R, Diez-Sebastian J, Lopez-Acinero MJ, Banegas-Banegas JR. Surgical site infection of 7301 traumatologic inpatients (divided in two sub-cohorts, study and validation): modifiable determinants and potential benefit. *Eur J Epidemiol* 2004;**19**:163–9.

74. Malone DL, Genuit T, Tracy JK, Gannon C, Napolitano LM. Surgical site infections: reanalysis of risk factors. *J Surg Res* 2002;**103**:89–95.

75. Moro ML, Sommella L, Gialli M, Tavanti L, Ciolli L, Masetti R, *et al.* Surgical infections surveillance: results of a six-month incidence study in two Italian hospitals. *Eur J Epidemiol* 1991;**7**:641–8.

76. Moro ML, Carrieri MP, Tozzi AE, Lana S, Greco D. Risk factors for surgical wound infections in clean surgery: a multicenter study. Italian PRINOS Study Group. *Ann Ital Chir* 1996;**67**:13–19.

77. Rantala A, Lehtonen OP, Niinikoski J. Alcohol abuse: a risk factor for surgical wound infections? *Am J Infect Control* 1997;**25**:381–6.

78. Reid R, Simcock JW, Chisholm L, Dobbs B, Frizelle FA. Postdischarge clean wound infections: incidence underestimated and risk factors overemphasized. *ANZ J Surg* 2002;**72**:339–43.

79. Reilly J. Evidence-based surgical wound care on surgical wound infection. *Br J Nurs* 2002;**11**:S4–S12.

80. Ronveaux O, Mertens R, Dupont Y. Surgical wound infection surveillance: results from the Belgian hospital network. *Acta Chir Belg* 1996;**96**:3–10.

81. Dwan K, Altman DG, Arnaiz JA, Bloom J, Chan AW, Cronin E, *et al.* Systematic review of the empirical evidence of study publication bias and outcome reporting bias. *PLoS ONE* 2008;**3**:e3081.

82. Avato JL, Lai KK. Impact of postdischarge surveillance on surgical-site infection rates for coronary artery bypass procedures. *Infect Control Hosp Epidemiol* 2002;**23**:364–7.

83. Delgado-Rodriguez M, Gomez-Ortega A, Sillero-Arenas M, Llorca J. Epidemiology of surgical-site infections diagnosed after hospital discharge: a prospective cohort study. *Infect Control Hosp Epidemiol* 2001;**22**:24–30.

84. Lecuona M, Torres-Lana A, Delgado-Rodriguez M, Llorca J, Sierra A. Risk factors for surgical site infections diagnosed after hospital discharge. *J Hosp Infect* 1998;**39**:71–4.

85. Medina-Cuadros M, Sillero-Arenas M, Martinez-Gallego G, Delgado-Rodriguez M. Surgical wound infections diagnosed after discharge from hospital: epidemiologic differences with in-hospital infections. *Am J Infect Control* 1996;**24**:421–8.

86. Oliveira AC, Carvalho DV. Postdischarge surveillance: the impact on SSI incidence in a Brazilian university hospital. *Am J Infect Control* 2004;**32**:358–61.

87. Perencevich EN, Sands KE, Cosgrove SE, Guadagnoli E, Meara E, Platt R. Health and economic impact of surgical site infections diagnosed after hospital discharge. *Emerg Infect Dis* 2003;**9**:196–203.

88. Simchen E, Wax Y, Galai N, Israeli A. Differential effect of risk factors on early and late wound infections in patients undergoing herniorrhaphy. *Ann Epidemiol* 1992;**2**:263–72.

89. Simchen E, Wax Y, Galai N, Israeli A. Discharge from hospital and its effect on surgical wound infections. The Israeli Study of Surgical Infections (ISSI). *J Clin Epidemiol* 1992;**45**:1155–63.

90. Weigelt JA, Dryer D, Haley RW. The necessity and efficiency of wound surveillance after discharge. *Arch Surg* 1992;**127**:77–81.

91. Taggart DP, D'Amico R, Altman DG. Effect of arterial revascularisation on survival: a systematic review of studies comparing bilateral and single internal mammary arteries. *Lancet* 2001;**358**:870–5.

92. Lu JC, Grayson AD, Jha P, Srinivasan AK, Fabri BM. Risk factors for sternal wound infection and mid-term survival following coronary artery bypass surgery. *Eur J Cardiothorac Surg* 2003;**23**:943–9.

93. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol* 1992;**13**:606–8.

94. Wilson JA, Ward VP, Coello R, Charlett A, Pearson A. A user evaluation of the nosocomial infection national surveillance system: surgical site infection module. *J Hosp Infect* 2002;**52**:114–21.

95. Wilson AP, Treasure T, Sturridge MF, Gruneberg RN. A scoring method (ASEPSIS) for postoperative wound infections for use in clinical trials of antibiotic prophylaxis. *Lancet* 1986;**i**:311–13.

96. Wilson APR, Gibbons C, Reeves BC, Hodgson B, Liu M, Plummer D, *et al.* Surgical wound infection as a performance indicator: agreement of common definitions of wound infection in 4773 patients. *BMJ* 2004;**329**:720.

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

98. Wilson AP, Helder N, Theminimulle SK, Scott GM. Comparison of wound scoring methods for use in audit. *J Hosp Infect* 1998;**39**:119–26.

99. Beaujean D, Veltkamp S, Blok H, Gigengack-Baars A, van der Werken C, Verhoef J, *et al.* Comparison of two surveillance methods for detecting nosocomial infections in surgical patients. *Eur J Clin Microbiol Infect Dis* 2002;**21**:444–8.

100. Streiner DL, Norman GR. *Health measurement scales: a practical guide to their development and use*. 4th edn. Oxford: Oxford University Press; 2008.

101. Ridgeway S, Wilson J, Charlett A, Kafatos G, Pearson A, Coello R. Infection of the surgical site after arthroplasty of the hip. *J. Bone Joint Surg* 2005;**87**:844–50.

102. Green J, Wintfeld N. Report cards on cardiac surgeons. *N Eng J Med* 1995;**332**:1229–32.

103. Lefebvre C, Manheimer E, Glanville J. Searching for studies. In Higgins JPT, Green S, editors. *Cochrane handbook for systematic reviews of interventions version 5.0.1*. 2008. URL: www.cochrane.org/training/cochrane-handbook (accessed 27 February 2011).

104. Reeves BC, Deeks JJ, Higgins JPT, Wells GA. Including non-randomized studies. In Higgins JPT, Green S, editors. *Cochrane handbook for systematic reviews of interventions version 5.0.1*. 2008. URL: www.cochrane.org/training/cochrane-handbook (accessed 27 February 2011).

105. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *PLoS Med* 2007;**4**:e296.

106. Vandenbroucke JP, Von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: explanation and elaboration. *PLoS Med* 2007;**4**:e297.

107. Lilford R, Mohammed MA, Spiegelhalter D, Thomson R. Use and misuse of process and outcome data in managing performance of acute medical care: avoiding institutional stigma. *Lancet* 2004;**363**:1147–54.

Appendix 1

Study protocol

1.1 Details of the proposed research

Background to the study

Wound infections are frequent complications of surgery that cause significant postoperative morbidity.[1] They are costly to the National Health Service (NHS; and to other health services and sectors), inconvenient, painful and potentially fatal to affected patients and potentially pose a risk to unaffected patients.[2] Rates of SSI have been observed to vary widely by hospital and it is widely believed that rates are, to a greater or lesser extent, influenced by surgical management and other aspects of the quality of care.[3,4] Therefore, SSI is a potential indicator of the quality of care for use in performance monitoring in the NHS.

The work outlined in the tender for this commissioned research has emerged from both research evidence and health policy:

- publication of HTA monograph[1];
- the subsequent workshop organised by the National Coordinating Centre for Research Methodology (NCCRM) to explore how the findings of the review can be taken forward[5];
- the NHS Plan, with its focus on improving services,[6] the need for national standards and the development of national performance monitoring as the mechanism for achieving these goals.[7]

Definition of wound infection

The recent HTA review identified five nationally proposed definitions. Many studies used one or other of these definitions but over half used various non-standardised combinations of components from these definitions or new components. From the review, it was clear that CDC definitions,[8,9] more recently the 1992 definition,[9] have been most widely adopted, especially for hospital-based monitoring.[1] The 1992 modification[9] stressed that wound infections should be described as 'surgical site infections' (SSIs) to distinguish surgical wound infections from other infected wounds, e.g. burns. For the rest of this proposal, we shall adopt this terminology and use the term SSI rather than wound infection. The 1992 CDC definition[9] is based on the presence of purulent drainage, the ability to culture organisms from an aseptic tissue sample from the wound or organ/space, local pain, tenderness, swelling, redness or heat, spontaneous wound separation or deliberate opening of the wound by a surgeon, presence of an abscess or other evidence from direct examination of deep infection or organ/space, other evidence of an organ/space infection, diagnosis by a surgeon or attending physician.

Both the review[1] and the NCCRM workshop[5] recommended that surveillance programmes should use the 1992 CDC definition.[9] This proposal also chooses the CDC definition as its 'primary' outcome. However, the 1992 CDC definition is not without critics.[1] Inevitably, CDC definitions have considerable authority but this does not necessarily mean that the definition is ideal. Practising clinicians are concerned that the definition is too microbiological and that SSIs detected using the definition do not necessarily reflect SSIs that are of most concern in ordinary practice, both from the point of view of threats to the patient and additional resource use in the health service (see 1.3.2). The consequences of different classes of infections may vary

considerably. Some infections can be catastrophic (fatal or permanent disability) and others relatively minor (extra NHS resource use, cost and inconvenience to patients, but no long term consequences). There may therefore be a need to prioritise investigation of some types of SSI. There is certainly a need for consensus between microbiologists and surgeons about an appropriate working definition of SSI in order to ensure that practising clinicians comply with surveillance programmes and take notice of their findings, and that the surveillance programmes themselves are cost-effective. Exploration of alternative definitions of SSI, created by modifying the CDC 1992 definition and in consultation with surgical specialists, is one of the objectives of the proposed research. The existence of a validated scale for assessing the severity of SSIs, and the inclusion of the data required for the scale in a single-centre surveillance programme will facilitate this objective.[10,11]

Risk factors

The HTA review also reviewed systems for hospital and postdischarge monitoring of SSI and considered as part of this review available methods for risk adjustment. Any system for assessing observed against expected rates of outcome and making comparisons between surgical centres needs to able to adjust for potential differences in the distribution of risk between centres (cf. adjustment for 'case-mix').[12]

The review identified three main risk indices, namely the National Research Council (NRC)[13], Study of the Efficacy of Nosocomial Infection Control (SENIC)[14] and the National Nosocomial Infections Surveillance (NNIS)[15] indices. Bacterial contamination at operation contributes to the risk of SSI and all three of these indices include the 4-class NRC wound classification system (class I – clean; class II – clean-contaminated; class III – contaminated; class IV – dirty).[13] Duration of operation is also common to the latter two systems, although the NNIS index uses a procedure specific cut-off criterion rather than an absolute cut-off [SENIC]. The SENIC and NNIS indices also include a measure of the 'host resistance', i.e. three or more different diagnoses (SENIC) or ASA class (NNIS; see 1.3.3).

The HTA review found that the NNIS index is the most widely used method of risk adjustment and has the advantage that it allows stratification of risk by procedure. Bruce *et al.* concluded that, although it has been criticised for not including other potential risk factors, it is the best available method for stratification of SSI rates, thereby achieving a degree of risk adjustment.[1] However, they also commented that the NNIS index has yet to be validated in the UK patient and hospital setting, particularly with regard to the application of cut-off times for specific procedures, a point worth noting for the proposed research.

It is clear from the literature, for example guidelines for the prevention of SSI,[16] that there are many risk factors for SSI which are not included in any of these risk indices. The combination of risk factors most predictive of SSI is also dependent on the site of surgery.[17] Risk adjustment programmes may choose not to include variables that are directly under the control of hospitals, for example extent of compliance with protocols for antibiotic prophylaxis, since adjusting for these factors will reduce differences in SSI rates between centres. Ideally, surveillance programmes should feedback SSI rates (expected to be higher than average) to hospitals that comply poorly with SSI prevention measures, unadjusted for compliance, together with information about the likely reduction in SSI rates that would be achieved with improved compliance (see 1.3.3). However, there are risk factors that are not clearly under the control of surgeons or hospitals, or dictated by the procedure, for example the requirement for surgical drains, transfusion or 'implanted' (but non-prosthetic) materials (e.g. staples, clips, wires,

autologous vs. synthetic graft, etc., where there is some discretion about whether to use the material or not). Other patient risk factors have also been suggested, e.g. tobacco use, obesity,[18] diabetes,[18] steroid medication, although these are not established.[16]

The aetiology of SSIs in different procedures and settings may vary. If so, the completeness of ascertainment of SSIs may affect the risk factors identified and their empirical weights in risk-adjustment models. Ascertainment is likely to vary most depending on whether or not postdischarge surveillance has been carried out. If only hospital infections are included, 72% of all SSIs may be missed.[19] The proposed research will estimate the effect of including postdischarge surveillance on the identification of risk factors.

Requirement of systems for risk adjustment and target setting

A system for establishing valid targets for SSI rates, and making meaningful comparisons of SSI rates between hospitals, needs:

- Complete ascertainment;
- Adequate characterisation of important risk factors;
- A statistical model to weight risk factors appropriately in order to take account of differences in case-mix between hospitals.[20,21]

Describing the extent to which existing databases achieve these requirements is a key objective of the proposed research.

A final note of caution concerns bias in data collection. Publication of centre-specific performance measures can create strong pressures to bias data collection to improve risk-adjusted outcomes. Susceptibility to bias should be a further consideration when choosing the data items required for statistical models that aim to adjust comparisons between centres for varying case-mix.

1.2 Purpose of the research

The aim of the proposed research is to investigate methods for the risk adjustment of rates of surgical wound infection. We propose to address the following specific objectives:

- To identify risk factors for surgical SSI (CDC definition), criteria for stratification of surgical procedures and evidence about the importance of PDS for methods of risk-adjustment by systematic reviews of the literature.
- To test whether 'short-listed' variables from the literature are risk factors in the databases being analysed, to identify in univariable analyses other potential risk factors from available databases and to investigate interactions between risk factors.
- To develop models for making risk-adjusted comparisons between units, with expert review of the appropriateness of inclusion of independent variables in the models
- To develop models to set absolute risks for infection, with expert review of the appropriateness of inclusion of independent variables in the models.
- To investigate modifications of CDC definition of SSI (as suggested in NCCRM workshop) and the impact of modified definitions on the importance (use for prediction) of risk factors identified.

1.3 Plan of investigation

1.3.1 Details of databases on which it is proposed to carry out the research (sample information on 'size, type and location' representativeness)

There are two main UK databases available, namely the multi-centre Nocosomial Infection National Surveillance Service (NINNS) database administered by the Public Health Laboratory Service (PHLS)[22] and a database administered by University College of London Hospitals (UCLH).[10,11]

The dominance of these two databases means that competing bids for the tender must necessarily have secured the agreement in principle from the custodians of the databases to use the data. This proposal includes representatives of the databases as co-applicants because we believe that collaboration with those who have in-depth knowledge of the databases (rather than simply gaining access to the data) is essential to optimise the value of the databases to the project. Other bidders may have taken the same view, so the same representatives may be represented on competing bids.

An ideal database would:

- include records of many thousands of operations;
- collect data from multiple centres;
- span several years;
- document potential risk factors as well as data required for established risk indices;
- carry out post-discharge, as well as in-hospital, surveillance.

The two main databases together cover all of these features although individually they cover only a subset.

Nosocomial Infection National Surveillance Service (NINNS) database

The NINSS is a national surveillance programme. Collection of the dataset needs to be feasible to implement in all participating hospitals. Therefore the dataset is relatively small (see Table). Data collection began in October 1997; approx 150 hospitals in England and the database currently stands at about 100 000 procedures in 12 categories of surgical procedure: abdominal hysterectomy; CABG, hip prosthesis; knee prosthesis; large bowel surgery; limb amputation; open reduction of fracture of the long bone; vascular surgery; bile duct, liver or pancreatic surgery; cholecystectomy; gastric surgery; small bowel surgery. Operations were chosen to have long lengths of stay, so that SSIs likely to become apparent before discharge. To date, data have only been analysed in detail for eight operation types, since there are too few events in four surgical categories (bile duct, liver or pancreatic surgery; cholecystectomy; gastric surgery; small bowel surgery).

The NINSS database relies on collection of information by infection control nurses in each hospital covered. SSIs are only identified while patients are still in hospital. The definition of SSI is a modified version of that of the CDC. The method and intensity of collection varies between hospitals. Post-discharge follow-up has only been performed in a small proportion. The NINSS database therefore satisfies the first three of the five criteria listed above.

University College of London Hospital (UCLH) database

The UCLH database is a single-centre database, which documents alternative measures of SSI and a larger number of potential risk factors but relatively few operations. Two small datasets were

collected in 1993 an 1994 (approx 500 operations only), but routine data collection only started in 2000; data collection continues. The total number of operations documented will exceed 5000 by April 2003.

Surgical patients with a hospital stay longer than 2 days are eligible for inclusion. Some information including patient demographics, microbiology results and operation duration are entered directly by linkage with the hospital administration system or from other hospital databases. Patient data are collected on to paper by 4 full-time employees; the data are then entered by hand into an Access programme. Patients are visited before operation and at least twice after operation. Most details are completed from the medical and nursing notes but wound appearance is determined by direct observation or interrogation of nursing staff. The exact days of surveillance vary but are never more than 3 days apart. The surveillance workers themselves do not determine if the wound is infected or not; SSIs are identified from the individual data items that are collected and entered in the database. Post discharge follow up is carried out by telephone questionnaire at 4–8 weeks following discharge; this method of post-discharge surveillance has been demonstrated to have acceptable validity and reliability[23] The information collected on each patient is shown in the Table. Follow-up data are available for about 95% of all patients in the database. Sufficient information is collected to allow SSI to be registered by ASEPSIS, the CDC and National Prevalence Survey definitions of SSI. The modified CDC definition used by the UK Nosocomial Infection National Surveillance Scheme (NINSS) is also included. Many risk factors for SSI are collected.

Analysis of the UCLH database has been used for the development of the ASEPSIS method of wound 'scoring' ('Additional treatment; Serous discharge, Erythema; Purulent exudate, Separation of deep tissues; Isolation of bacteria; Stay as in-patient prolonged over 14 days'), in which a score for the probability of SSI is determined by the extent of signs of infection in a wound during the first postoperative week and consequences of infection at 1–2 months after surgery. Many small objective decisions are made to determine the score which has a high degree of reproducibility between observers.[10,11] The method has already been used to determine risk factors for infection in cardiac surgery.[23] The UCLH database therefore satisfies the final criterion listed above and partly satisfies criteria 1, 3 and 4.

Other databases

Agreement in principle to use data from other UK databases has been obtained, although these databases have fewer features than the two described above:

- Northern Ireland PHLS surveillance data: permission from Dr E Smythe; duration of collection 5–10 years; single centre database. Dataset assumed to be similar to NINNS but no detailed information are available at present.
- Inverclyde database: permission from Dr E Taylor; details of dataset and duration of collection are not known at present; single centre database. This database is potentially of interest because it has been reported that established risk indices do not predict the probability of SSI in the dataset.[5]
- Scottish PHLS surveillance data: permission from Dr J Reilly; details of dataset and duration of collection are not known at present; multi centre database; currently few operations are documented.

We do not know of any other multi-centre UK databases. As suggested in the tender, the NNIS database held by CDC, USA may be a valuable resource but the applicability of these data to UK is uncertain, given major differences in the health care systems. We intend to explore the possibility of accessing these data.

TABLE Information available in UCLH and NINNS databases

UCLH database information	NINSS database information
Hospital number, surname, initial	
	Surveillance period
Sex, date of birth	Sex, date of birth
Height and weight	Height and weight
Date of hospital admission	Date of hospital admission
Ward, consultant	
Date of operation	Date of operation
Operation 1	Type of surgery
Operation 2	OPCS codes for surgical procedures
Category of surgical procedure (12 types)	Category of surgical procedure (12 types)
Operation due to trauma	Operation due to trauma
Implant	Implant
Multiple surgical procedures through same incision	Multiple surgical procedures through same incision
Emergency or elective	
NNIS risk index variables:	NNIS risk index variables:
Wound class	Wound class
ASA class	ASA class
Duration of operation	Duration of operation
Consultant, surgeon, assistant	Surgeon code
Drains	
Dressing	
	Date and reason surveillance discontinued
Detection of SSI, date of onset, type of SSI	Detection of SSI, date of onset, type of SSI
Specific sites for organ space SSI	Specific sites for organ space SSI
Criteria for SSI	Criteria for SSI
New SSI from same surgical procedure	New SSI from same surgical procedure
Causative micro-organism	Causative micro-organism
Antibiotic sensitivities	Antibiotic sensitivities
Antibiotic 1: Dose mg, # doses, interval hrs	Peri-operative prophylaxis
Antibiotic 2 and 3 same fields	
Date of discharge	
Following fields collected for days 1–16 but completed only once every 2–3 days:	
Temp1 – C	
Erythema (%)	
Serous (%)	
Purulent (%)	
Wound separation (%)	
First, second, third antibiotics/bacteria	
Deep infection away from site of incision	
Pus from drain	
Localised swelling, pain, tenderness	
Surgeon diagnosis	

TABLE Information available in UCLH and NINNS databases *(continued)*

UCLH database information	NINSS database information
Following data collected after discharge from hospital (Y/N to each question):	
Antibiotics for wd infn required at 1 mth	
Drainage required required at 1 mth	
Isolation of bacteria required at 1 mth	
Stay prolonged required at 1 mth	
Erythema required at 1 mth	
Serous discharge required at 1 mth	
Pus required at 1 mth	
Open wound required at 1 mth	

1.3.2 Outcome

This research will focus primarily on SSI, as defined by the CDC 1992 modified definition.[9] This definition classifies infections into subcategories according to their location, namely superficial, deep and organ/space. The data required to apply this definition are available in the two main databases that will be analysed (see 1.3.1), although both databases have also investigated alternative definitions of a SSI. Reports of the main findings from the NINNS database have used a modification of the 1992 CDC definition, allowing diagnosis of a SSI by a surgeon or trained health care worker.

The frequency of the outcome is an important consideration since the power of the analyses to detect risk factors depends more on the number of infections than on the total number of patients' operations recorded. Examination of the distribution of infection rates by category of surgical procedure in the NINNS database, based on the modified CDC definition, demonstrated approximately a tenfold range across hospitals within surgical procedure categories (2–3% to 20–30%), with median frequencies ranging from about 2% (for abdominal hysterectomy) to about 9% (for large bowel surgery).[22]

The definition of SSI used is an important issue (see 1.1). Among surgeons and practising clinicians, there is not a clear consensus that the CDC definition is optimal. The tender for this research did not specify that researchers should use a particular definition of SSI and did not consider the possibility of investigating alternative definitions. However, we believe that this is a critical issue to investigate alongside the investigation and modelling of risk factors, since the important risk factors or their weighting in a risk index may vary depending on the definition chosen. For example, there are potentially different 'aetiologies' for different classes of infection. The UCLH database in particular offers the opportunity to explore different definitions of SSI and we have therefore included this as an objective.

The definition of an SSI also involves defining the time period over which surveillance for SSIs occurs. Ideally, a definition would be based on a 'window in time' from surgical procedure to a follow-up date after which infection arising from hospital admission is extremely unlikely. It has been suggested that an SSI is unlikely to be diagnosed more than 21 days after an operation although this window in time is likely to vary by class of infection and by category of operation;

for example, deep infections following total hip replacement may not become apparent for some months after the operation. The problem is that, if the time period for surveillance is not constant, the probability of detecting an SSI is likely to vary depending on the length of surveillance for individual patients. Unfortunately, the data required for a definition based on a constant window of time are not available in the NINNS database, which only carried out surveillance until patients were discharged from hospital. In contrast, the UCLH database includes post-discharge surveillance of SSIs for 4–8 weeks after discharge.

1.3.3 Exposures

The most widely adopted risk index is the one developed by the NNIS surveillance programme.[15] The NNIS index has largely superseded SENIC[14] and NRC risk indices.[13] This index uses a three 3-point scale, scored simply by summing yes/no answers to three questions:

- ASA class > 2;
- wound class (contaminated or dirty, classes III and IV);
- duration of operation > 75th percentile for specific operation being performed.[24]

Operation type is also considered to be a risk factor, in so much as commentators and researchers agree that SSI rates should be stratified by operation type for comparisons between centres. This approach is widely accepted, although wound class and duration of operation are strongly associated with operation type. For specific operations, it is not clear what underlying factors predispose patients to SSIs. It appears that decisions about specific strata to use for stratification by operation type have been taken on the basis of both pragmatic (face validity, number of operations) and empirical grounds, e.g. recommendation in NINNS report to stratify hip prosthesis operations (hemi-arthroplasty, primary THR, revision THR, THR resulting from trauma).[22]

A broader consideration of potential risk factors is required for this project. Risk factors can be categorised into four groups:

- Patient factors: ASA class and specific comorbidities;
- Operation factors: type of operation, wound class, duration of operation, need for surgical drain;
- Factors characterising surgical and hospital practice;
- Specific surgical teams and hospitals/centres.

Patient factors are outside the control of the surgical team and the hospital. These should definitely be included in any model comparing performance between centres (typical situation requiring control for case-mix). However, it should also be recognised that the assessment of patient factors may be susceptible to bias, for example differential misclassification of ASA class towards higher classes would lead to optimistic SSI rates after adjusting for ASA class (NNIS index). Bias of this kind, i.e. in recording case-mix factors, has previously been observed when cardiac mortality rates comparing the performance of surgeons were published.[25]

Operation factors are generally considered to be dictated by the type of operation being carried out. However, some are also potentially under the control of the surgical team, at least to some extent. In so much as operation factors are an intrinsic part of a specific operation (and within the normative range for the specific operation), they should be included in any model comparing performance between centres. However, some operation factors may reflect poor performance of the surgical team (e.g. undue length of operation, higher rate of contaminated or dirty wound class than typical for the specified operation) rather than intrinsic risks. As with patient factors,

it should also be recognised that the assessment of operation factors may be susceptible to bias since the key risk factors are necessarily assigned by the surgeon or the surgical team.

Factors characterising surgical and hospital practice, i.e. routine measures taken to minimise the risk of an SSI, should be directly under control of the surgical team or hospital. These factors should not be included in any model comparing performance between centres, since inclusion would mean that the model would be controlling for factors that are likely to explain differences in performance. However, these factors should be included in models seeking to establish (absolute) target SSI rates, with targets being set for circumstances representing optimal practice for the prevention of SSIs. The effect on comparative performance of including these factors in addition to patient and operation factors would be of particular interest; if these factors are truly important in reducing the risk of an SSI, inclusion should reduce differences between centres.

There is, inevitably, overlap between the third and fourth categories, since surgical and hospital practices are closely associated with specific surgical teams and hospitals/centres. However, coding of the identities of specific surgical teams and hospitals/centres is separated out here because of the need to take account of the hierarchical nature of the dataset, i.e. 'clustering' of operation episodes within surgical teams and hospitals. (Ideally, the analysis should take into account individual surgeons, including trainees, as well as consultant teams.) Failure to take account of this data hierarchy is likely to result in overestimation of the precision of the effects of risk factors, misleading estimates of heterogeneity and, potentially, inappropriate modelling of interactions between risk factors (see below). It should also be recognised that, because of the incomplete characterisation of patients, operations and clinical and hospital practice, there will be unexplained variation between surgical teams and centres.

Ability to investigate the various risk factors identified depends on the risk factors having been documented in the NINNS and UCLH databases:

- Variables required for NNIS index are recorded in both databases
- Most important operative factors are recorded in both databases, although the UCLH database contains additional variables, e.g. use of surgical drain. However, choice of operative factors to record appears to have been guided mainly by previously published risk indices. It is not clear whether important operative risk factors have been omitted.
- Some factors characterising surgical and hospital practice are recorded in the UCLH database but very few are included in the NNIS/PHLS database
- Codes to distinguish specific surgical teams and hospitals/centres are recorded in both databases.

Finally, thorough PDS to an established protocol is essential to investigate whether risk factors for infections that become apparent during the hospital phase are also risk factors (and carry the same weighting) for infections that become apparent after hospital discharge.

1.3.4 Methods to be used

Further systematic review of the literature is required for this project to inform the proposed investigation of risk modelling for surgical SSI (see 1.3.5). Existing literature needs to be reviewed to answer questions about: (a) potential risk factors, (b) evidence relating to stratification by procedure type and (c) evidence about how the inclusion of infections identified after hospital discharge may require modification of systems for risk-adjustment.

Data collection is not a consideration for this project, since a 'download' will simply be obtained at a specific point in time. The choice of date will depend on how fast data cleaning is carried out

for the two databases. Both database custodians (i.e. co-applicants PW and AP) have emphasised that data 'cleaning' and preparation will be a key preliminary task. It is also important to describe exactly what data are recorded in each database, the methods of data collection and potential biases arising from data definitions and methods of collection.

Data analysis steps are described in more detail at 3.6. In brief, the second objective will be addressed by uni-variable analyses of individual risk factors and potential two-way interactions between risk factors. The third and fourth objectives will be addressed by multi-variable modelling, initially without and subsequently with consideration of the data hierarchy. Objective 5, exploration of alternative definitions of SSI, will mainly be carried out in parallel with uni-variable analyses, although key alternative definitions will also be investigated in multi-variable models if resources permit this.

There are potential ethical problems with the proposed research. Researchers who have recruited hospital and health care staff to contribute to the main databases have assured health care staff treating patients whose care is documented in the databases that the data would be kept confidential. Anonymising individual patient records assures patient confidentiality, but anonymising centres and surgical teams does not assure their confidentiality, since the identity of some centres and surgeons may be deduced from their operative workloads. This is likely to be an obstacle to making datasets publicly available after the research is completed. The data are also being used for a purpose not specified at the time of data collection. This issue requires further investigation. The applicants are currently preparing an application to the London MREC.

1.3.5 Systematic review of the literature

Additional systematic reviews of the literature are required to update the existing review[1] and to identify additional evidence on three key aspects that were not covered systematically by the review and which are critical to the proposed research:

- potential risk factors;
- evidence relating to stratification by procedure type;
- evidence about how the inclusion of infections identified after hospital discharge may require modification of systems for risk-adjustment.

The following databases will be used: MEDLINE, EMBASE, British Library Catalogue, Science Citation Index, Cochrane Library, DARE. With the help of the Ms Bruce, who carried out the literature searches for the HTA review, and LSHTM librarians new strategies will be designed to identify relevant literature for each of the three aspects. Selection of relevant literature and extraction of data (e.g. study population, sample sizes, definition of SSI used, risk factors investigated, risk estimates and confidence intervals, extent of control for confounding, % lost to follow-up) will be carried out by at least two members of the research team. A quality instrument (chosen on the basis of a review of quality instruments for observation studies[26]), will be used to appraise the validity and applicability of individual papers. Narrative syntheses will be carried out. Principles of systematic reviewing laid out in the Cochrane Reviewers' Handbook will be followed,[27] also taking into account complementary guidance available from the Cochrane Non-Randomised Studies Methods Group.[28]

1.3.6 Plan for data analyses

The plan for analysis is as follows:

Step 1: Data preparation; check that the primary outcome (CDC definition[9]) can be calculated in all the databases being analysed and describe the period of surveillance used. Summarise the information available in the databases, including data definitions and the methods of data

collection. Describe the number of patients, their age, sex and general health profile, the numbers undergoing various types of surgical procedures, hospital and surgical procedure variables that are available and measures of data quality (extent of missing and suspect data, following validation checks).

Step 2: Tabulate the crude risks of SSI by classes of procedure and by database. Similarly, tabulate patient profiles and hospital and surgical procedure variables by classes of procedure and database. Information from this step of the analysis, together with information from the systematic review, will help to address the question of how best to stratify further analyses by procedure. It is anticipated that decisions about stratification will be based on a combination of evidence, expertise and pragmatism. Explore the effects of modifications of CDC 1992 definition with a view to 'optimising' the definition of SSI (by maximising the detection of serious infections and minimise the inclusion of trivial infections).

Step 3: Within procedure types, and within and between centres/databases use unadjusted regression methods and expert clinical opinion to identify key risk factors and possible interactions between them. Given the multiplicity of risk factors and likely complexity of their associations with SSI, and their susceptibility to bias, we are particularly keen to use expert opinion, including relevant specialist surgeons, to identify possible biases, interpret and understand unexpected associations.

Step 4: Use multi-variable regression modelling to refine the set of risk factors.[14] Models will be reviewed with subject experts to understand the importance and possible causes of heterogeneity between procedures, hospitals and databases.

Step 5: Use the established technique of random effects modelling[12,29] to build a model for predicting risk based on (a) patient characteristics alone, (b) patient and operation characteristics and (c) patient, operation surgical and centre practice characteristics. These models will explore at what level in the data hierarchy (i.e patients, surgeons/surgical teams and hospitals) it is most appropriate to model important interactions. Models will be checked for goodness of fit using, for example, Lemeshow's chi-square statistics[30] and the ROC.[31] As in step 4, models 'short-listed' on statistical grounds will be reviewed with subject experts to understand the importance and possible causes of heterogeneity between procedures, hospitals and databases.

Following review of the models by experts, the models will be refined to achieve a model that predicts risk of SSI conditional on patient characteristics, category of operation and, possibly, operation characteristics (depending on collective view of susceptibility to bias of operation characteristics and the development of methods to identify and minimise sources of bias). This model will then be used to compare outcomes between surgical teams and hospitals in the NINNS database. Point estimates for frequency of infection for particular operation types, rank order and CIs for both frequencies and ranks will be calculated for illustrative purposes (see 5 below).

The results of this model will be presented in terms of a simple score for evaluating a patient's risk of SSI, similar to the APACHE system for intensive care[32] and risk scores for cardiovascular disease.[33] The scoring system could be made available on the internet, if this was considered appropriate by the steering group after consideration of its limitations (see 1.4).

Step 6: The final step in the analysis will be to derive a further model that seeks to explain the remaining differences between surgical teams and hospitals after allowing for case mix and surgical type by risk factors presumed to be under the 'control of' the hospitals, in so far as these variables are available in the databases. This model will help to identify areas where changes in

practice are likely to be beneficial and to predict the effect that would be expected if appropriate changes in practice were to implemented in a particular centre, given that centre's case mix and surgical mix.

Analyses will consider carefully heterogeneity by centre and by time (and an interaction between centre and time). A 'main effect' of centre implies differences between centres that may or may not be 'performance/quality' related. A main effect of time suggests that the importance of risk factors may be changing over time, e.g. as SSI-preventation measures are adopted. An interaction of centre by time (particularly if there is evidence of relatively constant workload/case-mix) is perhaps the strongest evidence that some centres may be doing better than others for reasons attributable to 'process' or infection control measures.

Validation of the goodness of fit of models is not considered necessary. Although estimates of goodness-of-fit are likely to be optimistic, there is no reason to suspect that the rank order of goodness-of-fit of competing models would be altered by methods used to correct this optimistic bias.

1.3.7 Potential areas of difficulty for analysis

It will be necessary to consider carefully the merits of logistic regression and survival analysis for analysis of 'time-to-event' data, when last follow-up differs between groups of patients. The results of logistic regression modelling may be biased in these circumstances. Survival analysis takes account of varying lengths of follow-up but (i) the results are less obviously interpretable, (ii) there is still potential for ascertainment bias (if censorship is not independent of outcome) and (iii) random effects modelling, the natural way to account for heterogeneity, is far from straightforward.

There is no obvious way to determine whether unusual or extreme operative characteristics, e.g. long duration of operation, should be regarded as risk factors or as markers of poor performance. Alternative models will be reviewed with surgical specialists to inform this issue.

The amount of data and, potentially, the quality of the data, varies by operation type. In the UCLH database, Caesarian section and CABG are considered to be procedures for which there are large numbers of patients and 'clean data'. However, these may not be the most important operation types, despite their high frequency, because the risk of a serious SSI is low. These procedures can be contrasted with operations on the large bowel for which the measurement of risk factors may be complex (e.g. wound class; issues of reverse causality and susceptibility to bias) and the risk of serious SSIs relatively high.

1.4 Likely outputs from the study

We believe that the programme of work that we have set out is 'preliminary' rather than definitive. We strongly maintain that the work is necessary and that a longer programme of work will, ultimately, be required. However, we cannot justify a more detailed programme at present until we know better what can be done with existing databases.

We anticipate that the project will deliver the following outputs:

- Findings from the three systematic review topics.
- An overview of state of databases and UK surveillance programmes (single and multi-centre); the comparability of these programmes; recommendations about developments

in surveillance programmes to improve the measurement of exposure and outcome, data quality and comprehensiveness.
- Description of the main risk factors for SSI and problems in their measurement and collection, including statistical and clinical insights about potential biases in surveillance programmes, e.g. from methods of data collection and differential ascertainment.
- A provisional understanding of the relationship (or lack of it) between case-mix and the risk of SSI, leading to publishable risk score (i.e. given a patient's characteristics, what is the probability of a patient undergoing procedure X developing a SSI). This could be used as an extremely provisional tool for comparing centres, taking into account the reservations expressed below.
- Identification of procedure variables that have an impact on risk.
- A comparison of alternative definitions of SSI for use in surveillance programmes.
- A description of heterogeneity of rates of SSI by centre and over time. Variation by centre and time may be useful indicators of the capacity for improvement through prevention measures.

Although we acknowledge that surveillance programmes have identified extreme outliers, we have reservations about using models from this research to compare or rank SSI rates across centres. There are considerable problems in achieving the ideal circumstances set out in 1.3.1 and it is clear that the available databases do not satisfy all of these criteria.

First, CIs for ranks are very wide, which implies that apparently large difference in ranks are likely to have arisen by chance.[34] Even when quantitative performance estimates are calculated, in most circumstances, large sample sizes are required to produce sufficiently precise estimates to identify outliers with confidence. Large sample sizes can be generated by collecting data over longer periods of time. However, data from further away in time are likely to be increasingly unrepresentative of current practice, especially if trends in outcome are apparent.

Second, models for risk-adjustment are inevitably affected by residual confounding, which will be more serious when the model is less well specified. It is clear that the available databases do not include data on all potential risk factors; available databases have resulted from single or multi-centre surveillance programmes with datasets that have focused on the inclusion of existing risk indices rather than comprehensive prospective collection of possible risk factors. Therefore, there is a considerable danger that final models will still be substantially confounded.

Third, it is known that a large proportion, perhaps the majority, of SSIs are diagnosed after discharge from hospital. This proportion is likely to vary depending on local hospital discharge policies and other factors. (The distribution of LOS for a particular procedure by centre can be investigated, to describe the extent to which the medians and ranges vary.) Such differences may obscure or be dominant over differences between centres that arise from varying quality of surgical care.

Fourth, the susceptibility of risk factors to bias is unknown and could markedly affect estimates for centres. Investigation of heterogeneity in this project is likely to provide insights about this issue and, potentially, recommendations for preventing bias in future surveillance programmes but cannot 'control for' biases that already exist.

Any statistical model is only as good as the data on which it is based. Given the limitations outlined above, statistical models resulting from the proposed research should be interpreted with caution. Hence, our view that the project represents only the first step in the development of a system for risk adjustment of SSI rates.

1.5 Proposal for an extension

1.5.1 Systematic review of the literature

The original proposal identified three review areas relevant to the project:

- potential risk factors;
- evidence relating to stratification by procedure type;
- evidence about how the inclusion of infections identified after hospital discharge may require modification of systems for risk-adjustment.

Based on further scoping, these three review areas have been restructured as follows:

- potential generic risk factors;
- potential surgery specific risk factors, including stratification by subprocedures;
- evidence about how the inclusion of infections identified after hospital discharge may require modification of systems for risk-adjustment.

The proposed content of the reviews is outlined in the table below.

Review topic	Content
Potential risk factors:	
Generic risk factors;	Provide quantitative summary (but not necessarily a quantitative synthesis) or risk factors identified and quality assessment of eligible papers.
Operation specific factors;	**Limit to:** ■ CABG ■ Joint replacement ■ Large bowel surgery Provide quantitative summary (but not necessarily a quantitative synthesis) and quality assessment of eligible papers.
Stratification by subprocedures	(Varying risks of SSI for subprocedures are considered under operation specific factors)
Differences in risk factors for in-hospital and post-discharge surveillance	Review carried out as described in the original protocol.

The main issues identified in doing the systematic reviews are as follows:

- It is relatively easy to extract risk factors identified, but time consuming to extract all of the associated information about unadjusted and adjusted risk estimates, CIs, etc. Lists of risk factors, with examples of their effects from particular papers subjectively judged to be of higher quality, would illustrate whether or not documentation of generic risk factors is likely to be sufficient to control for case mix.
- We do not anticipate that it will be appropriate to carry out meta-analyses of risk estimates across studies, but nevertheless believe that it would be useful to provide plots similar to 'forest plots', simply as graphical, quantitative summaries of the variation in risk factor estimates, possibly distinguished by clinical setting or other relevant variables.
- There is no established instrument for assessing the quality of observational studies of risk factors; this process is also time consuming. Nevertheless, we believe quality assessment may be an important source of heterogeneity in risk factor estimates between studies.

1.5.2 Validation of SSI definitions

We already propose to describe in the final report (a) the agreement between different SSI definitions and (b) the strength of association between 'presence of SSI' and outcomes that SSI

would be expected to influence (e.g. length of hospital stay for infections identified in hospital). However, the detailed consideration of different SSI definitions has highlighted that none of them have been psychometrically evaluated, as would be the case for example for a patient reported measure of health outcome. The only evaluation that has been carried out relates to the reliability of the ASEPSIS scale, but the method of data collection the ASEPSIS scale has since been modified. The steering group considers this to be a serious omission, since all three of the commonly used definitions (CDC, NINSS and ASEPSIS) all require infection control practitioners to observe wounds and make subjective assessments.

Prospective data collection by multiple trained infection control staff is currently underway at UCLH for a sample of patients. Additional funding would allow the inter-rater reliability of different SSI definitions to be described, including investigation of specific items within definitions. We would also use standard psychometric 'item reduction' methods to investigate whether it is possible to produce a 'slimmed down' but psychometrically robust definition of SSI, that is more practicable for surveillance.

1.5.3 Other important future research that the Steering Group has identified

Other research questions that we have identified as important and possible using the existing databases:

- Investigate how the important risk factors for case mix adjustment vary depending on whether or not wounds detected after discharge are included (using the UCLH database); this would represent an empirical test of the systematic review question that we set out to answer, but for which we have so far failed to identify any evidence.
- Investigate how the important risk factors for case mix adjustment vary for different SSI definitions (using the UCLH database).
- Investigate the importance for case-mix adjustment of surgery specific factors identified from the review (using the UCLH database); this question would be limited by the number of other variables available in the UCLH database, but would nevertheless be illustrative of the potential need to record additional surgery specific factors in order to adjust more fully for case-mix.
- Investigate the extent to which hospitals can be 'finger-printed' with respect to variations in their data collection practices, from the data in the NINSS database; we are concerned that variation between hospitals may be largely attributable to these factors, but the NINSS database does not include any variables that allow us to investigate this question directly. Nevertheless, we believe we can derive 'meta'-data for hospitals and test the extent to which these hospital-level data characteristics are associated with variation between hospitals that remains unexplained after applying our 'best' case-mix adjustment models.

1.6 References

1. Bruce J, Russell EM, Mollison J, Krukowski ZH. The measurement and monitoring of surgical adverse events. *Health Technol Assess* 2001;**5**(22):1-12.
2. The Scottish Office, Department of Health. *Hospital acquired infection: a framework for national surveillance for the NHS in Scotland.* 1999, Edinburgh, The Scottish Office.
3. Holmes J, Readman R. A study of wound infections following inguinal hernia repair. *Journal of Hospital Infection* 1994;**28**:153-6.
4. Platell C, Hall JC. The role of wound infection as a clinical indicator after colorectal surgery. *Journal of Quality in Clinical Practice* 1997;**17**:203-207.

5. Reeves BC. *Proceedings of a workshop on: Standard Measures of Generic Surgical Outcomes report*. NHS National Coordinating Centre for Research Methodology, University of Birmingham, 2002. http://publichealth.bham.ac.uk/nccrm/workshops.htm (accessed October 2002).
6. Department of Health. *The NHS Plan. A Plan for Investment. A Plan for Reform.* London, HMSO, 2000.
7. NHS Performance Indicators. *National Figures: February 2002*. http://www.doh.gov/nhsperformanceindicators/(accessed October 2002).
8. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections. *Am J Infect Control* 1988;**16**:128-140.
9. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infection Control & Hospital Epidemiology* 1992;**13**:606-8.
10. Wilson AP, Treasure T, Sturridge MF, Gruneberg RN. A scoring method (ASEPSIS) for postoperative wound infections for use in clinical trials of antibiotic prophylaxis. *Lancet* 1986;**i**:311-313.
11. Wilson AP, Webster A, Gruneberg RN, Treasure T, Sturridge MF. Repeatability of asepsis wound scoring method. *Lancet* 1986;**1**(8491):1208-9.
12. Goldstein H, Spiegelhalter DJ. League tables and their limitations: statistical issues in comparisons of institutional performance (with discussion). *J R Statist Soc A* 1996;**159:**385-443.
13. Cruse PJ, Foord R. The epidemiology of wound infection. A 10-year prospective study of 62,939 wounds. *Surgical Clinics of North America* 1980;**60**:27-40.
14. Haley RW. Nosocomial infections in surgical patients: developing valid measures of intrinsic patient risk. [Review] [31 refs]. *Am J Med* 1991;**91**:145S-51S.
15. Gaynes RP, Culver DH, Horan TC, Edwards JR, Richards C, Tolson JS. Surgical site infection (SSI) rates in the United States, 1992-1998: the National Nosocomial Infections Surveillance System basic SSI risk index. *Clin Infect Dis* 2001;**33** Suppl 2:S69-77.
16. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infection Control & Hospital Epidemiology* 1999;**20**: 250-78.
17. Tang R, Chen HH, Wang YL, Changchien CR, Chen JS, Hsu KC, *et al.* Risk factors for surgical site infection after elective resection of the colon and rectum: a single-center prospective study of 2,809 consecutive patients. *Ann Surg* 2001;**234**(2):181-9.
18. Russo PL, Spelman DW. A new surgical-site infection risk index using risk factors identified by multivariate analysis for patients undergoing coronary artery bypass graft surgery. *Infect Control Hosp Epidemiol* 2002;**23**(7):372-6.
19. Avato JL, Lai KK. Impact of postdischarge surveillance on surgical-site infection rates for coronary artery bypass procedures. *Infect Control Hosp Epidemiol* 2002;**23**(7):364-7.
20. Anonymous. Nosocomial infection rates for interhospital comparison: limitations and possible solutions. A Report from the National Nosocomial Infections Surveillance (NNIS) System. *Infect Control Hosp Epidemiol* 1991;**12**:609-21.
21. Anonymous. National Nosocomial Infections Surveillance (NNIS) System report, data summary from January 1990-May 1999, issued June 1999. *Am J Infect Control* 1999;**27**:520-32.

22. Public Health Laboratory Service. *Surveillance of surgical site infection in English Hospitals 1997-2000*. http://www.phls.org.uk/publications/ninns/NINSS-SSI2000.pdf (accessed October 2002).

23. Wilson AP, Livesey SA, Treasure T, Gruneberg RN, Sturridge MF. Factors predisposing to wound infection in cardiac surgery. A prospective study of 517 patients. *Eur J Cardiothorac Surg* 1987;**1**(3):158-64.

24. Gaynes RP, Culver DH, Horan TC, Edwards JR, Richards C, Tolson JS. Surgical site infection (SSI) rates in the United States, 1992-1998: the National Nosocomial Infections Surveillance System basic SSI risk index. *Clin Infect Dis* 2001;**33** Suppl 2:S69-77.

25. Green J, Wintfeld N. Report cards on cardiac surgeons. *N Eng J Med* 1995;**332**:1229-32.

26. Deeks J (personal communication). Systematic review of instruments for assessing the quality of non-randomised studies. Chapter in HTA monograph, submitted for review.

27. Cochrane Collaboration. *Cochrane Reviewers' Handbook. Cochrane Library* 2002; issue **2**.

28. Cochrane Non-Randomised Studies Methods Group. Draft guidance for inclusion of non-randomised studies in systematic reviews. http://www.cochrane.dk/nrsmg/guidelines.htm

29. Spiegelhalter DJ, Aylin P, Best NG, Evans SJW, Murray GD. Commissioned analysis of surgical performance using routine data: lessons from the Bristol inquiry (with discussion). *J R Statist Soc A* 2002;**165:**191-231.

30. Lemeshow S, Hosmer DW. A review of goodness of fit statistics for use in the development of logistic regression models. *Am J Epidemiol* 1982;**115**:92-106

31. Cleves M. Receiver operating characteristic analysis. *Stata Technical Bulletin* 1999; **52**:slg120.

32. Rowan K, Kerr J, Major E, McPherson K, Short A, Vessey M. Intensive Care Society's APACHE II study in Britain and Ireland – 1: variations in casemix of adult admissions to general intensive care units and impact on outcome. *BMJ* 1993;**307**:972-7.

33. Pocock SJ, McCormack V, Gueyffier F, Boutitie F, Fagard H, Boissel J-P on behalf of the INDANA project steering committee. A score for predicting risk of death from cardiovascular disease in adjust with raised blood pressure, based on individual patient data from randomised controlled trials. *BMJ* 2001;**323**:75-81. See also www.riskscore.org.uk

34. Marshall EC, Spiegelhalter DJ, Sanderson C, McKee M. Reliability of league tables of in vitro fertilisation clinics: retrospective analysis of live birth rates. *BMJ* 1998;**316**:1701-5.

Appendix 2

Database searches

Surgery-specific search: colon surgery

Databases: MEDLINE 1966 to July 2004 (week 3)

Search terms

1. exp surgical wound infection/
2. surgical wound infection.tw
3. surgical site infection.tw
4. or/1–3
5. exp risk factor/
6. exp risk assessment/
7. exp risk adjustment/
8. risk stratification
9. risk modelling.tw
10. risk factors.tw
11. or/5–10
12. 4 and 11
13. exp colorectal surgery/
14. exp colectomy/
15. colon surgery.tw
16. exp proctocolectomy/
17. exp proctocolectomy, restorative
18. exp colostomy/
19. large bowel surgery.tw
20. or/13–19
21. 20 and 12

EMBASE 1980 to July 2004

Search terms

1. exp surgical wound infection/
2. exp postoperative infection/
3. surgical wound infection.tw
4. surgical site infection.tw
5. or/1–4
6. exp risk factor/
7. exp risk assessment/
8. risk adjustment.tw
9. risk stratification.tw
10. risk modelling.tw
11. risk factor.tw
12. postoperative infection risk.tw
13. or/6–12
14. exp colon surgery/
15. exp colon anastomosis/
16. exp colostomy/

17. exp colon resection/
18. exp hemicolectomy
19. exp sigmoidectomy/
20. exp total colon resection/
21. exp colorectal surgery/
22. exp colorectal anastomosis/
23. exp proctocolectomy/
24. colorectal surgery.tw
25. colon surgery.tw
26. large bowel surgery.tw
27. or/14–26
28. 5 and 13
29. 27 and 28

Surgery-specific search: hip and knee replacement surgery

MEDLINE 1966 to June 2004 (week 3)

Search terms

1. exp surgical wound infection/
2. surgical wound infection.tw
3. surgical site infection.tw
4. or/1–3
5. exp risk factor/
6. exp risk assessment/
7. exp risk adjustment/
8. risk stratification.tw
9. risk modelling.tw
10. risk factors.tw
11. or/5–10
12. 4 and 11
13. exp hip prosthesis/
14. exp knee prosthesis/
15. exp joint prosthesis/
16. exp orthopaedics/
17. exp arthroplasty, replacement, knee
18. exp arthroplasty, replacement, hip
19. exp arthoplasty, replacement/
20. or/13–19
21. 12 and 20

EMBASE 1980 to June 2004

Search terms

1. exp surgical wound infection/
2. exp postoperative infection/
3. surgical wound infection.tw
4. surgical site infection.tw
5. or/1–4
6. exp risk factor/
7. exp risk assessment/
8. risk adjustment.tw
9. risk stratification.tw

10. risk modelling.tw
11. risk factor.tw
12. postoperative infection risk.tw
13. or/6–12
14. exp hip prosthesis/
15. exp knee prosthesis/
16. exp joint prosthesis/
17. exp orthopaedics/
18. exp hip arthroplasty/
19. exp knee arthroplasty/
20. hip prosthesis.tw
21. knee prosthesis.tw
22. hip replacement.tw
23. knee replacement.tw
24. hip arthroplasty.tw
25. knee arthroplasty.tw
26. or/14–25
27. 5 and 13
28. 26 and 27

Search for generic risk factors for surgical site infections

MEDLINE 1966 to June 2004 (week 3)

Search terms

1. exp surgical wound infection/
2. surgical wound infection.tw
3. surgical site infection.tw
4. or/1–3
5. exp risk factor/
6. exp risk assessment/
7. exp risk adjustment/
8. risk stratification
9. risk modelling.tw
10. risk factor.tw
11. senic.tw
12. nnis.tw
13. or/5–12
14. 4 and 13

EMBASE 1980 to June 2004

Search terms

1. exp surgical wound infection/
2. exp postoperative infection/
3. surgical wound infection.tw
4. surgical site infection.tw
5. exp risk factor/
6. exp risk assessment/
7. risk adjustment.tw
8. risk stratification.tw
9. risk modelling.tw
10. risk factor.tw

11. senic.tw
12. nnis.tw
13. postoperative infection risk.tw
14. or/1–4
15. or/5–13
16. 14 and 15

Search for risk factors for surgical site infections identified by postdischarge surveillance

MEDLINE 1966 to August 2004 (week 3)

Search terms

1. exp surgical wound infection/
2. surgical wound infection.tw
3. surgical site infection.tw
4. or/1–3
5. exp risk factor/
6. exp risk assessment/
7. exp risk adjustment/
8. risk stratification.tw
9. risk modelling.tw
10. risk factors.tw
11. or/5–10
12. 4 and 11
13. Exp population surveillance/
14. Post discharge surveillance.tw
15. Exp patient discharge/
16. Followup.tw
17. Postdischarge.tw
18. Post-discharge.tw
19. Or/13–18
20. 12 and 19

EMBASE 1980 to August 2004

Search terms

1. exp surgical wound infection/
2. exp postoperative infection/
3. surgical wound infection.tw
4. surgical site infection.tw
5. or/1–4
6. exp risk factor/
7. exp risk assessment/
8. risk adjustment.tw
9. risk stratification.tw
10. risk modelling.tw
11. risk factor.tw
12. postoperative infection risk.tw
13. or/6–12
14. 5 and 13
15. Exp hospital discharge/
16. Patient discharge.tw

17. Post discharge surveillance.tw
18. Postdischarge.tw
19. Post-discharge.tw
20. Exp follow-up/
21. Or/15–20
22. 14 and 21

Appendix 3

Methods for deriving surgical site infection definitions based upon CDC, NINSS and ASEPSIS criteria in the UCLH wound monitoring data set

Introduction

This appendix describes the data management steps taken by the applicants to calculate SSI scores and classifications based upon a joint research team/UCLH interpretation of the SSI criteria from CDC, NINSS and ASEPSIS definitions. The steps are tailored to obtain these data from the UCLH wound monitoring data set.

Tables used

All tables originally kept in the UCLH Microsoft Access database were exported and saved in Stata format at the outset. All data management was carried out using these exported tables, independently of the UCLH Microsoft Access database environment.

The main tables extracted from Access and converted to Stata format were:

Patients admissions	Daily follow-up	Lab results
		Lab positives
		Gram stains

Lab, laboratory.

Routines used and differences with University College London Hospitals database

The set of do-files developed in Stata replicated the functionality of the UCLH database in cleaning and otherwise treating raw data tables prior to applying the scoring algorithms for CDC, NINSS and ASEPSIS. The main differences (agreed jointly) related to:

- derivation of individual SSI criteria from imperfect data sources
- dealing with missing data, including imputation of blank values.

Matching laboratory data to wounds

All laboratory (lab) results were stored at the admission ID level. It was impossible to match, in a systematic way, data from lab results with specific wound numbers. Therefore, it was necessary to arbitrate in some way the assignment of lab data to wounds.

Before assigning data to wounds, lab specimens that were not relevant to wounds were removed from all tables according to a set of rules defined partly by expert appraisal and partly by a table in the Access database.

The method of assignment of data to wounds used was different from that employed in the UCLH database. It was assumed that all important findings from lab data should be assigned to all wounds in the admission (for all definitions). By contrast, the UCLH database employs a mixed mode of arbitration which is summarised in *Table 37*.

Handling multiple observations in laboratory data

Several records were often recorded against each patient admission, often with mixed positive/negative status on the three variables of interest. For a given variable [e.g. white blood cells (WBCs)], if any of the records within an admission tested positive, a 'yes' is recorded for that variable. *Tables 38* and *39* demonstrate using WBCs as an example.

Creating summary variables

White blood cells (in Gram stain table)

Many observations describe Gram-stained slides taken from wound specimens. Data management captured WBC information as follows (*Table 40*).

TABLE 37 University College London Hospitals method of assigning summary data from lab tables to wounds

Lab information	Mode of assignment to wound in UCLH database	Mode of assignment to wound in project data set
Isolation of bacteria	Assign to wound number one only	Assign to all wounds under the admission
WBCs	Assign to all wounds under the admission	Assign to all wounds under the admission
Positive culture	Assign to all wounds under the admission	Assign to all wounds under the admission

TABLE 38 Example of collapse operation upon the lab results of two patient admissions – precollapse

Admission ID	Gram stain data	WBCs?
5	SNUM-WBCINUM-GPC	Yes
5	SFEW-WBCINOSI	Yes
5	SFEW-WBCINOSI	Yes
5	HIDEI	No
6	SMOD-WBCINOSI	Yes
6	SWBC-NSENEIMOD-G	No
6	SMOD-WBC-NSENEIFE	No
6	HIDEI	No

TABLE 39 Example of collapse operation upon the lab results of two patient admissions – postcollapse

Admission ID	WBCs?
5	Yes
6	Yes

TABLE 40 Calculation of 'WBCs seen' from Gram stains data table

String seen in Gram stains table	Action
WBC	Assign 'yes' to WBCs for all wounds in the admission
HIDE	Ignore the observation even if 'WBC' is recorded
NSE (i.e. NSEEN NSENE)	Ignore the observation even if 'WBC' is recorded

This method generated nearly identical results to the processing in the UCLH Access database (99.89% agreement), but the project method had higher sensitivity (picks out two extra wounds with WBCs).

Isolation of bacteria (in lab positives table)

The project adopted the same method used by the UCLH database to flag the 'bacteria isolated field'.

As in the UCLH database, lab positives were examined for each admission, and the organisms and antibiotics recorded were matched against an extensive list of antibiotics and organisms from the UCLH Access database. Organisms and antibiotics within this list that have been assigned a 'NINSS code' were considered to be 'valid'.

If both a valid organism and antibiotic were seen simultaneously in a lab positives record, the bacteria isolated criterion was set to 'yes' for the parent admission.

Positive culture from wound specimen (in lab results table)

This variable is taken directly from 'culture positive' field in the lab results table and assigned to all wounds in the admission.

Final product

At the conclusion of the lab summary data management, all values were saved in one table which recorded, against each admission (and all wounds under each), the presence or absence of a positive culture, WBCs on Gram slide and isolation of bacteria.

Daily summary: Centers for Disease Control and Prevention

Using the daily table, a do-file created a summary data set that documented for each wound the adverse events that inform CDC/NINSS definitions of SSI.

The continuous time-element of the daily table was kept only in the summary sense. At the end of the do-file the daily table was 'collapsed' so that there was one record per wound, with most observations distilled to a set of 'yes/no' variables, plus two 'count' variables.

Duplicated observations on single days (which occur occasionally in the daily table) were accounted for and did not bias any results.

Variables are explained in *Table 41*, along with their method of calculation.

For the two count-variables, there was no imputation of missing data if dailies 'skipped' a day. Thus, a patient who had a fever recorded against a discontinuous set of days, say a Tuesday and a Thursday, would have only a score of '2' on fever count, even though it is likely that she/he also had fever on the Wednesday which was not observed (*Table 42*).

To facilitate the calculation of the CDC definition for 'superficial' infection, some 'yes/no' criteria were calculated in two forms that handled time differently. The forms were:

- form 1 (standard): first 30 days following operation considered, unless implant was used in operation, in which case first 365 days considered
- form 2: first 30 days following operation only considered.

TABLE 41 Daily wound measurements – method of collapse to 'yes/no' or count variables

Daily measurement	Original level of measurement in daily	Derivation of 'yes/no' or count variable(s) (variable name in capitals followed by description)
Wound dehiscence	Per cent of wound affected	DEHISCE
		If 'wound separation' percentage exceeds zero on any day assign 'yes'
Redness and/or heat	Per cent of wound affected	REDHEAT
		If 'erythema' percentage exceeds zero on any day assign 'yes'
Purulent drainage	Per cent of wound affected	PUS
		If 'purulent exudate' percentage exceeds zero on any day assign 'yes'
		PUSCOUNT
		# unique dates on which 'purulent exudate' percentage exceeded zero
Patient's temperature	Degrees Celsius	FEVER
		If this ever exceeds 38°C on any day assign 'yes'
		FEVERCOUNT
		# unique dates on which the observed temperature exceeded 38°C
Surgeon diagnosed superficial infection	Binary	SURG. SUPER
		If survey nurses ticked this field on any day, record 'yes'
Surgeon diagnosed deep infection	Binary	SURG. DEEP
		If survey nurses ticked this field on any day, record 'yes'

TABLE 42 Collapse of new (April 2002) 'yes/no' criteria from daily table

Daily measurement	Derivation of 'yes/no' score
Deep infection away from wound site	If this is ever observed during daily, assign 'yes'
Evidence of abscess	If 'pus from drain' is seen during daily, assign 'yes'
Localised swelling	If ever observed during daily, assign 'yes'
Pain or tenderness	If ever observed during daily, assign 'yes'

Special notes

Owing to its incomplete and unreliable recording in the daily table, the surgeon's diagnosis field was not used at all. Instead, the surgeon's diagnosis was imputed in other ways at follow-up. Refer to the description of the follow-up summary do-file for further information [see *Follow-up preparation and follow-up summary (surgical site infection definitions)*].

Final product

The final product of the daily summary, CDC routine, is a data set that records against each wound the presence, absence, and in two cases frequency, of CDC-relevant adverse events.

Daily summary: ASEPSIS

In this step, the daily table was processed to obtain the first part of the ASEPSIS scoring routine; namely daily wound scores from week 1.

Daily data preparation

Initial steps taken to prepare daily observations are documented below:

1. replace with missing any implausible values on scores recorded as 'per cent of wound affected' (namely erythema, serous exudate, ooze in dressing, purulent exudate, wound separation)
2. de-duplicate daily observations so that no one date may contribute an inflated score. If two percentage scores are mistakenly recorded for one day, keep the larger of the two
3. make a new score called 'wound weeping' – a composite of the percentage scores recorded for 'serous exudate' and 'ooze in dressing'. This composite will preferentially take the percentage value for serous exudate, but if serous exudate score is missing or zero, it will look for and use any available scores for ooze in dressing.

Daily wound scoring

Following this initial clean-up, the percentage values captured on each day were assigned a number of points on the ASEPSIS scale, corresponding with *Table 43*. The table differs slightly from that originally published in the 1986 *Lancet* and reflects a modification to scoring rules made by Dr Peter Wilson around the time of establishment of the UCLH database. The table is also used in the UCLH database.

The resulting scores were added together so that each date has recorded against it the sum of all observed ASEPSIS points. There are some assumptions about missing data, which are demonstrated by *Table 44* below.

As can be seen, missing ASEPSIS points are assumed to be zero unless all points are missing for a given date, in which case the routine assigned a blank combined daily score (to be imputed later as will be explained).

Coping with missing days

To avoid any bias because of unequal numbers of available observations, the ASEPSIS calculation requires strictly 5 days' worth of combined points to be used in calculating total ASEPSIS scores during the first postoperative week.

If more than 5 days of complete data are available in the first week, then some days of observation are dropped, starting with weekend days.

TABLE 43 Daily ASEPSIS score assignment rules for measurements made as 'per cent of wound affected'

Measurement	Method of scoring (per cent of wound affected)					
Purulent exudate	0% = 0	1–20% = 2	21–40% = 4	41–60% = 6	61–80% = 8	81–100% = 10
Wound separation	0% = 0	1–20% = 2	21–40% = 4	41–60% = 6	61–80% = 8	81–100% = 10
Erythema	0% = 0	1–20% = 1	21–40% = 2	41–60% = 3	61–80% = 4	81–100% = 5
Wound weeping	0% = 0	1–20% = 1	21–40% = 2	41–60% = 3	61–80% = 4	81–100% = 5

TABLE 44 Example of calculation of daily ASEPSIS points

			ASEPSIS points (original percentage)				
Administration ID	Wound number	Date	Purulent exudate	Wound separation	Erythema	Wound weeping	Combined daily score
55	1	1 November 2002	0 (0)	0 (0)	1 (5)	1 (7)	2
55	1	4 November 2002					
55	1	7 November 2002	2 (11)	2 (18)	3 (56)	3 (48)	10
55	1	10 November 2002	4 (26)	2 (20)		1 (12)	7

If less than a full 5 days' worth of points is available to contribute to the total, a more elaborate method of coping with missing data is specified in the 1986 ASEPSIS definition. The definition requires that missing scores in the first week be either interpolated linearly from abutting observations; or propagated from the first/last available observation. *Table 45* gives a demonstration of these processes.

This step filled out missing scores, as seen in *Table 45*, to make 7 whole days of scores for the first week for each wound. The totals from these 7-day sets are subsequently scaled by 5/7 to correct the weight of their contribution.

In practice, wounds with ASEPSIS points scored on only a single day can quickly have scores imputed by scaling, leaving only wounds with 2, 3 or 4 days' worth of scores actually eligible for the above manipulation.

Final product

The product of the routine was a table that recorded for each wound, the ASEPSIS totals from the first postoperative week. All total scores were scaled to represent the equivalent contribution from 5 days' worth of points.

Follow-up preparation and follow-up summary (surgical site infection definitions)

These two do-files worked together, first to unite summary data obtained by previous steps, and then to calculate CDC, NINSS and ASEPSIS scores.

Merging tables to make master file

Follow-up was used as a 'master' data set to which the information distilled in previously described steps was attached. The diagram below clarifies the process using an example data set.

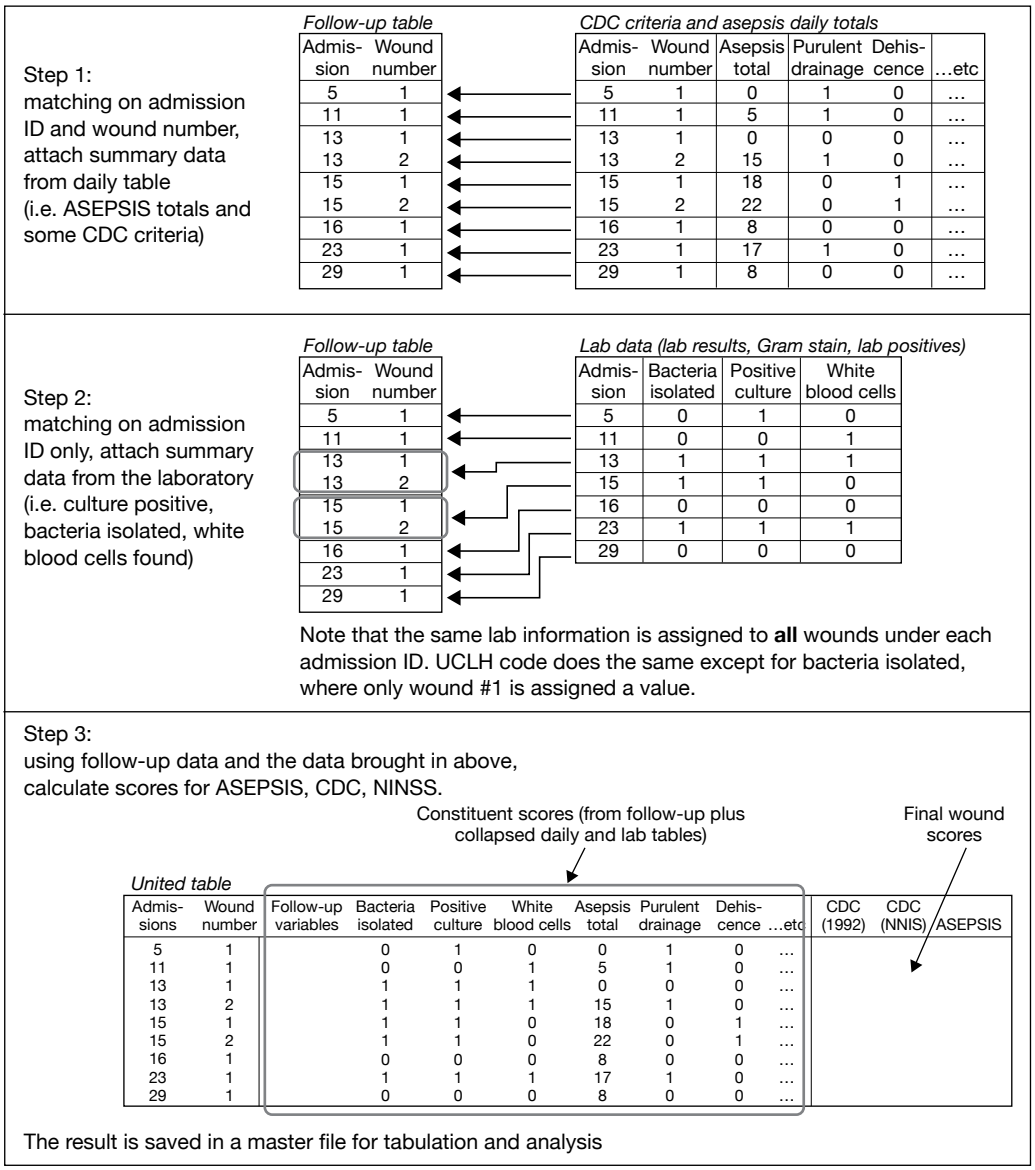
Wounds with missing laboratory data were kept and treated as if they had 'no' recorded against each of the three lab criteria (positive culture, WBCs and bacteria isolated). As mentioned previously, wounds with no daily records had already been discarded.

Step 3 in the table involved more than one computation. The details of these computations is described next.

TABLE 45 Example of algorithm to fill in missing daily ASEPSIS scores

Day since operation (1 = operation date)	Date of actual observation	Combined daily score	Imputation rule
1	<no observations>	6	Propagate from nearest observation
2	<no observations>	6	Propagate from nearest observation
3	3 July 2002	6	<real observations>
4	<no observations>	7.333	Interpolate between abutting observation
5	<no observations>	8.666	Interpolate between abutting observation
6	6 July 2002	10	<real observations>
7	<no observations>	10	Propagate from nearest observation
	Total	54	
Total (scaled to 5 days):		54 × 5/7 = 38.57	

Follow-up data with summary data tables



Handling missing data

After discussions with Dr Peter Wilson about the intention of participating research staff in respect of the database, it was apparent that binary variables representing criteria such as 'pain and tenderness' were usually left blank unless the diagnosis was positive.

Although legitimate zero values were more diligently recorded in some fields, the intention of research staff was impossible to clarify variable by variable.

Given the large number of variables involved in the CDC definition, and given Dr Peter Wilson's comments about how significant adverse events were detected, even whole days of observation were missed; the do-file treated all blank values for individual CDC criteria as legitimate zeros. The exception was when all criteria are blank, in which case the wound was excluded.

Although slightly more varied in its approach, the UCLH database made similar assumptions throughout when deriving variables for the CDC SSI definition.

Centers for Disease Control and Prevention classification of surgical site infection (1992 and Nosocomial Infection National Surveillance Scheme versions)

Save for a single variable, the NINSS adaptation of the CDC score is identical to the original 1992 definition. The 1992 version will thus be described.

Summary variables used

The 1992 CDC definition determines wound classification by the use of nested conditional statements which refer to criteria such as 'purulent drainage' and 'fever'. To make these criteria easier to manage and the calculations more transparent, the do-file made some new composite variables to address specific conditions in the CDC definition.

Table 46 describes the origin and nature of variables used to interpret CDC classifications and gives information about composite or new variables defined following creation of the master file.

Note, that some single variables were used in more than one of the composite variables and have been repeated in this table for clarity.

TABLE 46 Variables consulted in creation of CDC classification for SSI (1992 and NINSS versions)

Single variable	Source table	Description	Composite variables (where applicable)
April 2002	New	Whether wound was made in an operation after April 2002	
Pus	Daily	Wound discharged pus during daily observation	
Pus	Follow-up	Wound discharged pus on follow-up	
Pus 30	Daily	Wound discharged pus during daily observation (days 1–30)	
Dehisce	Follow-up	Wound separated on follow-up	Dehisce: true if either are seen
Dehisce	Daily	Wound separated during daily observation	
Erythema	Follow-up	Wound was red	Redpain 30: true if any of the four are seen
Redheat 30	Daily	Redness or heat during daily observation (days 1–30)	
Pain/tenderness 30	Daily	Pain or tenderness during daily observation (days 1–30)	
Localised swelling 30	Daily	Swelling around wound during daily observation (days 1–30)	
Redheat	Daily	Redness or heat during daily observation	
Pain/tenderness	Daily	Pain or tenderness during daily observation	
Localised swelling	Daily	Swelling around wound	
Fever	Daily	Fever > 38°C during daily observation	
Deep infection	Daily	Evidence of deep infection away from wound site	
Pus from drain	Daily	Pus from drain placed in wound (evidence of abscess)	
Pus count	Daily	Number of times pus seen during daily observation	
Fever count	Daily	Number of times fever seen during daily observation	
Positive culture	Lab results	Whether lab results for parent admission ID registered any organism-positive results	Organisms/WBC: NINSS criterion, both conditions must be true
WBCs	Gram stains	Whether WBCs were found in any Gram slides taken during the parent admission	
Antibiotics	Follow-up	Antibiotics prescribed by GP	Surgeon's diagnosis (general): imputed if any of the four are seen
Nurse	Follow-up	District nurse despatched	
Drain GA	Follow-up	Wound opened by surgeon (under GA)	
Drain LA	Follow-up	Wound opened by surgeon (under LA)	

TABLE 46 Variables consulted in creation of CDC classification for SSI (1992 and NINSS versions) *(continued)*

Single variable	Source table	Description	Composite variables (where applicable)
Surg. Super	Daily	Surgeon's explicit diagnosis of superficial infection during daily observation	Surgeon's diagnosis (specific): assign '1. Superficial' if Surg. Super seen, or if both Antibiotics and Drain LA seen
Antibiotics	Follow-up	Antibiotics prescribed by GP	
Drain LA	Follow-up	Wound opened by surgeon (under LA)	
Surg. Deep	Daily	Surgeon's explicit diagnosis of deep infection during daily observation	Surgeon's Diagnosis (Specific): Assign '2. Deep' if Surg. Deep seen, or if both Antibiotics and Drain GA seen
Antibiotics	Follow-up	Antibiotics prescribed by GP	
Drain GA	Follow-up	Wound opened by surgeon (under GA)	

GA, general anaesthetic; LA, local anaesthetic.

Assessment of final Center for Disease Control and Prevention score

Assessment of the status of a wound on the CDC 1992/NINSS scales was done through evaluation of the presence/absence of positive values in the variables from *Table 46*. To account for the fact that categories of the CDC definition were not mutually exclusive with respect to which variables in this data set, it was necessary to assign scores in a specific order to prevent the 'superficial' and 'deep' wound classifications 'stealing' wounds from one another. The criteria for infection categories and the order of their assignment are shown below.

To start, all wounds were assigned a CDC category of 'none'. Any wounds not meeting the criteria below are thus assumed to have no SSI.

Note, however, that wounds with 'no' daily data were already excluded from the data set.

Superficial

The first two conditions ('no' dehiscence, 'no' pus from drain) must be true to satisfy the definition, in addition to at least one of the four conditions (*Box 3*).

BOX 3 Definition criteria – superficial

Conditions

'no' dehiscence **AND** 'no' pus from drain **AND** one or more of:

- pus 30 (daily observation)
- positive culture
- redpain 30 (daily observation) **AND** drain GA/drain LA **AND** positive culture
- surgeon's diagnosis (specific) coded '1. Superficial'

GA, general anaesthetic; LA, local anaesthetic.

Deep infection

The first condition ('not already superficial') must be true, in addition to at least one of the four conditions (*Box 4*).

BOX 4 Definition criteria – deep infection

Conditions

Not already assigned superficial infection **AND** one or more of:

- [pus (daily observation) **OR** pus (follow-up)] **AND** dehiscence
- [dehiscence **AND** drain GA/drain LA] **AND** [fever **OR** pain/tenderness] **AND** positive culture
- [fever **AND** drain GA/drain LA] **OR** [pus count > 1 **AND** drain GA/drain LA]
- surgeon's diagnosis (specific) coded '2. Deep'

GA, general anaesthetic; LA, local anaesthetic.

Organ/space

If the daily variable deep infection is true, organ/space may be assigned if one or more of the following conditions is also true (*Box 5*).

BOX 5 Definition criteria – organ/space

Conditions

Deep infection **AND** one or more of:

- pus from drain (daily observation)
- positive culture
- [fever **AND** drain GA/drain LA] **OR** [pus count > 1 **AND** drain GA/drain LA]
- surgeon's diagnosis (general)

GA, general anaesthetic; LA, local anaesthetic.

Assessment of final Centre for Disease Control and Prevention (National Nosocomial National Surveillance Scheme version) score

The NINSS version of the CDC SSI definition differs significantly not only in its approach to bacteria and surgeon's diagnosis, but also with respect to its handling of the plainer wound diagnostics such as pus.

Superficial

The first two conditions ('no' dehiscence, 'no' pus from drain) must be true to satisfy the definition, in addition to at least one of the three conditions (*Box 6*).

BOX 6 Definition criteria – superficial

Conditions

'no' dehiscence, 'no' pus from drain **AND** one or more of:

- pus 30 (daily observation)
- organisms/WBC
- [at least two of: erythema, redheat 30, localised swelling 30, pain/tenderness 30] **AND** [(drain GA/drain LA **AND** positive culture) **OR** surgeon's diagnosis (specific) coded '1. Superficial']

GA, general anaesthetic; LA, local anaesthetic.

Deep infection

The first condition ('not already superficial') must be true, in addition to at least one of the four conditions (*Box 7*).

BOX 7 Definition criteria – deep infection

Conditions

Not already assigned superficial infection **AND** one or more of:

- [pus (daily observation) **OR** pus (follow-up)] **AND** dehiscence
- organisms/WBC
- [dehiscence **AND** drain GA/drain LA] **AND** [fever **OR** pain/tenderness] **AND** positive culture
- [fever **AND** drain GA/drain LA] **OR** [pus count > 1 **AND** drain GA/drain LA]

GA, general anaesthetic; LA, local anaesthetic.

Organ/space

If the daily variable deep infection is true, organ/space may be assigned if one or more of the conditions in *Box 8* is also true.

BOX 8 Definition criteria – organ/space

Conditions

Deep infection **AND** one or more of:

- pus from drain (daily observation)
- organisms/WBC
- [fever **AND** drain GA/drain LA] **OR** [pus count > 1 **AND** drain GA/drain LA]

GA, general anaesthetic; LA, local anaesthetic.

TABLE 47 Follow-up events that augment the ASEPSIS score accumulated in the first week of daily observation

Event recorded at follow-up	Points added to ASEPSIS score
Antibiotics administered for infection	10
Doctor drained wound under GA	10
Doctor drained wound under LA	5
Bacteria Isolated	10
Stay prolonged ≥ 14 days	5
Pus seen for first time post discharge	5
Nurse dispatched to attend to wound/wound dressing	5

GA, general anaesthetic; LA, local anaesthetic

TABLE 48 ASEPSIS categories by range of scores

Score range	Category
0–10	Wound healed satisfactorily
11–20	Disturbance of healing
21–30	Minor wound infection
31–40	Moderate wound infection
≥ 41	Severe wound infection

ASEPSIS score

ASEPSIS scores calculated from the first postoperative week in 'daily' were augmented with additional points assigned if certain events were recorded at follow-up. The scoring rules for this latter calculation came from a recent amendment to the original 1986 definition of Dr Peter Wilson and were consistent with those used by UCLH database (*Table 47*).

After adding the extra points assigned through the list in *Table 47*, the ASEPSIS score was saved, and also made into a categorical variable with the levels shown in *Table 48*.

Final output file

At this stage, the final file was complete and was available for summaries and analysis.

Appendix 4

Risk factors excluded from modelling

Summary of actions taken to exclude some risk factors from surgery-specific models

Category	Action
CABG	
Trauma	Excluded: CABG is rarely initiated in response to trauma
Wound class	Excluded: the vast majority of CABG wounds are uncontaminated
Large bowel surgery	
ASA score	Dropped observations: removed patients with ASA scores of 5
Abdominal hysterectomy	
Gender	Excluded: all female patients
Implant used	Excluded: insufficient SSI events at each level of variable for analysis
Trauma	Excluded: insufficient SSI events at each level of variable for analysis
Emergency surgery	Excluded: insufficient SSI events at each level of variable for analysis
Wound class	Excluded: almost all wounds have same classification
ASA score	Dropped observations: removed patients with ASA scores of 5
Hip replacement	
Implant used	Excluded: implant routine in this category of surgery
Wound class	Recoded: clean and clean/contaminated wound classifications combined
ASA score	Dropped observations: removed patients with ASA scores of 5
Knee replacement	
Implant used	Excluded: implant is standard procedure in this category of surgery
Trauma	Recoded: clean and clean/contaminated wound classifications combined
Emergency surgery	Recoded: clean and clean/contaminated wound classifications combined
Wound class	Recoded: wound classifications recoded to two categories – (1) clean or clean/contaminated (2) contaminated/dirty
ASA score	Dropped observations: removed patients with ASA scores of 5
Limb amputation	
Implant used	Excluded: insufficient SSI events at each level of variable for analysis
Trauma	Excluded: insufficient SSI events at each level of variable for analysis
ASA score	Dropped observations: removed patients with ASA scores of 5
Open reduction of fractures of long bones	
Trauma	Excluded: 'trauma' difficult to interpret in this type of surgery
Vascular surgery	
Wound class	Recoded: clean and clean/contaminated wound classifications combined
ASA score	Dropped observations: removed patients with ASA scores of 5

Category	Action
Small bowel surgery	
Implant used	Excluded: implants very rarely observed
Trauma	Excluded: this surgery is rarely initiated in response to trauma
Wound class	Recoded: clean and clean/contaminated wound classifications combined
ASA score	Dropped observations: removed patients with ASA scores of 5

Appendix 5

Univariable summaries of risk factors measured as continuous variables

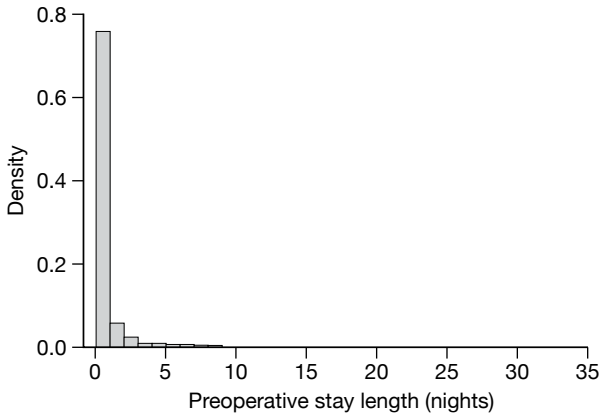


FIGURE 23 Preoperative stay length (nights).

TABLE 49 Preoperative stay length (nights)

Valid observations (*n*)	Mean	Standard deviation	Minimum	Maximum
112,152	1.8	3.1	0	32

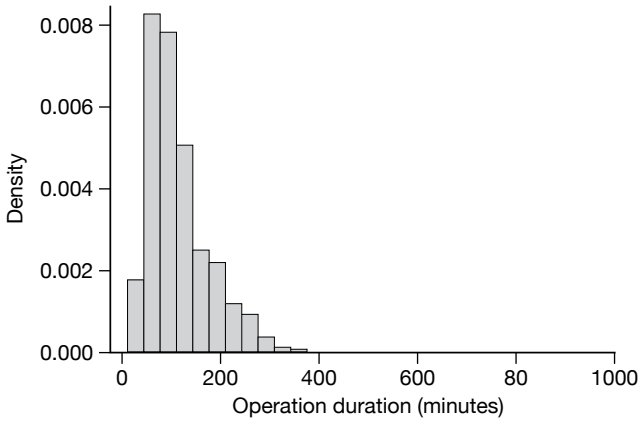


FIGURE 24 Operation duration.

TABLE 50 Operation duration

Valid observations (*n*)	Mean	Standard deviation	Minimum	Maximum
110,650	113.7	65.0	10	995

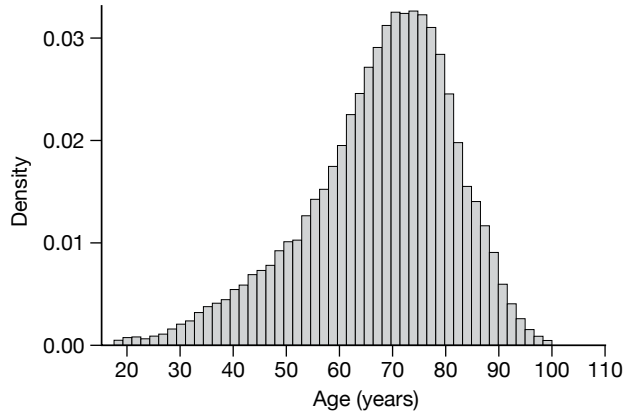


FIGURE 25 Age.

TABLE 51 Age

Valid observations (*n*)	Mean	Standard deviation	Minimum	Maximum
110,442	68.3	13.7	18.02	102.01

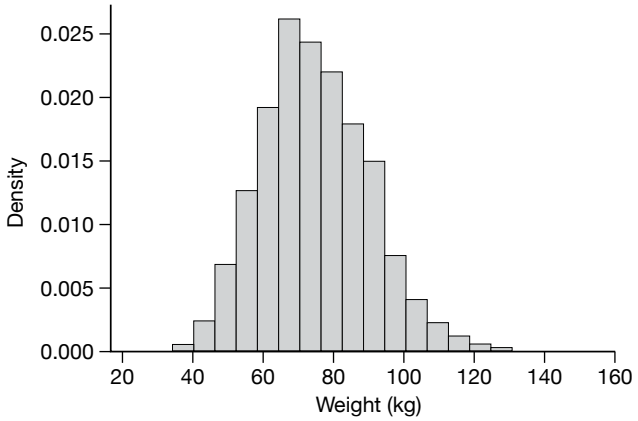


FIGURE 26 Weight.

TABLE 52 Weight

Valid observations (*n*)	Mean	Standard deviation	Minimum	Maximum
56,321	75.2	15.7	28	150

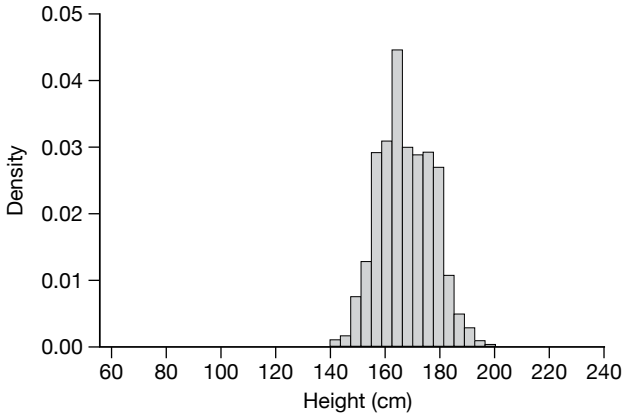


FIGURE 27 Height.

TABLE 53 Height

Valid observations (*n*)	Mean	Standard deviation	Minimum	Maximum
45,344	166.1	11.9	60	248

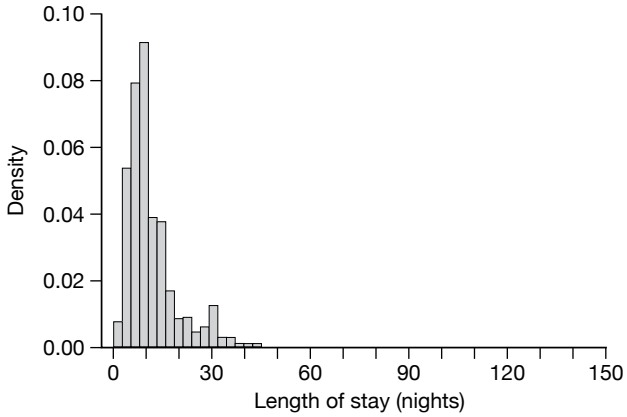


FIGURE 28 Length of hospital stay (nights).

TABLE 54 Length of hospital stay (nights)

Valid observations (*n*)	Mean	Standard deviation	Minimum	Maximum
112,738	12.0	10.5	0	130

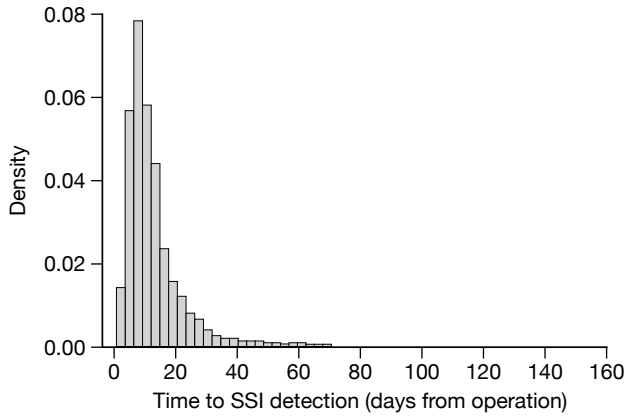


FIGURE 29 Time to SSI detection (days, SSI cases only).

TABLE 55 Time to SSI detection (days, SSI cases only)

Valid observations (*n*)	Mean	Standard deviation	Minimum	Maximum
5064	12.1	10.5	0	149

Tabulations of categorisations of potential risk factors other than components of National Nosocomial Infections Surveillance risk index, age and gender

Number of surgical site infections in categories of preoperative stay, with univariable odds ratio estimates, by surgery category

TABLE 56 Number of SSIs in categories of preoperative stay, with univariable OR estimates, by surgery category

Category of surgical procedure	Categories of preoperative stay (number of nights)				Missing	Main effect χ^2 (*p*-value)
	0	1	2–7	≥8		
Abdominal hysterectomy (*n* = 9119)						
SSI cases (*n*)	82 (2809)	169 (5744)	14 (464)	6 (96)	0 (6)	2.78 ($p = 0.43$)
OR (95% CI)	1.0 [Ref]	1.01 (0.77 to 1.32)	1.03 (0.58 to 1.84)	2.22 (0.94 to 5.21)		
Bile duct, liver, pancreatic surgery (*n* = 188)						
SSI cases (*n*)	1 (12)	11 (87)	8 (44)	1 (40)	0 (5)	4.09 ($p = 0.25$)
OR (95% CI)	1.0 [Ref]	1.59 (0.19 to 13.57)	2.44 (0.27 to 21.75)	0.28 (0.02 to 4.88)		
Cholecystectomy (*n* = 117)						
SSI cases (*n*)	0 (22)	3 (56)	0 (23)	2 (13)	0 (3)	1.43 ($p = 0.23$)
CABG (*n* = 15,384)						
SSI cases (*n*)	28 (534)	473 (11,218)	139 (2392)	97 (1131)	8 (109)	42.80 ($p < 0.01$)
OR (95% CI)	1.0 [Ref]	0.80 (0.54 to 1.18)	1.11 (0.73 to 1.69)	1.70 (1.10 to 2.62)		
Gastric surgery (*n* = 221)						
SSI cases (*n*)	5 (38)	14 (106)	5 (39)	4 (31)	4 (7)	0.21 ($p = 0.90$)
OR (95% CI)	1.0 [Ref]	1.00 (0.34 to 3.00)	0.97 (0.26 to 3.67)	0.98 (0.24 to 4.00)		
Hip replacement (*n* = 43,226)						
SSI cases (*n*)	136 (4102)	978 (31,699)	301 (5975)	87 (1175)	24 (275)	94.70 ($p < 0.01$)
OR (95% CI)	1.0 [Ref]	0.93 (0.77 to 1.11)	1.55 (1.26 to 1.90)	2.33 (1.77 to 3.08)		
Knee replacement (*n* = 22,585)						
SSI cases (*n*)	27 (1592)	402 (19,637)	29 (1071)	11 (204)	7 (81)	10.90 ($p = 0.01$)
OR (95% CI)	1.0 [Ref]	1.21 (0.82 to 1.79)	1.61 (0.95 to 2.74)	3.30 (1.61 to 6.77)		
Large bowel surgery (*n* = 9514)						
SSI cases (*n*)	107 (775)	391 (4779)	255 (2802)	143 (965)	20 (148)	52.90 ($p < 0.00$)
OR (95% CI)	1.0 [Ref]	0.56 (0.44 to 0.70)	0.63 (0.49 to 0.80)	1.09 (0.83 to 1.42)		

continued

TABLE 56 Number of SSIs in categories of preoperative stay, with univariable OR estimates, by surgery category *(continued)*

Category of surgical procedure	Categories of preoperative stay (number of nights)				Missing	Main effect χ^2 (*p*-value)
	0	**1**	**2–7**	**≥8**		
Limb amputation (*n*=1528)						
SSI cases (*n*)	16 (143)	34 (340)	74 (455)	84 (453)	32 (137)	13.90 ($p<0.00$)
OR (95% CI)	1.0 [Ref]	0.88 (0.47 to 1.65)	1.54 (0.87 to 2.74)	1.81 (1.02 to 3.20)		
Open reduction of fractures (*n*=4593)	**0**	**1**	**2**	**≥3**		
SSI cases (*n*)	55 (1167)	84 (1929)	33 (621)	54 (832)	4 (44)	5.66 ($p=0.13$)
OR (95% CI)	1.0 [Ref]	0.92 (0.65 to 1.30)	1.13 (0.73 to 1.77)	1.40 (0.95 to 2.07)		
Small bowel surgery (*n*=1091)	**0**	**1**	**2–6**	**≥7**		
SSI cases (*n*)	13 (178)	33 (494)	22 (217)	34 (171)	4 (31)	23.00 ($p=0.00$)
OR (95% CI)	1.0 [Ref]	0.91 (0.47 to 1.77)	1.43 (0.70 to 2.93)	3.15 (1.60 to 6.21)		
Vascular surgery (*n*=5502)						
SSI cases (*n*)	77 (892)	169 (2757)	142 (1227)	89 (556)	14 (70)	67.60 ($p=0.00$)
OR (95% CI)	1.0 [Ref]	0.69 (0.52 to 0.92)	1.39 (1.03 to 1.85)	2.02 (1.46 to 2.79)		
All surgery types (*n*=113,068)						Interaction: 72.2 ($p<0.01$)

Number of surgical site infections by year of admission, with univariable odds ratio estimates, by surgery category

TABLE 57 Number of SSIs by year of admission, with univariable OR estimates, by surgery category

Category of surgical procedure	Year of admission						Main effect χ^2 (*p*-value)
	1996	1997	1998	1999	2001	2002	
Abdominal hysterectomy (*n* = 9119)							
SSI cases (*n*)	3 (402)	34 (1585)	90 (2178)	49 (1567)	62 (1757)	33 (1630)	30.70 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	2.92 (0.89 to 9.54)	5.73 (1.81 to 18.2)	4.29 (1.33 to 13.8)	4.86 (1.52 to 15.6)	2.75 (0.84 to 9.01)	
Bile duct, liver, pancreatic surgery (*n* = 188)							
SSI cases (*n*)	4 (33)	9 (75)		1 (4)	0 (18)	7 (58)	0.49 ($p=0.92$)
OR (95% CI)	1.0 [Ref]	0.99 (0.28 to 3.47)		2.42 (0.20 to 29.2)		1.00 (0.27 to 3.69)	
Cholecystectomy (*n* = 117)							
SSI cases (*n*)	0 (24)	1 (20)	0 (3)	0 (14)	3 (26)	1 (30)	4.40 ($p=0.22$)
CABG (*n* = 15,384)							
SSI cases (*n*)	23 (584)	113 (3209)	96 (1971)	133 (2869)	122 (2855)	258 (3896)	41.00 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	0.89 (0.56 to 1.41)	1.25 (0.78 to 1.99)	1.19 (0.75 to 1.86)	1.09 (0.69 to 1.72)	1.73 (1.12 to 2.67)	
Gastric surgery (*n* = 221)							
SSI cases (*n*)	2 (23)	11 (36)	5 (34)	0 (16)	10 (63)	4 (49)	8.45 ($p=0.08$)
OR (95% CI)	1.0 [Ref]	4.62 (0.92 to 23.2)	1.81 (0.32 to 10.3)		1.98 (0.40 to 9.81)	0.93 (0.16 to 5.51)	
Hip replacement (*n*=43,226)							
SSI cases (*n*)	23 (886)	111 (4045)	214 (5243)	299 (8829)	426 (10,836)	453 (13,387)	21.20 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	1.06 (0.67 to 1.67)	1.60 (1.03 to 2.47)	1.32 (0.86 to 2.02)	1.54 (1.00 to 2.35)	1.31 (0.86 to 2.01)	
Knee replacement (*n* = 22,585)							
SSI cases (*n*)	15 (601)	40 (1994)	81 (2834)	90 (4123)	121 (5583)	129 (7450)	13.10 ($p=0.02$)
OR (95% CI)	1.0 [Ref]	0.80 (0.44 to 1.46)	1.15 (0.66 to 2.01)	0.87 (0.50 to 1.52)	0.87 (0.50 to 1.49)	0.69 (0.40 to 1.18)	
Large bowel surgery (*n* = 9514)							
SSI cases (*n*)	31 (249)	165 (1652)	144 (1386)	197 (1916)	203 (2328)	176 (1938)	7.10 ($p=0.21$)
OR (95% CI)	1.0 [Ref]	0.78 (0.52 to 1.17)	0.82 (0.54 to 1.23)	0.81 (0.54 to 1.21)	0.67 (0.45 to 1.01)	0.70 (0.47 to 1.06)	
Limb amputation (*n* = 1528)							
SSI cases (*n*)	8 (50)	44 (340)	23 (148)	61 (433)	67 (339)	37 (218)	7.17 ($p=0.21$)
OR (95% CI)	1.0 [Ref]	0.78 (0.34 to 1.77)	0.97 (0.40 to 2.32)	0.86 (0.39 to 1.92)	1.29 (0.58 to 2.88)	1.07 (0.47 to 2.47)	

continued

TABLE 57 Number of SSIs by year of admission, with univariable OR estimates, by surgery category *(continued)*

Category of surgical procedure	Year of admission						Main effect χ^2 (*p*-value)
	1996	1997	1998	1999	2001	2002	
Open reduction of fractures (*n* = 4593)							
SSI cases (*n*)	7 (298)	13 (312)	25 (445)	51 (731)	67 (1277)	67 (1530)	13.10 (*p* = 0.02)
OR (95% CI)	1.0 [Ref]	1.81 (0.71 to 4.59)	2.47 (1.06 to 5.80)	3.12 (1.40 to 6.95)	2.30 (1.05 to 5.07)	1.90 (0.87 to 4.19)	
Small bowel surgery (*n* = 1091)							
SSI cases (*n*)	5 (53)	6 (84)	12 (124)	13 (121)	37 (361)	33 (348)	0.98 (*p* = 0.96)
OR (95% CI)	1.0 [Ref]	0.74 (0.21 to 2.55)	1.03 (0.34 to 3.08)	1.16 (0.39 to 3.42)	1.10 (0.41 to 2.93)	1.01 (0.37 to 2.70)	
Vascular surgery (*n* = 5502)							
SSI cases (*n*)	9 (154)	64 (758)	83 (874)	142 (1504)	94 (1085)	99 (1127)	3.20 (*p* = 0.67)
OR (95% CI)	1.0 [Ref]	1.49 (0.72 to 3.05)	1.69 (0.83 to 3.44)	1.68 (0.84 to 3.37)	1.53 (0.75 to 3.10)	1.55 (0.77 to 3.14)	
All surgery types (*n* = 113,068)							Interaction: 112 (*p* < 0.01)

Number of surgical site infections by reasons for discontinuing surveillance, with univariable odds ratio estimates, by surgery category

TABLE 58 Number of SSIs by reasons for discontinuing surveillance, with univariable OR estimates, by surgery category

Category of surgical procedure	Discharged home/to another care facility	Died	Late reoperation (after 72 hours)	30th day postoperative stay (if no implant)	Follow-up completed after end of surveillance period	Missing	Main effect χ^2 (p-value)
Abdominal hysterectomy (n=9119)							
SSI cases (n)	251 (8977)	3 (19)	3 (23)	7 (14)	3 (21)	4 (65)	46.10 (p<0.01)
OR (95% CI)	1.0 [Ref]	6.52 (1.89 to 22.5)	5.21 (1.54 to 17.7)	34.8 (12.1 to 99.9)	5.79 (1.70 to 19.80)		
Bile duct, liver, pancreatic surgery (n=188)							
SSI cases (n)	10 (153)	5 (9)	4 (17)	1 (7)	1 (1)	0 (1)	16.40 (p<0.01)
OR (95% CI)	1.0 [Ref]	17.9 (4.14 to 77.2)	4.40 (1.21 to 16.0)	2.38 (0.26 to 21.8)			
Cholecystectomy (n=117)							
SSI cases (n)	3 (102)	1 (3)	1 (4)	0 (4)		0 (4)	5.20 (p=0.07)
OR (95% CI)	1.0 [Ref]	16.5 (1.15 to 236.20)	11.0 (0.87 to 139.20)				
CABG (n=15,384)							
SSI cases (n)	584 (14653)	35 (359)	48 (100)	40 (87)	23 (89)	15 (96)	367 (p<0.01)
OR (95% CI)	1.0 [Ref]	2.60 (1.82 to 3.72)	22.2 (14.9 to 33.2)	20.5 (13.3 to 31.5)	8.40 (5.19 to 13.6)		
Gastric surgery (n=221)							
SSI cases (n)	18 (170)	2 (17)	3 (9)	9 (21)	0 (2)	0 (2)	14.20 (p<0.01)
OR (95% CI)	1.0 [Ref]	1.13 (0.24 to 5.33)	4.22 (0.97 to 18.35)	6.33 (2.35 to 17.09)			
Hip replacement (n=43,226)							
SSI cases (n)	1155 (40,305)	99 (1064)	64 (206)	24 (195)	161 (1064)	23 (392)	575 (p<0.01)
OR (95% CI)	1.0 [Ref]	3.48 (2.80 to 4.31)	15.3 (11.3 to 20.6)	4.76 (3.09 to 7.32)	6.04 (5.06 to 7.22)		
Knee replacement (n=22,585)							
SSI cases (n)	410 (21,927)	4 (87)	15 (37)	8 (31)	30 (372)	9 (131)	139 (p<0.01)
OR (95% CI)	1.0 [Ref]	2.53 (0.92 to 6.93)	35.8 (18.4 to 69.5)	18.3 (8.12 to 41.1)	4.60 (3.13 to 6.77)		

continued

TABLE 58 Number of SSIs by reasons for discontinuing surveillance, with univariable OR estimates, by surgery category *(continued)*

Category of surgical procedure	Discharged home/to another care facility	Died	Late reoperation (after 72 hours)	30th day postoperative stay (if no implant)	Follow-up completed after end of surveillance period	Missing	Main effect χ^2 (*p*-value)
Large bowel surgery (*n* = 9514)							
SSI cases (*n*)	572 (8135)	68 (578)	112 (295)	140 (363)	13 (59)	16 (84)	465 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	1.76 (1.35 to 2.30)	8.09 (6.30 to 10.39)	8.30 (6.61 to 10.42)	3.74 (2.01 to 6.96)		
Limb amputation (*n* = 1528)							
SSI cases (*n*)	67 (904)	22 (120)	55 (169)	94 (314)	2 (11)	0 (10)	126 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	2.80 (1.66 to 4.74)	6.03 (4.01 to 9.05)	5.34 (3.77 to 7.55)	2.78 (0.59 to 13.10)		
Open reduction of fractures (*n* = 4593)							
SSI cases (*n*)	161 (3886)	17 (171)	7 (71)	15 (123)	28 (301)	2 (41)	35.30 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	2.55 (1.51 to 4.32)	2.53 (1.14 to 5.61)	3.21 (1.83 to 5.64)	2.37 (1.56 to 3.61)		
Small bowel surgery (*n* = 1091)							
SSI cases (*n*)	66 (852)	7 (68)	11 (62)	18 (83)	3 (10)	1 (16)	21.40 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	1.37 (0.60 to 3.11)	2.57 (1.28 to 5.16)	3.30 (1.85 to 5.89)	5.10 (1.29 to 20.20)		
Vascular surgery (*n* = 5502)							
SSI cases (*n*)	341 (4652)	38 (414)	31 (138)	55 (168)	23 (101)	3 (29)	130 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	1.28 (0.90 to 1.82)	3.66 (2.42 to 5.55)	6.15 (4.38 to 8.65)	3.73 (2.31 to 6.01)		
All surgery types (*n* = 113,068)							Interaction: 210 ($p<0.01$)

Number of surgical site infections after non-emergency and emergency procedures, with univariable odds ratio estimates for emergency procedures, by surgery category

TABLE 59 Number of SSIs after non-emergency and emergency procedures, with univariable OR estimates for emergency procedures, by surgery category

	Procedure			
Category of surgical procedure	**Non-emergency**	**Emergency**	**Missing**	**Main effect χ^2 (*p*-value)**
Abdominal hysterectomy (*n* = 9119)				
SSI cases (*n*)	261 (8886)	3 (43)	7 (190)	1.78 ($p = 0.18$)
OR (95% CI)	1.0 [Ref]	2.48 (0.76 to 8.06)		
Bile duct, liver, pancreatic surgery (*n* = 188)				
SSI cases (*n*)	21 (177)	0 (11)		
OR (95% CI)	1.0 [Ref]			
Cholecystectomy (*n* = 117)				
SSI cases (*n*)	3 (105)	1 (11)	1 (1)	0.85 ($p = 0.36$)
OR (95% CI)	1.0 [Ref]	3.40 (0.32 to 35.8)		
CABG (*n* = 15,384)				
SSI cases (*n*)	695 (14,612)	41 (550)	9 (222)	7.27 ($p = 0.01$)
OR (95% CI)	1.0 [Ref]	1.61 (1.16 to 2.24)		
Gastric surgery (*n* = 221)				
SSI cases (*n*)	20 (169)	12 (52)		3.72 ($p = 0.05$)
OR (95% CI)	1.0 [Ref]	2.23 (1.01 to 4.96)		
Hip replacement (*n* = 43,226)				
SSI cases (*n*)	1291 (38,924)	212 (3721)	23 (581)	48.80 ($p < 0.01$)
OR (95% CI)	1.0 [Ref]	1.76 (1.52 to 2.04)		
Knee replacement (*n* = 22,585)				
SSI cases (*n*)	461 (22,202)	3 (50)	12 (333)	2.51 ($p = 0.11$)
OR (95% CI)	1.0 [Ref]	3.01 (0.93 to 9.71)		
Large bowel surgery (*n* = 9514)				
SSI cases (*n*)	680 (8066)	237 (1354)	4 (94)	93.30 ($p < 0.01$)
OR (95% CI)	1.0 [Ref]	2.30 (1.96 to 2.71)		
Limb amputation (*n* = 1528)				
SSI cases (*n*)	185 (1223)	53 (286)	2 (19)	1.96 ($p = 0.16$)
OR (95% CI)	1.0 [Ref]	1.28 (0.91 to 1.79)		
Open reduction of fractures (*n* = 4593)				
SSI cases (*n*)	154 (3578)	69 (968)	7 (47)	11.90 ($p < 0.01$)
OR (95% CI)	1.0 [Ref]	1.71 (1.27 to 2.29)		
Small bowel surgery (*n* = 1091)				
SSI cases (*n*)	80 (857)	23 (226)	3 (8)	0.15 ($p = 0.70$)
OR (95% CI)	1.0 [Ref]	1.10 (0.67 to 1.79)		

continued

TABLE 59 Number of SSIs after non-emergency and emergency procedures, with univariable OR estimates for emergency procedures, by surgery category *(continued)*

	Procedure			
Category of surgical procedure	**Non-emergency**	**Emergency**	**Missing**	**Main effect χ^2 (*p*-value)**
Vascular surgery ($n=5502$)				
SSI cases (n)	378 (4478)	103 (959)	10 (65)	4.94 ($p=0.03$)
OR (95% CI)	1.0 [Ref]	1.31 (1.04 to 1.64)		
All surgery types ($n=113,068$)				Interaction: 26.0 ($p<0.01$)

Number of surgical site infections after procedures using or not using an implant, with univariable odds ratio estimates for emergency procedures, by surgery category

TABLE 60 Number of SSIs after procedures using or not using an implant, with univariable OR estimates for emergency procedures, by surgery category

Category of surgical procedure	No implant used	Implant used	Missing	Main effect χ^2 (*p*-value)
Abdominal hysterectomy (*n* = 9119)				
SSI cases (*n*)	271 (9110)	0 (6)	0 (3)	
OR (95% CI)	1.0 [Ref]			
Bile duct, liver, pancreatic surgery (*n* = 188)				
SSI cases (*n*)	20 (185)	1 (3)		1.06 (*p* = 0.30)
OR (95% CI)	1.0 [Ref]	4.13 (0.36 to 47.60)		
Cholecystectomy (*n* = 117)				
SSI cases (*n*)	5 (115)	0 (1)		Not estimable
CABG (*n* = 15,384)				
SSI cases (*n*)	307 (7447)	436 (7883)	0 (1)	17.16 (*p* = 0.00)
OR (95% CI)	1.0 [Ref]	1.36 (1.17 to 1.58)		
Gastric surgery (*n* = 221)				
SSI cases (*n*)	32 (216)	0 (5)		
OR (95% CI)	1.0 [Ref]		2 (54)	
Hip replacement (*n* = 43,226)				
SSI cases (*n*)		1526 (43,226)		
Knee replacement (*n* = 22,585)				
SSI cases (*n*)		476 (22,585)		
Large bowel surgery (*n* = 9514)				
SSI cases (*n*)	909 (9385)	3 (47)	4 (37)	0.66 (*p* = 0.42)
OR (95% CI)	1.0 [Ref]	0.64 (0.20 to 2.05)		
Limb amputation (*n* = 1528)				
SSI cases (*n*)	238 (1510)	2 (13)	0 (5)	0.00 (*p* = 0.97)
OR (95% CI)	1.0 [Ref]	0.97 (0.21 to 4.41)		
Open reduction of fractures (*n* = 4593)				
SSI cases (*n*)	19 (687)	211 (3900)	0 (6)	9.90 (*p* = 0.00)
OR (95% CI)	1.0 [Ref]	2.01 (1.25 to 3.24)		
Small bowel surgery (*n* = 1091)				
SSI cases (*n*)	106 (1076)	0 (12)	0 (3)	
Vascular surgery (*n* = 5502)				
SSI cases (*n*)	253 (2618)	234 (2842)	4 (42)	3.43 (*p* = 0.06)
OR (95% CI)	1.0 [Ref]	0.84 (0.70 to 1.01)		
All surgery types (*n* = 113,068)				Interaction: 23.3 (*p* = 0.00)

Number of surgical site infections after procedures involving trauma or not, with univariable odds ratio estimates for emergency procedures, by surgery category

TABLE 61 Number of SSIs after procedures involving trauma or not, with univariable OR estimates for emergency procedures, by surgery category

Category of surgical procedure	Not involving trauma	Involving trauma	Missing	Main effect χ^2 (*p*-value)
Abdominal hysterectomy ($n=9119$)				
SSI cases (*n*)	239 (7522)	1 (36)	31 (1561)	0.02 ($p=0.89$)
OR (95% CI)	1.0 [Ref]	0.87 (0.12 to 6.38)		
Bile duct, liver, pancreatic surgery ($n=188$)				
SSI cases (*n*)	9 (81)	0 (3)	12 (104)	
Cholecystectomy ($n=117$)				
SSI cases (*n*)	4 (75)	0 (1)	1 (41)	
CABG ($n=15,384$)				
SSI cases (*n*)	599 (11446)	1 (33)	145 (3905)	0.38 ($p=0.54$)
OR (95% CI)	1.0 [Ref]	0.57 (0.08 to 4.15)		
Gastric surgery ($n=221$)				
SSI cases (*n*)	19 (158)	0 (3)	13 (60)	
Hip replacement ($n=43,226$)				
SSI cases (*n*)	838 (29,345)	573 (9576)	115 (4305)	181.70 ($p<0.01$)
OR (95% CI)	1.0 [Ref]	2.17 (1.94 to 2.41)		
Knee replacement ($n=22,585$)				
SSI cases (*n*)	414 (20,051)	2 (140)	60 (2394)	0.31 ($p=0.58$)
OR (95% CI)	1.0 [Ref]	0.69 (0.17 to 2.79)		
Large bowel surgery ($n=9514$)				
SSI cases (*n*)	725 (7697)	8 (35)	183 (1737)	5.48 ($p=0.02$)
OR (95% CI)	1.0 [Ref]	2.85 (1.29 to 6.30)		
Limb amputation ($n=1528$)				
SSI cases (*n*)	190 (1138)	6 (54)	44 (336)	1.29 ($p=0.26$)
OR (95% CI)	1.0 [Ref]	0.62 (0.26 to 1.48)		
Open reduction of fractures ($n=4593$)				
SSI cases (*n*)	6 (151)	207 (3903)	17 (539)	0.56 ($p=0.45$)
OR (95% CI)	1.0 [Ref]	1.35 (0.59 to 3.10)		
Small bowel surgery ($n=1091$)				
SSI cases (*n*)	88 (939)	3 (11)	15 (141)	2.84 ($p=0.09$)
OR (95% CI)	1.0 [Ref]	3.63 (0.94 to 13.90)		
Vascular surgery ($n=5502$)				
SSI cases (*n*)	437 (4791)	5 (60)	49 (651)	0.05 ($p=0.83$)
OR (95% CI)	1.0 [Ref]	0.91 (0.36 to 2.27)		
All surgery types ($n=113,068$)				Interaction: 18.2 ($p=0.02$)

Appendix 6

Alternatives to the National Nosocomial Infections Surveillance risk index: a test using large bowel surgery data

Introduction

The NNIS risk index is a combined score that distils information from patient- and operation-related variables to give an estimate of SSI risk. Three variables are dichotomised, then added together, as shown in *Table 62*.

It has been observed previously that the components of the NNIS risk index score often do not vary within specific categories of surgery. This gives the score less room to explain SSI than its notional range of 0–3 might initially suggest. For example, in CABG operations it is extremely rare for wounds to be classed as 'dirty' or 'contaminated', meaning that the upper score of 3 is rarely observed.

The research team proposed a set of logistic regression analyses to determine whether or not alternative combinations of the NNIS risk index's 'ingredients' could give a better model of SSI than the index itself. The analyses were done for large bowel surgery – a category of surgery where all three constituents of NNIS risk index are known to vary. Below are summaries of the NINSS risk index (*Tables 63* and *64* and *Figures 30* and *31*) and its ingredients for large bowel surgery observations. Note that, for a fair comparison of the scores, it was necessary to drop all observations with missing data (n=1890), cutting down the original number of observations from 9266 to 7376. All of the following summaries and analyses were obtained from this trimmed sample.

TABLE 62 National Nosocomial Infections Surveillance risk index calculation

Risk factor	Treatment for NNIS risk index
ASA score	Dichotomise to:
	0. ASA score 1–2
	1. ASA score ≥ 3
Wound classification	Dichotomise to:
	0. Clean or clean/contaminated
	1. Contaminated/dirty
Operation duration	Dichotomise to:
	0. Duration is below 75th percentile for associated category of surgery
	1. Duration exceeds 75th percentile for associated category of surgery
	(Note the '75th percentile' is a fixed value specified by the HPA, and is not to be calculated from the NINSS data set)
NNIS risk index	**Sum above 3 binary scores**

HPA, Health Protection Agency.

TABLE 63 American Association of Anesthesiologists score by NNIS risk index

	Risk index			
ASA score	**0**	**1**	**2**	**3**
Class 1	747	380	48	
Class 2	2247	1190	167	
Class 3		1265	756	85
Class 4		217	190	48
Class 5		18	12	6

TABLE 64 Wound classification by NNIS risk index

	Risk index			
Wound class	**0**	**1**	**2**	**3**
Clean	19	12	1	
Clean/contaminated	2975	2300	409	
Contaminated		606	553	92
Dirty		152	210	47

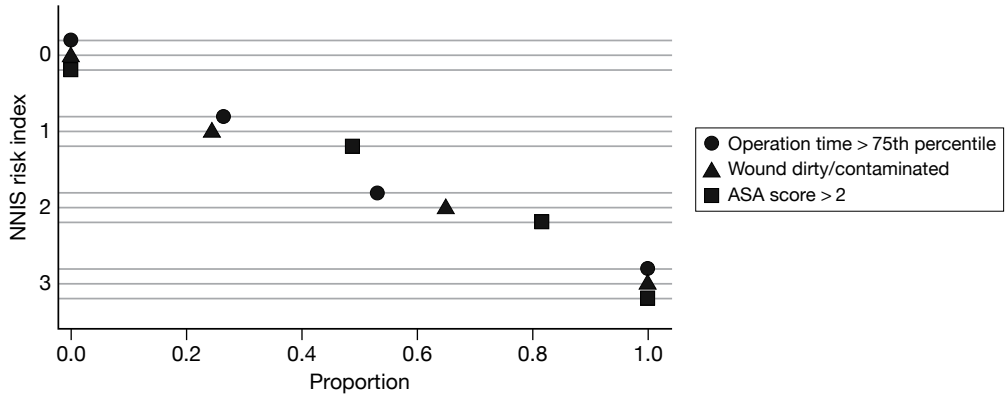


FIGURE 30 Percentage incidence of NNIS risk index's constituents (dichotomised) by risk index score.

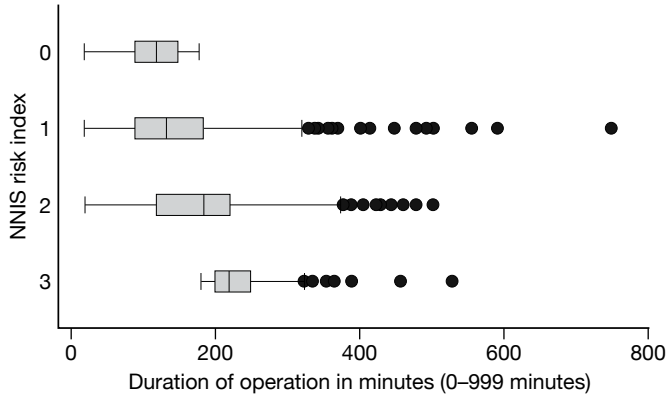


FIGURE 31 Operation duration by NNIS risk index.

Logistic regression analysis for large bowel surgery

Next, logistic regression analyses were carried out to determine which combination of the NNIS risk index and/or its 'ingredients' would give the best fit for SSI. The models fitted all categories of ASA class, continuous operation duration and operation duration squared as well as the full categories for wound classification. The most relevant STATA output is shown below after the tabular summary (*Tables 65–71*).

Conclusion

The findings demonstrate the value in seeking to model the constituent variables of the NNIS risk score.

TABLE 65 Summary of diagnostic analyses to determine 'optimal from NNIS risk index (large bowel surgery data only)

Variable/model	Model log likelihood	Comment
NNIS risk index only	–2291.7914	This score and its constituents are arithmetically connected. In this analysis it will be preferable to work with these constituents rather than the score as it will enable more detailed diagnosis of the NNIS scale in each category of surgery
NNIS risk index ingredients:	–2290.5213	
ASA score dichotomised		
Wound classification dichotomised		
Operation duration dichotomised		
NNIS – detailed ingredients:	–2258.2848	Each of these three 'ingredients' gave a significant increase in log-likelihood when they were used in preference to their dichotomised versions
ASA score full		
Wound classification full		
Operation duration		
Operation duration^2		
Advanced ingredients + NNIS risk index ingredients	–2258.0314	Dichotomised versions of the variables could be removed from a combined model with no significant impact on log likelihood

TABLE 66 Model: NNIS risk index only

Logistic regression				Number of obs = 7376		
				LR chi2(3) = 143.12		
				Prob > chi2 = < 0.0001		
Log likelihood = –2291.7914				Pseudo R2 = 0.0303		
ssi	**Odds Ratio**	**Std. Err.**	**z**	**P>|z|**	**[95% Conf. Interval]**	
Risk index = 0	0.5307186	0.0521155	–6.45	0.000	0.4378023	0.643355
Risk index = 2	1.757446	0.1720518	5.76	0.000	1.450609	2.129185
Risk index = 3	2.694197	0.5602701	4.77	0.000	1.792331	4.049864

TABLE 67 Model: NNIS risk index basic ingredients – i.e. 3 × dichotomised variables

Logistic regression				Number of obs = 7376		
				LR chi2(3) = 145.66		
				Prob > chi2 = < 0.0001		
Log likelihood = –2290.5213				Pseudo R2 = 0.0308		
ssi	**Odds Ratio**	**Std. Err.**	**z**	**P>|z|**	**[95% Conf. Interval]**	
Wound classification dichotomised	1.933199	0.1630556	7.82	0.000	1.638634	2.280716
Operation duration dichotomised	1.561279	0.1386117	5.02	0.000	1.311928	1.858022
ASA score dichotomised	1.827388	0.1453015	7.58	0.000	1.563684	2.135564

TABLE 68 Model: NNIS risk index detailed ingredients – i.e. 3 × variables with all available detail, not dichotomised

Logistic regression				Number of obs = 7376		
				LR chi2(9) = 210.13		
				Prob > chi2 = < 0.0001		
Log likelihood = –2258.2848				Pseudo R2 = 0.0445		
ssi	**Odds Ratio**	**Std. Err.**	**z**	**P>|z|**	**[95% Conf. Interval]**	
Wound class = 1	0.8439923	0.6203838	–0.23	0.818	0.1998276	3.564688
Wound class = 3	1.613929	0.1605062	4.81	0.000	1.328104	1.961268
Wound class = 4	2.891777	0.3799399	8.08	0.000	2.235263	3.741115
ASA score = 1	0.7161574	0.098869	–2.42	0.016	0.5463814	0.9386874
ASA score = 3	1.510218	0.137437	4.53	0.000	1.263503	1.805107
ASA score = 4	2.414941	0.3269817	6.51	0.000	1.852057	3.148899
ASA score = 5	0.9861356	0.5397987	–0.03	0.980	0.3372867	2.883195
Operation duration	1.007263	0.0018719	3.89	0.000	1.003601	1.010938
Operation duration squared	0.9999915	$4.74e^{-06}$	–1.80	0.073	0.9999822	1.000001

TABLE 69 Model: detailed and simple ingredients from NNIS risk index

note: _lwoundclas_3 dropped due to collinearity
note: _lasascore_4 dropped due to collinearity
Logistic regression — Number of obs = 7376
LR chi2(10) = 210.64
Prob > chi2 = < 0.0001
Log likelihood = –2258.0314 — Pseudo R2 = 0.0446

ssi	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf. Interval]	
Wound class = 1	0.8471088	0.6226857	–0.23	0.821	0.2005603	3.577942
Wound class = 4	1.784371	0.2658577	3.89	0.000	1.332486	2.389504
ASA score = 1	0.7164356	0.0989056	–2.42	0.016	0.5465964	0.9390475
ASA score = 3	0.6244209	0.0860932	–3.42	0.001	0.4765587	0.8181605
ASA score = 5	0.4084801	0.2267785	–1.61	0.107	0.1375953	1.212657
Operation duration	1.007857	0.0020362	3.87	0.000	1.003874	1.011855
Operation duration squared	0.9999913	$4.67e^{-06}$	–1.87	0.062	0.9999821	1
ASA score dichotomised	1.618774	0.1611362	4.84	0.000	1.331852	1.967509
Operation duration dichotomised	0.9049873	0.1270096	–0.71	0.477	0.6873556	1.191526
Wound classification dichotomised	2.418036	0.3274673	6.52	0.000	1.854331	3.153105

Wound class = 3 dropped due to collinearity.
ASA class = 4 dropped due to collinearity.

TABLE 70 Likelihood ratio test: basic ingredients only versus combined model

likelihood-ratio test LR chi2(7) = 64.98
(Assumption: ni nested in nf_ni) Prob > chi2 = < 0.0001

TABLE 71 Likelihood ratio test: detailed ingredients only versus combined model

likelihood-ratio test LR chi2(1) = 0.51
(Assumption: nf nested in nf_ni) Prob > chi2 = 0.4765

Health Technology Assessment programme

HTA Commissioning Board *(continued)*

Professor Barney Reeves, Professorial Research Fellow in Health Services Research, Department of Clinical Science, University of Bristol

Professor Martin Underwood, Professor of Primary Care Research, Warwick Medical School, University of Warwick

Professor Marion Walker, Professor in Stroke Rehabilitation, Associate Director UK Stroke Research Network, University of Nottingham

Dr Duncan Young, Senior Clinical Lecturer and Consultant, Nuffield Department of Anaesthetics, University of Oxford

Observers

Dr Tom Foulks, Medical Research Council

Dr Kay Pattison, Senior NIHR Programme Manager, Department of Health

HTA Clinical Evaluation and Trials Board

Chair,
Professor Sallie Lamb,
Director, Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick and Professor of Rehabilitation, Nuffield Department of Orthopaedic, Rheumatology and Musculoskeletal Sciences, University of Oxford

Deputy Chair,
Professor Jenny Hewison,
Professor of the Psychology of Health Care, Leeds Institute of Health Sciences, University of Leeds

Programme Director,
Professor Tom Walley, CBE,
Director, NIHR HTA programme, Professor of Clinical Pharmacology, University of Liverpool

Members

Professor Keith Abrams, Professor of Medical Statistics, Department of Health Sciences, University of Leicester

Professor Martin Bland, Professor of Health Statistics, Department of Health Sciences, University of York

Professor Jane Blazeby, Professor of Surgery and Consultant Upper GI Surgeon, Department of Social Medicine, University of Bristol

Professor Julia M Brown, Director, Clinical Trials Research Unit, University of Leeds

Professor Alistair Burns, Professor of Old Age Psychiatry, Psychiatry Research Group, School of Community-Based Medicine, The University of Manchester & National Clinical Director for Dementia, Department of Health

Dr Jennifer Burr, Director, Centre for Healthcare Randomised trials (CHART), University of Aberdeen

Professor Linda Davies, Professor of Health Economics, Health Sciences Research Group, University of Manchester

Professor Simon Gilbody, Prof of Psych Medicine and Health Services Research, Department of Health Sciences, University of York

Professor Steven Goodacre, Professor and Consultant in Emergency Medicine, School of Health and Related Research, University of Sheffield

Professor Dyfrig Hughes, Professor of Pharmacoeconomics, Centre for Economics and Policy in Health, Institute of Medical and Social Care Research, Bangor University

Professor Paul Jones, Professor of Respiratory Medicine, Department of Cardiac and Vascular Science, St George's Hospital Medical School, University of London

Professor Khalid Khan, Professor of Women's Health and Clinical Epidemiology, Barts and the London School of Medicine, Queen Mary, University of London

Professor Richard J McManus, Professor of Primary Care Cardiovascular Research, Primary Care Clinical Sciences Building, University of Birmingham

Professor Helen Rodgers, Professor of Stroke Care, Institute for Ageing and Health, Newcastle University

Professor Ken Stein, Professor of Public Health, Peninsula Technology Assessment Group, Peninsula College of Medicine and Dentistry, Universities of Exeter and Plymouth

Professor Jonathan Sterne, Professor of Medical Statistics and Epidemiology, Department of Social Medicine, University of Bristol

Mr Andy Vail, Senior Lecturer, Health Sciences Research Group, University of Manchester

Professor Clare Wilkinson, Professor of General Practice and Director of Research North Wales Clinical School, Department of Primary Care and Public Health, Cardiff University

Dr Ian B Wilkinson, Senior Lecturer and Honorary Consultant, Clinical Pharmacology Unit, Department of Medicine, University of Cambridge

Observers

Ms Kate Law, Director of Clinical Trials, Cancer Research UK

Dr Morven Roberts, Clinical Trials Manager, Health Services and Public Health Services Board, Medical Research Council

Diagnostic Technologies and Screening Panel

Members

Chair,
Professor Lindsay Wilson Turnbull,
Scientific Director of the Centre for Magnetic Resonance Investigations and YCR Professor of Radiology, Hull Royal Infirmary

Professor Judith E Adams,
Consultant Radiologist, Manchester Royal Infirmary, Central Manchester & Manchester Children's University Hospitals NHS Trust, and Professor of Diagnostic Radiology, University of Manchester

Mr Angus S Arunkalaivanan,
Honorary Senior Lecturer, University of Birmingham and Consultant Urogynaecologist and Obstetrician, City Hospital, Birmingham

Dr Diana Baralle,
Consultant and Senior Lecturer in Clinical Genetics, University of Southampton

Dr Stephanie Dancer,
Consultant Microbiologist, Hairmyres Hospital, East Kilbride

Dr Diane Eccles,
Professor of Cancer Genetics, Wessex Clinical Genetics Service, Princess Anne Hospital

Dr Trevor Friedman,
Consultant Liason Psychiatrist, Brandon Unit, Leicester General Hospital

Dr Ron Gray,
Consultant, National Perinatal Epidemiology Unit, Institute of Health Sciences, University of Oxford

Professor Paul D Griffiths,
Professor of Radiology, Academic Unit of Radiology, University of Sheffield

Mr Martin Hooper,
Public contributor

Professor Anthony Robert Kendrick,
Associate Dean for Clinical Research and Professor of Primary Medical Care, University of Southampton

Dr Nicola Lennard,
Senior Medical Officer, MHRA

Dr Anne Mackie,
Director of Programmes, UK National Screening Committee, London

Mr David Mathew,
Public contributor

Dr Michael Millar,
Consultant Senior Lecturer in Microbiology, Department of Pathology & Microbiology, Barts and The London NHS Trust, Royal London Hospital

Mrs Una Rennard,
Public contributor

Dr Stuart Smellie,
Consultant in Clinical Pathology, Bishop Auckland General Hospital

Ms Jane Smith,
Consultant Ultrasound Practitioner, Leeds Teaching Hospital NHS Trust, Leeds

Dr Allison Streetly,
Programme Director, NHS Sickle Cell and Thalassaemia Screening Programme, King's College School of Medicine

Dr Matthew Thompson,
Senior Clinical Scientist and GP, Department of Primary Health Care, University of Oxford

Dr Alan J Williams,
Consultant Physician, General and Respiratory Medicine, The Royal Bournemouth Hospital

Observers

Dr Tim Elliott,
Team Leader, Cancer Screening, Department of Health

Dr Joanna Jenkinson,
Board Secretary, Neurosciences and Mental Health Board (NMHB), Medical Research Council

Professor Julietta Patnick,
Director, NHS Cancer Screening Programme, Sheffield

Dr Kay Pattison,
Senior NIHR Programme Manager, Department of Health

Professor Tom Walley, CBE,
Director, NIHR HTA programme, Professor of Clinical Pharmacology, University of Liverpool

Dr Ursula Wells,
Principal Research Officer, Policy Research Programme, Department of Health

Disease Prevention Panel

Members

Chair,
Professor Margaret Thorogood,
Professor of Epidemiology, University of Warwick Medical School, Coventry

Dr Robert Cook,
Clinical Programmes Director, Bazian Ltd, London

Dr Colin Greaves,
Senior Research Fellow, Peninsula Medical School (Primary Care)

Mr Michael Head,
Public contributor

Professor Cathy Jackson,
Professor of Primary Care Medicine, Bute Medical School, University of St Andrews

Dr Russell Jago,
Senior Lecturer in Exercise, Nutrition and Health, Centre for Sport, Exercise and Health, University of Bristol

Dr Julie Mytton,
Consultant in Child Public Health, NHS Bristol

Professor Irwin Nazareth,
Professor of Primary Care and Director, Department of Primary Care and Population Sciences, University College London

Dr Richard Richards,
Assistant Director of Public Health, Derbyshire County Primary Care Trust

Professor Ian Roberts,
Professor of Epidemiology and Public Health, London School of Hygiene & Tropical Medicine

Dr Kenneth Robertson,
Consultant Paediatrician, Royal Hospital for Sick Children, Glasgow

Dr Catherine Swann,
Associate Director, Centre for Public Health Excellence, NICE

Mrs Jean Thurston,
Public contributor

Professor David Weller,
Head, School of Clinical Science and Community Health, University of Edinburgh

Observers

Ms Christine McGuire,
Research & Development, Department of Health

Dr Kay Pattison,
Senior NIHR Programme Manager, Department of Health

Professor Tom Walley, CBE,
Director, NIHR HTA programme, Professor of Clinical Pharmacology, University of Liverpool

External Devices and Physical Therapies Panel

Members

Chair,
Dr John Pounsford,
Consultant Physician North Bristol NHS Trust

Deputy Chair,
Professor E Andrea Nelson,
Reader in Wound Healing and Director of Research, University of Leeds

Professor Bipin Bhakta,
Charterhouse Professor in Rehabilitation Medicine, University of Leeds

Mrs Penny Calder,
Public contributor

Dr Dawn Carnes,
Senior Research Fellow, Barts and the London School of Medicine and Dentistry

Dr Emma Clark,
Clinician Scientist Fellow & Cons. Rheumatologist, University of Bristol

Mrs Anthea De Barton-Watson,
Public contributor

Professor Nadine Foster,
Professor of Musculoskeletal Health in Primary Care Arthritis Research, Keele University

Dr Shaheen Hamdy,
Clinical Senior Lecturer and Consultant Physician, University of Manchester

Professor Christine Norton,
Professor of Clinical Nursing Innovation, Bucks New University and Imperial College Healthcare NHS Trust

Dr Lorraine Pinnigton,
Associate Professor in Rehabilitation, University of Nottingham

Dr Kate Radford,
Senior Lecturer (Research), University of Central Lancashire

Mr Jim Reece,
Public contributor

Professor Maria Stokes,
Professor of Neuromusculoskeletal Rehabilitation, University of Southampton

Dr Pippa Tyrrell,
Senior Lecturer/Consultant, Salford Royal Foundation Hospitals' Trust and University of Manchester

Dr Nefyn Williams,
Clinical Senior Lecturer, Cardiff University

Observers

Dr Kay Pattison,
Senior NIHR Programme Manager, Department of Health

Dr Morven Roberts,
Clinical Trials Manager, Health Services and Public Health Services Board, Medical Research Council

Professor Tom Walley, CBE,
Director, NIHR HTA programme, Professor of Clinical Pharmacology, University of Liverpool

Dr Ursula Wells,
Principal Research Officer, Policy Research Programme, Department of Health

Interventional Procedures Panel

Members

Chair,
Professor Jonathan Michaels,
Professor of Vascular Surgery, University of Sheffield

Deputy Chair,
Mr Michael Thomas,
Consultant Colorectal Surgeon, Bristol Royal Infirmary

Mrs Isabel Boyer,
Public contributor

Mr Sankaran Chandra Sekharan,
Consultant Surgeon, Breast Surgery, Colchester Hospital University NHS Foundation Trust

Professor Nicholas Clarke,
Consultant Orthopaedic Surgeon, Southampton University Hospitals NHS Trust

Ms Leonie Cooke,
Public contributor

Mr Seumas Eckford,
Consultant in Obstetrics & Gynaecology, North Devon District Hospital

Professor Sam Eljamel,
Consultant Neurosurgeon, Ninewells Hospital and Medical School, Dundee

Dr Adele Fielding,
Senior Lecturer and Honorary Consultant in Haematology, University College London Medical School

Dr Matthew Hatton,
Consultant in Clinical Oncology, Sheffield Teaching Hospital Foundation Trust

Dr John Holden,
General Practitioner, Garswood Surgery, Wigan

Dr Fiona Lecky,
Senior Lecturer/Honorary Consultant in Emergency Medicine, University of Manchester/Salford Royal Hospitals NHS Foundation Trust

Dr Nadim Malik,
Consultant Cardiologist/Honorary Lecturer, University of Manchester

Mr Hisham Mehanna,
Consultant & Honorary Associate Professor, University Hospitals Coventry & Warwickshire NHS Trust

Dr Jane Montgomery,
Consultant in Anaesthetics and Critical Care, South Devon Healthcare NHS Foundation Trust

Professor Jon Moss,
Consultant Interventional Radiologist, North Glasgow Hospitals University NHS Trust

Dr Simon Padley,
Consultant Radiologist, Chelsea & Westminster Hospital

Dr Ashish Paul,
Medical Director, Bedfordshire PCT

Dr Sarah Purdy,
Consultant Senior Lecturer, University of Bristol

Dr Matthew Wilson,
Consultant Anaesthetist, Sheffield Teaching Hospitals NHS Foundation Trust

Professor Yit Chiun Yang,
Consultant Ophthalmologist, Royal Wolverhampton Hospitals NHS Trust

Observers

Dr Kay Pattison,
Senior NIHR Programme Manager, Department of Health

Dr Morven Roberts,
Clinical Trials Manager, Health Services and Public Health Services Board, Medical Research Council

Professor Tom Walley, CBE,
Director, NIHR HTA programme, Professor of Clinical Pharmacology, University of Liverpool

Dr Ursula Wells,
Principal Research Officer, Policy Research Programme, Department of Health

Pharmaceuticals Panel

Members

Chair,
Professor Imti Choonara,
Professor in Child Health, University of Nottingham

Deputy Chair,
Dr Yoon K Loke,
Senior Lecturer in Clinical Pharmacology, University of East Anglia

Dr Martin Ashton-Key,
Medical Advisor, National Commissioning Group, NHS London

Dr Peter Elton,
Director of Public Health, Bury Primary Care Trust

Dr Ben Goldacre,
Research Fellow, Epidemiology London School of Hygiene and Tropical Medicine

Dr James Gray,
Consultant Microbiologist, Department of Microbiology, Birmingham Children's Hospital NHS Foundation Trust

Dr Jurjees Hasan,
Consultant in Medical Oncology, The Christie, Manchester

Dr Carl Heneghan,
Deputy Director Centre for Evidence-Based Medicine and Clinical Lecturer, Department of Primary Health Care, University of Oxford

Dr Dyfrig Hughes,
Reader in Pharmacoeconomics and Deputy Director, Centre for Economics and Policy in Health, IMSCaR, Bangor University

Dr Maria Kouimtzi,
Pharmacy and Informatics Director, Global Clinical Solutions, Wiley-Blackwell

Professor Femi Oyebode,
Consultant Psychiatrist and Head of Department, University of Birmingham

Dr Andrew Prentice,
Senior Lecturer and Consultant Obstetrician and Gynaecologist, The Rosie Hospital, University of Cambridge

Ms Amanda Roberts,
Public contributor

Dr Gillian Shepherd,
Director, Health and Clinical Excellence, Merck Serono Ltd

Mrs Katrina Simister,
Assistant Director New Medicines, National Prescribing Centre, Liverpool

Professor Donald Singer,
Professor of Clinical Pharmacology and Therapeutics, Clinical Sciences Research Institute, CSB, University of Warwick Medical School

Mr David Symes,
Public contributor

Dr Arnold Zermansky,
General Practitioner, Senior Research Fellow, Pharmacy Practice and Medicines Management Group, Leeds University

Observers

Dr Kay Pattison,
Senior NIHR Programme Manager, Department of Health

Mr Simon Reeve,
Head of Clinical and Cost-Effectiveness, Medicines, Pharmacy and Industry Group, Department of Health

Dr Heike Weber,
Programme Manager, Medical Research Council

Professor Tom Walley, CBE,
Director, NIHR HTA programme, Professor of Clinical Pharmacology, University of Liverpool

Dr Ursula Wells,
Principal Research Officer, Policy Research Programme, Department of Health

Psychological and Community Therapies Panel

Members

Chair,
Professor Scott Weich,
Professor of Psychiatry, University of Warwick, Coventry

Deputy Chair,
Dr Howard Ring,
Consultant & University Lecturer in Psychiatry, University of Cambridge

Professor Jane Barlow,
Professor of Public Health in the Early Years, Health Sciences Research Institute, Warwick Medical School

Dr Sabyasachi Bhaumik,
Consultant Psychiatrist, Leicestershire Partnership NHS Trust

Mrs Val Carlill,
Public contributor

Dr Steve Cunningham,
Consultant Respiratory Paediatrician, Lothian Health Board

Dr Anne Hesketh,
Senior Clinical Lecturer in Speech and Language Therapy, University of Manchester

Dr Peter Langdon,
Senior Clinical Lecturer, School of Medicine, Health Policy and Practice, University of East Anglia

Dr Yann Lefeuvre,
GP Partner, Burrage Road Surgery, London

Dr Jeremy J Murphy,
Consultant Physician and Cardiologist, County Durham and Darlington Foundation Trust

Dr Richard Neal,
Clinical Senior Lecturer in General Practice, Cardiff University

Mr John Needham,
Public contributor

Ms Mary Nettle,
Mental Health User Consultant

Professor John Potter,
Professor of Ageing and Stroke Medicine, University of East Anglia

Dr Greta Rait,
Senior Clinical Lecturer and General Practitioner, University College London

Dr Paul Ramchandani,
Senior Research Fellow/Cons. Child Psychiatrist, University of Oxford

Dr Karen Roberts,
Nurse/Consultant, Dunston Hill Hospital, Tyne and Wear

Dr Karim Saad,
Consultant in Old Age Psychiatry, Coventry and Warwickshire Partnership Trust

Dr Lesley Stockton,
Lecturer, School of Health Sciences, University of Liverpool

Dr Simon Wright,
GP Partner, Walkden Medical Centre, Manchester

Observers

Dr Kay Pattison,
Senior NIHR Programme Manager, Department of Health

Dr Morven Roberts,
Clinical Trials Manager, Health Services and Public Health Services Board, Medical Research Council

Professor Tom Walley, CBE,
Director, NIHR HTA programme, Professor of Clinical Pharmacology, University of Liverpool

Dr Ursula Wells,
Principal Research Officer, Policy Research Programme, Department of Health

Expert Advisory Network

Members

Professor Douglas Altman,
Professor of Statistics in Medicine,
Centre for Statistics in Medicine,
University of Oxford

Professor John Bond,
Professor of Social Gerontology
& Health Services Research,
University of Newcastle upon Tyne

Professor Andrew Bradbury,
Professor of Vascular Surgery,
Solihull Hospital, Birmingham

Mr Shaun Brogan,
Chief Executive, Ridgeway
Primary Care Group, Aylesbury

Mrs Stella Burnside OBE,
Chief Executive, Regulation and
Improvement Authority, Belfast

Ms Tracy Bury,
Project Manager, World
Confederation of Physical Therapy,
London

Professor Iain T Cameron,
Professor of Obstetrics and
Gynaecology and Head of the
School of Medicine, University of
Southampton

Professor Bruce Campbell,
Consultant Vascular & General
Surgeon, Royal Devon & Exeter
Hospital, Wonford

Dr Christine Clark,
Medical Writer and Consultant
Pharmacist, Rossendale

Professor Collette Clifford,
Professor of Nursing and Head
of Research, The Medical School,
University of Birmingham

Professor Barry Cookson,
Director, Laboratory of Hospital
Infection, Public Health
Laboratory Service, London

Dr Carl Counsell,
Clinical Senior Lecturer in
Neurology, University of Aberdeen

Professor Howard Cuckle,
Professor of Reproductive
Epidemiology, Department
of Paediatrics, Obstetrics &
Gynaecology, University of Leeds

Professor Carol Dezateux,
Professor of Paediatric
Epidemiology, Institute of Child
Health, London

Mr John Dunning,
Consultant Cardiothoracic
Surgeon, Papworth Hospital NHS
Trust, Cambridge

Mr Jonothan Earnshaw,
Consultant Vascular Surgeon,
Gloucestershire Royal Hospital,
Gloucester

Professor Martin Eccles,
Professor of Clinical Effectiveness,
Centre for Health Services
Research, University of Newcastle
upon Tyne

Professor Pam Enderby,
Dean of Faculty of Medicine,
Institute of General Practice
and Primary Care, University of
Sheffield

Professor Gene Feder,
Professor of Primary Care
Research & Development, Centre
for Health Sciences, Barts and The
London School of Medicine and
Dentistry

Mr Leonard R Fenwick,
Chief Executive, Freeman
Hospital, Newcastle upon Tyne

Mrs Gillian Fletcher,
Antenatal Teacher and Tutor and
President, National Childbirth
Trust, Henfield

Professor Jayne Franklyn,
Professor of Medicine, University
of Birmingham

Mr Tam Fry,
Honorary Chairman, Child
Growth Foundation, London

Professor Fiona Gilbert,
Consultant Radiologist and NCRN
Member, University of Aberdeen

Professor Paul Gregg,
Professor of Orthopaedic Surgical
Science, South Tees Hospital NHS
Trust

Bec Hanley,
Co-director, TwoCan Associates,
West Sussex

Dr Maryann L Hardy,
Senior Lecturer, University of
Bradford

Mrs Sharon Hart,
Healthcare Management
Consultant, Reading

Professor Robert E Hawkins,
CRC Professor and Director of
Medical Oncology, Christie CRC
Research Centre, Christie Hospital
NHS Trust, Manchester

Professor Richard Hobbs,
Head of Department of Primary
Care & General Practice,
University of Birmingham

Professor Alan Horwich,
Dean and Section Chairman,
The Institute of Cancer Research,
London

Professor Allen Hutchinson,
Director of Public Health and
Deputy Dean of ScHARR,
University of Sheffield

Professor Peter Jones,
Professor of Psychiatry, University
of Cambridge, Cambridge

Professor Stan Kaye,
Cancer Research UK Professor of
Medical Oncology, Royal Marsden
Hospital and Institute of Cancer
Research, Surrey

Dr Duncan Keeley,
General Practitioner (Dr Burch &
Ptnrs), The Health Centre, Thame

Dr Donna Lamping,
Research Degrees Programme
Director and Reader in
Psychology, Health Services
Research Unit, London School of
Hygiene and Tropical Medicine,
London

Professor James Lindesay,
Professor of Psychiatry for the
Elderly, University of Leicester

Professor Julian Little,
Professor of Human Genome
Epidemiology, University of
Ottawa

Professor Alistaire McGuire,
Professor of Health Economics,
London School of Economics

Professor Neill McIntosh,
Edward Clark Professor of Child
Life and Health, University of
Edinburgh

Professor Rajan Madhok,
Consultant in Public Health, South
Manchester Primary Care Trust

Professor Sir Alexander Markham,
Director, Molecular Medicine
Unit, St James's University
Hospital, Leeds

Dr Peter Moore,
Freelance Science Writer, Ashtead

Dr Andrew Mortimore,
Public Health Director,
Southampton City Primary Care
Trust

Dr Sue Moss,
Associate Director, Cancer
Screening Evaluation Unit,
Institute of Cancer Research,
Sutton

Professor Miranda Mugford,
Professor of Health Economics
and Group Co-ordinator,
University of East Anglia

Professor Jim Neilson,
Head of School of Reproductive
& Developmental Medicine
and Professor of Obstetrics
and Gynaecology, University of
Liverpool

Mrs Julietta Patnick,
Director, NHS Cancer Screening
Programmes, Sheffield

Professor Robert Peveler,
Professor of Liaison Psychiatry,
Royal South Hants Hospital,
Southampton

Professor Chris Price,
Director of Clinical Research,
Bayer Diagnostics Europe, Stoke
Poges

Professor William Rosenberg,
Professor of Hepatology and
Consultant Physician, University
of Southampton

Professor Peter Sandercock,
Professor of Medical Neurology,
Department of Clinical
Neurosciences, University of
Edinburgh

Dr Philip Shackley,
Senior Lecturer in Health
Economics, Sheffield Vascular
Institute, University of Sheffield

Dr Eamonn Sheridan,
Consultant in Clinical Genetics, St
James's University Hospital, Leeds

Dr Margaret Somerville,
Director of Public Health
Learning, Peninsula Medical
School, University of Plymouth

Professor Sarah Stewart-Brown,
Professor of Public Health,
Division of Health in the
Community, University of
Warwick, Coventry

Dr Nick Summerton,
GP Appraiser and Codirector,
Research Network, Yorkshire
Clinical Consultant, Primary Care
and Public Health, University of
Oxford

Professor Ala Szczepura,
Professor of Health Service
Research, Centre for Health
Services Studies, University of
Warwick, Coventry

Dr Ross Taylor,
Senior Lecturer, University of
Aberdeen

Dr Richard Tiner,
Medical Director, Medical
Department, Association of the
British Pharmaceutical Industry

Mrs Joan Webster,
Consumer Member, Southern
Derbyshire Community Health
Council

Professor Martin Whittle,
Clinical Co-director, National
Co-ordinating Centre for Women's
and Children's Health, Lymington

Current and past membership details of all HTA programme 'committees' are available from the HTA website (www.hta.ac.uk)

Feedback

The HTA programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (www.hta.ac.uk) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

NETSCC, Health Technology Assessment
Alpha House
University of Southampton Science Park
Southampton SO16 7NS, UK
Email: hta@hta.ac.uk
www.hta.ac.uk

ISSN 1366-5278