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BMJ Open How do we evaluate the cost of nosocomial infection? The ECONI protocol: an incidence study with nested case-control evaluating cost and quality of life

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ABSTRACT

Introduction Healthcare-associated or nosocomial infection (HAI) is distressing to patients and costly for the National Health Service (NHS). With increasing pressure to demonstrate cost-effectiveness of interventions to control HAI and notwithstanding the risk from antimicrobial-resistant infections, there is a need to understand the incidence rates of HAI and costs incurred by the health system and for patients themselves.

Methods and analysis The Evaluation of Cost of Nosocomial Infection study (ECONI) is an observational incidence survey with record linkage and a nested case-control study that will include postdischarge longitudinal follow-up and qualitative interviews. ECONI will be conducted in one large teaching hospital and one district general hospital in NHS Scotland. The case mix of these hospitals reflects the majority of overnight admissions within Scotland. An incidence survey will record all HAI cases using standard case definitions. Subsequent linkage to routine data sets will provide information on an admission cohort which will be grouped into HAI and non-HAI cases. The case-control study will recruit eligible patients who develop HAI and twice that number without HAI as controls. Patients will be asked to complete five questionnaires: the first during their stay, and four others during the year following discharge from their recruitment admission (1, 3, 6 and 12 months). Multiple data collection methods will include clinical case note review; patient-reported outcome; linkage to electronic health records and qualitative interviews. Outcomes collected encompass infection types; morbidity and mortality; length of stay; quality of life; healthcare utilisation; repeat admissions and postdischarge prescribing.

Ethics and dissemination The study has received a favourable ethical opinion from the Scotland A Research Ethics Committee (reference 16/SS/0199). All publications arising from this study will be published in open-access peer-reviewed journal. Lay-person summaries will be published on the ECONI website.

Trial registration number NCT03253640; Pre-results.

Strengths and limitations of this study

- This study will describe the whole hospital incidence of all healthcare-associated or nosocomial infection (HAI) types using internationally comparable case definitions including causative organisms and antibiotic susceptibilities within two hospitals.
- Postdischarge information on the outcome quality of life is rarely available; this will be achieved by following up patients after discharge with questionnaires.
- Routine health record linkage in Scotland allows post discharge outcome data which otherwise would require review of general practitioner's case notes for all patients recruited to the case-control study.
- Infections without laboratory-confirmed HAI may be under-represented.
- Some patients may be too unwell to participate in the case-control study and may not wish to participate in the case-control study inevitably, some patients will be lost to follow-up.

INTRODUCTION

Healthcare-associated or nosocomial infections (HAIs) are infections acquired as a result of an episode of healthcare. HAIs are distressing for patients, increase their length of stay (LOS) and incur additional costs to both patient and the healthcare system. WHO reports acquisition of infection while receiving healthcare as the most frequently occurring adverse events.¹ HAI affects all healthcare systems from the most advanced to the lowest resourced. While high-income countries have surveillance systems which describe the prevalence and incidence of selected HAIs, the burden in terms of numbers of cases and the attributable impact on cost of treatment, patients' quality of life and impact on society is not well described.

Antimicrobial resistance (AMR) is an increasing concern worldwide and HAI surveillance including AMR is being implemented worldwide.^{2–4} Studies which assess the impact of HAI tend to focus on patient morbidity and mortality in the hospital, specifically the additional LOS in acute care. With average LOS currently decreasing and patients with increasingly complex disease being managed in the community there is a need to address the impact of HAI from the perspectives of acute care, community care, individual patient and the broader society.

Within the UK and Europe, point prevalence surveys have become the reference point for policy makers to plan infection prevention and control (IPC) strategies. Within Europe, each country undertakes a national HAI point prevalence survey every 5 years coordinated by the European Centre for Disease Prevention and Control (ECDC).⁵ In order to ensure that HAI prevention is targeted towards infections with the highest impact on patient quality of life and/or the greatest reduction in incidence or cost, robust incidence surveillance is required.⁶ While point prevalence study design is a measure of disease burden and reports the proportion of infection types at a given point, it is a limited measure. Prevalence surveys use a cross-sectional approach identifying active cases and as such are biased towards identifying HAI of longer duration. Prevalence surveys do not capture risk exposure, or duration of risk exposure and are therefore subject to bias if used to evaluate increased LOS. Incidence data can be used to estimate how many patients will develop HAI over time, show seasonal variations, allow assessment of risk of HAI and describe the outcomes of HAI.

This will be the first whole hospital incidence study of its kind undertaken within the UK in over 20 years. The last similar study by Plowman *et al* collected data in the UK in 1995.^{7,8} Since that time, the HAI landscape has changed in terms of ageing population, increasingly complex procedures and the emergence of antimicrobial resistance. A well-designed incidence survey is necessary to provide information on risk, aetiology and outcome of HAI within the current healthcare system.

Objectives

The Evaluation of Cost of Nosocomial Infection (ECONI) survey will investigate the health impact and consequent costs of HAI for patients, the health service and the wider community. Epidemiological and health economic analytical techniques will be used. There are three broad aims to the study: to describe the epidemiology of HAI in terms of risk, time, place and person; to describe the impact of HAI on care in hospital, LOS, impact on health-related quality of life and cost from an acute care perspective and to describe the impact of HAI postdischarge in terms of health-related quality of life; health and social care utilisation and socioeconomic impact. Each of these aims is broken down into research objectives with associated research questions (see supplementary appendix A).

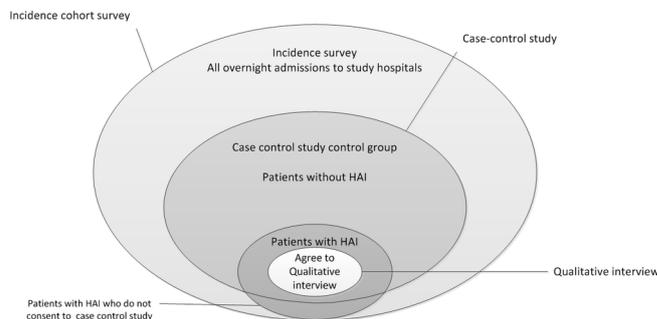


Figure 1 Representation of the Evaluation of Cost of Nosocomial Infection nested study design. The incidence cohort represents all adult overnight admission to the study hospitals. The case-control study will be a subset of cases and controls (two controls for each case) and the nested qualitative study will recruit a subset of patients who develop healthcare-associated or nosocomial infection (HAI) and have consented to participate in the case-control study. A proportion of HAI cases will not be able or willing (including by proxy) to provide consent to participate in the case-control study.

METHODS AND ANALYSIS

Study design

ECONI is a two-centre, prospective observational incidence study with record linkage, nested case-control and qualitative study. The case-control study component includes a longitudinal follow-up for 1 year postdischarge also encompassing a second nested study that includes qualitative interviews with a selected group of patients who acquire HAI during their hospital stay. A maximum variation purposive sample of patients with HAI will be recruited to take part in a qualitative research study during their hospital stay, and will be interviewed by phone after discharge. The aim of this sampling strategy is to ensure that as wide a range of perspectives from patients experiencing different types of HAI are included. A diagram of the ECONI study is shown in figure 1.

Hospital setting

All Scottish acute hospitals were reviewed based on the number of staffed beds, annual inpatients, distribution of emergency, elective and transfer admissions and mean LOS within their hospital type.⁹ One large teaching hospital (981 beds and a 24 hours Accident and Emergency (A&E) department and a number of national specialist services) and a large general hospital (492 beds with a 24 hours A&E department and a regional cardiovascular centre) were selected as study sites. The study hospitals represent 82% of clinical specialties served within Scotland and fall within the mid-range of HAI cases in the National HAI prevalence survey 2012.¹⁰ Teaching and general hospitals accounted for 91% of all admissions to acute care in Scotland in 2015 while the study was being developed.¹¹ The two study hospitals served 100 000 patients during 2015.¹¹

Box 1 The criteria that are required to meet the European Centre for Disease Prevention and Control case definitions of healthcare-associated or nosocomial infection (HAI). HAI must meet both criteria a and b.

- a. HAI is an infection that met the HAI case definitions during the patient's stay.
- b. In addition, the onset of infection must have occurred within one of the following time frames:
 - i. The infection occurred on day 3 of current admission onwards (if day 1 is day of admission).
 - ii. Present on admission (or presenting on day 1 or 2) in patients discharged from hospital in previous two days.
 - iii. Surgical site present on admission (or presenting day 1 or 2) if surgery within 30 days of signs and symptoms appearing if no implant and within 90 days of signs and symptoms appearing if an implant was present.
 - iv. *Clostridium difficile* infection present on admission (or presenting day 1 or 2) in patients discharged from hospital in previous 28 days.
 - v. Device associated infection (pneumonia, urinary tract infection, bloodstream infection and catheter-related infection following the insertion of the device (including day 1 or 2 of admission)).

Case definitions

The ECONI study will use the microbiologically confirmed ECDC HAI epidemiological case definitions that are based on internationally recognised case definitions for incidence of HAI (based on the Centres for Disease Control (CDC) nosocomial infection definitions 1988).¹² These definitions were used within the 2012 and 2017 European HAI Prevalence survey.¹³ Data on HAIs will be recorded on all hospital patients who meet the relevant case definitions. The use of these definitions will allow a comparison between the current HAI incidence study, the national prevalence survey and international HAI studies.

The definitions define 14 infection types which can affect adult patients. The timeframe for developing an HAI according to the ECDC case definitions¹³ is 48 hours or more after admission or day 3 of admission onwards. The additional onset criteria take account of cases where a patient is re-admitted to hospital after receiving care within the study hospital or another acute care facility (box 1). Infections originating in other acute and non-acute hospitals will be included but those originating in long-term care facilities, care homes or nursing homes will be excluded (these will be classified as community acquired).

Study period

In-hospital data collection began in April 2018 and will continue for one calendar year. Recruitment to the nested case-control study will take place over the same period. Patients will be followed up by postal questionnaires at 1, 3, 6 and up to 12 months after their date of discharge. A subset of patients will be recruited for qualitative interviews on their experience of HAI. Record linkage data for

the cohort will include information on their healthcare during the year before the start date and 1 year after the final in-hospital data collection date.

Incidence cohort survey

The incidence survey is an observational epidemiological surveillance study. The incident or outcome event for the incidence survey is HAI as defined by the ECDC case definitions. ECONI study nurses will work closely with local infection control teams; they will have full access to local patient management systems, infection control systems (IC Net) and laboratory data. ECONI nurses will identify patients with one or more suspected HAI through searching laboratory systems for positive laboratory reports, consultation with infection control teams and ward staff. Case note review will be undertaken to assess whether these suspected cases meet the ECDC case definitions.

Inclusion criteria

- ▶ Age 18 years or over.
- ▶ Admitted to hospital for an overnight stay at study hospitals.
- ▶ Any sex.
- ▶ HAI diagnosed using ECDC case definitions and time scales

Exclusion criteria

- ▶ Age under 18 years.
- ▶ Admitted as a day case to a study hospital.
- ▶ Patient does not acquire HAI according to ECDC case definitions and time scales.

Routine data sets

The Community Health Index (CHI) number is a unique identifier allocated to every patient and can be used to link to routine data sets collected by NHS Scotland. CHI will be collected for all patients with HAI and this will enable analysis to separate patient-level data for cases and non-cases in the admission cohort. Linkage to routine data sets will be used to collect information for all patients within the admission cohort. These databases include the Scottish Morbidity Register 'SMR01': a record of all hospital admissions and discharges to acute hospitals. The SMR01 data set links to the Scottish death register which records the date of death and the cause of death as described by the International Classification of Disease version 10 (ICD-10)¹⁴ and operations are recorded using OPCS-4¹⁵ classification. The 'SMR00' database records information on attendance at outpatient clinics for treatment or investigation. Linkage will also be made to the data sets which record patient-level community prescribing in Scotland (the 'Prescribing Information System for Scotland') and the Community Health Activity Data—District Nursing data set which is a relatively new data set (dates from 2015) that records information on community nursing visits to patients. Both SMR00 and SMR01 data sets are estimated to be 97% complete.¹⁶ It is acknowledged that newer data sets

will have lower completion rates and this will be considered in the analysis.

Case-control study

For the nested case-control study an incidence density sampling approach will be used. The protocol aims to recruit all eligible patients with HAI and two patients without HAI at time of recruitment. Cases will have been identified within the incidence survey.

Inclusion criteria

- ▶ Admitted to hospital for an overnight stay at study hospital.
- ▶ Subjects capable of giving informed consent, or if appropriate, subjects having an acceptable individual capable of giving consent on the subject's behalf.
- ▶ Any sex.
- ▶ Age 18 years and over.
- ▶ Good English language skills (sufficient to read and understand the participant information sheet without help).

Exclusion criteria

- ▶ Admitted to hospital as a day case.
- ▶ Admitted to hospitals other than the study hospitals.
- ▶ Age under 18 years.
- ▶ Admitted to the study hospital during the study period and recruited to the study during a previous stay.
- ▶ Subjects not capable of giving informed consent unless legal representative or relative can provide proxy consent.
- ▶ Patients who do not have sufficient English language skills to read and understand the information sheet without help.
- ▶ Patients cared for under the hospital at home care pathway.
- ▶ Admitted to hospital as a day case.

Controls will be selected at random from the cohort of patients without HAI who are being cared for on the same ward as the cases. Controls will be selected using a random number generator from the same ward as the case at the same time period. The ECONI nurses will approach the clinical teams to ensure that patients meet the inclusion criteria, and if being recruited as a case, they must be aware of their infection and considered well enough to be invited to take part. The initial approach to the patient will be by the clinical team caring for the patient. Patients will be asked to provide consent after reviewing the patient information sheet provided. ECONI nurses will seek a guardian, welfare attorney or family member to provide consent for patients who are unable to consent for themselves. This approach will ensure that the case-control study includes the most unwell and patients potentially at risk of HAI.

Patients or their proxies who have provided informed consent will be sent a short paper questionnaire at 1, 3, 6 and 12 months after discharge from the episode of care when they were recruited. They will be provided with a

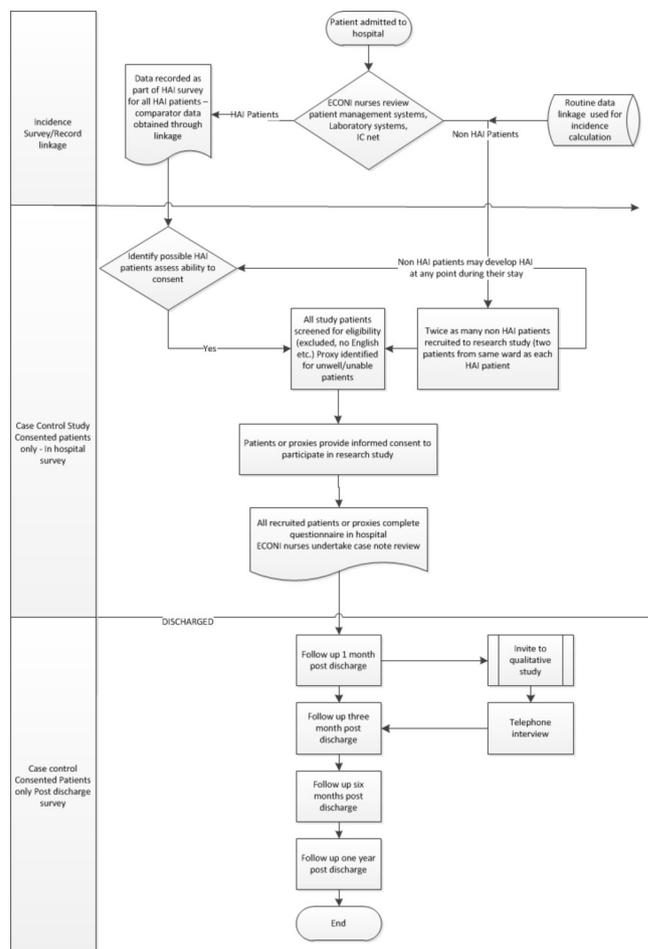


Figure 2 Evaluation of Cost of Nosocomial Infection study flow chart. HAI, Healthcare Associated Infection or Nosocomial Infection.

prepaid return envelope. The National Death Registry will be contacted in order to identify any patients who have died since discharge; this will ensure that their families will not be contacted after their relatives have died. The ECONI nurses will also undertake a case note review collecting clinical data which is not routinely available.

A flow chart showing the patient pathway and data collection/recruitment points is shown in [figure 2](#). ECONI nurses will be trained to collect data using a bespoke data collection tools for each study design using REDCap software.¹⁷

Variables

[Table 1](#) shows the outcomes of interest for the ECONI study.

Data sources/measurement

[Table 2](#) shows the variables which will be recorded for the study and the sources of these data. Extrinsic risk factors which are patient care practices inclusive of devices, surgeries and isolation will be included in the analysis. Known confounding intrinsic patient characteristics will also be included within the analyses. These include: sex, age, ethnicity, socioeconomic status as defined by Scottish

Table 1 ECONI outcomes for incidence survey and case-control study

Incidence survey	
Epidemiological outcomes	Data items
Infection	Type of infection ECDC case definitions ¹³ Causative organism Antimicrobial resistance of causative organism
Duration of infection	Start date of infection End date of infection
Morbidity	Attributable additional bed days required as a result of infection
Mortality	30-Day mortality
Case-control study	
Socioeconomic outcomes	Data items
Cost of illness from hospital perspective	Attributable additional bed days required as a result of infection Cash treatment costs (including tests, treatment, IPC measures, equipment)
Cost of illness from acute care perspective	Attributable additional visits to outpatient clinic Re-admission to hospital
Cost of illness from a primary care perspective	GP prescribing District nurse visits
Cost of illness from patient's perspective	Quality of life (EQ-5D, ²⁸ SF-12 ²⁹) Lost income
Cost of illness from patient's family perspective	Caring responsibilities to be covered Additional care requirements to be provided by family
Cost of illness from a societal perspective	Days of work lost Bed days used Social care provided

ECDC, European Centre for Disease Prevention and Control; ECONI, Evaluation of Cost of Nosocomial Infection; EQ-5D, EuroQol-5D; GP, general practitioner; IPC, infection prevention and control; SF-12, 12-Item Short Form Health Survey.

Index of Multiple Deprivation and comorbidities from the SMR01 data set using ICD-10 definitions.¹⁸ For the case-control study, factors like underlying comorbidities, health status measured by McCabe score, age and complexity of surgeries will be considered within the analysis as potential confounders in terms of increased LOS.

Data linkage

Data from the incidence survey, routine data sets and case-control study will be combined to form an ECONI data set (figure 3).

Qualitative interview

A subgroup of patients who have been identified as having HAI will be invited to take part in a qualitative interview between 1 and 3 months after they have been discharged from hospital. This will investigate the experiences of patients who have had an HAI; the effect this infection has had on their life since discharge from hospital, how they have coped with having this infection and how this experience could have been improved.

Inclusion criteria

- ▶ Patients who consented to be contacted for follow-up interview.
- ▶ Patients who acquired HAI.
- ▶ Patients who are able to consent for themselves (this will be checked to ensure that they remember the study and are still willing and physically able to take part).
- ▶ Good English language skills (sufficient to read and understand the participant information sheet).
- ▶ Willing and able informant.

Exclusion criteria

- ▶ Patients who did not consent to follow-up.
- ▶ Patients who did not acquire HAI.
- ▶ Patients who are not able to consent for themselves.
- ▶ Patients who do not have English language skills.
- ▶ Patients who are not willing to participate in a telephone interview.

Study size

The ECONI study is an observational study. The two study hospitals admitted 100 000 patients during 2015 when the study was planned. A hospital HAI incidence of about 0.5%–1% per admission is anticipated, yielding around 500–1000 incident HAI cases from an admission cohort of 100 000 admissions over the period of 1 year. Individuals may have multiple HAIs during their stay in hospital so the power for this part of the study is evaluated for the comparison of Poisson rates.¹⁹ For a rare exposure factor in 5% of patients, risk ratios in the exposed group in excess of 1.47 will be detected with a power in excess of 90% when around 700 HAI cases are anticipated. If the anticipated number of HAI cases is lower at around 500 then the detectable risk ratio is 1.55 and if it is higher at around 1000 HAI cases then the detectable risk ratio is 1.4, both at a power of 90%. If the risk factor is more prevalent at 30% then for powers in excess of 90%, the detectable risk ratios are >1.28 for around 500 anticipated HAI cases, 1.24 for around 700 anticipated HAI cases and 1.2 for around 1000 anticipated HAI cases. This demonstrates that the study is expected to be large enough to detect moderate risk ratios associated with the acquisition of an HAI.

Statistical analysis

Baseline characteristics will be summarised for the whole admission cohort; for patients who develop HAI and those who do not. Missing data will be reported for each variable. The analysis of the rate of acquisition of HAI in hospital will be carried out using time to event models, such as Poisson regression, Cox or parametric survival models. This will be reported as the rate per 1000 patient days, or per 1000 admissions, together with 95% CIs. For each patient, time will begin on admission to hospital and will end with discharge, death or acquisition of an HAI. Multiple admissions from the same patients will be modelled using a frailty component or adjusting the SEs of the estimated effect to account for the multiple

**Table 2** ECONI data items for incidence survey and case-control study and sources of data

Concept	Data items	Data sources
Incidence survey—data collected by ECONI nurses		
HAI infection type	Infection type ¹³ Causative organism ¹³ Antibiotic resistance ³⁰ Date infection identified	Patient clinical records, laboratory systems, nursing notes including GP letters
Record linkage—linked using CHI number		
Age	Date of birth	SMR01 ³¹
Patient health	International Statistical Classification of Diseases and Related Health Problems ^{14 32} from SMR01	
Socioeconomic status	Scottish Index of Multiple Deprivation ¹⁸	
Ethnicity	Ethnicity as defined by census	
Hospital admissions post discharge	Date of hospital admission Date of discharge	
Outpatient clinic attendance	Date and number of outpatient clinic visits	SMR00 ¹⁹
GP prescribing of antibiotics	Antimicrobial agents prescribed Dosage Frequency of dosage No. of days	Prescribing Information System for Scotland ³³
District nurse visits	Number of district nurse visits	Community Health Activity Data—District Nursing ³⁴
Deaths	Date of death Cause of death	National records of Scotland death records ³⁵
Case-control study—recorded by ECONI nurses		
Lifestyle	Smoking Drinking	
Severity of illness	McCabe score ³⁶ Continence	Clinical case note review
Screening	MRSA screening CPE screening	
Antimicrobial use	Type of antimicrobial agent ¹³ Route of administration Dose Frequency No. of days Indication for prescribing	Drug Kardex
Surgery	Surgery type Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures (fourth revision) ¹⁵ Wound classification American Society of Anaesthesiologists score ³⁷ Date of operation Duration of surgery Patient weight/height	Surgical note review
Device use	Type of device present PVC, Urinary catheter CVC I have Date inserted Date removed	Clinical case note review
Complications in hospital	Adverse events	
Case-control studies—patient questionnaires		

Continued

Table 2 Continued

Concept	Data items	Data sources
Quality of life	EQ-5D ²⁸ SF-12 ²⁹	Patient self-report by questionnaire or completed by proxy. A proxy version of the questionnaire has been prepared.
Living arrangements	Current residence Marital status	
Education	Education	
Work	Current employment Work days lost Salary	
Caring	Care provided Care received	
Healthcare utilisation	Use of healthcare services not available through record linkage	
Date questionnaire completed		

CHI, Community Health Index; CPE, Carbapenemase Producing Enterobacteriaceae; CVC, Central venous catheter; ECONI, Evaluation of Cost of Nosocomial Infection; EQ-5D, EuroQol-5D; GP, general practitioner; HAI, healthcare-associated or nosocomial infection; IPC, infection prevention and control; MRSA, Meticillin Resistant *Staphylococcus aureus*; PVC, Peripheral venous catheter; SF-12, 12-Item Short Form Health Survey.

observations per patient. This analysis can also deal with multiple HAI events during the one admission episode. The impact of HAI on mortality or LOS will also be estimated using Cox or parametric survival models. Time will begin on admission to hospital and the occurrence of an HAI will be a time-dependent variable. Patients will initially be in the no HAI group on admission to hospital and some will then move into the HAI group during their hospital stay.

The nested case-control study, where additional data are collected on HAI cases and two controls, will be analysed

using matched logistic regression to estimate the impact of risk factors on HAI. Time to event models will be used to estimate the impact of HAI on mortality and additional LOS. In this analysis, time will begin on the date when the case receives the initial HAI diagnosis. The matched controls will also use this date. Comparing LOS for the cases and matched controls will provide the additional LOS associated with HAI. Analysis will be undertaken using R statistical software.²⁰

Health economic analysis

This study will estimate the cost of HAI by HAI type to acute healthcare, to community care, social care services and costs to patients. This study will report an estimated of cost of HAI in Scotland and the UK using a number of approaches including accounting costs, cash treatment costs and willingness to pay.

EuroQol-5D (EQ-5D) and 12-Item Short Form Health Survey (SF-12) questions will be completed by all consented patients or proxies. The wording of the proxy questionnaires to be completed by the guardians, welfare attorneys or family members has been adjusted so as to reflect the perspective of the person completing the questionnaire. This includes use of the proxy version of EQ-5D. Utility values will be calculated from the EQ-5D and from the Short-Form Six-Dimension (derived from the SF-12).²¹ These utility values are required in the calculation of quality-adjusted life-years, which is a multidimensional measure of health outcome incorporating quality of life and length of life. Existing studies on the impact of HAI on patients' quality of life are limited to a specific organisms (*Clostridium difficile*^{22 23}) or hospital settings.²⁴

Costs will be calculated from a range of perspectives including acute hospital care, primary care and the patient's perspective. Cost within acute care will be primarily based on additional attributable LOS using multistate modelling. The costs of each infection

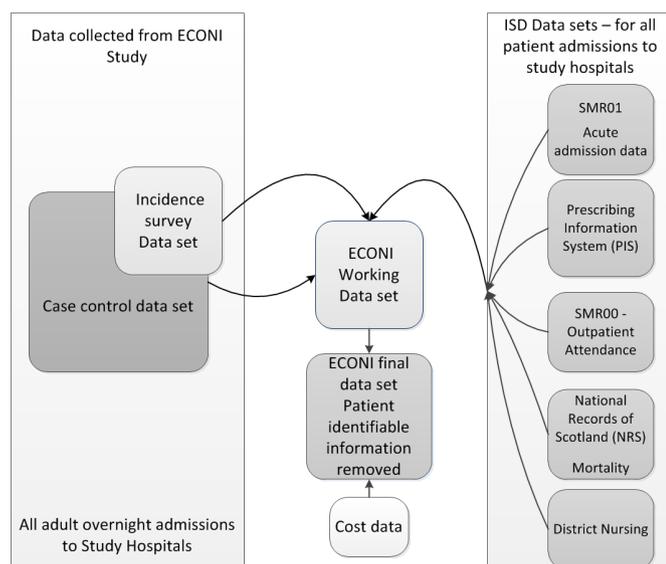


Figure 3 ECONI data linkage. Data sets which will be combined in order to address the study research questions. ECONI, Evaluation of Cost of Nosocomial Infection; ISD, Information Services Division.

will be calculated using the cost of the laboratory tests required to identify the infection including follow-up tests; infection prevention and control measures implemented according to infection type and resistance of the organism and specific treatment costs for the infection. Indirect costs to patients including forgone earnings due to changes in employment circumstances and impact on personal care requirements will also be reported.

Strengths and limitations of this study

Whole hospital incidence is rarely available. The study will also report causative organisms and antibiotic susceptibilities for all HAI incident infections which is currently unknown. Data collection will take place over one calendar year to ensure that infections that show seasonal variation will be included within the data set. However, the single year of data collection will not be sufficient to identify seasonal trends which would require multiple annual surveys. The study will link high-quality health data for recruited patients, in order to evaluate risk factors, healthcare utilisation and mortality, which will mitigate absent data from patients who are lost to follow-up. Post-discharge information on detailed follow-up for socioeconomic outcome is rarely available; this will be achieved by following up patients after discharge with questionnaires. The study will report quality of life scoring using the EQ-5D and SF-12 instruments for up to 1 year after patients have been discharged from hospital. This is novel since there are no HAI-specific instruments available as yet and if they do exist are disease or setting specific.^{22–24} Similarities and differences for HAI patients between the instruments are not available in the literature. Previous studies have a narrow definition of cost focusing only on historical accounting costs that may not be representative of economic costs. HAI's burden in a public health system such as the National Health Service (NHS) can be better described in terms of wasted resources. ECONI will produce a unique detailed set of HAI costs information that can be used in the economic evaluation of IPC programmes. Finally, the inclusion of a qualitative interview will collect personal accounts of the experience of developing HAI which will provide a patient-centred perspective to the study.

A limitation of the case-control study is the fact that the patients at greatest risk of HAI constitute the most elderly and unwell and these patients may not have the capacity to consent for themselves. This limitation is mitigated by the option to ask a guardian, welfare attorney or family member, who can make decisions about the study on the patient's behalf. If patients are temporarily unable to provide consent but recover capacity before they are discharged, then they will be asked to provide their consent to take part in the remainder of the study, should they wish to do so. Patients may be lost to follow-up during the postdischarge phase and this would impact on patient-reported outcomes. Such a limitation has been largely mitigated by the fact that information on mortality, repeat hospitalisations, community prescribing

and use of district nursing teams will be available for all patients.

Potential for bias

Selection bias will be addressed because all newly admitted patients will be included within the admission cohort and the outcome will not be known at the time of admission (unless patients are readmitted with active HAI). Patients will be observed during their hospital stay, they will be monitored using patient management systems (including laboratory databases) so the loss to follow-up for the incidence study will be minimal. Chronology bias will be reduced as all patients (with and without HAI) will be admitted over same 1-year period. Data will be collected over one calendar year in order to account for variations in case mix and causative organisms throughout the seasons. Interobserver bias is addressed through inter-rater reliability tests being undertaken before and during the study to ensure that their application of the case definitions are consistent and validation of diagnosed cases undertaken by the study manager on a fortnightly basis.

Patients who do not have sufficient English language skills to read and understand the patient information sheet will be excluded from the case-control study. There is potential for bias from this because patients who have lived abroad may be at increased risk of antibiotic-resistant infections. These patients will be included within the incidence cohort and the infection type, and causative organism and antibiotic susceptibilities will be recorded as part of the surveillance part of the study.

Using record linkage means that key events do not rely on patient recall. For the postdischarge phase of the case-control study it is anticipated that patients will be lost to follow-up. These patients will be well described from the incidence study and the demographics of any lost patients can be clearly reported. Response bias for cases and controls will be assessed by comparing the characteristics of the cases and controls with the admission characteristics of all admissions during the study period.

Governance summary

The study reports to the ECONI Steering Committee who provided overall supervision of the trial. The committee contains members independent of the investigators and their employers and includes two members of the public.

Patient and public involvement

Two members of the public were recruited to the steering committee to represent the patients' and their families' perspective. These public representatives reviewed the research questions, patient facing information and questionnaires. A recent review of the literature on patient experience of HAI identified 17 studies which had investigated the impact of HAI on patients.²⁵ The findings of this paper will be used to inform the qualitative interview questions. Patients have not been involved in recruitment and conduct of the study due to the rapidly changing hospital population. The public representatives will work

with researchers to prepare a lay summary of each of the publications from the study, which will be available from the ECONI study website. Patients will be sent a summary of the findings of the study in a final communication which will thank them for their participation.

Ethics and dissemination

The incidence study is led by NHS Health Protection Scotland and was deemed ineligible for ethical review as it was a public health surveillance study.²⁶ The incidence survey and record linkage protocol was approved on 1 February 2017 by the NHS Scotland Public Benefit and Privacy Panel for Health and Social Care (PBPP) (reference 1617–0037). The PBPP is the governance structure of NHS Scotland and they exercise delegated decision-making on behalf of NHS Scotland Chief Executive Officers and the Registrar General. The panel operates as a centre of excellence for privacy, confidentiality and information governance expertise in relation to Health and Social Care in Scotland.

The main ethical issues with the study are the balance between the patients' frailty and the need to collect data from the patients' perspective. The research nurses will discuss potential recruitment of patients with the nurses caring of them to ensure that the patients are aware of their infection (for cases) and that they are well enough to discuss consent before they are approached. In order to avoid any unnecessary distress to family members, a check will be undertaken with the national death registry before questionnaires are posted to patients. The protocol will seek consent from a proxy (the patient's legal representative, guardian, welfare attorney or nearest relative) authorised to take decisions regarding research. This phase of the study was approved by PBPP on the 25 May 2017 (reference 1617–0329).

All publications arising from the ECONI study will be published in open-access peer-reviewed journals. Lay summaries will be made available to participants. The study will follow the NHS Information Services Division protocol for statistical disclosure²⁷ in order to ensure patient confidentiality is maintained. An anonymised data set will be produced at the end of the study and these data will be available for future studies. This will be subject to agreement with the Chief Investigator JR.

CONCLUSIONS

ECONI will be a multisite study on the current incidence and impact of HAI in Scotland. This will include the incidence of causative organisms and AMR data. These incidence rates will be extrapolated based on specialty of treatment to generate estimates of Scotland and UK wide HAI. It will provide detailed epidemiological information on the occurrence of HAI and identify patients who are at increased risk of developing HAI. The study will report previously unreported health utility values for a range of HAIs, which can be used to inform modelling

and decision making on HAI prevention and control interventions.

International implications

While this study will benefit NHS Scotland, the findings will elicit health state utility values for HAI types which can be used in the economic evaluation of IPC interventions elsewhere. The epidemiology of HAI in Scotland in terms of causative organisms and antibiotic resistance patterns are comparable to countries within northern Europe at this time. Data collected during the ECONI study will allow comparison with the findings of the 2016 European HAI prevalence survey. The use of electronic health data will allow validation of the representativeness of the recruited patients and the generalisability at a national and international level.

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Collaborators The ECONI Steering Committee reviewed and approved the protocol and will review publications from their area of expertise. Professor Mahmood Adil represented the funder, Professor Alistair Leanord, Rachel Dunk, Abigail Mullings represented the Scottish Government HAI policy unit on the Steering Committee. Elaine Ross and Dr Lisa Ritchie represented Infection Prevention Society (IPS). Moira Whyte and Louise Brown were lay representatives on the Steering Committee and contributed to the development of the patient facing materials for the study. All authors have reviewed and commented on this paper, approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Contributors SS led the study design, wrote study protocols and ethics and PBPP approvals, patient facing materials, contributed to the design of the collection tools and developed the manuscript. CR contributed to the concept of the study, study design and statistical analysis plan. SM contributed to the design of data collection for economic analysis. HM contributed to the study design and health economic aspects of the study design. AMcF contributed to design of questionnaire. LH contributed the development of study design, protocol and plans for data management. SD and BC are the Principal Investigators at the recruiting site. NG contributed to the health economic elements of the study design. JR conceived the study and is Chief Investigator for the study.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The case-control component of the ECONI study received a favourable ethical opinion from the Scotland A Research Ethics Committee on 3 March 2017 (reference 16/SS/0199).

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