

■ INFECTION

Surgical site infection after hip fracture surgery

A SYSTEMATIC REVIEW AND META-ANALYSIS OF STUDIES PUBLISHED IN THE UK



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Aims

This study explores the reported rate of surgical site infection (SSI) after hip fracture surgery in published studies concerning patients treated in the UK.

Methods

Studies were included if they reported on SSI after any type of surgical treatment for hip fracture. Each study required a minimum of 30 days follow-up and 100 patients. Meta-analysis was undertaken using a random effects model. Heterogeneity was expressed using the I² statistic. Risk of bias was assessed using a modified Newcastle-Ottawa Scale (NOS) system.

Results

There were 20 studies reporting data from 88,615 patients. Most were retrospective cohort studies from single centres. The pooled incidence was 2.1% (95% confidence interval (CI) 1.54% to 2.62%) across ‘all types’ of hip fracture surgery. When analyzed by operation type, the SSI incidences were: hemiarthroplasty 2.87% (95% CI 1.99% to 3.75%) and sliding hip screw 1.35% (95% CI 0.78% to 1.93%). There was considerable variation in definition of infection used, as well as considerable risk of bias, particularly as few studies actively screened participants for SSI.

Conclusion

Synthesis of published estimates of infection yield a rate higher than that seen in national surveillance procedures. Biases noted in all studies would trend towards an underestimate, largely due to inadequate follow-up.

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Article focus

- A large-scale meta-analysis of 20 studies from the UK considering over 80,000 patients.
- Analysis was undertaken according to major categories of surgery and study definition of infection.

- Definitions used across studies were varied and may explain the variation in rates between studies.

Strengths and limitations

- A large number of patients were considered from a single healthcare system with recognized standards for hip fracture care and SSI prevention.
- Data were heterogenous and therefore pooled data should be interpreted in that context.

Key messages

- Rates of surgical site infection (SSI) after hip fracture in the published literature may be higher than surveillance suggests.

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Introduction

Hip fracture is one of the biggest challenges facing patients and healthcare systems. Worldwide there are 1.3 million hip fractures and more than 70,000 hip fractures in the UK every year.¹ These figures are projected to rise to over 100,000 by 2020 in the UK¹ and more than six million by 2050 worldwide.²

The overwhelming majority of hip fractures are treated with surgery.³ Given that 60% of hip fracture patients have at least one major medical comorbidity, such as malignancy or diabetes, these patients are particularly vulnerable to surgical site infection (SSI).^{4,5}

Deep infection has profound consequences for hip fracture patients including five-times higher mortality. Survivors experience prolonged hospital admissions and much higher need for discharge to residential care.^{6,7}

Understanding the rate of infection is a critical component of research and disease management for SSI. Various bodies are responsible for SSI surveillance in their respective countries. In the UK, this falls under the remit of Public Health England's Surgical Site Infection Surveillance Programme.^{8,9} However, the surveillance process may underestimate the true rate of infection.¹⁰ The underestimation of SSI in hip fracture by public bodies has important implications for the time, energy, and resources being employed to tackle a problem which is a research priority for patients.¹¹

Published studies may act as an important source of incidence data for this complication for patients and in turn inform future studies.

The principal aim of this study was to determine the rate of SSI after hip fracture surgery in the UK. The analysis was limited to the UK due to the single payer health provider and national guidelines regarding hip fracture care and SSI.

The secondary aim was to consider the SSI rates alongside the subtypes of surgery and study definitions of infection.

Methods

A systematic review of published studies was undertaken. The methodology was conducted and reported in line with the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) process.¹² The study protocol was registered prospectively (Prospero CRD42017050685).

Search strategy. The search was designed with a specialist information librarian to capture any study that reported infection after hip fracture surgery (Supplementary Table i). The Embase and Medline databases were searched from inception to 1 May 2018 and all items imported into specialist systematic review software.¹³ Statistical analysis was undertaken using Stata version 15.1 (StataCorp, College Station, Texas, USA).

Inclusion criteria. All studies reporting SSI after hip fracture surgery in the UK were included. All studies had to report on a minimum of 100 consecutive hip fracture patients undergoing surgery in order for each included

study to have a reasonable chance of capturing SSI within their study population. Each study needed a minimum of 30 days of follow-up. Only studies published in English were included.

Exclusion criteria. Patients treated with external fixation were excluded as were studies focusing on highly selected populations, e.g. high-energy trauma patients were excluded. Studies published before 2000 were also excluded as they were unlikely to help determine contemporary SSI rates. Review articles were used as a source of further original studies.

Selection of studies. The review of titles and abstracts was done in full by one of the authors (JM). A 10% random sample of these items was reviewed independently by a second author (DM). Disagreement at each stage was resolved by discussion and where necessary arbitration by a senior colleague (MLC). Once the titles and abstracts were reviewed, relevant possible full UK paper reference lists were also reviewed. Additional studies not identified in the original search were added to the list of full papers to review. No grey literature or conference abstracts were searched. An overview of this process is outlined in Figure 1.

Once full studies were identified, they were categorized into the respective type of surgery, e.g. 'all hip fractures', 'hemiarthroplasty'. When multiple publications reported data from a single database, only the largest study was included. When the patients were derived from non-overlapping study periods, both studies were included. If there was lack of clarity about dual counting or dates from which the study came from, then the authors were contacted.

Data extraction. The author performed data extraction in parallel and independently with a third author (JSH). Disagreement was resolved by discussion and arbitration where necessary.

Data for extraction were based on demographic features (e.g. age and sex), surgical features (e.g. type of hip fracture surgery), and study features (e.g. definition of infection). Definition for infection was considered for each study and where possible reported by either superficial or deep SSI. Where reoperation was reported as part of the SSI definition, this was assumed to represent deep infection and recorded accordingly. Authors were contacted for additional data where required.

Statistical analysis. Descriptive statistics were used to represent the patient demographics included in the study. Summary statistics including expressions of uncertainty were used to calculate the rate of infection as a percentage. Meta-analysis was undertaken where appropriate based on the number of cases available. This was undertaken using a meta-analysis of proportions with a random effects model. Study heterogeneity was expressed using the I^2 statistic. All proportions were transformed to percentages. No meta-regression was possible due to the limited and variable reporting of covariates within individual studies.

Figure 1- Study Flow Diagram Selection Process

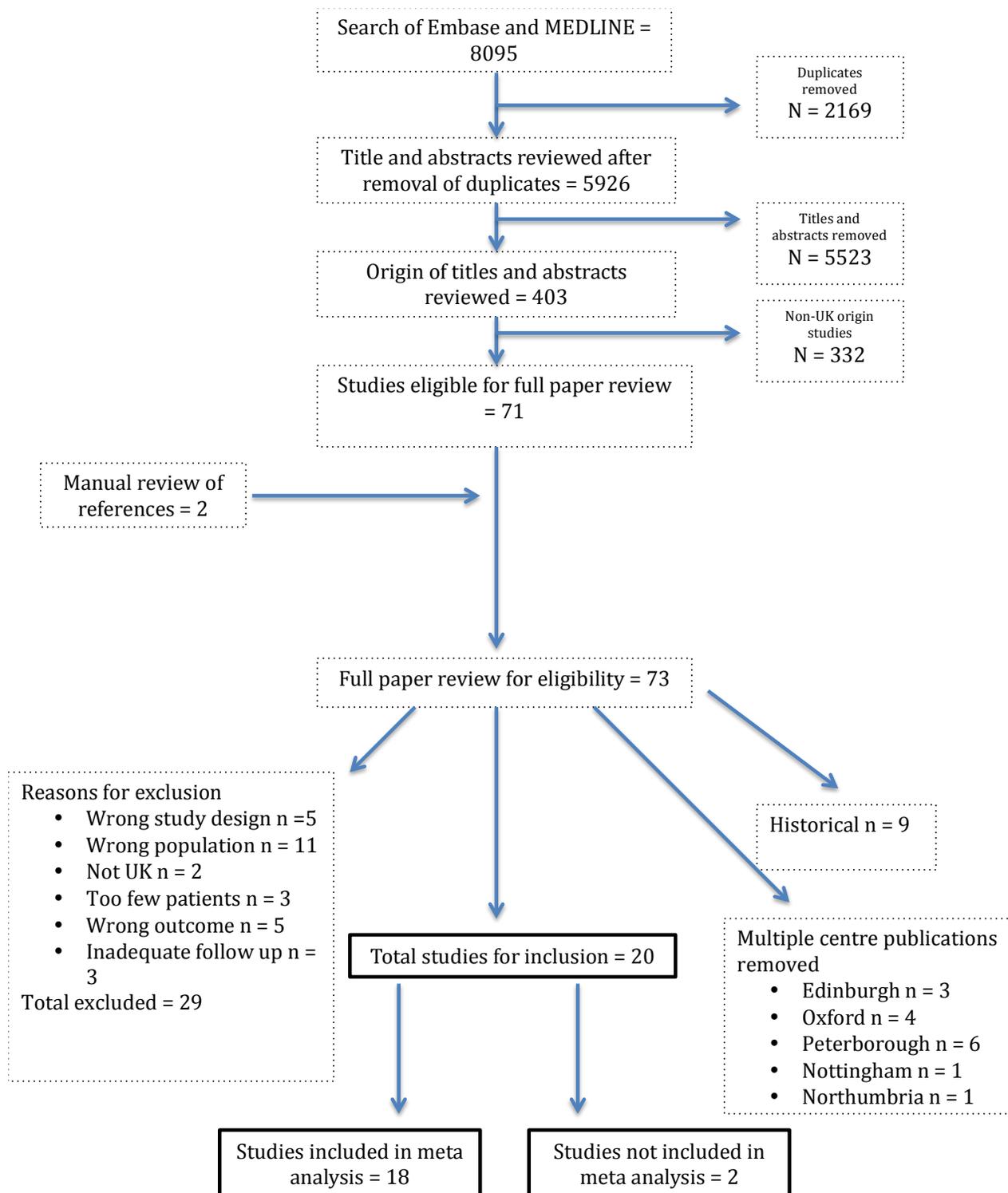


Fig. 1

Outline of the process of study selection.

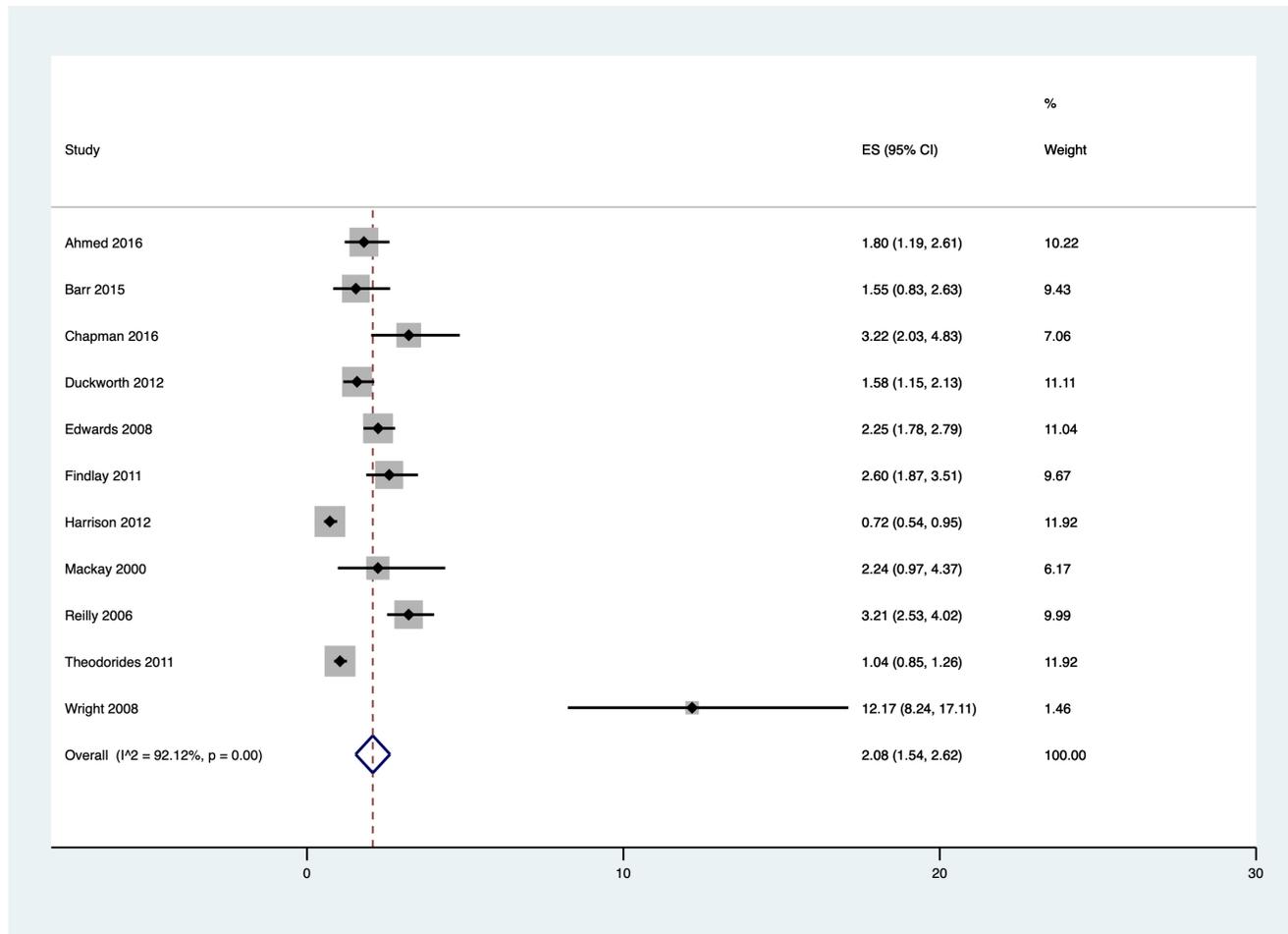


Fig. 2

Synthesis of studies reporting surgical site infection (SSI) for hip fracture of all surgical types. Meta-analysis of reported rates of SSI in 'all hip fracture surgery' using random effects model. Heterogeneity is expressed using the I^2 statistic. CI, confidence interval; ES-SSI, estimate from each study.

Quality assessment/risk of bias. The Newcastle-Ottawa Scale (NOS) for observational studies was used to assess study quality.¹⁴ The NOS was modified by including only the 'selection' and 'outcome' quality assessment questions. The comparative component of the standard NOS was removed as there was no comparison of treatments in this systematic review question. The results are presented in Supplementary Table ii.

Results

A total of 20 studies were selected, with reasons for exclusion outlined in Figure 1.^{6,15–33} Of the 20 studies, 18 were included in the quantitative synthesis. This was undertaken according to the type of surgery reported. Two studies were multicentre studies or reporting administrative data from across the UK. After contacting the authors, it was not possible to determine whether or not these patients would be double-counted and so these studies were only included in the qualitative synthesis.^{22,27} Overall 29 studies were excluded. A summary of all the studies identified and included is presented in Supplementary

Table iii. A separate table of studies that were identified as 'historical' is outlined in Supplementary Table iv.

All hip fractures. A total of 11 of the 20 studies reported data from 'all types' of hip fracture surgery. Across these studies, 491 surgical infections were observed in 30,740 hip fractures. A range of study sizes and rates of infection were seen. The largest study reported on 105 infections from 10,061 cases (1.04%) from two high-volume centres.³² The smallest study contained only 230 cases, with 28 infections (12.2%).³³

The pooled estimate for infection across these studies was 2.1% (95% confidence interval (CI) 1.54% to 2.62%). There was notable variance between the studies as measured by the I^2 statistic (92.1%). These data are highlighted in Figure 2.

This is unsurprising given the mixture of study designs, case definitions, and study sizes. One study was a marked outlier in that the infection rates were substantially higher than the other studies and the pooled estimate.³³ Although this study was relatively small in the context of all the studies assembled here, it still represents a sizeable

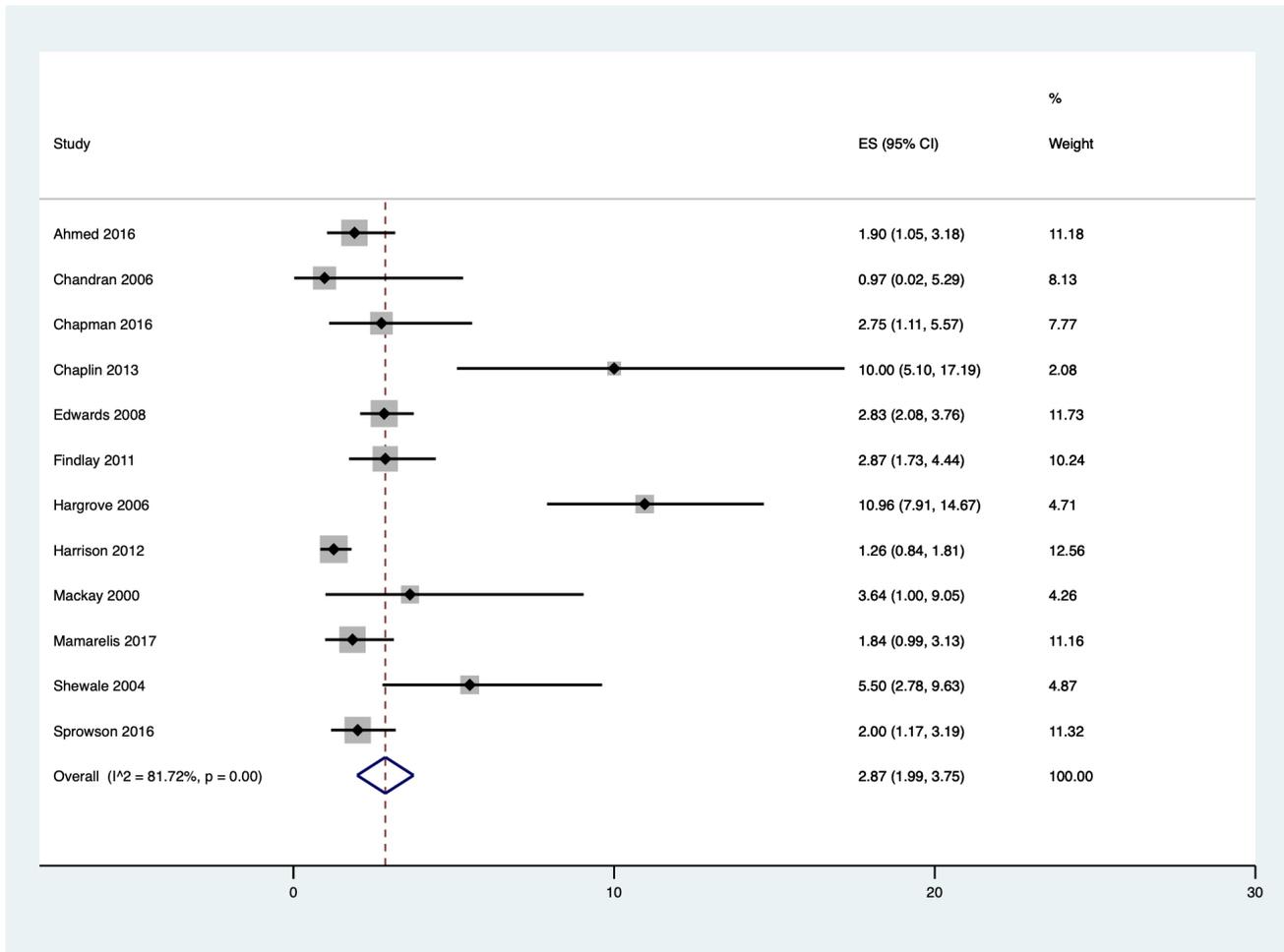


Fig. 3

Summary of studies reporting hemiarthroplasty. Meta-analysis of reported rates of surgical site infection (SSI) in hemiarthroplasty using random effects model. Heterogeneity is expressed using the I^2 statistic. CI, confidence interval; ES-SSI, estimate from each study.

study population. This study did not report the definition used for identifying cases of SSI, therefore it is possible this higher rate can be explained by a very inclusive definition of SSI.

Hemiarthroplasty. Data from 12 studies reported infection after hemiarthroplasty. The pooled estimate percentage rate of infection in the 7,941 hemiarthroplasty cases was 2.87% (95% CI 1.99% to 3.75%) (Figure 3). Within these studies, a range of infection rates were identified, the highest being two studies of over 10% surgical infection.

Similar to the 'all hip fracture' synthesis, there was high between-study heterogeneity (I^2 81.7%).

It was not possible to pool or report on the hip fracture population treated with total hip arthroplasty from the study dataset, as no cases of infection were reported against this treatment category.

Sliding hip screw. Fewer studies reported data on the sliding hip screw (SHS; $n = 6$). A total of 68 infections in 5,383 cases treated with SHS give a pooled estimate of 1.35% (95% CI 0.78% to 1.93%) (Figure 4).

The largest study that reported data on SHS is not included in the synthesis as it was reporting administrative data, and it was not possible to determine which centres it reported and hence any possible overlap.²²

This study reported on 18,014 undisplaced intracapsular hip fractures treated with SHS and found 80 cases of infection (0.44%).²²

Study types. Most studies were single-centre cohort studies. There was a mixture of prospective and retrospective study designs. A third category of 'prospective database' was also used to cover a number of the eligible studies. One study was of administrative data, named Hospital Episode Statistics (HES).²²

There were two randomized controlled trials;^{23,31} each used SSI as its primary outcome measure. Both trials were comparing interventions that are used in NHS care and therefore all patients were retained and treated as a single cohort.

Definition of infection. There were differing definitions of infection across the included studies. Seven studies reported using either a formally recognized diagnostic system

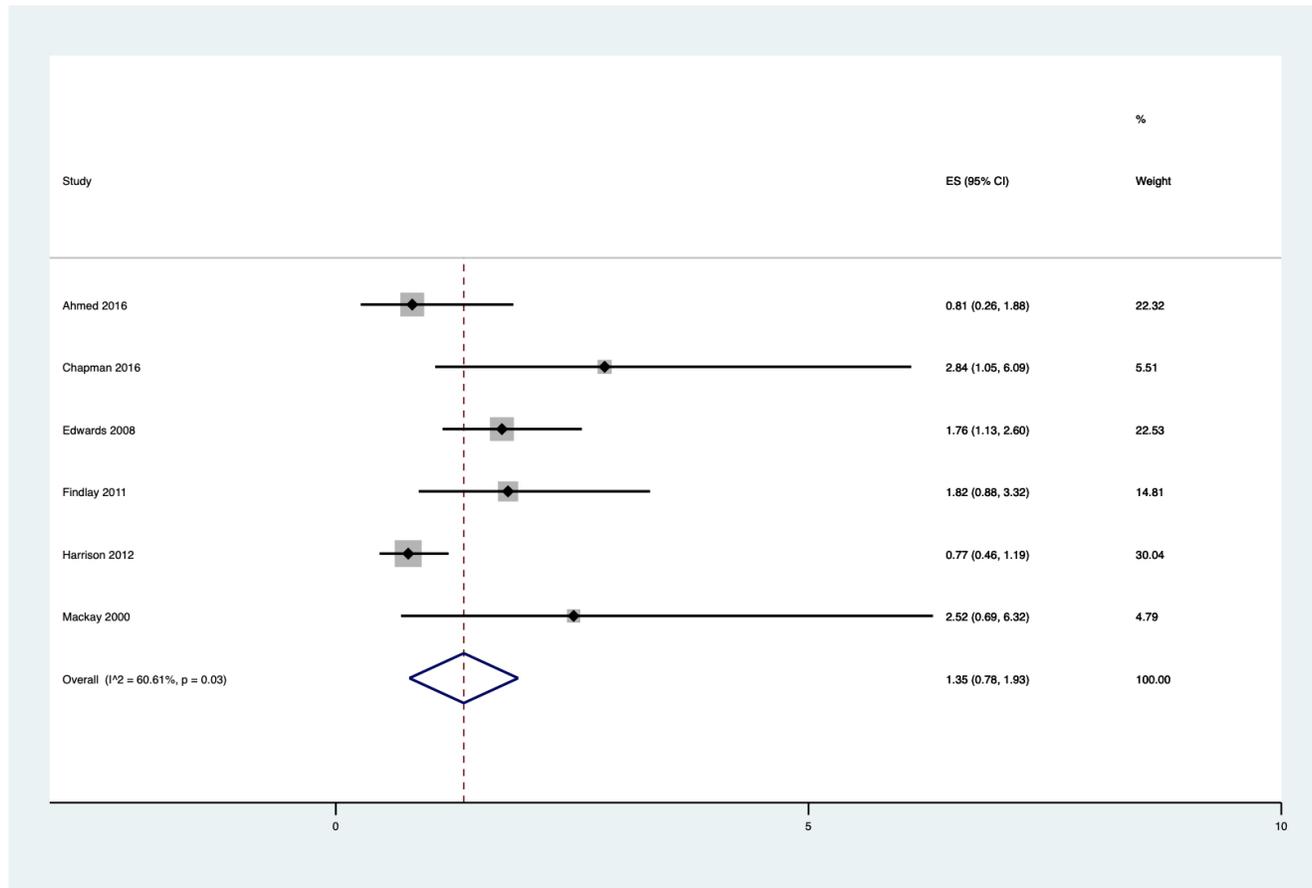


Fig. 4

Summary of studies reporting surgical site infection (SSI) after sliding hip screw (SHS). Meta-analysis of reported rates of SSI in SHS using random effects model. Heterogeneity is expressed using the I^2 statistic. CI, confidence interval; ES-SSI, estimate from each study.

such as the Centers for Disease Control and Prevention (CDC) definition or another validated definition.³⁴ Six studies failed to give a definition of infection, and the remainder used their own definition.

Figure 5 outlines the effect of three types of case definition on estimated rate of SSI. Studies of 'all hip fracture' were clustered into three categories: self-defined or 'study's own'; use of formally recognized criteria, e.g. CDC; no definition given.

The definition used by each study is outlined in Supplementary Table iii. The estimate for those studies with no definition is 5.56%, the relatively broad confidence intervals (95% CI 4.65% to 6.58%) relative to the other two clusters highlights that the absolute numbers in each are quite different. Of the two studies of 'all hip fractures' with no definition, Wright et al³³ was an outlier with a rate of 12%.

Superficial and deep infections. Across studies and definitions, the reporting and differentiation between superficial and deep SSI was inconsistent. These data were extracted where reported. Of the 20 studies identified, eight distinguished between superficial and deep infection. General observations suggest that those studies where this distinction was made had a similar spread of reported

rates of SSI - lowest (1.55%)¹⁶ and highest (13.92%)²⁹ - compared to where this distinction was not made.

Figure 6 plots the percentage rate of infection against the study sample size. The largest studies also reported the lowest infection rates, however there were still a majority of studies clustered around the 2.1% rate.^{22,24,32} Jettou et al's²² study of intracapsular fractures focused on two treatment methods and used administrative data. On the plot in Figure 6 this is the extreme outlier with over 50,000 cases. This focus on a specific population and the lack of identifiable centres meant that the study was not incorporated into any of the pooled estimates. The outliers for high rates of infection were all smaller studies of fewer than 500 patients.

Supplementary Table ii outlines the scores accrued for the modified NOS system.

Discussion

Summary of findings. The primary aim for this study was to identify studies reporting SSI after hip fracture surgery in the UK.

The search process identified 20 studies that reported on 88,615 cases of hip fracture and 938 cases of SSI.

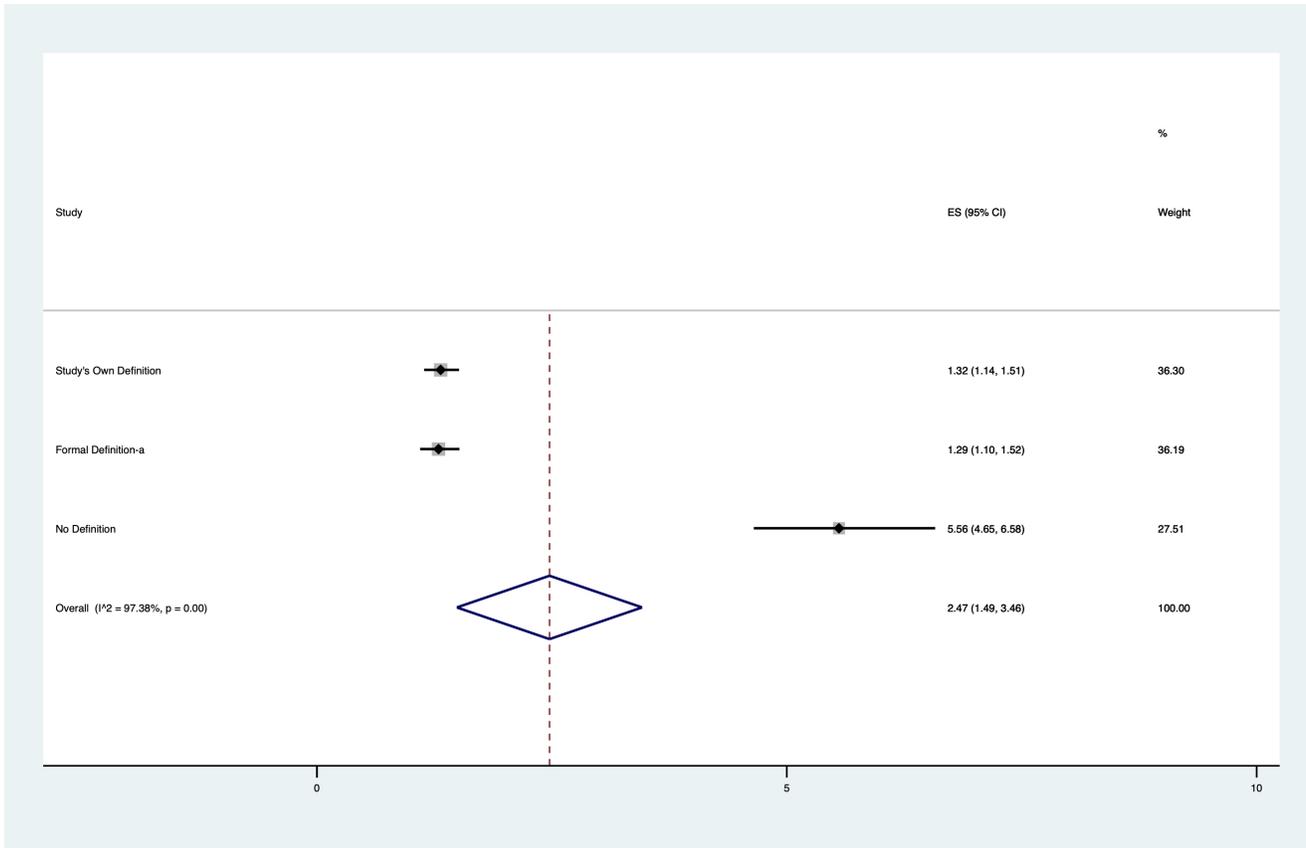


Fig. 5

Summary of studies clustered by definition of surgical site infection (SSI). Meta-analysis of reported rates of SSI according to study definition using random effects model. Heterogeneity is expressed using the I^2 statistic. Formal definitions encompass either a referenced study on SSI or a formal definition used by a public health body, e.g. Centers for Disease Control and Prevention. CI, confidence interval; ES-SSI, estimate from each cluster.

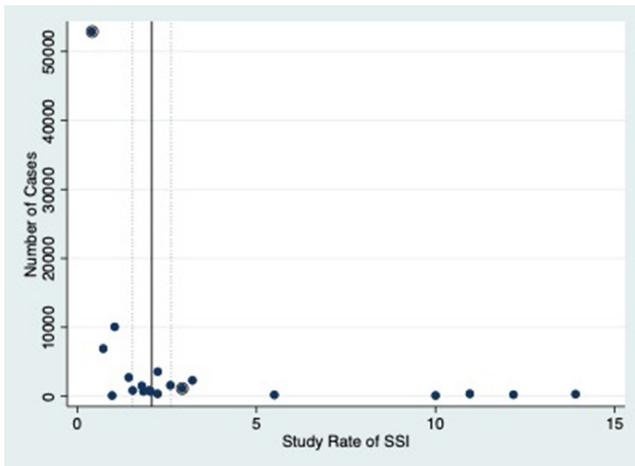


Fig. 6

Percentage rate of surgical site infection (SSI) for studies included in systematic review by study population. Summary data plotting reported rate of SSI against the study population size. The pooled estimate for 'all hip fractures' is also plotted with 95% confidence intervals. Studies not included in the pooled estimate are circled for reference.

The aggregate of 'all hip fracture' identified a rate of 2.1% (95% CI 1.84% to 3.09%). These data are derived

from studies from 18 centres. Many different types of hospital such as major trauma centres, trauma units, and traditional district general hospitals are included in the analysis, improving the generalizability of the results. Similarly, the characteristics of patients included were defined in the broadest possible terms. The previously reported rate of SSI from Public Health England is 1.1% (95% CI 1.1% to 1.2%).⁹ This estimate is notably lower than the pooled estimate from this study. This is in-keeping with previous work on the limitations of the current surveillance process.³⁵

When SHS and hemiarthroplasty were considered as subcategories of procedure, different rates were observed.

Sliding hip screw. For the SHS category, the pooled estimate was 1.35% (95% CI 0.78% to 1.93%). The review process also identified a single large study (18,014 patients) reporting patients who underwent a SHS procedure for a less common subset indication - intracapsular fracture. This estimate was lower than the pooled estimate (0.44%).²² The difference between these two is most likely explained by the different data sources and highly specific subset of fractures studied by Jettoo et al.²² There is possible further confounding by the use of

administrative data in the Jettoo et al²² study compared to medical records for the pooled estimate.³⁶ Few published studies focus on SSI after SHS for the more common indication of intertrochanteric fractures. In this review, all of the data were from studies reporting the generality of hip fractures. Other published estimates are as high as 3.9%.³⁷

Hemiarthroplasty. The hemiarthroplasty pooled estimate of 2.87% (95% CI 1.99% to 3.75%) is notably higher than the estimate for SHS and the national surveillance estimate for hip fracture. There were a greater number of studies reporting hemiarthroplasty cases, which likely reflects a broader general interest in the implants and techniques around this procedure. Despite being the highest pooled estimate in this study, a rate of 2.87% may still be conservative. Other systematic reviews have identified rates as high as 7%.³⁸ Explanations for the higher rate of infection following arthroplasty are likely multifactorial, but may be based on a higher risk population and a more invasive surgical procedure requiring more extensive surgical dissection and surgical duration.

Study size and quality. The two largest study sizes had the lowest rates of infection (< 1.5%).^{24,32} Similarly, the studies with the highest rates of infection were the smallest.³³ However, this observation cannot be purely attributed to the size of the study as similar small-sized studies also reported low infection rates.

The explanation for this association may be related to the study design and the method of case capture. As studies become larger, the resources needed to assess many thousands of patients grow dramatically. The most frequent solution is to use routinely collected data, either from the medical record or an institutional database. The process of retrospectively reviewing this type of data may require the patient being diagnosed and treated in the same institution, and returning to secondary care. This type of study is therefore quite 'specific' for the SSI cases, but not very 'sensitive'. The tendency of the larger studies to rely on local medical record database data may introduce under-reporting bias, as they rely on coders to identify SSI cases and may not capture patients re-presenting to other institutions.

Definitions of infection. The definitions used in these studies vary considerably. For those studies using institutional data, the retrospective nature of their data collection necessitated the use of particular metrics such as culture, reoperation, and treatment with antibiotics. Clinical examination parameters are much more difficult to review in this way, but are also a valid means by which diagnosis can be achieved. The widespread use of reoperation and culture to define cases in this literature may therefore lead to under-reporting; in particular only considering patients who have undergone reoperation as having SSI is highly problematic. Hip fracture patients often represent very high anaesthetic risk, and as such the decision to operate may well be a last resort. Where no clear diagnostic criteria were used it is possible that

speculative infections were included, e.g. erythematous wound treated with antibiotics.

There are a number of important limitations to acknowledge in this study. First, the use of only published studies meant that we did not include unpublished data and grey literature. The studies identified used a mixture of methods and definitions for the cases of infection. For this reason, these study findings should be interpreted cautiously. The heterogeneity observed across all of the pooled estimates could not be fully explored due to the limited covariate reporting. However, sensitivity analysis using study definition seemed to explain some of the observed variation. Similarly, the study size seemed to also explain some of the differences in the reported rates. It is also important to acknowledge that these data are derived from the UK. The findings of this study may therefore be particularly relevant to other high income health-care systems where hip fracture is a disease of the frail elderly population. The implications for other settings are less clear.

In conclusion, the published literature reporting SSI after hip fracture demonstrates a range of rates, study designs, and case definitions. The 'true' proportion of hip fracture cases complicated by SSI is likely to be higher than 2.1%. However, this should be interpreted with great caution given the many potential sources of bias and heterogeneity. Further work should aim to overcome the study limitations identified in this review and to distinguish between superficial and deep SSI.

Supplementary material



Tables showing the online search string used for study identification and summaries of modified Newcastle-Ottawa Scales, studies included in systematic review and meta-analysis, and historical studies identified by search.

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Author contributions:

- J. Masters: Conceptualized and managed the study, Wrote the manuscript.
- D. Metcalfe: Selected the studies, Wrote the manuscript.
- J. S. Ha: Extracted the data, Wrote the manuscript.
- A. Judge: Supervised the study, Edited the manuscript.
- M. L. Costa: Supervised the study, Edited the manuscript.

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Ethical review statement

- No ethical approval was sought as this is an analysis of existing published data.

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