The economic benefits of surgical site infection prevention in adults: a systematic review

McFarland, Agi; Reilly, Jacqui; Manoukian, Sarkis; Mason, Helen

Published in:
Journal of Hospital Infection

DOI:
[10.1016/j.jhin.2020.05.011](https://doi.org/10.1016/j.jhin.2020.05.011)

Publication date:
2020

Document Version
Author accepted manuscript

[Link to publication in ResearchOnline](#)

Citation for published version (Harvard):
McFarland, A, Reilly, J, Manoukian, S & Mason, H 2020, 'The economic benefits of surgical site infection prevention in adults: a systematic review', *Journal of Hospital Infection*, vol. 106, no. 1, pp. 76-101.
<https://doi.org/10.1016/j.jhin.2020.05.011>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

If you believe that this document breaches copyright please view our takedown policy at <https://edshare.gcu.ac.uk/id/eprint/5179> for details of how to contact us.

Title page

Title: The economic benefits of surgical site infection prevention in adults: A systematic review

Name and title of each author:

Mrs Agi McFarland

Professor Jacqui Reilly

Dr Sarkis Manoukian

Professor Helen Mason

Department and institution where the work was completed:

Department of Nursing and Community Health, School of Health and Life Sciences, Glasgow
Caledonian University

Author responsible for correspondence and proofs:

Agi McFarland
Department of Nursing and Community Health
School of Health and Life Sciences
Glasgow Caledonian University
Cowcaddens Road
Glasgow G4 0BA
Tel: +44 (0) 141 331 8328
Email: agi.mcfarland@gcu.ac.uk

Running title: Economic benefits of SSI prevention

Funding: This work was supported by Glasgow Caledonian University and Health Protection
Scotland via the Evaluation of the Cost of Nosocomial Infection Study

Structured Summary

Background: Surgical site infections (SSI) present a significant burden to healthcare and patients in terms of excess length of stay, distress, disability and death. SSI risk and the associated economic burden may be reduced through adherence to prevention guidelines although the irreducible minimum is unclear.

Aim: To evaluate the methods used to estimate the cost effectiveness of prevention strategies for all SSI.

Methods: Pubmed, Medline, CINAHL and NHS Economic Evaluation Database were searched from inception to January 2020 to identify English language economic evaluation studies, embedded economic evaluations and studies with some analysis in relation to cost and benefit in adult patients receiving surgical care in any setting. Risk of bias was assessed using the Drummond [1] and Philips [2] checklists.

Findings: 32 studies involving 24 043 participants were included. Most studies evaluated SSI prevention in orthopaedic surgeries. Antibiotic prophylaxis, screening, treating or decolonisation of MRSA and surgical wound closure were the main methods evaluated. Methods ranged from cost analyses to cost effectiveness and cost utility analyses. Synthesis of results was not possible due to heterogeneity. All studies reported some economic benefit associated with preventing SSI however measures of benefit were not reported consistently and the quality of studies was low to moderate. Limited evidence in relation to SSI impact on quality of life was identified.

Conclusion: Current evidence in relation to the economic benefits of SSI prevention is limited. Further robust studies which utilise sound economic and epidemiological methods are required to inform future investment decisions in SSI prevention.

(248 words including headings)

Keywords

Surgical site infection

SSI

Healthcare acquired infection

Economic evaluation

Quality of life

Main text

Introduction

Healthcare associated infection (HAI) are infections associated with patients receiving health care and are globally the most frequently reported adverse event. They present a significant burden in terms of excess length of stay and disability and contribute to the development of resistant organisms through the increased use of antimicrobials. A significant economic burden is also presented by HAI in relation to the increased cost of health care, costs for the patient and their family, societal costs from lost productivity and excess deaths [3]. Globally, SSI is the most surveyed and frequent HAI in low and middle income countries and the second most frequent HAI in Europe and the United States of America [4].

Once SSI develops, post-operative recovery is extended and increased use of healthcare resource is required [5]. Estimates on the burden posed by excess length of stay attributed to SSI are complicated by methodological limitations [6], and although monetary estimates may vary depending on method used there is agreement in the literature that this burden is substantial. It is therefore logical to assume that one way to minimise the impact of this burden is through the prevention of SSI. Although not all HAI are preventable [7], a recent systematic reviews' findings [8] highlighted that prevention strategies aimed specifically at SSI could have a substantial effect on risk reduction. Annual costs of preventable SSI are estimated in the range of \$166 million to \$345 million in the USA alone [9]. However, the economics of SSI prevention is not as simple as costs avoided through the elimination of infection. The prevention strategies themselves will incur a cost, and not including these in any analysis will overestimate the economic gains offered by specific strategies.

Systematic identification and analysis of all relevant alternatives is integral to effective decision making. Economic evaluation can provide a robust decision-making framework to inform resource allocation decisions. Given the recognition in the literature that SSI substantially impact both costs and health outcomes [10], cost effectiveness analysis methodology using health related quality of life as the patient outcome measure is the obvious choice for capturing the economic burden posed by these infections. It is imperative to have accurate estimations of this burden to enable any meaningful evaluation of infection preventions and control (IPC) strategies aimed at reducing SSIs.

In order to establish the current evidence base in relation to the economic impact of prevention measures for SSI, a systematic review was undertaken. The primary aim of the literature review was to assess the methods used to estimate the cost effectiveness of prevention strategies for surgical site infection. A secondary objective focussed on the assessment of the quality of economic evaluation methods used within the extant literature and identify any methodological limitations. The PICOS were as follows:

- *Participants*: All adult patients, as defined by the trialists, with a confirmed surgical site infection using any diagnostic criteria in hospital and community settings
- *Interventions*: Any prevention strategy aimed at reducing SSI
- *Comparisons*: No intervention or a standard care intervention where the prevention strategy represents an alternative or adjunct to standard care
- *Outcomes*: Economic data in relation to cost and efficacy of SSI prevention methods
- *Study Design*: All economic evaluation studies, economic modelling studies or studies reporting embedded economic evaluations, including randomised controlled trials or quasi randomised controlled trials, controlled trials and pilot studies. Studies which were primarily clinical but had some analysis in relation to cost and benefit (using an economic tool or

method to calculate outcome) were also included. Studies which did not consider an analysis plan for economics data in the main methods and/or completed narrative costings as part of a discussion or conclusion were excluded.

Methods

Search

The systematic review was registered with PROSPERO, the International prospective register of systematic reviews (Registration number CRD42017056340). Studies which met the PICO criteria and published in English were included. The following databases were searched from inception to January 2020:

- Pubmed
- Medline via EBSCO host
- CINAHL via EBSCO host
- NHS Economic Evaluation Database.

A pre specified search strategy was formulated for each database and adapted for each database's conventions. The main search strategy is included in Appendix A. NHS Economic Evaluation Database was searched using medical subject headings only. Reference lists within relevant evaluations were screened to identify any further potential papers.

Study selection and data extraction

Two authors (AMcF and HM) independently examined the titles and abstracts identified by the search strategy to remove any duplicate records and obviously irrelevant reports. Full text versions of potentially relevant studies identified by at least one author were retrieved and evaluated. Two authors (AMcF and HM) independently assessed each study to determine if they met the eligibility criteria and extracted data utilizing a standardized data extraction form developed for this review. Any disagreements were resolved by discussion between the authors (AMcF and HM), with a further author (SM) acting as arbiter. The data extraction form included the following:

- General information: author(s), title, source, contact address, year of study, country of study, year of publication
- Trial characteristics: design, time horizon, perspective
- Participants: baseline characteristics (including surgery type), inclusion and exclusion criteria, sample size and number of patients allocated to each group or hypothetical patient cohort details (for modelling studies)
- Interventions: detailed description of the comparison SSI prevention strategies
- Outcomes: Costs and economic outcomes

Synthesis of results was planned via a four grid decision matrix which categorises costs and effectiveness in one diagram.

Quality assessment

Study quality assessment was completed independently by three authors (AMcF, JR and SM) using the Drummond Checklist [1] for economic evaluations. Modelling studies were further evaluated using the Phillips Checklist [2]. Study components were either rated as Yes, No or Not Clear for all

criteria. Any disagreement was resolved through discussion between all three authors (AM, JR, SM). Quality assessment was evaluated both within and across all included studies.

Results

Study selection and characteristics

The search identified 2465 titles and abstracts following removal of duplicates. A total of 89 articles were initially identified as having the potential and full texts of these were retrieved. Of these 57 articles were subsequently excluded and 32 studies met the inclusion criteria (see PRISMA flow diagram Figure 1). Study characteristics for all included studies can be found in Table I. All monetary values are reported here in US dollars, converted to the year of study using historical national currency conversion rates. Where no year of study was provided, the year of publication was used for the calculation.

The range of SSI prevention strategies evaluated included training programmes for staff [11, 12], SSI prevention bundles [13], wound dressings [14 – 19] or preoperative skin antisepsis [20, 21]. Strategies in relation to MRSA such as preoperative decolonisation [22, 23] or a combination of both screening and treating MRSA [24 – 28], various prophylactic antibiotic regimens [29 – 38] and surgical wound closure methods [39 – 42] were the main IPC measures evaluated in the literature. The majority of the studies were from the USA [11, 13, 16, 19, 20 - 22, 24 - 27, 35, 38, 42] four from Australia [17, 18, 33, 34] three from the UK [29, 30, 40] and Japan [14, 39, 41] two from the Netherlands [23, 28] India [32, 42] and single studies from Egypt [31], Nigeria [37] Spain [15] and Turkey [36]. Publication dates ranged from 1996 to 2017, with a peak in publication in the years 2013-14. Methods used ranged from simple cost analyses [11 - 15, 19, 21, 26, 29, 31, 34 - 39, 41] to cost benefit analysis [16], cost effectiveness analyses [20, 23, 27, 28, 32, 38, 42] and cost utility analyses [17, 18, 22, 24, 25, 30, 33, 40]. Synthesis of results via the four grid decision matrix to categorise costs and effects into one diagram was not possible due to the variability in methods, interventions and patient populations. Consequently, results are presented as a narrative overview and grouped according to methods used.

Cost analyses

The 16 studies in this grouping were predominantly efficacy studies with calculation of costs. Studies which included a consideration of costs or collection of economic variables within their methods were included. Studies which completed descriptive costings in the discussion or conclusion sections only with no considerations of the economic component in the formal methods were excluded. A summary of the studies is presented in Table II.

A mixed approach to costings were used in this group, with two studies only including cost differences for the consumables required for the interventions [31, 39]. Three studies collected information on resource use [14, 15, 39] although only one attributed any costs [15]. Six studies considered subsequent treatment related to SSI and additional impacts on length of stay [13, 19, 29, 34 – 36] although the scope of this was limited in one study with a focus exclusively on antibiotic usage [36] rather than all treatment. Some studies used historical SSI costs from previously published sources [21, 26, 34] with no details of any price adjustments between the year of study and the original estimates. When reported, SSI were predominantly diagnosed using CDC criteria [12, 15, 19, 29, 31, 34, 36, 39, 41].

Estimates for cost of SSI interventions in this group ranged from \$3.35 [36] (prophylactic antibiotics in neurosurgery) to \$111 794 [11] (comprehensive unit based safety programme in colorectal

surgery). Interventions reported to reduce the rates of SSI from 0.26% [19] to 100% [21, 39] or have no effect [14, 20, 41, 36]. Economic gains reported as “savings” ranged from \$40 219 [41] to \$501 605 [19] annually.

Cost benefit analysis

Only one study used cost benefit methodology [16]. Benefit was defined as costs saved by avoiding SSI after caesarean section using negative pressure wound therapy. The intervention was found to be cost beneficial compared to standard dressings only if SSI rates and efficacy of the intervention were high (see Table III).

Cost effectiveness analyses

Of the seven studies in this grouping, four used economic modelling for their analysis [20, 27, 38, 42]. Sources of efficacy data ranged from prospective observational data collection [23, 27, 32] routine audit [28] or published sources [11, 38, 42]. Cost data was sourced from the study sites [11, 23, 28, 32] previously published estimates [38, 42] or a combination [27]. All but one study [28] stated a hospital or third party payer perspective (see Table IV).

There was variation in the presentation of cost effectiveness results with some reports of incremental cost savings per surgical case resultant from the intervention [20], per SSI averted [23] overall savings [20, 28] or lifetime healthcare costs [38]. These incremental cost savings ranged from \$16 [20] to \$416 663 [23]. One study only presented the results of the sensitivity analysis so conclusions about the base case cost effectiveness are not possible to draw [27]. Two studies reported incremental cost effectiveness in terms of cost savings per person ranging from \$234.45 for screen and treat with mupirocin [28] to \$16 for single use applicator and \$26 bottled chlorhexidine for pre-operative skin preparation [20]. Any further direct comparison of single study metrics were not possible due to the lack of consistency in how cost effectiveness outcome measures were reported.

Cost utility analyses

Cost utility analysis may be thought of as a specific form of economic evaluation where the effectiveness of the intervention is evaluated in terms of health related quality of life as measured by utility. Utility is a valuation of health, with 0 being death and 1 being perfect health [43]. The health state valuation is then multiplied by the time the person spends in that health state, to give a measure of the quality adjusted life years (QALYs) associated with the outcomes of each treatment under comparison. As such, cost utility analyses have the potential to address the limitations identified in the previous studies in relation to the variability in outcomes reporting. The majority of the eight included cost utility analyses used decision analytical modelling for their analysis [8, 17, 18, 24, 25, 30, 33] and a summary is included in Table V.

Utilities were drawn from existing literature specific to the study population [22, 24, 30, 33], from a comparable population [25, 18] or through primary prospective data collection using a survey instrument [40, 17]. All but one of the studies [33] assumed a payer perspective. Six studies [17, 18, 24, 30, 33, 40] reported a cost per QALY gained from various prevention methods. The remaining two studies reported probabilities of the intervention being cost effective. Estimates ranged from a \$4174.43 saving [33] to a cost of \$273 817.28 [40] (see Table VI).

Study quality assessment

Results of the study quality assessments for all included studies can be found in Table VII. Criteria relating to study design were generally completed well. The alternatives under comparison were described in all studies but the rationale for these was not always clear or provided. Around half of the included studies did not explicitly state or were not clear in the form of economic evaluation [14, 15, 19, 25 - 29, 31 - 33, 35, 37, 39 - 41] the majority of these were in the Cost Analyses group (11 studies from 16).

The source of effectiveness estimates were stated in all studies, however the reporting of single source estimates or methods used to combine studies if estimates of effectiveness came from multiple sources was variable. Where health state valuations were used, methods used to elicit these lacked enough detail to be reproducible [11, 12, 17, 18, 20, 22, 24, 30, 38]. Most studies did not report resource use separately from unit costs. There was considerable variation in the reporting of criteria in relation to currency, time horizons, and discounting. Even in studies which reported a discount rate [11-13, 20, 22, 23, 30] only three [20, 23, 30] provided a justification for this figure. Sensitivity analysis was generally reported, although again variation existed in the studies whereby some studies covered this well and others provided little or no information. Less than half of the studies reported findings in disaggregated form as a minimum in terms of costs and effects in addition to an overall aggregated estimate [11, 12, 15 - 18, 20, 23 - 26, 30, 36, 38]. On the whole, answers to the research question were provided except in the 10 studies where there was ambiguity in relation to the objectives of the economic evaluation [26 - 28, 31, 33, 34, 37, 39, 40, 41]. Modelling studies were generally reported fairly but there was consistent lack of reporting in relation to methodological uncertainty, heterogeneity, testing of the mathematical logic of the model and calibration against independent data in all the studies (see Table VIII). Overall, the quality of the included studies was variable. Costs analysis methodology was associated with poorer levels of reporting as judged by all criteria in the checklists used, and cost utility analyses with the most robust.

Discussion

The primary aim of the literature review was to assess the range of methods used to estimate the cost effectiveness of prevention strategies for SSI. A secondary objective focussed on the assessment of the quality of economic evaluation methods used within the extant literature and identify any methodological limitations. Overall 32 studies were identified which met the inclusion criteria for the review using a range of economic evaluation methods. Regardless of methodology, all of the studies reported economic benefit associated with the prevention of SSI. However, measures of this benefit were not reported consistently. Only a handful of studies considered quality of life when making value for money judgements of the prevention strategies under comparison.

Mupirocin for the prevention of MRSA SSI was the only intervention which was evaluated across each of the main methodologies identified in the review in the same setting of joint arthroplasty [24, 26, 27]. Yet despite these similarities and potential economic gains identified, even in this relatively homogenous group of studies different estimates of effect were reported. This not only highlights the impact of using different economics methodologies to evaluate comparable questions, but also the general difficulty in attempting to synthesise the evidence from the identified studies.

The current evidence base is limited in a number of ways. The lack of SSI specific quality of life information in the literature was highlighted by the cost utility analyses included in this review. Where utility values were used from previously published literature, the transferability of the values for the study of SSI impact may be questionable. An example of this is the use of utilities [38] from the Beaver Dam Health Outcomes Study which was a longitudinal cohort study aiming to study

health related quality of life in a random sample of adults from a community population [44]. A clear limitation of the current literature base identified from this review is, therefore, a lack of health utility data specifically for people with an SSI. Although a previous review [45] did manage to synthesise a utility decrement estimate in the range of 0.04 – 0.48 from 29 studies, the authors acknowledge that the majority of this estimate came from study participants who were undergoing revision arthroplasty for deep infections. As such, these utilities represented an outcome of SSI rather than an ongoing SSI. A clear need is therefore identified to gather health related quality of life information specifically to determine the impact that SSI may have on health utility, in hospital and beyond for any future modelling work aimed at evaluating the economic impact of any SSI prevention strategy.

Although a number of studies claimed a societal perspective, none collected true socioeconomic costs which would account for costs beyond the health care sector such as informal care and loss of labour productivity due to SSI. Not only will this restrictive view of costing hide the effect of cost shifting to other sectors (for example, from hospital to community or the patient), but it will also prohibit a true estimation of the opportunity costs of the interventions under comparison which is the theoretically preferred strategy for accurate cost estimates [46]. The majority of the studies used accounting costs from hospital databases which may be used as a cheaper and quicker alternative. However, given that these are based on historical costs they cannot give actual opportunity costs, only reasonable estimates [47]. In the single study which collected indirect costs in relation to lost productivity and out of pocket expenses for the patient and carer as a result of HAI [12], these indirect costs were not reported separately for SSI. This is a clear gap in the current knowledge base which needs to be addressed for a true estimate of economic burden to enable long term impacts of SSI prevention strategies to be evaluated.

A further consideration in terms of long term impact is the development of antimicrobial resistance which will inevitably change the efficacy profile of antibiotic and antiseptic based IPC measures. For example, the development of resistant bacterial strains in the presence of excessive use of chlorhexidine has been documented in various settings [48]. If short term data in relation to efficacy is extrapolated over the life time horizon, some consideration of resistance will need to be considered in the model structure. One study [33] acknowledged the lack of consideration for the development of resistance in their model as a limitation. One further study also briefly considered this issue [38] and built a 2% annual resistance rate in to their model and found that the initial recommendations for Vancomycin prophylaxis was no longer the dominant strategy after 6 years. They present this only as an overview and advise that there is a lack of robust data in relation to the development of resistance therefore have not included it in the formal model structure and analysis.

The studies in this review are further limited by the epidemiological methods used. Many were retrospective reviews of available data rather than well designed studies for the purpose intended and few met the criteria for reporting epidemiology required by STROBE [49]. As such, there was a high risk of bias therein.

The protocol of any future economic evaluations of SSI prevention strategies should use standardised internationally recognised definitions of infection such as those available from the Centers for Disease Control and Prevention [50]. Economic evaluations should clearly state the type of evaluation they are conducting, and with the widely acknowledged impact of SSI on quality of life, cost utility analysis would be the methodology of choice. Given the paucity of quality of life data specific to SSI, any future studies should also prospectively collect these measures using recognised instruments such as EQ-5D [51] and SF-36 [52]. Studies should report methods used to estimate and value resource use associated with the alternative interventions. Costings should also include costs

associated with the delivering the prevention strategy itself and any additional healthcare costs, cognisant that these may be post discharge from the acute hospital setting. If studies aim to capture the socioeconomic value of SSI prevention, societal costs beyond healthcare utilisation should also be included. All prospective data should be gathered for the full time period specified in the diagnostic criteria. Finally, any economic models with a long term time horizon (i.e. greater than 12 months) should consider the impact of the development of resistance on the efficacy of the prevention measure under study. Studies should be reported according to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement along with the associated checklist [53].

The findings of this systematic review are in agreement with recent work looking at the economic case for SSI prevention in the pre [54] and intraoperative phase of treatment [55]. The inclusion of a wider scope of the patient journey and economic modelling studies in this review provides a wider perspective. Improvements need to be made in terms of the overall quality of economic evaluations in this area. Similar to a recent systematic review of economic evaluations of IPC measures for all HAI types [56], the reporting quality of studies in this review were found to be poor to fair. More high quality studies are required which address the limitations identified above which adhere to current methodological reporting guidelines.

Appendix

Appendix A – Main search strategy

((“Cross Infection”[Mesh] OR (cross infection*) OR (healthcare associated infection*) OR (health care associated infection*) OR (hospital acquired infection*) OR (hospital-acquired infection*) OR (hospital associated infection*) OR (healthcare-associated infection*) OR (healthcare acquired infection*) OR (health care acquired infection*) OR (nosocomial*) OR (cross transmission) OR (infectious disease transmission))

AND (“Surgical Wound Infection”[Mesh] OR (surgical site infection*) OR (SSI))

AND (“Costs and Cost Analysis”[Mesh] OR “Health Care Costs”[Mesh] OR “Economics” [Mesh] OR (economics) OR (economic*) OR (costs and cost analysis”[Mesh]) OR (cost) OR (direct cost*) OR (economic eval*) OR (economic analys*) OR (cost analy*) OR (cost utili*) OR (cost effect*) OR (cost benefit*))

AND (“Primary prevention [Mesh] OR “Prophylactic Surgical Procedures” [Mesh])

References

- [1] Drummond MF, Jefferson TO. Guidelines for the authors and peer reviewers of economic submissions to the BMJ. *BMJ* 1996; 313: 275 – 83. <https://doi.org/10.1136/bmj.313.7052.275>
- [2] Phillips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, et al. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technol Assess* 2014; 8: 1 – 158. <https://doi.org/10.3310/hta8360>
- [3] WHO. Report on the Burden of Endemic Health Care-Associated Infection Worldwide, http://apps.who.int/iris/bitstream/10665/80135/1/9789241501507_eng.pdf?ua=1; 2010 [Accessed on 12 February 2020]
- [4] World Health Organisation. Global Guidelines for the Prevention of Surgical Site Infection <http://www.who.int/gpsc/ssi-prevention-guidelines/en/>; 2016 [Accessed on 12 February 2020]
- [5] Owens CD, Stoessel K. Surgical site infections: epidemiology, microbiology and prevention. *J of Hosp Infect* 2008; 70: 3 – 10. [https://doi.org/10.1016/S0195-6701\(08\)60017-1](https://doi.org/10.1016/S0195-6701(08)60017-1)
- [6] Manoukian S, Stewart S, Dancer S, Graves N, et al. Estimating excess length of stay due to healthcare-associated infections: a systematic review and meta-analysis of statistical methodology. *J of Hops Infect* 2018; 100: 222 – 35. <https://doi.org/10.1016/j.jhin.2018.06.003>
- [7] Brown J, Doloresco F, Mylotte JM. (2009) “Never Events”: Not Every Hospital Acquired Infection Is Preventable. *Clin Infect Dis* 2009; 49: 743 – 6. <https://doi.org/10.1086/604719>
- [8] Harbarth S, Sax H, Gastmeier P. The preventable proportion of nosocomial infection: an overview of published reports. *J of Hosp Infect* 2003; 54: 258 – 66. [https://doi.org/10.1016/s0195-6701\(03\)00150-6](https://doi.org/10.1016/s0195-6701(03)00150-6)
- [9] Umscheid CA, Mitchell MD, Doshi JA, Agarwal R, et al. Estimating the Proportion of Healthcare-Acquired Infections The Are Reasonably Preventable and the Related Mortality and Costs. *Infect Control and Hosp Epidemiol* 2011; 32: 101 – 14. <https://doi.org/10.1086/657912>
- [10] NICE. Surgical site infections: prevention and treatment (NG125). <https://www.nice.org.uk/guidance/ng125> 2019 [Accessed on 12 February 2020]
- [11] Lee BY, Berenholtz SM, Hobson DB, Demski RJ, Yang T, et al. Building a Business Case for Colorectal Surgery Quality Improvement. *Dis Col Rectum* 2013; 56: 1298 – 1303. <https://doi.org/10.1097/DCR.0b013e3182a4b973>
- [12] Singh S, Kumar RK, Sundaram KR, Kanjilal B, Nair P. Improving outcomes and reducing costs by modular training in infection control in a resource-limited setting. *Int J for Qual in Health* 2012; 24: 641 – 8. <https://doi.org/10.1093/intqhc/mzs059>
- [13] Keenan JE, Speicher PJ, Thacker JKM, Walter M, Kuchibhatla M, et al. The Preventive Surgical Site Infection Bundle in Colorectal Surgery. An Effective Approach to Surgical Site Infection Reduction and Health Care Cost Savings. *JAMA Surg* 2014; 149: 1045 – 52. <https://doi.org/10.1001/jamasurg.2014.346>
- [14] Akagi I, Furukawa K, Miyashita M, Kiyama T, Matsuda A, et al. Surgical wound management made easier and more cost effective. *Onc Lett* 2012; 4: 97 – 100. <https://doi.org/10.3892/ol.2012.687>

- [15] Arroyo AA, Casanova, PL, Soriano JV, i Bou JT. Open-label clinical trial comparing the clinical and economic effectiveness of using polyurethane film surgical dressing with gauze surgical dressings in the care of post-operative surgical wounds. *Int Wound Journal* 2015; 12: 285 – 92. <https://doi.org/10.1111/iwj.12099>
- [16] Echebiri NC, McDoom MM, Aalto MM, Fauntleroy J Nagappan N, et al. Prophylactic Use of Negative Pressure wound Therapy After Cesarean Delivery. *Obs and Gyn* 2015; 125: 299 – 307. <https://doi.org/10.1097/AOG.0000000000000634>
- [17] Heard C, Chaboyer W, Anderson V, Gillespie BM, Whitty JA. Cost-effectiveness analysis alongside pilot study of prophylactic negative pressure wound therapy. *J of Tissue Viability* 2017; 26: 79 – 84. <https://doi.org/10.1016/j.jtv.2016.06.001>
- [18] Tuffaha HW, Gillespie BM, Chaboyer W, Gordon LG, Scuffham PA. Cost-utility analysis of negative pressure wound therapy in high-risk cesarean section wounds. *J of Surg Res* 2015; 195: 612 – 22. <https://doi.org/10.1016/j.jss.2015.02.008>
- [19] Mueller S, Krebsbach LE. Impact of antimicrobial – impregnated gauze dressing on surgical site infections including methicillin-resistant *Staphylococcus aureus* infections. *Am J of Infect Con* 2008; 36: 651 – 5. <https://doi.org/10.1016/j.ajic.2007.12.005>
- [20] Lee I, Agarwal RK, Lee BY, Fishman NO, Umscheid CA. Systematic Review and Cost Analysis Comparing Use of Chlorhexidine with Use of Iodine for Preoperative Skin Antisepsis to Prevent Surgical Site Infection 2010. *Infect Control and Hosp Epidemiol* 2010; 31: 1219 – 29. <https://doi.org/10.1086/657134>
- [21] Watson PA., Watson L, Torres-Cook A. Institution of the Steiros algorithm outpatient surgical protocol reduced orthopaedic surgical site infections (SSI) rates. *The Iowa Orthop J* 2012; 32: 116 – 9. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3565391/>
- [22] Bailey RR, Stuckey DR, Norman BA, Duggan AP, Bacon KM, et al. Economic Value of Dispensing Home-Based Preoperative Chlorhexidine Bathing Cloths to Prevent Surgical Site Infection. *Infect Control and Hosp Epidemiol* 2011; 32: 465 – 71. <https://doi.org/10.1086/659763>
- [23] VandenBergh MF, Kluytmans JA, van Hout AP, Seerden RJ, McDonnal, et al. Cost-Effectiveness of Perioperative Mupirocin Ointment in Cardiothoracic Surgery. *Infect Control and Hosp Epidemiol* 1996; 17: 786 – 92. <https://doi.org/10.1086/647237>
- [24] Courville XF, Tomek IM, Kirkland KB, Bihle M, Kantor SR, et al. Cost-Effectiveness of Preoperative Nasal Mupirocin Treatment in Preventing Surgical Site Infection in Patients Undergoing Total Hip and Knee Arthroplasty: A Cost-Effectiveness Analysis. *Infect Control and Hosp Epidemiol* 2012; 33: 152 – 9. <https://doi.org/10.1086/663704>
- [25] Lee BY, Wiringa AE, Mitgang EA, McGlone SM, Afriyie AN, et al. Routine Pre-cesarean *Staphylococcus aureus* Screening and Decolonization: A Cost-Effectiveness Analysis. *Am J Manag Care* 2011; 17: 693 – 700. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3836821/>
- [26] Rao N, Cannella B, Crossett LS, Yates AJ Jr, McGough R 3rd. A Preoperative Decolonization Protocol for *Staphylococcus aureus* Prevents Orthopaedic Infections. *Clin Orthop and Relat Res* 2008; 466: 1343 – 8. <https://doi.org/10.1007/s11999-008-0225-4>

- [27] Slover J, Haas JP, Quirno M, Phillips MS, Bosco JA 3rd. Cost-Effectiveness of a Staphylococcus aureus Screening and Decolonization Program for High-Risk Orthopedic Patients. *J Arthroplasty* 2011; 26: 360 – 4. <https://doi.org/10.1016/j.arth.2010.03.009>
- [28] Wassenberg MWM, Ardine de Wit G, Bonten MJM. Cost-Effectiveness of Preoperative Screening and Eradication of Staphylococcus aureus Carriage. *PLoS One* 2011; 6: e14815. <https://doi.org/10.1371/journal.pone.0014815>
- [29] Dhadwal K, Al-Ruzzeh S, Althanasious T, Choudhury M, Tekkis P, et al. Comparison of clinical and economic outcomes of two antibiotic prophylaxis regimens for sternal wound infection in high-risk patients following coronary artery bypass grafting surgery: a prospective randomised double-blind controlled trial. *Heart* 2007; 93: 1126 – 33. <https://doi.org/10.1136/hrt.2006.103002>
- [30] Elliot RA, Weatherly HL, Hawkins NS, Cranny G, Chambers D. An economic model for the prevention of MRSA infections after surgery: non-glycopeptide or glycopeptide antibiotic prophylaxis? *Eur J of Health Econ* 2010; 11: 57 – 66. <https://doi.org/10.1007/s10198-009-0175-0>
- [31] El-Mahallway HA, Hassan SS, Khalifa HI, Safa MME, Khafagy MM. Comparing a combination of penicillin G and gentamicin to a combination of clindamycin and amikacin as prophylactic antibiotic regimens in prevention of clean contaminated wound infections in cancer surgery. *J Egypt Natl Canc Inst* 2013; 25: 31 – 5. <https://doi.org/10.1016/j.jnci.2012.12.001>
- [32] Mathur P, Trikha V, Farooque K, Sharma V, Jain N, et al. Implementation of a short course of prophylactic antibiotic treatment for prevention of postoperative infections in clean orthopaedic surgeries. *Indian J Med Res* 2012; 137: 111 – 16. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3657872/>
- [33] Merollini K, Crawford RW, Whitehouse SL, Graves N. Surgical site infection prevention following total hip arthroplasty in Australia: A cost-effectiveness analysis. *Am J of Infect Con* 2013; 41: 803 – 9. <https://doi.org/10.1016/j.ajic.2012.11.015>
- [34] Spelman D, Harrington G, Russo P, Wesselingh S. Clinical, Microbiological, and Economic Benefit of a Change in Antibiotic Prophylaxis for Cardiac Surgery. *Infect Con and Epidemiol* 2002; 23: 402 – 4. <https://doi.org/10.1086/502074>
- [35] Theologis AA, Demirkiran G, Callahn M, Pekmezci M, Ames C, et al. Local Intrawound Vancomycin Powder Decreases the Risk of Surgical Site Infections in Complex Adult Deformity Reconstruction. *Spine* 2014; 39: 1875 – 80. <https://doi.org/10.1097/BRS.0000000000000533>
- [36] Ulu - Kilic A, Alp E, Cevahir F, Tucer B, Demiraslan H, et al. Economic evaluation of appropriate duration of antibiotic prophylaxis for prevention of neurosurgical infections in a middle income country. *Am J of Infect Con* 2015; 43: 44 – 7. <https://doi.org/10.1016/j.ajic.2014.09.010>
- [37] Yinusa W, Onche II, Thanni LOA. Short-Term Antibiotic Prophylaxis In Implant Surgery: A Comparison Of Three Antibiotics. *The Niger Postgrad Med J* 2007; 14: 90 – 3. PMID: 17599102
- [38] Zanetti G, Goldie SJ, Platt R. Clinical Consequences and Cost of Limiting Use of Vancomycin for Perioperative Prophylaxis: Example of Coronary Artery Bypass Surgery. *Emerg Infect Dis* 2001; 7: 820 – 7. <https://doi.org/10.3201/eid0705.010508>
- [39] Ando M, Tamaki T, Yoshida M, Sasaki S, Toge Y, et al. Surgical site infection in spinal surgery: a comparative study between 2-octyl-cysnoacrylate and staples for wound closure. *Eur Spine J* 2014; 23: 854 – 62. <https://doi.org/10.1007/s00586-014-3202-5>

- [40] Gheorghe A, Roberts TE, Pinkney TD, Bartlett DC, Morton M, et al. The Cost-Effectiveness of Wound-Edge Protection Devices Compared to Standard Care in Reducing Surgical Site Infection after Laparotomy: An Economic Evaluation alongside the ROSSINI Trial. *PLoS One* 2014; 9: e95595. <https://doi.org/10.1371/journal.pone.0095595>
- [41] Nakamura T, Kashimura N, Noji T, Suzuki O, Ambo Y, et al. Triclosan-coated sutures reduce the incidence of wound infections and the costs after colorectal surgery: A randomised controlled trial. *Surgery* 2013; 153: 576 – 83. <https://doi.org/10.1016/j.surg.2012.11.018>
- [42] Singh A, Bartsch SM, Muder RR, Lee BY. An Economic Model of Antimicrobial-Coated Sutures to Society, Hospitals and Third-Party payers in Preventing Abdominal Surgical Site Infections. *Infect Con Hosp Epidemiol* 2014; 35: 1013 – 20. <https://doi.org/10.1086/677163>
- [43] McFarland A. Economic evaluations of interventions in health care. *Nurs Stan* 2014; 29: 49 – 58. <https://doi.org/10.7748/ns.29.10.49.e9315>
- [44] Fryback DG, Dasbach EJ, Klein R, Klein BE, Dorn N, et al. The Beaver Dam Health Outcomes Study: initial catalog of health-state quality factors. *Med Decis Making* 1993; 13: 89 – 102. <https://doi.org/10.1177/0272989X9301300202>
- [45] Gheorghe A, Moran G, Duffy H, Roberts T, Pinkney T, et al. Health Utility Values Associated with Surgical Site Infection: A Systematic Review. *Value Health* 2015; 18: 1126 – 37. <https://doi.org/10.1016/j.jval.2015.08.004>
- [46] Palmer S, Raftery J. Opportunity cost. *BMJ* 1999; 318: 1551 – 2. <https://doi.org/10.1136/bmj.318.7197.1551>
- [47] Mogyorosy Z, Smith P. The main methodological issues in costing health care services. A literature review, <https://www.york.ac.uk/che/pdf/rp7.pdf>; 2005 [Accessed 12 February 2020].
- [48] Kampf G. Acquired resistance to chlorhexidine – is it time to establish an ‘antiseptic stewardship’ initiative? *J Hosp Inf* 2016; 94: 213 – 27. <https://doi.org/10.1016/j.jhin.2016.08.018>
- [49] STROBE. STROBE Checklists, <https://www.strobe-statement.org/index.php?id=available-checklists>; 2007 [Accessed 12 February 2020].
- [50] CDC. Surgical Site Infection (SSI) Event, <https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscscssicurrent.pdf> ; 2020 [Accessed 29 April 2020].
- [51] EuroQol. EQ-5D, <https://euroqol.org/>; 2020 [Accessed 29 April 2020].
- [52] RAND. 36 Item Short-Form Survey (SF-36), https://www.rand.org/health-care/surveys_tools/mos/36-item-short-form.html; 2020 [Accessed 29 April 2020].
- [53] Husereau D, Drummond M, Petrou S, Greenberg d. et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. *BMJ* 2013; 346: f1049. <https://doi.org/10.1136/bmj.f1049>
- [54] Allen J, David M, Veerman JL. Systematic review of the cost-effectiveness of preoperative antibiotic prophylaxis in reducing surgical-site infection. *BJS Open* 2018; 2: 81 – 98. <https://doi.org/10.1002/bjs5.45>

[55] Gillespie BM, Chaboyer W, Erichsen – Andersson A, Hettiarchchi RM, Kularatna S. Economic case for intraoperative interventions to prevent surgical site infection. *Br J Surg* 2017; 104: e55 – e64.
<https://doi.org/10.1002/bjs.10428>

[56] Arefian H, Vogel M, Kwetkat A, Hartmann M. Economic Evaluation of Interventions for Prevention of Hospital Acquired Infections: A Systematic Review. *PLoS One* 2016; 11: e 0146381.
<https://doi.org/10.1371/journal.pone.0146381>

Economic benefits of SSI prevention

Table I – Included Studies

Study	Data collection year	Country	Participants	SSI Definition	Prevention strategy	Comparator	Design	Time horizon	Perspective	Costs	Economic outcomes
Akagi et al (2012)	May 1 st – October 31 st 2003	Japan	All patients undergoing operative treatment at study site	“suspected...based on the appearance or odor of the wound or systemic signs”	Gauze dressing changed once daily for 2 days post operatively	Gauze dressing changed once daily for 7 days post operatively	“cost implications” (p97)	6 months	Hospital	Cost of operation, nursing hours for dressing change, consumables associated with dressing change	No significant difference in SSI rates (4 vs 3) Nursing time for dressing reduced (3.7 min to 0.9 min), material costs per dressing reduced by \$14.70.
Ando et al (2014)	April 2007 - March 2010 (Control), April 2010 - Feb 2012 (Intervention)	Japan	Patients undergoing spinal surgery	CDC (Non implant and implant)	Wound adhesive for wound closure (Dermabond)	Metal staples	"Cost evaluation" (p854)	Not stated	Hospital	Wound closure method only	Difference in costs of closure methods \$13.50 and took 28 seconds shorter for Dermabond
Arroyo et al (2015)	Not stated	Spain	Patients undergoing clean scheduled surgery at study site	CDC	Polyurethane film dressing with absorbent pad	Gauze and tape	“economic analysis” (p289)	Not stated	Hospital	Cost of dressing, staff time, SSI related hospital bed days, antibiotics to treat SSI	Investing an additional €2900 (\$3295.37) in the new dressing resulted in €45,000 (\$51 135.12) savings from avoidance of additional bed days, treatment and reduction in staff time for dressing changes
Bailey et al (2011)	2010	USA	Hypothetical cohort of 63 year olds undergoing hip and knee surgery	Not applicable - modelling study	Preoperative chlorhexidine bathing cloths	Usual care (no bathing cloth)	Cost effectiveness analysis using decision tree	1 year	Hospital	Cloth costs, inpatient costs associated with SSI	At baseline cost, washcloths were dominant when cloth efficacy was at least 10% and compliance was 1.5 x baseline. Cloth costs, excess LOS, compliance and cloth efficacy were the main drivers of model outcomes. Cloths remain dominant over a range of efficacy and compliance values

Economic benefits of SSI prevention

Courville et al (2012)	2005	USA	Hypothetical cohorts of 65 year old pts undergoing THA or TKA	Deep SSI CDC definition	1: test and treat carriers with Mupirocin, 2: treat all	3: do nothing	Cost effectiveness analysis using decision tree	1 year	Hospital	Costs associated with procedure and acute hospitalisation, bacterial culture costs, 30 minutes nursing time, 11 minutes lab time, cost of mupirocin 5 day course	Treat all dominant strategy in both TKA and THA. THA cost per QALY treat all \$30380, TKA \$35916, although differences in cost per QALY for other strategies were small
Dhadwal et al (2007)	June 2003 - May 2004	UK	Coronary bypass graft of one artery and either BMI>30kg/m, diabetes or use of other artery	CDCP; presence of wound infection and/or positive blood culture and/or positive swab	Antibiotic prophylaxis: oral rifampicin, gentamicin and intravenous vancomycin pre operatively and intravenous vancomycin post operatively	Intravenous Cefuroxime 4 times daily	"Economic analysis" (p1127)	90 days	Hospital	Antibiotics, post op stay, vacuum therapy, debridement, microbiology costs and out patient attendance	Study group antibiotics \$358.31 (\$31 - \$12714) Hospital \$14,800 (\$5,700-\$126,800) Control group antibiotics \$454.9 (\$9-\$21316) Hospital \$18,600 (\$5700 - \$97,300)
Echebiri et al 2015	2014	USA	Hypothetical cohort of patients undergoing non emergent caesarean delivery	Not applicable - modelling study	Application of negative pressure wound therapy after closure of skin incision	Application of standard wound dressing only	Cost benefit analysis using decision tree	Not stated	Third party payer	Negative pressure wound therapy costs, rehospitalisation and reoperation, outpatient management costs of SSI	Standard wound dressing cost \$547, negative pressure therapy \$804 per patient Negative pressure wound therapy cost beneficial if priced below \$192. Standard dressings preferred if SSI rate 14% or less. If SSI rate above 14%, negative pressure beneficial only at certain levels of infection reduction (e.g. 30% reduced to 15%)
Elliot et al (2010)	2005	UK	Hypothetical cohort of patients undergoing primary hip arthroplasty	Not applicable - modelling study	1: Vancomycin, 2: Cephalosporin, 3: a combination of both	Only 3 regimens outlined in Prevention Strategy considered	Cost effectiveness analysis using decision tree	Not stated	Third party payer	30 different pathway treatment costs, including None, Superficial and Deep or Joint	Where MRSA infection rate is $\geq 0.25\%$ and rate infections is $\geq 0.2\%$, cephalosporin and vancomycin combined is optimal

Economic benefits of SSI prevention

EL-Mahallawy et al (2013)	March 2008 – Sep 2010	Egypt	Patients undergoing clean contaminated cancer surgery	CDC	Group A: IV penicillin G sodium and gentamicin 80mg, pre operatively 20 prior to skin closure	Group B: IV clindamycin 600mg and amikacin 500mg, pre operatively prior to skin closure	“to compare...cost” (p32)	2yrs 6 months	Hospital	Cost of prophylactic antibiotic regimens	Statistically significant difference in prophylactic antibiotic costs between 2 groups, A: 21.96±3.22 LE (\$3.99 ± \$0.59), B: 117.05±12.74 LE (\$21.28 ± \$2.31), (p<0.001)
Gheorghe et al (2014)	Feb 2010 - Jan 2012	UK	Patients undergoing laparotomy	Not stated	Wound edge protection devices	Usual care (no WEPD)	Cost effectiveness	30 days	Health care provider	Cost of intervention, inpatient and primary care resource costs, medication costs	WEPD was £290 (\$463.83) more expensive and 0.00002 QALYs less beneficial than standard care. WEPD is less than 30% likely to be cost effective in all analyses for the WTP NICE threshold
Heard et al (2017)	2014	Australia	Obese (BMI > 30kg/m ²) women undergoing elective caesarean section	CDC	Negative pressure wound therapy	Standard care (Comfeel Plus dressing)	Cost utility analysis	4 weeks	Health care provider	Cost of intervention including nurse time to apply, cost of hospital care and post discharge care	ICER AU\$1347 (\$1173.38) per SSI prevented (95% CI dominant to AU\$ 41 873, \$36 475,57)) and AU\$42 340 (\$36 882.37) per QALY gained (95% CI dominant to AU\$884 019, \$770 068. 95), although CI are very wide
Keenan et al (2014)	Jan 2008 – Dec 2012	USA	Patients undergoing major colorectal surgery	Not stated	Preventive colorectal surgery SSI bundle	Usual care (pre bundle implementation)	“cost analysis” (p1051)	30 days	Hospital	Variable direct costs for index admission and total LOS	Superficial SSI pre bundle associated with 35.5% increase in variable direct costs (\$13,253 vs \$9779) Bundle reduced LOS from 7.9 to 4.6 days Preventing SSI associated with \$3474 decrease in variable direct costs

Economic benefits of SSI prevention

Lee et al (2010)	2009	USA	All surgical cases at study site	Not applicable - modelling study	Chlorhexidine for preoperative skin antisepsis	Iodine	Cost benefit analysis using decision tree	1 year	Hospital	Cost of implementation, mean treatment costs with and without SSI including all direct variable supply costs	Base case analysis: switching from iodine to single use chlorhexidine applicators results in cost savings of \$16 per case, translating to \$349,904 over the year for the study site. Findings favouring chlorhexidine robust over a range of values in sensitivity analyses.
Lee et al (2011)	Not stated	USA	Hypothetical cohort of 27.1 year old pregnant women undergoing elective caesarean sections	Not applicable - modelling study	MRSA screening and decolonisation	Do nothing	Cost effectiveness analysis using decision tree	1 month	Third party payer	Inpatient stay costs, pharmaceutical costs, procedure and laboratory costs	Routine screening and decolonization in this patient demographic is rarely cost effective; intervention unlikely to be cost saving given current epidemiological circumstances of MRSA colonisation in the USA
Lee et al (2013)	July 2010 - June 2012	USA	Patients undergoing open and lap colectomies and proctectomies	Not stated	Comprehensive unit based safety programme (CUSP)	Surgeon who did not participate in the CUSP	Prospective cohort study with costings	2 years	Hospital	Programme costs (including personnel and supplies) and variable direct costs of each case	The CUSP saved \$955 per case, overall annual cost of prevention \$111,794
Mathur et al (2013)	April 2009 – Dec 2010	India	Patients undergoing open reduction and internal fixation of closed limb fractures	Diagnosed clinically: one or more “classic signs and symptoms” of inflammation + pus at site	3 doses of 1g IV cefuroxime over 12 hours	Conventional regimen (5 days IV cefuroxime and amikacin, oral cefuroxime twice per day until suture removal)	2 group parallel randomised controlled trial with costings	20 months	Hospital	Average cost of medicine and hospital stay in both groups	Average cost in intervention group 150 INR (\$per patient, control group 1900 INR per patient (converts to \$2.39 Intervention and \$30.27 Control)
Merollini et al (2013)	Not stated	AUS	Hypothetical cohort of 30,000 total hip arthroplasty	Not applicable - modelling study	1: no use of antibiotic prophylaxis, 2: additional use of antibiotic-	Routine preoperative antibiotic prophylaxis	Cost effectiveness analysis using decision tree	30 years	Health services	Cost of IPC strategies, cost of infection treatment	Antibiotic-impregnated cement prophylaxis and vancomycin would prevent 46 deep SSI

Economic benefits of SSI prevention

			patients aged over 65 years		impregnated cement, 3: additional use of laminar air operating rooms						and save \$3909 per QALY compared to prophylaxis alone, no prophylaxis would increase costs by \$1.5million and lose 163 QALYs. Laminar air operating rooms in all surgeries would increase costs by \$4.6 million and lose 127 QALYs. Antibiotic impregnated cement remains dominant in sensitivity analyses.
Mueller and Krebsbach (2008)	July 2004 - May end 2005 (control), July 2005 May end 2006 (intervention)	USA	All patients undergoing surgery at the study site	"CDC surgical site criteria" (p652)	Institution wide replacement of sterile gauze with antimicrobial gauze	Sterile gauze, historical control	"Cost effective" (p654)	11 months x 2 (for both groups)	Hospital	Consumables, cost per infection	Cost of implementing \$15, 604, annual costs \$30, 008. 8 SSIs prevented, 9 MRSA SSIs prevented through use of antimicrobial gauze
Nakamura et al 2013	April 2009 – March 2011	Japan	All patients undergoing elective colorectal operations at study site	"CDC guidelines of 1999"	Triclosan coated polyglactin antimicrobial sutures	Conventional polyglactin sutures	"evaluate the impact on costs associated with wound infection after colorectal surgery" (p576)	30 days	Hospital	Medical costs generated during additional treatment for infections, material cost of sutures	19 pts had SSI in control group., 9 intervention group, median cost of treating SSI \$2,310; total costs of treatment \$60, 814 control group \$18,370 in intervention. Cost of intervention increased cost by \$2,225 over control, \$10.80 per patient. Savings \$40,219 (\$42,444 - \$2,225) Cost effective if 0.5% of SSI prevented
Rao et al (2008)	Oct 2005 - Oct 2006	USA	Prospective cohort of all patients undergoing total joint arthroplasty at study site	Not stated	Preoperative MRSA screening and decontamination	Concurrent control with patients of surgeons who did not take part and	Cost analysis (p1345)	1 year	Hospital	Hospital costs for infected and non infected patients	Lower infection rates reduced lost revenue by \$270,000 compared to pre intervention, total

Economic benefits of SSI prevention

					in patients with positive screen	a historical comparator group					economic gains estimated at \$231,741 when adjusted for actual number of operations completed
Singh et al (2012)	Jan 2009 - Dec 2010	India	All adult patients (2838) undergoing cardiovascular surgical procedures	CDC	Two module training step by step teaching programme and delivered to 184 health care workers	Previous practice	Not given, although refers to "total savings" (p646) and "return on investment" (p646)	1 year	Societal and Hospital	Direct costs of health care, indirect costs including loss of job days for patients and attendants, additional LOS and opportunity cost of blocked beds from HAI	Overall costs of SSI \$120,938 (not including opportunity costs), direct and indirect costs of SSI \$5396 per infection. Cost of training \$5 per staff member. For every \$1 on training, \$236.70 returned on investment (although this is for all infection types, not SSI specific)
Singh et al 2014	Not stated	USA	Hypothetical cohort of adult patients undergoing abdominal surgeries	SSSI "occur within 30 days...involving only skin and subcutaneous tissues...deep incisional infections are more severe, including those that occur within 30 or 90 days after an operative procedure involving deeper soft tissues" (p1014)	Triclosan coated sutures	Uncoated sutures	Cost effectiveness	Not stated Model ran 1 million trials (cohort 1,000)	Hospital, third party payer and societal	Varied with perspective Hospital: suture costs, opportunity cost of bed days Third party: direct hospitalisation, treatment and suture costs Societal: direct costs (hospitalisation, treatment, sutures) and indirect (productivity losses, mortality costs)	Triclosan coated sutures saved progressively greater costs per surgery if SSI risk was at least 15% and efficacy 5%. 3 rd party payer followed same trend but saved more costs per SSI. Societal perspective: \$40,127 - \$53,244 per SSI prevented if SSI risk at least 15%
Slover et al (2011)	Not stated	USA	Patients undergoing primary knee and hip arthroplasty and spinal fusion surgery	MRSA/MSSA	Preoperative mupirocin for all, cephalosporin for MRSA negative, vancomycin for MRSA positive. Non compliant patients (to preoperative mupirocin) were	Only 4 regimens outlined in Prevention Strategy were considered	Markov decision analysis	Not stated	Hospital	Costs of nasal culture, mupirocin, vancomycin (vancomycin costs, cephalosporin costs), average cost of knee/hip arthroplasty/spinal fusion/septic joint revision, cost of	Programme more likely to be cost saving in spine population due to higher infection rates and costs of treatment. If hip and knee arthroplasty costs \$15,000, screening needs to

Economic benefits of SSI prevention

					given post operative mupirocin					treating spine infection	result in 35% reduction in revision rate for it to be cost saving. For spine, this is only 10%
Spelman et al (2002)	12 months before and after February 2000	AUS	Patients undergoing CABG surgery at study site	CDC	1g IV vancomycin, 600mg oral rifampicin preoperatively and 2nd dose of IV vancomycin 12 hrs post op	1g IV cephazolin; 1 dose pre op and 3 doses post operatively	"Cost analysis" (p403)	12 months	Hospital	Cost of antibiotics, cost of deep SSI at study site	Rate of deep sternal SSIs fell (4.2% to 0.6%) which converts to 19 infections prevented. At a cost of \$31597 each (from previous work by study authors), net savings over 12 months were \$579, 655 (SSIs averted - cost of prevention \$23, 688)
Theologis et al (2014)	Jan 2008 – Dec 2009 (control) Jan 2011 – June 2012 (intervention)	USA	Adults with complex adult deformity reconstruction by 2 surgeons with a minimum of 3 months follow up	"SSI requiring revision surgery within 90 days" (p1876)	2g vancomycin powder applied locally in wound	Normal care, no vancomycin powder in wound	Not stated but refers to "cost savings" throughout	90 days	Hospital	Direct costs including supplies, services, room and care and pharmacy	Index procedure significantly more expensive (absolute diff \$6,399), 3 less SSI in Intervention group, average cost of SSI Intervention group \$780 vs \$3224 Control group Intervention results in \$244,402 savings per 100 operations
Tuffaha et al (2015)	2014	Australia	Obese women undergoing elective caesarean section	Not applicable - modelling study	Negative pressure wound therapy	Standard care with hydrocolloid dressing	"cost effectiveness analysis" (p63)	6 months	Third party payer	Costs of dressing, treatment of SSI, staff time to apply dressing	Negative pressure wound therapy costs AUD30 (\$26.13) more than standard treatment with a gain of 0.002 QALYs. Incremental net benefit was 70AUD (\$60.98)., probability of cost effectiveness 65% at a willingness to pay threshold of 50, 000 AUD (\$43 555)

Economic benefits of SSI prevention

Ulu-Kilic et al (2015)	June 2012 - June 2013	Turkey	Patients undergoing operations for spinal fusion, craniotomy and ventricular shunt and over 15 years of age	"an infection related to an operative procedure that occurred at or near the surgical incision within 30 days of the procedure or within 90 days if prosthetic material was implanted during surgery" (p45) Classified according to the CDC criteria, ASA and NNIS risk index	Weight based dose of cefazolin, at appropriate time, frequency and duration	Patients who did not receive appropriate antibiotic regimen	"Cost analysis" (p47)	30 days or 90 days with implant	Hospital	Cost of prophylactic antibiotics, total antibiotics for treatment of infections	Prophylactic antibiotics Study group \$3.35, Control \$20.41; Total antibiotics Study group \$51.26, Control \$57.61
VandenBergh et al (1996)	March 1991 - August 1992 (intervention), Aug 1989 - Feb 1991 (control)	NL	Patients undergoing cardiothoracic surgery	CDC	Mupirocin applied to each nostril twice daily for 5 days beginning the day before surgery	Do nothing	Cost effectiveness	18 months	Hospital	Mupirocin, postoperative costs, hospital days, SSI attributable costs	Cost effectiveness ratio \$16,633 per SSI prevented. Ratio relatively insensitive to changes in mupirocin effectiveness, cost and incidence of SSI but sensitive to SSI attributable costs. If SSI attributable cost is <\$245, ratio would exceed zero
Wassenberg et al (2011)	2009	NL	Hypothetical cohort of patients undergoing orthopaedic and cardiac surgical procedures	Not applicable - modelling study	Screen and treat for MRSA and treat all for MRSA no screening	No screening no treatment	Cost effectiveness analysis	? Life time	Societal	Cost for readmission for treatment for SSI, cost of screening	Both interventions were cost saving and improved health outcomes, despite big cost differences between both, when compared to base case (no screen, no treat). Treat all strategy dominant. RR of SSI needs to be less than 0.53/0.62 for either intervention to be cost saving.

Economic benefits of SSI prevention

Watson et al (2012)	July 2005 – Dec 2008 (control), Jan 2009 – Feb 2011 (intervention)	USA	Patients undergoing orthopaedic surgery	CDC for superficial and deep infections	Steiros Algorithm Outpatient Surgery Protocol (patient applies skin sanitiser night before and morning of surgery, continue 5 days after)	Usual care	Not stated but refers to “cost savings” (p118)	3yrs 5 m (control), 2yrs 1 m (intervention)	Hospital	“lowest previously published estimated direct costs” (p118)	100% reduction in SSI rate (13 SSI down to 0) \$154,059 cost savings over 26 months
Yinusa et al (2007)	July 1999 - Dec 2003	Nigeria	Patients undergoing elective implant surgery (open reduction and internal fixation, hemi-arthroplasty)	Superficial infection "finding of wound erythema or discharge associated with positive microbiological culture within four weeks of surgery" and deep infection "if infection extended deep into the wound with a positive bacteriological culture and characteristic radiological findings" (p91)	Antibiotic regimens 1: Ceftriazone 1g at induction, 1g 12 hours later, 2: Cefuroxime 1.5g at induction, 2 more doses of 750mg six hourly, 3: Ciprofloxacin 400mg at induction then 2 doses 200mg six hourly	Only 3 regimens outlined in Prevention Strategy considered	"Cost effectiveness" (p91)	33 months	Hospital	Drug costs only	Overall drug costs for each regimen: 1: N3572, 2:N1872, 3: N1780 Cost benefit ratio stated as N 1864 (\$14.99)
Zanetti et al (2001)	1998	USA	Hypothetical cohort of 10,000 patients undergoing coronary artery bypass grafting	Not applicable - modelling study	Routine Cefazolin and Vancomycin for those with allergy, Routine Vancomycin: for preoperative prophylaxis	No prophylaxis	Cost effectiveness analysis using decision tree	3 months	Payer	Cost of SSI and hospital death, prophylaxis related adverse events, antibiotic costs, preparation costs (Vancomycin Only), cost of follow up care	Routine vancomycin dominated cephazolin and no prophylaxis; results most sensitive to cost of vancomycin (over \$215, cephazolin was not dominated), efficacy and prevalence of resistance.

CI: Confidence interval

LOS: Length of stay

N: Nigerian Naira

Economic benefits of SSI prevention

NICE: National Institute for Health and Clinical Excellence

QALY: Quality adjusted life year

THA: Total hip arthroplasty

TKA: Total knee arthroplasty

WEPD: Wound edge protection device

WTP: Willingness to pay

Table II – Overview of cost analyses

<i>Study</i>	<i>Intervention</i>	<i>Effectiveness</i>	<i>Cost</i>
Akagi et al (2012)	Changing sterile gauze dressings daily for 7 days or 2 days post operatively	4 wound infections developed in the 7-day group, 3 in the 2-day group. Report states “no significant difference”	Average nursing time for dressings reduced by 2.8 minutes. Material costs for dressing changes reduced by \$14.70
Ando et al (2014)	Surgical adhesive vs. staples for wound closure in patients undergoing spinal surgery (total n = 609)	8 patients using staples developed SSI (6 with positive MRSA isolates) compared to none using surgical adhesive (p < 0.01)	Staples took longer to close the surgical wound (48.0 ± 12.6 seconds vs. 19.9 ± 10.7 seconds) and were more costly (\$38.50 vs. \$25.0)
Arroyo et al (2013)	Polyurethane film dressing compared to gauze and tape in management of postoperative wounds (n = 196 intervention, 215 control)	Superficial SSI identified in 13 patients (6.6%) in control group, 3 (1.4%) in film dressing group (p = 0.006)	SSI adds incremental 2 days in hospital. Polyurethane dressing is more expensive (€2.9 or \$3.30 per patient) but involves less time (-€900 or -\$1022.70 for a cohort of 1000 patients). Investing €2900 (\$3295.37) in the more expensive dressing is associated with cost savings of €45 000 (\$51 135.12) for every 1000 patients (preventing 52 superficial SSI)
Dhadwal et al (2007)	Two antibiotic prophylaxis regimens: 1: Gentamicin, Rifampicin and Vancomycin (intervention) 2: Cefuroxime (control) for high risk cardiac surgery patients (n = 244)	SSI at 30 days 12.1% control, 4.6% intervention and at 90 days 25.2% control, 9.2% intervention (p = 0.004). Reduction in infection noted across both superficial and deep categories.	Total antibiotic costs (prophylaxis and treatment) and total hospital costs were lower for the intervention group (-\$96 and -\$3800)
El-Mahallawy et al (2013)	Two antibiotic prophylaxis regimens: A: IV penicillin G sodium and gentamicin 80mg IV; 20 minutes pre operatively and further dose prior to skin closure (n = 100) B: IV clindamycin 600mg and amikacin 500mg; 20 minutes pre operatively and further dose prior to skin closure (n = 100)	19 patients developed SSI, 11 in Group A and 8 in Group B (p = 0.469)	Direct costs of prophylaxis only considered: Group A: 21.96 ±3.22 LE Group B: 117.05±12.74 LE (converts to Group A \$3.99 ± \$0.59 and Group B \$21.28 ± \$2.31) Difference in costs between groups was statistically significant (p < 0.001)
Keenan et al (2014)	Preventative multidisciplinary SSI bundle specific to colorectal surgery (included pre, intra and postoperative recommendations) (n = 213). Historical control group who had surgery prior to the adoption of the bundle (n = 346)	Adjusted superficial SSI rates were reduced by 13.6% post bundle (19.3% to 5.7%, p < 0.001). No significant difference noted in deep or organ-space SSI	Variable direct costs incurred by patients after propensity matching of subset (n = 212) went up (median \$8391, range \$6781 - \$11 311 pre bundle and \$9681, range 7915 - \$11 745 post bundle) Post bundle superficial SSI associated with increase in variable direct costs (£13, 253 - \$9779, p = 0.001) and length of stay (7.9 vs 4.6 days, p< 0.001)

Economic benefits of SSI prevention

Lee et al (2013)	A comprehensive unit based safety programme focussing on colorectal SSI. Control group were patients whose surgeon did not participate in the programme (n = 626)	SSI rate did not differ (adjusted OR 1.14, CI 0.73 – 1.83), ITU stay (OR 0.9, CI 0.61 – 1.34) or LOS (-0.57, CI -1.48 – 0.34) between the two groups	Intervention group had significantly lower lab costs (\$191, p = 0.009), operating room utilisation (\$149, p = 0.05) and use of supplies (\$615, p = 0.003). Overall cost saving \$955 per case. Total cost of delivering the intervention was \$111 794 per year, participating surgeons complete 222 cases therefore net impact estimated around \$100 000 annually.
Mueller and Krebsbach (2008)	Sterile gauze dressings were replaced throughout the study site hospital with a sterile antimicrobial gauze dressing. Pre and post study design.	SSI rates fell from 1.08% (101/9372 procedures, 20 MRSA +ve) to 0.82% (84/1020, 11 MRSA +ve)	Annual costs of intervention \$30 008, cost difference in treating each observed SSI/MRSA SSI \$538 613, minus cost of intervention \$508 605 “total savings”
Nakamura et al (2013)	RCT evaluating triclosan coated polyglactin sutures (intervention, n = 206) vs conventional polyglactin sutures (control, n = 204) for wound closure in patients undergoing colorectal surgery	SSI in intervention group 9/206 (4.3%) control group 19/204 (9.3%) (p = 0.047) No difference in noted in incidence of organ/space SSI	Median cost of wound infection \$2310 Actual cost of infections in intervention group \$18 370 vs \$60 814 control. Material cost of intervention \$2225, therefore overall cost savings reported as \$40 219
Rao et al (2008)	Preoperative screening and decolonisation of MRSA positive patients with mupirocin and chlorhexidine for patients undergoing total knee and hip arthroplasty. Control group of patients whose surgeons did not want to participate in the screening and decolonisation (n = 1966)	164/636 S.aureus positive patients in intervention group, none of whom developed an SSI. Estimated 345/1330 were S.aureus positive (based on intervention rates), 12 of whom (3.5%) developed SSI (7 MSSA, 5 MRSA)	Lower infection rate during intervention reduced lost revenue by \$27000, adjusted for lower number of operations performed, economic gain estimated at \$231741
Singh et al (2012)	Before and after study examining the impact of the introduction of formal infection control practices and structured training for staff on HAI rates for patients undergoing cardiovascular surgical procedures (total n = 2838). Subgroup analysis completed for SSI, only these results used here.	Significant reductions in annual growth rate of SSI infection rate per 100 surgeries (-0.25 to -31, p<0.001), length of stay (0.11 days to -17, p<0.001) and percentage mortality (-1.59% to -77%, p = 0.05).	Direct costs of SSI \$46 938, indirect costs \$19 778 and cost of excess LOS \$54 222. Opportunity cost of all HAI \$190 657. Extra expense per SSI was calculated at \$1173. Cost of training one member of staff was \$5. Return on investment: \$1 on training returned \$236.70 through infection prevention (this figure is for all infections)
Spelman et al (2002)	Cardiothoracic routine prophylactic antibiotics were changed from intravenous cephazolin (n = 599) to intravenous vancomycin with oral rifampicin (n = 515)	SSI rate fell from 10.5 infections/100 (95% CI 8.2 – 13.3) to 4.9/100 (95% CI 3.2 – 7.1, p<0.001). Relative risk reduction 55.3%, numbers needed to treat was 18 to prevent one infection	Prophylaxis initiative cost AUS\$ 23 688, and 19 deep SSIs were averted at a cost of AUS\$600 343 giving overall net savings of AUS\$576 655 (converts to \$326 502)
Theologis et al (2014)	Retrospective analysis of adult patients undergoing complex deformity reconstruction (spinal) and subdivided into 2 groups.	Total number of 90 day SSI requiring readmission dropped (from 7/64, 10.9% to 4/151, 2.6%, p = 0.01)	Average cost of treating postoperative SSI higher in control group; readmission costs +\$6219 (\$34 388 vs \$28 169) and average

Economic benefits of SSI prevention

	Intervention group received routine IV antibiotics and 2g vancomycin powder applied locally to surgical wound (n = 151), control group received routine IV antibiotics only (n = 64)		cost of SSI per index case +\$2444 (\$3224 vs \$780) Cost savings per 100 operations reported as \$244 402
Ulu-Kilic et al (2015)	Weight based dose of cefazolin at induction, repeated every 4 hours during surgery and for less than 24 hours for patients undergoing neurosurgical procedures (spinal fusion, craniotomy, ventricular shunt). Control group of patients had the same but for more than 24 hours (n = 822)	SSI rates did not differ between the groups 3.5% (17/488) for control, 3.6% (12/822) for intervention	Prophylactic antibiotic cost per patient was significantly lower in intervention group (\$3.35 vs \$20.41, p<0.01), and total antibiotic costs were also significantly lower (\$51.26 vs \$57.61, p<0.01)
Watson et al (2012)	Retrospective analysis of SSI outcomes before (n = 1292) and after (n = 875) implementation of Steiros Algorithm Outpatient Surgery Protocol for patient cleaning; applying skin sanitiser the night before and morning of surgery to continue 5 days post-surgery	SSI rates fell from 1% (13/1292) to 0% (0/875)	Previously published lowest estimated direct cost of SSI was used (\$17 708) Cost savings reported as \$154 059
Yinusa, Onche and Thanni (2007)	Three short term antibiotic regimens for patients undergoing elective orthopaedic implant surgery; Ceftriaxone, Cefuroxime and Ciprofloxacin (n = 101 surgeries)	SSI rates were lower in Ceftriaxone group (2/32, 6.3%) than Cefuroxime (3/41, 7.3%) and Ciprofloxacin (2/28, 7.1%) but this difference was not statistically significant (p>0.05). Deep wound infection occurred in one patient but unclear which group this was in	Cost of Ceftriaxone regimen N 3572, Cefuroxime regimen N 1872 and Ciprofloxacin regimen N 1708. Cost benefit ratio stated as N 1864 (converts to \$14.99) between Ceftriaxone and Ciprofloxacin (but this is actually cost difference).

AUS\$: Australian Dollar

CI: Confidence interval

LE: Egyptian Pound

LOS: Length of stay

N: Nigerian Naira

OR: Odds ratio

Table III – Overview of cost benefit analysis

<i>Study</i>	<i>Intervention</i>	<i>Cost</i>	<i>Cost benefit</i>
Echebiri et al 2015	Application of negative pressure wound therapy (NPWT) after closure of skin incision after elective caesarean section	Standard wound dressing cost \$547, negative pressure therapy \$804 per patient	NPWT cost beneficial if priced below \$192. Standard dressings preferred if SSI rate 14% or less. If SSI rate above 14%, negative pressure beneficial only at certain levels of infection reduction (e.g. 30% reduced to 15%) Standard dressings optimal 85% of the time, NPWT 15%

Table IV – Overview of cost effectiveness analyses

<i>Study</i>	<i>Intervention</i>	<i>Effectiveness</i>	<i>Cost</i>	<i>Cost effectiveness</i>
Mathur et al (2013)	RCT evaluating two different prophylactic antibiotic regimens undergoing open reduction and internal fixation of closed limb fractures: Group 1: 3 doses of 1g IV cefuroxime spaced 12 hours apart (Intervention n = 100) Group 2: 5 days of IV cefuroxime and amikacin twice per day, 500mg oral cefuroxime until suture removal (Control n = 97)	4 SSI were observed from 197 procedures, 2 in Group 1 and 2 in Group 2	Cost of antimicrobial prophylaxis was 150 INR for the Intervention Group 1 and 1900 INR for the Control Group 2 (converts to \$2.39 Intervention and \$30.27 Control)	Intervention was found to be cost effective due to no difference in SSI rate between comparator groups
Lee et al (2010)	Chlorhexidine (single use applicators or bottled) or iodine for skin antisepsis for surgery of any type	Results of meta-analysis of 7 studies: Chlorhexidine significantly decreased risk of SSI (adjusted RR 0.64, CI 0.51 - 0.80) Results of meta-analysis of 4 studies: Chlorhexidine significantly decreased positive skin culture results after application (adjusted RR 0.44, CI 0.35 – 0.56)	Mean cost per case for patients who did not develop SSI \$5356, and \$13,537 for those who did develop SSI Purchase prices of antiseptics: \$6.0736 for single applicator chlorhexidine, \$1.678 per 113g bottle. Povidone iodine \$1.416 per 118ml	Use of chlorhexidine single use applicators associated with incremental cost savings of \$16 per case, saving an annual \$349,904 at the study site. Chlorhexidine remained cost effective if reduction in SSI was 10% or over. Use of bottled chlorhexidine associated with incremental cost savings of \$26 per case, saving an annual \$568,594 at the study site
Singh et al (2014)	Triclosan coated sutures or traditional uncoated sutures for the prevention of incisional infections in abdominal surgeries	Probabilities from previously published literature, databases and some expert opinion Efficacy of triclosan sutures in preventing SSI was explored over a range of efficacies (from 5 – 50%)	Various costs entered into model depending on severity of infection Costs analysed from the hospital, third part payer and societal perspective	Triclosan coated sutures saved progressively greater costs per surgery if SSI risk was at least 15% and efficacy 5%. 3rd party payer followed same trend but saved more costs per SSI. Societal perspective: \$40,127 - \$53,244 per SSI prevented if SSI risk at least 15%
Slover et al (2011)	Preoperative screening and mupirocin 1. If compliant and positive MSSA on screen, vancomycin for prophylaxis 2. If non compliant and positive MRSA on screen, vancomycin and mupirocin prophylaxis 3. If non compliant and positive MSSA on screen, mupirocin and cephalosporin	Probability of compliance with mupirocin 0.6% THA and TKA patients: - Probability of positive MRSA 0.00329 - Probability of positive MSSA 0.2027 Spine patients: - Probability of positive MRSA 0.00174 - Probability of positive MSSA 0.223	Revision of infected joint surgery for THA and TKA \$70,000 and \$100,000 for spinal fusion. Nasal culture \$20 Mupirocin \$90	In THA and TKA patients, if screening produces a 10% reduction in relative revision rate and cost of revision is less than \$70,000, screening is cost effective. In spinal fusion patients the program is more likely to be cost saving due to the higher cost and incidence of infection

Economic benefits of SSI prevention

	4. All negative screens received cephalosporin prophylaxis For all patients undergoing THA, TKA and spinal fusion surgery at the study site (n = 365+287)			
VandenBergh et al (1996)	Mupirocin ointment applied for 5 days starting the day before cardiothoracic surgery, with a historical control group (total n=1796)	Incidence of SSI decreased (7.3% to 2.8%), calculated mupirocin effectiveness as 62%. 45 SSIs prevented per 1,000 patients	Mean SSI attributable costs \$16,878 (95% CI \$15,575 – 18,181).	Cost effectiveness ratio \$16,633 per SSI prevented. Impact of cost and efficacy of mupirocin and changes in the incidence of SSI did not significantly impact ratio. SSI attributable costs had substantial effect. If SSI attributable costs were <\$245, intervention would not be cost effective
Wassenberg, Ardine de Wit and Bonten(2011)	Two scenarios evaluated for preoperative screening and decolonisation of Staphylococcus aureus in patients undergoing prosthetic joint and cardiac surgery to the base case of do nothing: 1. Screen all and treat all positive patients with mupirocin and chlorhexidine 2. Screen all and treat all positive patients and any patient who could not be screened with mupirocin and chlorhexidine	Compared to the base case of do nothing, scenario 1 prevented 7 deep SSIs and gained an extra 14 life years, Scenario 2 prevented 3 deep SSIs and gained an extra 24 life years	Scenario 1 saved €47,746 (\$67 589) Scenario 2 saved €178,970 (\$253 349.93)	Both scenarios were cost effective compared to the base case, but overall scenario 2 was the most cost effective
Zanetti, Goldie and Platt (2001)	Three strategies for antibiotic prophylaxis in patients undergoing CABG: 1. No prophylaxis 2. Cephazolin, vancomycin for those with a history of allergy to beta-lactam antibiotics 3. Routine vancomycin	No prophylaxis (Strategy 1) there were 570 deep SSI, 1141 superficial SSI and 405 deaths in a cohort of 10,000 patients. Routine cephazolin (Strategy 2) resulted in 173 fewer deep SSI, 347 fewer superficial SSI and 14 fewer deaths than no prophylaxis. Routine vancomycin (Strategy 3) resulted in 29 fewer deep SSI and 3 fewer deaths in comparison to routine cephazolin (Strategy 2)	Routine vancomycin had the lowest direct medical costs (\$23.36 million) compared to routine cephazolin (\$24.53 million) and no prophylaxis (\$33.41 million)	Routine vancomycin dominated due to being more effective and less costly. Reference case of 65-year-old man undergoing CABG - Per person lifetime costs \$62,892 with no prophylaxis - With cephazolin, \$876 less and extra 0.023 QALYs gained compared to no prophylaxis - With vancomycin additional \$103 saved compared to cephazolin (dominant Strategy 3)

CABG: Coronary artery bypass graft

CI: Confidence interval

INR: Indian Rupees

IV: Intravenous

RCT: Randomised controlled trial

RR: Risk ratio

THA: Total hip arthroplasty

TKA: Total knee arthroplasty

Table V – Overview of cost utility analyses

Study	Intervention	Cost utility
Bailey et al (2011)	Chlorhexidine bathing with polyester cloths the evening before and the morning of surgery for orthopaedic patients aged 63 years undergoing hip and knee procedures compared to standard preoperative preparation alone	The cloths dominated standard care if: <ul style="list-style-type: none"> - Efficacy was at least 10% and compliance at least 1.5 times baseline (15.3%), - Efficacy 25% and compliance 75% - Efficacy 50% and compliance 50% Cost of cloths, additional LOS attributable to SSI, efficacy and compliance impacted on estimates.
Courville et al (2012)	Analysis of 3 strategies for 65 year old patients undergoing TKA and THA: <ol style="list-style-type: none"> 1. Screen and treat with mupirocin 2. Treat all with mupirocin 3. No screen, no treat 	Treat all was the dominant strategy in the base case for both TKA (\$35, 916 per QALY gained) and THA (\$30, 379 per QALY gained). Differences between strategies were small: <ul style="list-style-type: none"> - TKA screen and treat +\$354, no screen no treat +\$449 compared to treat all - THA screen and treat +\$279, no screen no treat +\$330 compared to treat all Treat all remained dominant in a variety of sensitivity analyses varying the price of mupirocin and/or screening, effectiveness of mupirocin.
Elliot et al (2010)	Analysis of 3 strategies of antibiotic prophylaxis for 65 year old males undergoing THA: <ol style="list-style-type: none"> 1. Vancomycin 2. Cephalosporin 3. A combination of vancomycin and cephalosporin 	Vancomycin delivered 8.52 QALYs at £6119 (\$11 144.23) Cephalosporin delivered 8.52 QALYs at £6120 (\$11 146.05) Cephalosporin and vancomycin delivered 8.52 QALYs at £6135 (\$11 173.37) <ul style="list-style-type: none"> - Cephalosporin is dominant when MRSA SSI rate is 0.0% or MRSA infection rate is $\geq 0.2\%$ and other non MRSA infection rate is $\leq 0.1\%$. - Vancomycin alone is dominant when MRSA SSI rate is $\leq 0.15\%$ and other non MRSA SSI is $\geq 0.1\%$, or MRSA infection rate $\leq 0.2\%$ and other infection rates is $\geq 0.2\%$. - The combination of vancomycin and cephalosporin is dominant if MRSA SSI rate $\geq 0.25\%$ or above and non MRSA SSI rate 0.2% or above.
Gheorghe et al (2014)	The use of wound edge protection devices for patients undergoing laparotomy versus standard care	Wound edge protection devices were £290 (\$463.83) more expensive and delivered 0.00002 QALYs less than standard care (i.e. more expensive and less effective). Cost effectiveness acceptability curve found the wound edge protection device is 30% likely to be cost effective for all analyses in the willingness to pay threshold recommended by UK government (£20 000 - £30 000, \$31 988 – \$47 982) Base case adjusted ICER: £171,200 (\$273 817.28) per QALY gained.
Heard et al (2017)	Negative pressure wound therapy for SSI prevention in obese women undergoing elective caesarean section	ICER AU\$1347 (\$1173.38) per SSI prevented (95% CI dominant to AU\$ 41 873, \$36 475.57)) and AU\$42 340 (\$36 882.37) per QALY gained (95% CI dominant to AU\$884 019, \$770 068. 95). Small sample size highlighted by large confidence intervals in ICER estimates therefore only preliminary support suggested adoption of intervention.
Lee et al (2011)	Screening and subsequent decolonisation with mupirocin and chlorhexidine washes for 5 days in 27.1 year old women undergoing planned caesarean delivery	Screen and treat only cost effective if: <ul style="list-style-type: none"> - Probability of decolonisation success was $\geq 50\%$ and colonisation prevalence was $\geq 40\%$ - Decolonisation success was $\geq 75\%$ successful and colonisation prevalence was $\geq 20\%$ - Decolonisation success was $\geq 90\%$ and colonisation prevalence was $\geq 20\%$ Therefore, screen and treat considered rarely cost effective.
Merollini et al (2013)	Baseline antibiotic prophylaxis compared to: <ol style="list-style-type: none"> 1. No antibiotic 2. antibiotic prophylaxis and antibiotic cement 3. antibiotic prophylaxis and laminar air operating rooms In 65 year old patients undergoing THA	Compared to baseline, antibiotic prophylaxis and antibiotic cement was the dominant strategy preventing 46 deep SSIs for AUS\$3909 (\$4174.43) less per QALY. No antibiotic prophylaxis would result in costs of AUS\$1.5million (\$1.601 million) and a QALY loss of 163. Antibiotic prophylaxis and laminar air operating rooms would increase cost by AUS\$4.6million (\$4.912 million) at QALY loss of 127. At willingness to pay of AUS\$40,000 – AUS\$64,000 (\$42 716.08 - \$68 345.73) antibiotic prophylaxis and antibiotic cement had a $\geq 98.5\%$ chance of being cost effective.
Tuffaha et al (2015)	Negative pressure wound therapy for SSI prevention in obese women undergoing caesarean section	Negative pressure wound therapy associated with an additional AU\$30 (\$26.13) cost but delivered an additional 0.002 QALYs. At Australian willingness to pay threshold (AU\$ 50 000 QALY, \$43 555) incremental net benefit is AU\$ 70 (\$60.98).

Economic benefits of SSI prevention

	compared to standard hydrocolloid dressing	Probability of negative pressure wound therapy being cost effective was 65%.
--	--	--

AU\$: Australian dollar

ICER: Incremental cost effectiveness ratio

TKA: Total knee arthroplasty

THA: Total hip arthroplasty

QALY: Quality adjusted life year

Table VI – Cost per QALY gained across studies presented incrementally according to cost

<i>Study</i>	<i>Intervention</i>	<i>Cost per QALY gained</i>
Merollini et al 2013 [33]	Antibiotic impregnated cement for joint replacement in 65 year olds undergoing total hip replacement	\$4174.43 saving*
Elliot et al 2010 [30]	Vancomycin prophylaxis in 65 year old males undergoing total hip replacement	\$1308.00
	Cephalosporin prophylaxis in 65 year old males undergoing total hip replacement	\$1308.22
	Combination prophylaxis in 65 year old males undergoing total hip replacement	\$1311.43
Tuffaha et al 2015 [18]	Negative pressure wound therapy for obese women undergoing elective caesarean section	\$13 066.59
Courville et al 2012 [24]	Treat all 65 year old patients undergoing total hip and knee arthroplasty with mupirocin	\$30 379 (total knee) \$35 916 (total hip)
Heard et al [17]	Negative pressure wound therapy for obese women undergoing elective caesarean section	\$36 882.37
Gheorghe et al 2014 [40]	Wound edge protection device	\$273 817.28

* the intervention delivered a cost saving rather than cost incurring

Table VII: Overview of quality assessment of all included studies

Dimension of quality	Number of studies			
	Yes	No	Not clear	Not applicable
Study design				
The research question is stated	29	0	3	
The economic importance of the research question is stated	26	3	3	
The viewpoint(s) of the analysis are clearly stated and justified	14	12	6	
The rationale for choosing the alternative programmes or interventions compared is stated	27	3	2	
The alternatives being compared are clearly described	31	0	1	
The form of economic evaluation is stated	16	9	7	
The form of economic evaluation is justified in relation to the questions addressed	13	12	7	
Data collection				
The source(s) of effectiveness estimates used are stated	32	0	0	
Details of the design and results of effectiveness study are given (if based on a single study)			2	9
Details of the method of synthesis or meta-analysis of estimates are given	5	1	3	23
The primary outcome measure(s) for the economic evaluation are clearly stated	17	13	2	
Methods to value health states and other benefits are stated	8	0	1	23
Details of the subjects from whom valuations were obtained are given	1	3	3	25
Productivity changes (if included) are reported separately	1	2	0	29
The relevance of productivity changes to the study question is discussed	5	19	0	8
Quantities of resources are reported separately from their unit costs	6	25	1	
Methods for the estimation of quantities and unit costs are described	18	5	9	
Currency and price data are recorded	19	7	6	
Details of currency of price adjustments for inflation or currency conversion are given	18	11	0	2
Details of any model used are given	12	7	2	11
The choice of model used and the key parameters on which it is based are justified	10	6	5	11
Analysis and interpretation of results				
Time horizon of costs and benefits is stated	16	10	6	
The discount rate(s) is stated	7	21	1	3
The choice of rate(s) is justified	3	20	1	8
An explanation is given if costs or benefits are not discounted	3	20		9
Details of statistical tests and confidence internals are given for stochastic data	15	11	6	
The approach to sensitivity analysis is given	10	18	3	1
The choice of variables for sensitivity analysis is justified	10	11	2	9
The ranges over which the variables are varied are stated	10	12	1	9
Relevant alternatives are compared	20	7	5	
Incremental analysis is reported	15	15	0	2
Major outcomes are presented in a disaggregated as well as aggregated form	14	17	1	
The answer to the study question is given	22	0	10	
Conclusions follow the data reported	25	3	4	
Conclusions are accompanied by the appropriate caveats	21	6	5	

Total n = 32 studies

Table 8: Overview of quality assessment of modelling studies

Dimension of quality		Number of studies			
		Yes	No	Not clear	Not applicable
<i>Structure</i>					
S1. Statement of decision problem/objective	S1.1.	11			
	S1.2	11			
	S1.3	9	2		
S2. Statement of scope/perspective	S2.1	10	1		
	S2.2	9	1	1	
	S2.3	9		2	
	S2.4	11			
S3. Rationale for structure	S3.1	10		1	
	S3.2	10		1	
	S3.3	9		2	
S4. Structural assumptions	S4.1	8	1	2	
	S4.2	8	2	1	
S5. Strategies/comparators	S5.1	11			
	S5.2	9	1	1	
	S5.3		2		9
S6. Model type	S6.1	11			
S7. Time horizon	S7.1	9		2	
	S7.2	6	2	3	
S8. Disease states/pathways	S8.1	10		1	
S9. Cycle length	S9.1	6	4	1	
<i>Data</i>					
D1. Data identification	D1.1	7	1	3	
	D1.2	3	2	6	
	D1.3	5		6	
	D1.4	1	1	9	
	D1.5		4	1	6
D2. Data modelling	D2.1	11			
D2a. Baseline data	D2a.1	7		4	
	D2a.2	9		2	
	D2a.3		6		5
	D2a.4		6		5
D2b. Treatment effects	D2b.1	3		8	
	D2b.2	1	4	5	1
	D2b.3	9	2		
	D2b.4		8	3	
	D2b.5	4	7		
D2c. Costs	D2c.1	10		1	
	D2c.2	9	1	1	
	D2c.3	6	3	1	1
D2d. Quality of life weights (utilities)	D2d.1	5		2	4
	D2d.2	7			4
	D2d.3	5		2	4
D3. Data incorporation	D3.1	10		1	
	D3.2	6		2	3
	D3.3	11			
	D3.4	1	2	3	5
	D3.5	4	1	1	5

Economic benefits of SSI prevention

D4. Assessment of uncertainty	D4.1	1	10		
	D4.2		10		1
D4a. Methodological	D4a.1	1	10		
D4b. Structural	D4b.1	9		2	
D4c. Heterogeneity	D4c.1	3	8		
D4d. Parameter	D4d.1	7	1	3	
	D4d.2	8			3
<i>Consistency</i>					
C1. Internal consistency	C1.1		11		
C2. External consistency	C2.1				11
	C2.2	3	7		1
	C2.3	5	6		

Total n = 11 studies