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Review

Evaluation of the costing methodology of published studies estimating costs of surgical site infections: A systematic review

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Abstract

Objectives: Surgical site infections (SSIs) are associated with increased length of hospitalization and costs. Epidemiologists and infection control practitioners, who are in charge of implementing infection control measures, have to assess the quality and relevance of the published SSI cost estimates before using them to support their decisions.
In this review, we aimed to determine the distribution and trend of analytical methodologies used to estimate cost of SSIs, to evaluate the quality of costing methods and the transparency of cost estimates, and to assess whether researchers were more inclined to use transferable studies.

Methods: We searched MEDLINE to identify published studies that estimated costs of SSIs from 2007 to March 2021, determined the analytical methodologies, and evaluated transferability of studies based on 2 evaluation axes. We compared the number of citations by transferability axes.

Results: We included 70 studies in our review. Matching and regression analysis represented 83% of analytical methodologies used without change over time. Most studies adopted a hospital perspective, included inpatient costs, and excluded postdischarge costs (borne by patients, caregivers, and community health services). Few studies had high transferability. Studies with high transferability levels were more likely to be cited.

Conclusions: Most of the studies used methodologies that control for confounding factors to minimize bias. After the article by Fukuda et al, there was no significant improvement in the transferability of published studies; however, transferable studies became more likely to be cited, indicating increased awareness about fundamentals in costing methodologies.

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Hospital-acquired infections (HAIs) are one of the preventable adverse events that impose significant economic consequences on the healthcare system. Surgical site infections (SSIs) account for 20% of all HAIs and are associated with increased morbidity, length of hospital stay, readmission rates, and healthcare costs.[1,2] Costs due to SSIs have been recently reported to be $3.45–$10.07 billion in the United States.[3] Because of this significant economic burden as well as high expectations of their prevention, reducing SSIs has become a major target of quality improvement initiatives, especially in the era of expanding healthcare costs. Thus, estimating the cost of SSIs has been a matter of great interest and the number of healthcare economic studies has increased. Accurate estimation of the HAI costs has important implications for hospitals, patients, and payers. Decisions concerning the extent of resources that hospitals assign to infection control (IC) and the incentives third-party payers provide to reduce infection rates require accurate information.[4]

Estimating costs due to nosocomial infections requires that incremental costs associated with the infection must be distinguished from those attributable to the problems for which the patient was admitted.[5] Researchers differ on the best estimation technique to accurately capture cost. Consequently, the number of published studies that have conducted different costing methodologies to produce valid cost estimates has increased. Most studies have used case reviews, unmatched comparison, matched comparison, or regression analyses.[6]

In case review, each patient medical record is reviewed to distinguish between resources related to original causes of hospitalization and resources related to SSI.[5]

Unmatched comparison of the cost outcomes for patients with SSI and for those without is not useful because of the heterogeneity unrelated to SSI and difference in time to start of infection between the 2 groups. Those with SSI might have more comorbid conditions and so might generate quite greater cost outcomes regardless of the SSI.[7]

Matching is used to replicate randomization by identifying uninfected controls that are similar as much as possible for observed covariates to infected cases.[8] This leads to a balanced number of cases and controls across levels of the matching

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variables that improves statistical efficiency.[9] One method of matching is propensity score matching (PSM). Patients with SSI are matched to uninfected control patients if their propensity scores are within a prespecified range.[10,11] Regression analysis summarizes the association between the cost and the SSI while controlling for other observable factors that might explain variation in cost.[12] Regression can be used in combination with matching.[11]

Cost components associated with SSIs include inpatient, outpatient, out of pocket, capital/overhead (indirect costs that have to be paid even if there is no production, include rent, utilities, insurance and staff salaries, office supplies, etc), productivity losses (costs due to loss of labor productivity due to illness or death) and opportunity costs (costs that could have been produced or purchased with the same resources if the treatment of an SSI-case was avoided). Cost estimates differ according to the chosen perspective, which determines which resources should be included and whether to use charges or costs to value them. Illustrations of types of perspective, charges, and costs are presented in Box 1.

Box 1. Illustrations of Types of Perspective, Charges, and Costs

The perspective of a cost analysis refers to the standpoint at which costs are determined.[114] The economic impact of SSIs can be assessed from patient, provider or hospital, payer, and society perspective.[115] Costing will differ dependent on the perspective; therefore, it is important to identify those who bear these costs. [116] Cost analysis can be conducted from a single or multiple perspectives.

The choice of the perspective depends upon the point of view of decision makers[114] and should be in harmony with the objective of the study.[14] In assigning monetary value to resource utilization, costing should be aligned with the study perspective.[114]

Patient perspective. Costs from the patient perspective are the expenses that patients pay for medical products or health care services not covered by their health insurance.[115]

Provider perspective. Providers can be hospitals, managed care organizations, or private practice physicians. Costs from the provider perspective are the ***true costs*** of providing a product or service, regardless of the charge.[115] Providers usually use charges instead of the true economic costs because ***charge data*** are more readily available but are usually not reflective of the true costs of health care.[117]

Payer perspective. Payers include insurance companies, the government, or employers. Costs from the payer perspective are charges for health care services allowed, or reimbursed, by the payer. They may include lost workdays and decreased productivity.

Societal perspective. Costs from the societal perspective are all costs and all health outcomes, regardless of who incurs the costs.[118]

Although the latest guidelines allow researchers to utilize cost estimates from published literature, the results of economic evaluations may be inaccurate. Thus, the decision to implement a control program may be misled.[13,14]Also, these results may not be directly applied elsewhere due to differences in the context and circumstances in which original results were produced. Therefore, epidemiologists and decision makers must assess the quality of the costing methods and transparency of cost estimates, and their suitability to their setting.[15]

In 2008, Fukuda et al[13] developed criteria for assessing transferability of the cost estimates, by reviewing publications dealing with economic evaluations. This assessment is based on 2 axes. The first is the clarification of the scope of costing. It assesses the transparency on reporting cost components and how cost estimates were calculated to enable readers to judge the potential applicability to their own cost-effectiveness and cost-savings analyses of infection control measures. The second assesses the accuracy of the costing methods which are of 2 types: micro costing or quasi–micro costing (higher accuracy) and gross costing (lower accuracy). Gross costing methods include relative value units (RVUs), cost to charge ratios (RCCS), and charges. In 2011, Fukuda et al[16] conducted a systematic review of published studies that have produced cost estimates of HAI from 1980 to 2006 to evaluate the transferability of these estimates.

In this study, we conducted a systematic review of published studies that (1) estimated the costs of SSIs, (2) determine the distribution and trend of the analytical methodology used, and (3) evaluated the costing methods' quality and the transparency of the cost estimates. Also, we investigated whether studies of high transferability were more likely to be cited.

Methods

Data collection

Inclusion criteria

We included primary studies that produced original costs estimates of SSI published in English from January 1, 2007, to March 23, 2021.

Exclusion criteria

Studies that had utilized existing cost estimates obtained from other published studies, studies in a language other than English, studies without full text, studies reflecting biomedical or laboratory research, studies reporting quantities of resource utilization (length of stay) rather than costs, studies focusing on identifying cost predictors (analyze impact of patient sociodemographic on cost) rather than evaluating costs, studies used infected patients in the control group, and studies in which the primary aim was economic evaluation of intervention or infection control programs (ICPs). We also excluded reviews, conceptual papers, commentaries, letters, editorials, meta-analyses, and research protocols.

Search strategy

We searched the MEDLINE database via PubMed using the following keywords ((surgical wound infection MeSH Terms) AND ((economics MeSH Terms) OR (hospital cost MeSH Terms))) AND ((“2007/1/1"Date - Publication : “2021/3/23"Date - Publication)) and used Human and English as filters. We hand-searched the references of the included studies after the MEDLINE search.

Study selection

We reviewed the identified studies in 2 steps: an initial abstract review followed by a full-text review. The initial abstract review was conducted to identify studies focusing on SSI that produced original cost estimates while excluding those that used published cost estimates.

The subsequent full-text review included studies identified as eligible and studies that could not be fully evaluated from the abstract review. The abstract review and the full-text review were conducted independently by 2 evaluators (R.H. and G.A.) with backgrounds in economic evaluations and infectious diseases. Disagreements were discussed and resolved by consensus. If a disagreement cannot be resolved, a third evaluator (O.G.) was consulted to resolve disagreement and to determine whether the article is suitable for inclusion.

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Data extraction

Data were extracted as reported in the studies without judgment or deduction using a data collection form (Supplementary Materials 1 online). It included:

(1) The analytical methodology used to estimate the cost of SSI

(2) The transferability of cost estimates which was assessed according to the evaluation axes developed by Fukuda et al (2009).[13] These evaluation axes as described below:

Evaluation axis 1: Clarification of the scope of costing. Studies were classified according to the following definitions:

- Level A: All cost components were described, and data for both quantity and unit price of resources were reported for each component.
- Level B: All cost components were described, and data for costs in each component were reported.
- Level C: All cost components were described, but data for costs in each component were not reported.
- Level D: Only the scope of costing was described, but the components of costs were not described. Studies that only reported terms such as "hospital stay" or "direct costs" without further exposition were evaluated at Level D.

Evaluation axis 2: Evaluating the costing method. Studies were further classified according to the following definitions:

- α: The use of micro- or quasi-microcosting, i.e., activity-based costing
- β: The use of relative value units (RVU)
- γ: The use of charge data based on the ratio of costs to charges (RCC).
- δ: The use of unmodified charge data
- ϵ: Studies that offer no information to readers about the methodology used.

The α level was assigned for studies that reported using the "actual costs" in valuing resources without determining how these costs were estimated.

Level of transferability was considered high when the level of clarification of scope of costing was A or B and costing method was α.

(3) Relevant criteria for reporting which were adopted from Drummond et al[17] and the CHEERS checklist[18] as follows: economic perspective, cost description measure, time horizon, discounting, price year and/or inflation adjustment, sensitivity analysis, currency and currency conversion.

The data items were independently extracted by 2 members of the review team (R.H. and G.A.). Disagreements were discussed and resolved. When disagreements could not be resolved, a third researcher
(O.G.) was consulted.

Statistical analysis

The Monte-Carlo test and the Fisher's exact test were used to test the difference in the distribution of the analytical methodologies, scope of costing, costing method, length of stay adjustment, and transferability through the study periods. The Monte-Carlo test was conducted to test wheather or not the costing method is aligned with the chosen economic perspective. Also, 2 Poisson log-linear models were used to test whether transferability level, as well as scope of costing and costing method, affect the number of citations while adjusting for the time since publication. The numbers of citations (from the year of publication to 2021) were obtained from Google scholar. The effect size was summarized using the adjusted incident rate ratio. Significance level was set at $P < .05$.

Results

We identified 541 studies after searching MEDLINE, and hand-searching the references of relevant studies. After title and abstract review, 81 were assessed by full literature review, and 70 were included (Fig. 1). The reasons of exclusion after full literature review were: utilizing existing cost estimates from published studies,[19] estimating the cost based on expert opinion,[20] estimating the incremental cost associated with bacterial resistance because the comparison group were also infected,[21] estimating cost of SSI as a part of economic evaluation of intervention or ICPs,[22–25] studies in which SSI was not a single component of the cost object (eg, complications of certain surgery, HAI, or wound healing[26–28]), and using contribution margin rather than cost to evaluate the impact of SSI.[29]

Among the studies included in the review, 38 were conducted in the United States, 20 were conducted in Europe, 6 were conducted in Asia, and 5 were conducted in Australia, Brazil, Canada, and Egypt. Half of the studies (52.9%) were multicenter, 17 studies (24.3%) were conducted in university hospitals, and 7 studies (10%) were conducted in tertiary-care hospitals (Tables 1 and 2).

Analytical methodologies and adjustment on time to start of infection

The most frequent analytical methodologies were matched comparison, and regression models (82.9%) (Table 3). Moreover, 6 studies (8.6%) used case review; one of these was standardized using used appropriateness evaluation protocol (AEP).[30] Regression on a matched sample was used in 3 studies (4.3%).[31–33] The distribution of the studies through the different analytical methodologies was not significantly different between the periods 2007–2013 and 2014–2020.

In matched comparisons, 13 studies (46.4%) used 1:1 matching in which each infected patient was matched to a single control patient, and 6 studies (21.4%) used 1:2 matching. Matching based on propensity scores was performed in 7 studies.[34–40]

Regarding the regression models, 24 studies (88.9%) used multiple regression, 9 of them used normal distribution of costs as the dependent variable, and 15 used logarithmic and/or γ transformation. Other regression models used include multiple logistic regression (1 study),[26,41] multiple Poisson regression (1 study),[42] and quantile regression (1 study).[43] Also, 2 studies[34,35] compared total cost between SSI cases and controls matched based on propensity scores as well as regression model (Table 1).

The statistical comparison between SSI and non-SSI patients was reported in 63 studies (98.4%), P value was mentioned in 44 studies (69.8%), and P was <.05 in all but 1 study (Table 1).[48]

Only 9 studies (12.9%)[32,40,49–55] accounted for the time to start of SSI. Also, 4 studies[40,49,52,53,55] used the time to start of SSI itself, and 5 studies[32,50,51,54,55] used the preoperative LOS or "having the surgery on same day of admission" as regression covariate instead. The percentage of studies that accounted for time to start of SSI from 2007 to 2020 has not statistically significantly changed.

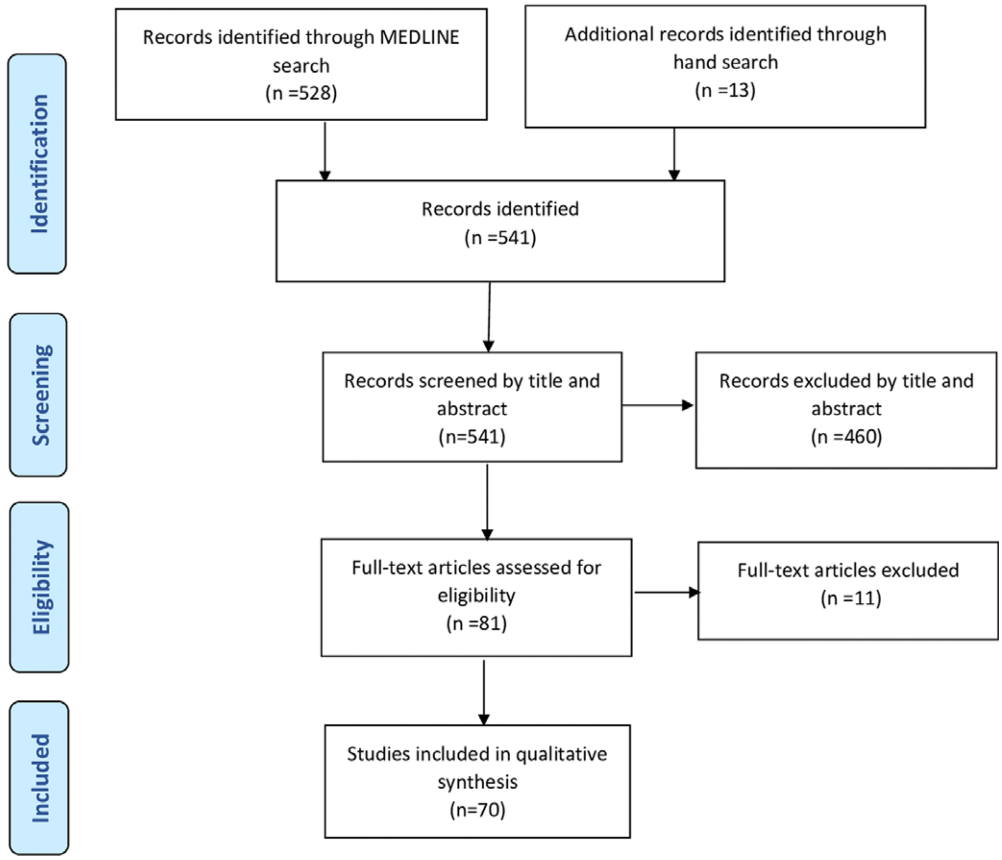

Fig. 1. PRISMA flow diagram showing identification and selection of published studies that estimated the cost of SSIs from 2007 to 2020.

Transferability

Regarding the scope of costing, the most common level was D (38 studies, 54.3%) and B (22 studies, 31.4%) levels, only 2 studies[45,50] were classified as level A studies (Table 3). The distribution of the studies through the levels of the scope of costing was not significantly different between the 2 periods (2007–2013 and 2014–2020).

The most frequently reported costing method was the charge method in 29 studies (41.4%). The method of costing was unknown in 19 studies (27.1%). Among the 15 studies that reported the use of actual costs, 5 studies did not determine the method of estimating these costs. In our review, only 7 studies (10%) had a high level of transferability. The distribution of costing methods and transferability were not significantly different between the periods 2007–2013 and 2014–2020.

Economic perspective

Of the included studies, 40 (57.1%) did not state the economic perspective. The cost was estimated from hospital or provider perspective in 18 studies (25.7%), from the payer perspective in 13 studies (18.6%), and from the patient perspective in 2 studies.[30,46] No studies estimated the cost from societal perspective. However, 3 studies[30,56,57] estimated the cost from 2 perspectives. Ho et al[56] and Eagye et al[57] estimated the cost from hospital and payer. Abu-Sheashae et al[30] estimated the cost from provider and patient perspectives.

Among the 18 studies conducted in the United States and that also mentioned the economic perspective, 9 studies (50%) estimated the cost from the payer perspective, 8 studies (44.4%) estimated the cost from the hospital or provider perspective, and 1 study (5.6%) estimated the cost from the patient perspective. In Europe, hospital or provider perspective was the most common.

The reported costing method was significantly aligned with the chosen perspective among 21 of the 28 studies with reported perspective and costing method. Also, 11 studies (73.3%) adopted provider or hospital perspective and used actual costs directly or indirectly by converting charges to actual cost using RVU or RCC, while 10 studies (76.9%) considered payer or patient perspective and used unmodified charges ($P = .008$). An unsuitable costing method was used in the remaining 7 studies (25%), where actual costs were used with payer or patient perspective in 3 studies[37,57,59] and unmodified charges were used with provider perspective.[42,49,58,60]

In addition, 2 studies estimated the cost from 2 perspectives. Abu-Sheasha et al[30] used microcosting for hospital perspective and charges for patient perspective. Ho et al[56] also used microcosting for hospital perspective and charges for payer perspective.

Types of cost

Overall, the types of costs included were aligned with the chosen perspective. In the 18 studies that estimated the cost from the provider perspective, in addition to the inpatient cost, capital and overhead costs,[35,63–65] opportunity costs,[58,60,63] and outpatient costs,[30,34,50,55] were considered. Inpatient and outpatient costs[33,43,48,66–69] as well as productivity losses[56,57,66] and out-of-pocket costs[47,47,68] were included in 13 studies in which the payer perspective was adopted. With patient perspective,[30,46] inpatient, outpatient and out-of-pocket costs were included. Also, opportunity costs were considered by Lee et al.[46]

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Table 1. Analytical Methodology, Additional Estimates, Matching Variables or Regression Analysis Covariates, Economic Perspective Used in the Studies Cited in the Systematic Review

First Author	Year	Setting	Country	Analytical Methodology	Additional Cost to HAI (Infected vs Uninfected)	Matching Variables or Regression Analysis Covariates	Perspective	Scope of Costing	Costing Method
Large bowel surgery									
Eagye[57]	2009	University	US	Multiple linear regression (logarithmic transformation), mean	$31,517 ($P < .05$)	Age, sex, race, procedure type, development of deep SSI, diabetes, COPD, and smoking status	Hospital/ payer	D	α (actual cost)
Mahmoud[41]	2009	Multicenter	US	Logistic regression, OR (95% CI) ≥$15,000	$7.46 ($P < .05$)	Age, sex, race, Body mass index, high SENIC score	Not mentioned	C	δ
Wick[67]	2011	Multicenter	US	Unmatched, mean	$17,324 ($31,933 vs $14,608) ($P < .001$)	NA	Payer	B	δ
Kashimur[75]	2012	Multicenter	Japan	Matching (1:1), mean, median	$5,938 ($11,400 $5,462) ($P < .001$)	Surgery, institution, age, the date of surgery, ASA score	Not mentioned	B	δ
Ohno[58]	2018	University	Japan	Matching (1:1), total, median	¥16,972,780 + opportunity cost= ¥491,764 ($P < .0002$)	Surgical category, age, gender, wound class, presence of stoma, and SSI risk index of the National Nosocomial Infection Surveillance	Provider	C	δ
Gantz[39]	2019	Multicenter	US	Propensity score matching, mean	$18,410 (Elective) & $20,890 (nonelective)	Age, sex, admission, transfusion, comorbidities	Not mentioned	D	δ
Abdominal surgery (liver, bile ducts, pancreas, stomach, colon, rectum, etc.)									
Mora-Guzmán[96]	2020	University	Spain	Case review, mean	€29,946	NA	Not mentioned	D	ϵ
Reduction of long bone fracture									
Metsemakers[54]	2017	Multicenter	Not clear	Multiple linear regression (normal distribution), median	€44,468 vs €6,855 ($P < .001$)	Age, gender, ASA score, fracture type, open fractures, delayed stage surgery, type of surgery, infection, nonunion, other complications	Not mentioned	B	ϵ
Olesen[80]	2017	University	Denmark	Unmatched, mean	€ 81,155 vs € 49,817.00 ($P < .05$)	NA	Not mentioned	B	α (Actual)
Parker[48]	2018	Specialist trauma	UK	Multiple linear regression (normal distribution), median	£1950.93 ($P = .25$)	Age, gender, trial site, Gustilo–Anderson wound grade, presence of diabetes, height, weight, and smoking status	Payer	D	ϵ
Chitnis[69]	2019	Multicenter	US	Unmatched, mean, median	$67,494 vs $13,434 ($P < .001$)	NA	Payer	D	δ
Hip fracture surgery									
Edwards[97]	2008	University	UK	Unmatched, mean	£25940 vs £8979 ($P < .001$)	NA	Not mentioned	D	ϵ
Wijeratna[61]	2015	General	UK	Matching (1:2), mean	£15,576 vs £6,922 ($P < .001$)	Age, sex and ASA score	Not mentioned	D	ϵ
Mok[98]	2018	Specialist trauma	Singapore	γ regression, total	$27,010 vs $18,502	Age, gender, race, number of comorbidities, fracture type, and door-to-surgery duration	Not mentioned	D	δ
Knee and/or hip replacement									
Kurtz[42]	2008	Multicenter	US	Poisson regression, Charge ratio (infected vs noninfected)	$1.76	Hospital size, hospital setting, age, sex, race, census region, and calendar year	Provider	D	δ
Dal-Paz[45]	2010	Tertiary	Brazil	Case review, total, mean	US$91,843.75	NA	Not mentioned	A	ϵ

Kurtz[44]	2012	Multicenter	US	Case review, mean	\$93,600 (infected hip revision) and \$74,900 (infected Knee revision)	NA	Not mentioned	D	ϒ
Poultsidesa[99]	2013	Multicenter	US	Unmatched, mean	\$31,432 (THA), \$24,558 (TKA) vs \$14,286 (THA), \$13,334 (TKA) ($P < .001$)		Not mentioned	D	δ
Bohensky[77]	2014	Multicenter	Australia	GLM with γ-distributed errors and a log-link function, mean, median	\$US6,646	Patient age, gender, comorbidity, socioeconomic status	Payer	D	δ
Kapadia[100]	2014	Tertiary	US	Matching (1:2), mean	\$116,382.65 vs \$28,249.57 ($P < .001$)	Type of surgical procedure, date of surgery, surgeon, age, gender and National Healthcare Safety Network risk category	Not mentioned	B	δ
Miletic[47]	2014	Multicenter	US	Case review, mean, median, total	\$23,952 for first hospitalizations, \$20,001 for subsequent hospitalizations	NA	Payer	D	δ
González-Véleza[65]	2016	University	Spain	Matching (1:1), median	€25,288 vs €10,828 ($P < .001$)	ASA classification, age, sex, date of surgery and main diagnosis at admission.	Provider	C	ϵ
Kapadia[101]	2016	Tertiary	US	Matching (1:2), mean	\$88,623 vs \$25,659 ($P < .001$)	Type of surgical procedure, date of surgery, surgeon, age, gender, and the NHSN risk category	Not mentioned	B	δ
Rennert-May[59]	2018	Multicenter	Canada	Multiple linear regression (normal distribution), mean	\$69,699 vs \$13,203 ($P < .001$)	Age, sex, First Nations status, and patient comorbidities	Payer	C	α
Adeyemi[31]	2019	Multicenter	US	propensity score matching and GEE (γ distribution), mean	\$12,890 (\$29,288 vs \$16,398) ($P < .001$)	Age, gender, and primary payer status. Other baseline variables included ZIP income quartile, hospital bed size, hospital teaching status, and CCI	Not mentioned	D	ϒ
Orthopedic procedures (Not specified)									
Kandilov[33]	2014	Multicenter	US	Matching (1:5) & multiple linear regression (logarithmic transformation), β (95% CI)	33.2% (20.8%–47.0%) ($P < .001$)	Age, sex, race, and DRG, present- on-admission risk factors as well as provider fixed effects	Payer	B	δ
Cystectomy									
Gili-Ortiza[38]	2015	Tertiary	Spain	Propensity score matching (1:4), mean	€14,875.70 (€33,533.40 vs €18,657.70) ($P < .001$)	Age group, sex, hospital group, alcohol consumption disorders, tobacco consumption disorders, and CCI	Not mentioned	D	δ
Wolters[52]	2017	University	Germany	Matching (1:2), median (95% CI)	€–4,343 (€–5,471 (€–7,499 to profit €3,219) vs €–1,128 (€–3,555 to profit €1,024) ($P = .0130$)	Age; gender; type of urinary diversion; DRG in the same year (adjusting for underlying disease and reimbursement conditions); preoperative LOH (adjusting for time at risk before surgery); LOH after the urologic surgical procedure	Not mentioned	B	α (Actual)
Kim[102]	2012	Multicenter	US	GEE (γ distribution and log link), total	\$25,234,960 ($P < .001$)	Age, race, gender, comorbidity, primary health insurance, annual income, hospital, type of AE and hospital level	Not mentioned	D	ϒ
Kidney transplant									
Ho[56]	2010	University	US	Multiple linear regression (normal distribution), Mean	\$13,862 (hospital cost-provider) \$11,132 (reimbursement- payer) ($P < .001$)	Body mass index, race, gender, donor type, age, diabetes, induction, rejection, delayed graft function, smoking history, cold and warm ischemia times, operative time, necessity and number of blood products given perioperatively, and method of skin closure	Provider & payer	D	α (provider), δ (payer)
Spinal surgery									
Kuhns[66]	2015	Not clear	US	Matching (1:1), total	\$21,778 vs \$9,159 ($P < .001$)	Sex, age, body mass index, same operating surgeon, same instrumentation, date of surgery, and duration of follow-up, cervical levels operated on, comorbidities	Payer	B	δ

(*Continued*)

Table 1. (*Continued*)

First Author	Year	Setting	Country	Analytical Methodology	Additional Cost to HAI (Infected vs Uninfected)	Matching Variables or Regression Analysis Covariates	Perspective	Scope of Costing	Costing Method
Atkinsona[62]	2017	Tertiary	UK	Matching (1:x), total, mean	£217,416 vs £108,852	Age, gender, body mass index, ASA, and RTS scores	Not mentioned	B	α
Blumberg[71]	2018	Specialist trauma	US	Multiple linear regression (normal distribution), mean, median	$16,242	Albumin, no. of I&Ds, Total posterior levels fused	Not mentioned	D	ϵ
Provenzano[68]	2019	Multicenter	US	GLM (γ distribution and a log link function), mean	$59,716 (95% CI, $48,965–$69,480) (initial group), $64,833 (95% CI, $37,377–$86,519) (replacement group) ($P < .05$)	Presence of infection before generator implant, CCI, patient demographics (age, gender, region, and insurance type)	Payer	B	δ
Rosenthal[103]	2019	Multicenter	US	Generalized linear regression model, mean	$88,353 (Invasive S. aureus Infection), $64,356 (any S. aureus Infection) vs $47,366 ($P < .001$)	Age, race, fusion type, fusion level, CCI, hospital size, teaching status, and hospital region.	Not mentioned	D	ϵ
Cranial surgery									
O ' Keeff[104]	2012	Multicenter	UK	Matching (1:1), total, mean	£ 1 85 660	Gender, age, ASA grade, indication for craniotomy, indication for craniotomy.	Not mentioned	B	ϵ
Hweidi[79]	2018	University	Jordan	Matching (1:1), mean	JOD 10,411.11 vs JOD 4,768.91	Age, gender, medical diagnosis	Not mentioned	D	ϵ
Head & neck surgery									
Penel[72]	2008	Not clear	France	Unmatched, mean	€17,434 (€39,957 vs €22,523) ($P < .001$)	NA	Provider	D	ϵ
Al-Qurayshi[105]	2019	Multicenter	US	Multivariate linear regression model, mean	$20,953.00 ($P < .001$)	Age, sex, modified CCI, body mass index, history of tobacco use, diagnosis of a head and neck cancer, history of radiotherapy, history of chemotherapy, trauma, trauma as the indication for admission, and site and class of primary procedure, class of surgery, others include neck dissection, tracheostomy, blood transfusion, location and type of hospital and hospital volume	Provider	D	ϒ
CABG and/or valve surgery									
Kobayashi[78]	2015	Multicenter	Japan	Matching (1:1), mean, median	$27,631 ($3,453,2 vs $6,901) ($P < .001$)	Operation code, sex, age, preoperative corticosteroid use, hemodialysis, same combined operation, preoperative, ASA score, and operation	Not mentioned	B	δ
Cardiac electronic device implantation									
Daneman[55]	2020	Multicenter	Canada	GLM with a log link and γ distribution, adjusted cost ratio (% increase in mean cost associated with the variable)	early-onset infections (RR, 3.1; 95% CI, 2.3–4.1), mid-onset infections (RR, 2.8; 95% CI, 2.4–3.3) and late-onset infections (RR, 4.7; 95% CI, 3.6–6.2) compared with uninfected patients ($P < .001$)	Age, sex, lowest income quintile, CCI, type of hospitalization, type of device, and timing of device	Provider	C	β
Cardiothoracic surgery									
Grafa[53]	2010	Tertiary	Germany	Matching (1:2), median	€36,261 vs €13,356 ($P < .001$)	Age, gender, underlying disease and reimbursement conditions, preoperative LOS (adjusting for time at risk before surgery) and LOS after procedure	Not mentioned	B	α (Actual)

Hysterectomy									
Roy[106]	2014	Multicenter	US	GLM with γ-distributed errors and a log-link function, mean	$19,203 vs $8,239	Age, race, marital status, APR-severity score hospital size, teaching or non-teaching function, geographic location, and type of payer	Not mentioned	D	ε
Endometrial cancer									
Bakkum-Gameza[36]	2013	Clinic	US	Propensity score matching (1:1), median	$5,447 ($25,788.10 vs $19,341.60) ($P < .001$)	Age, BMI, ASA score, medical history, Surgical characteristics	Not mentioned	D	δ
Cesarean delivery									
Olsen[34]	2010	Tertiary	US	-GLS (logarithmic transformation), mean -Propensity score matching, median	$3,529 (GLS), $2,852 (PSM) ($P < .05$)	Demographics, Procedures, Medical Conditions	Provider	B	ϒ
Breast surgery									
Olsen[35]	2008	University	US	-Propensity score matching (1:1) -Feasible GLS regression using natural log-transformed costs, mean, median	$5,700 (PSM) $4,091 (regression), ($P < .001$)	Age, sex, race, comorbidities, operative variables, malignancy, metastatic diseases, CVC, gynecomastia	Provider	D	α
Vascular surgery									
Turtiainen[107]	2010	Multicenter	Finland	Unmatched, mean	€3,320	NA	Not mentioned	B	α (Actual)
Dua[108]	2016	Multicenter	US	Unmatched, median	$30,949 vs $16,939 ($P < .001$)	NA	Not mentioned	D	ϵ
General & vascular surgery									
Hollenbeak[87]	2011	Multicenter	US	GLM with the γ distribution and the log link function, total	$6,681.81 ($P = .001$)	Age, sex, race, wound class, ASA classification, CCI, payer, surgery department.	Not mentioned	D	ϒ
Boltz[109]	2011	University	US	Multiple linear regression (normal distribution), mean	$10,497 ($P = .003$)	Age, gender, race, surgery, steriod use, ASA class, operative time, emergent operation, transfer	Not mentioned	D	ϒ
Multiple surgical procedures									
Sparling[110]	2007	Children	US	Matching (1:1), mean	$27,288 ($52,706 vs $25,418) ($P = .01$)	Surgical procedure, age, procedure date, comorbidities, diagnosis codes. elective/emergency admission	Not mentioned	D	ϵ
Alfonso[70]	2007	General	Spain	Matching (1:2), mean, total	$97,433 (mean), $1,084,639 (total)	Age, gender, diagnosis, duration of surgical intervention, comorbidity, and surgical procedure	Not mentioned	B	ϵ
Weber[74]	2008	University	Switzerland	Matching (1:1), mean	SwF19,638 (SwF52,027 vs SwF34,930) ($P < .001$)	Age, procedure code, and NNIS risk index	Not mentioned	D	α, ϵ
Kaye[32]	2009	Multicenter	US	Matching (1:1) & multiple linear regression (logarithmic transformation), mean	$43,970	Type and year of procedure and hospital (matching), Age, CCI, McCabe score, BMI, treatment at a tertiary care hospital, Admission to the hospital before	Not mentioned	D	δ

(*Continued*)

Table 1. (*Continued*)

First Author	Year	Setting	Country	Analytical Methodology	Additional Cost to HAI (Infected vs Uninfected)	Matching Variables or Regression Analysis Covariates	Perspective	Scope of Costing	Costing Method
						surgery, undergoing coronary artery bypass graft surgery, duration of surgery, and postoperative serum glucose (regression)			
Anderson[51]	2009	Multicenter	US	Multiple linear regression (logarithmic transformation), mean	\$61,681 (\$112,144 vs \$50,463)	Procedure at a tertiary-care hospital, coronary artery bypass graft procedure, surgical duration, procedure on same day as admission, ASA score, the interaction between MRSA SSI and need assistance with 3 or more ADLs and the interaction between MRSA SSI and procedure at a tertiary-care hospital	Not mentioned	D	δ
de Lissovoy[37]	2009	Multicenter	US	Propensity score matching (1:1), mean, median	\$20,842	Surgical category, age, sex, elective admission, comorbid condition	Payer	D	ϒ
Kusachi[76]	2012	Multicenter	Japan	Matching (1:1), mean	\$8,791 (\$13,237 \$4,446) ($P < .001$)	Operation code, sex, age, preoperative corticosteroid use, and operation date	Not mentioned	B	δ
Lamarsalle[111]	2013	Multicenter	France	Matching (1:x), total	€43,019,936 (public) and €14,872,779 (private)	Procedures only	Provider	D	ϵ
Shepard[60]	2013	Multicenter	US	Matching (1:x), mean	\$58,822 vs \$35,827 ($P < .001$)	Admission APR-DRG and complexity score	Provider	B	δ
Schweizer[64]	2014	Multicenter	US	GLM with γ-distributed errors and a log-link function, mean	\$11,876	Age, sex, preoperative laboratory values, preoperative condition, wound classification, ASA, surgery type, emergency surgery, and work relative value	Provider	C	α
Jenks[63]	2014	University	UK	Matching (1:8), median, total	£5,239 (£5,837 vs £12,928) ($P < .001$)	Surgical category, HRG code, age and the NNIS system risk index	Provider	B	α
Campbell[112]	2015	Multicenter	US	GLMwith γ-distributed errors and a log- link function, total	\$165,651 (MRSA), \$134,313 (MSSA) vs \$52,077 ($P < .001$)	Age; gender; race; insurance type; CCI; the presence of chronic cardiac disease, kidney disease, cancer, respiratory disease, liver disease, and diabetes; procedure year; surgery subgroup; major procedure; procedure with a permanent device; time to index/pseudo-index culture; and hospital indicators for region, teaching hospital, and number of beds	Not mentioned	D	δ
Olsen[43]	2017	Multicenter	US	Quantile regression, median	\$6,959 (serious BCS)	Patient demographics, comorbid conditions, medications, type of facility, operative factors, and postoperative factors	Payer	D	ϵ
Juchler[73]	2018	University	Switzerland	GLM, median	−2,223 (colon), −2,485 (CABG) ($P < .001$)	ASA classification, emergency surgery, surgery year, age, number of secondary diagnoses, and surgical procedure	Not mentioned	C	α (Actual)
Koek[50]	2019	Multicenter	Netherlands	Linear regression, mean, total	€14,084 (€24,198 vs €6,854) ($P < .05$)	Hospital, type of surgery, age, sex, ASA, duration of surgery, surgical wound class and preoperative hospital stay	Provider	A	α

Plastic surgery									
Lee[46]	2018	University	US	Case review, mean		NA	Patient	C	δ
Unclear surgery									
Defeza[49]	2008	University	France	Matching (1:1), mean	€1,814	Sex, age, McCabe index, type of ward, length of hospital stay before inclusion and diagnosis	Provider	B	δ
Carey[113]	2011	Multicenter	US	GLMs using a γ-distributed log-linked structure, mean	$18,256 (deep SSI) ($P < .001$)	Severity, demographics, and facility-level variables	Provider	D	α
Glied[40]	2016	Multicenter	US	Propensity score matching (1:1), mean	$69,626 ($362,006 vs $292,380) ($P < .001$)	Sex, age; date of admission; hospital; organism; infection site; prior hospitalization; diabetes; chronic dermatitis; trauma; wounds; burns; prior stay in a skilled nursing facility; renal failure; history of substance abuse; having ≥1 hospital roommate; CCS categories; use of and no. of days of use of chemotherapeutic, immunosuppressive, and anti-inflammatory medications; mechanical ventilation; urinary, central venous, or cardiac catheterization; catheter angiography; vascular stenting; dialysis; surgical procedure; general anesthesia; intubation; intensive care unit stay; and day of hospital stay on which the infection occurred	Not mentioned	D	δ
Abu-Sheashaa[30]	2018	University	Egypt	AEP, Total	EGP13,818 (provider), EGP26,510 (payer)	NA	Provider & payer	B	α (provider), δ (payer)

Note. AE, adverse event; APR DRG, all-patients refined diagnosis-related groups; ASA, American Society of Anesthesiologists classification;
BCS, breast-conserving surgery; BMI, body mass index; CABG, coronary artery bypass graft; CCI, Charlson Comorbidity Index; CCS, Clinical Classifications Software; CI, Confidence Interval; COPD, chronic obstructive pulmonary disorder; CVC, central venous catheter; I&D, irrigation and debridement; GEE, generalised estimating equation; GLM, generalized linear model; GLS, generalized least squares; HRG, Healthcare Resource Group; LOS, length of hospital stay; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; NA, Not Applicable; NHSN, National Health Safety Network; OR, Odds ratio; NNIS, National Nosocomial Infection Surveillance;
PSM, propensity score matching; RTS, Revised Tokuhashi Score; RR, rate ratio; SENIC, Study on the Efficacy of Nosocomial Infection Control; SSI, surgical site infection; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Table 2. Characteristics of the Published Studies Used to Estimate the Cost of SSI Between 2007 and 2020

Study Characteristics	n (%)
Study Setting[a]	
Multicenter	37 (52.9)
University	17 (24.3)
Tertiary	7 (10)
Others	9 (12.9)
Country[b]	
United States	38 (54.3)
Europe	20 (28.6)
Asia	6 (8.6)
Others	6 (8.6)
Year of publication	
2007–2013	31 (44.3)
2014–2020	39 (55.7)

[a]Others: specialist trauma (n = 3 studies), general (n = 2), not stated (n = 2), clinic (n = 1), children (n = 1)[b]Country: Europe includes United Kingdom (n = 6 studies), France (n = 3), Spain (n = 4), Germany (n = 2), Switzerland (n = 2), Denmark (n = 1), Finland (n = 1), and Netherlands (n = 1), Asia includes Japan (n = 4), Jordan (n = 1) and Singapore (n = 1), others include Australia (n = 1), Brazil (n = 1), Canada (n = 2), Egypt (n = 1), and not clear (n = 1).

Time horizon and discounting

In total, 63 studies (90%) stated the duration over which cost was calculated, ranging from 1–3 months to lifetime (Table 4).[70] Discounting was applicable when the time horizon was 1 year or more[33,47,54,59,66,69,71] in 8 studies; however, costs were discounted only in 1 study,[70] and 2 studies[32,51,70] discounted their costs although they were collected over 3 months only.

Price year and inflation adjustment

In 36 studies (51.4%), the price year was reported in which the cost was adjusted for inflation except for 1 study[48] in which inflation adjustment was not required because costs were reported in the same year (Table 4) (Supplementary Material 2 online).

Currency and currency conversion

The most commonly reported currency was USD (39 studies, 55.7%), converted from other currencies in 13 studies (18.6%)[40,45,59,65,70,72–80] that reported the method of conversion and exchange rate. Exchange using purchasing power exchange was used in only 1 study (Table 4) (Supplementary Material 2 online).[65]

Cost description measure

Among these studies, 47 (67.1%) reported the mean or total cost. We included studies that reported the total cost with those that reported the mean cost because the total cost can be used to calculate the mean. Median cost was reported in 9 studies (12.9%). Also, 11 studies (15.7%) reported both median and total and mean cost. Other measures used for reporting were the ratio of the charges for infected versus noninfected,[42] adjusted cost ratio,[55] and odds ratio of logistic regression.[41] In a study in which logistic regression was used, Mahmoud et al[41] did not mention how they determined the cost threshold (Table 4).

Sensitivity analysis

Only 5 studies[40,50,60,72,77] undertook sensitivity analysis to explore the impact of the of variation in per diem cost of hospitalization and length of hospitalization, change of prevalence of SSI, imputation of missing cost data for cases, and excluding deaths during follow-up.

Citation analysis

Studies with high transferability were statistically significantly 1.4 times more likely to be cited than low transferability studies (95% CI, 1.15–1.58). Studies with a scope of costing A/B were statistically significantly 1.1 times more likely to be cited relative to D studies (95% CI, 1.032–1.257). Studies with a scope of costing C were as cited as D studies. Studies that used actual costing, ratio of costs to charges (RCC), or relative-value units (RVU) methods were 1.2 times more likely to be cited than studies with unknown costing method (95% CI, 1.031–1.319). Studies that used unmodified charges were 1.3 times more likely to be cited than those with an unknown costing method (95% CI, 1.12–1.43).

Discussion

Recently, many studies and reviews have focused on the impact of SSI on medical costs.[75] Accurate information on the cost of SSI is required to support decisions concerning the extent of resources hospitals devote to infection control.[4] Published cost estimates may not be transferable, and thus, the decision based on them to implement a program may result in undesirable consequences.[13,14] Also, these estimates are not necessarily comparable due to the variation in the costing scopes, cost accounting systems, unit costs, clinical practice, costing methods, statistical methods used to determine attributable costs, and duration of follow-up.[4,35] Thus, it is crucial to assess the quality of the costing methods and the transferability of cost estimates before using them. In this review, we aimed to critically appraise published articles after the reviews made by Fukuda et al[6,16] to explore whether researchers addressed their recommendations. However, most researchers did not address these recommendations that make their cost estimates unlikely to be transferable.

Matching and regression analysis represented 80% in our review. Both methods are easy to implement given the hospital information system's availability. Matching on covariates, unlike regression analysis, does not require complicated statistical analysis. However, with many covariates, the proportion of unsuccessful matches increases.[12] Although it is easier to base matching on a propensity score (PS), one scalar that summarizes all covariates is still associated with unsuccessful matches. Thus, reporting the proportion of successful matches to measure the potential bias is recommended.[6] Of the 31 studies that used matching on PS or covariates, only 10 (32.3%) had reported the proportion of successful matches. With a lack of controls matching to severely infected cases, the latter is likely to be excluded with subsequent underestimation of SSI cost (ie, selection bias).[34]

The whole study sample could only be preserved using regression analysis and PS-based weighting approaches as inverse probability weighting (IPW).[10,12,81] This might explain why more studies used regression analysis than was reported by Fukuda et al (39% vs 26%). Also, regression analysis was used after matching to control for any remaining imbalances in 2 studies.

The impact of different analytical methods on estimated costs is unclear. In the current review, 2 studies compared matching with

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Table 3. Analytical Methodology, Time to Infection Adjustment and Transferability of the Cost Estimates of SSI in the Included Studies by Publication Year

Variable	Total (2007–2020) (N = 70)	Year: 2007-2013 (n = 31) n (%)	Year: 2014-2020 (n = 39) n (%)	Statistical test *P* value
Analytical Methodology				
Regression[a]	30 (42.9)	12 (38.7)	18 (46.2)	*MCp* > .05[b]
Matched comparisons	28 (40)	14 (45.2)	14 (35.9)	
Case review	6 (8.6)	2 (6.5)	4 (10.3)	
Unmatched	8 (11.4)	5 (16.1)	3 (7.7)	
Adjustment on time to start of infection				
Yes	9 (12.9)	4 (12.9)	5 (12.8)	*FEp* = .992[c]
No	61 (87.1)	27 (87.5)	34 (87.5)	
Scope of costing				
A & B	24 (34.3)	11 (35.5)	13 (33.3)	*MCp* > .05[b]
C	8 (11.4)	1(3.2)	7 (17.9)	
D	38 (54.3)	19 (61.3)	19 (48.7)	
Costing method[d]				
α (Actual cost)	15 (21.4)	7 (22.6)	8 (20.5)	*MCp* > .05[b]
β (RVU)	1 (1.4)	0 (0)	1 (2.6)	
γ (RCC)	8 (11.4)	6 (19.4)	2 (5.1)	
δ (Unmodified charge)	29 (41.4)	12 (38.7)	17 (43.6)	
ϵ (Unknown)	19 (27.1)	7 (22.6)	12 (30.8)	
Transferability				
High	7 (10)	2 (6.5)	5 (12.8)	*FEp* = .452[c]
Low	63 (90)	29 (93.5)	34 (87.2)	

[a]3 studies that used regression on matched sample were included in regression category while the 2 studies that used regression as well as PSM as analytical methodologies were counted twice (with matched comparison and with regression). [b]*MCp* = Monte Carlo test *P* value. [c]*FEp* = Fisher's exact *P* value. [d]2 studies that estimated the cost from 2 perspectives used 2 different costing methods, microcosting method for hospital perspective and charges for patient or payer, each study was counted in the corresponding category of the costing method twice.

regression analyses. One study found no difference between them[35], and the other revealed higher estimates with regression.[34] A similar unclear pattern was observed by Fukuda et al.[6]

As reported by Fukuda et al,[6] case review was the least used method to estimate the cost as it is labor intensive. Additionally, if the criteria for inclusion of SSI-related resources were unclear as in the AEP method,[82] expert reviewers as physicians or nurses might be required to review records.[83]

SSI increases total costs by extending the LOS. Concurrently, extended time to start of SSI (LOS before SSI) is by itself a cause of SSI. Thus, LOS is an endogenous variable because it simultaneously affects and is affected by SSI. Without adjustment for time to start of SSI, the cost of SSI is usually overestimated as the time to start of SSI is incorrectly assigned to the cost of SSI.[4,12,84] Contrarily, adjustment for the "whole LOS" underestimated the cost of SSI.[4,85] In the current review, only a few studies (13%) adjusted for time to start of SSI. None of them adjusted for the whole LOS. Even when the time to start of an SSI was unknown, researchers adjusted for only a part of this time, eg, adjusting for preoperative LOS.

Half of the studies did not report the type of perspective. In a recent systematic review, Sculpture et al[14] found that the perspective was defined in only 42% of the studies. When researchers neglect to report the perspective, decision-makers could not interpret if the relevant costs and selected costing methods are consistent with the objective of costing. This will affect the generalizability and transferability of the reported results.

Most of the studies which reported perspectives assigned the monetary values of resources according to the chosen perspective. Since hospital perspective was the most common, studies mainly included inpatient costs and excluded post-discharge costs, mainly borne by patients, caregivers, and the community health service. Excluding post-discharge costs might considerably underestimate the burden of SSI. Perencevich et al[88] found that the inclusion of post-discharge costs increased SSI cost by a factor of 3. Thus, the choice of hospital perspective should be considered carefully.

Although ICPs are implemented by and in hospitals, considering their perspective provides little incentive to implement ICP because hospitals might not bear the consequences of SSI. We recommend estimating the costs from the perspective of whoever bears the consequences, either the patients or the society. If it proves to be substantial, then legislation should be set to encourage hospitals to keep SSI rates low, even if the hospitals will not gain monetary benefit from reducing SSI.

Overall, researchers chose a perspective that aligns with the main source of health financing in their countries. In the United States, where private insurance dominates,[89] payer perspective was mainly adopted. In Europe, where universal health coverage predominates,[89] provider perspective was the most common.

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Table 4. Reporting Characteristics of the Cost Estimates of Surgical Site Infections in Published Studies Between 2007 and 2020

Reporting characteristics	n (%)
Cost Description Measure	
Total/Mean	47 (67.1)
Median	9 (12.9)
Both	11 (15.7)
Others	3 (4.3)
Time horizon	
Yes	63 (90)
Not stated	7 (10)
Price year	
Yes	36 (51.4)
Not stated	34 (48.6)
Inflation adjustment[a]	
Yes	35 (50.7)
No[b]	1 (1.4)
Not clear	33 (47.8)
Currency[c]	
USD	39 (55.7)
Euros	13 (18.6)
British sterling	5 (7.1)
Japanese yen	4 (5.7)
Others	9 (12.9)
Currency conversion	
Yes (converted original currency into USD)	13 (18.6)
No (Reported original currency)	57 (81.4)

[a]1 study[48] was not applicable for inflation adjustment because price year was same year over which the study was conducted. [b]As mentioned by Ohno et al.[52] [c]Others in currency include Canadian dollars (n = 2 studies), Swiss francs (n = 2), Egyptian pound (n = 1), Australian dollars (n = 1), Jordanian dollars (n = 1), Danish kroner (n = 1), Real (Brazilian currency) (n = 1).

Table 5. Recommendations to Improve Costing Methodologies for Surgical Site Infections

For accurate cost estimates
• Track postdischarge surgical site infections (SSI) and adopt patient as well as societal perspectives • Choose a suitable costing method in accordance with the perspective of whoever bears the consequences. For instance, charges could be the most suitable choice to measure the burden of SSI considering patient perspective and not depending on the cost of SSI from hospital perspective to implement infection control procedures (ICP) • Control for confounders and adjust for time to start of infection (and not for the whole length of stay [LOS]) using statistical techniques that preserves the whole study sample • Conduct sensitivity analyses to evaluate the robustness of the estimated costs • Conduct further research to study the impact of different analytical methodologies on the validity of estimated costs
For transferability of cost estimates to other settings
• Include the perspective, time horizon, the currency used, price year, inflation adjustment, and discounting if applicable • Report detailed information of methodological approach • Clarify cost components and how the cost estimates were calculated • Describe cost by the mean, not the median, with confidence intervals • Use purchasing power exchange rate in currency conversion • Conduct multicenter studies rather than single-center studies to have comparable standardized cost data applicable to other settings • Ensure the applicability of cost estimates to their settings when using them as a decision-making tool

Also, researchers were aware of how the chosen perspective affects the assigned costing method. Inconsistent methods of costing were observed in only 25% of the studies. Moreover, 80% of studies that took payer or patient perspective used unmodified charges. Unlike Fukuda et al, we believe that unmodified charges are not always less accurate than actual costs. In countries where out-of-pocket payments constitute the main sources of financing healthcare services, as in low-income countries, charges might be more realistic to evaluate the burden of illnesses or the impact of interventions.

As reported by Fukuda et al,[16] few studies (10%) had a high transferability level, and D was the most common scope of costing. No increase in the percentage of studies was reported at the B level, the recommended level that achieves the balance between clarity (which is essential for transferability) and practicality when estimating the cost.[13]

Half of the studies we reviewed were multicenter studies. In contrast to single-setting studies, multicenter studies[14,90] generate comparable standardized and transferable cost estimates. Most of the studies were conducted in the United States and Europe, and few were conducted in developing countries. The underrepresentation of low-income countries hinders the transferability to similar countries.

All of the studies that converted currency reported the type of exchange rate used. Unfortunately, all but 1 study[65] used the market exchange rate. The purchasing power parity exchange rate is superior to the market exchange rate because the former is determined by the relative cost of living and inflation rates in different countries. Thus, it allows for transferability and comparability of cost estimates.

In the current review, most studies reported the mean or total costs, and only 13% reported the median cost. Although cost data are known to be skewed, the use of median underestimates the burden of SSI. For decision making, the cost is best presented with the mean.[91] Additionally, such studies should be accompanied by sensitivity analysis to evaluate the robustness of the estimated costs.[92,93] In this review, only 5 studies conducted sensitivity analyses.

Lack of reporting does not only hinder the transferability of the cost estimates, it also might hinder their usage in clinical support decisions in the setting where they were estimated. For example, without reporting the time horizon (observed in 10% of the studies), readers are left unable to check whether the cost of SSI was entirely captured and whether discounting should have been applied. Neglecting the price year, which was reported in half of the studies, hinders the comparability and transferability of cost estimates between different settings and times.

Unlike Fukuda et al,[16] we found that researchers became more inclined to use transferable studies. We observed significantly higher numbers of citations of studies with high transferability as well as studies with a clear scope of costing (A/B) and studies that used actual costing/RCC/RVU.

Here, we updated the reviews by Fukuda et al.[6,16] Although we confined our review to only 1 type of HAI, we broadened the criteria for critically appraising the included studies to enhance cost studies' quality and transferability as economic perspective, types of cost (inpatient, outpatient, out of pocket, productivity losses, capital/overhead, opportunity), cost description measure, time horizon and discounting, price year and inflation adjustment, currency and currency conversion, and sensitivity analysis.

This study has several potential limitations. We limited our search to MEDLINE only via PubMed, included only published studies, and excluded studies in which evaluating intervention or ICPs was the primary aim, although they could have estimated the cost of SSI. The impact of these limitations might be minimal for the following reasons. MEDLINE was capable of identifying from 75% to 92% of relevant studies.[94,95] Unpublished studies are less likely to be sources of SSI cost to support decision for implementing ICP. Exclusion of the studies evaluating the economic impact of ICP kept the included studies more homogenous in methodology and reporting. Another limitation is that we did not address other aspects of the costing methodology, for example, which confounding variables are important to include, and how to refer to the time to start of the infection. These factors might be topics for further research.

In conclusion, over the past 14 years, matching and regression analysis were more likely used to control for confounding factors to minimize bias. Although LOS adjustment has decreased, researchers started to correctly use "time to start of infection" instead of "whole LOS" for adjustment. Researchers mainly adopted a hospital perspective and neglected patient and societal perspectives in the postdischarge setting. After Fukuda et al article, we observed no significant improvement in the transferability of published studies; however, unlike Fukuda et al, transferable studies became more likely to be cited. Researchers became selective in using cost estimates derived from other settings, indicating increased awareness about fundamentals in costing methodologies.

Researchers were less likely to consider reporting recommendations made by Drummond et al[17] and the CHEERS checklist[18] when estimating the cost of SSI (Table 5). We believe that these recommendations, while not new, are unfortunately not well considered by researchers and should be used when conducting their economic evaluations to estimate the cost.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2021.381

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