Discussion 3

- Ambulance use was significantly associated with increasing t-PA administration (OR 3.85)
  - In multi-hospital nationwide database
  - Adjusting for patient case mix
- Possible effects of ambulance*
  - time before calling the ambulance
  - time during transportation
  - time between arrival and initial diagnosis or treatment
- Our results may underline the importance of improving education and awareness for the general public for using ambulance in suspected stroke cases

** Iguchi Y 2006, Morris DL 2000, Yoneda Y 2001*

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Limitations

- Our administrative data analysis does not include the clinical reasons of non-use of t-PA and the underlying reasons for ambulance use
  - Further studies are desirable to investigate these issues

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Conclusions

- Using a large-scale cross-sectional retrospective analysis of Japanese hospitals, we found that the administration of t-PA was significantly associated with age and severity of stroke symptoms, which are congruent with current guidelines.
- Even after adjusting for patients' characteristics, the administration of t-PA was found to be associated with ambulance use.

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  - The authors have no financial conflict of interest to disclose concerning the presentation

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Evaluation of resource allocation and supply–demand balance in clinical practice with high-cost technologies

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Keywords
delivery of health care, ESWL, Japan, MRI, supply and distribution

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Abstract

Rationale, aims and objectives Japan has one of the highest numbers of high-cost medical devices installed relative to its population. While evaluations of the distribution of these devices traditionally involve simple population-based assessments, an indicator that includes the demand of these devices would more accurately reflect the situation. The purpose of this study was to develop an indicator of the supply–demand balance of such devices, using examples of magnetic resonance imaging scanners (MRI) and extracorporeal shockwave lithotripters (ESWL), and to investigate the relationship between this indicator, personnel distribution statuses and operating statuses at the prefectural level.
Methods Using data from nation-wide surveys and claims data from 16 hospitals, we developed an indicator based on the ratio of the supplied number of device units to the number of device units in demand for MRI and ESWL. The latter value was based on patient volume and utilization proportion. Correlation analyses were conducted between the supply–demand balances of these devices, personal distribution and operating statuses.
Results Comparisons between our indicator and conventional population-based indicators revealed that 15% and 30% of prefectures were at risk of underestimating the availability of MRI and ESWL, respectively. The numbers of specialist personnel/device units showed significant, negative correlations with our indicators in both devices.
Conclusions Utilization-based analyses of health care resource placement and utilization status provide a more accurate indication than simple population-based assessments, and can assist decision makers in reviewing gaps between health policy and management. Such an indicator therefore has the potential to be a tool in helping to improve the efficiency of the allocation and placement of such devices.

Introduction

As shown by Kissick's iron triangle of health care, all countries confront the same challenges with regard to balancing access to health services, quality of health care and cost containment [1]. When cost and quality have achieved a certain level of balance, the next step is to ensure that these health technologies are allocated in the most efficient and appropriate manner possible, and made equally available to every patient in need [2]. However, the diffusion of these technologies under market influence does not tend to occur in the most equitable or appropriate ways.

The dilemma of cost containment versus equitable availability of high-cost medical devices is not a new one, and continues to grow in importance [3,4]. In terms of resource allocation, the most common dilemma is the accurate determination of the number of high-cost medical devices needed within a region to adequately meet its health care demands, as opposed to the maximization of convenience to patients or the economic interests of physicians and hospitals [5,6]. Many countries have tried to examine how best to ensure sustainable health care investments by regulating the diffusion of high-cost medical devices [7,8].

In Japan, however, this dilemma has not been regarded as an issue of concern [9]. The Japanese government has adopted a hands-off approach, and encouraged the enhanced accessibility of high-cost medical devices through market behaviour under a low fee-for-service reimbursement schedule. However, results from a multiple regression analysis of OECD countries have shown that allowing flexible payment methods to hospitals appeared to be an influential factor in the diffusion of high-cost medical technologies [10]. The market system has caused a so-called medical arms race [11] and has contributed to the rapid diffusion of medical devices. In particular, the dramatic diffusion of magnetic resonance imaging scanners (MRI) was supported by other driving forces: for example, domestic medical equipment companies have developed high-quality products and market prices have thus declined [12]. Japan has recently become one of the world's leading countries in terms of the number of high-cost medical devices installed per population [13,14].

On the other hand, the consequent ubiquity of these medical devices has resulted in the associated procedures performed being taken for granted and many physicians, if pressed, tend to provide an intervention even if they did not think it was warranted or cost-effective [15]. It has been reported that many of the available high-cost medical devices had low utilization rates [16]. Thus, it has become necessary to treat the issue of allocative efficiency in Japan as seriously as in any other country.

The issue of allocative efficiency in high-cost medical devices could be regarded as consisting of the distributions of both these device units and the corresponding human resource. Because of the reasons outlined above, the issue of whether the distribution of devices is well-balanced with regional demands in Japan is in doubt. A number of previous studies have evaluated the geographic distribution of high-cost medical devices based on the number of device units per population [14,17–19]. There is a possibly that these previous indicators mislead decision making regarding the control of technology diffusion, as the relationship between the number of residents and the actual eligible population for a technology may not always correspond within a geographical area. Thus, an indicator that measures how the number of supplied device units differs from the number of device units in demand is required. As such, a more precise assessment of resource distribution can be attained by taking into account regional disease distributions.

The purpose of this study was to develop an indicator for the evaluation of the supply–demand balance of high-cost medical devices based on regional disease distribution and utilization, to apply this indicator to analyses of MRI and extracorporeal shock-wave lithotripters (ESWL) within all 47 prefectures in Japan, and to investigate the relationship between device distribution statuses, human resource distribution statuses and operating statuses.

Methods

Diffusion patterns of MRI and ESWL

We investigated the recent diffusion patterns of MRI and ESWL in Japan using data obtained from a National Survey of Medical Care Institutions conducted by the Ministry of Health, Labour and Welfare.

Data collection

Data were obtained from three sources: (1) the numbers of medical device units in each prefecture were obtained from a National Survey of Medical Care Institutions conducted in 2002 by the government [20]; (2) estimated patient volume was obtained from a National Patient Survey in 2002, also conducted by the government [21]; and (3) claims data for patients discharged between April 2001 and December 2005 from 16 sampled hospitals.

All of the 16 private hospitals were members of the Quality Indicator/Improvement Project (QIP), a program administrated by our department in which participating hospitals widely distributed throughout Japan voluntarily provide discharge summary data for analysis. All hospitals had at least one MRI installed, and only one out of 16 hospitals did not have an ESWL on-site. The QIP database includes information on demographics, disease classification, surgical procedures, other medical procedures and claims information.

For correlation analyses, the number of radiologists, radiological technologists and urologists were obtained from a Hospital Report [20] and National Survey of Physicians, Dentists and Pharmacists [22]. To calculate the operating rate of selected medical devices, the utilization volume (number of examinations/procedures) during 1 month was used.

Calculation procedure for the OE ratio

In this study, we developed an indicator based on the ratio of the observed number of device units (O) to the expected number of device units (E), henceforth the OE ratio. The observed number of device units reflects the actual number of supplied device units. The expected number reflects the number of device units in demand, and was estimated based on patient volumes and utilization proportions categorized according to primary diagnosis classifications. When the OE ratio is greater than 1 in a particular area, it implies that the area is in a state of relative excess supply. This approach is based on the concept of demand estimation, in which resources demanded are proportionally distributed in accordance with the expected frequency of use in each area. The expected frequency of use is obtained by multiplying the levels of resource utilization by the number of patients in each primary diagnosis classification.

The OE ratio can be obtained as follows: first, the crude expected frequency of use (CEF) in area r is represented by:

$$CEF_r = \sum_c \left(n_{c,r} \cdot \sum_h f_{h,c} \Big/ \sum_h s_{h,c}\right) \quad (1)$$

where $n_{c,r}$ is the number of patients in a disease classification c in area r, $f_{h,c}$ is the frequency of use among patients in disease classification c in sampled hospital h, and $s_{h,c}$ is the number of patients in disease classification c in sampled hospital h. This formula assumes that the proportions of medical device utilization according to disease classifications are the same in all hospitals. Next, the expected number of device units EU_r is given by the following formula:

$$EU_r = \sum_r OU_r \cdot \left(CEF_r \Big/ \sum_r CEF_r\right) \quad (2)$$

where OU_r is the observed number of device units. Finally, the OE ratio is derived from the observed number of device units divided by the expected number of device units. It should be noted that the OE ratio is not based on absolute demand estimates but instead represents relative assessments of demand.

The OE ratio was applied to evaluate the supply–demand balance of MRI and ESWL units at the prefectural level in Japan. We selected these capital-intensive devices primarily because of availability of data and because the installed numbers of these particular device units per population in Japan are extremely large when compared with other developed countries [23].

Evaluation of the OE ratio

To evaluate its usability as an indicator, the OE ratio was compared with the adjusted relative number of device units per population.

However, there is no benchmark for the ideal number of device units per population that could be used for validation of our indicator. Previous studies have used the number of device units per population as a conventional indicator to evaluate the relative appropriateness of the installed number. We have thus used this indicator for comparative purposes with the OE ratio. In order to ensure that this conventional indicator is capable of judging relative appropriateness, we have adjusted the number of device units per population in each prefecture by the national mean of the number of device units per population.

Correlation analyses

We conducted correlation analyses to investigate the relationship between OE ratio as the supply–demand balance of device units, the number of staff who operate MRI or ESWL to indicate human resource replacement status and the number of utilization per selected device units indicating the operating rate. In addition to these cross-section variables, the increasing rate of the number of these device units during the period between 2002 to 2005 was included. *P*-values were taken to be significant at $P < 0.05$ (two-tailed). Statistical analyses were conducted using SPSS ver.12.0. Choropleth maps were produced using ArcGIS 9.2.

Results

Table 1 shows the diffusion of MRI and ESWL in hospitals and clinics from 1996 to 2005. The numbers of units of both devices were observed to rise consistently throughout the study period. Furthermore, all prefectures had at least one MRI and ESWL by 2002.

Table 2 shows the summarized data of utilization proportions for MRI and ESWL by 16 major diagnosis categories derived from 465 primary diagnosis classifications. Data from a total of 387 644 patients from 16 hospitals utilizing MRI and 383 362 patients from 15 hospitals utilizing ESWL were used. Within our study population, the major diagnosis categories with the highest mean utilization proportions for MRI and ESWL were the nervous system (8.8%) and kidney, urinary tract, and male reproductive system (3.4%), respectively. The primary diagnoses within the major diagnosis categories with the highest utilization proportions were stroke (37.5%) and upper ureteral calculous (30.2%) for the MRI and ESWL, respectively.

Figures 1 and 2 illustrate the relationship between the OE ratio and the adjusted relative number of device units per population. To evaluate the assessment of demand based on utilization proportion for each primary diagnosis classification, we compared the OE ratio with the adjusted relative number of device units per population. The OE ratios of some prefectures were plotted within the second quadrant of the Cartesian coordinate system, in which the point of origin exists at the intersection where the abscissa unit and the ordinate value equal 1. Based on the conventional indicator, the second quadrant represents prefectures with a supply shortage of devices. However, the same quadrant represents prefectures with supply excess based on the new OE ratio indicator. There were seven prefectures plotted in the second quadrant with respect to MRI, and 14 prefectures with respect to ESWL. On the other hand, the fourth quadrant represents prefectures with an excess in supply based on the conventional indicator, while representing prefectures with a supply shortage based on our developed indicator. There were three prefectures plotted in the fourth quadrant with respect to MRI, and one prefecture with respect to ESWL.

The OE ratio according to prefectural distributions of MRI was calculated to be 1.05 ± 0.19 (mean $\pm$ SD), while the OE ratio for ESWL was found to be 1.18 ± 0.41. There were wide geographic variations in the supply–demand balance for these devices (0.69–

Table 1 Total number of MRI and ESWL by facilities for each fiscal year

	1996	1999		2002		2005	
	N	*N*	Rate of increase (%)	*N*	Rate of increase (%)	*N*	Rate of increase (%)
MRI							
Hospital							
Facility	2175	2622	20.6	3067	17.0	3322	8.3
Equipment	2360	2938	24.5	3505	19.3	3878	10.6
Clinic							
Facility	N/A	N/A	N/A	889	N/A	1242	39.7
Equipment	N/A	N/A	N/A	996	N/A	1250	25.5
ESWL							
Hospital							
Facility	483	586	21.3	763	30.2	867	13.6
Equipment	N/A	N/A	N/A	794	N/A	891	12.2
Clinic							
Facility	N/A	N/A	N/A	13	N/A	14	7.7
Equipment	N/A	N/A	N/A	20	N/A	21	5.0

MRI, magnetic resonance imaging scanner; ESWL, extracorporeal shock wave lithotripter; *N*, total number for each fiscal year in Japan; rate of increase, rate of increase over the previous three fiscal years; N/A, not available; clinic, a facility having fewer than 20 beds; hospital, a facility having equal to or more than 20 beds.

Source: National Survey of Medical Care Institutions.

The survey items on medical technology are included in a large-scale survey conducted every 3 years.

Table 2 Utilization proportions of MRI and ESWL by classification of primary diagnosis

Major diagnostic categories	No. of classifications of primary diagnosis	Utilization proportion of MRI (%)			Utilization proportion of ESWL (%)		
		Mean*	Min†	Max‡	Mean*	Min†	Max‡
Nervous system	37	8.8	0.0	37.5	0.0	0.0	0.2
Eye	37	0.4	0.0	6.5	0.0	0.0	0.0
Ear, nose, mouth and throat	37	0.8	0.0	20.0	0.0	0.0	0.0
Respiratory system	27	0.6	0.0	3.2	0.0	0.0	0.0
Circulatory system	26	1.2	0.0	7.7	0.0	0.0	0.0
Digestive system	37	1.5	0.0	9.8	0.0	0.0	0.3
Musculoskeletal system	37	1.8	0.0	12.5	0.0	0.0	0.0
Skin and subcutaneous tissue	25	1.1	0.0	2.2	0.0	0.0	0.0
Mammary gland	5	0.3	0.0	0.3	0.0	0.0	0.0
Endocrine and metabolic system	37	1.7	0.0	33.3	0.0	0.0	0.0
Kidney, urinary tract and male reproductive system	32	0.9	0.0	7.7	3.4	0.0	30.2
Female reproductive system, pregnancy and puerperium	29	0.0	0.0	2.6	0.0	0.0	0.0
Blood and blood forming organs	16	1.3	0.0	2.7	0.0	0.0	0.6
Neonates and congenital malformation	37	1.2	0.0	4.7	0.0	0.0	0.0
Other pediatrics	9	0.4	0.0	9.8	0.0	0.0	0.0
Injuries, burns, toxicosis and others	37	1.2	0.0	33.3	0.0	0.0	0.1

*Mean utilization proportion in each major diagnosis category.
†Minimum utilization proportion in each classification of primary diagnosis.
‡Maximum utilization proportion in each classification of primary diagnosis.
Number of sampled hospitals: 16 (MRI), 15 (ESWL).
Total number of patients in sampled hospitals: 387 644 (MRI), 383 362 (ESWL).
MRI, magnetic resonance imaging scanner; ESWL, extracorporeal shock wave lithotripter.

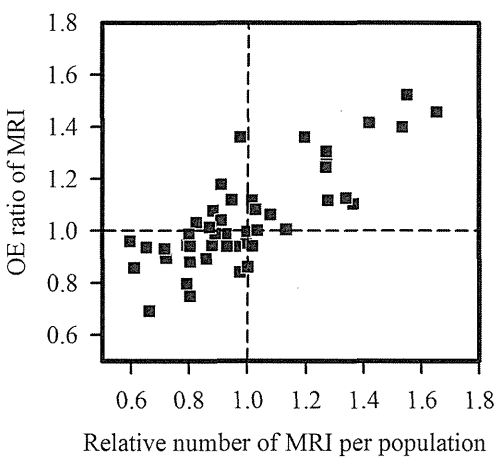

Figure 1 Relationship between OE ratio and relative number of MRI per population. MRI, magnetic resonance imaging scanner.

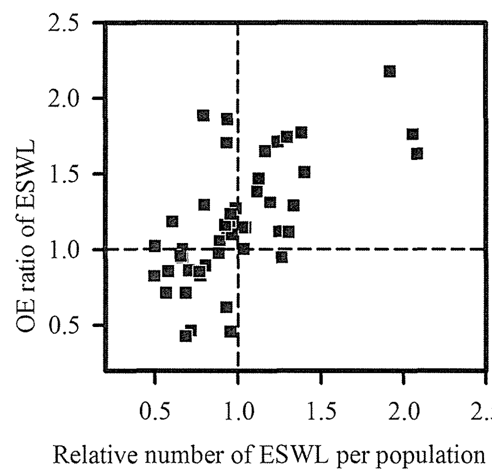

Figure 2 Relationship between OE ratio and relative number of ESWL per population. ESWL, extracorporeal shockwave lithotripter.

1.52 for MRI and 0.43–2.18 for ESWL estimations). The OE ratios according to prefectural distributions of MRI and ESWL in 2002 are shown in Figs 3 and 4, respectively. Regions with high OE ratios, implying a state of excess supply, show some clustering for both MRI and ESWL.

Table 3 shows summary statistics for each selected variable. The largest number of specialist personnel per MRI or ESWL in a prefecture was more than twice or fourfold that of the smallest one, respectively. Likewise, the largest operating rate of MRI or ESWL was more than thrice or fourfold that of the smallest one. In addition, there was no prefecture where the number of MRI had decreased from 2002 to 2005. On the other hand, as seen in Table 3, the negative value observed in the minimum increasing rate of number of ESWL implies that there was a least one prefecture where the number of ESWL had been decreasing.

The results of correlation analyses are shown in Table 4. With regard to MRI, there was a statistically significant, negative correlation between the OE ratio with the number of radiological

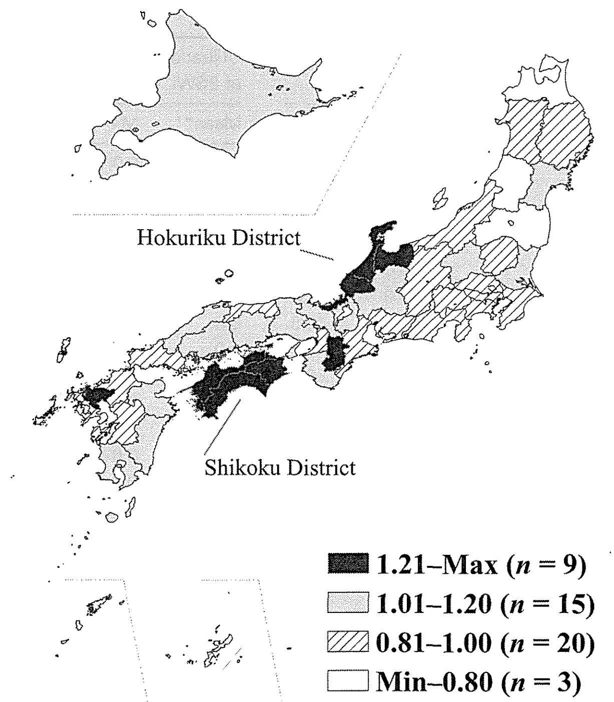

Figure 3 OE ratio by prefecture – MRI. MRI, magnetic resonance imaging scanner.

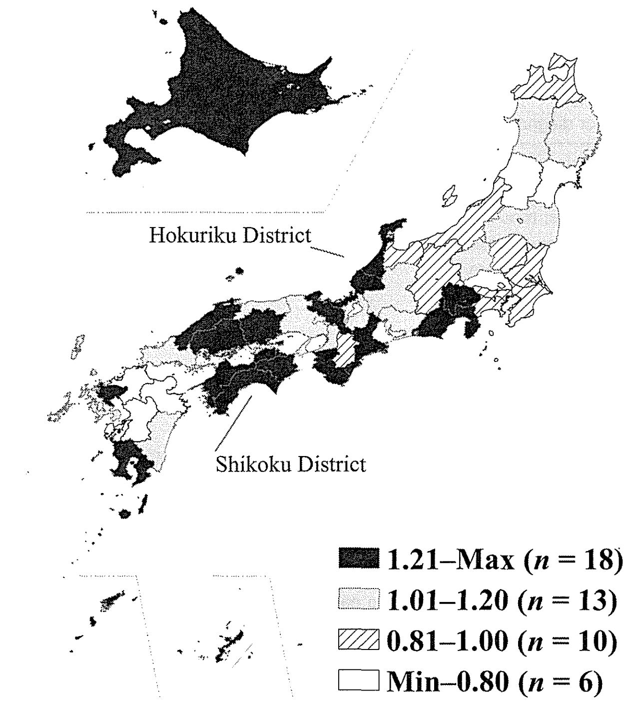

Figure 4 OE ratio by prefecture – ESWL. ESWL, extracorporeal shock-wave lithotripter.

Table 3 Summary statistics of OE ratio and supply indicators of MRI and ESWL at prefectural level ($n = 47$)

		Mean	Standard deviation	Min	Max
MRI	OE ratio of device units	1.05	0.19	0.69	1.52
	No. of radiologists per MRI	1.33	0.42	0.60	2.33
	No. of radiological technologists per MRI	9.20	1.64	5.80	13.20
	No. of examinations per MRI*	171.25	39.65	110.00	329.50
	Increasing rate of no. of MRI†	10.75	6.24	0.00	27.80
ESWL	OE ratio of device units	1.18	0.41	0.43	2.18
	No. of urologists per ESWL	7.59	2.27	3.30	14.20
	No. of procedures per ESWL*	11.08	3.27	3.60	17.60
	Increasing rate of no. of ESWL†	12.57	20.94	–37.50	63.60

*Survey period for utilization: 1 month.
†Reference period for increasing rate: 2002–2005.
MRI, magnetic resonance imaging scanner; ESWL, extracorporeal shock wave lithotripter.

Table 4 Correlations between OE ratio and supply indicators of MRI and ESWL at prefectural level ($n = 47$)

		OE ratio of MRI	OE ratio of ESWL
No. of specialist personnel per no. of device units*	r	–0.701	–0.417
	P-value	<0.001	0.004
No. of examinations/procedures per no. of device units	r	–0.221	–0.377
	P-value	0.136	0.009
Increasing rate of no. of device units	r	–0.303	0.047
	P-value	0.038	0.753

*Specialist personnel consists of radiological technologists (MRI) and urologists (ESWL). The number of radiologists per MRI was not included as it was found to have a non-significant correlative coefficient ($r = 0.023$, $P = 0.876$) with the OE ratio of MRI.
MRI, magnetic resonance imaging scanner; ESWL, extracorporeal shock wave lithotripter.

technologists per MRI ($r = -0.701$) and the increasing rate of the number of MRI ($r = -0.303$). On the other hand, there was no significant correlation between the OE ratio with the number of radiologists per MRI. In the case of ESWL, the OE ratio, the number of urologists per ESWL ($r = -0.417$) and the number of utilization per ESWL ($r = -0.377$) show a statistically significant, negative correlation.

Discussion

In this study, we developed an indicator for evaluating the supply–demand balance of high-cost medical devices that takes into account differences in regional patient volume and utilization patterns, and applied this indicator to evaluating MRI and ESWL. The conventional population-based indicator is based on the assumption that the proportion of devices in demand to population size is constant in all prefectures. While both the volume of stroke (which accounted for the highest utilization proportion of MRI) and upper ureteral calculous (which accounted for the highest utilization proportion of ESWL) were positively correlated to population size in all prefectures, sub-analysis revealed that for both devices, the largest patient number per million population ratio in a prefecture was three times that of the smaller one (data not shown). The existence of such a large variation implied that a disease-specific patient-based indicator would have the advantage of taking into account differences in prefectural distribution of diseases when compared with the conventional indicator.

By comparisons between our developed indicator and the conventional population-based indicator, the OE ratio can be expected to decrease the possibility of misreading as to whether a situation represents one of excess or shortage in supply. Applying this concept to the dataset in this study, 21% (10/47) and 32% (15/47) of prefectures were at risk of misreading the supply–demand balance of MRI and ESWL, respectively. In addition, more than half of the prefectures at risk (MRI: 7/10, ESWL: 14/15) were likely to be judged as being undersupplied when they were in actuality facing a situation of excess supply for high-cost medical devices. Furthermore, the numbers of these device units continue to increase in hospitals and even in clinics (Table 1).

Choropleth maps displaying the distribution of OE ratios (Figs 3 & 4) showed that there were some oversupplied areas for both MRI and ESWL that tended to cluster, such as in the Shikoku and Hokuriku districts. Additionally, some prefectures which showed an oversupply of MRI also tended to be oversupplied with ESWL. Furthermore, some prefectures in the north tended to be in a situation of supply shortage. This might be indicative of the chronic workforce shortage from which many hospitals suffer, particularly in the northern districts [22].

A possible priority issue of resource planning of MRI could be that the adoption of MRI and the placement of human resource should be treated in parallel. With regard to manpower involved with MRI operation, we analysed both radiologists and radiological technologists. Japan has only one-third the OECD average of the number of radiologists per population [24]. Thus, the assessment of the regional distribution of radiologists should be treated as seriously as that of radiological technologists in order to ensure sufficient manpower for this particular resource. Our results showed that there was no statistically significant correlation between the OE ratio of MRI and the number of radiologists per MRI, although there was a statistically significant negative correlation between the OE ratio and the number of radiological technologists per MRI (Table 4). This could be caused by the diffusion of telemedicine and the working pattern of radiologists who work for more than one medical institution, sometimes covering more than one regional area. According to a report on the regional distribution of telemedicine in Japan, telemedicine projects are developing in the rural areas of the Tohoku district and Hokkaido prefecture [25]. The small OE ratios of MRI were shown in many prefectures in the Tohoku district. These findings would indicate that hospitals have tried to meet increasing workload requirements by sharing a finite radiological manpower resource.

As previously mentioned, it has often been argued that a market-oriented diffusion of high-cost medical devices would have a risk of excess placement. The results from correlation analysis, however, show that areas with excess supply tended to have lower increasing rates of the number of MRI and a lower number of radiological technologists. This could imply that the supply–demand imbalances of MRI units are in the process of improvement because of constraints on human resources, rather than pressures arising from competitions for patients.

Because of the fact that there are still waiting lists for MRI utilization [26] and that there was no prefecture where the number of MRI has declined (Table 3), it is assumed that MRI would continue to increase in numbers. On the other hand, the human resource shortage for operating MRI has been found to hinder the establishment of emergency delivery systems [27]. Thus, a policy that is based on selection of health care delivery functions and in particular, focusing on the control of health care resource should be implemented at the regional level. In order for this policy to work, there needs to be a continuous assessment of the relationship between health care demands, distributions of MRI and human resource placement.

As the MRI is a diagnostic device, and not a treatment device like the ESWL, it is possible that excessive utilization may occur in areas of excess supply because of inappropriate utilization by patients who may not fit the application criteria for MRI [28]. However, it is difficult to claim that excessive use of MRI is being aggressively driven because a negative correlation was observed between the OE ratio of MRI and the operating rate, although this correlation was statistically insignificant. Furthermore, the Japanese hospital payment system has partly changed to a case-mix payment system in place of a fee-for-service payment system since 2003 [29]. Inpatient care in hospitals that fall under the case-mix payment system would therefore have less economic incentives for changing the application criteria for MRI utilization.

A priority issue of resource planning in the case of ESWL could be that, in addition to facing the same issues as MRI, the decision making concerning the adoption of ESWL by hospitals should take into greater account the regional demand of these devices. This is because the correlation between the OE ratio in ESWL and the increasing rate of the number of ESWL was positive, unlike the trend observed in MRI. From an operational standpoint, it is highly unlikely that excessive use of ESWL frequently occurred as it is only used in limited diseases, there are strict clinical guidelines for treatment with ESWL, and also because the reimbursement charge is constant regardless of how many times a single patient utilizes an ESWL per month. This assumption would be supported by the result that the OE ratio in ESWL was negatively and significantly correlated with the operating rate.

With regard to data availability, OE ratios were estimated under the following assumptions: first, as outpatient claims data are not structured, we assumed that outpatient utilization numbers are proportional to inpatient utilization numbers. Second, given that data involving multiple utilizations by a single patient of medical devices in 1 month could not be obtained, we assumed that there was a proportional relationship between initial utilization and subsequent utilization of each device within a given month. Furthermore, our dataset was limited to private hospitals.

However, we do not consider that these factors would significantly introduce bias into our indicator. Approximately 80% of hospitals in Japan are, like the hospitals used in this study, privately owned and not-for-profit, according to a National Survey of Medical Care Institutions [20], and this therefore minimizes selection bias. Furthermore, regardless of whether they are privately or publicly owned, Japanese health care providers are paid according to the nationally uniform reimbursement schedule. This implies that there may be few, if any, significant differences between private and public hospitals with regard to medical device utilization, and may thus reduce the impact on our indicator's validity. The hospitals used in our sample are relatively large, and may therefore be thought to have a higher proportion of severe cases in need of greater resource utilization. However, as our indicator was based not on an absolute value of utilization, but rather a relative scale between diagnoses, any bias that may arise because of the aforementioned conditions should be minimized.

Public health policy implications

In order to obtain a greater allocative efficiency of high-cost medical devices within the health care system, active regulation of the distribution of these devices by the government may be a useful intervention. We believe the OE ratio may assist such regulation, and may even be applicable to monitor changes in the supply–demand balance post-intervention.

As an alternative, in place of government regulations, committees consisting of representatives from hospitals, physicians' associations, local governments and other stakeholders may be able to redefine hospital roles and cooperative utilization of high-cost medical devices within a given area [30]. Even in such cases, the OE ratio would still be applicable as an indicator of allocative efficiency.

Conclusions

As international comparisons of the diffusion of high-cost medical devices continue, the need for a thorough evaluation of the supply–demand balance of these devices grows. Previous attempts at such evaluations have relied on indicators that do not take into account variations in patient volume or utilization. Therefore, we derived the OE ratio as a more realistic estimate by combining the level of resource utilization with the number of patients in primary diagnosis classifications. When compared with population-based assessments, the OE ratio would be less inclined to misread the supply–demand balance of high-cost medical devices.

When considering the rational reformation of a health care delivery system, it is necessary that resources with a complementary relationship to each other should be treated in parallel during resource allocation planning. Our studies revealed that there were mismatches between the distribution of device units and human resources. Furthermore, we found that areas of excess MRI and ESWL supply were not always related to excessive device utilization. However, the characteristics of the Japanese health care delivery system, in which a fee-for-service payment system with no governmental regulations regarding the purchase of such devices, may have driven the diffusion of high-cost medical devices and thus influenced a state of excess supply. The methodology in this study will contribute to assisting decision makers review gaps between health policy and health management under other reimbursement systems and regulation, and help motivate further research geared towards efficient health care resource planning at hospital, regional and governmental levels.

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Review

Variations in analytical methodology for estimating costs of hospital-acquired infections: a systematic review

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S U M M A R Y

Quantifying the additional costs of hospital-acquired infections (COHAI) is essential for developing cost-effective infection control measures. The methodological approaches to estimate these costs include case reviews, matched comparisons and regression analyses. The choice of cost estimation methodologies can affect the accuracy of the resulting estimates, however, with regression analyses generally able to avoid the bias pitfalls of the other methods. The objective of this study was to elucidate the distributions and trends in cost estimation methodologies in published studies that have produced COHAI estimates. We conducted systematic searches of peer-reviewed publications that produced cost estimates attributable to hospital-acquired infection in MEDLINE from 1980 to 2006. Shifts in methodologies at 10-year intervals were analysed using Fisher's exact test. The most frequent method of COHAI estimation methodology was multiple matched comparisons (59.6%), followed by regression models (25.8%), and case reviews (7.9%). There were significant increases in studies that used regression models and decreases in matched comparisons through the 1980s, 1990s and post-2000 ($P = 0.033$). Whereas regression analyses have become more frequently used for COHAI estimations in recent years, matched comparisons are still used in more than half of COHAI estimation studies. Researchers need to be more discerning in the selection of methodologies for their analyses, and comparative analyses are needed to identify more accurate estimation methods. This review provides a resource for analysts to overview the distribution, trends, advantages and pitfalls of the various existing COHAI estimation methodologies.

Introduction

In 2008, the Centers for Medicare & Medicaid Services adopted a 'no pay for errors' policy in the USA in which hospitals would no longer be reimbursed for preventable adverse events. As an indication of the recognition of their effects, these adverse events included several hospital-acquired infections (HAIs).[1] Accurate estimations of the additional costs associated with HAIs (COHAI) support the decision-making process for infection control measures by making possible the accurate assessments of these measures.

Most studies in the existing literature that produce COHAI estimates have used case reviews, matched comparison analyses or regression analyses as their estimation methodologies. In case reviews, researchers are able to accurately distinguish between resources used in the treatment of the primary diagnosis of patients, and the additional resources used for HAIs. Recent development of methods such as appropriateness evaluation protocols (AEP) have allowed for more rigorous evaluations.[2] The accuracy of the case review approach is dependent on the quality of information recorded in patient charts, and hampered by the associated labour intensiveness.

The main advantage of the matched comparisons method is its relative simplicity, which eschews the need for overly complicated statistical knowledge on the part of analysts. However, variations in patient attributes make it extremely difficult to find a corresponding uninfected patient for every infected case. Selection bias may consequently arise due to the exclusion of unmatched cases and controls.

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The regression analysis approach enables the inclusion of almost all infected and uninfected patients in analysis, and therefore provides a means to avoid selection bias. Though vulnerable to the influence of endogenous variables, methods such as instrumental variable models have been developed in order to minimise the effects.[3]

Other biases may arise from the failure to account for the influence of confounding factors such as disease severity or patient time at risk.[3–5] The occurrence of an HAI generally extends the hospital length of stay (LOS) of a patient, and therefore contributes to increased healthcare costs.[6] Longer LOS prior to infection may also represent a risk factor for infections, and this presents a potential endogeneity problem in COHAI estimates.[3,7,8]

Graves *et al.* have recently highlighted the importance of accurate HAI cost estimations, and the need for more stringent measurement methodologies.[9] Over the years, pioneering researchers have developed new strategies to minimise the aforementioned issues and produce more accurate COHAI estimates for downstream use.[3,10] There has been an increase in the number of published studies that have conducted COHAI estimates, and it is entirely plausible that these estimates have been used in downstream research such as the assessments of infection control measures. However, the trends and distribution of methodologies that have been used in COHAI estimation studies remain unknown. Furthermore, researchers who intend to conduct COHAI estimates, as well as third parties who use the published estimates may benefit from a review of the trends, advantages and pitfalls of the various methodologies. Therefore, the first objective of this study was to conduct a systematic review of the analytic methodologies used in published studies that produced COHAI estimates, and observe the distribution of approaches employed to deal with the issues as described above. The second objective was to observe changes in trends, if any, of methodologies over time.

Methods

Data sources and search strategies

This systematic review was conducted according to the general principles of the Cochrane Collaboration framework.[11] We conducted a systematic review of studies published in the English language from 1980 to 2006 that had produced original COHAI estimates. Candidate studies were identified using a MEDLINE search using the following keywords: 'economics'[Subheading] OR 'Hospital Costs'[MeSH]) AND ('Cross Infection'[MeSH] OR 'Surgical Wound Infection'[MeSH] OR 'Bacteremia'[MeSH] OR 'Bacterial Infections'[MeSH] OR 'Sepsis'[MeSH] OR 'Staphylococcal Infections'[MeSH] OR 'Pseudomonas Infections'[MeSH] OR 'Pneumonia'[MeSH] OR 'Urinary Tract Infections'[MeSH].

Study selection

Studies that corresponded to the abovementioned search keywords were subjected to a two-step review process consisting of an abstract review and a full literature review. The abstract review was conducted in order to identify studies that had produced original cost estimates for the treatment of HAIs and excluded (1) studies that had utilised existing cost estimates obtained from other published studies, (2) studies that had included community-acquired infections in their sample, and (3) studies that had included infected patients in the reference comparison group. The subsequent full literature review stage included studies identified as having produced original COHAI estimates, and studies that could not be fully evaluated from the abstract review stage. In the full literature review stage we confirmed the suitability of the studies for inclusion in analysis, and through the use of data collection forms we evaluated the analytic methodologies used for COHAI estimation.

Additionally, we conducted a hand-search of the references cited in the studies obtained in the MEDLINE search, and identified other publications that had also produced original COHAI estimates using the same two-step review method as outlined above.

All reviews were conducted independently by two evaluators (H.F. and J.L.), and non-congruent evaluations were discussed before decisions were made.[11]

Analytic methodologies

There are three major analytic approaches used in COHAI estimation research: (1) case reviews, (2) matched comparisons, and (3) regression analysis.[2,4,5] We evaluated the distribution of analytic methodologies categorised by infection type, and analysed the matching variables in matched comparisons and independent variables used in regression analysis. COHAI estimates were also reported for reference purposes.

Trends in methodology

Several treatises regarding novel methodologies have been published, and these studies may have influenced shifts in trends in COHAI estimation approaches: of particular importance are those developed by McGowan in 1981, Haley in 1991, and Howard *et al.* in 2001.[3–5] Taking into account the year of publication of these studies, we analysed the methodology of COHAI estimates by categorising the papers according to whether they were published in the 1980s, 1990s or post 2000. Statistical analysis of the shifts in trends over the years was conducted using Fisher's exact test.

Results

Of the 3069 studies that matched our search terms on MEDLINE, we identified 79 studies that produced estimates on incremental COHAI using the abstract review and full literature review. The subsequent hand-search identified a further 110 non-duplicate candidate publications from the references in the original 79 studies, 10 of which were evaluated as suitable for our analysis. Therefore, the final analysis consisted of 89 studies.[A1–A89]

Analytic methodologies

The characteristics of the studies used in our analysis are presented in Table I. Of the 89 studies, 28 studies produced estimates on surgical site infections (SSI), 20 bloodstream infection (BSI) studies, 12 pneumonia/ventilator-associated pneumonia (VAP) studies, 10 urinary tract infection (UTI) studies, 5 respiratory tract infection (RTI) studies, and 40 studies with unspecified infections. There was an observed increase in studies producing COHAI estimates over the years, with 10 of the studies published in the 1980s, 21 in the 1990s, and 58 from 2000 to 2006. With regard to the distribution of analytical approaches used in producing COHAI estimates, the most frequent method used was multiple matched comparisons (53 studies, 59.6%), followed by regression models (23 studies, 25.8%), case reviews (7 studies, 7.9%), unmatched comparisons (3 studies, 3.4%) and unspecified methods (3 studies, 3.4%).

Forty of the studies that used matched comparisons employed a 1:1 matching method in which each case (infected) patient was matched to a single reference patient. An approximately equal number of studies assumed a normal distribution for regression models (10 studies), or used a logarithm transformation for the dependent variable of healthcare costs (9 studies). While there

Table I
Characteristics of published studies that had produced estimates of additional healthcare costs due to hospital-acquired infections ($N = 89$)

Study characteristics	No. (%) of studies
Type of infection	
Surgical	28 (31.5%)
Bloodstream	20 (22.5%)
Pneumonia/ventilator-associated pneumonia	12 (13.5%)
Urinary tract	10 (11.2%)
Respiratory tract	5 (5.6%)
General	40 (44.9%)
Country/region	
USA	41 (46.1%)
Europe	26 (29.2%)
Asia	13 (14.6%)
Other	9 (10.1%)
Year of publication	
1980–1984	7 (7.9%)
1985–1989	3 (3.4%)
1990–1994	9 (10.1%)
1995–1999	12 (13.5%)
2000–2004	35 (39.3%)
2005–2006	23 (25.8%)
Methods for estimating cost of hospital-acquired infection	
Case review	7
Standardised case review (AEP)	3 (3.4%)
Standardised case review	1 (1.1%)
Case review	3 (3.4%)
Unmatched comparison (1:*x*)	3 (3.4%)
Matched comparison	53
Multiple matched comparison (1:1)	40 (44.9%)
Multiple matched comparison (1:*x*)	8 (9.0%)
Multiple matched comparison (1:2)	4 (4.5%)
Multiple matched comparison (1:all)	1 (1.1%)
Regression analysis	23
Multiple linear regression (normal distribution)	10 (11.2%)
Multiple linear regression (logarithmic transformation)	9 (10.1%)
Multiple linear regression (gamma model)	1 (1.1%)
Generalised estimating equation	1 (1.1%)
Heckman's two-stage model	1 (1.1%)
Multiple regression (unknown)	1 (1.1%)
Unknown	3 (3.4%)

AEP, appropriateness evaluation protocol.
Europe includes UK (5), France (5), Belgium (4), Germany (3), Spain (3), Netherlands (2), Ireland (1), Italy (1), Scotland (1), and Switzerland (1). Asia includes Turkey (6), Taiwan (4), India (1), Thailand (1), and China (1). Others include Canada (2), Argentina (2), Mexico (1), Trinidad and Tobago (1), Australia (1), New Zealand (1), and multi-country study (1).

were no studies that addressed the endogeneity problem by employing an instrumental variables model, there was one publication that used Heckman's two-stage model in order to reduce bias. There was also one study that used matched comparisons as the primary approach with regression analysis as the secondary approach, and five studies that used regression analysis as the primary approach with matched comparisons as the secondary approach.

The details of the studies used in analysis, including year of publication, country of origin, types of healthcare institution, patient sample, analytic methodologies, COHAI estimates and matching variables or independent variables are presented in Table II.

We observed that 18 of the 53 publications that used matched comparison analyses, and 8 out of the 23 publications that used regression analyses, had included time at risk in the estimation of COHAI. In matched comparisons, the selection of control reference patients with an LOS of at least the same duration as infected cases was the most frequently used method of taking into account time at risk. However, none of the studies had used the methods proposed by Schulgen.[7] In studies that employed regression analysis, time at risk was taken into account by the inclusion of LOS before surgery, ventilator duration, or intensive care unit duration in the independent variables.

Trends in methodology

Table III shows the changes in methodologies by publication year. Regression analyses had not been used for COHAI estimations in the 1980s. In the 1990s, there were three studies that had used regression analyses, and this number rose to 20 (34.5%) in studies published after 2000. While matched comparisons accounted for the majority of studies in our sample in the 1980s and the 1990s, this method was less popular in studies published post 2000. Also, the proportion of studies using case reviews has also decreased greatly in recent years. These changes in COHAI estimation methodologies were found to be statistically significant ($P = 0.033$).

There was a transition in the number of studies that accounted for LOS relating to both HAI rates and resource use for patients: in the 1980s, there were no studies that had included LOS as a variable, but this has increased in recent years. These studies have accounted for about one-third of all COHAI estimate publications since 2000, showing a marginally statistically significant change over the years ($P = 0.058$).

Discussion

Quantifying the additional costs associated with HAIs supports the decision-making process in infection control measures, and is therefore essential to healthcare policy development and hospital management. There are many potential biases that can affect the validity of these estimates, and methods have been developed to minimise their effect. In this study, we have conducted a systematic review of the methodologies used in studies that produced COHAI estimates published from 1980 to 2006. It was found that studies that had used measures to minimise biases and deal with confounding factors were in the minority, and there is a strong possibility that many of the published COHAI estimates are biased to varying extents. Furthermore, we observed a gradual shift from matched comparisons to regression analyses in recent years. This is a desirable trend as regression analyses are generally preferable to the matched comparisons method in order to obtain estimates with reduced bias. Within regression analyses, it has also been suggested that instrumental variable models can address the issues of endogenous variables.[3,8]

Haley *et al.* analysed the differences in COHAI estimates produced by clinicians' assessments, unmatched comparisons and matched comparisons. It was found that the lowest estimate arose from the clinicians' assessments, followed by matched comparisons and unmatched comparisons.[12] In the case of clinicians' assessments, the distinction between healthcare costs for the primary diagnosis at admission and the additional treatment costs for HAIs are based on subjective opinions, and therefore vulnerable to the effects of bias.[2,4,5] Another study has conducted a comparative analysis of the additional LOS due to surgical site infections (SSI) as calculated by two different methodological approaches. In the case of general SSIs, the standardised case reviews method produced shorter LOS extensions, but with no statistically significant difference.[13] To the best of our knowledge there are no reports of comparisons between standardised case reviews and regression analyses. Furthermore, standardised case reviews have the disadvantage of requiring high labour intensiveness. The current evidence therefore provides little incentive to conduct standardised case reviews for the purpose of COHAI estimates.

By contrast, there have been several studies comparing matched comparisons and regression analyses, with results ranging from no significant difference between the two methods, higher estimates in regression analysis, and higher estimates in matched comparisons.[14–17] Warren *et al.* found that a matched comparison using a propensity score produced COHAI estimates more than twice

Table II
Analytical methodology, estimates of additional costs of hospital-acquired infections, matching variables and regression analysis covariates used in the studies cited in the systematic review

First author	Year	Country	Type of setting	Type of patients	Analytical methodology	Additional cost to HAI if stated [infected vs uninfected]	Matching variables or regression analysis covariates
Surgical site infection							
Herwaldt[A1]	2006	USA	Mixed: 2 hospitals	Surgical	Linear regression (log)	<Non-fatal> + US$1,574 [3,473 vs 1,899] ($P < 0.001$) <Fetal> + US$2,005 [3,904 vs 1,899] ($P < 0.001$)	(1) Karnofsky score*, (2) NNIS risk index*, (3) No. of comorbid illnesses*, (4) Obesity*, (5) Preoperative LOS*, (6) Age*, (7) Interaction of type of surgery and the McCabe and Jackson classification*
Vogel[A2]	2006	USA	University hospital	Surgical	Regression	+US$94,331 [264,778 vs 170,447] ($P < 0.001$)	Not specified
Gavalda[A3]	2006	Spain	Teaching hospital	Mixed	Standardized case review (AEP): mean	+€3,816	NA
Wilson[A4]	2006	UK	University hospital	Surgical	Unknown: mean	+£4,018 [7,718 vs 3,700]	Not specified
Kasatpibal[A5]	2005	Thailand	University hospital	Surgical	Matched comparison (1:1): mean & median	Mean: +TB43,658 [75,544 vs 31,886] ($P < 0.001$) Median: +TB31,140 [50,951 vs 24,568] ($P < 0.001$)	(1) Surgical operation, (2) Diagnosis, (3) ASA
Sheng[A6]	2005	Taiwan	University hospital	Admissions	Matched comparison (1:1): median	+T$117,802 [357,013 vs 126,519] ($P < 0.001$)	(1) Age, (2) Sex, (3) Underlying medical illness, (4) Types of surgery, (5) Diagnosis at admission, (6) Admission date, (7) Types of wards and disease severity
Coskun[A7]	2005	Turkey	University hospital	Surgical	Matched comparison (1:1): mean	<Deep sternal> + US$6,851 <Superficial sternal> + US$3,741	(1) Operation year, (2) Sex, (3) Age
McGarry[A8]	2004	USA	Mixed: 2 hospitals	Surgical	Linear regression (log)	+US$41,117 ($P < 0.001$)	(1) Diabetes*, (2) Renal disease*, (3) ASA score*, (4) Duration of surgery*, (5) Preoperative LOS*, (6) Rheumatological disorder*, (7) Malignancy*, (8) Hospital*
Hollenbeak[A9]	2003	USA	Mixed: 3 hospitals	Surgical (children)	Linear regression (normal)	+US$132,507 ($P < 0.05$)	(1) Race*, (2) Ventilator support*, (3) Age, (4) Packed red blood cells, (5) Cold ischaemia time, (6) HLA-A and -B mismatches, (7) Sex
Engemann[A10]	2003	USA	Mixed: 2 hospitals	Surgical	Matched comparison (1:x): median	<MSSA> + US$23,336 [52,791 vs 29,455] ($P < 0.001$) <MRSA> + US$62,908 [92,363 vs 29,455] ($P < 0.001$)	(1) Type of surgical procedure, (2) Calendar years of surgery
Apisarnthanarak[A11]	2003	USA	Community hospital	Surgical	Matched comparison (1:x): mean	+US$12,477	(1) Surgery, (2) Time period
Whitehouse[A12]	2002	USA	University hospital	Surgical	Matched comparison (1:1): median	+US$27,969 [38,640 vs 10,671] ($P < 0.001$)	(1) Operative procedure, (2) NNIS risk index, (3) Age, (4) Date of surgery within the same year, (5) Surgeon
Hollenbeak[A13]	2002	USA	Community hospital	Surgical	1. Linear regression (normal) 2. Heckman's two-stage method 3. Matched comparison (1:1): mean 4. Unmatched comparison: mean	<Linear regression> + US$20,103 ($P < 0.001$) <Heckman's two-stage> + US$14,211 ($P = 0.0553$) <Matched> + US$19,579 ($P = 0.0001$) <Unmatched> + US$20,012 ($P = 0.0001$)	[Matched comparison] (1) Age, (2) Sex, (3) Diabetes, (4) Renal insufficiency, (5) Length of surgical procedure [Linear regression] (1) Intra-aortic balloon pump*, (2) Diabetes [Heckman's two-stage] (1) Intra-aortic balloon pump*, (2) Diabetes, (3) Hazard function (1. Obesity*, 2. Renal insufficiency*, 3. Connective tissue disease, 4. Antibiotic prophylaxis > 60 min, 5. OR duration >240 min, 6. Re-exploration for bleeding, 7. diabetes)
Jenney[A14]	2001	Australia	Tertiary hospital	Surgical	Matched comparison (1:1): mean	+A$12,419 [20,888 vs 8,468] ($P = 0.001$)	(1) Sex, (2) Age, (3) NNIS risk index scores, (4) No. of principal comorbidities
Hollenbeak[A15]	2001	USA	Mixed: 3 hospitals	Surgical	Linear regression (normal)	+US$131,276 ($P < 0.001$)	(1) Karnofsky scale*, (2) Packed red blood cells*, (3) Cold ischaemia time, (4) HLA-A and -B mismatches, (5) Oedema*, (6) Sex, (7) Race
Plowman[A16]	2001	UK	General hospital	Mixed	Linear regression (gamma)	+£1,594 ($P < 0.05$)	(1) Age, (2) Sex, (3) Diagnosis, (4) No. of comorbidities, (5) Admission specialty, (6) Admission type
Reilly[A17]	2001	UK	Not stated	Surgical	Unmatched comparison (1:x): mean	+£1,743	NA

Hollenbeak[A18]	2000	USA	Community hospital	Surgical	Linear regression (normal)	+US$18,938 ($P < 0.001$)	(1) Intra-aortic balloon pump*, (2) Age*, (3) Smoker, (4) COPD, (5) Renal insufficiency, (6) Obese, (7) Preoperative LOS, (8) Re-exploration for bleeding, (9) Clamp duration, (10) Surgery duration, (11) CHF, (12) Diabetes
Kirkland[A19]	1999	USA	Community hospital	Surgical	Matched comparison (1:1): median	+US$3,089 [7,486 vs 3,842] ($P < 0.05$)	(1) Procedure code, (2) NNIS risk index, (3) Age, (4) Date of surgery, (5) Surgeon
Zoutman[A20]	1998	Canada	University hospital	Surgical	Standardized case review (AEP): mean & median	Mean: +CA$3,937 Median: +CA$1,737	Not specified
VandenBergh[A21]	1996	Netherlands	University hospital	Surgical	Unknown: median	<Postoperative> + US$9,320 [14,560 vs 5,240] ($P < 0.001$)	Not specified
Coello[A22]	1993	UK	General hospital	Surgical	Matched comparison (1:1): mean	+£1,456	(1) Sex, (2) Age, (3) Surgical service, (4) Underlying condition or complication
Vegas[A23]	1993	Spain	Tertiary hospital	Surgical	Matched comparison (1:1): mean	+US$4,449 ($P < 0.01$)	(1) Primary diagnosis, (2) Operative procedure, (3) No intervention if the infected patient was not operated on, (4) Category of surgical procedures classification, (5) Age, (6) Neoplastic or endocrine disease, (7) Elective and emergency procedures, (8) Duration at risk (LOS)
Lynch[A24]	1992	Scotland	Teaching hospital	Surgical	Matched comparison (1:1): mean	+£1,072 [2,680 vs 1,607]	(1) Age, (2) Sex, (3) Type of operation, (4) Surgeon
Boyce[A25]	1990	USA	University hospital	Surgical	Matched comparison (1:1): mean	+US$13,162 [25,957 vs 12,795] ($P = 0.0002$)	(1) DRG, (2) Age, (3) Sex, (4) Urgency of surgery, (5) Type of cardiac surgery, (6) No. of vessels bypassed, (7) Internal mammary artery graft, (8) Type of valve
Mugford[A26]	1989	Several countries	Mixed: several hospitals	Surgical	Unmatched comparison (1:x): mean	+£716 [1,435 vs 719]	NA
Fabry[A27]	1982	France	Teaching hospital	Surgical	Matched comparison (1:x): mean	+FF4,258	(1) Age, (2) Surgical procedure, (3) Level of medical risk (infection at entry, heavier surgery, and associated chronic conditions)
Scheckler[A28]	1980	USA	Teaching hospital	Admissions	Case review: mean	+US$1,329	NA
Bloodstream infection							
Herwaldt[A1]	2006	USA	Mixed: 2 hospitals	Surgical	Linear regression (log)	<UTI & RTI & BSI> <Non-fatal> + US$6,536 [8,435 vs 1,899] ($P < 0.001$) <Fetal> + US$3,249 [5,148 vs 1,899] ($P < 0.001$)	(1) Karnofsky score*, (2) NNIS risk index*, (3) No. of comorbid illnesses*, (4) Obesity*, (5) Preoperative LOS*, (6) Age*, (7) Interaction of type of surgery and the McCabe and Jackson classification*
Vogel[A2]	2006	USA	University hospital	Surgical	Regression	+US$86,500 [247,440 vs 160,940] ($P < 0.001$)	Not specified
Warren[A29]	2006	USA	Suburban hospital	Patients with CVC – ICU	Linear regression (log) & matched comparison by propensity score: median	<CABSI: Regression> + US$11,971 [29,256 vs 17,285] ($P < 0.05$) <CABSI: Matched comparison> US$26,241 [54,242 vs 26,001] (P: unknown)	[Matched comparison] (1) Duration at risk (LOS), (2) CHF, (3) Age, (4) APACHE II, (5) Mechanical ventilation [Regression analysis] (1) APACHE II*, (2) CHF*, (3) Haemodialysis*, (4) Ventilator days*, (5) Age, (6) Sex, (7) Chronic obstructive pulmonary disease, (8) Cancer, (9) Diabetes, (10) Sepsis, (11) Surgical procedure, (12) Renal failure
Laupland[A30]	2006	Canada	Mixed: 3 hospitals	Intensive care	Matched comparison (1:1): median & mean	Median: +CA$12,321 [85,137 vs 67,879] ($P < 0.05$) Mean: +CA$16,867 [103,987 vs 87,120] (P: unknown)	(1) Regional ICU location, (2) Surgical/medical diagnosis, (3) Chronic renal dialysis dependence, (4) Duration at risk (LOS), (5) Age, (6) Sex, (7) APACHE II, (8) Hospital LOS

(continued on next page)

Table II (*continued*)

First author	Year	Country	Type of setting	Type of patients	Analytical methodology	Additional cost to HAI if stated [infected vs uninfected]	Matching variables or regression analysis covariates
Blot[A31]	2005	Belgium	University hospital	Intensive care	Linear regression (normal) & matched comparison (1:2 or 1:1): median	<CABSI: Regression> + €16,814 ($P<0.001$) <CABSI: Matched comparison> + €13,585 [51,405 vs 37,820] ($P<0.001$)	[Matched comparison] (1) APACHE II, (2) Diagnostic category, (3) Duration at risk (ICU LOS), (4) CVC [Regression analysis] (1) LOS*, (2) Age, (3) APACHE II*, (4) Surgical or medical admission diagnosis, (5) Need for mechanical ventilation, (6) Need for renal replacement therapy*, (7) Need for vasopressors, (8) Need for inotropic treatments
Sheng[A6]	2005	Taiwan	University hospital	Admissions	Matched comparison (1:1): median	+T$101,536 [323,479 vs 199,365] ($P<0.001$)	(1) Age, (2) Sex, (3) Underlying medical illness, (4) Types of surgery, (5) Diagnosis at admission, (6) Admission date, (7) Types of wards and disease severity
Elward[A32]	2005	USA	Tertiary hospital	Admissions – PICU	Linear regression (log)	+US$39,219 [45,615 vs 6,396] ($P<0.001$)	(1) PRISM III*, (2) Ventilator days*, (3) CHF*, (4) Transplant*, (5) Underlying lung disease*, (6) Age
Payne[A33]	2004	USA	Mixed: 17 hospitals	Inborn and outborn infants	Generalised estimating equations (log)	+US$5,875 [128,887 vs 123,012] ($P=0.141$) ~ +US$12,480 [94,060 vs 81,580] ($P=0.009$)	(1) Birth weight, (2) Birth location, (3) Sex, (4) Race, (5) Prenatal care, (6) Antenatal steroids, (7) Multiple birth, (8) Apgar score, (9) Respiratory distress syndrome, (10) CLD, (11) Necrotizing enterocolitis (NEC), (12) NEC surgery, (13) Other surgery, (14) Mechanical ventilation
Wisplinghoff[A34]	2003	Germany	University hospital	Patients with a haematological malignancy	Matched comparison (1:1): mean	+US$3,170	(1) Date of admission, (2) Duration at risk (LOS), (3) Age, (4) Sex, (5) Type and stage of underlying malignancy, (6) Radiation therapy, (7) Duration and severity of neutropenia prior to BSI
Rosenthal[A35]	2003	Argentina	Mixed: 3 hospitals	Patients with CVC – ICU	Matched comparison (1:1): mean	<CVC-associated BSI> + US$4,888 [7,972 vs 3,083]	(1) Hospital, (2) ICU type, (3) Year of admission, (4) LOS, (5) Sex, (6) Age, (7) ASIS
Orsi[A36]	2002	Italy	University hospital	Admissions	Matched comparison (1:2): mean	+€16,356	(1) Duration at risk (LOS), (2) Primary diagnosis, (3) Ward of admission, (4) CVC, (5) Age, (6) Sex
Liu[A37]	2002	Taiwan	Tertiary hospital	Surgical	Matched comparison (1:2): median	+T$66,302 [131,584 vs 65,282] ($P<0.001$)	(1) Primary diagnosis at admission, (2) Date of admission, (3) Age, (4) Duration at risk (LOS), (5) Sex, (6) No. of discharge diagnoses
Plowman[A16]	2001	UK	General hospital	Mixed	Linear regression (gamma)	+£6,209 ($P<0.05$)	(1) Age, (2) Sex, (3) Diagnosis, (4) No. of comorbidities, (5) Admission specialty, (6) Admission type
Dimick[A38]	2001	USA	Tertiary hospital	Surgical – ICU	Linear regression (log)	<CABSI> + US$56,167 [102,973 vs 46,806] ($P=0.001$)	(1) APACHE III*, (2) Age*, (3) Sex, (4) Univariate factors of significance
Slonim[A39]	2001	USA	Children's hospital	Admissions – PICU	Matched comparison (1:1): mean	+US$58,344 [99,177 vs 45,038] ($P<0.001$)	(1) Age, (2) PRISM III, (3) Primary diagnosis, (4) Admission date
Rello[A40]	2000	Spain	Tertiary hospital	Admissions – ICU	Matched comparison (1:1): mean	+€3,124 [10,052 vs 6,914]	(1) Level of severity, (2) Underlying disease, (3) Age, (4) Duration at risk (LOS)
Digiovine[A41]	1999	USA	University hospital	Medical – ICU	Matched comparison (1:1): median	+US$15,965 [60,650 vs 36,899] ($P<0.001$)	(1) Predicted mortality, (2) Sex, (3) Age, (4) Race, (5) LOS, (6) Admission during the study period, (7) Admitting diagnosis, (8) Chronic health
Abramson[A42]	1999	USA	University hospital	Admissions	Matched comparison (1:1): median	<MSSA> + US$9,661 ($P<0.01$) <MRSA> + US$27,083 ($P<0.01$)	(1) Primary diagnosis, (2) No. of secondary diagnosis, (3) Age, (4) Sex, (5) Hospital ward
Pittet[A43]	1994	USA	University hospital	Surgical intensive care	Matched comparison (1:1): mean	+US$33,268 [91,241 vs 57,973] ($P<0.01$)	(1) Primary diagnosis for admission, (2) Age, (3) Sex, (4) Duration at risk (LOS), (5) No. of discharge diagnoses
Pneumonia/VAP							
Vogel[A2]	2006	USA	University hospital	Surgical	Regression	<VAP> + US$89,187 [232,080 vs 142,893] ($P<0.001$)	Not specified
Gavalda[A3]	2006	Spain	Teaching hospital	Mixed	Standardised case review (AEP): mean	<Pneumonia & RTI> +€358	NA
Thompson[A44]	2006	USA	Mixed: 994 hospitals	Surgical	Linear regression (normal)	<Pneumonia> + US$28,161 ($P<0.05$)	(1) Surgical procedure, (2) Age, (3) Sex, (4) Race
Cocanour[A45]	2005	USA	Tertiary hospital	Ventilated patients – ICU	Matched comparison (1:1): mean	<VAP> + US$57,158 [82,195 vs 25,037] ($P<0.05$)	(1) Age, (2) Injury severity score
Rosenthal[A46]	2005	Argentina	Mixed: 3 hospitals	Intensive care	Matched comparison (1:1): mean	<Pneumonia> + US$2,253 [4,946 vs 2,694] ($P<0.001$)	(1) Hospital, (2) ICU type, (3) Admission year, (4) LOS, (5) Sex, (6) Age, (7) ASIS at admission
Hugonnet[A47]	2004	Switzerland	University hospital	Ventilated patients – ICU	Matched comparison (1:1): mean	<VAP> + US$10,450 [24,727 vs 17,438] ($P<0.05$)	(1) No. of discharge diagnoses, (2) Duration at risk (ventilation), (3) Age, (4) Diagnosis at admission, (5) Sex, (6) Study period

van Nieuwenhoven[A48]	2004	Netherlands	University hospital	Intensive care	Unknown: mean	<VAP> + US$15,623 [29,360 vs 13,737]	Not specified
Warren[A49]	2003	USA	Tertiary hospital	Ventilated patients – ICU	Linear regression (log)	<VAP> + US$11,897 [27,033 vs 15,136] ($P < 0.05$)	(1) CHF*, (2) Corticosteroid use*, (3) APACHE II*, (4) Tracheostomy*, (5) No. of CVC*, (6) Bacteraemia*, (7) H2-histamine antagonist use*
Dietrich[A50]	2002	Germany	University hospital	Admissions	Matched comparison (1:1): mean	<Pneumonia> + DM29,610	(1) Severity of disease, (2) Age, (3) Primary ward, (4) Status of ventilation, (5) Immunosuppression, (6) Sex, (7) Duration at risk (LOS)
Merchant[A51]	1998	India	Teaching hospital	Admissions	Unmatched comparison (1:x): mean	<Pneumonia> + US$496	None
Kappstein[A52]	1992	Germany	University hospital	Ventilated patients – ICU	Matched comparison (1:x): mean	<VAP> + DM14,253 (US$8,800)	(1) Underlying condition, (2) Age, (3) Duration at risk (ventilation), (4) Time that control patients were subjected to the risk of acquiring nosocomial infections
Scheckler[A28]	1980	USA	Teaching hospital	Admissions	Case review: mean	<Pneumonia> + US$878	NA
Urinary tract infection							
Herwaldt[A1]	2006	USA	Mixed: 2 hospitals	Surgical	Linear regression (log)	<UTI & RTI & BSI> <Non-fatal> + US$6,536 [8,435 vs 1,899] ($P < 0.001$) <Fetal> + US$3,249 [5,148 vs 1,899] ($P < 0.001$)	(1) Karnofsky score*, (2) NNIS risk index*, (3) No. of comorbid illnesses*, (4) Obesity*, (5) Preoperative LOS*, (6) Age* (7) Interaction of type of surgery and the McCabe and Jackson classification*
Gavalda[A3]	2006	Spain	Teaching hospital	Mixed	Standardised case review (AEP): mean	+€1,792	NA
Sheng[A6]	2005	Taiwan	University hospital	Admissions	Matched comparison (1:1): median	+T$114,662 [354,608 vs 159,953] ($P < 0.001$)	(1) Age, (2) Sex, (3) Underlying medical illness, (4) Types of surgery, (5) Diagnosis at admission, (6) Admission date, (7) Types of wards and disease severity
Lai[A53]	2002	USA	University hospital	Admissions	Case review: mean & median	<CAUTI>Mean: +US$1,214 <CAUTI>Median: +US$614	NA
Tambyah[A54]	2002	USA	University hospital	Admissions	Case review: mean	<CAUTI> + US$589	NA
Plowman[A16]	2001	UK	General hospital	Mixed	Linear regression (gamma)	+£1,122 ($P < 0.05$)	(1) Age, (2) Sex, (3) Diagnosis, (4) No. of comorbidities, (5) Admission specialty, (6) Admission type
Coello[A22]	1993	UK	General hospital	Surgical	Matched comparison (1:1): mean	+£467	(1) Sex, (2) Age, (3) Surgical service, (4) Underlying condition or complication
Fabry[A27]	1982	France	Teaching hospital	Surgical	Matched comparison (1:x): mean	+FF2,726	(1) Age, (2) Surgical procedure, (3) Level of medical risk (infection at entry, heavier surgery, and associated chronic conditions)
Givens[A55]	1980	USA	Teaching hospital	Surgical	Matched comparison (1:x): mean	<CAUTI> + US$558	NA
Scheckler[A28]	1980	USA	Teaching hospital	Admissions	Case review: mean	+US$146	NA
Respiratory tract infection							
Herwaldt[A1]	2006	USA	Mixed: 2 hospitals	Surgical	Linear regression (log)	<UTI & RTI & BSI> <Non-fatal> + US$6,536 [8,435 vs 1,899] ($P < 0.001$) <Fetal> + US$3,249 [5,148 vs 1,899] ($P < 0.001$)	(1) Karnofsky score*, (2) NNIS risk index*, (3) No. of comorbid illnesses*, (4) Obesity*, (5) Preoperative LOS*, (6) Age*, (7) Interaction of type of surgery and the McCabe and Jackson classification*
Gavalda[A3]	2006	Spain	Teaching hospital	Mixed	Standardised case review (AEP): mean	<Pneumonia & RTI> +€358	NA
Sheng[A6]	2005	Taiwan	University hospital	Admissions	Matched comparison (1:1): median	+T$117,100 [368,435 vs 180,059] ($P < 0.001$)	(1) Age, (2) Sex, (3) Underlying medical illness, (4) Types of surgery, (5) Diagnosis at admission, (6) Admission date, (7) Types of wards and disease severity
Plowman[A16]	2001	UK	General hospital	Mixed	Linear regression (gamma)	+£2,080 ($P < 0.05$)	(1) Age, (2) Sex, (3) Diagnosis, (4) No. of comorbidities, (5) Admission specialty, (6) Admission type
Fabry[A27]	1982	France	Teaching hospital	Surgical	Matched comparison (1:x): mean	+FF2,060	(1) Age, (2) Surgical procedure, (3) Level of medical risk (infection at entry, heavier surgery, and associated chronic conditions)

(*continued on next page*)

Table II (*continued*)

First author	Year	Country	Type of setting	Type of patients	Analytical methodology	Additional cost to HAI if stated [infected vs uninfected]	Matching variables or regression analysis covariates
General							
Gavalda[A3]	2006	Spain	Teaching hospital	Mixed	Standardised case review (AEP): mean	+€2,730	NA
Esatoglu[A56]	2006	Turkey	Clinics	Not stated	Matched comparison (1:1): mean	+US$2,027 [3,907 vs 1,524] ($P<0.001$)	(1) Age, (2) Sex, (3) Clinic, (4) Primary diagnosis
Sanchez-Velazquez[A57]	2006	Mexico	National hospital	Intensive care	Matched comparison (1:2): median	+US$12,155	(1) Duration at risk (LOS), (2) Age, (3) APACHE II
Lazarus[A58]	2005	USA	Teaching hospital	Trauma admissions	Linear regression (log)	2.04 times	(1) Age, (2) Sex, (3) Injury Severity Score*
Noskin[A59]	2005	USA	Mixed: 986–994 hospitals	Admissions	Linear regression (log) & matched comparison (1:1): mean	Regression: +US$32,856 ($P<0.001$) Matched comparison: +US$36,119 ($P<0.001$)	[Matched comparison] (1) Hospital, (2) Age, (3) Sex, (4) Race, and (5) Comorbidity [Regression analysis] (1) Hospital (2) DRG, (3) Age, (4) Sex, (5) Race, (6) Payer, (7) Comorbidities
Sheng[A6]	2005	Taiwan	University hospital	Admissions	Matched comparison (1:1): median	+T$127,354 [363,425 vs 165,965] ($P<0.001$)	(1) Age, (2) Sex, (3) Underlying medical illness, (4) Types of surgery, (5) Diagnosis at admission, (6) Admission date, (7) Types of wards and disease severity
Chen[A60]	2005	Taiwan	Tertiary hospital	Intensive care	Linear regression (log)	+US$3,306 ($P<0.05$)	(1) LOS in ICU*, (2) Age, (3) Sex, (4) Service (medical or surgical), (5) APACHE II, (6) Albumin level*, (7) Pulmonary artery catheter*, (8) Mechanical ventilator*, (9) Urinary catheter*
Upton[A61]	2005	NZ	Specialised hospital	Surgical	Matched comparison (1:1): mean	+NZ$45,577 [76,104 vs 30,527] ($P<0.001$)	(1) Sex, (2) Age, (3) Surgical procedure, (4) Month of procedure, (5) Diabetes mellitus
Sheng[A62]	2005	Taiwan	Mixed: 3 hospitals	Admissions	Matched comparison (1:1): mean	<Hospital 1> + US$5,335 [13,426 vs 8,092] ($P<0.001$) <Hospital 2> + US$5,058 [8,014 vs 2,955] ($P<0.001$)	(1) Age, (2) Sex, (3) Underlying medical illness and surgical operation, (4) Diagnosis at admission, (5) Admission date, (6) Ward, (7) Disease severity
Pirson[A63]	2005	Belgium	General hospital	Admissions	Matched comparison (1:all): mean	+€12,853 [18,288 vs 5,440] ($P<0.001$)	(1) DRG
Watters[A64]	2004	Ireland	Tertiary hospital	Surgical	Matched comparison (1:*x*): mean	+£8,955 [11,795 vs 2,840]	(1) Procedure
Piednoir[A65]	2003	France	University hospital	Child admissions	Matched comparison (1:1): mean	+€1,930 [3,097 vs 1,167]	(1) Primary diagnosis for admission, (2) Admission to the infant ward during the same period, (3) Age, (4) Sex, (5) Duration at risk (LOS), (6) No. of discharge diagnoses
Roberts[A66]	2003	USA	Teaching hospital	Admissions	Linear regression (normal)	+US$15,275 ($P<0.001$)	(1) APACHE III*, (2) ICU care*
Song[A67]	2003	USA	University hospital	Admissions	Matched comparison (1:1): median	+US$81,208	(1) Age, (2) Year of admission, (3) Duration at risk (LOS), (4) Principal diagnosis at admission, (5) Primary procedure, (6) All patient refined – DRG
Zhan[A68]	2003	USA	Mixed: 994 hospitals	Not stated	Matched comparison (1:*x*): mean & linear regression (mixed-effect model)	<Postoperative sepsis> Mean: +US$57,727 ($P<0.001$) <Selected infection due to medical care> Mean: +US$38,656 ($P<0.001$)	[Matched comparison] (1) Hospitals, (2) DRG, (3) Sex, (4) Race, 5) Age, (6) Comorbidity [Regression analysis] Not specified
Oncul[A69]	2002	Turkey	Teaching hospital	Burned admissions	Matched comparison (1:*x*): mean	+US$502 [579 vs 77] ($P=0.001$)	(1) Age, (2) Sex, (3) Medical and surgical setting, (4) Total burn surface area
Onen[A70]	2002	Turkey	Surgery clinic	Child admissions	Matched comparison (1:1): mean	+US$452 [963 vs 511] ($P<0.001$)	(1) Age, (2) Sex, (3) Primary illness
Mahieu[A71]	2001	Belgium	University hospital	Neonates in NICU	Matched comparison (1:1): mean	+€11,750 [24,722 vs 12,972] ($P<0.001$)	(1) Gestational age, (2) Patent ductus arteriosus, (3) Surgery, (4) Ventilator support
Plowman[A16]	2001	UK	General hospital	Mixed	Linear regression (gamma)	+£2,917 ($P<0.05$)	(1) Age, (2) Sex, (3) Diagnosis, (4) No. comorbidities, (5) Admission specialty, (6) Admission type
Khan[A72]	2001	Turkey	Tertiary hospital	Admissions	Matched comparison (1:1): mean	+US$442 [2,419 vs 1,977] (*P*-value: NS)	(1) Age, (2) Sex, (3) ICU location, (4) Principal diagnosis

Dominguez[A73]	2001	USA	Tertiary children's hospital	Admissions – PICU	Linear regression (normal) & matched comparison (1:1): mean	Regression: +US$50,362 ($P$ < 0.001) Matched comparison: +US$32,040 [63,971 vs 32,291]	[Matched comparison] (1) Diagnosis category, (2) Duration at risk (LOS), (3) PRISM [Regression analysis] (1) Age, (2) Severity of illness, (3) Organ system failure, (4) Diagnosis, (5) Chronic disease, (6) Ventilator use, (7) Vascular catheter use, (8) Referral source, (9) Sex, (10) Complication categories
Macartney[A74]	2000	USA	Children's hospital	Child admissions	Matched comparison (1:1): mean	+US$45,335	(1) RSV season, (2) Principal discharge diagnosis, (3) No. of secondary diagnoses, (4) Approximate age
Chaix[A75]	1999	France	University hospital	Medical – ICU	Matched comparison (1:1): median & mean	Mean: +US$9,275 [30,225 vs 20,950] (P = 0.004) Median: +US$5,885 [24,525 vs 17,105] (P = 0.003)	(1) Age, (2) McCabe and Jackson classification, (3) Simplified acute physiology score, (4) No. of organ system failures at ICU admission, (5) Duration at risk (ICU LOS)
Orrett[A76]	1998	Trinidad and Tobago	Tertiary hospital	Admissions	Matched comparison (1:1): mean	+US$1,910	(1) Age, (2) Sex, (3) Operative procedures, (4) Services, (5) Discharge diagnoses
Yalcin[A77]	1997	Turkey	University hospital	Not stated	Matched comparison (1:1): mean	+US$1,582 [2,280 vs 698] ($P$ < 0.001)	(1) Age, (2) Sex, (3) Medical and surgical setting, (4) Underlying disease
Leroyer[A78]	1997	France	Paediatric hospital	Neonates	Matched comparison (1:1): mean	+FF52,192 [502,837 vs 450,645] (P = 0.03)	(1) Birthweight, (2) Gestational age, (3) Admission route, (4) Previous stay in an ICU, (5) CVC
Wilcox[A79]	1996	UK	Teaching hospital	Admissions	Matched comparison (1:2): mean	+£4,107	(1) Ward, (2) Date of admission, (3) Sex
Gray[A80]	1995	USA	Mixed: **2 hospitals	Admissions – NICU	Linear regression (normal)	+US$25,090	(1) Birth weight, (2) Score for Neonatal Acute Physiology, (3) Retrotransport
Vegas[A23]	1993	Spain	Tertiary hospital	Surgical	Matched comparison (1:1): mean	+US$2,850 ($P$ < 0.01)	(1) Primary diagnosis, (2) Operative procedure, (3) No intervention if the infected patient was not operated on, (4) Category of surgical procedures classification, (5) Age, (6) Presence of neoplastic or endocrine disease, (7) Elective and emergency procedures, (8) Duration at risk (LOS)
Shulkin[A81]	1993	USA	University hospital	Surgical	Linear regression (normal)	+US$12,542 ($P$ < 0.01)	Not specified
Li[A82]	1990	China	Specialised hospital	Surgical	Matched comparison (1:1): mean	+£290 [717 vs 427] (P < 0.001)	(1) Sex, (2) Underlying disease, (3) Surgical procedure, (4) Age, (5) Preoperative stay, (6) Duration at risk (LOS)
Taylor[A83]	1990	USA	Teaching hospital	Surgical	Linear regression (normal)	+US$41,559 ($P$ < 0.001)	(1) Complication*, (2) Respiratory failure*, (3) Left ventricular failure requiring intra-aortic balloon counterpulsation*, (4) Death*
Wakefield[A84]	1988	USA	University hospital	Admissions	Standardized case review (AEP): mean & median	Mean: +US$3,198 Median: +US$1,058	NA
Nelson[A85]	1986	USA	Not stated	Surgical	Matched comparison (1:1): mean	+US$6,605 [14,443 vs 7,838]	(1) Type of operation, (2) Age, (3) Sex, (4) Date of operation, (5) Non-invasive procedure
Girard[A86]	1983	France	University hospital	Neonates hospitalized	Matched comparison (1:1): mean	+FF6,038 [25,170 vs 19,132] (P < 0.001)	(1) Hospital unit, (2) Birth weight, (3) Duration of pregnancy, (4) Diagnosis
DeClercq[A87]	1983	Belgium	Not stated	Admissions – ICU	Matched comparison (1:1): mean	+BF1,639 [3,442 vs 1,803]	(1) Sex, (2) Age, (3) Operative procedure, (4) Diagnosis
Haley[A88]	1981	USA	Mixed: 3 hospitals	Admissions	Standardized case review: mean	<Hospital 1> + US$680 <Hospital 2> + US$721 <Hospital 3> + US$671	NA
Scheckler[A28]	1980	USA	Teaching hospital	Admissions	Case review: mean	+US$636	NA
Haley[A89]	1980	USA	General hospital	Admissions	Matched comparison (1:1): mean	+US$1,018 [1,733 vs 714]	(1) First discharge diagnosis, (2) Main procedure, (3) Second operative procedure, (4) Hospital service, (5) Sex, (6) Age

TB, Thai Baht; T$, New Taiwan dollar; FF, French franc; DM, Deutsche Mark; BF, Belgian franc.
HAI, hospital-acquired infection; SSI, surgical site infection; NNIS, National Nosocomial Infection Surveillance system; LOS, length of stay; AEP, appropriateness evaluation protocol; NA, not applicable; ASA, American Society of Anesthesiologists; MSSA/MRSA, meticillin-susceptible/resistant *Staphylococcus aureus*; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; DRG, diagnosis-related group; UTI, urinary tract infection; RTI, respiratory tract infection; BSI, bloodstream infection; CVC, central venous catheter; ICU, intensive care unit; CABSI, catheter-associated bloodstream infection; APACHE II, Acute Physiological Assessment and Chronic Health Evaluation; PRISM, Paediatric risk of mortality score; ASIS, American Spinal Injury Association; VAP, ventilator-associated pneumonia; NICU, neonatal ICU; PICU, paediatric ICU; RSV, respiratory syncytial virus.
*Significant variables (if stated).

Table III
Changes in analytical methodologies for estimating additional healthcare cost of hospital-acquired infection (HAI) ($N = 89$)

	Year of publication			*P*-value
	1980–1989	1990–1999	2000–2006	
	($N = 10$)	($N = 21$)	($N = 58$)	
Analytic approaches for estimating cost of HAI				0.033
Case review	3 (30%)	1 (4.8%)	3 (5.2%)	
Matched comparison	6 (60%)	15 (71.4%)	32 (55.2%)	
Regression analysis	0	3 (14.3%)	20 (34.5%)	
Unknown	0	1 (4.8%)	2 (3.4%)	
Unmatched comparison	1 (10%)	1 (4.8%)	1 (1.7%)	
Adjustment by length of stay				0.058
Adjusted by LOS	0 (0%)	6 (28.6%)	21 (36.2%)	
Not adjusted	10 (100%)	15 (71.4%)	37 (63.8%)	

LOS, length of stay.
Statistical analysis conducted using Fisher's exact test.

that of regression analysis.[18] Due to this high degree of variation in the published literature, the degree of influence of methodological approach on estimates remains unclear.

In recent years, there has been an increase in analyses that use models that make it possible to adjust for endogenous variables and confounding factors in linear regression models.[8,10,14] In a comparison of matched comparison analysis, linear regression analysis and Heckman's two-stage model, it was found that whereas the difference was not statistically significant, Heckman's two-stage model produced lower COHAI estimates than both of the other methods.[14] The lack of statistical significance supported the conclusion that matching and linear regression analyses could be used as valid methodologies. Graves has stated with regard to instrumental variable models that 'the conventional wisdom has been that the endogeneity between length of stay and lower respiratory tract infection should bias the traditional estimates upwards, not downwards'.[19]

A major issue in the matched comparisons approach is the trade-off required in the quality of matching: if matching is conducted with the utmost stringency, the exclusion of unused cases and controls can lead to selection bias. However, reducing the stringency for matching criteria may increase the number of possible matched references, but also result in insufficient accounting for detailed patient characteristics such as disease severity. The use of stepwise fashion matching and a scoring system has been recommended to increase the quality of matching, but this technique was used by only seven studies in our analysis.[20] Furthermore, while patient factors such as age and sex are used in virtually all of the matching comparison analyses, patient disease severity factors were used in less than half of these studies.

In order to evaluate the possible effects of bias, the proportion of successful matches should be reported as part of the results in all studies, using a ratio of the final number of infected cases used in analysis to the number of all original infected cases. Of the 53 studies that used matched comparisons, only 28 (52.8%) had reported the proportion of successful matches. Given its simplicity, we advocate the reporting of this indicator in all matched comparison analyses. Furthermore, the use of propensity scores as summaries of covariate information has been recommended, and analysts should endeavor to use this method if employing the matched comparisons approach.[18,21]

The shifts in analytic methodologies for COHAI estimates over the years have shown that analysts have started to lean towards regression analysis. More than half of the studies published post 2000 had used matched comparisons, and there was only a marginally significant difference between studies that had accounted for LOS and those that did not. LOS is a highly important factor to include in analysis, even in the matched comparisons method. In the 89 studies in our sample, only 27 (30.3%) had included LOS as a factor in COHAI estimation. This highlights the fact that the inclusion of time at risk variables has yet to become sufficiently adopted among analysts.

Based on an analysis of the citation rates of the studies in our sample using the ISI Web of Science® database, we found that studies using the more stringent methodology of regression analysis were not cited with a significantly higher frequency than studies that had less stringent methodologies (data not shown). This indicates the possibility that COHAI estimates with biases have been used in downstream analyses, and may even have influenced decision-making by supporting inaccurate business cases.

The Society for Healthcare Epidemiology of America (SHEA) has produced guidelines that permit the extrapolation of estimates calculated from the published literature; we feel that this is a risky stance, as COHAI estimates have a high degree of uniqueness based on the particular conditions in which they were calculated.[22] There is a large degree of variation in costing scopes, unit costs per item, clinical practice variations for HAI treatment, and costing methodologies (actual costs vs ratio of costs-to-charges (RCC) vs charges), and these factors have a direct and substantial influence on the resulting estimates (H. Fukuda, J. Lee, Y. Imanaka, unpublished data).

A limitation was that the dearth of detailed information concerning methodological approach might be due to space limitations set by the various journals. However, as these data are essential for editors, reviewers and readers to evaluate the quality of the methods used, the authors feel this information should be reported in all COHAI estimate studies.

Greater insight is needed on the characteristics and limitations of different COHAI estimation methodologies, as this would allow analysts to identify and select more accurate methods, as well as employ the correct tools for avoiding biases. More transparency in the reporting of methodologies and limitations would provide readers with the necessary information to evaluate the appropriateness of extrapolating published COHAI estimates in their own research. Accurate methodologies would produce COHAI estimates of better quality, and provide better support for the decision-making process in infection control.

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None declared.

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Appendix. Studies used in systematic review

A1 Herwaldt LA, Cullen JJ, Scholz D, *et al.* A prospective study of outcomes, healthcare resource utilization, and costs associated with postoperative nosocomial infections. *Infect Control Hosp Epidemiol* 2006;**27**:1291–1298.

A2 Vogel TR, Diaz JJ, Miller RS, *et al.* The open abdomen in trauma. *Surg Infect (Larchmt)* 2006;**7**:433–441.

A3 Gavalda L, Masuet C, Beltran J, *et al.* Comparative cost of selective screening to prevent transmission of methicillin-resistant *Staphylococcus aureus* (MRSA), compared with the attributable costs of MRSA infection. *Infect Control Hosp Epidemiol* 2006;**27**:1264–1266.

A4 Wilson AP, Hodgson B, Liu M, *et al.* Reduction in wound infection rates by wound surveillance with postdischarge follow-up and feedback. *Br J Surg* 2006;**93**:630–638.

A5 Kasatpibal N, Thongpiyapoom S, Narong MN, Suwalak N, Jamulitrat S. Extra charge and extra length of postoperative stay