Asia-Pacific Economic Cooperation

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A Review of the Literature

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November 2013

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Cost of Healthcare-Associated Infections (HAIs) in APEC Economies

A Review of the Literature

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Executive Summary

The APEC Health Working Group and Life Sciences Innovation Forum (LSIF) have been leading efforts in the region to advance understanding of the economic and public health impact of healthcare-associated infections (HAIs). Enhancing awareness of the prevalence and costs of HAIs is a critical element for the development and analysis of policies that aim to reduce waste in healthcare systems and improve the quality and efficiency of care. This is particularly important at a time when many APEC economies are actively expanding and investing in their healthcare systems and are seeking to ensure the best utilization of scarce resources. However, efforts to do so can be impeded by a lack of quality data on the prevalence and costs of HAIs.

In many developed economies within APEC a robust body of published literature demonstrates the costs of HAIs and provides a basis for policies and protocols to reduce their incidence and improve the quality and efficiency of care. However, in many developing economies there is a deficit of data. A deficit of data in itself is not an indication that HAIs are not imposing significant adverse costs to an economy's healthcare systems. Rather, a deficit of data could present a costly missed opportunity for economies to integrate sound policies to promote efficiency at a critical time when many are rapidly expanding their health systems to meet the needs of growing populations and economic activity.

This reports aims to add to the dialogue on HAIs by assessing the available studies on the costs and length of hospital stay attributable to HAIs in APEC economies. The analysis is conducted in three parts: (1) a search for existing data; (2) an evaluation of the data quality and completeness; and (3) a discussion on future research to inform policy.

The search for existing data resulted in a variable quantity and quality of data across the studied APEC economies. This is not surprising given the current state of infrastructure and investment in infection prevention and control within healthcare settings. The analysis then turned to an attempt to develop a model based on existing data. In order to accomplish this, four parameters are identified: (1) information on the incidence rates of HAIs is needed; (2) information is required to describe the extra time a patient must receive care in a healthcare setting due to an incidence of an HAI (referred to as the length of stay per case); (3) the treatment costs need to be understood; and (4) the economic value of bed days lost to HAIs needs to be understood.

The results of the model indicate costs attributable to HAIs, but with a high degree of variability and uncertainty. This reflects the quality of available data and is not surprising. Because of the uncertainties, it is difficult to draw conclusions and policy recommendations directly from the model. However, the results, coupled with the strong body of evidence of the costs of HAIs in developed economies, indicate that further study of the economic impact

of HAIs is warranted in the developing economies within APEC to ensure that inefficiencies in healthcare delivery are appropriately identified, measured, and reduced.

This analysis leads to support for recommendations endorsed by APEC for member economies to establish collection of surveillance data on HAIs in order to better quantify the problem and identify cost-effective solutions to improve the efficiency and quality of healthcare delivery.

1. Background

The APEC Health Working Group and Life Sciences Innovation Forum (LSIF) have been exploring the public health and economic impact of healthcare-associated infections (HAIs) in member economies. In July 2012 in Manila, Republic of the Philippines, APEC hosted the first of its kind "APEC High-Level Workshop on Reducing the Economic Burden of Healthcare-Associated Infections," which produced a series of recommendations at both the economy and institutional levels. Subsequently, in July 2013 in Medan, Indonesia, APEC hosted an "APEC HWG-LSIF Policy Dialogue on Building Capacity to Address HAIs," during which a toolkit for policymakers to consider as they evaluate and develop policies to address HAIs was submitted for APEC consideration, along with proposed "APEC Medan Principles for Public-Private Partnerships in Infection Prevention & Control." In order to supplement and support the ongoing work of APEC in HAIs, the APEC Technical Assistance and Training Facility requested a review of literature on the economic impact of HAIs in developing APEC economies.

Having a robust awareness of the prevalence of HAIs provides a foundation for the development and analysis of policies that aim to reduce waste in healthcare systems and improve the quality and efficiency of care. While policies at the economy level and clinical interventions at the institutional level need to be evaluated for their effectiveness, efforts to do so can be impeded by a lack of quality surveillance data on HAIs. In many developed economies within APEC, data on the prevalence of healthcare-associated infections (HAIs) and the costs that they incur on healthcare systems are well-documented. However, data on the economic impact of HAIs in many developing economies within APEC are not as well documented. A deficit of data in itself is no indication that HAIs are not imposing significant adverse costs to an economy's healthcare systems. Rather, a deficit of data could present a costly missed opportunity for economies to integrate sound policies to promote efficiency at a critical time when many are rapidly expanding their health systems to meet the needs of growing populations and economic activity.

Measuring and valuing the costs of healthcare associated infection (HAI) is a difficult yet important consideration for any decision to strengthen public policies and protocols and increase investment in infection control programs. They represent the potential savings that will offset the positive costs of an essential infection control program, such as increasing hand hygiene compliance. The health benefits of decreased morbidity and mortality from reduced infections must also be quantified [1].

The costs of HAIs are likely to be diffused throughout healthcare services, and there are private and difficult-to-value costs like pain and suffering for patients and inconvenience and stress for their families. In the US around 99,000 deaths were attributed to HAIs in 2002, and the annual HAI-associated economic costs were estimated at US$6.5 billion [2]. In European

developed economies, HAIs cause 16 million extra days of hospital stay, direct medical costs of €7 billion a year, and an additional 110,000 deaths [3,4].

The largest component of total costs will arise from prolongation of stay in acute care hospitals due to HAIs [5]. The opportunity cost of numbers of bed days lost to HAIs is a key statistic to be included in any economic argument for making investments in prevention programs. At least three tasks need to be achieved to measure the cost of lost bed days: The frequencies of infections need to be counted reliably; the extra days stay per average case need to be quantified; and the economic value of the bed days needs to be found. There are challenges at every stage with definitions, accurate diagnoses, and the routine surveillance of HAIs [6,7]. When attributing extra stay to an average case of HAI, the large biases arising from time dependency need to be controlled [8-10]. When valuing bed days, economic rather than accounting costs need to be used [11]. The real value of bed days depends on the need to access hospital services among the general population and the willingness of decision makers to pay for these.

HAIs introduce inefficiencies into healthcare systems and health risks for patients and are a challenge for those who manage healthcare services in all economies. In developing economies, risks may be higher. However, these economies are also constrained in available funding for infection control, and therefore there is a strong need to show how costs can be reduced and health benefits increased by investing in infection control. Knowledge of the economic impact of HAIs in middle-income settings is low because data on HAIs are incomplete and almost nonexistent in developing economies.

At present there is no systematic review undertaken to assess the economic impact of HAIs in developing economies. While HAI surveillance systems are in place at the national or sub-national level in many developed economies, less than 16 percent of developing economies reported a functioning national surveillance system, according to a survey conducted by the WHO [4,12].

This report aims to systematically assess available studies on the costs and length of hospital stay (LOS) attributable to HAIs in APEC economies. Because we currently have good knowledge of the costs of HAIs in North America [2] and Australia [13] these economies are excluded, and the work concentrates on the remaining economies. This report has four sections:

- Searching for data
- Data quality and completeness
- Future research to inform policy
- Summary

2. Searching for Data

We undertook a systematic literature search to identify studies on the costs and LOS attributable to healthcare associated infection in APEC economies. We excluded North America and Australia, for which separate searches have been conducted. We searched CINAHL, PubMed, and EconLit using MeSH and non-MeSH terms including "cross infection," "healthcare acquired infection," "hospital acquired infection" and "nosocomial infection," combined with "healthcare costs," "hospital costs, " "treatment costs," "economics," and "length of hospital stay." In addition, we searched Google and Google Scholar for relevant studies. Reference lists of retrieved cost studies and systematic reviews were examined to locate relevant studies for inclusion. We limited the above searches to studies published in English between January 1, 2000, and April 30, 2013. The detailed search strategies are in Appendix A.

SELECTION CRITERIA

Studies were included if their measures of outcomes included costs and LOS attributable to HAIs in APEC economies (excluding Australia, Canada, and the United States). Studies were excluded if they reported only incidence and prevalence of HAIs, or costs or LOS unrelated to HAIs. Studies on HAI-associated costs and LOS in non-APEC economies were excluded. The detailed selection process is in Figure 2-1.

DATA EXTRACTION

Two independent reviewers conducted the selection of studies for inclusion and data extraction. Discrepancies were resolved by consensus. The extracted data included: authors, year of publication, economy and study setting, study design, study period, study population, site and type of HAI, incidence, prevalence, study method, HAI-associated LOS and costs, and currency of denomination. The data extracted from the selected studies are shown in Appendix B.

SEARCH RESULTS

The search strategy yielded 632 studies after removing duplicates; of those 632 studies, 18 studies met the selection criteria for inclusion (Figure 2-1).

Figure 2-1
Flow Charts Used to Select Studies

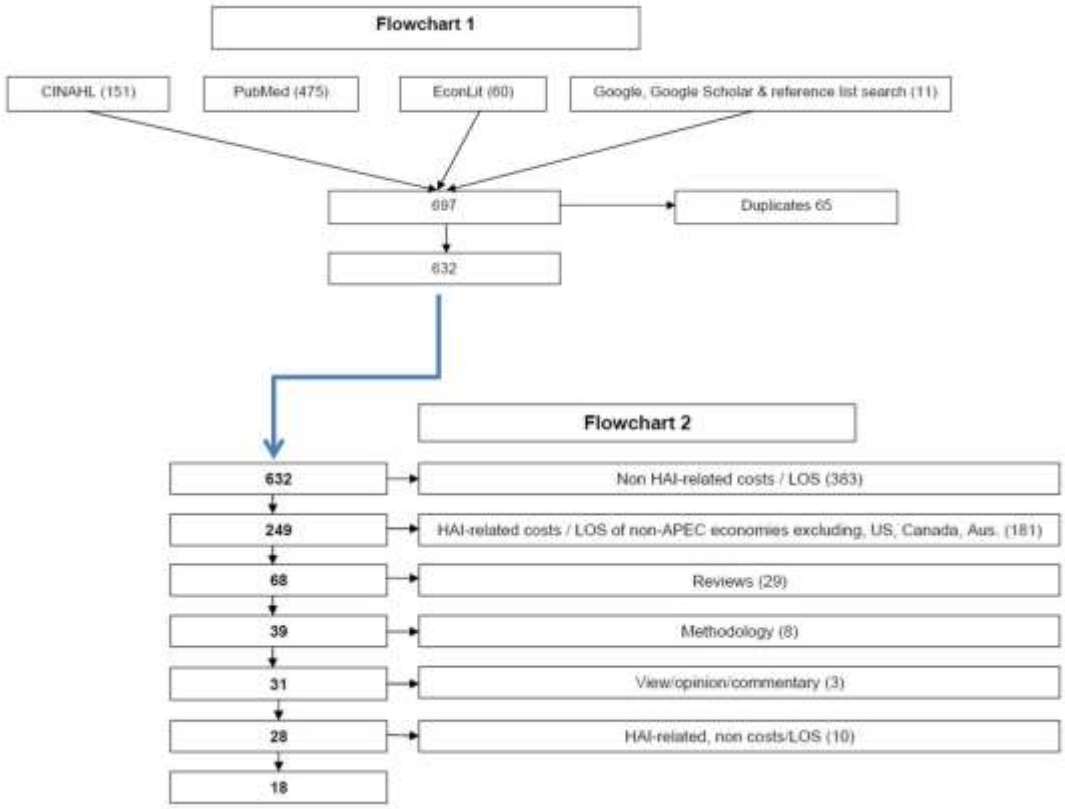
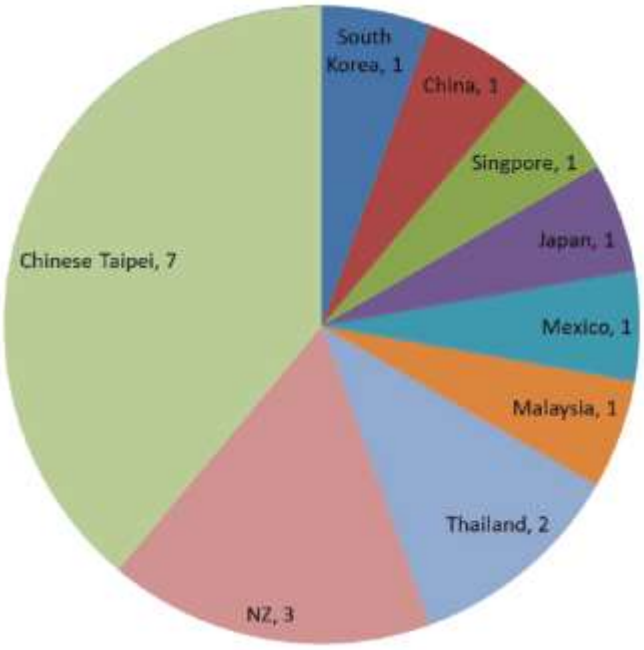
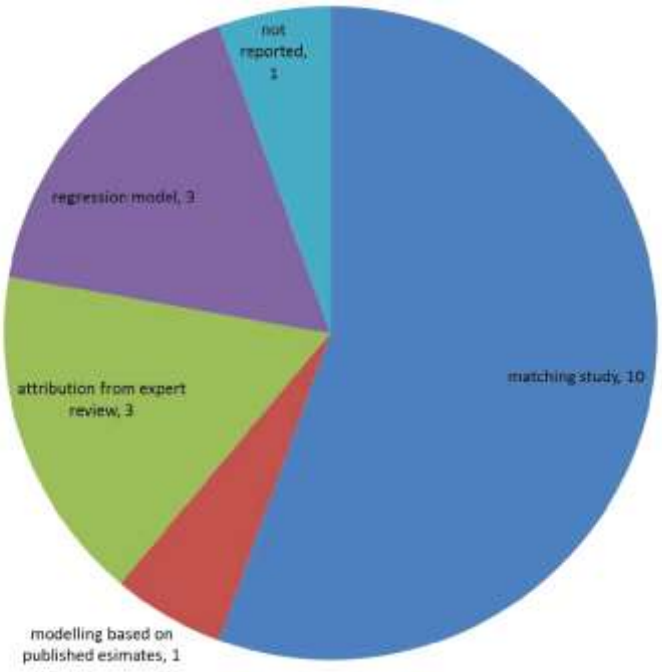


Figure 2-2
Where Studies Were Done



Three studies were conducted in New Zealand [14-16]; seven in Chinese Taipei [17-23]; two in Thailand [24,25]; and one each in Japan [26], Singapore [27], China [28], Korea [29], Mexico [30], and Malaysia [31].

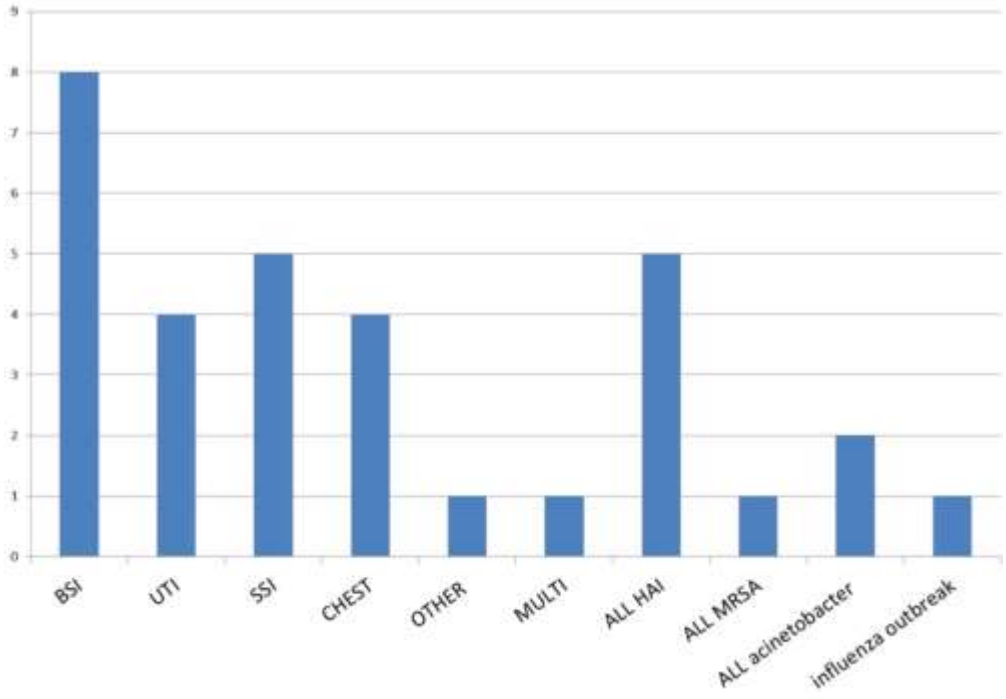
Figure 2-3
Different Study Designs Used



As for design, 10 were matching studies [14, 16, 17, 19-23, 27, 29, 30], one was a modeling study based on published estimates [15], three were attribution studies from expert review [25, 31, 32], and three were based on statistical regression models [18, 22, 26].

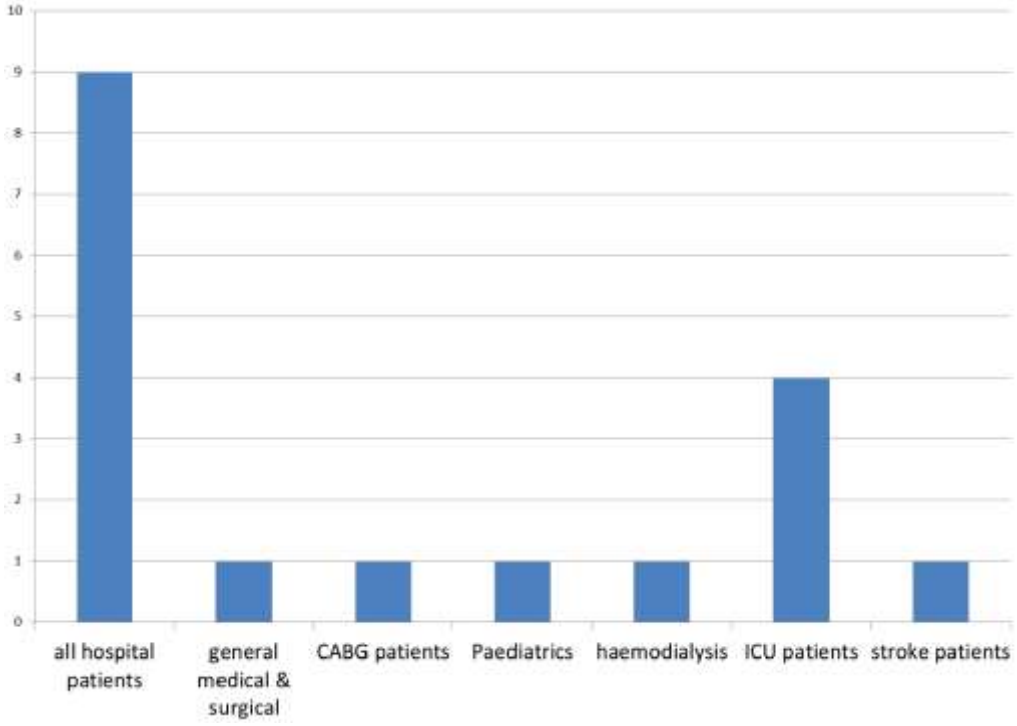
The types of infection included were bloodstream [14, 15, 17, 21, 23, 29-31], urinary tract [15, 21, 23, 31], surgical site [15, 16, 21, 23, 31], chest [15, 21, 23, 31], other and multiple sites of HAI [15], methicillin-resistant Staphylococcus aureus [27], Acinetobacter [19, 20] and an influenza outbreak [32].

Figure 2-4
Sites of Infection Studied



The patient groups studied included the following groups: all hospital patients [14, 19, 21, 22, 25, 27, 29, 31, 32]; general medical and surgical patients [15]; coronary artery bypass grafting (CABG) patients [16]; pediatrics patients [28]; hemodialysis patients [17]; intensive care unit (ICU) patients [18, 20, 23, 30]; and stroke patients [26].

Figure 2-5
Patient Groups Studied



3. Data Quality and Completeness

The extra lengths of stay estimated by each study for the different types of HAI are shown in Table 3-1. There is large variability among these results with bloodstream infections (BSI) found to prolong stays between 5 and 18.9 days, surgical site infections (SSI) between 7 and 32.2 days, and urinary tract infections (UTI) between 2 and 17.5 days. This high degree of uncertainty means we know little about the factors that influenced the actual increased stay caused by these infections. The incidence rates and point prevalences reported for each study for the different types of HAI are shown in Table 3-2.

Table 3-1

Extra Lengths of Stay Found by Each Study

Reference	Economy	Patient Group Studied	Estimated Extra Stay (days)
[14]	NZ	All hospital patients	BSI = 9.7 or 7.9
[15]	NZ	General medical & surgical	BSI = 5; UTI = 2 (medical) & 4 (surgical); SSI =8 (medical) & 10 (surgical); Chest = 6; other = 5
[16]	NZ	CABG patients	SSI = 32.2
[29]	Korea	All hospital patients	BSI = 18.9
[28]	China	Pediatrics	All HAIs = 5
[27]	Singapore	All hospital patients	All MRSA = 25
[17]	Chinese Taipei	Hemodialysis	BSI = 14
[18]	Chinese Taipei	ICU patients	All HAIs = 27
[19]	Chinese Taipei	All hospital patients	Acinetobacter = 13.4
[20]	Chinese Taipei	ICU patients	Acinetobacter = 8.7 (ICU) and 19.1 (ward)
[22]	Chinese Taipei	All hospital patients	All HAIs = 19.2; BSI = 15.5; UTI = 17.5; SSI = 14.4; Chest = 18.4
[21]	Chinese Taipei	All hospital patients	All HAIs = 15
[23]	Chinese Taipei	ICU patients	BSI (N/A)
[25]	Thailand	All hospital patients	All HAIs = total stay 22.9 (not extra stay)
[32]	Thailand	All hospital patients	Influenza outbreak (only $ estimated)
[26]	Japan	Stroke patients	All HAIs = 16·3 (range 5.1-25.1)
[30]	Mexico	ICU patients	BSI = 6.05
[31]	Malaysia	All hospital patients	Only treatment $ reported

Table 3-2

Incidence Rates and Point Prevalence Found by Each Study

Reference	Economy	Patient Group Studied	Estimated Incidence Rates and Point Prevalence (%)
[15]	NZ	General medical and surgical	BSI = 1.77/0.48 UTI = 1.4/2.54 SSI = 0.51/2.31 Chest = 1.04/1 Other = 1/0.88
[28]	China	Pediatrics	12 (2000) 6 (2008)
[18]	Chinese Taipei	ICU patients	10.2
[19]	Chinese Taipei	All hospital patients	55.6 episodes per 100,000 discharges (annual)
[20]	Chinese Taipei	ICU patients	0.56 per 1,000 patient-days
[23]	Chinese Taipei	ICU patients	All HAIs = 14.5 Chest = 3.7 BSI = 5.1 UTI = 5.6SSI = 1.4
[26]	Japan	Stroke patients	All HAIs = 16·4 (inter-hospital range of 4.7-28.3)
[30]	Mexico	ICU patients	BSI = 7.1
[31]	Malaysia	All hospital patients (point prevalence)	HAIs = 13.9 UTI = 12.2 Chest = 21.4 BSI = 12.2SSI = 11.2

The quality of the data is difficult to judge. Making unadjusted comparisons of the stays of those with and without HAIs is not useful due to other differences, unrelated to HAIs, between the two groups. For example, those with HAIs might have more comorbidities and more complex diagnoses, and so might generate quite different length-of-stay outcomes regardless of their HAI status. The challenge is to estimate the independent effect of HAIs on length of stay by making allowances for sources of biases. Graves and Weinhold [33] review the method of "direct attribution" used by the authors of these papers found by this review [25, 31, 32], and "comparative attribution" used by the authors of these papers found by this review [14, 16, 17, 19-23, 27, 29, 30]. Direct attribution requires experts to assess the prolongation of stay due to HAIs. This method has been suggested to be "subjective" and not reproducible [34]. Comparative attribution studies tend to be preferred as they are perceived as objective measures. Authors of these studies use data from a cohort of patients. Then, either (1) a subset of infected patients is manually matched with uninfected controls on variables thought likely to affect length of stay, such as age, sex, comorbidities; or (2) multivariable statistical regression models are built to describe the relationship between HAI and cost outcomes, with controls for other factors thought likely to affect cost outcomes [35]. A disadvantage of manual matching is that infected patients are being matched on a limited number of variables. Matching with greater than five or six variables requires a much larger size of controls, making the research costly and difficult and possibly biased because of "omitted variables." The likely consequence is that too much of the observed variation in cost is attributed to an HAI and the cost of the HAI is overstated [36]. If cases of infection are excluded from the analysis to allow matching on more variables, then a selection bias could arise, because not all cases have the same opportunity to be included in the comparison of lengths of stay.

The use of statistical regression avoids selection bias and offers the opportunity to reduce bias arising from omitted variables. A statistical regression model will show the association between length of stay and the independent variables of HAIs, and other observable factors that might explain variation. Another important source of bias arises from the relationship between an HAI and length of stay. We know that HAIs increase length of stay and evidence exists that a prolonged length of stay also increases the risks of HAIs. This reverse causality induces correlation between the error terms and the independent variables, leading to biased estimates and tests of hypotheses [37]. This problem is called "endogenous variables bias" and has been discussed in the context of HAIs [38, 39]. Graves and Weinhold [33, 40] describe the problem in detail and report preliminary attempts at a solution, using an instrumental variables method. Controlling bias from endogenous variables and interpreting the results of an unbiased model is a methodological challenge for future research. Great progress has been made in recent years with the application of multistate models that correctly account for the timing of events [8-11, 41-58] and produce estimates of extra stay that are free from time-related biases, this is a good example [44]. All the estimates of extra stay reported in Table 3-1 arose from studies that failed to account for the timing of the infection.

The incidence rates and point prevalences reported do not emerge from common definitions, audit methods or similar data collection processes [59]. It is highly likely that outcomes are being measured differently, making comparison or extrapolation unreliable.

In addition to the weaknesses of methods in the data discussed, they are also incomplete. An economic modeling study that aims to predict the costs of HAIs requires, for each site or type of infection, data to inform four separate parameters that are discussed below.

First, information on the incidence rates of HAI is needed, and this review identified patchy and poor quality data for this parameter. Second, information is required to describe the extra stay per case, and this review identified estimates that mostly used methods fraught with sources of bias. Third, the treatment costs need to be understood and we found limited information for this. Presumably, clinicians working in each of the economies could make fairly good estimates of the typical treatment protocol for HAIs. Finally, the economic value of bed days lost to HAIS needs to be understood. No information was found for this issue in the literature retrieved. Economists would take a different approach to valuing bed days from the approach taken by cost accountants. Economists would estimate the value of bed days in their next-best alternative use; they wish to find the opportunity cost of losing bed days to treat an HAI. Cost accountants would estimate the cash expenditures in the hospital per bed day by dividing total expenditure by total bed days. The goal of the hospital accountant is to keep the organization financially viable [60]. Opportunity cost is the appropriate value for decision making and represents the amount that someone is willing to pay to access the marginal bed day. As long as the effective demand exceeds supply for hospital-based services, marginal bed days will be economically valuable.

4. Future Research Needs

In order to predict the costs of HAIS in the APEC economies, an economic model needs to be built. Five parameters are essential, which are shown in the black boxes marked A to E below. This allows predictions to be made for the outcomes in the remaining boxes with rounded corners.

Figure 4-1
A Suggested Economic Model

The at-risk population (A) represents the number of hospital admissions who are at risk of acquiring an infection. These might be broad categories, such as “all surgical patients” or “all medical patients,” or could be subgroups, such as “ICU admissions” or “oncology patients.” Regardless, this is a simple parameter to measure and should be accessed from routine hospital-level statistics in many economies. The period in which the risk arises must be specified, such as 12 months. In order to build a hypothetical case illustrating the method, we will assign 1,400 ICU patients admitted to a 20-bed ICU over a 12- month period as the first parameter. The incidence rates (B) will be taken from Chen et al. [61]who reported 114 episodes of bloodstream infection among 2,757 ICU admissions (giving an incidence rate of 4.1 percent). For a modeling study, this information can be used to reveal uncertainty in this parameter by fitting a beta distribution using the number of events (114) as the alpha and the number of non-events (2757-114) as the beta. This type of distribution is suitable for risks, as it produces values constrained between zero and one. The extra stay (C) per case of BSI is taken from Sheng et al. [22] who used a statistical regression model to estimate the extra stay for BSI at 15.5 days (standard deviation 24.7); this estimate is likely biased upwards because of failure to account for the timing of infection. Uncertainty in the parameter can be shown by fitting a gamma distribution to the mean and variance estimates. The procedure is to estimate

the alpha by (mean/sd)^2 and the beta by (sd^2)/mean. Treatment costs (D) are not known; but for this example we estimate they lie between $100 and $200 per case. The value of a bed day (E) is also not known; we estimate the value is between $500 and $800 per case. In the absence of better data, it is assumed both parameters are distributed uniformly.

These five parameters (A-E) can be used to generate a range of powerful outcomes, as shown by the green boxes with rounded corners in the previous figure. The modeling also shows uncertainties in the data and includes this in the output. This model (below) predicts economic outcomes of bloodstream infections for a 12-month period in one ward in Chinese Taipei; remember this model is for illustration purposes only. Table 4-1 shows the data used for estimating parameters B to E. The mean and variance are shown as well as the minimum and maximum possible values.

Table 4-1

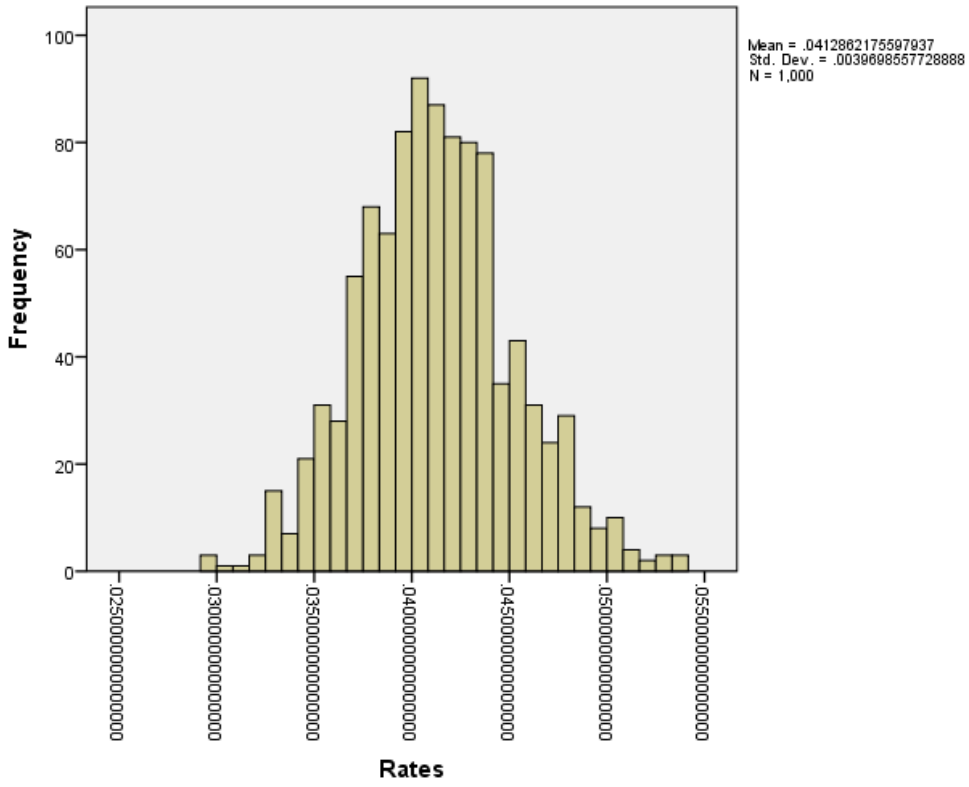
Prediction Measures and Level of Uncertainty for Each

Measure	Mean	Standard Deviation	Minimum	Maximum
Rates	4.13%	0.40%	2.92%	5.41%
Extra stay in days	16.5	26.3	0.0	200.9
Treatment cost	$150	$30	$100	$200
Bed-day cost	$649	$88	$500	$800

The "Rates" reflect plausible ranges of infection risks and are moderately uncertain and, Figure 4-2 shows the prior distribution of this parameter.

Figure 4-2

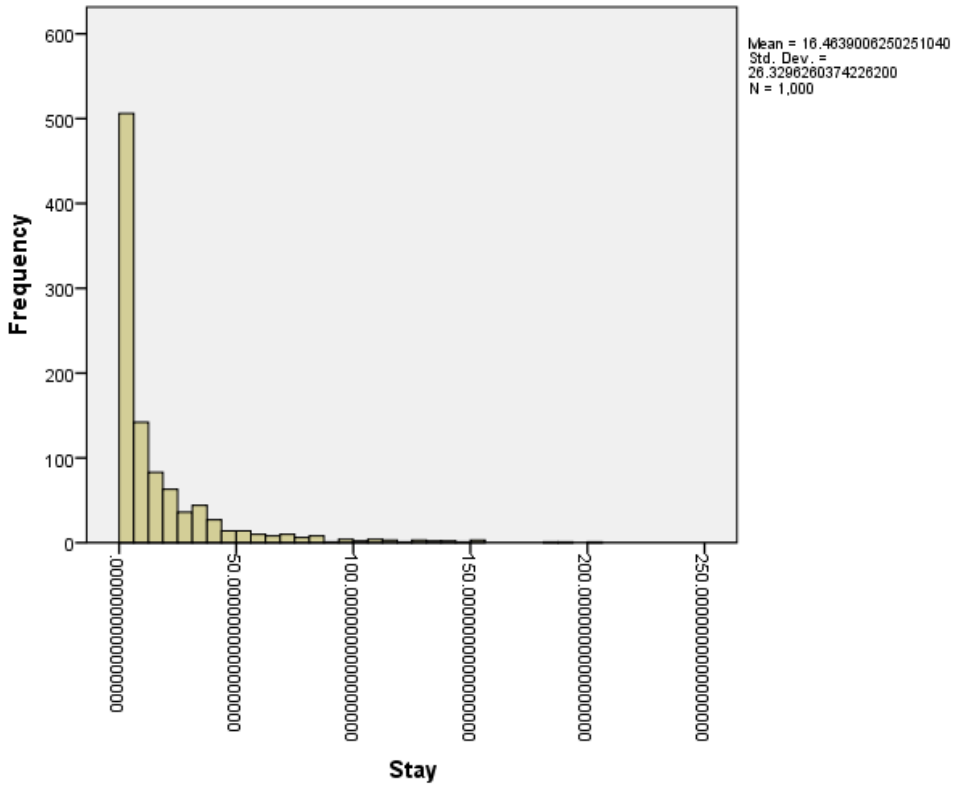
Prior Distribution for 'Rates' Parameter



The "extra stay in days" due to a BSI has a very high maximum value of 200 days, which shows nicely the skew in length-of-stay data (Figure 4-3). The very long stays due to infection are possible but highly unlikely to happen in the model.

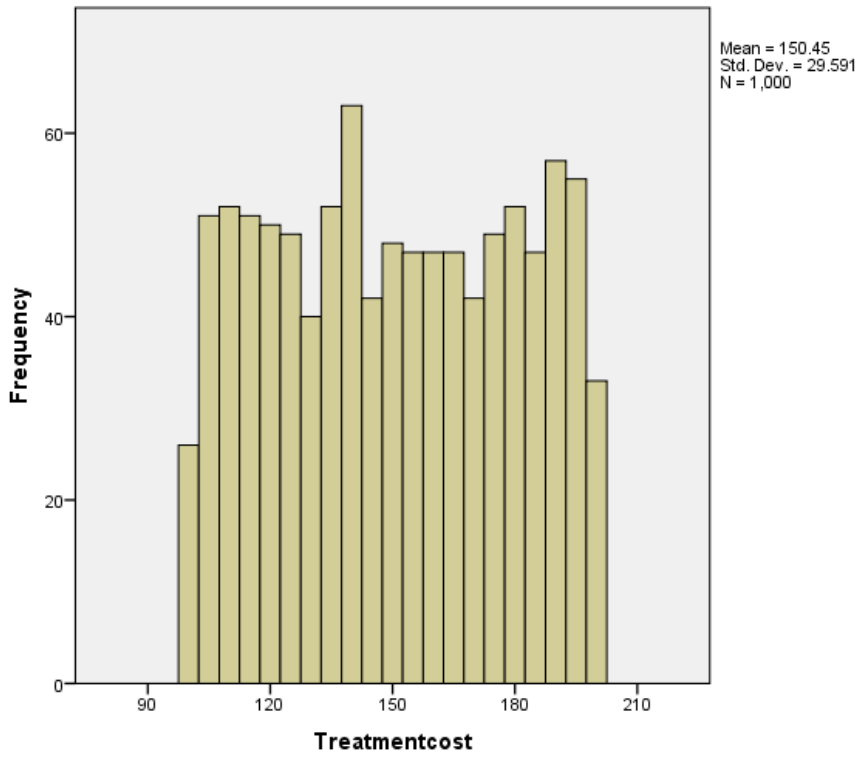
Figure 4-3

Prior Distribution for 'Extra Stay' Parameter



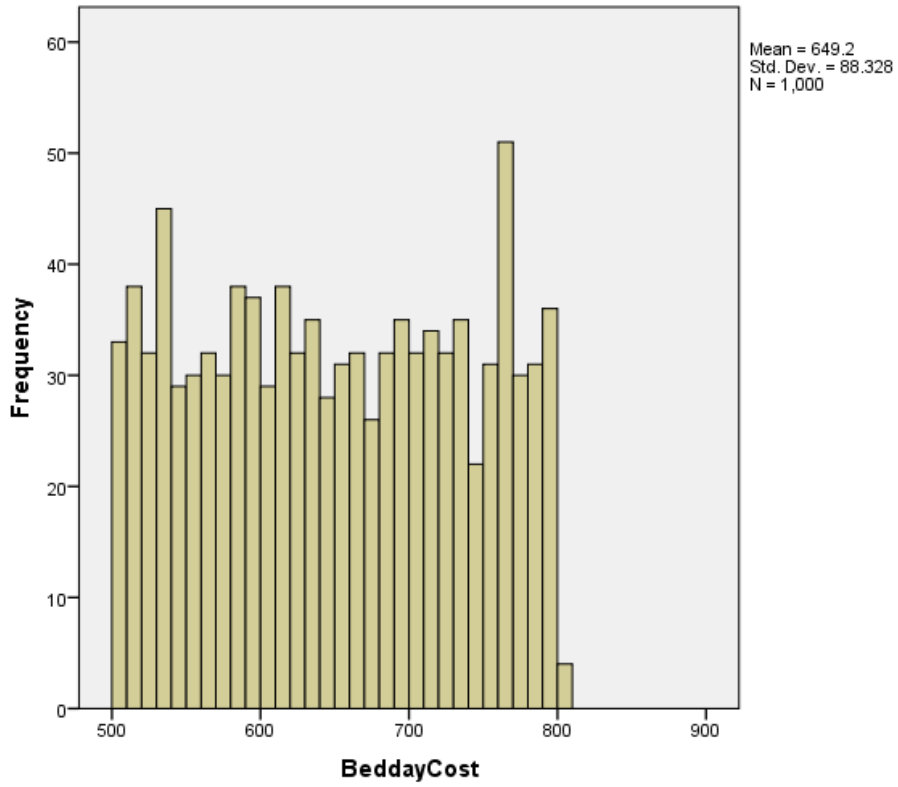
The extra treatment costs are uniform and show close to an equal chance of being in a range of $100 to $200 (Figure 4-4).

Figure 4-4
Prior Distribution for 'Treatment Costs' Parameter



The costs of a bed day are again uniform and show a close to equal chance of being in a range of $500 to $800 as expected (Figure 4-5).

Figure 4-5
Prior Distribution for 'Bed Days Cost' Parameter



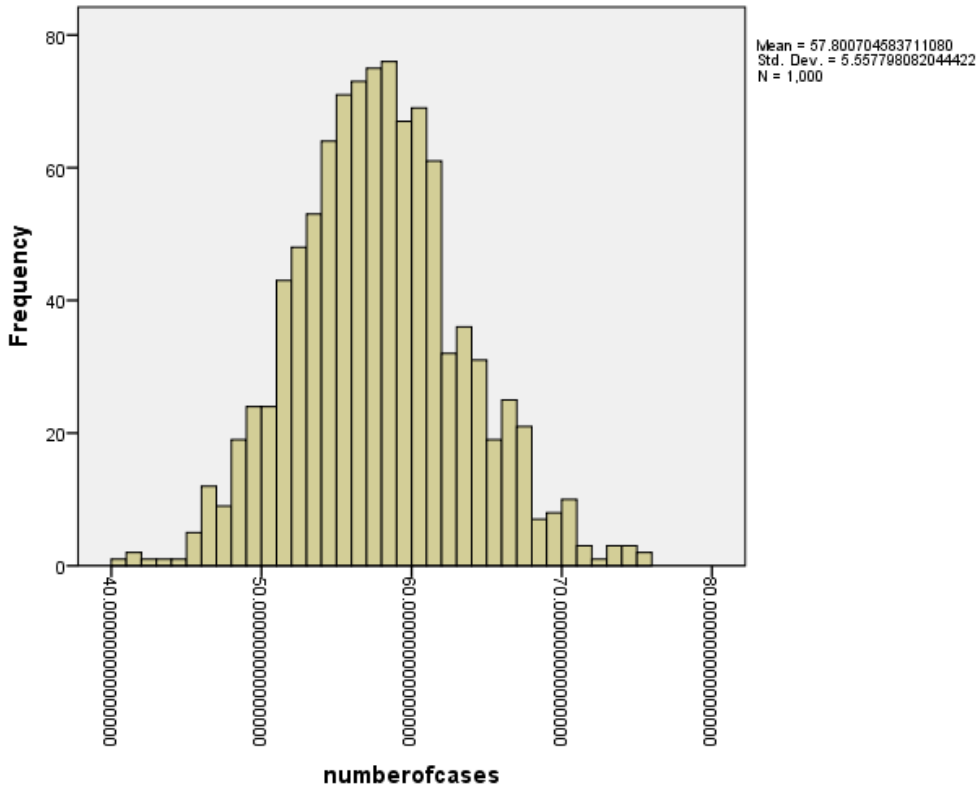
The outputs of the modeling are shown in Table 4-2, with uncertainties included.

Table 4-2
Economic Indicators for Hospitals and Level of Uncertainty for Each

Indicator	Mean	Standard Deviation	Minimum	Maximum
Number of cases	58	6	41	76
Bed-days lost	950	1512	0	10242
Total treatment costs	$8,692	$1,888	$4,717	$15,058
Cost of bed-days	$37,488	$6,078	$23,900	$58,869
Total costs	$46,179	$6,749	$29,277	$73,926

The number of cases from the model lies in a moderate range between 41 and 76 and reflects the uncertainty in the estimates published by Chen et al. [61] (Figure 4-6).

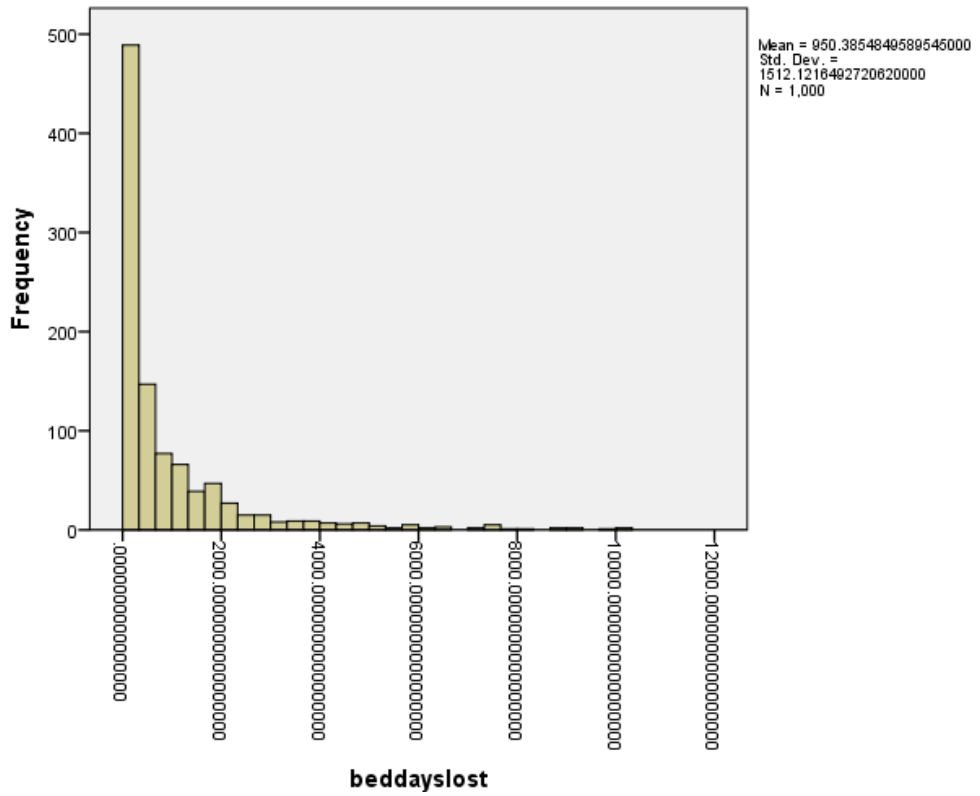
Figure 4-6
Model Output for 'Number of Cases' of BSI



The number of bed days lost to BSI follows the skew in the data, but the mean expected value is 950 days (Figure 4-7).

Figure 4-7

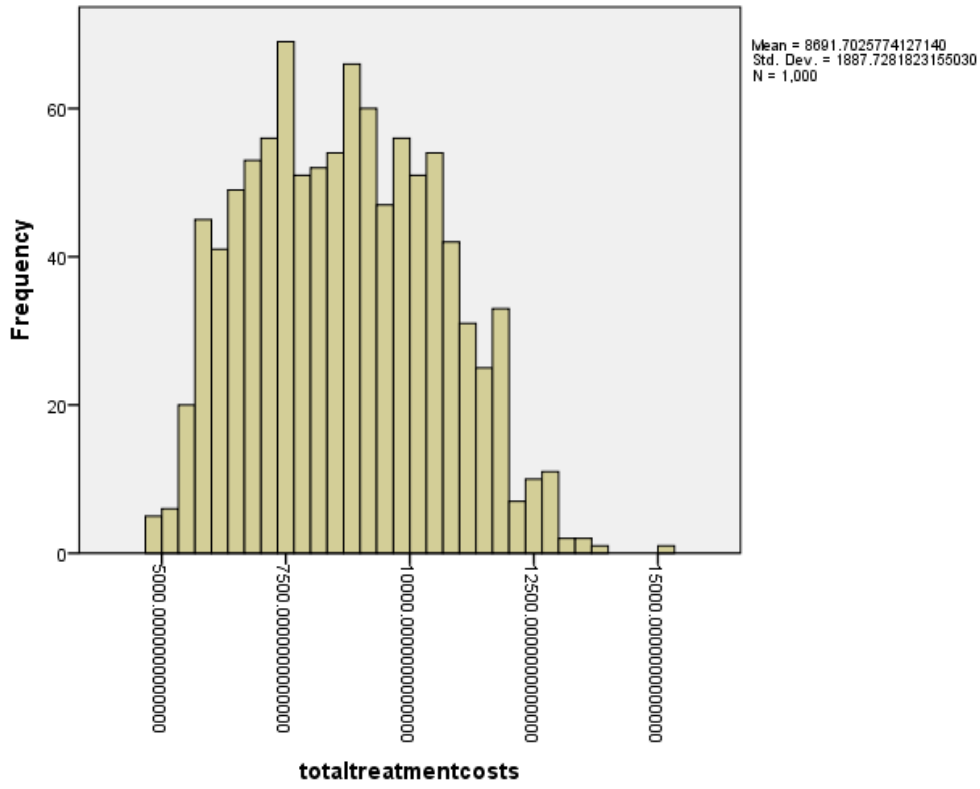
Model Output for 'Number of Bed Days Lost' to BSI



The value of treatment costs ranges between $4,700 and $15,000 (Figure 4-8)

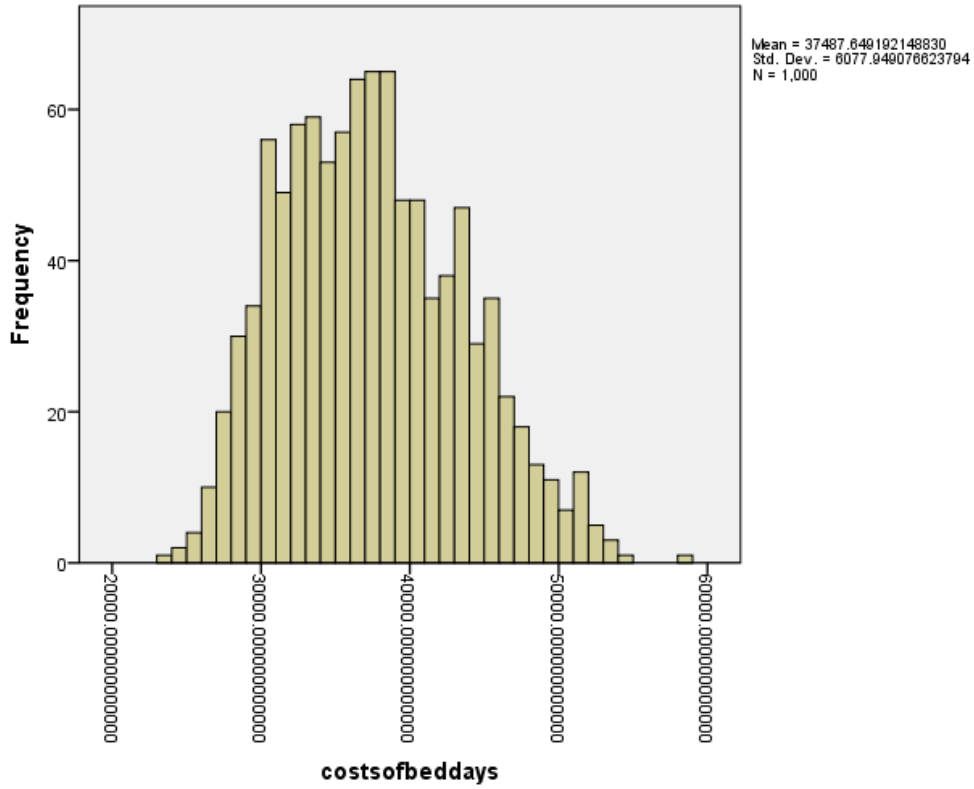
Figure 4-8

Model Output for 'Treatment Costs' of BSI



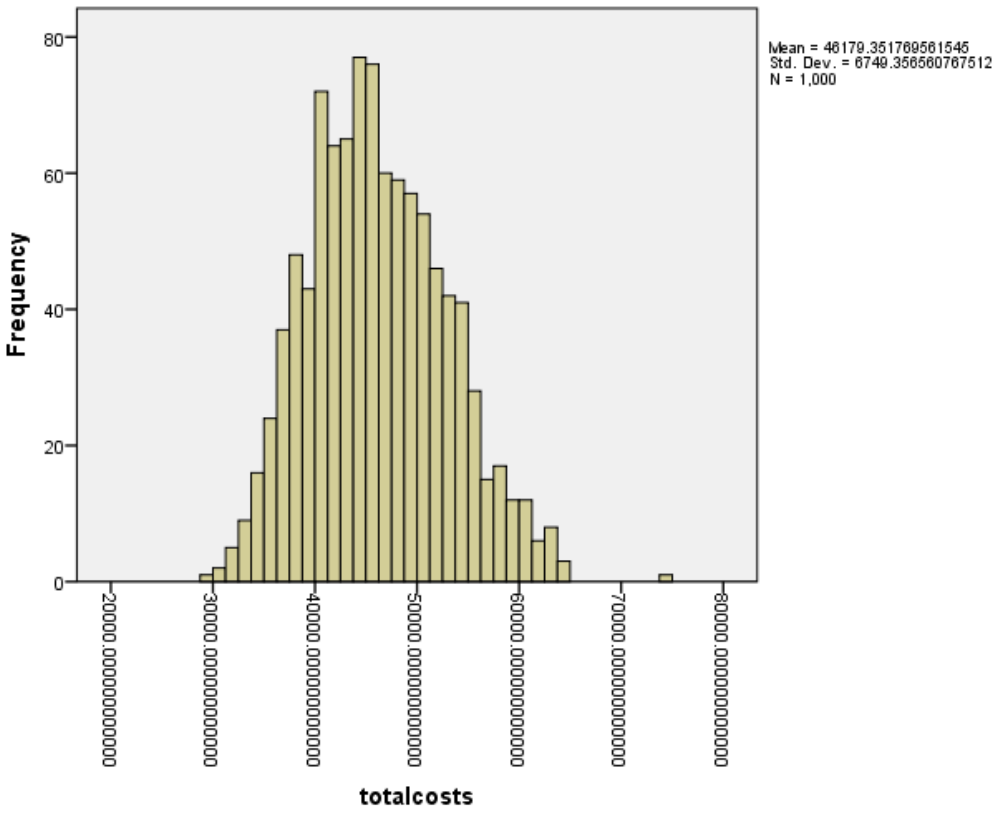
The value of treatment costs ranges between $23,900 and $58,869 (Figure 4-9).

Figure 4-9
Model Output for 'Bed Day' Costs' of BSI



The values of the total costs range between $29,277 and $73,926, which is a reflection of the uncertainty among the input parameters. The truth is likely between these numbers and the mean value; the most likely value is $46,179.

Figure 4-10
Model Output for 'Total Costs' of BSI



This economic model generates some powerful data on the costs of HAIs. However, significant gaps in understanding remain in most APEC economies. We are a long way from having all the information needed to build these models for every type of site of HAIs in every APEC economy. The information in Figure 4-11 summarizes the information we have and where the major omissions are.

Figure 4-11

Completeness of Data Needed for Studies to Describe HAI Costs in All APEC Economies

	Have estimates	At risk pop	Risks	Days	Bed day $	Treatment Costs
Australia	✓					
Brunei Darussalam	x	?	x	x	?	?
Canada	✓					
Chile	x	?	x	x	?	?
People's Republic of China	x	?	Some	Some	?	?
Hong Kong, China	x	?	x	x	?	?
Indonesia	x	?	x	x	?	?
Japan	x	?	Some	Some	?	?
Republic of Korea	x	?	x	Some	?	?
Malaysia	x	?	x	x	?	?
Mexico	x	?	Some	Some	?	?
New Zealand	✓					
Papua New Guinea	x	?	x	x	?	?
Peru	x	?	x	x	?	?
The Republic of the Philippines	x	?	x	x	?	?
The Russian Federation	x	?	x	x	?	?
Singapore	x	?	x	Some	?	?
Chinese Taipei	x	?	Some	Some	?	?
Thailand	x	?	x	Some	?	?
United States of America, and	✓					
Viet Nam.	x	?	x	x	?	?

The green rows are the economies where we already have a good understanding of the costs of HAIs; no further work in these economies would be useful. For 10 of the remaining economies, no data exist for any of the parameters we need for economic models: Brunei, Chile, Hong Kong, Indonesia, Malaysia, Papua New Guinea, Peru, Philippines, Russian Federation, and Vietnam. Some data exist for the parameters required for the remaining APEC economies. This has been summarized in earlier sections of this report.

5. Summary

In order to assess the available body of published evidence on the economic burden of HAIs in developing economies in APEC, a thorough literature search was done and 632 published papers were reviewed. A final set of 18 publications was included. Relevant data were extracted from these studies and summarized to build and evaluate an indicative economic model. The data on incidence rates and costs of HAIs are limited and variable in both scope and quality, with only a small number of APEC counties represented. The range of infections included was variable, and the methods used to estimate extra costs were subject to biases, which are discussed. An illustrative economic model shows relevant outcomes for one of the economies. There is scope to improve the data used in the economic models and make meaningful predictions of costs in selected APEC economies. It might be that economies in which no data exists can be matched and data generalized to them. It may be that more data, currently unpublished, are available from each of the economies and can be used. Overall, the lack of accessible data in the public domain is a challenge to broader modeling. It is also clear that significant gaps exist in data that are necessary for policymakers to understand the public health and economic impact of HAIs and make informed decisions about policies and programs that could address these impacts.

A lack of data on HAIs cannot be interpreted to mean that these infections do not impose a serious economic burden on the developing economies in this analysis. In contrast, the robust body of evidence on the economic burden of HAIs in many developed economies with higher levels of infrastructure for infection prevention and control indicates that HAIs are a likely burden to all healthcare systems. A lack of robust surveillance may in fact impede the development and implementation of evidence-based policies that could enhance the efficiency and quality of healthcare systems. The evidence from this review supports the need for APEC economies to continue working toward carrying out the recommendations from the APEC High-Level Workshop on Reducing the Economic Burden of Healthcare-Associated Infections, held in July 2012 in Manila. These Manila Recommendations, as they are referred to in brief, call on APEC members to strengthen infection prevention and control programs and policies; establish surveillance and data collection; and encourage partnerships and collaboration among governments, patients, the private sector, and academia to help work towards these goals.

Making progress based on the information we have available today, while continuing to enhance the body of evidence to support continued improvement in policy and practice in infection prevention and control should be goals of policymakers in all APEC economies.

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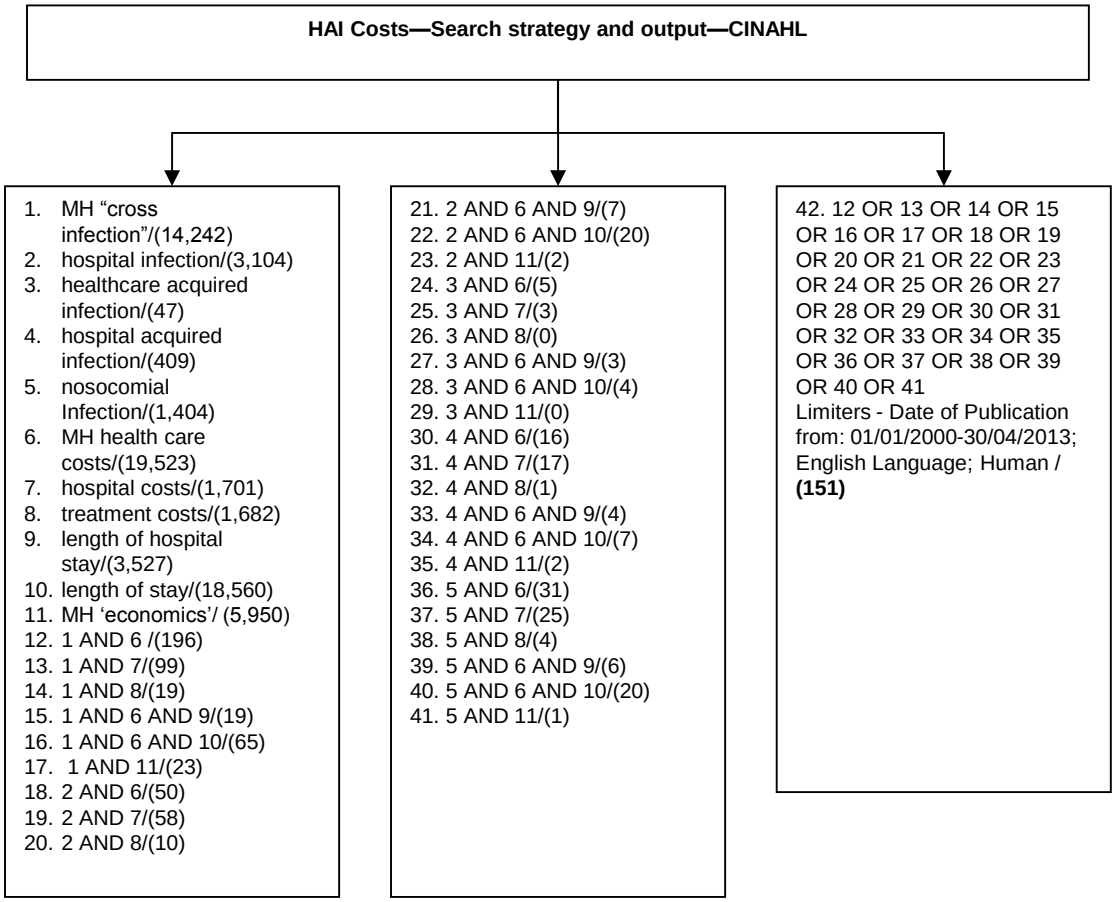
Appendix A. Search Strategies



HAI Costs—Search strategy and output—CINAHL

1. MH "cross infection"/(14,242)
2. Hospital infection/(3,104)
3. Healthcare acquired infection/(47)
4. Hospital acquired infection/(409)
5. Nosocomial infection/(1,404)
6. MH health care costs/(19,523)
7. Hospital costs/(1,701)
8. Treatment costs/(1,682)
9. Length of hospital stay/(3,527)
10. length of stay/(18,560)
11. MH 'economics'/ (5,950)
12. 1 AND 6 /(196)
13. 1 AND 7/(99)
14. 1 AND 8/(19)
15. 1 AND 6 AND 9/(19)
16. 1 AND 6 AND 10/(65)
17. 1 AND 11/(23)
18. 2 AND 6/(50)
19. 2 AND 7/(58)
20. 2 AND 8/(10)

21. 2 AND 6 AND 9/(7)
22. 2 AND 6 AND 10/(20)
23. 2 AND 11/(2)
24. 3 AND 6/(5)
25. 3 AND 7/(3)
26. 3 AND 8/(0)
27. 3 AND 6 AND 9/(3)
28. 3 AND 6 AND 10/(4)
29. 3 AND 11/(0)
30. 4 AND 6/(16)
31. 4 AND 7/(17)
32. 4 AND 8/(1)
33. 4 AND 6 AND 9/(4)
34. 4 AND 6 AND 10/(7)
35. 4 AND 11/(2)
36. 5 AND 6/(31)
37. 5 AND 7/(25)
38. 5 AND 8/(4)
39. 5 AND 6 AND 9/(6)
40. 5 AND 6 AND 10/(20)
41. 5 AND 11/(1)

42. 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41
Limiters: Date of publication from 01/01/2000 to 30/04/2013; English language; Human / **(151)**

HAI Costs—Search strategy and output—PubMed

1. MH cross infection AND MH health care costs/(447)

2. MH cross infection AND MH hospital costs/(230)

3. MH cross infection AND MH health care costs AND MH length of hospital stay/(158)

4. MH cross infection AND health care costs AND length of stay/(252)

5. MH hospital infection AND hospital costs/(230)

6 MH hospital infection AND MH health care costs AND length of hospital stay/(184)

7. Health care acquired infection AND MH health care costs/(354)

8. Health care acquired infection AND MH hospital costs/(117)

9. Health care acquired infection AND MH health care costs AND MH length of hospital stay/(88)

10. Nosocomial infection AND MH health care costs/(512)

11. Nosocomial infection AND MH hospital costs/(248)

12. Nosocomial infection AND MH health care costs AND MH length of hospital stay/(169)

13. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7OR 8 OR 9 OR 10 OR 11

Limiters: Date of publication from 01/01/2000 to 30/04/2013; English language; Human / **(475)**

Appendix B. Selected Studies

Study	Economy	Design	Period	Group	Infection	Incidence	Point Preva-lence	Cost/ LoS Method	Extra LoS (days)	Extra Costs/ Infection
Burns A, Bowers L, Pak N, Wignall J, Roberts S. (2010). The excess cost associated with healthcare-associated bloodstream infections at Auckland City Hospital. N Z Med J, 123 (1324):7-24	NZ	Cohort, 1:1 & 1:2 match with controls	July 2004-Dec. 2006	All admitted patients	Bloodstream	N/A	N/A	Matching (1:1) nd (1:2)	Group 1 (with matched control): 9.7 Group 2 (by itself): 7.9	(2005 NZ$) Group 1: $20,394 Group 2: $11,139
Graves N, Nicholls TM, Morris AJ (2003) Modelling the costs of healthcare acquired infections in New Zealand. Infect Control Hosp Epidemiol, 24:214-223	NZ	Monte Carlo simulation model	14 May - 17 June 1999	All patients admitted to general medical and surgical services in Auckland District Health Board Hospitals	Urinary tract (UT) Surgical wound (SW); chest (CHEST); Bloodstream (BS); Other (OTHER); Multiple sites (MULTI)	UT: 1.40% / 2.54% SW: 0.51% / 2.31% CHEST:1.04% / 1% BS: 1.77%/ 0.48% OTHER: 1%/0.88% MULTI: 0.99%/ 0.61%	N/A	N/A	UT: 1, .5, 5.1 / 4.7, 3.6, 5.1 SW: 4, 7.5, 11 / 12, 5.7, 12.9 CHEST: 6.5, 3.7, 8.7 (for both) BS: 4, 0, 12 (both) OTHER: 2.5, 0, 12.4 (both) MULTI: 29 / 25, 18, 26.2	(NZ$) UT: $2,816 / $15,562 SW: $3,489 / $32,134 CHEST: $5,992 / $8,555 BS: $8,438 / $3,500 OTHER: $4,549 / $6,057 MULTI: $26,068 / $19,460
Upton A, Smith P, Roberts S. (2005). Excess cost associated with staphylococcus aureus poststernotomy mediastinitis. N Z Med J. 2005, 118(1210):U1316.	NZ	Retrospective case control	Pending paper delivery	Adults who developed staphylo-coccus aureus PSM after median sternotomy for coronary, artery bypass grafting, heart valve, or thoracic artery surgery	Post-sternotomy mediastinitis (PSM)	N/A	N/A	Matching (1:1)	32.2	NZ$45,677
Park SY, Son JS , Oh IH , Choi JM , Lee MS. (2011). Clinical impact of methicillin-resistant Staphylococcus aureus	Korea	Propensity-matched case control	2003 - 2008	All patients with clinically significant Staphylo-coccus	MRSA, or MRSA bacteremia	N/A	N/A	Matching (1:1) Note: pair-matched	Mean 25.0 vs. 6.1 days	(National currency n/a) $9,369.6 vs. $8,355.8; P = 0.62:

Study	Economy	Design	Period	Group	Infection	Incidence	Point Prevalence	Cost/ LoS Method	Extra LoS (days)	Extra Costs/ Infection
bacteremia based on propensity scores. Infection, 39 (2): 41-7				aureus bloodstream infections						Difference is not statistically significant.
Zhang QL, Xu XN, Langley JM, Zhu BQ, Zhang N, and Tang YY. (2010). Health-associated infections in a pediatric nephrology unit in China. Am J Infect Control. 38:473-5.	China	Prospective infection control surveillance program	2000 - 2008	All pediatric patients admitted to pediatric nephrology unit	HAI	2000: 12% 2008: 6%	9.16%	Surveil-lance data	5	N/A
Pada SK , Ding Y, Ling ML, Hsu LY, Earnest A, Lee TE, Yong HC, Jureen R, Fisher D. (2011). Economic and clinical impact of nosocomial methicillin-resistant Staphylococcus aureus infections in Singapore: a matched case control study. Journal of Hospital Infection, 78 (2011) 36 - 40	Singapore	Prospective matched case control study	Sept. 2007 - March 2008	All inpatients culture positive for MRSA	MRSA	N/A	N/A	Matching (1:2)	25	US$13,639
Liu JW, Su YK, Liu CF, Chen JB. (2002) Nosocomial blood-stream infection in patients with end-stage renal disease: excess length of hospital stay, extra cost and attributable mortality. Journal of Hospital Infection, 50: 224 - 27.	Chinese Taipei	Retrospective matched (1:2) case-control	Jan 1998 – Dec. 1998	All patients with end-stage renal disease undergoing hemodialysis	Nosocomial BSI (bloodstream)		N/A	Matching (1:2)	14	(New China Taipei Dollars—NT$) $70,145 (mean costs)
Chen YY, Chou YC, Chou P. (2005) Impact of nosocomial infection on costs of illness and length of stay in intensive care units. Infect Control Hosp Epidemiol, 26:281-287	Chinese Taipei	Regression modelling	Oct. 2001 - June 2002	Patients admitted to adult ICUs	Nosocomial infections	10.20%	N/A	Covariates-adjusted comparison	27	N/A
Lee NY, Lee HC, Ko, NY, Chang CM, Shih, HI, Wu CJ, Ko, WC. (2007). Clinical and economic impact of multidrug resistance in	Chinese Taipei	Retrospective matched cohort	1996-2001	Hospitalized patients with multidrug-resistant (MDR)	MDR Acinetobacter baumannii bacteremia	55.6 episodes/ 100,000 annual discharges	N/A	Matching (1:1)	13.4	US$3,758

Study	Economy	Design	Period	Group	Infection	Incidence	Point Prevalence	Cost/ LoS Method	Extra LoS (days)	Extra Costs/ Infection
nosocomial Acinetobacter baumannii bacteremia. Infect Control Hosp Epidemiol. 28(6):713-9				Acinetobacter baumannii bacteremia						
Jang TN, Lee SH, Huang CH, Lee CL, Chen WY. (2009). Risk factors and impact of nosocomial Acinetobacter baumannii bloodstream infections in the adult intensive care unit: a case-control study. Journal of Hospital Infection, 73: 143 - 150.	Chinese Taipei	Matched case-control	Oct. 1997 – Sept. 2006)	Patients admitted to adult intensive-care unit	Nosocomial Acinetobacter baumannii bloodstream	0.56 per 1,000 patient-days		Matching (1:1)	8.7 (IUC); 19.1 (hospital stay)	US$8,480
Sheng WH, Wang JT, Lu DCT, Chi WC, Chen YC, Chang SC. (2005). Comparative impact of hospital-acquired infections on medical costs, length of hospital stay and outcome between community hospitals and medical centres. Journal of Hospital Infection. 59: 205–214.	Chinese Taipei	Matched case-control	Oct. 1, 2002-Dec. 31, 2002	All hospitalized patients with hospital-acquired infection	Urinary tract (UT); Respiratory tract (RT) Bloodstream (BS) Surgical site (SS)	N/A	N/A	Matching (1:1)	Medical Center All HAI: 19.2 UT:17.5 RT:18.4 BS:15.5 SSI:14.4 Community Hospital All HAI: 20.1 UT:20.7 RT:21.3 BS:16.6 SS:14.4 (No statistical difference)	($USD) Medical Center All HAI: $5,335 UT:$3,725 RT:$5,146 BS:$4,872 SSI:$4,471 Community Hospital All HAI:$5,058 UT:$2,832 RT:$6,078 BS:$4,643; SS:$2,482 (No statistical difference)
Sheng WH, Chie WC, Chen YC, Hung CC, Wang JT, Chang SC. (2005). Impact of nosocomial infections on medical costs, hospital stay, and outcome in hospitalized patients. J Formos	Chinese Taipei	Atched case-control	Oct. 1, 2002-Dec. 31, 2002	Hospitalized patients with HAI	Nosocomial	N/A	N/A	Matching (1:1)	15	NTD$12,7354

Study	Economy	Design	Period	Group	Infection	Incidence	Point Preva-lence	Cost/ LoS Method	Extra LoS (days)	Extra Costs/ Infection
Med Assoc. 04(5):318-26.										
Chen YY, Wang FD, Liu CY, Chou P. (2009) Incidence rate and variable cost of nosocomial infections in different types of intensive care units. Infect Control Hosp Epidemiol. 30:39-46	Chinese Taipei	Retrospective cohort	2003 - 2005	All patients admitted to adult ICUs	Nosocomial (NI): BS, RT, UT, SS	Overall NI incidence: 14.5% in mixed medical and surgical ICUs: UT: 5.6% BS: 5.1% RT: 3.7% SS: 1.4%	N/A	Multiple statistical analysis including generalized linear model	N/A	(2007 $USD) BS:$6,056 RT: $4,287 UT: $1,955 SS: $1,051
Pancharti P, Leksawas N, Sukamwang K, Tantisiriwat W, Danchaivijitr S. (2005). Impacts of nosocomial infection among elderly patients in Inburi Hospital. J Med Assoc Thai. 8 Suppl 10:S83-5.	Thailand	Descriptive study based on NI surveillance data	Feb. 2002 - May 2002	All elderly patients admitted to Inburi Hospital	Nosocomial	N/A	N/A	Surveillance data	Average length of stay (not extra LoS): 22.9 days	Average medical expenditure (not extra cost): 67,265 baht per patient
Apisarnthanarak A, Puthavathana P, Kitphati R, Auewarakul P, Mundy LM. (2008). Outbreaks of Influenza A among nonvaccinated healthcare workers: implications for resource-limited settings. Infect Control Hosp Epidemiol; 29:777–780.	Thailand	Influenza surveillance & outbreak investi-gation	Jan. 1, 2004–Dec. 31, 2006	Healthcare workers (HCW)	Influenza outbreak attack	Medical intensive care unit:23%; coronary care unit: 18%;surgical infection care unit:24%	N/A	N/A	N/A	Influenza investigation cost per outbreak: US$3,321 at medical intensive care unit; $2,245 at coronary care unit; $2,565 at surgical infection care unit
Lee J, Imanaka Y, Sekimoto M, Ikai H, Otsubo T. (2011). Healthcare-associated infections in acute ischaemic stroke patients from 36 Japanese hospitals: risk-adjusted economic and clinical outcomes. International Journal Of Stroke. 6(1):16-24	Japan	Logistic regression model using admini-strative data	N/A	All ischemic stroke patients admitted to Japanese hospitals	Healthcare-associated infection in ischemic stroke patients	Overall healthcare-associated infection incidence of 16·4%, with an interhospital range of 4.7%–28·3%	N/A	Logistic regression analysis	Additional 16.3 days; interhos-pital range: 5.1-25.1 days	$US3,067 per admission; interhospital range: $434- $7,151

Study	Economy	Design	Period	Group	Infection	Incidence	Point Preva-lence	Cost/ LoS Method	Extra LoS (days)	Extra Costs/ Infection
Higuera F, Rangel-Frausto MS, Rosenthal VD, Soto JM, Castañon J, Franco G, Tabal-Galan N, Ruiz J, Duarte P, Graves N. (2007). Attributable cost and length of stay for patients with central venous catheter- associated bloodstream infection in Mexico City intensive care units: a prospective matched analysis. infect Control Hosp Epidemiol. 28(1):31-35	Mexico	Prospective, nested case-control study of patients with and without BSI.	June 2002 – Nov. 2003	Patients with central venous catheter–associated BSI admitted to intensive care units (ICUs) in Mexico City.	Central venous catheter–associated BSI	10.6% over 18 months or 7.1% per year for central venous catheter-related BSI	N/A	Matching (1:1)	6.05 per case patient	$US11,591 per case of BSI
Hughes AJ, Ariffin N, Huat TL, Abdul MH, Hashim S, Sarijo J, Abd Latif NH, Abu Hanifah Y, Kamarulzaman A. (2005). Prevalence of nosocomial infection and antibiotic use at a university medical center in Malaysia. Infection Control And Hospital Epidemiology. 26(1):100-104	Malaysia	Point-prevalence study of nosocomial infection and antibiotic prescription	July 16-17, 2001	All patients admitted to hospitals	Urinary tract, pneumonia, laboratory-confirmed bloodstream, deep surgical wound, and clinical sepsis	N/A	Overall prevalence: 13.9%. urinary tract: 12.2% pneumonia: 21.4% lab confirmed blood infections: 12.2% deep surgical wound infections: 11.2% clinical sepsis: 22.4%	One-day point survey recording cost of antibioticuse	N/A	Cost of antibiotics used to treat 237 patients with NI per day: US$1,429, US$6.03 per patient/day

LoS=Length of Stay