Costs and length of sepsis-related hospitalizations in Taiwan

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Abstract
To investigate the healthcare expenditures and length of stay (LOS) of sepsis-related hospitalizations in Taiwan. This is a retrospective claim database study. Data were obtained from the two-million-sample longitudinal health and welfare database (LHWD). Adult patients hospitalized with sepsis between 2010 and 2014 were identified by International Classification of Diseases 9th Edition Clinical Modification (ICD-9-CM) codes, and these patients were divided into three levels of sepsis severity. The amount and distribution of their total medical expenditures were investigated. In total, 62,517 patients with 97,790 sepsis-related hospitalizations were included in the present study. It was found that ward fees and medicines comprised the largest component of expenses for sepsis-related hospitalizations. In addition, our study results indicated that the median sepsis-related hospitalization cost was 66.4 thousand New Taiwan Dollar (NT dollars) in 2014, and a significant temporal change was found between 2010 and 2014. The median LOS in a hospital and in an intensive care unit were 11 and 7 days, respectively. Both expenditures and LOS were found to increase with sepsis severity. This study provides an updated and better understanding of the costs and LOS of sepsis-related hospitalizations in Taiwan. It was found that ward fees and medicine fees were the major components of hospital costs.

Abbreviations: LHWD = Health and Welfare Database, ICD-9-CM = International Classification of Diseases 9th Edition Clinical Modification, ICU = intensive care unit, IQR = interquartile range, LHWD = Longitudinal Health and Welfare Database, LOS = length of stay, NT Dollar = New Taiwan dollar, SD = standard deviation.

Keywords: cost, healthcare expenditure, sepsis, septic shock, severe sepsis, Taiwan

1. Introduction
Sepsis is a severe condition with a high mortality rate. There are 31.5 million sepsis cases and 19.4 million severe sepsis cases across the world annually, resulting in 5.3 million deaths.[11] In addition, each of septic patients requires considerable and costly medical treatment. In the US, sepsis was the most expensive medical condition, with its treatment accounting for 5.2% and 6.2% of the nation’s healthcare expenditures in 2011 and 2013, respectively,[2,3] and the more severe the level of sepsis, the higher the cost.[4] The total hospital cost per sepsis case was estimated between 11,413 and 16,100 dollars[5–7] whereas that of severe sepsis was 37,161 dollars in 2003 and 34,142 dollars in 2007.[8] More recently, Jones et al reported that the cost per case was 19,997, 39,736, and 51,307 dollars for sepsis, severe sepsis, and septic shock, respectively.[4] Costs of sepsis are largely impacted by hospital length of stay (LOS), which varies from country to country. In the US, the LOS of sepsis and severe sepsis was estimated at 10.9 to 14.1 days and 14.2 to 17.3 days, respectively.[4,5,8–10] Moreover, the mean LOS of men was found to be similar to that of women (19.6 days vs 19.5 days),[11] but longer for youths than for the elderly.[12] In Europe, the median LOS in the hospital and the intensive care unit (ICU) were estimated at 9 and 2.2 to 2.6 days, respectively, for patients with septic shock in England,[13] whereas the average LOS in Canada, Germany, and Brazil were 10.8, 32.5, and 24 days, respectively.[14–16]

Like LOS, the hospital cost of sepsis varies from country to country, but little is known about the cost and resource use of sepsis in Taiwan. An exception is the study of severe sepsis by Shen et al, where the LOS in the hospital and in the ICU was estimated at 11 to 14 days and 6 to 9 days, respectively, with no significant change over time.[17] The study further showed that the total hospital cost of severe sepsis increased from 1718 dollars in 1997–1998 to 2911 dollars in 2005–2006.[17] In spite of these findings, neither the cost distribution of sepsis nor the temporal...
change of those costs has been recently investigated in Taiwan. In addition, no study has investigated the difference in LOS or health expenditures of the three severity levels of sepsis in Taiwan. We aimed to fill these knowledge gaps and hope the study results will assist the government with healthcare resource allocation.

2. Methods

This is a retrospective claim database study. Data were obtained from the 2-million-sample longitudinal health and welfare database (LHWD). Adult patients hospitalized with sepsis between 2010 and 2014 were identified by the International Classification of Diseases 9th Edition Clinical Modification codes (ICD-9-CM). In addition, based on their medical records during hospitalization, these patients were divided into three levels of severity. The Taipei Medical University Joint Institutional Review Board approved this study (TMU-JIRB-N201708040).

2.1. Data source

In Taiwan, the government provides the national health insurance to ensure everyone has equal medical resources, and in 2009, the National Health Insurance covered 99.3% of residents. Therefore, the Health and Welfare Database (HWD) has been the most comprehensive medical database in Taiwan. The LHWD is a subset of the HWD extracted by stratified random sampling, and it includes two million people, or 8.6% of the total population. In this study, we used the LHWD of 2010 that provided the 2000–2015 claim records and other medical information.

2.2. Patient

Adult patients who were hospitalized between 2010 and 2014 and suffered from any severity of sepsis during the hospitalization were identified and selected for analysis. The exclusion criteria were a lack of a discharge record or missing sex or age information during hospitalization. We included multiple hospital admissions of a single patient as long as they have met the selection criteria. If the patient was re-hospitalized within 2 days of discharge, the two admissions were regarded as one. Although all of the identified patients suffered from sepsis at admission, we used “sepsis-related” to mean that sepsis was documented at some point in his/her hospitalization.

We identified the patients with any severity of sepsis by ICD-9-CM codes. A patient was regarded as having a sepsis if he/she had a medical record with an ICD-9-CM code of “038.xx” or having a code of “995.91” combined with an infection code (Appendix Table 1 in supplemental materials, http://links.lww.com/MD/E302). In addition, following the study by Angus et al and Weycker et al, patients having both an infection and an acute organ dysfunction (Appendix Table 2 in supplemental materials, http://links.lww.com/MD/E326) were regarded as having a severe sepsis. Among the patients with sepsis or severe sepsis identified, those who were administered norepinephrine or experienced a shock (i.e., ICD9 code of “785.50”, “785.52”, or “785.59”) during hospitalization were considered to have a septic shock. If an admission met the definition of more than one sepsis level, we classified it to the most severe level.

Within these severity groups, we investigated temporal change by dividing all sepsis-related hospitalizations into five 1-year periods (from 2010 to 2014) based on admission date. Furthermore, in order to investigate outcome variation by age, we also divided the patients into 14 age groups with an interval of 5 years (i.e., 20–24, 25–30 . . . , 75–84, 85+).

2.3. Outcomes

The overall healthcare expenditure of sepsis-related hospitalizations was calculated and then divided by 8.6% to estimate the annual national economic burden of sepsis in Taiwan. The temporal change of overall healthcare expenditures and the total hospital costs per patient by severity level were also examined. Furthermore, we investigated cost distribution by dividing the expenditures into 8 categories: ward, medicine, medicine services, therapeutic treatment, laboratory, diagnosis, surgery, and others (including rehabilitation therapy, special medical supply, etc.) The cost data in the study database were reported as points. As the value of one point is close to 1 NT dollar, for ease of calculation and interpretation, we regarded one point as one NT dollar, and all costs were presented as NT dollars (NT $30.17 = US $1[24]). Finally, for all sepsis-related hospitalizations, we investigated the LOS in a hospital (including the days in an ICU) and the LOS in an ICU.

2.4. Statistical analysis

Mean (with standard deviation (SD)) and median (with interquartile range (IQR)) were used to present the continuous variables. The percentages were used to present the discrete variables. Temporal changes were assessed by linear regression. The Kruskal-Wallis test with the post-hoc Dunn test were used compare the different severity groups. In this study, we used the SAS for Windows version 9.4. In addition, a two-tailed P < 0.05 was considered significant.

2.5. Patient and public involvement

This study is a claim database analysis. Patients and the public were not directly involved in the development of this research.

3. Results

3.1. Healthcare expenditure per sepsis-related hospital admission

In total, 62,517 patients with 97,790 sepsis-related hospitalizations were included in the present study. Healthcare expenditures during sepsis-related hospital admission were calculated for each selected patient. For those with multiple admissions involving the same severity level of sepsis, an average was calculated and used in the analysis. The 2014 expenditure data were right-skewed, with a mean of 138.4 ± 84, 85+ thousand NT dollars, and the median was 66.4 (30.3–151.7) thousand NT dollars (Table 1). There was a significant temporal change both in the mean and median (P = .001 and .02, respectively). In 2014, ward fees made up the largest component of costs (24.3%), followed by other fees (21.0%), medicine fees (18.9%), and therapeutic treatment fees (15.8%). The proportions of expenditures were similar over the 5-year observation period.

It was also found that both the mean and median expenditures of the older groups were generally higher than those of the younger ones (Appendix Figure 1 in supplemental materials,
When stratified by sepsis severity, the expenditures of severe sepsis and septic shock significantly decreased over time ($P=0.01$) (Fig. 1). Furthermore, the Kruskal-Wallis test and post-hoc Dunn test results showed that the expenditures increased with severity (all $P<0.0001$). The median (IQR) hospital costs were 39.6 (21.2–74.5), 63.6 (30.2–136.6), and 136.3 (55.5–306.8) thousand NT dollars per admission for sepsis, severe sepsis, and septic shock, respectively, in 2014. In addition to the total cost, the distribution of cost items was slightly different among the three severity groups. Medicine fees

### Table 1
Mean/Median hospital cost per case.

|       | 2010   | 2011   | 2012   | 2013   | 2014   |
|-------|--------|--------|--------|--------|--------|
| Mean ± SD | 163.8 ± 305.4 | 158.6 ± 267.7 | 148.3 ± 261.8 | 144.5 ± 245.1 | 138.4 ± 221.9 |
| Median (IQR) | 74.5 (32.0–181.5) | 71.5 (31.1–170.7) | 67.7 (30.6–156.9) | 68.7 (31.0–155.1) | 66.4 (30.3–151.7) |

Thousand NT dollars.

Figure 1. Temporal change in healthcare expenditure per sepsis-related hospital admission by severity group (A) Median (B) Mean.
made up the largest component of hospital expenditure for sepsis while ward fees represented the majority of the costs in both severe sepsis and septic shock (Appendix Figure 2 in supplemental materials, http://links.lww.com/MD/E328).

### 3.2. Length of stay of sepsis-related hospital admissions

The mean (±SD) and median (IQR) total LOS in the hospital per sepsis-related hospital admission were 18.0 (±27.9) days and 11 (6.0–21.0) days, respectively, in 2014. There was a significant change in mean LOS over time during the study period (P = .0002) but no change in median (P = .18) (Fig. 2). In addition, the total LOS increased with age (Appendix Figure 3 in supplemental materials, http://links.lww.com/MD/E329). The median (IQR) total LOS was 6 (4–12) and 12 (7–21) days for the youngest group and the oldest group, respectively, in 2014. In addition, the differences in total LOS among the three sepsis severity groups were all significant (P < .0001 for all three pairwise comparisons). The median (IQR) was 9 (6–15), 11.5 (7–21), and 15 (7–29) days for sepsis, severe sepsis, and septic shock, respectively, in 2014 (Fig. 3).

Overall, 40.8% of the study patients stayed in an ICU during their hospitalization; the proportions of patients who did so were 11.1%, 35.5%, and 72.0% for sepsis, severe sepsis, and septic shock, respectively. The median (IQR) LOS in an ICU was 7 (3–13) days in 2014, and there was no significant change over time (P = .56) (Appendix Figure 4 in supplemental materials, http://links.lww.com/MD/E330). In addition, the LOS in an ICU increased significantly with severity (P < .0001), with a median (IQR) LOS of 4 (2–6), 7 (3–12), and 7 (3–16) days for sepsis, severe sepsis, and septic shock, respectively (Appendix Figure 5 in supplemental materials, http://links.lww.com/MD/E331).

### 4. Discussion

An extrapolation from our analysis results suggests that an average of 33.5 billion NT dollars, or 3.6% of the national healthcare expenditure, was spent on sepsis-related hospital care in Taiwan annually. The estimated national health expenditure for sepsis-related hospitalizations in this study was higher than those for cancer and diabetes, which were estimated at 23.0 and 1.5 billion NT dollars, respectively. Nevertheless, it is noteworthy that not all costs incurred in sepsis-related hospitalizations were for sepsis treatment. In addition, as sepsis is typically accompanied by comorbidities, the costs of sepsis could have been overestimated. Despite these concerns, the economic burden of sepsis cannot be overlooked.

In the present study, the mean LOS and costs of sepsis-related hospitalizations significantly decreased over time. For comparison purposes, 2 studies that were also conducted in Asia are noteworthy: the total hospital cost of severe sepsis was estimated at 11,390 dollars in China in 2004 to 2005 and at 4498 dollars in Thailand in 2008 to 2011. In 2008, the total hospital cost in Thailand was 5335 dollars, and in 2011 it decreased to 4493 dollars. As for cost distribution, an ICU study conducted in Thailand indicated that the largest cost was “other” (including costs of staff, surgical procedures, and nursing care), followed by medications. The LOS in the hospital was estimated at 22 days in China and 15 days in Thailand with a decrease in the LOS in an ICU over time.

In the present study, the ward fee was the largest cost component, followed by medicine and therapeutic treatment fees. However, in other similar studies, staffing was the greatest costs, followed by medication. The difference may be because our study database did not list staffing as a separate cost item and, instead, embedded it in various other items, including the ward fees. Moreover, ward fees significantly decreased over the 5-year study period, which correlated with the decrease in LOS and total costs per sepsis-related hospital admission over time.

As the major contributor to sepsis-related hospital costs is ward fees, which fees are mainly determined by the LOS, to avoid medical resource waste, we recommend that patients with life-threatening conditions who have been stabilized should leave the ICU as soon as possible and that patients who have been hospitalized for a long time should transfer to a long-term care setting.
facility as appropriate. Currently, there are respiratory care centers and respiratory care wards in Taiwan that can provide care to the patients who need long-term use of mechanical ventilation but do not have other organ dysfunctions. The effectiveness and cost-effectiveness of long-term care facilities for hospitalized septic patients is worth further research.

There are several limitations to our study. First, the severity of sepsis may have been misclassified, because we identified patients by the limited (5 only) diagnostic codes recorded in the database. Second, we could not identify the onset date of sepsis, as the information about diagnosis time or drug administration time was not provided in the database. Therefore, we were unable to tell which costs were incurred after the onset of sepsis, and some of the hospital costs and LOS could have resulted from a cause other than sepsis, thus leading to possible overestimation. Lastly, as the patients were from the same cohort and may have had multiple sepsis-related hospital admissions over the study period, the patient samples for each of the five years in the study period were not independent of each other.

5. Conclusion
In this study, it was estimated that in 2014 the median hospital cost per sepsis-related admission was 66.4 thousand NT dollars. The cost significantly decreased over time and increased with severity of sepsis between 2010 and 2014. In addition, the costs of ward fees and medicine fees were the major components of hospital costs. In 2014, the median LOS in a hospital per sepsis-related admission was 11 (6.0–21.0) days, while the median LOS in an ICU was 7 (3–13) days.
This study provides an updated and better understanding of the cost of sepsis in Taiwan. Nevertheless, due to the limitations of the study database, caution is needed when interpreting the study findings.

**Author contributions**

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