Health Policy and Technology 7 (2018) 149–155

Contents lists available at ScienceDirect

Health Policy and Technology

journal homepage: www.elsevier.com/locate/hlpt

Segmented regression analysis of emergency departments patient visits from Septicemia in Taiwan

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ARTICLE INFO

Article history:
Available online 20 February 2018

Keywords:
Septicemia
Segmented regression analysis
Program evaluation
Policy intervention
Emergency care

ABSTRACT

Background: The protocol for early goal-directed therapy (EGDT) is effective for improving both the costs and outcomes of septicemia treatment, including a significant reduction in case fatality. However, this complicated protocol may have a downside. Furthermore, the Joint Taiwan Critical Care Medicine Committee has launched a nationwide educational program after the publication of the Surviving Sepsis Campaign (SSC) to improve the overall survival rate from septicemia in the emergency care system of Taiwan.

Objectives: To assess the impact of the EGDT protocol and SSC education programs on island-wide septicemia-related emergency department (ED) visits.

Methods: Segmented regression techniques were utilized to assess the differences in annual rates and changes in septicemia-related ED visits between 1998 and 2012. We considered annual incidence of two medical comorbidities as potential confounders: metastatic malignant neoplasms and malignant neoplasms of the lymphatic and hematopoietic tissues.

Results: The EGDT protocol was associated with decreased septicemia-related ED visits in 2002 (level change; $p < 0.001$), while the SSC education program led to a slight increase in septicemia-related ED visits in 2007 (slope change; $p < 0.001$). For the EGDT protocol, the number of patient visits decreased by 32.9% after the protocol was implemented in 2002 compared with the expected number without the intervention. For the SSC education program, the number of patient visits increased by 20.2% (compared with the predicted number) in 2007 after the education program was implemented.

Conclusions: The EGDT protocol and SSC education program were associated with significant immediate changes and lagged intervention effects on island-wide septicemia-related ED visits.

Abbreviations: CVC, Central Venous Catheterization; CVP, Central Venous Pressure; ED, Emergency Department; EGDT, Early Goal-Directed Therapy; EMS, Emergency Medicine Service; GRHAC, Grading Responsible Hospitals for Acute Care; ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification; ICU, Intensive Care Units; MAP, Mean Arterial Pressure; MERS, Middle East Respiratory Syndrome; MOI, Ministry of the Interior; MOHW, Ministry of Health and Welfare; NHI, National Health Insurance; SARS, Severe Acute Respiratory Syndrome; ScvO2, Central Venous Oxygen Saturation; SSC, Surviving Sepsis Campaign.

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https://doi.org/10.1016/j.hlpt.2018.01.010
2211-8837/

Introduction

In recent years, emerging infectious septicemia has been one of the major causes of death in numerous developed countries [1–3]. Particularly, infectious diseases such as severe acute respiratory syndrome (SARS), flu, and Middle East respiratory syndrome (MERS) may be frequently accompanied by septicemia in the early course of illness. According to a report published by the Ministry of Health and Welfare (MOHW) in 2016, septicemia is the thirteenth leading cause of death in Taiwan. The incidence of septicemia has increased over the past few decades [4–7], and numerous studies have explored its pathogenesis [8,9].

The protocol for early goal-directed therapy (EGDT) has been shown to be effective for improving both the costs and outcomes of septicemia treatment, including a significant reduction in case fatality [10]. Usual care for septicemia lacks aggressive assessment and treatment, whereas the EGDT protocol has physicians employ intravenous fluids, vasopressors, packed red-cell transfusions, and dobutamine to achieve prespecified targets for central venous catheterization (CVC) to monitor central venous pressure (CVP) and central venous oxygen saturation (ScvO2), which are monitored via central venous catheterization. Most intensive care units (ICUs) in Taiwan face such a situation. Most ICUs utilize a written form when carrying out EGDT, and the entire form must be completed [11].

However, the EGDT protocol is highly complicated, so there is controversy over whether it actually reduces case fatalities. Moreover, numerous clinical trials have been conducted to provide other evidence-based clinical practice protocols, such as the Surviving Sepsis Campaign (SSC) guidelines, to be delivered in education programs or different protocols control to improve patient outcomes [12–16]. These protocols or education programs aim to change physician behavior and guarantee that critically ill patients receive effective treatment [17–20]. The Joint Taiwan Critical Care Medicine Committee has in fact launched a nationwide education program after the publication of the SSC [21]. This education program involves at least 10 h of training for participating intensivists.

To adequately evaluate the effect of the EGDT protocol and SSC education program on emergency department (ED) to be delivered in education programs patient visits due to septicemia, it is necessary to examine the underlying temporal trend in the incidence of septicemia over the past decade, as has been suggested by several studies conducted in Western developed countries [22,23]. Currently, little is known about the secular trend in ED visits due to septicemia in the general population of Taiwan. It is also necessary to consider the confounding risk factors that might have affected the incidence of septicemia during the same calendar period [24], such as annual incidence of metastatic malignant neoplasms and malignant neoplasms of the lymphatic and hematopoietic tissues [25].

Multiple studies have indicated that both the EGDT protocol and SSC education program are associated with survival [10,12–20]. Particularly, research in Asia has shown that implementation of EGDT and SSC were associated with improvements in outcome and survival rates. However, there has been little research on awareness of the diagnosis of patient visits for septicemia in the ED during implementation of EGDT and SSC, or how patient visits for septicemia are influenced by implementation of these programs. In the current study, we expected that EGDT protocol and SSC education program would increase awareness of the diagnosis of patient visits from septicemia in the ED, which in turn would increase the number of visits due to septicemia. We used segmented regression to determine the immediate impact of the EGDT protocol and SSC education program on the annual rates of septicemia-related ED visits by comparing the visit rates before EGDT implementation (1998–2001), during EGDT and SSC implementation (2002–2005), and after SSC implementation (2006–2012).

Methods and materials

Data source and study population

The National Health Insurance (NHI) program in Taiwan was launched on March 1, 1995. Taiwan's NHI scheme can be viewed as the most important social milestone in recent years, and is generally regarded as the most extensive and satisfying public investment in the country. The Health Promotion Administration of the MOHW publishes the NHI Health Statistics Annual Report to enhance understanding of the NHI system. We used this Report, which includes data on all ED visits indexed by the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) Codes, to assess the number of visits (disease code and ID card number were key data points allowing for patient-centered review and removal of duplicate information) [26]. The publicly available datasets for this report can be downloaded in an aggregate format—namely, contingency tables consisting of the number of ED visits by sex, age (in one-year intervals), and ICD-9-CM codes for each year. This aggregate data format is managed and validated by the Department of Statistics of the Ministry of the Interior (MOI) of Taiwan.

All patients aged 0–65 years or older who were diagnosed with septicemia (ICD-9-CM code group: 038) in the ED in 1998–2012 were included in the analysis. In the Poisson regression model, we estimated the effect of the main independent variables on the outcome variable. Male sex (defined as the proportion of men) was found to significantly influence the level of the outcome variable—in other words, every one-unit increase in the proportion of males. The category variable had a relative effect on the outcome variable. We stratified age groups as follows: 0–19, 20–39, 40–64, and $\geq$ 65 years. We used the ED visits by younger adults (aged 20–39) as a comparison group in the following analysis.

Outcome and derived variables

The outcome variable, denoted as Y_i (i =1998–2012), was the number of septicemia-associated patient visits to the ED for the three calendar periods**:** 1998–2001, 2002–2005, and 2006–2012, which represent the years before EGDT, during EGDT and SSC implementation, and after their implementation, respectively. Visit rate per year, per 100,000 persons, was defined as follows:

$$\frac{\text{The number of patient visits to the ED per year}}{\text{Mid} - \text{year population per year}} \times 100,000$$

The inverse formula for practice outcome was as follows:

$$\text{The number of patient visits to the ED per year} = \frac{\text{Visit rate per year per 100,000 persons}}{100,000} \times \text{Mid} - \text{year population per year}$$

We used de-identified data from the NHI patient-centered review claims for septicemia from 1998 to 2012. We identified the changes in the secular trend of septicemia-related ED visits after implementation of the EGDT protocol and SSC education program in order to determine the impact of these interventions both immediately and over time. We also assessed whether factors other than the interventions could explain the change.

The covariates related to the outcome variable included male sex (proportion of men in the mid-year population covered by the NHI program), age (in four groups), and presence of medical comorbidities (malignant neoplasms [ICD-9-CM codes: 140–208]) [27].

Statistical analysis

All data were analyzed using *R* (version 3.3.2) for Windows [28]. All analyses were performed at a two-sided significance level of 0.05. The number of septicemia-related ED visits (count data) was estimated using Poisson regression models. Poisson regression models were also used to estimate the difference in the number of septicemia-associated patient visits between pre- and post-intervention. Regression dummy variables were used to indicate the different segmented periods (the pre-intervention periods were coded as 0 and the post-intervention periods as 1), and the difference in the number of septicemia-related ED visits between these periods was estimated using the regression coefficient. Besides graphically displaying the number of septicemia-related ED visits for the overall population and each age group, we performed a descriptive analysis of septicemia-related ED visits by sex, age group, and the presence of medical comorbidities for the three observation periods separately. The proportion of patients with septicemia who had a concurrent diagnosis of malignant neoplasm was calculated for each calendar period separately. Chi-square tests were used to examine differences in the distribution of sex, age, and major comorbidities among the three observation periods, assuming that each included patient had only one medical comorbidity during the entire study period.

Next, we used segmented regression analysis of interrupted time series [29] to estimate the associations between number of septicemia-related ED visits per year, intervention, and time (period) after intervention using multiple linear regression models. Segmented regression models can illustrate more than one intervention at a time. For instance, we might be interested in the effects of the different components of a larger intervention introduced at different times. The level and slope are the parameters that define the intercept and slope, respectively, of each successive segment of the time series. The level parameter was defined as the expected or mean number of patient visits at a particular time interval, and the slope parameter quantifies the change in the number of patient visits over a single unit of time (per year). A disjointed or interrupted intervention effect is reflected in the step-change (change in intercepts) in the outcome variable between any two consecutive periods after the intervention. Before-and-after changes in the number of septicemia-related ED visits were estimated by testing differences in the slopes between the pre- and post-intervention periods. The specific estimators of the segmented regression include *time* (calendar years before intervention), *intervention* (the index year(s)), and *time after intervention* (calendar years after intervention). The multivariate linear regression model containing the two change points (interventions) is as follows:

$$\begin{aligned} Y = {} & \beta_0 + \beta_1 time + \beta_2 intervention_1 \\ & + \beta_3 time\ after\ intervention_1 + \beta_4 intervention_2 \\ & + \beta_5 time\ after\ intervention_2 + \beta_6 male\ sex + \beta_7 age \\ & + \beta_8 malignant\ neoplasm + random\ error \end{aligned}$$

Expressing intervention effects

We can express the results of the segmented regression model by reporting level and slope changes, or by comparing the estimated post-intervention values for the outcome with the values estimated at a particular time based on the baseline level (intercept) and slope only (if the intervention had been implemented). In this study, we calculated the absolute difference in predicted outcomes between when the intervention was implemented and when it was not, which we deemed as indicative of an intervention effect.

Results

Between 1998 and 2012, there were 521,064 septicemia-related ED visits, more than 50% of which were for men (53.1%, Table 1). Middle-aged patients (aged 40–64 years) and older patients (aged ≥ 65 years) made up 27.3% (*N* = 142,166) and 49.7% (*N* = 259,081) of the visits, respectively. Older patients (aged ≥ 65 years) were the predominant source population for the different calendar periods (Table 1). A predominance of male and elderly patients was consistently observed across the three calendar periods (Table 1).

Overall, septicemia-related ED visits increased from 20,565 in 1998 to 43,957 in 2012, representing a total increase of 23,392 visits during the 15-year observation period. Note that septicemia-related ED visits did not always increase throughout the study period (1998–2012). The mean annual increment was 1670 visits, with an average annual growth rate of 8.3% (95% CI: -6.8–23.4%).The mean annual growth rate for male and female visits was 2.2% (95% CI: -13.4–17.7%) and 2.1% (95% CI: -13.0–16.7%), respectively, during the 15-year observation period. Only the 0–19 age group showed negative growth in septicemia-related ED visits; for the other three age groups, 20–39, 40–64, and ≥ 65 years, the mean annual growth rates for visits were 0.05% (95% CI: -28.2–28.2%), 3.4% (95% CI: -15.4–22.3%), and 4.1% (95% CI: -6.5–14.7%), respectively.

In this study, the number of septicemia-related ED visits (count data) was estimated using the Poisson regression model. This means that the estimated coefficients of the segmented regression model were transformed; these results are presented inTable 2. As shown in Table 2, there was a significant change point for the intercepts (i.e., the level parameter) and a statistically significant overall trend in the number of patient visits ($P < 0.0001$). In particular, the level change in septicemia-related ED visits was significant for the 0–19 group as well as for middle-aged and older adult groups (for level change, both $P < 0.0001$).

Fig. 1 shows the fitted numbers of septicemia-related ED visits by age group across the three calendar periods. Both the observed and the model-based estimates are shown for comparison. Variation in the overall septicemia-related ED visits over the 15-year period mainly resulted from the decreases observed in all age groups for 2003–2006 and the increases in the middle-aged and older adult groups between 2008 and 2012, whose upward trends appeared parallel to each other (Fig. 1).

Fig. 2 shows the significant estimated change points (for 2002 and 2007) for the two interventions (EGDT protocol and SSC education program). After comparing septicemia-related ED visits of the intervention period, there were one-to two-year lags in the effect of the intervention. Theoretically, the intervention effects might occur over several periods, which embed in rolling periods. To better quantify the early impact of the EGDT protocol and SSC education program, we additionally compared model-predicted ED visits with and without the intervention to confirm the intervention effects. In expressing the results of the segmented regression modeling, we either report the level and trend changes in ED visits following implementation of the EGDT protocol and SSC education program (see Table 2) or compare estimated numbers of ED visits in the post-intervention period when the intervention was implemented and when it was not (i.e., the counterfactual value). We considered the Poisson regression models for 2002 and 2007 to express the intervention effects, respectively. In practice, the intervention effect can be expressed as the absolute difference in predicted visits between when the intervention was implemented and the counterfactual value. Alternatively, we can present the ratio of the absolute difference value to the counterfactual value. We can express the ratio as a percentage increase or decrease by multiplying by 100.

To estimate the intervention effect of the EGDT protocol, we used the following regression equation (the expected results are shown in Table 2):

Table 1
Number of ED patient visits.

Characteristics	Intervention Phases: Overall	EGDT (1998–2001)	During EGDT and SSC (2002–2005)	Post-SSC (2006–2012)
	Total $N = 521{,}064$	Total $N = 123{,}822$	Total $N = 141{,}036$	Total $N = 256{,}206$
Gender*				
Male	53.1%	53.3%	53.2%	52.9%
Female	46.9%	46.7%	46.8%	47.1%
Age*				
0–19	11.4%	16.8%	17.6%	5.3%
20–39	11.6%	12.8%	12.8%	10.3%
40–64	27.3%	26.8%	25.8%	28.3%
≥ 65	49.7%	43.6%	43.8%	56.1%

Chi-square tests of significance were used to examine differences in the distribution of sex, age during the entire study period.
* Significant at the 0.05 level (*P*-value< 0.0001).

Table 2
Parameter estimates, standard errors, and *P*-values from full-segmented regression model predicting annual numbers of septicemia-related ED visits.

Segmented regression model	Coefficient	95% CI (LL, UL) Patient-visits	*P*-value
Intercept (Baseline level) β_0	16.89	(14.92–19.13)	< 0.0001*
Baseline slope β_1	1.35	(1.34–1.35)	< 0.0001*
Level change (EGDT)β_2	1.04	(1.02–1.05)	< 0.0001*
Slope change (EGDT)β_3	0.65	(0.64–0.65)	< 0.0001*
Level change (SSC)β_4	1.04	(1.02–1.05)	< 0.0001*
Slope change (SSC)β_5	1.16	(1.15–1.16)	< 0.0001*
Male vs. Female β_6	10,280.46	(8082.92–13075.45)	< 0.0001*
Age β_7			
Level change for adults aged 0–19 years	0.73	(0.72–0.74)	< 0.0001*
Level change for adults aged 40–64 years	1.10	(1.09–1.12)	< 0.0001*
Level change for adults aged ≥ 65 years	0.83	(0.81–0.86)	< 0.0001*
malignant neoplasm β_8	1.00	(1.00–1.00)	< 0.0001*

CI=confidence interval; LL=lower level; UL=upper level
The coefficient had been transformed by the exponential function
* Significant at the 0.05 level.

$$g(\hat{Y}_{2002(\text{without intervention})}) = \hat{\beta}_0 + \hat{\beta}_1 \times 5(\textit{2002 is coded as 5}\text{ while 1998 is coded as 1})$$
$$+\ \hat{\beta}_2 \times 1(\text{intervention}_1 = 1) + \hat{\beta}_3 \times 1(\text{time after intervention}_1 = 1)$$
$$+\ \hat{\beta}_4 \times 0(\text{intervention}_2 = 0) + \hat{\beta}_5 \times 0(\text{time after intervention}_2 = 0)$$
$$+\ \hat{\beta}_6 \textit{male sex} + \hat{\beta}_7 \textit{age} + \hat{\beta}_8 \textit{malignant neoplasm}$$
$$= \hat{\beta}_0 + \hat{\beta}_1 \times 5 + \hat{\beta}_2 \times 1 + \hat{\beta}_3 \times 1 + \hat{\beta}_6 \textit{male sex} + \hat{\beta}_7 \textit{age} + \hat{\beta}_8 \textit{malignant neoplasm}$$

In this equation, g is a link function that connects the outcome and independent variables. Next, to estimate the impact of the EGDT protocol not being implemented, we used the following regression equation:

$$g(\hat{Y}_{2002(\text{without intervention})}) = \hat{\beta}_0 + \hat{\beta}_1 \times 5$$
$$+\ \hat{\beta}_2 \times 0(\text{intervention}_1 = 0) + \hat{\beta}_3 \times 0(\text{time after intervention}_1 = 0)$$
$$+\ \hat{\beta}_4 \times 0(\text{intervention}_2 = 0) + \hat{\beta}_5 \times 0(\text{time after intervention}_2 = 0)$$
$$+\ \hat{\beta}_6 \textit{male sex} + \hat{\beta}_7 \textit{age} + \hat{\beta}_8 \textit{malignant neoplasm} = \hat{\beta}_0 + \hat{\beta}_1 \times 5 + \hat{\beta}_6 \textit{male sex} + \hat{\beta}_7 \textit{age} + \hat{\beta}_8 \textit{malignant neoplasm}$$

The ratio of the outcome's association with the EGDT protocol is calculated as $\hat{Y}_{2002(\text{with intervention})} - \hat{Y}_{2002(\text{without intervention})}/\hat{Y}_{2002(\text{without intervention})}$, and can be expressed a percentage change by multiplying by 100.

For the EGDT protocol, we found that the number of septicemia-related ED visits would decrease by 32.9% (calculated by the ratio of the outcome: (46,476–69,318)/69318≅0.329 × 100%) in 2002 if the protocol were implemented, compared to if it were not. For the SSC education program, the number of septicemia-related ED visits would increase by 20.2% in 2007 (calculated by the ratio of the outcome: (32,414–26,946/26,946) ≅ 0.202 ×100%) if the education program were implemented.

Discussion

We performed a secondary analysis to evaluate the temporal changes in septicemia-related ED visits and the intervention effects of the EGDT protocol and SSC education program. In this

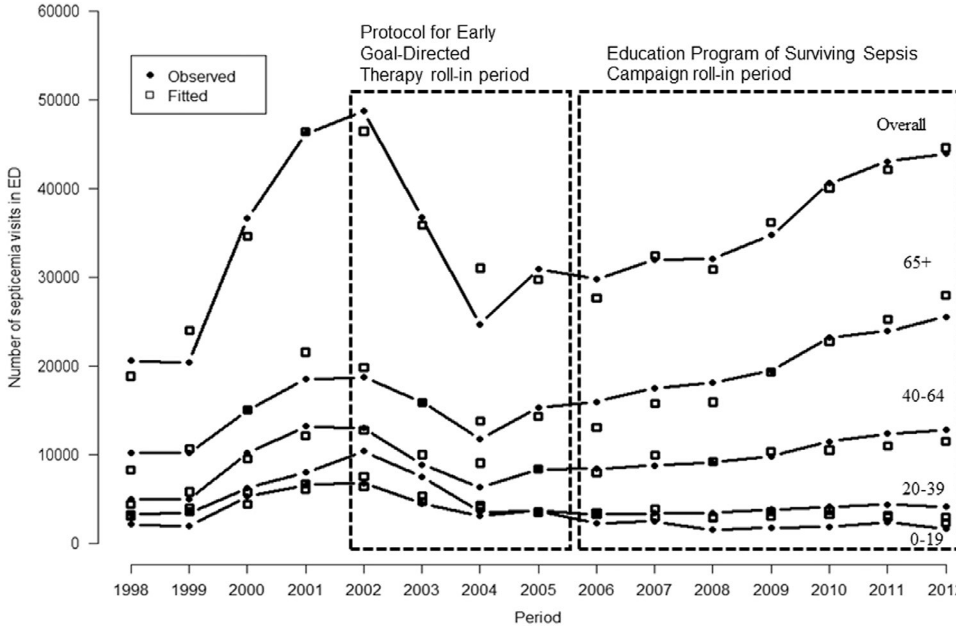

Fig. 1. Number of septicemia-related ED visits between 1998 and 2012.

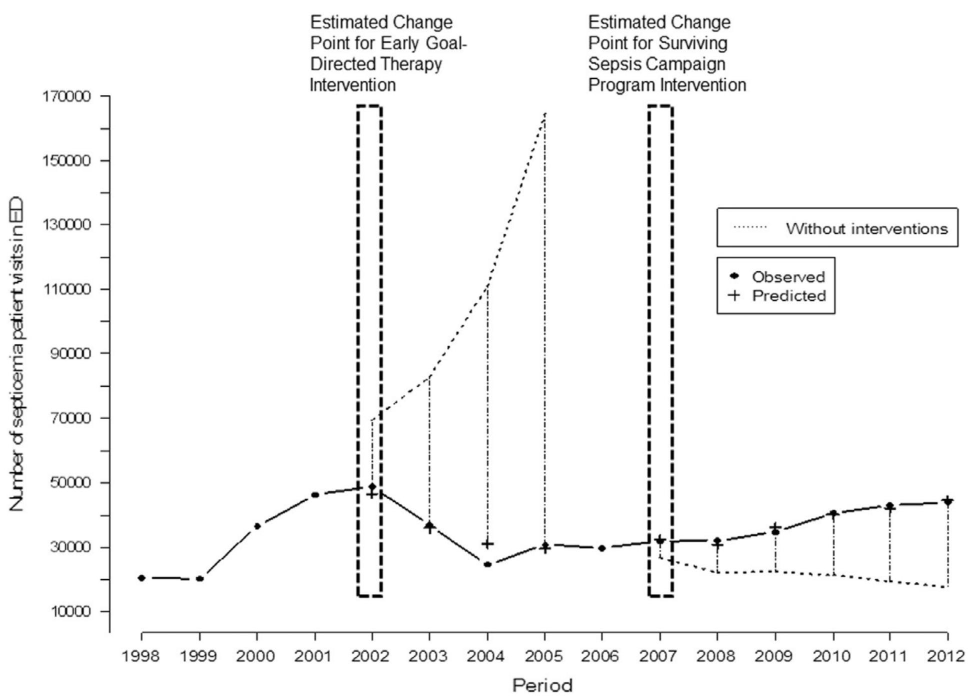

Fig. 2. Plot effects of the intervention on the primary outcome measure using segmented regression model.

study, we compared changes in the expected level and growth rate of septicemia-related ED visits using insurance claims data. We also quantified the potential intervention effects based on comparisons between model-predicted values following implementation of the intervention and when the intervention was not implemented. Moreover, we identified the impact model as a level and slope change model [30].

We observed an immediate decrease in septicemia-related ED visits in the first post-intervention year (2003); however, it is impossible for the septicemia incidence rate to decrease so dramatically within such a short time frame when looking at the worldwide trend. In the United States, the National Hospital Discharge Survey found that the septicemia incidence rate increased from 0.83 to 2.4 per 1000 population between 1997 and 2000 [31]. Discharge data from the Nationwide Inpatients Sample found that the hospitalization rate for septicemia ranged from 0.65 to 1.35 per 1000 population in 1993–2003 [32]. The findings can be attributed to a gap between the true and reported incidence of septicemia, a phenomenon that might be explained by advances in diagnostic devices used by hospital infection control teams [33], a higher likelihood of ED physicians to make septicemia-related diagnoses (i.e., surveillance bias), and overall increased awareness of septicemia-related symptoms and signs by the general population, including at-risk patients and their family members. Indeed, we found that the number of septicemia-related ED visits was about the same in 2012 as in 2002.

Since 2001, randomized, double-blinded studies have indicated that EGDT can improve mortality rates in patients with severe septicemia and septic shock. The EGDT protocol can be implemented within six hours of a diagnosis of severe sepsis or septic shock and involves maintaining the airway, placing CVC to maintain a CVP of 8–12 mmHg, a mean arterial pressure (MAP) of greater than 65 mmHg, an ScvO2 of greater than 70%, more than half of the weight per ml of urine (urine output $\geq$ 0.5 mL/kg/h), etc. However, recent studies have shown no statistically significant difference between EGDT and usual treatment in 28-day, 60-day, or a year in hospital mortality [34–36].

Despite the implementation of interventions designed to improve critically ill patients' overall survival rates for septicemia, we observed a persistent growth in septicemia-related ED visits over time. However, these visits showed differing trends after the two interventions. The EGDT protocol is regarded as so complicated that it remains controversial whether it actually reduces case fatalities. On the other hand, the SSC guidelines can be delivered as part of an education program, which has been shown to improve outcomes. Potentially counter-intuitive to these findings is the finding that there were fewer estimated septicemia-related ED visits when the SSC intervention was not implemented. This can be explained by an increase in physician awareness. Physicians' awareness of septicemia-related symptoms might be promoted through education programs. Chen et al. investigated the effect of a nationwide educational program based on the SSC guidelines on hospitalizations for severe sepsis. The annual severe sepsis incidence rate increased slightly after the program (by 0.4 on average). Furthermore, physicians' clinical practice of sepsis care and patient mortality rate for severe sepsis both decreased [37]. Thus, it is important to evaluate the effectiveness and outcomes of the SSC education program.

One finding that is relevant to public health is that the incidence of emergency septicemia differed between males and females [38]. In this study, we noted that ED visits by older adults ($\geq$ 65 years) might serve as a sentinel event for the observed substantial growth in septicemia-related ED visits. Therefore, we suggest further prospective investigation of older patients after their discharge from the ED. This prospectively collected information might provide valuable insights on clinical, psychosocial, and EMS risk factors for repeated ED attendance by the elderly population. Such studies might also generate an evidence base for evaluating the success of the SSC education program in meeting the acute healthcare needs of this critical population.

In Taiwan, because the size and infection situation of each hospital differ, the implementation times of the interventions are not the same for each hospital. However, the emergent rescuer responsive hospitals for acute care must implement SSC quickly because of requirements by the MOHW—namely, the Grading Responsible Hospitals for Acute Care (GRHAC) audit program, which was implemented from 2007 to 2009 [39]. The MOHW has annually audited and updated the list of responsible acute care hospitals since 2009. The current lag between the implementation of the SSC intervention and its actual rollout, which is about three years, allows for a dramatic growth in septicemia ED visits to the ED. With the implementation of the SSC program, public health decision-makers might be able to increase the period for protocol administration, and thereby better evaluate the impact of the SSC intervention on septicemia-related ED visits. Therefore, it might be important to consider the length of the intervention period when developing health care plans that can help public health programs achieve their goal.

This study has several limitations. First, the covariates were limited in number and were rather specific categories since there is a shortage of individual-level claims data. Therefore, there is a potential risk of unmeasured and uncontrolled confounding variables in the current analysis. Second, we investigated the impact of the EDGT protocol and SSC education program on septicemia-related ED visits between 1998 and 2012 due to data availability. Besides, the relatively short pre-intervention period (1998–2001 and 2002–2005) might have limited the statistical power for the segmented regression analysis to detect minimal changes in the level or slope parameters [29]. Third, the aggregated format datasets make it difficult to completely adjust for confounders (such as comorbidities, education levels, or lifestyle) in the multivariable linear regression model. Further completed studies need to resolve this limitation when using individual data. Fourth, the number of cases of septicemia was relatively low (Table 1) compared to another study using aggregate claims data (which reported the incidence rates for severe sepsis) [37]. One potential reason is the coding method of sepsis we adopted. Gender differences might be another reason: For example, women might be less likely to develop septicemia than men [40].

Previous studies have demonstrated that the implementation of the EGDT protocol and SSC education program in developed countries is associated with improved outcomes, including shorter length of stay in the ICU and hospital, and even decreased mortality [10,17–19]. However, the impact of these interventions on ED visits for septicemia was unclear. The present study demonstrated that the EGDT protocol and SSC education program were associated with significant immediate changes and lagged intervention effects on island-wide septicemia-related ED visits. We successfully demonstrated these findings through segmented regression analysis.

Acknowledgments

All authors report no conflicts of interest relevant to this article. We have no financial support.

Author Statements

Funding

The authors declare that there is no funding supporting.

Competing interests

The authors declare that there are no conflicts of interest.

Ethical approval

Not required.

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