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Predicting emergency departments visit rates from septicemia in Taiwan using an age–period–cohort model, 1998 to 2012

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Abstract

The aim of this study was to determine the age–period–cohort (APC) effects on the rate of infection-related emergency department (ED) visits from septicemia for predicting the same in recent periods.

In our study, we investigated the longitudinal trends in septicemia-related visit rates. Using an APC model to decompose the septicemia visit rates into the effects of age, time period, and cohort, and examine whether their effects varied by sex.

The septicemia ED visit rate was classified as the International Classification of Disease Code 038 by primary and secondary diagnosis between 1998 and 2012.

In both males and females, the visit rate of septicemia showed an increase from 2003 through 2012. An increase in septicemia visit rate after 2003 was observed in all age groups. An APC model indicated a reversal increasing period effect, which increased prominently from 2003 to 2012 in both males and females. The age effect showed an increasing trend. The cohort effect tended to show a slight oscillation from 1913 to 1988. With reference to the prediction of the logarithms of the age-specific 5-year visit rates, we observed that the younger cohorts exhibited a slightly increasing trend, as compared to the older cohorts.

The period effect can explain the increase in septicemia visit rates, suggesting the role of screening for septicemia. Furthermore, it is well known that aging is a relevant risk variable for infectious diseases. The present study concludes that the aged population exhibited a strong increasing future trend for septicemia-related ED visit rates.

Abbreviations: APC = age, period, and cohort, CD = ambulatory care expenditures by visits, ED = emergency department, EMS = emergency medical service, HCAI = healthcare-associated infections, ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification, ID = identification, MOHW = Ministry of Health and Welfare, NHI = National Health Insurance, NHIRD = National Health Insurance Research Database, NHS = National Health Service, OEMQ = optimizing emergency medicine quality.

Keywords: age–period–cohort predicting, emergency department visit, septicemia

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Authors' contributions: I-ST created the research idea, performed the analysis, wrote the results and discussion, and contributed to the literature review. S-HL assisted in the literature review and supported the analysis and results interpretation. K-FC participated in critical discussion, contributed to analysis, and aided in editing of the manuscript. J-CC participated in the study design and revised the manuscript. YTC helped cope with the NHIRD dataset. C-HH, C-JL, C-YC, S-CH, and Y-MW provided clinical suggestions and helped revise the manuscript. I-ST prepared the manuscript for submission. All authors read and approved the final manuscript.

Ethical approval: Ethical approval is not required since this study is a secondary analysis of septicemia-associated ED visits data available in the public domain.

Informed consent: The septicemia-associated ED visits data available to the public are not individually identifiable, and therefore their analysis would not involve human subjects. Informed consent is not required for this study.

Availability of data and materials: The dataset supporting the conclusions of this article is included within the article (refer to table, Supplemental Content, which records the septicemia-related ED visit rates calculated by mid-year population and visit number of patients, http://links.lww.com/MD/B451).

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1. Introduction

The past 150 years has seen a progressive decline in premature deaths associated with infectious diseases such as septicemia. This decline is thought to be the result of several contributing factors, such as technological advances in the fields of medicine (vaccination), engineering (sanitation), and administration (healthcare delivery).[1] These factors would affect all individuals in a given cohort, depending on the given age of the cohort.

According to this concept, life expectancy may be embodied by the maximum survival rate over a long period. However, there are several types of bacteria that potentially threaten our survival.[2] For example, septicemia is a life-threatening infection caused by large bacteria or germs present in the blood.[3] Indeed, the emergency medical service (EMS) system has to bear the brunt of life-threatening infections.[4] However, in case of early septicemia or with the presence of certain host factors, clinical manifestations may be hidden, making it difficult to clinically diagnose the infection. Since 2004, the national campaign was launched to devote toward decreasing the incidence of health-care-associated infections (HCAI) in the United Kingdom; another campaign was launched during 2007.[5] These campaigns were proposed to improve infection control and awareness in English National Health Service (NHS) hospitals. It is important to require robust methods, such as interrupted time series analysis, used to assess (or evaluate) the impact of national and regional HCAI interventions on rates of meticillin-resistant *Staphylococcus aureus* and meticillin-sensitive *S. aureus* bacteremia in NHS acute hospitals in the East Midlands of the United Kingdom. In addition, initial hospitalization for severe sepsis in Taiwan, the age-standardized annual incidence rates of first episodes increased from 135 per 100,000 in 1997 to 217 per 100,000 in 2006, with annual growth percent about 3.9%. Based on direct observations of the long-term trends in septicemia-associated hospitalization from 1997 to 2006 in Taiwan, it is important for physicians to observe a sustained period effect on hospitals' capacity for managing patients.[6]

In epidemiology, age–period–cohort (APC) model has been used for describing the secular trend in disease incidence or mortality.[7–12] A 3-factor multiplicative model separates effects from APC for the incidence or rates of a particular event. Age effects are associated with the outcome of time, so change in the number of outcome (deaths caused by cancer). Period effects can affect all ages simultaneously over time. Birth cohort effects involve changes across groups with the same birth year who presented the same outcome during the same period. These effects separated by APC model may provide epidemiologists with important insights on identifying health determinants[13]; hypothesis testing[14]; or potential sources of heterogeneities in the literature.[15] However, less effort has been made previously to the outcome-forecasting potential of the APC model.

In our study, we investigated the longitudinal trends in the rate of infection-related emergency department (ED) visits, focusing only on septicemia. We decomposed the septicemia-related ED visit rates to identify the effects of age, time period, and cohort, and examined whether these effects varied by sex.

We investigated septicemia-related visit rates because the capacity of the emergency physicians to provide medical services has not only been linked with patients' health status, but it has also been associated with the labor provided for critical infection diseases. Thus, in this paper, we examined the longitudinal trends in the septicemia-related visit rate, attempted to predict the potential increase in visit rates due to infections, and aimed to provide generalized etiological insights by utilizing an aggregated report obtained from a claims database of the National Health Insurance (NHI) program in Taiwan.

2. Methods

2.1. Data sources

The NHI system is compulsory and covers all citizens except prisoners. The NHI research database (NHIRD) covers nearly all (99%) inpatient and outpatient claims for its population of approximately 23 million which has been used widely in various studies. The NHIRD provided encryption participated patients' identification (ID) numbers, sex, date of birth, dates of hospital admission and discharge, medical institutions providing the services that are indexed by the International Classification of Diseases (ICD), 9th Revision, Clinical Modification (ICD-9-CM) Codes. The Health Promotion Administration of the Ministry of Health and Welfare (MOHW) in Taiwan has maintained electronic databases of all annual ED visits according to relevant emergency case files as ambulatory care expenditures by visits (CD), since 1998 to 2012. The duplicated visit with the same diagnostic codes from the same patient each year such as repeated visit or interhospital transfer are excluded specifically to facilitate the calculation of the annual disease burden on each patient. Split-year treatment occasionally has little effect on the trend. The publicly available datasets can be downloaded in the aggregated format of contingency tables consisting of numbers of ED visits by patient (ID number for the key calculation made by households and remove duplication for each year), sex, age (in 1-year intervals), and ICD-9-CM codes for each year.[16] The septicemia ED visit rate was classified as the ICD Code 038 by primary and secondary diagnosis.

There were 14 age groups ranging from 20 to 85+ years (defined as 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, and ≥85 years) and 3 time periods (defined as 1998–2002, 2003–2007, and 2008–2012) with 16 cohorts (defined as1913–1917, 1918–1922, 1923–1927, 1928–1932, 1933–1937, 1938–1942, 1943–1947, 1948–1952, 1953–1957, 1958–1962, 1963–1967, 1968–1972, 1973–1977, 1978–1982, 1983–1987, and 1988–1992). From these, we calculated the age-specific and the age-adjusted (using the 2000 World Standard Population)[17] visit rates. The present study was approved by the Institutional Review Board of Chang Gung Memorial Hospital (no. 103-6269B).

2.2. Statistical analysis

We modeled septicemia-related ED visits by using Poisson APC models which decomposes visit rates over time by age, time period, and cohort. In more detail, visit rates per year, per 100,000 persons, were 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 inversion formula for practice outcome, number of patient visits to the ED per year, was calculated as follows:

$$\frac{\text{Visit rate per year per } 100,000 \text{ persons}}{100,000} \times \text{Mid} - \text{year population per year}$$

The framework of APC modeling has been applied to describe the secular trend in patient visit.[18] It is reasonable to perform

Table 1

Case numbers of ED patient visits from septicemia.

Characteristics	Overall Total, % N=179,975	1998–2002 Total, % N=60,538	2003–2007 Total, % N=53,618	2008–2012 Total, % N=65,819	P
Gender					
Male	92,943 (51.6)	30,861 (50.9)	27,424 (51.1)	34,657 (52.7)	<0.0001*
Female	87,032 (48.4)	29,677 (49.1)	26,193 (48.9)	31,162 (48.3)	
Age					
20–39	6452 (3.6)	2387 (3.9)	1907 (3.6)	2158 (3.3)	<0.0001*
40–64	23,141 (12.9)	8872 (14.7)	6719 (12.5)	7551 (11.5)	
≥65	150,382 (83.5)	49,279 (81.4)	44,992 (83.9)	56,111 (85.2)	

ED = emergency department.
* Significant at the 0.05 level.

APC model to investigate the factors for visit rates among septicemia-related ED patients, because age is related to visit rates. These results can provide clues for testing the hypotheses of issue.

In this study, a log-linear Poisson model for the rates was fitted to the data for both genders separately by assuming a Poisson distribution for the number of septicemia-related visits. The particular parameter estimates was maximum likelihood estimates, which were used by free R software (version 3.1.0) (Vienna, Austria) [19] for analysis.

Estimates of the parameters of the above APC model were set out to predict the septicemia-related ED visit rate. There are 2 prediction scenarios in this study. In this context, it was unnecessary to extrapolate the age effects. The period effects are extrapolated using a quadratic regression into the time period, 2013 to 2017. The cohort effects were extrapolated using a cubic multiple-regression on the birth cohorts from 1991 to 1995. Finally, we combined the age effects and extrapolated period and cohort effects to obtain the point estimates of visit rate prediction (marked A). For a comparison, using a quadratic regression to extrapolate the observed log age-adjusted visit rates themselves into the time period, 2013 to 2017 (marked B).

To check model fitness, we plot deviance residuals, progressively from the null model, the age model, the age-period model, and then to the APC model.

3. Results

From 1998 to 2012, there were 179,975 septicemia-related ED visits by adults aged 20 years or older, out of which, more than 50% were males (51.6%, Table 1). Middle-aged patients contributed to 12.9% of the sample (N=23,141) and 83.5% (N=150,382) of the septicemia-related ED visits, whereas the elderly (age ≥ 65 years) comprised the predominant patient population (N=173,523, 96.4%, Table 1). This predominance of male and elderly patients was consistent across the 3 observation periods (Table 1).

Figure 1 presents the APC effects for males and females. It is evident that the age effects are quite similar for both the sexes. Septicemia-related ED visits increased exponentially with age in both sexes. There was an upturn in the period effects in both sexes, steeper in male than female for recent period. The birth cohort curves had notable downward inflections in both sexes in about 1938, earlier in female than male.

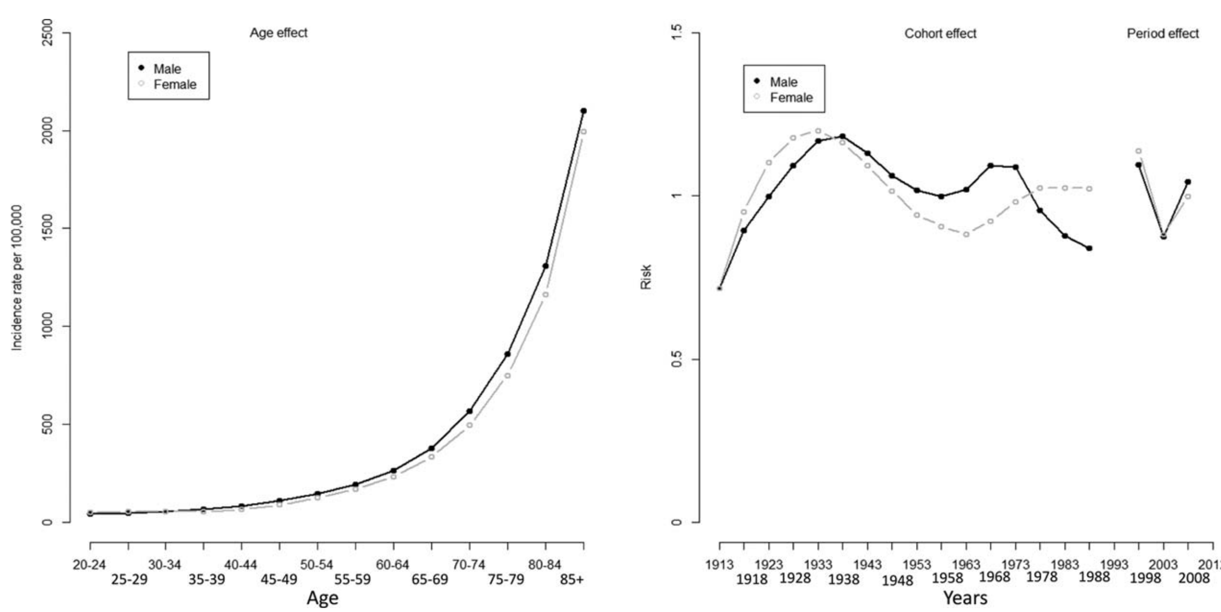

Figure 1. The effect of septicemia-associated emergency department visits rates by age, time period, birth cohort for male and female in Taiwan, 1998 to 2012.

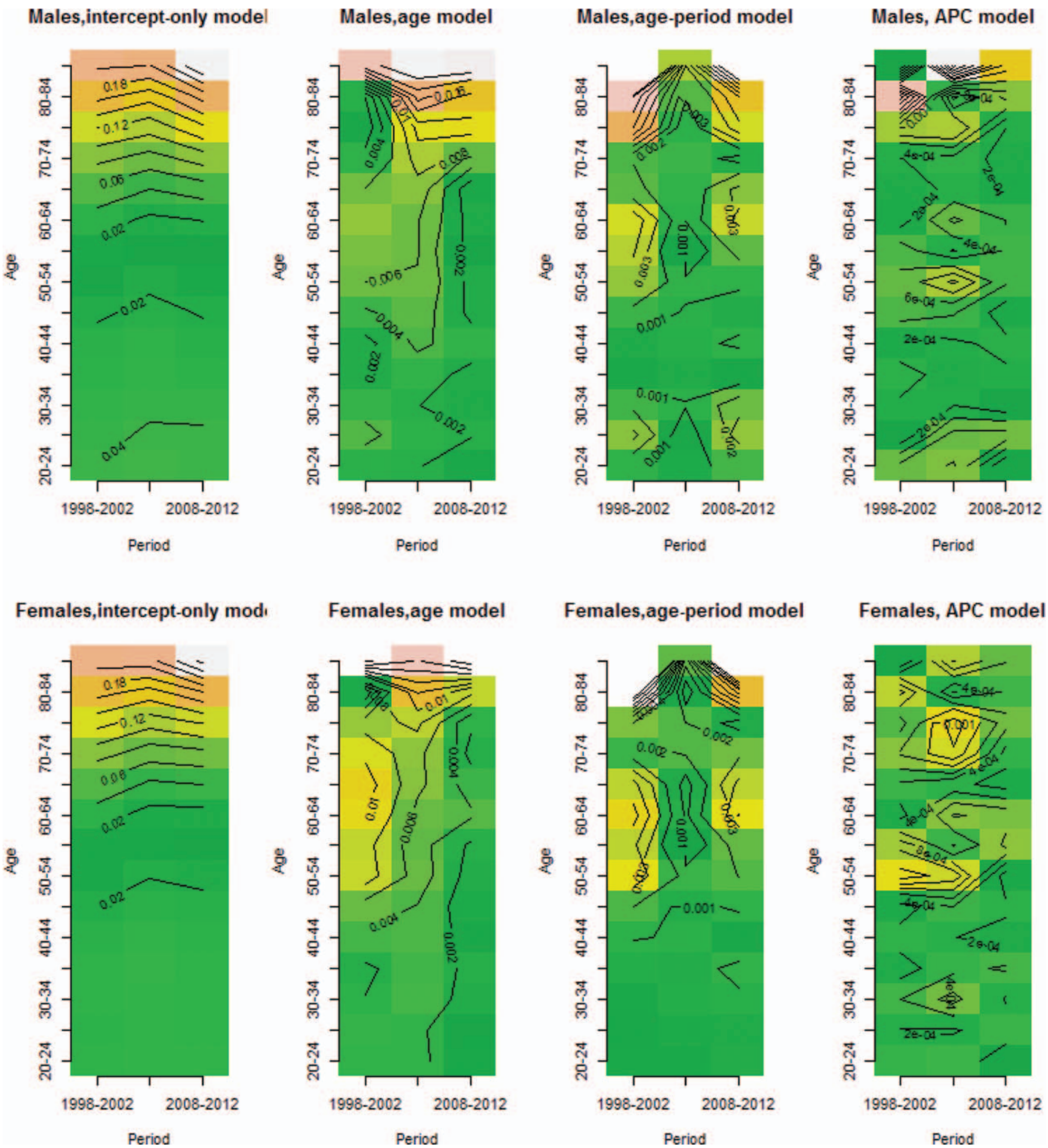

Figure 2. Residual plots for the null models, the age models, the age-period models, and the age–period–cohort models.

Figure 2 displays the deviance residual plots for males (upper panels) and females (lower panels). We found that the systematic patterns existed in residuals, most obviously in the null models (leftmost panels) progressively disappear in the age model (panels in second column) and the age–period model (panels in third column). As for the residual plots of the APC model (rightmost panels), it can be seen that no systematic pattern is observed.

Figure 3 presents the logarithms of the age-specific 5-year visit rates (for aforementioned 14 age groups) for males and females, respectively. It also presents the 5-year visit rate predicted values based on Scenario A (dash lines). It is evident that the age-specific visit rates continued to increase from 2008 to 2012, and this trend will continue for the next 5-year period of 2013 to 2017 in both genders.

Figure 4 shows the age-adjusted visit rates of age categories 20 to 39, 40 to 64, and ≥65 years, respectively. The predicted values using the APC model have also been shown in Fig. 4, Scenario A. It is clear that the trend increases dramatically in the period 2013 to 2017 for the elderly population in both genders. The extrapolation of the observed log age-adjusted visit rates, the same figure also presents the predictions for Scenario B. The predictions using such a direct and simple method show a continuously increasing trend, for 5 years, for both males and females.

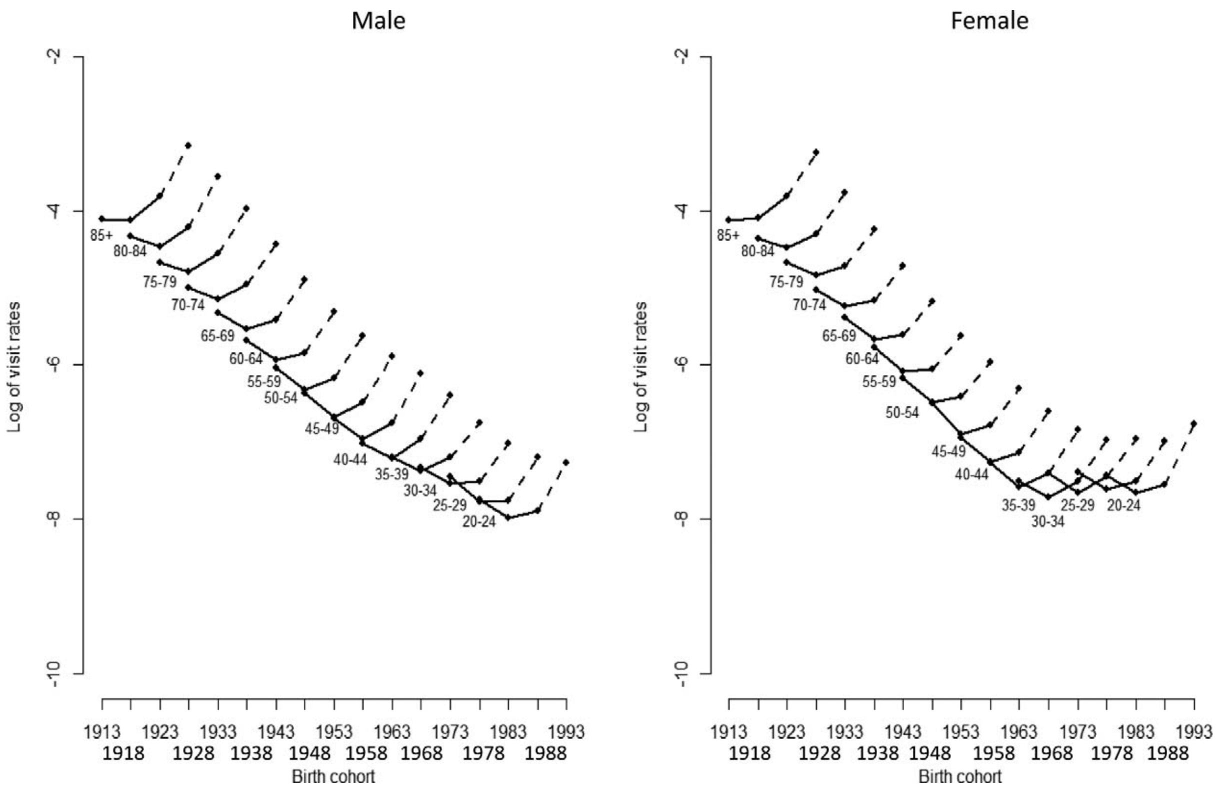

Figure 3. Age-specific emergency department visit rates of septicemia-associated in log scale by birth cohort for male and female in Taiwan, 1998 to 2012. Solid line: observations; dotted line: forecasts.

4. Discussion

The current study investigated the trends in the septicemia-related ED visit rates by simultaneously applying APC perspectives. Indeed, the APC model predictions can provide an advanced warning based on the future trend. APC effects provide a formal clue to guide the analysis through an explicit consideration of these effects with sufficient goodness-of-fit in the APC model.

Urging growth of ED visits rates due to septicemia, results showed that effects on women were stronger than on men in the recent cohort. We found no gender differences among the cohort effects of mid-20th century generations on the variations in

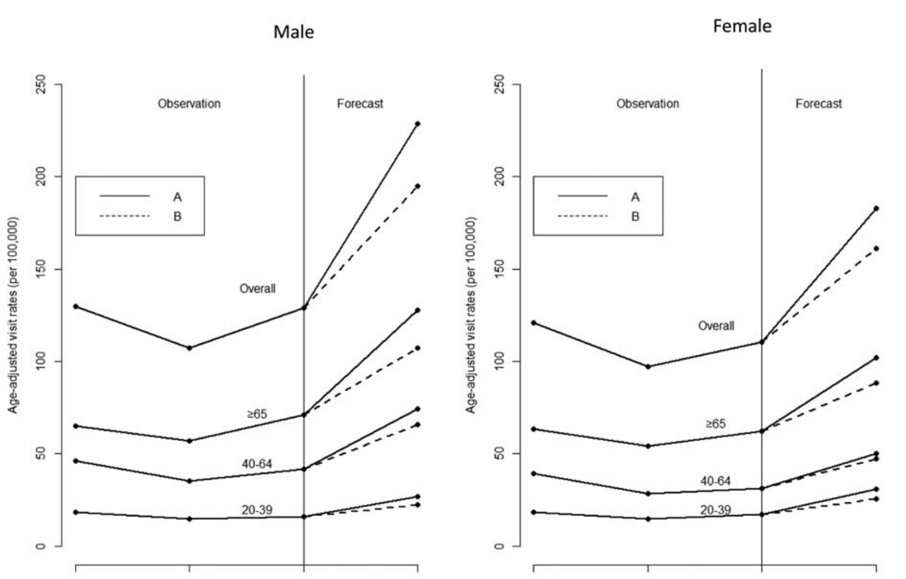

Figure 4. Observation and prediction of age-adjusted visit rates from septicemia for stratified males and females in Taiwan (mark [A] age–period–cohort analysis; mark [B] quadratic regression analysis of logarithm of age-adjusted visit rates, 2013–2017).

septicemia-related ED visit rates. From these results, we speculate that the overall external changes affect all age groups in 1988 to 2012, while imposing different cohort effects on visit rates due to septicemia, while this difference may be provided to explain the causation rather than the effect on the entire ED visit rates.

According to the latest researches, there have been many studies explaining the overall trend of septicemia. In general, there were studies presented an increase trend in (severe) sepsis.[20,21] Although we observed a decline trend in septicemia-related ED visit rates at an early stage (Fig. 3), which reversed itself by increasing. Viewpoint of public health for gender, the incidence of some infectious diseases had differences in male and female. For example, the adult female has higher incidence of urinary tract infection than male.[22] The incidence of bacteremia (but not the case–fatality ratio) was significantly higher in males than in females.[23] Another study also indicated that Gram-positive bacteria caused more sepsis in males than in females.[24] We similarly observed the adult male has higher incidence of septicemia than female in ED (Fig. 1). Thus, our observations are somewhat consistent with previous studies. Of note, to our knowledge, previous studies did not decompose septicemia visit rates into the effects of APC or examine influences in age-stratified groups.

Further, the quality of medical care for critical illnesses has become an issue of great concern.[25] In Taiwan, to improve the quality of care for critically ill patients in the EMS, the MOHW has emphasized the importance of the quality of care for critical illnesses and the efficiency of disposition by initiating the optimizing emergency medicine quality (OEMQ) program of the NHI in 2012.[26] The OEMQ program provides a protocol for critically ill patients to receive standard treatment and provides reward as accreditation as an NHI-privileged hospital when a set of standards has been reached. Septicemia was one of the index diagnoses for upgrading the critical care performance of hospital EDs in the OEMQ program. Overall, this program may increase visit rates due to septicemia in EDs because of the more aggressive disposition decisions, with a higher likelihood for ED physicians to make septicemia-associated diagnoses. Moreover, the impact of the OEMQ program on septicemia-associated ED visit rates should be measured in future.

For predictions of the logarithms of the age-specific 5-year visit rates, a simple quadratic extrapolation revealed that the younger cohorts exhibited slightly increased trends, which was less than that of the older cohorts. However, a simple quadratic extrapolation of the log age-adjusted visit rates may underestimate some important features hidden in the data (i.e., the cohort effects), especially in the elderly population. Based on a direct observation of the recent trends in visit rates from 2008 to 2012 in Taiwan, we can undoubtedly confirm that the trends will continue to increase in the next few years.

Despite these interesting results, some potential limitations of our study should be noted. First, our study is descriptive and we can only infer about the etiologies of the changes observed. The visit rates derived by APC effects are reamenable for an APC prediction. However, it is important to note that there are set assumptions for the prediction method that we used in the present study. As we based our prediction on visit rates across 15 years, we limited our APC prediction to only the next 5 years. Second, APC analysis can be used extensively in epidemiology and social economic fields in populations of developing or recently developed countries, where there is a lack of long-running cohort studies. Third, we do not have information from the aggregated format datasets to adjust confounders, such as comorbidities, education levels, or lifestyle in the APC model. Further studies using individual data are needed to solve this limitation. Fourth, the number of cases of septicemia was comparatively low (Table 1), compared to the incidence rates of severe sepsis reported in another claims data-based studies.[6] We suspected one of the reasons of utilizing the coding of sepsis. Moreover, women may be less likely to develop septicemia. In general, the age standardized rates for septicemia decreased and then increased during the period, as presented in the period effects. The phenomenon can be explained by a more aggressive disposition by ED physicians and a higher awareness about making septicemia diagnoses as well as an overall increase in the number of cases of septicemia-relevant symptoms and signs in the general population, including at-risk patients. In addition, general progress has been made in medical technology and practices to detect bacteremia.[27,28] Lastly, the diagnostic codes were given to the patients at discharge of the ED to either inpatient or outpatient departments. Under the ED crowding condition in Taiwan, many patients would stay in the ED for 2 to 3 days in average.[29] Therefore, the emergency physicians could observe the patients before they give the final discharge diagnosis in the ED. However, the results of blood culture may still be unavailable at the time patients were discharged from ED, which would result in the underestimated prevalence of sepsis in the ED.

5. Conclusion

The capacity of emergency physicians to provide medical services should be planned by age, time period, and cohort effects on the incidence of infectious diseases. Predicting the EDs visit rates from septicemia-related data is an important element in the process of planning for the future. Since 1993, Taiwan became an aging society because the percentage of the population aged 65 years and over reached 7%.[30] It is known that aging is a relevant risk variable for infectious diseases.[31] Thus, the present study concluded that the aged population will contribute to the increase in the infection-related ED visit rates in the future.

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References

[1] Van Bodegom D, May L, Meij HJ, et al. Regulation of human life histories: the role of the inflammatory host response. Ann N Y Acad Sci 2007;1100:84–97.
[2] Rozanska A, Wojkowska-Mach J, Adamski P, et al. Infections and risk-adjusted length of stay and hospital mortality in Polish Neonatology Intensive Care Units. Int J Infect Dis 2015;35:87–92.
[3] Yeh CF, Chen KF, Ye JJ, et al. Derivation of a clinical prediction rule for bloodstream infection mortality of patients visiting the emergency department based on predisposition, infection, response, and organ dysfunction concept. J MicrobiolImmunol Infect 2014;47: 469–77.
[4] Jones AE, Puskarich MA. The Surviving Sepsis Campaign guidelines 2012. Update for emergency physicians. Ann Emerg Med 2014;63:35–47.
[5] Newitt S, Myles PR, Birkin JA, et al. Impact of infection control interventions on rates of *Staphylococcus aureus* bacteraemia in National Health Service acute hospitals, East Midlands, UK, using interrupted time-series analysis. J Hosp Infect 2015;90:28–37.
[6] Shen HN, Lu CL, Yang HH. Epidemiologic trend of severe sepsis in Taiwan from 1997 through 2006. Chest 2010;138:298–304.

[7] Holford TR. The estimation of age, period and cohort effects for vital rates. Biometrics 1983;39:311–24.
[8] Holford TR. Understanding the effects of age, period and cohort on incidence and mortality rates. Annu Rev Public Health 1991;12:425–57.
[9] Lee WC, Lin RS. Autoregressive age-period-cohort models. Stat Med 1996;15:273–81.
[10] Keyes KM, Li G. A multiphase method for estimating cohort effects in age-period contingency table data. Ann Epidemiol 2010;20: 779–85.
[11] Tu YK, Smith GD, Gilthorpe MS. A new approach to age-period-cohort analysis using partial least squares regression: the trend in blood pressure in the Glasgow Alumni Cohort. PLoS One 2011;6:e19401.
[12] Tzeng IS, Lee WC. Forecasting hepatocellular carcinoma mortality in Taiwan using an age-period-cohort model. Asia Pac J Pub Health 2015;27:N65–73.
[13] Lin SF, Beck AN, Finch BK, et al. Trends in US older adult disability: exploring age, period, and cohort effects. Am J Public Health 2012;102:2157–63.
[14] Chang CH, Lin JW, Tu YK. Secular trends were considered in the evaluation of universal hepatitis B vaccination in Taiwan. J Clin Epidemiol 2015;68:405–11.
[15] Liu SH, Tzeng IS, Hsieh TH, et al. Associations between excessive adiposity and seroprevalence of herpes simplex virus type 1 and type 2 among US adults: a population-based age–period–cohort analysis. BMJ Open 2016;6:e012571.
[16] Ministry of Health and Welfare, R.O.C. National Health Insurance Health Statistics Annual Report. 2007. Available from: http://www.mohw.gov.tw/EN/Ministry/Statistic.aspx?f_list_no=474. Accessed December 3, 2014.
[17] Ahmad OB, Boschi-Pinto C, Lopez AD, et al. Age Standardization of Rates: A New WHO Standard. GPE Discussion Paper Series, No. 31. Geneva:World Health Organization; 2005.
[18] Ju X, Brennan DS, Spencer AJ. Age, period and cohort analysis of patient dental visits in Australia. BMC Health Serv Res 2014;14:13.
[19] R Development Core Team. R: A Language and Environment for Statistical Computing. 2008; Vienna, Austria: R Foundation for Statistical Computing, ISBN 3-900051-07-0, URL. Available at: http://www.R-project.org. Accessed May 5, 2014.
[20] Chen YC, Chang SC, Pu C, et al. The impact of nationwide education program on clinical practice in sepsis care and mortality of severe sepsis: a population-based study in Taiwan. PLoS One 2013;8:e77414.
[21] van der Wekken LC, Alam N, Holleman F, et al. Epidemiology of sepsis and its recognition by emergency medical services personnel in the Netherlands. Prehosp Emerg Care 2015;20:90–6.
[22] Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Am J Med 2002;113:5–13.
[23] McGowan JEJr, Barnes MW, Finland M. Bacteremia at Boston City Hospital: occurrence and mortality during 12 selected years (1935–1972), with special reference to hospital-acquired cases. J Infect Dis 1975;132:316–35.
[24] Esper AM, Moss M, Lewis CA, et al. The role of infection and comorbidity: factors that influence disparities in sepsis. Crit Care Med 2006;34:2576–82.
[25] Schramm GE, Kashyap R, Mullon JJ, et al. Septic shock: a multidisciplinary response team and weekly feedback to clinicians improve the process of care and mortality. Crit Care Med 2011;39:252–82.
[26] Ministry of Health and Welfare, R.O.C. Modification of “Optimizing Emergency Medicine Quality program under the National Health Insurance”; 2012. Available from: http://www.nhi.gov.tw/webdata/webdata.aspx?menu=20&menu_id=712&webdata_id=4167. Accessed October 28, 2015.
[27] Sogaard M, Engebjerg MC, Lundbye-Christensen S, et al. Changes in blood culture methodology have an impact on time trends of bacteraemia: a 26-year regional study. Epidemiol Infect 2011;139:772–6.
[28] Reimer LG, Wilson ML, Weinstein MP. Update on detection of bacteremia and fungemia. Clin Microbiol Rev 1997;10:444–65.
[29] Hsu NC, Shu CC, Lin YF, et al. Why do general medical patients have a lengthy wait in the emergency department before admission? J Formos Med Assoc 2014;113:557–61.
[30] Tsai WH. The growth of Taiwan’s aging population and its socio-economic consequences. Taiwanese Gerontol Forum 2008;1:1–0. http://www.ncku.edu.tw/forum/vol1/article1. Accessed November 2, 2015.
[31] Henriksen DP, Pottegard A, Laursen CB, et al. Risk factors for hospitalization due to community-acquired sepsis - a population-based case-control study. PLoS One 2015;10:e0124838.