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醫療照護相關感染長期趨勢統計模式分析

Statistical Modelling for Time Trends of Healthcare-Associated Infections

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論文中文題目：醫療照護相關感染長期趨勢統計模式分析

論文英文題目：Statistical Modelling for Time Trends of Healthcare-Associated Infections

本論文係王瑞芳君（學號 D99842004）在國立臺灣大學流行病學與預防醫學研究所完成之博士學位論文，於民國 104 年 01 月 28 日承下列考試委員審查通過及口試及格，特此證明。

口試委員：

（簽名）

（指導教授）

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中文摘要

國立臺灣大學

背景

對於時間數列因子(時間趨勢、季節性及自相關性)及源自醫療照護相關感染之異質性因子進行系統評估，對於醫療照護相關感染的監視扮演重要角色，特別是對於病菌或起因於抗藥性造成的大流行時及對介入方案進行評估。然而，欲對介入效益進行長期動態性時間數列預測，傳統時間數列模式往往會遭遇一連串方法學上的議題，包括非常態資料、穩定性及可轉性(自我相關階數與平均移動之交換)、階層式資料結構所導致相關性、以及異質性之時間數列因子等。

研究目的

本研究利用醫學中心時間序列之分析並以此評估長期追蹤之醫療照護相關感染(Healthcare-associated infections, HAI)資料進行感染控制實務介入成效之探討，主要目的：

(1)醫療照護相關感染發生之相關因素探討

(2)利用傳統時間序列分析方法，探討時間序列相關因素對於醫療照護相關感染發生之影響，例如時間趨勢、季節變異及自我回歸次序等等：並進一步利用 Poisson 時間序列模式進行整體醫療照護相關感染、特定部位感染、特殊菌種及住院部門之醫療照護相關感染發生因素進行分析

(3)考量上述(2)發現影響醫療照護相關感染之時間序列因素及年齡、性別對於醫療照護相關感染異質性後，進一步預測醫療照護相關感染發生趨勢演變

(4)評估醫療照護相關感染控制介入之成效，包括整體醫療照護相關感染、特定部位感染、特殊菌種及住院部門之醫療照護相關感染控制成效評估

(5)發展創新性廣義線性混合 ARIMA 模式(Autoregressive Integrated Moving Average model)應用於(3)之分析

(6)在非隨機分派試驗設計下，本研究結合上述(5)發展之分析模式應用於醫療照護相關感染控制介入之成效評估

資料來源

本研究資料以位於台北市都市型之 921 床醫學中心主體，該院平均每年約有 27000 名住院病患。研究族群收集自 1994 年 1 月 1 日至 2013 年 12 月 31 日之住院病患為醫療照護相關感染之研究世代。

醫療照護相關感染控制介入措施

該期間醫療照護相關感染控制介入包括醫療照護之目標管理循環(PDCA)概念模式、衛生計畫、疾病管制署洗手衛生政策及台灣醫療品質策進會(台灣醫策會)對於泌尿道感染醫療照護品質提升計畫(CDC/TJCHA)及、醫療照護組合式措施

(Bundle Care)等。

研究設計

第一部份利用該長期資料進行醫療照護相關感染發生率趨勢及其相關因素探討。

本研究採用兩種模式進行醫療照護相關感染控制介入評估，首先以控制策略介入前與介入後之醫療照護相關感染個案數比較，以模式獲得參數後，估算事後個案數分佈並與介入後個案數進行比較，以獲得相同年數期間的個案數差異作為介入成效指標。第二種研究設計以類隨機分派試驗設計進行評估，本研究以介入前資料進行模式分析，並以其結果預測醫療照護相關感染發生數以作為對照組，即為在無介入控制時所產生的個案數(2005 年之前)，該對照組與政策介入後所觀察到的醫療照護相關感染數進行比較，則可獲得該政策介入成效。

方法學特點

本論文在分析架構上，首先進行傳統時間數列模式例如時間數列分解模式以及貝氏動態線性模式，接著再逐步發展貝氏廣義線性混合自我相關平均移動模式，運用臨床醫療照護相關感染資料進行感染之長期趨勢預測及針對介入政策進行效益評估。

結果及結論

有關醫療照護相關感染發生之研究結果如下:

結果

(1) 醫療照護相關感染發生研究，本研究發現較年長男性比年輕女性有較高危險性

(2) 本研究資料發現以泌尿道感染及菌血症為最高，且隨著不同部門其變異性大

(3) 醫療照護相關感染於夏季發生率高，但於冬季則較低；依不同感染部位及特殊菌種的自我迴歸次序，醫療照護相關感染隨著時間有線性及非線性(二次方及三次方線性)下降趨勢

有關醫療照護相關感染控制策略介入評估，本研究結果及結論發現摘要如下:

(1) 研究結果顯示，調整年齡、性別、時間趨勢、季節變異性及三次方自我回歸趨勢後，疾病管制署/台灣醫策會及醫療照護組合式措施於 2010 年介入後成效分別可降低 26%及 39%的醫療照護相關感染發生。然而，目標管理循環(PDCA)概念模式及衛生計畫僅能降低約 10%且未達統計顯著意義。

(2) 調整年齡、性別、時間趨勢、季節變異性及三次方自我回歸趨勢後，疾病管制署/台灣醫策會及醫療照護組合式措施於 2010 年介入後，考慮 6 個月延遲效應，可有效降低 36%醫療照護相關感染發生。

(3) 本研究以隨機效應模式考量醫院部門、感染部位及菌種之階層次結構後，其

介入成效結果與(1)及(2)發現非常相近。

(4) 疾病管制署/台灣醫策會介入成效隨著感染部位不同而有所差異。對於菌血症及外科手術部位感染可以降低 36%、泌尿道感染可降低 16%、對於其他部位可以降低 81%，但對於肺炎則無成效。醫療照護組合式措施介入可有效降低 37%菌血症、44%外科手術部位感染、38%泌尿道感染及 88%其他部位感染，而對肺炎僅能降低 3%。

(5) 疾病管制署/台灣醫策會介入對於急診部成效最佳(約可降低 94%)，而於小兒科最差。對於腫瘤科沒有任何成效。醫療照護組合式措施介入對於感染科成效最顯著(約可降低 77%)且對於外科手術部位感染成效最低(約可降低 34%)，而對於腫瘤科及小兒科不具任何成效。

(6) 疾病管制署/台灣醫策會政策或醫療照護組合式措施介入隨著菌種不同而不同。疾病管制署/台灣醫策會政策對於厭氧菌種成效最佳(約下降 65%)、革蘭氏陽性 (約下降 31%)及革蘭氏陰性 (約下降 30%)次之，但對於黴菌成效很小(5%)，而其他菌種都無任何效果。醫療照護組合式措施對於其他菌種成效最大(約下降 91%)、厭氧菌種(82%)、黴菌(52%)、革蘭氏陽性 (約下降 32%)及革蘭氏陰性 (約下降 31%)次之。

(7) 利用時間數列模型 2005 年前(介入前)後觀察 HAIs 數目發現，疾病管制署/台灣醫策會政策介入可以減少 643 位 HAIs，但若以預測值(考慮估計值不確

定性)則降低數目減少 283 位。

結論

本論文在方法學上的創新性，包括使用貝氏廣義線性混合 ARIMA 模式的發展，以及在非隨機試驗下對於介入效益評估之模式設計。這樣的貝氏廣義線性混合 ARIMA 模式結合廣泛地運用在長期追蹤研究之廣義線性混合模式及廣泛應用於經濟研究之 ARIMA 模式。當進行與時間數列特性之醫療照護相關感染的預測上，藉由貝氏分析估計相關參數時可以同時考量時間數列及異質性成分。在研究設計上之創新，應用時間數列模型之估計及預測，可以在非隨機試驗研究設計下仍可對介入政策進行效益評估。此模式相當彈性，不一定要進行隨機試驗設計，即可推展至任何與醫療照護相關感染介入方案之評估。

關鍵字: 醫療照護相關感染，時間序列分析，介入措施，統計模式

ABSTRACTS

Background

Systematic evaluation of time-series factors (time trend, seasonal variations, and autocorrelation) and factors responsible for heterogeneity accounting for healthcare-associated infections (HAIs) plays an important role in the surveillance of HAIs, particularly for evaluation of the efficacy of interventions and the outbreak of pathogens probably due to drug-resistance. However, forecasting for the long-term dynamic evolution and evaluation of the efficacy of interventions is often confronted with a series of methodological issues if the conventional time-series model is applied, including non-Gaussian data, stationarity and invertiblity, hierarchical data structure, and heterogeneity beyond time-series factors.

Aims

By using a longitudinal follow-up time-series data on HAIs from a medical center, my thesis aimed to, from the practical aspect of HAIs control,

(1) identify the risk factors responsible for HAIs incidence;

(2) elucidate how time-series factors such as time trend, seasonal variation, and autoregressive order made contribution to incident HAIs using the conventional

time series model and the extended Poisson time-series model for the overall HAIs, site-specific, pathogen-specific and department-specific HAIs;

(3) to forecast the evolution of HAIs making allowance for time-series components as identified in (2) and heterogeneity contributed from other covariates such as age and gender with 95% confidence interval;

(4) to evaluate the efficacy of interventions related to HAIs control in the site-specific, pathogen-specific, and department-specific reduction in HAIs.

My thesis also aimed to, form the aspect of methodology,

(5) to develop a novel generalized linear mixed ARIMA model to achieve the objective (3);

(6) devise a time-series model-based design together with the proposed model in (5) to evaluate the efficacy of interventions associated with HAIs in the absence of randomized controlled trial as mentioned in (4) .

Data Sources: A cohort of healthcare-associated infections was followed during the period of January 1, 1994 and December 31, 2013 in an urban tertiary medical center in northern Taipei with 921-bed and approximately 27,000 inpatient admission annually.

Intervention programs indicators: Intervention of PDCA, Hygiene programs, Taiwan Centers for Disease Control (CDC) National Hand Hygiene Campaign and the urinary tract infection quality improvement program of Taiwan Joint Commission on Hospital Accreditation (TJCHA) called CDC/TJCHA, and Bundle care program.

Study Design: The first part of study design was in the light of an incident follow-up cohort over time to identify the HAI episode. There are two study designs proposed for evaluation of efficacy of these intervention programs. The first is based on before and after comparison of counts of HAIs. The estimated HAIs counts that were computed on the basis of the posterior distribution with the same length of period conducted with the intervention program were compared with the observed HAIs after the intervention program. The second study design was based on a pseudo randomized controlled trial design. The HAIs counts in the observed were compared with the control group created by predicting rather than estimating the HAIs counts based on the predictive distribution formed by the posterior distribution estimated from the time series data before interventions (i.e. the year before 2005).

Model Specification

The analysis framework began with the conventional time-series model including decomposition method and Bayesian dynamic linear model and then step-by-step developed the proposed Bayesian linear mixed autoregressive moving average model, combining with for forecasting the long-term time trend of HAIs based on the empirical data presented here and also for evaluation of the efficacy of intervention programs.

Results and Conclusions

As far as factors affecting the occurrence of HAIs are concerned, the summary of results and conclusions consists of the following points:

(1) The elderly males are more likely to be susceptible to HAIs than the young female by using demographic features.

(2) The most frequent infection sites are UTI and bacteremia and there is much variation of HAIs across departments.

(3) There was much preponderance in summer but less in winter seasons, a decreasing time trends with linear and non-linear (quadratic and cubic) pattern, the consideration of autoregressive orders depending on the site of infection and pathogens.

Regarding the efficacy of intervention, the summarized findings and conclusions were as follows.

(1) Around 26% and 39% reduction resulting from CDC/TJCHA and Bundle care program, respectively, after 2010 were estimated with adjustment for age,

gender, time trend, seasonal variation, and third-order of autoregressive order. However, there was a 10% non-significant reduction for hygiene program and lacking of significant benefit for PCDA.

(2) The 36% reduction resulting from time lag (6 months) of either CDC/TJCHA or Bundle care program after 2010 was estimated with adjustment for age, gender, time trend, seasonal variation, and autoregressive order.

(3) The similar findings on (1) were found when random-effects considering the hierarchical structure of department, infection site, and pathogen were allowed.

(4) The results of efficacy of CDC/TJCHA and Bundle care varied with site of infection. CDC/TJCHA was conducive to 36% reduction in HAIs for bacteremia and SSI, 16% for UTI, 81% for others but there was lacking of any benefit for pneumonia. Bundle care was conducive to 37% reduction in HAIs for bacteremia, 44% for SSI, 38% for UTI, 88% for others but only 3%for pneumonia.

(5) The reduction in HAIs for CDC/TJCHA was the greatest in emergency department (almost 94%) and the least in pediatrics (7%). There was lacking any benefit for oncology. The reduction in HAIs for Bundle care was the greatest in infection department (almost 77%) and the least in surgical (34%).

There was lacking any benefit for oncology and pediatric department.

(6) The results of efficacy of CDC/TJCHA and Bundle care largely varied with pathogen. The reduction in HAIs with CDC/TJCHA was the greatest for anaerobic pathogen (65%), followed by Gram-positive (31%) and Gram-negative (30%), but smallest for Fungi pathogen (5%). There was lacking of any benefit for other pathogens. The reduction in HAIs with Bundle care was the greatest for others (91%), followed by anaerobic pathogen (82%), by Fungi (52%), Gram-positive (34%), and Gram-negative (31%).

Regarding the novelty of methodology, there are two parts pertaining to the novelty of methodology presented in this thesis, the development of a Bayesian generalized linear mixed ARIMA model and the model-based design for evaluation of the efficacy of intervention dispensing with the randomized controlled trial. Specifically, this thesis developed a generalized linear mixed effect ARIMA model by combining the generalized linear mixed model widely used in longitudinal follow-up study and ARIMA model widely used in economic studies. It can be useful for monitoring the episodes of HAIs by projecting time-series-featuring HAIs with the relevant parameters estimated by Bayesian approach making allowance for both properties of heterogeneity and time series components. The thesis has devised a time-series

model-based design to evaluate the efficacy of intervention associated with HAIs in the absence of randomized controlled trial. Such a time-series model-based design is very flexible in the evaluation of any kind of evaluation of intervention in association with HAIs without needing a randomized controlled trial design.

Keywords: Healthcare-associated infections, Time series analysis, Intervention, Statistical analysis

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Chapter 1 Introduction

1.1 Surveillance of healthcare-associated infections with statistical time-series model

Healthcare-associated infections (HAIs), which are known as nosocomial infections, pose a threat to hospital infection control. Zimlichman et al. has asserted that the costs involved with the HAIs imposed on the healthcare system are enormous according to the results of their meta-analysis. The total annual cost for the major HAIs was counted $9.8 billion (95% CI, $8.3-$11.5 billion) in the United States, with surgical site infections contributing the most to overall cost [1]. It is of importance for the policy maker, public health experts, and clinicians to quantify the diseases evolution with time and forecast diseases burden caused by HAIs.

Harbarth et al. found that at least 20% of all nosocomial infections were probably preventable[2]. Many countries have established national surveillance systems[2-5]. Several studies have already shown that the surveillance and the subsequent policy changes can lead to a decrease in HAIs[6-9]. The continued dynamic monitoring for disease incidence, risk factor identification, and evaluation of the efficacy of intervention in reducing HAIs (such as hand hygiene and Bundle care) taking the properties of time-series data into account and the corresponding forecasting models can provide a new insight into evaluation and prioritization of programs.

Dynamic evolution with time is one of the characteristics of infectious diseases. The dynamic changes includes seasonal variations, trends, periodic cycling, and fluctuations (innovation), which have been already found in urinary tract healthcare-associated infections [10]. The incidence of several other viral and bacterial infections also shows seasonal patterns[11-18]. However, systematic evaluation of seasonal variations of infectious diseases together with time trend, particularly nosocomial infection, has been hardly addressed. Many authors have focused on studying specific infections sites or some microorganisms over the past few decades. It is possible to postulate the impact of intervention on occurrence of HAIs may vary with site of infection, pathogens, and department. In addition to lacking of dynamic properties, few studies provide a comprehensive and systematic evaluation for the surveillance of long-term HAIs.

1.2 Methodological issues of conventional time-series model

There are many imperfect methodological issues raised when the traditional autoregressive moving average time series model is applied to monitoring and assessing long-term time trend of HAIs. First, it assumes normality of the observations. However, both incidence and mortality of HAIs are often regarded as count data and have rare disease assumption. The use of Poisson distribution or negative binomial distribution in time series analysis seems more justified for time series analysis. The extension of linear time-series model to generalized linear time-series model is therefore indispensable.

Second, one of the most obstacles for forecasting HAIs is that occurrence of infectious diseases tends to be correlated when the observations are taken in successive time points and the correlations decreases as they are taken separately far apart. Autocorrelations, the dependency with itself through time, is an important concern when considering the evaluation of the dynamic quantity. These characteristics form the basis for forecasting long-term sequence of infectious diseases. Nonetheless, the application of traditional time-series statistical method often requires the assumption of stationarity for autoregressive (AR) process and invertiblity for moving-average (MA) process. The use of Bayesian approach to explosive and non-explosive studies is an alternative. Moreover, Bayesian is also very flexible in predicting the dynamics of infectious disease as Bayesian perspectives from the philosophy of statistical viewpoint seems more appropriate to treat the parameters of interest as certain kind of distribution (the uncertainty of parameter) when various patterns of the incidence of infectious diseases have been modelled. For example, Bayesian state-space time series modelling, consisting of an observation equation and a state equation, is a very useful technique for the dynamic modelling of HAIs with the flexibility through parameter updating process.

Third, given the limited resources, logistics of long-term follow-up, and ethical concern, it is infeasible to perform randomized control trials on intervention related to infectious control studies. To solve this issue, a model-based time-series design with Bayesian approach would be envisaged in this thesis to create a pseudo control group comparable to the control group based on a randomized controlled trial.

1.3 Aims

By using a longitudinal follow-up time-series data on HAIs from a medical center, my thesis aimed to, from the practical aspect of HAIs control,

(1) identify the risk factors responsible for HAIs incidence;

(2) elucidate how time-series factors such as time trend, seasonal variation, and autoregressive order made contribution to incident HAIs dynamics using conventional time series model and the extended Poisson time-series model for the overall HAIs, site-specific, pathogen-specific and department-specific HAIs;

(3) to forecast the evolution of HAIs making allowance for time-series components as identified in (2) and heterogeneity contributed from other covariates such as age and gender;

(4) to evaluate the efficacy of intervention related to HAIs control in the overall site-specific, pathogen-specific, and department-specific reduction in HAIs.

My thesis also aimed to, form the aspect of methodology,

(5) to develop a novel generalized linear mixed ARIMA model to achieve the objective (3);

(6) devise a time-series model-based design together with the proposed model in (5) to evaluate the efficacy of intervention associated with HAIs in the absence of randomized controlled trial as mentioned in (4) .

Chapter 2 Literature Review

2.1 Surveillance of HAIs

The establishment of HAIs control systems depends on the facilities of the hospitals. Manual medical records data key-in is labor-consuming. Automated laboratory monitoring surveillance is mandatory [19,20]. The emergence of new diseases or outbreak of specific diseases, such as Severe Acute Respiratory Syndrome (SARS), West Nile virus, and HIV outbreaks needs real-time, automated outbreak detection. In recent years, many detection systems developed [21-26].

The methodology of detection systems varies. Hutwagner et al. use time series model to detect Salmonella outbreaks [27]. The Serfling method and its modifications has been used for influenza surveillance and other diseases [28]. The trimmed seasonal model is used as a monitoring system for statewide real-time population health. Zhang et al. applied wavelet transform time series to artificial disease outbreaks and tested its sensitivity and specificity. The wavelet transform could deal with the problems found in long-term trends and negative singularity [29]. Owing to the changes in patient characteristics, medical services, and clinical practice, the monitoring models used should be flexible and easily updating. Traditional time series analysis consists of fixed parameters which is performed well in the short-term predictions but it may be difficult in coping with long-term predictions. It is reasonable to apply Bayesian methods in which parameters are not fixed for the long-term disease monitoring.

2.2 Dynamic infectious diseases

Knowledge of the dynamic trends in infectious diseases will allow for improved designs, modelling, interpretation, and policy-making.

2.2.1 Seasonality of infectious diseases and meteorological factors

The importance of seasonal variations in disease patterns are well recognized in many studies, mostly in viral diseases, such as influenza, measles, hepatitis B virus, Japanese encephalitis, rotavirus gastroenteritis, respiratory syncytial virus [11-14], e.t.c. Panackal showed that the invasive fungal infections also had seasonal, and spatio-temporal effect in his U.S. national hospital survey study [30]. Some bacterial infections also have seasonal phenomenon shown in previous studies, for instance, *Escherchia coli*, *Acinetobacter* species, *Klebsiella pneumoniae*, *Enterobacter* species, *Pseudomonas aeruginasa*, *Campylobacter* and S*taphylococcus aureus* [15-18].

However, the seasonality and its correlation with meteorological factors such as temperature varies with infection sites and locations [31].

Bloodstream infections (BSIs)

In bloodstream infections (BSIs), Goncalves-Pereira et al. studied community-acquired BSIs in 17 intensive care units in Portugal. BSIs of Gram-positive infections were more common in the winter, whereas those of Gram-negative infections were more in the summer. They also noted that the primary site of BSIs seems to be largely from lung in the winter and from both urinary tract and intra-abdominal during the rest of the year. However, the patients enrolled in this study limited for 12-month period and had a relative small sample size. This study focused on the count but not the incidence [32]. Another study of multiple bacterial species by Eber et al. in 2011, which is a database of BSIs from 132 U.S. hospital inpatients, demonstrated that higher temperature was positively associated with Gram-negative bacilli BSIs in summer. *Acinetobacter* exhibited the greatest seasonal variation, whereas *E. coli* had the most modest summer peaks on Gram-negative bacterial BSIs. Higher relative humidity was associated with increased frequency of *Pseudomonas aeruginosa* BSIs. *Enterococcus* BSIs did not have significant association with temperature. Increased precipitation was associated with decreased BSIs frequency in *Staphylococcus aureus* and *Escherichia coli*. This study was not able to identify healthcare-associated infections and did not use infection incidence as the measurement unit [17]. Chazan et al. performed a hospital-based study in northern Israel and found 72.4% of the BSIs was community-acquired and 67.4% of the BSIs source was urinary tract infections. The incidence of *Escherichia coli* was higher in summer with the positive correlation with the temperature; however, there was no association within seasons. This study used BSI episode per admission per month as the unit of incidence [33]. A population-based investigation by Al-Hassan et al. showed a 35% increase in the *Escherichia coli* BSIs incidence (50.2 per 100,000 person-years) in the warmest months (June-September) after gender and age adjustment. It also had correlation with temperature. 59% of the cases were community-acquired [34].

The seasonality of *Klebsiella pneumoniae* (*K. pneumoniae*) in BSIs is still controversial. A four-hospital retrospective surveillance data by Anderson et al. revealed that the temperature and dew point were predictive of increased incidence rates of *K. pneumoniae*. This study was limited by its inability to adjust for patients' characteristics or diseases [35]. In the population-based BSIs study by Al-Hasan et al. did not show the seasonal variation or temperature association after age and gender adjustment. There were only 127 patients with *Klebsiella* species enrolled in this study that may be too small to detect the seasonal change[36].

Al-Hasan et al. also had a study of *Enterobacter* species in BSIs in 2011. There was no significant seasonality shown in their study[37].

Healthcare-associated infections (HAIs)

In a case-control study of pediatric oncology central-venous catheter-associated BSIs patients by Smith et al. found an increase in *Pseudomonas* species during the summer months [38]. The extended-spectrum β-lactamase (ESBL)-producing *E.coli* and *Klebsiella* species were noted to be significantly associated with higher mean temperature and in the summer[16]. Cho et al. studied the patients with peritoneal dialysis, they found that the fungal and Gram-negative bacteria peritonitis had summer and autumn peaks, whereas *corynebacteria* peritonitis had winter peaks, coagulase-negative *Staphylococci* had spring and summer peaks. *Pseudomonas* peritonitis also had summer peaks [39].

Hypothesis of seasonality in infectious diseases

The causes of seasonal variation may be different in community-acquired (CAIs) and healthcare-associated infections. The environmental factors such as humidity, temperature and precipitation are more likely to influence the community-acquired infections; whereas in the hospital with air-conditioner, the variations of these factors tend to be relative small. The healthcare staffs' experiences and workload may be different in a year that could be a point of concern in the seasonality variation in HAIs. Therefore, for the studies which did not show their population origin (CAIs or HAIs), one could not make the inference about the possible causes of the seasonality.

Recreational summer water activities had been found in more than 50% in both case group and control group in Smith et al.'s study [38]. The increased growth in nonendogenous Gram-negative microorganisms were associated with higher ambient temperature [40].

Increased environmental *E. coli* growth has been found in the study of Ishii et al. They detected that the greatest population density of soilborne *E. coli*, isolated from northern temperate soils in three Lakes Superior watersheds, were in summer to fall (June to October) [41]. The seasonal variations in *E. coli* BSIs were noted in many studies, however, whether the seasonal factor influences the primary sites of infection or is a promoter for E. coli to disseminate to bloodstream still unknown. Freeman suggested that the primary sites of infection leading to BSIs should be analyzed separately [42].

The seasonal variations of complex human behavior could be another explanations of the infectious diseases, including water consumption, recreational water exposure, travel, sex activities, and food preference [15,42]. Freeman also suggested that human vulnerability to disease, host immunity, and microorganism virulence could change with seasons [42]. There are still gaps in our understanding of the relationships between seasonal variations and infectious diseases.

2.2.2 Autocorrelations

In viral infectious diseases, many studies apply time series analysis to catch the phenomenon of autocorrelation [13]. Still very few studies consider the autocorrelations of the observations in the analysis the seasonality infectious bacterial diseases [16,18,43]. Kaier et al's study on ESBL-producing *Klebsiella* and *E. coli* showed that the lagged temperature of one to four, autoregressive term, and moving average term were significant variables affecting the incidence [16]. Fernandez-Perez et al. used multivariate autoregressive integrated and moving average (ARIMA) time series modelling in the cumulative incidence of nosocomial infection in Spain. This study showed that medical strike and each new employment corresponded to an increase of infection incidence, whereas the urinary tract infection prevention program and continuous personnel training were associated with the decrease of the incidence. The autoregressive term of order 12 was noted to represent the seasonal phenomenon of the nosocomial infection [43]. This study did not incorporate meteorological variables in their modelling. Weisent et al. compared three time-series models for predicting campylobacteriosis risk. Decomposition model was the fastest, most accurate, and user-friendly method as compared to regression and Box-Jenkins models. However, the decomposition and regression models could not achieve white noise in their residuals. The distinct seasonal pattern of campylobacteriosis in June to August were revealed by three models. No explanatory variable were included in their study [18].

2.3 Intervention programs for HAI

In the past decades, several studies showed that the infection control programs could reduce the incidence of HAI[7-9,44,45] .

2.3.1 Surveillance-based intervention

Geubbles et al. studied the impact of multicenter surveillance in a network on the surgical site infections. They found reduced risk of SSI during the fourth surveillance year (RR=0.69, 95% CI: 0.52-0.89) and it was reduced further during the fifth year (RR=0.43, 95% CI: 0.24-0.76) [44]. In Nicotra's study, they used FOCUS-PDCA project and revealed that the ventilator-associated pneumonia rate had decreased [45]

2.3.2 Hand hygiene-based intervention

Hand hygiene has long been regarded as the basis of the infection control and prevention. The WHO announced guidelines on hand hygiene in health care [46,47].

In 38 Australian hospitals, Barnett et al. evaluated the National Hand Hygiene Initiative intervention and found that it was associated with a reduction in the monthly incidence rate of healthcare-associated *Staphylococcus aureus* bloodstream infections. An immediate 17% and 28% rate reduction in 2 states and a linear decrease in rates of 8% and 11% per year, and no change was found in 2 states [48]. Dumpa et al. had a retrospective study in the central line–associated bloodstream infection (CLABSI) in the neonatal intensive care unit. They found the CLABSI decreased from 4.4/1000 to 0/1000 catheter-days during the intervention including tubing care and hand hygiene [49]. In Grayson’s study, methicillin-resistant *Staphylococcus aureus* bacteremia was significantly decreased from 0.05/100 patient discharges to 0.02/100 patient discharges following 24 months after the implementation of Hand Hygiene culture-change program (HHCCP) [50].

Alp et al studied adult ICUs at a university teaching hospital in Turkey, the hand hygiene program was initiated since 2004, the HAI rate was decreased from

42.6/1,000 patient-days to 33.6/1,000 patient-days in 2012 (IRR, 0.8; P=0.001). The ventilator-associated pneumonia rate was stable from 31.66/1,000 ventilator-days to 24.04/1,000 ventilator-days in 2012 (IRR, 0.88; P=0.574). Similar stable findings were noted in catheter-associated urinary tract infection from 7.92-4.97/1,000 catheter-days. Significant increase was noted in central line-associated bloodstream infections from 7.85 to 12.04/catheter-days (IRR, 1.5; P=0.024). The incidence of microorganisms including *Pseudomonas aeruginosa*, *Acinetobactor baumannii*, and methicillin-resistant *Staphylococcus aureus* was declined [51].

2.3.3 Bundle-based intervention

In Cheng et al's study in ICU in Chi Mei medical center, they introduced a catheter-associated urinary tract infection (CAUTI) bundle since August, 2013. They found that the CAUTI was reduced to zero [52]. Interestingly, they also reported that the bundle effect could affect other infection sites and decreased the incidence, including ventilator-associated pneumonia (from 3.69 to 2.90/1,000 ventilator days), central line-associated bloodstream infection (from 2.08 to 1.92/1,000 catheter days) and HAI (from 7.30 to 4.91 per 1,000 inpatient days) [53].

2.4 HAIs modelling

Many longitudinal follow-up health issues can be quantified and represented as time series tracings. Time series analysis have been well applied in many areas, such as mechanics, physics, meteorology, genetics and finances. In the area of epidemiology, incidence and mortality studies using time series analysis have become commonplace in these decades.

Multivariable Poisson regression was used for the analysis of *Escherichia coli* BSIs incidence by Al-Hassam et al. in a population-based study and *K. pneumoniae* by Anderson et al. [34,35]. Chazan et al. used Poission generalized linear models with the assumption of constant dispersion over time to evaluate *Escherichia coli* BSIs [33]. Multivariable ARIMA time series with trend and lagged temperature was applied in the Kaier et al.'s study on ESBL-producing *E.coli* and *Klebsiella* species [16].

The incidences of infectious diseases have the characteristics of seasonality, autocorrelations, cyclic pattern which were noted in several studies [15]. Observations close in time tend to have higher correlations with each other. The cardinal assumption of traditional regression model, chi-square test and ANOVAs is independent of the observations, which violates the characteristics of clinical infectious diseases. Moreover, the intervention policy lunched needs time to take effect. When effects persist over time, an appropriate model will include lagged variables.

Interventional time-series were used in many studies to evaluate the intervention impact. Vernaz et al. studied the effects of antibiotics use and hand rub consumption on the incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile*. They used ARIMA model with transfer functions and demonstrated that the lagged effects were seen in different antibiotics classes and the consumption of alcohol-based hand rub. No seasonal variation was detected in the monthly incidence of MRSA. This study did not distinguish the community-acquired or healthcare-associated MRSA infections [54]. Another study of MRSA incidence in neonate intensive care unit by Sakamoto et al. also applied ARIMA (0,1,1) model and included 4 lag zero covariates. Although they showed that there were no significant association seen in the patient-to-nurse ratio, bed occupancy rates, and MRSA colonization pressure, there was possibility that the delayed effect of these factors could affect the incidence of MRSA. Still there was no seasonal variation noted in their study [55].

The prior studies have been limited by their inability to incorporate covariates that might be important confounding factors [56], to assess the dependence structure of consecutive observations [15,17,35], or limited to some specific microorganisms [15,35,56]. Time series models, however, take correlations of the successive observations (incidences) into account and give more valid inferences. Time series applying Box-Jenkins model and state-space model can manage these problems.

Some empirical methods can also be used in the time series forecasting. Exponential weighted moving average is very popular for economical use, such as forecasting inventory level, monthly sales, etc. In a non-seasonal time series without trend, the future value of the observation can be obtained.

$$\hat{y}_{t+1|t} = \lambda \sum_{j=0}^{t-1} (1-\lambda)^j y_{t-j} \ \ (0 \le \lambda < 1) \qquad \text{(2-1)}$$

It shows that the future value is the linear combinations of the past observations, with different weights. It is known as exponential smoothing.

$$\hat{y}_{t+1|t} = \lambda y_t + (1-\lambda)\hat{y}_{t|t-1} \qquad \text{(2-2)}$$

$\hat{y}_{t+1|t}$ is a weighted average of y_t and $\hat{y}_{t|t-1}$, and the updating of the time t-1 forecast is achieved when the new observation y_t is available. Though it is friendly for the user, the forecast uncertainty or estimate uncertainty cannot be assessed easily by exponentially weighted moving average method.

2.4.1 Poisson models

Since the incidence of HAIs and associated covariates were of interest, the Poisson model can be expressed as follows. $\log\{n_i\} = \log\{N_i\} + \mathbf{x}_i'\boldsymbol{\beta}$, where n_i denotes number of events of interest (episodes of HAIs), Ni denotes patient-days (offset) in each level, **x** is the covariates vector, and **β** was the corresponding regression coefficients. Poisson regression models were used to calculate the relative risk of developing HAIs [57]. The study by Shen showed that attack rate together with case-fatality rate led to an increase in mortality, particularly seen in *E.coli* and fungus [57].

2.4.2 Negative binomial models

Negative binomial regression models were used to estimate the relative risk of developing HAIs in the cases of over-dispersion noted in the Poisson model.

The negative binomial distribution describes the number of failures before the *r*th success. The probability of the number of failures required before having the *r*th success given r, p is expressed as

$$\mathrm{P}(\mathrm{Y} = y|r, p) = \binom{y + r - 1}{y} p^r (1-p)^y,\ y = 0,1,2,\ldots \qquad (2\text{-}3)$$

Y is the negative binomial random variable and it denotes the number of failures before the *r*th success; *p* is the probability of success and *r* is the number of success events [58]. Let $Y_1, Y_2, \ldots, Y_n$ be a set of count data. The data is negative binomial distributed and can be expressed as

$$P(Y_i = y_i|\alpha, \mu_i) = \frac{\Gamma(y_i + {}^1/_\alpha)}{y_i!\Gamma({}^1/_\alpha)}\left(\frac{1}{1+\alpha\mu_i}\right)^{1/\alpha}\left(1 - \frac{1}{1+\alpha\mu_i}\right)^{y_i} \quad (2\text{-}4)$$

In Poisson distribution, the variance of Y_i, var(Y_i), is equal to the expectation of Y_i, say E(Y_i). When the var(Y_i) is larger than E(Y_i), it is called the over-dispersion. Negative binomial model is well known for its advantage for adjusting over-dispersion by introducing an additional parameter. It provides a model with var(Y_i)=αE(Y_i). The α is the parameter that can be estimated and α is larger than one [59]. Over-dispersion occurs in many situations, such as lack of independence between the observations, inappropriate link functions between the random component and the systemic components, and the existence of unmeasured covariates. In ecological bird migration studies, Linden et al. showed that sampling, flocking behavior or aggregation, environmental variability, or combinations of these factors could results in over-dispersion [60]. Luo J. et al. uses negative binomial distribution to model hypoglycemic events with baseline hypoglycemic event rate adjustment [61].

2.4.3 Autoregressive models

Let y_t denote the random component of generalized linear model (GLM) for a stationary time series data. A *p*th order autoregressive regression model under the context of GLM is expressed as follows.

$$Y_t = \emptyset_1 Y_{t-1} + \emptyset_2 Y_{t-2} + \cdots + \emptyset_p Y_{t-p} + u_t \quad (2\text{-}5)$$

$$t = 1,2, \dots, \mathrm{T}$$

When $\mathrm{p} = 1$, it is often called the first-order autoregressive model denoted by AR(1) with the following expression

$$Y_t = \emptyset Y_{t-1} + u_t \quad (2\text{-}6)$$

If the data are centered, the equation is re-expressed as

$$(Y_t - \mu) = \emptyset(Y_{t-1} - \mu) + u_t \quad (2\text{-}7)$$

u is the mean of the series.

Note that $|\emptyset| < 1$ is required to meet the stationarity. From the equation (2-5), we have

$$\mathrm{V}(Y_t) = \emptyset^2 \mathrm{V}(Y_{t-1}) + V(u_t)$$

$$\Rightarrow \quad V_0 = \emptyset^2 V_0 + \sigma_u^2 \tag{2-8}$$

$$V_0 = \frac{\sigma_u^2}{1-\emptyset^2}$$

$$\Rightarrow \quad \mathrm{E}(Y_t Y_{t-m}) = \emptyset E(Y_{t-1} Y_{t-m}) + E(Y_{t-m} u)$$

Applying the property of stationarity of the series and the independence of $Y_{t-1}$and

u_t

$$V_m = \emptyset V_{m-1}$$

$$m = 1,2,\ldots$$

For $m = 1,$

$$V_1 = \emptyset V_0 = \emptyset \frac{\sigma_u^2}{1-\emptyset^2}$$

For $m = 2,$

$$V_2 = \emptyset V_1 = \emptyset \left(\emptyset \frac{\sigma_u^2}{1-\emptyset^2}\right) = \emptyset^2 \frac{\sigma_u^2}{1-\emptyset^2} = \emptyset^2 V_0$$

By induction, we have autocorrelation function

$$V_m = \emptyset^m V_0$$

$$\Rightarrow \quad \rho_m = \frac{V_m}{V_0} = \emptyset^m \tag{2-9}$$

As $|\emptyset| < 1$, the autocorrelation function is exponentially decreasing in *m*.

For $0 < \emptyset < 1$, all ρ_m are positive.

For $-1 < \emptyset < 0$, $\rho_1 < 0$, the sign of subsequent autocorrelations alternate.

When $= 2$, a stationary series Y_t is the second-order autoregressive model denoted by AR(2) with the following expression.

$$Y_t = \emptyset_1 Y_{t-1} + \emptyset_2 Y_{t-2} + u_t \quad (2\text{-}10)$$

Using a similar derivation, as done for the AR(1), we have

$$V_k = \emptyset_1 V_{k-1} + \emptyset_2 V_{k-2} \quad (2\text{-}11)$$

$$\rho_m = \emptyset_1 \rho_{m-1} + \emptyset_2 \rho_{m-2} \quad (2\text{-}12)$$

To meet stationarity, the coefficients $\emptyset_1$ and $\emptyset_2$ have to satisfy the following constraints

$$\emptyset_1 + \emptyset_2 < 1, \emptyset_2 - \emptyset_1 < 1, -1 < \emptyset_2 < 1$$

for the AR(2) model.

The equation (4.3.8) is so called Yule-Walker equation.

For $m = 1$,

$$\rho_1 = \emptyset_1 \rho_0 + \emptyset_2 \rho_{-1}$$

$\rho_0 = 1$ and $\rho_{-1} = \rho_1$, we have

$$\rho_1 = \frac{\emptyset_1}{1 - \emptyset_2}$$

For $m = 2$,

$$\rho_2 = \emptyset_1 \rho_1 + \emptyset_2$$

$$\Rightarrow \ \rho_2 = \emptyset_2 + \frac{\emptyset_1^2}{1-\emptyset_2}$$

From (2-10), we also have

$$\mathrm{V}(Y_t) = \emptyset_1^2 \mathrm{V}(Y_{t-1}) + \emptyset_2^2 V(Y_{t-2}) + 2\emptyset_1\emptyset_2 Cov(Y_{t-1}, Y_{t-2}) + \sigma_u^2 \qquad (2\text{-}13)$$

Following (2-11), we have

$$V_1 = \emptyset_1 V_0 + \emptyset_2 V_{-1}$$

$$= \emptyset_1 V_0 + \emptyset_2 V_1$$

$$V_1 = \emptyset_1 \frac{V_0}{1-\emptyset_2}$$

Substituting of this equation into (2-13)

$$\Rightarrow \ V_0 = \frac{\sigma_u^2(1-\emptyset_2)}{(1-\emptyset_2)(1-\emptyset_1^2-\emptyset_2^2)-2\emptyset_1\emptyset_2} \qquad (2\text{-}14)$$

The use of AR(1) and AR(2) mentioned above is assumed with a stationary time-series. However, most of time series are not-stationary. To solve this problem, we first define.

$$\mathrm{B}(y_t) = y_{t-1}$$

B(.) represents backward shift parameter

$$y_t - \emptyset_1 y_{t-1} - \emptyset_2 y_{t-2} - \cdots - \emptyset_p\, y_{t-p}$$

$$= y_t(1 - \emptyset_1 B - \emptyset_2 B^2 - \cdots - \emptyset_P B^P) = u_t$$

$$\Rightarrow \emptyset(\mathrm{B}) y_t = ut$$

A non-stationary time series can be transformed to stationarity by differencing (of order d).

For instance,

$$Z_t - Z_{t-1} = (1-B)Z_t = (1-B)^2 y_t \text{ is stationary.}$$

$$\Rightarrow \mathrm{d}=2$$

2.4.4 Moving average models

$$\mathrm{y_t} = \mu_t - \theta_1\, \mu_{t-1} - \theta_2\, \mu_{t-2} - \cdots - \theta_q\, \mu_{t-q}$$

The moving average of order q is denoted by MA(q) with the following expression

$$\mathrm{y_t} = \mu_t - \theta\, \mu_{t-1} \qquad (2\text{-}15)$$

$$\mathrm{E(y_t)} = 0$$

$$\nu_0 = \nu(\mathrm{y_t}) = \sigma^2 + \theta^2\sigma_\mu^2 = \sigma^2(1+\theta^2)$$

$$\mathrm{Cov(y_t,\ y_{t-1})} = \mathrm{E(y_t\, y_{t-1})}$$

$$= \mathrm{E}[(\mu_t - \theta\, \mu_{t-1})(\mu_{t-1} - \theta\, \mu_{t-2})]$$

$$= \mathrm{E}(\mu_t\, \mu_{t-1}) - \theta[\mathrm{E}(\mu_{t-1}^2) + \mathrm{E}(\mu_t\, \mu_{t-2})] + \theta^2 \mathrm{E}(\mu_{t-1}\, \mu_{t-2})$$

$\because$ $\mu_1, \mu_2, \ldots$ are independent with $\mathrm{E}(\mu_t) = 0$ for all t.

$$\nu_1 = \mathrm{Cov(y_t,\ y_{t-1})} = -\theta\sigma_\mu^2$$

$$\mathrm{Cov}(y_t,\ y_{t-m}) = 0, \qquad m = 2,3,\ldots$$

The autocorrelation function is expressed as follows

$$\rho_1 = \frac{\nu_1}{\nu_0} = -\frac{\theta}{1+\theta^2} \qquad (2\text{-}16)$$

$$\rho_m = 0, \qquad m = 2,3,\ldots$$

Replacing θ with $\frac{1}{\theta}$, (2-16) gives the same autocorrelation.

The re-arrangement of 2-15 gives

$$\mu_t = y_t + \theta\ \mu_{t-1}$$

$$= y_t + \theta(y_{t-1} + \theta\ \mu_{t-2}) = y_t + \theta\ y_{t-1} + \theta^2\ \mu_{t-2}$$

$$\mu_t = y_t + \theta\ y_{t-1} + \theta^2\ y_{t-2} + \cdots$$

$$\Rightarrow y_t = -(\theta\ y_{t-1} + \theta^2\ y_{t-2} + \cdots) + \mu_t$$

If $|\theta| < 1$, it can be seen that MA(1) model is easily inverted to an infinite-order AR model.

Second-order Moving Average Model MA(2)

$$y_t = \mu_t - \theta_1\, \mu_{t-1} - \theta_2\, \mu_{t-2} \tag{2-17}$$

The auto covariance functions are

$$\nu_1 = \mathrm{Cov}(y_t, y_{t-1})$$

$$= -\theta_1\, \sigma_\mu^2 + \theta_1\, \theta_2\, \sigma_\mu^2 = -(\theta_1 + \theta_2)\sigma_\mu^2$$

$$\nu_2 = \mathrm{Cov}(y_t, y_{t-2}) = -\theta_2\, \sigma_\mu^2$$

$$\nu_0 = \nu(y_t) = \sigma_\mu^2 + \theta_1^2\sigma_\mu^2 + \theta_2^2\sigma_\mu^2$$

$$= (1 + \theta_1^2 + \theta_2^2)\, \sigma_\mu^2$$

The autocorrelation functions for MA(2) process are

$$\rho_1 = \frac{\nu_1}{\nu_0} = \frac{-\theta_1 + \theta_1\theta_2}{1 + \theta_1^2 + \theta_2^2} \tag{2-18}$$

$$\rho_2 = \frac{\nu_2}{\nu_0} = -\frac{\theta_2}{1 + \theta_1^2 + \theta_2^2} \tag{2-19}$$

$$\rho_k = 0, \qquad k = 3,4 \ldots$$

2.4.5 Autoregressive moving average models

With the application of the p-order of AR and the q-order of MA, the general form of combining AR with MA is expressed as follows

$$y_t = \left(\phi_1\, y_{t-1} + \phi_2\, y_{t-2} + \cdots + \phi_p\, y_{t-p}\right) \tag{2-20}$$
$$+ \left(\mu_t - \theta_1\mu_{t-1} - \theta_2\, \mu_{t-2} - \cdots - \theta_q\mu_{t-q}\right)$$

which is denoted as ARMA(p,q).

When p=1 and q=1, we have ARMA(1,1), which is expressed by

$$y_t = \phi\, y_{t-1} + \mu_t - \theta\, \mu_{t-1}$$

The auto covariance for the ARMA(1,1) is

$$E(y_t\, y_{t-m}) = \phi\, E(y_{t-1}\, y_{t-m}) + E(\mu_t\, y_{t-m}) - \theta E(\mu_{t-1}\, y_{t-m})$$

$$\Rightarrow \nu_k = \phi\, \nu_{k-1} + E(\mu_t\ \ y_{t-m}) - \theta\, E(\mu_{t-1}\, y_{t-m})$$

When k=0 $\Rightarrow \nu_0 = \phi\, \nu_1 + E(\mu_t\ \ y_t) - \theta\, E(\mu_{t-1}\, y_t)\ \ - (4.3.6)$

$$E(\mu_t\ \ y_t) = \sigma_\mu^2$$

Note that

$$E(\mu_{t-1}\, y_t) = \phi\, E(\mu_{t-1}\, y_{t-1}) + E(\mu_t\, \mu_{t-1}) - \theta E(\mu_{t-1}^2)$$

$$= \phi\sigma_\mu^2 - \theta\sigma_\mu^2 = (\phi - \theta)\sigma_\mu^2$$

$$\Rightarrow \nu_0 = \phi\, \nu_1 + \sigma_\mu^2 - \theta(\phi - \theta)\sigma_\mu^2$$

When k=1

$$\nu_1 = \phi\, \nu_0 + E(\mu_t\, y_{t-1}) - \theta\, E(\mu_{t-1}\, y_{t-1})$$

$$= \phi v_0 + E(\mu_t\ \ y_{t-1}) - \theta\, \sigma_\mu^2$$

$$E(\mu_t\ \ y_t) = \phi\, E(\mu_t\ \ y_{t-1}) + E(\mu_t^2) - \theta E(\mu_t\, \mu_{t-1})$$

$$\sigma_\mu^2 = \phi\, E(\mu_t\ \ y_{t-1}) + \mu_a^2$$

$$E(\mu_t\, y_{t-1}) = 0$$
$$\Rightarrow \nu_1 = \phi\nu_0 - \theta\, \sigma_\mu^2$$

$$\nu_0 = \phi^2\nu_0 - \phi\,\theta\,\sigma_\mu^2 + \sigma_\mu^2 - \phi\,\theta\,\sigma_\mu^2 + \theta^2\,\sigma_\mu^2$$
$$\Rightarrow \nu_0 = \frac{1 + \theta^2 - 2\phi\,\theta}{1 - \phi^2}\,\sigma_\mu^2$$

$$\nu_1 = \phi\left(\frac{1 + \theta^2 - 2\phi\,\theta}{1 - \phi^2}\right)\sigma_\mu^2 - \theta\,\sigma_\mu^2$$
$$= \frac{(\phi - \theta)(1 - \phi\,\theta)}{1 - \phi^2}\,\sigma_\mu^2$$

$$\because \nu_k = \phi\nu_{k-1}$$

The autocorrelation function for the ARMA(1,1) is

$$\rho_m = \begin{cases} 1 & m = 0 \\ \dfrac{(\phi - \theta)(1 - \phi\,\theta)}{1 + \theta^2 - 2\phi\,\theta} & m = 1 \\ \phi\,\rho_{m-1} & m \geq 2 \end{cases}$$

2.4.6 Dynamic linear models

In the early sixties, state-space models originated in the engineering fields. Its application in time series were noted in Akalke, Harrison and Stevens. It became established during the eighties by Aoki, Harvey, West and Harrison. It becomes more popular in the recent years and more applications are found in the area of molecular biology, ecology, space technology and finance [62-64].

The dynamic linear model can be a special case of a general state-space models, being Gaussian and linear. Dynamic linear models have flexibility to deal with nonstationary time series, parameter uncertainty, structural change, and statistical analysis. The dynamic linear models are often more interpretable than ARMA models, especially in the regression relationships. When the time series have discontinuity or shifts, the state-space model can deal with it directly.

In the case of nonstationary time series, one should do preliminary transformations in order to reach stationarity in ARMA analysis. State-space models can deal with nonstationary time series without preliminary transformation of the data. If we consider a system filled with disturbances, as in the real world, we may apply a time series with the build-in disturbances or noises.

The dynamic linear model is expressed as

$$\mathrm{Y}_t = \mathbf{F}_t'\boldsymbol{\theta}_t + v_t \tag{2-21}$$

$$\boldsymbol{\theta}_t = \mathbf{G}_t\boldsymbol{\theta}_{t-1} + \omega_t \tag{2-22}$$

$\mathbf{F}_t$ is a p-dimensional vector of regression vector or known constants.

$\boldsymbol{\theta}_t = (\theta_{t,1}, \theta_{t,2}, \ldots, \theta_{t,p})'$, a px1 state vector at time *t*.

$v_t \sim \mathrm{N}(0, \mathbf{V}_t)$ is observation noise

$\mathbf{G}_t$ is a *p* x *p* state evolution matrix at time *t*.

$\omega_t \sim \mathrm{N}(0, \mathbf{W}_t)$ is the state evolution noise at time *t*.

The dynamic linear model is a model with two sub-models. The first equation is an observation process. It is determined by a latent process called systemic process, the second equation. If we knew the latent process at successive time points, the $\mathrm{Y}_t{'s}$ would be independent. The second equation is the systemic process, which cannot be observed directly. This equation assumed that $\boldsymbol{\theta}_t$ depends on itself of the previous time point, $\boldsymbol{\theta}_{t-1}$, through an evolution matrix, $\mathbf{G}_t$. In the dynamic linear model, the assumption is linear relationship and Gaussianity. Then the forecasting of the future $\mathrm{Y}_{t+k}{'s}$ can be obtained sequentially.

The simple form of dependence among the $\mathrm{Y}_t{'s}$ is the Markov property.

$\pi(y_t | y_{1:t-1}) = \pi(y_t | y_{t-1})$ for any $t > 1$.

$(Y_t)_{t\geq 1}$ is a Markov chain with Markov property. The information about y_t carried by $y_{1:t-1}$ is the same with that carried by y_{t-1}. This means that y_t depends on y_{t-1} alone.

The finite-dimensional joint distributions can be expressed as

$$\pi(y_{1:t}) = \pi(y_1) \cdot \prod_{j=2}^{t} \pi(y_j | y_{j-1}) \qquad (2\text{-}23)$$

in a Markov chain.

Then the state-space model is specified as

$$\pi(\theta_{0:t}, y_{1:t}) = \pi(\theta_0) \cdot \prod_{j=1}^{t} \pi(\theta_j | \theta_{j-1}) \cdot \pi(y_j | \theta_j) \tag{2-24}$$

In the linear state space model, one can specify linear distributions. For instance, in normal linear model, one can use normal distributions in the following functions h_t and g_t.

A general state-space model:

$$Y_t = h_t(\theta_t, v_t) \tag{2-25}$$

$$\theta_t = g_t(\theta_{t-1}, w_t) \tag{2-26}$$

2.4.7 Regression models and ARMA models in DLM representation

Using state-space formulation, ARMA models can be expressed as dynamic linear models[65,66]. (See equation (2-21), (2-22))

$$\mathrm{Y}_t = \mathbf{F}_t' \boldsymbol{\theta}_t + v_t \tag{2-21}$$

$$\boldsymbol{\theta}_t = \mathbf{G}_t \boldsymbol{\theta}_{t-1} + \omega_t \tag{2-22}$$

$\mathbf{F}_t$ is a p-dimensional vector of regression vector or known constants.

$\boldsymbol{\theta}_t = (\theta_{t,1}, \theta_{t,2}, \ldots, \theta_{t,p})'$, a px1 state vector at time *t*.

$v_t \sim \mathrm{N}(0, \mathbf{V}_t)$ is observation noise

$\mathbf{G}_t$ is a p x p state evolution matrix at time t.

$\omega_t \sim \mathrm{N}(0, \mathbf{W}_t)$ is the state evolution noise at time t.

(a) Static regression model: (From equation (2-21), (2-22))

$$\mathrm{Y}_t = \mathbf{F}_t' \boldsymbol{\theta}_t + v_t \tag{2-21}$$

$$\boldsymbol{\theta}_t = \mathbf{G}_t \boldsymbol{\theta}_{t-1} + \omega_t \tag{2-22}$$

We have

$$\mathbf{G}_t = \mathbf{I}_p = \begin{bmatrix} 1 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & 1 \end{bmatrix} \text{ and } \mathbf{W}_t = \mathbf{0} \text{ for all } t. \tag{2-27}$$

For example, we can include an explanatory variable, x, as

$$Y_t = \theta_1 + \theta_2 x_t + v_t, \ v_t \ iid \sim \mathrm{N}(0, \sigma^2) \tag{2-28}$$

A DLM with ($\theta_t = \begin{bmatrix} \theta_1 \\ \theta_2 \end{bmatrix}$, $F_t = \begin{bmatrix} 1 \\ x_t \end{bmatrix}$, $\mathbf{G}_t = \mathbf{I}$, $\mathbf{W}_t = \mathbf{0}$) is a static regression with explanatory variable x, and the vector (Y_t, x_t), t=1,2,… is observed over time.

(b) Time-varying regression model: (From equation (2-21), (2-22))

$$\mathrm{Y}_t = \mathbf{F}_t' \boldsymbol{\theta}_t + v_t \tag{2-21}$$

$$\boldsymbol{\theta}_t = \mathbf{G}_t \boldsymbol{\theta}_{t-1} + \omega_t \tag{2-22}$$

$$\mathbf{G}_t = \mathbf{I}_p = \begin{bmatrix} 1 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & 1 \end{bmatrix} \text{ and } \mathbf{W}_t \neq \mathbf{0} \quad \textbf{, random walk.} \tag{2-29}$$

For example, we can include an explanatory variable, x, as

$$Y_t = \theta_{t,1} + \theta_{t,2} x_t + v_t, \;\; v_t \; iid \sim \mathrm{N}(0, \sigma^2) \tag{2-30}$$

$$\theta_t = \begin{bmatrix} \theta_{t,1} \\ \theta_{t,2} \end{bmatrix}, \;\; F_t = \begin{bmatrix} 1 \\ x_t \end{bmatrix}.$$

(c) Linear growth model (local linear trend with time-varying slope in the dynamics for μ_t) (From equation (2-21), (2-22),

$$\mathrm{Y}_t = \mathbf{F}_t' \boldsymbol{\theta}_t + v_t \tag{2-21}$$

$$\boldsymbol{\theta}_t = \mathbf{G}_t \boldsymbol{\theta}_{t-1} + \omega_t \tag{2-22}$$

$$\mathrm{Y}_t = \mu_t + v_t \tag{2-31}$$

$$\mu_t = \mu_{t-1} + \beta_{t-1} + \omega_{t,1} \tag{2-32}$$

$$\beta_t = \beta_{t-1} + \omega_{t,2} \tag{2-33}$$

That is,

$$v_t \sim \mathrm{N}(0, \mathrm{V}), w_{t,1} \sim \mathrm{N}\left(0, \sigma_\mu^2\right), w_{t,2} \sim \mathrm{N}\left(0, \sigma_\beta^2\right)$$

This is a dynamic linear model with $\theta_t = \begin{bmatrix} \mu_t \\ \beta_t \end{bmatrix}$, $\mathrm{G} = \begin{bmatrix} 1 & 1 \\ 1 & 0 \end{bmatrix}$,

system variance: $\mathrm{W} = \begin{bmatrix} \sigma_\mu^2 & 0 \\ 0 & \sigma_\beta^2 \end{bmatrix}$, $\mathrm{F} = \begin{bmatrix} 1 \\ 0 \end{bmatrix}$.

(d) Static autoregression, AR(p) model:

(From equation (2-21),

$$\mathrm{Y}_t = \mathbf{F}_t'\boldsymbol{\theta}_t + v_t \quad (2\text{-}21)$$

$$\mathbf{F}_t' = (y_{t-1}, y_{t-2}, \dots, y_{t-p}),\ \boldsymbol{\theta}' = (\emptyset_1, \emptyset_2, \dots, \emptyset_p),\ v_t = \epsilon_t, \text{ for all } \boldsymbol{t}.$$

(d-1) Alternatively, the Gaussian ARMA and DLM models are the same in the time-invariant case. (Hannan and Deistler, 1988). From equation (2-21) and (2-22),

$$\mathrm{Y}_t = \mathbf{F}_t'\boldsymbol{\theta}_t + v_t \quad (2\text{-}21)$$

$$\boldsymbol{\theta}_t = \mathbf{G}_t\boldsymbol{\theta}_{t-1} + \omega_t \quad (2\text{-}7)$$

$$\mathbf{F}_t = \mathbf{F},\ \mathbf{G}_t = \mathbf{G},\ \mathbf{W}_t = \mathbf{W} \quad (2\text{-}34)$$

For example,

$$\mathbf{F}_t = \mathbf{F} = (1,0,0,\dots,0)'$$

$$\mathbf{G}_t = \mathbf{G} = \begin{bmatrix} \emptyset_1 & 1 & 0 \cdots & 0 \\ \emptyset_2 & 0 & 1 & 0 \\ \vdots & & \ddots & \vdots \\ \emptyset_{p-1} & 0 & 0 \cdots & 1 \\ \emptyset_p & 0 & 0 & 0 \end{bmatrix},\ v_t = 0 \text{ for all t, and } \mathbf{W}_t = \mathbf{W} = \begin{bmatrix} w & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & 0 \end{bmatrix}, \text{w>}\mathbf{0}$$

(d-2) time-dependent variance

$$\mathbf{W}_t = \begin{bmatrix} w_t & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & 0 \end{bmatrix},\ w_t > 0 \quad (2\text{-}35)$$

(e) Time-varying autoregressive coefficients (TVAR) model: (also called random coefficient autoregressive (RCAR) model). (Congdon p145)

The lag coefficients $\boldsymbol{\theta_t}$ can vary over time.

From equation (2-21) and (2-22),

$$\mathrm{Y}_t = \mathbf{F}_t'\boldsymbol{\theta_t} + v_t \tag{2-21}$$

$$\boldsymbol{\theta_t} = \mathbf{G}_t\boldsymbol{\theta_{t-1}} + \omega_t \tag{2-22}$$

In which

$$\mathbf{F}_t' = \left(y_{t-1}, y_{t-2}, \ldots, y_{t-p}\right) \text{ and } \mathbf{W}_t \neq \mathbf{0} \text{ for all } t. \tag{2-36}$$

(f) Autoregressive moving average (ARMA) model,

(f-1) $\mu = 0$, ARMA(p,q)

$$Y_t = \sum_{r=1}^{p} \phi_r Y_{t-r} + \sum_{r=1}^{q} \psi_r \epsilon_{t-r} + \epsilon_t \tag{2-37}$$

$$\phi_r = 0 \; for \; r > p \; and \; \psi_r = 0 \; for \; r > q$$

DLM expression:

$$\mathrm{Y}_t = \mathbf{F}_t'\boldsymbol{\theta_t} + v_t \tag{2-21}$$

$$\boldsymbol{\theta_t} = \mathbf{G}_t\boldsymbol{\theta_{t-1}} + \omega_t = \mathbf{G}_t\boldsymbol{\theta_{t-1}} + \mathbf{R}\epsilon_t \tag{2-38}$$

$$\mathrm{m} = \max(\mathrm{p}, \mathrm{q}+1),$$

$$\mathrm{F} = [1\ 0\ \ldots\ 0]'$$

$$\mathbf{G}_t = \mathbf{G} = \begin{bmatrix} \emptyset_1 & 1 & 0 \ \cdots & 0 \\ \emptyset_2 & 0 & 1 & 0 \\ \vdots & & \ddots & \vdots \\ \emptyset_{m-1} & 0 & 0 \ \cdots & 1 \\ \emptyset_m & 0 & 0 & 0 \end{bmatrix}$$

$$\omega_t = (1, \psi_1, \dots, \psi_{m-1})' \epsilon_t = \mathbf{R}\epsilon_t$$

$$\text{V} = 0, \qquad \text{and W} = \mathbf{RR}'\sigma^2$$

$$\theta_t = (\theta_{1,t}, \dots, \theta_{m,t})'$$

σ^2: the variance of the error sequence (ϵ_t)

(f-2) observational noise-free DLM: $v_t = \mathbf{0}$ in equation (2-21)

$$\text{Y}_t = \mathbf{F}_t'\boldsymbol{\theta}_t \tag{2-39}$$

$$\boldsymbol{\theta}_t = \mathbf{G}_t\boldsymbol{\theta}_{t-1} + \omega_t \tag{2-22}$$

Dimension: m

Evolution variance matrix

$$\text{U} = \text{U}(1, \psi_1, \dots, \psi_{m-1})'(1, \psi_1, \dots, \psi_{m-1}).$$

(g) Polynomial trend model:

In equation (2-21) and (2-22),

$$\text{Y}_t = \mathbf{F}_t'\boldsymbol{\theta}_t + v_t \tag{2-21}$$

$$\boldsymbol{\theta}_t = \mathbf{G}_t\boldsymbol{\theta}_{t-1} + \omega_t \tag{2-22}$$

We have

$$\mathbf{F} \quad = (1, 1, 0, \dots, 0)'$$

$$\boldsymbol{\theta}' = (\mu_t, \emptyset_2, \dots, \emptyset_p) \quad (2\text{-}40)$$

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2.4.8 Stationary time series

Stationarity definition:

1. Strict Stationary if for any integer n, the distribution function of any random vector $Z_{t,n+1} = (Z_t, \dots, Z_{t+n})'$ is independent of the time t.
2. Weakly stationary if both $\mathrm{E}[Z_{t,n+1}]$ and $\mathrm{V}[Z_{t,n+1}]$ are independent of the time t.
3. Gaussian (normal) stationary if it is weakly stationary and the distribution of every $Z_{t,n+1}$ is normal.

A DLM $\{\mathrm{F}_t, G_t, \mathrm{V}_\mathrm{t}, W_t\}$ is a zero mean weakly stationary DLM if and only if

(1) It is equivalent to an observable constant DLM [67];

(2) The eigenvalues of G lie inside the unit circle, i.e., $|\lambda_i| < 1, for\ i = 1, \dots, n$

2.4.9 Filtering, Smoothing, and Forecasting in dynamic linear models

Filtering means to use the recent data to revise the previous values of the previous state. The filtering distribution is $\pi(\theta_t|y_{1:t})$. And $\pi(\theta_{t-k}|D_t), for\ k \geq 1$ is called the k-step time t filtered distribution for the state vector. Smoothing is a retrospective reconstruction of the time series system using the filtered distribution. Forecasting is to compute the value or the state of the future based on the filtering density of time t state, $\boldsymbol{\theta_t}$. $\pi(y_{t+1}|y_{1:t})$is the one-step-ahead predictive density.

2.4.10 Generalized autoregressive moving-average models

The problems of non-Gaussian time series is encountered in many research fields such as biology, epidemiology, and medical studies, in that the observations are likely to be positive and sometimes are integers or counts data. Time series models for counts have been used by several authors [68]. The extension of the normal distributed time series to the suitable distribution is reasonable. Poisson autoregressive model is therefore considered.

Hsu et al. applied generalized Poisson autoregressive model on the Japanese encephalitis to evaluate the secular time trend, seasonal variation pattern, autoregressive order of Japanese encephalitis incident cases and temporal relationship of lagged temperature and precipitation[13]. They also adjusted vaccination rate, pig density, and geographic area variation. The model form is written as follows.

$$\log\left(E\left(y_t|y_{t-1},\dots y_{t-l},x_1,x_2,x_3,\dots,x_p,t,m_1,\dots,m_{11}\right)\right)=\ln(PY)+ \quad (2.41)$$

$$\alpha+\sum_{k=1}^{n}v_kTM_{t-k}+\sum_{i=1}^{m}\pi_iRa_{t-i}+\delta_1t+\alpha_3+\beta_1x_1+\cdots+\beta_px_p+$$

$\omega_1 m_1 + \cdots + \omega_{11} m_{11} + \sum_{j=1}^{l} \gamma_j \, y_{t-j}$

Where y_t is the number of Japanese encephalitis cases by month at time t. $x_1, \ldots, x_p$ are covariates such as pig density and geographic area. $m_1, \ldots, m_{11}$ are dummy seasonal variables. y_{t-j} are autoregressive orders and $\ln(PY) = \ln(\text{Person} - \text{Years})$ is the offset. $\sum_{k=1}^{n} v_k TM_{t-k} + \sum_{i=1}^{m} \pi_i Ra_{t-i}$ is the combinations of lagged temperature and precipitation. v_k , π_i , δ_1 , $\beta_1, \ldots, \beta_p, \omega_1, \ldots, \omega_{11}$ are the corresponding regression coefficients [13].

The proposed model, albeit it has been extended form Gaussian data to non-Gaussian data, is the failure of taking into account the uncertainty of parameters, and correlated property and heterogeneity property due to hierarchical data.

Due to the limitation of the application of previous models for the infection data, we developed a novel Bayesian generalized linear mixed ARIMA model and applied it to HAIs.

Chapter 3 Materials and Methods

3.1 Setting

A cohort of healthcare-associated infections was followed during the period of January 1, 1994 and December 31, 2011 in an urban tertiary medical center in northern Taipei with 921-bed and approximately 27,000 inpatient admission annually.

3.2 Patient enrollment and Definition

Patients who fulfilled the criteria of healthcare-associated infections (HAIs) were eligible for this HAIs cohort since 1994. All confirmed cases and related factors were prospectively collected in the database.

Hospital information system

The nationwide health insurance has been launched since 1-March 1995 in Taiwan [69]. Before this significant change in medical system, the hospital information system, including inpatient, outpatient, emergency, prescription, bio-laboratory, etc., was established for automatic insurance reimbursement and payment. Besides those systems, the hospital-associated infection registry system also was separately set up to systematically collect the HAIs for quality control of hospital care which was independently from insurance payment. But, those could link with admission of hospitalized status and laboratory examination using chart number linkage. Therefore, the all hospitalized admission and infection status could be completed accessed since 1994. The database contains information about every admitted patient, includes, date of admission, date of discharge, and date of transfer, ward of admission, physician attending service, operation information if available, discharge condition, and the International Classification of Diseases (Ninth Revision) Clinical Modification (ICD-9-CM) codes of diagnoses, admission types (from emergency or outpatient department),

Hospital-associated infection registry system

The infection control team established a nosocomial infection registry system since 1993. Ever since then, a central infection committee has coordinated the infection control and confirmed enrolled cases every week. HAIs were defined according to the U.S. Centers for Disease Control and Prevention standards. The U.S. CDC defined an HAI as a localized or systemic condition resulting from an adverse reaction to the presence of an infectious agents or its toxins[70]. HAIs were classified as urinary tract infection (UTI), surgical site infection (SSI), pneumonia (PNEU), bloodstream (Bacteremia), skin and soft tissue (SST), gastrointestinal system (GI), eye, ear, nose, throat, or moth (EENT), and other (central nervous, reproductive tract, bone and joint, and cardiovascular system infections) [70,71]. The database contains comprehensive information about age, gender, infection sites, culture sampled date, indwelling bladder catheter, central venous catheter, admitted medical departments, and numbers of HAIs episodes during each admission. This registry system are used for clinical infectious diseases studies [72,73].

Incident cases: Incident cases were those free of HAIs hospitalized patients attacked by a new episode of HAI at least 48 hours after their admission in each month.

HAI episode: A HAI episode was defined as a new infection acquired in the hospital documented after at least 48 hours admission in the hospital.

HAI-related 30-day death: For the incident cases who died within 30 days and caused by the HAI were defined.

Patient-days: It was calculated since admission entrance and ended by the first infection occur. The patient-days of non-infectious patients was reckoned the duration of hospitalization.

Incidence rate: The incidence rate was expressed as number of infection episodes per 1,000 patient-days.

Death rate: Death rate was the number of deaths due to HAIs per 100 HAIs patients.

Mortality rate: Mortality rate was calculated as the death cases per 1,000 patient-days which was also the product of the incidence rate and the death rate.

Culture: Microbiological specimens were collected as recommended by the CDC. Thresholds of positive culture was defined according to the CDC for different infection sites[70,71].

3.3 Study design

This study was designed as an incidence-death follow-up cohort. The current study focused on the incidence part of the cohort (Figure 1). Those incident cases were followed up for 30 days, and those who died within 30 days and caused by the HAI episode were defined as HAIs related 30-day death. Since the seasonal variations exist in hospital admissions [17], this study use disease incidence as a measurement unit instead of counts.

During the study period of twenty-years, the hospital policy-maker conducted infection control interventions. The intervention programs of the hospital were Plan-Do-Check-Act (PDCA) program, Hygiene Programs, Centers for Disease Control, R.O.C. (Taiwan) (CDC) Hand-hygiene project and the urinary tract infection Quality Improvement Program of Taiwan Joint Commission on Hospital Accreditation

(TJCHA), and bundle care program were conducted by the hospital infection control team. The details of each intervention were described as follows.

PDCA program: The hospital infection control decision-makers initiated a program using Edward Deming's Plan-Do-Check-Act (PDCA) cycle-combined monitoring for each warning outbreak of HAI incidence since 2005. It was a warning-feedback system that the infection control team monitored the infection rate of wards. If the infection rate was above the 95% confidence interval, the ward-based unit should launch the act to improve the infection rate.

Hygiene programs: They were the combined facility improvement and continuing education programs. The infection control team both introduced an alcohol-based hand rub disinfection site for each ICU bed and set hand hygiene stands at ward entrances since 2007. They also set a red warning line to separate the ICU patients care from the healthcare member paperwork station.

CDC/TJCHA project: Centers for Disease Control, R.O.C. (Taiwan) (Taiwan CDC) and Taiwan Joint Commission on Hospital Accreditation (TJCHA) together setup the standards for the hospital healthcare-associated infection control audit since 2008. The Minister of Health Dr. Yeh approved Taiwan CDC to initiate National Hand Hygiene Campaign in May, 2009. The goals of the National Hand Hygiene Campaign were to form the culture of patient safety and to encourage hospitals to improve continually by evaluating performance indicators regularly. Shin Kong Wu Ho-Su Memorial Hospital participated the auditing program since 2010. In order to meet the standards of the auditing, the hospital increased the numbers of hand-hygiene stands in the ward, rewarded the healthcare staffs if they reached the points of infection control, and launched serial education classes. We also joined the Catheter-related Urinary Tract Infection Quality Improvement Project conducted by TJCHA. The catheter use rate and the indwelling time were monitored in the intensive care units.

Bundle care program: It was a multidisciplinary approach to decrease the catheter-related infection in intensive care unit since July, 2011.

3.4 Covariates

All confirmed cases and related factors were prospectively collected in the database.

Patient characteristics: age, gender, date of birth, admission, diagnosis of HAI, discharge, transfer to ICU, and death

Infection-related covariates: infection sites, cultures sampled date, indwelling bladder catheter and central venous catheter, microorganism cultures

Disease conditions: the International Classification of Diseases (Ninth Revision) Clinical Modification (ICD-9-CM) codes of diagnoses, admission types (from emergency or outpatient department), admitted medical departments, numbers of HAIs episodes during each admission, and cause of death.

Intervention programs indicators: Intervention of PDCA, Hygiene programs, Taiwan Centers for Disease Control (CDC) National Hand Hygiene Campaign and the urinary tract infection quality improvement program of Taiwan Joint Commission on Hospital Accreditation (TJCHA) called CDC/TJCHA, and Bundle care program.

Chapter 4 Model specification

Generalized linear time series models were used for analysis of HAIs incidence. Moreover, Bayesian state-space model was used for evaluating the time-dependent incidences and for forecasting future incidences in HAIs. Both were delineated as follows.

4.1 Generalized linear time series model

To accommodate various distributions of the outcome of interest covering from continuous to discrete types, a generalized linear time-series model following Zeger et al[74] study and applied to Japanese encephalitis by Hsu et al[13] was proposed in my thesis (Figure 4.1.1, Figure 4.1.2).

Under the context of GLM, three components are often defined, including

(1) Random component

It is the distribution of the outcome Y and expressed by $E(Y) = \mu$

(2) Link function

It is a function defined by $h(\mu)$, which can take varies kinds of distributions, mainly including identity function for normal distribution, logistic function for binomial distribution, logarithm function for Poisson distribution and so on.

(3) Systemic components

This part includes the major components covered in time-series analysis such as seasonal variation, time trend, the cyclic change, and autoregressive orders. The generalized form is written as follows.

$$h(\mu) = \eta \tag{4-1}$$

η represents systematic components. If the outcome of Y is specified by a Poisson distribution, the equation (4-1) is expressed by

$$\log \mu = \ln(PY) + \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_p X_p + g(t) + s(t) + \sum_{j=1}^{l} r_j y_{t-j} \tag{4-2}$$

$X_1, \ldots, X_p$ represent covariates such as age and gender.

$g(t)$ is a polynomial function of time trend.

$s(t)$ is a function of seasonality. Trigonometric function is one of choices. Here, we used dummy variables to denote spring, summer, autumn, and winter denoted by $s_1 - s_3$. Trigonometric function is used in Bayesian approaches for comparison.

4.2 Decomposition method with generalized linear time-series model

We extended the time series to the Poisson seasonal model in order to have a better fit with the HAIs incidence data. The algorithm consists of four steps. Firstly, the incidence was checked for its seasonality and de-seasonalized if any. Secondly, the residual of the first step was used for trend detection. De-trend procedure was applied if trend existed. Third, cycling was checked if any. Finally, the left residual of the above three steps was checked for discernible patterns or autocorrelations.

The algorithm is written as follows:

Step1.

$$\log\left(E\left(y_t|x_1, x_2, x_3, \dots, x_p, s_1, s_2, s_3, s_4, t\right)\right) \tag{4-3}$$

$$= \ln(PD) + \alpha_2 + \omega_1 s_1 + \omega_2 s_2 + \omega_3 s_3 + \omega_4 s_4 + \varepsilon_1$$

Step2.

$$E(\varepsilon_1|t) = \alpha_2 + \delta_1(t - \bar{t}) + \delta_2(t - \bar{t})^2 + \delta_3(t - \bar{t})^3 + \varepsilon_2 \tag{4-4}$$

Step3.

$$E(\varepsilon_2|c) = \alpha_3 + \beta_1 x_1 + \cdots + \beta_p x_p + \varepsilon_3 \tag{4-5}$$

Step4.

Residual plots for ε_3 to check

(a) Autocorrelations: autoregressive order, sample autocorrelation function plots (SAC) using ARIMA method, Ljung-Box statistics.

(b) Normality: Normal plot

4.3 Bayesian Dynamic linear models (DLM)

We are not only interested in the population microbiology on understanding temporal fluctuations in abundance of specific microorganisms, but also in the impact on its relation to the diseases. For instance, as the antibiotics-resistant microorganism grows rapidly, it may increase the possibility to invade the hosts, causes diseases, and the incidence of diseases will increase. However, this is the simplified model for microorganism-host interactions. There are still several interactions between microorganisms, environment, and hosts. Factors involving in the interactions make the interpretation of incidence-microorganism abundance status a complex phenomenon. Crucially, our understanding of disease incidence is also affected by errors in the observation process. Separating true microorganism abundance (biological signals) from observation error in data is of great importance.

In this study, we aimed at evaluating the population dynamics of HAIs microorganisms and its relationships with disease incidence. The disease incidence survey of HAIs time series sometimes include errors, and yet most previous studies have not explicitly been able to account for errors. Therefore, analysis that can manage the source of errors are needed in disease control.

Following the dynamic linear model mentioned in the literature in Chapter 2, we have used state-space model based on the equation (2-21) and (2-22).

To simplify the notation, we use state-space model with the form expressed by

$$y_t = X_t^T \beta + e_1^T C_t \tag{4-6}$$

, which is so-called observation equation, and

$$C_t = G C_{t-1} + e_1 v_t \tag{4-7}$$

, which is so-called state equation. e_1 is a px1 vector with a one in the first row and zeros elsewhere. Note that Y_t is the observed number of disease, C_t is the true pathogen state. Y_p is expressed as

$$Y_p = X_p \beta + C_p \tag{4-8}$$

$$X_r = \begin{pmatrix} X_p^T \\ X_{p-1}^T \\ \vdots \\ \vdots \\ X_{r-p+1}^T \end{pmatrix}$$

It follows that

$$\Omega_p = Var(Y_p) = Var(C_p)$$

$$= Var(GC_{p-1} + V_p e_1)$$

$$= GVar(E_{p-1})G^T + \sigma_v^2 e_1 e_1^T$$

$$= G\Omega_p G^T + \sigma_v^2 e_1 e_1^T \quad (4\text{-}9)$$

($\because$ $\mathrm{Var}(C_p) = \mathrm{Var}(C_{p-1})$ by stationary and C_p and C_{p-1} are independent)

By defining $\sum_p = (\frac{1}{\sigma_v^2})\,\Omega_p$, the distribution of Y_p will follow a normal distribution,

$Y_p \sim N_p(X_p\beta, \sigma_v^2\Sigma_p)$.

$\Sigma_p$can be written in terms of ϕ (autocorrelation) with vector form like the following

$$\mathrm{Vec}(\Sigma_p) = \mathrm{Vec}(\mathrm{G}\Sigma_p G^T) + \mathrm{Vec}(e_1 e_1^T)$$

$$= (\mathrm{G} \otimes \mathrm{G})\mathrm{Vec}(\Sigma_p) + \mathrm{Vec}(e_1 e_1^T)$$

$$= [\mathrm{I} - (\mathrm{G} \otimes \mathrm{G})]^{-1}\mathrm{Vec}(e_1 e_1^T) \quad (4\text{-}10)$$

The joint posterior distribution of the parameters is

$$\mathrm{P}(\beta, \phi, \sigma_v^2) \propto \left(\frac{1}{\sigma_v^2}\right)^{\frac{p}{2}} \times \frac{1}{|\Sigma_p|^{\frac{p}{2}}} \exp\left[-\frac{1}{2\sigma_v^2}(Y_p - X_p\beta)^T \Sigma_p^{-1}(Y_p - X_p\beta)\right] \quad (4\text{-}11)$$

$$\times \left(\frac{1}{\sigma_v^2}\right)^{\frac{(T-p)}{2}} \exp\left[-\frac{1}{2\sigma_v^2}\sum_{p+1}^{T}(\hat{y}_t - \hat{x}_t\beta)^T(\hat{y}_t - \hat{x}_t\beta)\right]$$

$$\times P(\beta)P(\sigma_v^2)P(\phi)$$

Assuming $\beta \sim N_k(\beta_0, \gamma_0)$.

It is easy to show that $\beta | y, \sigma_v^2, \ \phi \sim N_k(\bar{\beta}, \gamma_1)$.

$$\gamma_1 = \left[\sigma_v^{-2}\left(X_p^T \Sigma_p^{-1} X_p + \sum_{p+1}^{T} \hat{x}_t \hat{x}_t^T\right) + \gamma_0^{-1}\right]^{-1}$$

$$\bar{\beta} = \gamma_1 \left[\sigma_v^{-2}\left(X_p^T \Sigma_p Y_p + \sum_{p+1}^{T} \hat{x}_t y_t^T\right) + \gamma_0^{-1}\beta_0\right] \quad (4\text{-}12)$$

The derivation of $P(\sigma_v^2 | y, \beta, \phi)$ is straightforward by assuming that the prior distribution for $\frac{1}{\sigma_v^2}$ is $\text{Gamma}\left(\frac{\alpha_1}{2}, \frac{\delta_1}{2}\right)$.

$$\frac{1}{\sigma_v^2} | y, \beta, \phi \sim \text{Gamma}\left(\frac{\alpha_1}{2}, \frac{\delta_1}{2}\right)$$

$$\alpha_1 = \alpha_0 + T$$

$$\delta_1 = \delta_0 + \left(Y_p - X_p\beta\right)^T \Sigma_p^{-1}\left(Y_p - X_p\beta\right) + \sum_{p+1}^{T}(\hat{y}_t - \hat{x}_t^T\beta)^T(\hat{y}_t - \hat{x}_t^T\beta) \quad (4\text{-}13)$$

The conditional posterior distribution of β and σ_v^2 can be simulated by Gibbs sampling scheme.

To reflect the dependence of Σ_p on ϕ with $\Sigma_p(\phi)$, let

$$y_t^* = y_t - X_t^T\beta$$

$$y_t^* = \phi_1 y_{t-1}^* + \cdots + \phi_p y_{t-p}^* + v_t$$

$$= y_{t-1}^{*}\phi + v_t \quad (4\text{-}14)$$

Accordingly, for $t > p$ $y_t^{*} \sim N(y_{t-1}^{*}\phi, \sigma^2)$. The conditional posterior distribution of ϕ is therefore

$$\phi | y, \beta, \sigma_v^2 \propto \frac{1}{\left|\Sigma_p(\phi)\right|^{\frac{T}{2}}} exp\left[-\frac{1}{2\sigma_v^2}\left(Y_p - X_p\beta\right)^T \Sigma_p^{-1}(\phi)\left(Y_p - X_p\beta\right)\right]$$

$$\times exp\left[-\frac{1}{2\sigma_v^2}\sum_{p+1}^{T}(y^{*} - y_{t-1}^{*}\phi)^T(y_t^{*} - y_{t-1}^{*}\phi)\right]$$

$$\times P(\phi)1(\phi \in S_{\phi}) \quad (4\text{-}15)$$

Where S_{ϕ} is the region in which the process is stationary. Note that this distribution is a non-standard distribution but it may be sampled with an Metropolis-Hasting algorithm after specifying the prior distribution of ϕlike $\phi \sim \mathrm{N}(\phi_0, \Phi_0)$. A proposal candidate density may be obtained by multiplying $P(\phi)$by the terms involving y_t^{*}, $t > p$ with the distribution specified by $\phi \sim \mathrm{N}(\hat{\phi}, \widehat{\Phi})$.

$$\widehat{\Phi} = \left(\sigma_v^{-2}\sum_{p+1}^{T} {y_{t-1}^{*}}^{T} y_{t-1}^{*} + \Phi_0^{-1}\right)$$

$$\hat{\phi} = \widehat{\Phi}\left(\sigma_v^{-2}\sum_{p+1}^{T} {y_{t-1}^{*}}^{T} y_{t-1}^{*} + \Phi\phi_0\right) \quad (4\text{-}16)$$

Draws of ϕ from $\phi \sim \mathrm{N}(\hat{\phi}, \widehat{\Phi})$ will be performed with one is found that is in stationary region, which is subject to the usual Metropolis-Hasting acceptance region. The state-space form consists of the observation equation when regression coefficients evolve randomly through time following the equations (4-6) and (4-7).

$$y_t = X_t^T \beta_t + v_t \tag{4-17}$$

and the transition equation

$$\beta_t = \beta_{t-1} + e_t \tag{4-18}$$

where $t = 1, \dots, T$, y_t and v_t are scalars, X_t, β_t, and e_t are k x 1 vectors, $v_t \sim N(0, \sigma^2)$, and $e_t \sim N_k(0, \Sigma)$. v_t and e_t are assumed to be independent with each other through time.

To generalize this model as a vector autoregression, this model is defined as

$$\mathrm{Y} = (y_T, y_{T-1}, \dots, y_1)^T$$

$$\beta = (\beta_T, \beta_{T-1}, \dots, \beta_1)^T$$

$$\mathrm{v} = (v_T, v_{T-1}, \dots, v_1)^T$$

$$\mathrm{e} = (e_T, e_{T-1}, \dots, e_1)^T$$

$$\mathrm{X} = \begin{pmatrix} X_T^T & 0 & 0 & 0 \\ 0 & X_{T-1}^T & \cdots & 0 \\ \vdots & \vdots & \ddots & 0 \\ 0 & 0 & \cdots & X_1^T \end{pmatrix}$$

This likelihood function is

$$f(y|\beta, \sigma^2) \propto \frac{1}{\sigma^2}^{\frac{T}{2}} \exp\left[-\frac{1}{2\sigma^2}(y - \mathrm{X}\beta)^T (y - \mathrm{X}\beta)\right] \tag{4-19}$$

The prior distribution based on the transition equation for β can be defined by the kT x kT matrix F

$$\mathrm{F} = \begin{pmatrix} \mathrm{I}_k & -\mathrm{I}_k & 0 & \dots & 0 \\ 0 & \mathrm{I}_k & -\mathrm{I}_k & \dots & 0 \\ \vdots & 0 & \mathrm{I}_k & \ddots & 0 \\ \vdots & 0 & \ddots & \ddots & 0 \\ 0 & 0 & 0 & 0 & \mathrm{I}_k \end{pmatrix}$$

$\mathrm{F}\beta = \widetilde{\beta_0} + e$, where $\widetilde{\beta_0}$ is a Tk x 1 vector with β_0 in the last k rows and zero elsewhere. It follows that $\beta = \mathrm{F}^{-1}\widetilde{\beta_0} + \mathrm{F}^{-1}e$. The distribution of β is derived as follows. $\beta \sim N_k\left(\mathrm{F}^{-1}\widetilde{\beta_0}, \mathrm{F}^{-1}(\mathrm{I}_T \otimes \Sigma)(\mathrm{F}^{-1})^T\right)$

The priors for the remaining parameters are adopted with standard forms such as $\frac{1}{\sigma^2} \sim \mathrm{Gamma}\left(\frac{\alpha_0}{2}, \frac{\delta_0}{2}\right)$ and $\Sigma^{-1} \sim W_k(u_0, s_0)$.

The joint posterior distribution is

$$\mathrm{P}(\beta, \sigma^2, \Sigma|\mathrm{y}) \propto \frac{1}{\sigma^2}^{\frac{T}{2}} \exp\left[-\frac{1}{2\sigma^2}(y - \mathrm{X}\beta)^T(y - \mathrm{X}\beta)\right] \frac{1}{|\Sigma|^{\frac{T}{2}}} \times \exp\left[-\frac{1}{2}\left(\beta - \mathrm{F}^{-1}\widetilde{\beta_0}\right)^T \mathrm{F}^T(\mathrm{I}_T \otimes \Sigma^{-1})\mathrm{F}\left(\beta - \mathrm{F}^{-1}\widetilde{\beta_0}\right)\right] \times (\frac{1}{\sigma^2})^{\frac{\alpha_0}{2}-1} \exp\left[-\frac{\delta_0}{2\sigma^2}\right] \frac{1}{|\Sigma|^{\frac{(u_0-k-1)}{2}}} \exp\left[-\frac{1}{2} tr(s_0^{-1}\Sigma^{-1})\right] \quad (4\text{-}20)$$

Note that $|\mathrm{F}^T(\mathrm{I}_T \otimes \Sigma^{-1})\mathrm{F}| = |\mathrm{F}^T||\mathrm{I}_T \otimes \Sigma^{-1}||\mathrm{F}|, |\mathrm{F}| = 1$

The following conditional posterior distributions can be sampled with a Gibbs algorithm.

$$\beta|y, \sigma^2, \Sigma \sim N_{Tk}\left(\bar{\beta}, B_1\right)$$

$$\left(\frac{1}{\sigma^2}\right)|y, \beta, \Sigma \sim \mathrm{Gamma}\left(\frac{u_1}{2}, \frac{\delta_1}{2}\right)$$

$$\Sigma^{-1} \sim W_k(u_1, s_1) \tag{4-21}$$

Where $B_1 = \left[\left(\frac{1}{\sigma^2}\right) X^T X + \mathrm{F}^T (\mathrm{I}_T \otimes \Sigma^{-1}) \mathrm{F}\right]^{-1}$

$$\bar{\beta} = B_1 \left[\left(\frac{1}{\sigma^2}\right) X^T y + \mathrm{F}^T (\mathrm{I}_T \otimes \Sigma^{-1}) \widetilde{\beta_0}\right]$$

$$\alpha_1 = \alpha_0 + \mathrm{T}$$

$$\delta_1 = \delta_0 + (y - \mathrm{X}\beta)^T (y - \mathrm{X}\beta)$$

$$u_1 = u_0 + \mathrm{T}$$

$$s_1 = \left[s_0^{-1} + \sum_{t=1}^{T} (\beta_t - \beta_{t-1})(\beta_t - \beta_{t-1})^T\right]^{-1}$$

The expression for s_1 is derived from

$$\left(\beta - \mathrm{F}^{-1}\widetilde{\beta_0}\right)^T \mathrm{F}^T (\mathrm{I}_T \otimes \Sigma^{-1}) \mathrm{F} \left(\beta - \mathrm{F}^{-1}\widetilde{\beta_0}\right) = \tag{4-22}$$

$$\begin{pmatrix} \beta_T - \beta_{T-1} \\ \vdots \\ \beta_1 - \beta_0 \end{pmatrix} \begin{pmatrix} \Sigma^{-1} & 0 & 0 & 0 \\ 0 & \Sigma^{-1} & 0 & 0 \\ \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \Sigma^{-1} \end{pmatrix} \begin{pmatrix} \beta_T - \beta_{T-1} \\ \vdots \\ \beta_1 - \beta_0 \end{pmatrix} = \sum_{t=1}^{T} (\beta_t - \beta_{t-1})^T \Sigma^{-1} (\beta_t - \beta_{t-1}) = tr\left[\sum_{t=1}^{T} (\beta_t - \beta_{t-1})(\beta_t - \beta_{t-1})^T \Sigma^{-1}\right]$$

4.4 Bayesian Generalized Time-series Model

We can also combine observation equation with state-space equation to develop a unified framework for the extension of DLM model to generalized linear time-series model with Bayesian underpinning.

4.4.1 Bayesian Generalized Autoregressive Poisson Regression Model

Under the context of generalized linear model together with autoregressive model proposed in Chapter 2, a p-order autoregressive Poisson regression model is proposed to include autoregressive order, two classical components of time-series model (time trend and seasonal variation),

$$\log \mu_t = \beta_0 + \beta_1 S_1 + \beta_2 S_2 + \beta_3 S_3 + \beta_4 f(t) + \beta_5 X + \phi_1 y_{t-1} + \phi_2 y_{t-2} + \cdots + \phi_\beta y_{t-p} + u_t \quad (4\text{-}23)$$

$\mu_t = E(y_t)$: The expected count of HAIs

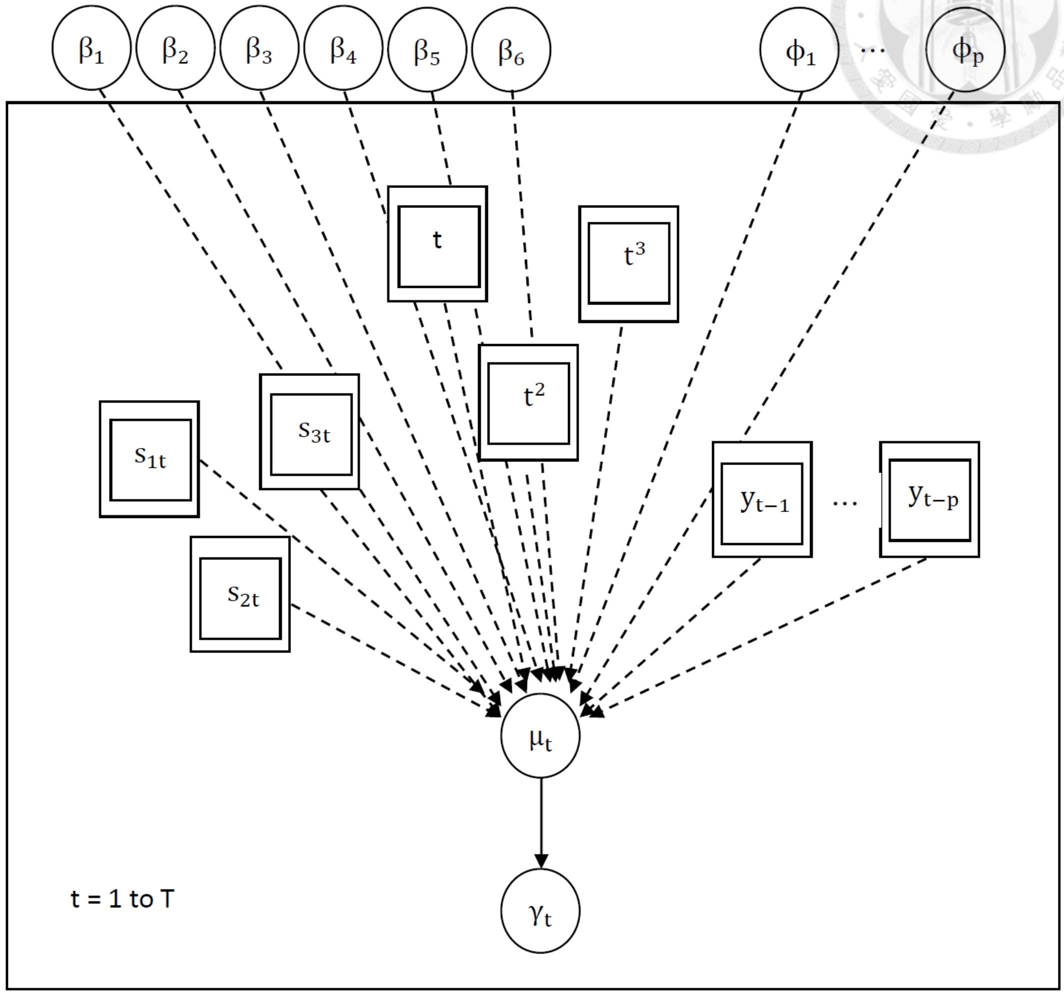
$f(t)$ represents the p polynomial time trend function

X includes age, gender, intervention, department and site of infection

The Doodle of Bayesian Directed Acyclic Graphic Model (DAG)

The proposed model is framework in the doodle of Bayesian directed acyclic graphic model (DAG).

Doodle



$f(t)$ represents the p polynomial time trend function

X includes age, gender, intervention, department and site of infection

$\gamma(t)$ is the observed count of HAI at time t. It is determined by $\mu(t)$, expected numbers of counts, with Poisson distribution (μ_t). The parent node of γ_t is the μ_t. μ_t is linked through a logical expression governed by the equation(4-23). β_s and ϕ_s are the corresponding regression coefficients.

The posterior distribution of $P(\theta|y)$ is formed in proportion to $P(\theta)$, prior distribution, and the likelihood function $\ell(y|\theta)$, where $\theta = (\beta_1 - \beta_k, \phi_1 - \phi_p)$.

4.4.2 Bayesian Generalized Moving Average Model

In a similar vein, a q-order moving average Poisson regression model is proposed with the model form like the following,

$$\log(\mu_t) = \beta_0 + \beta_1 S_1 + \beta_2 S_2 + \beta_3 S_3 + \beta_4 f(t) + \beta_5 X + u_t - \theta_1 u_{t-1} - \theta_2 u_{t-2} - \cdots - \theta_p u_{t-p} \quad (4\text{-}24)$$

The doodle of Bayesian DAG model and also the posterior distribution are derived in a similar manner as done for Bayesian AR process.

4.4.3 Bayesian Generalized ARMA Poisson Regression Model

Fixed –effect Model

The model form is expressed as follows,

$$\log(\mu_t) = \beta_0 + \beta_1 S_1 + \beta_2 S_2 + \beta_3 S_3 + \beta_4 f(t) + \beta_5 X + \phi_1 y_{t-1} + \phi_2 y_{t-2} + \cdots + \phi_\beta y_{t-p} + u_t - \theta_1 u_{t-1} - \theta_2 u_{t-2} - \cdots - \theta_p u_{t-p} \quad (4\text{-}25)$$

Random-effect Model

In addition to the property of time-series of HAIs data, it is also fraught with correlated property, partly because of hierarchical (multilevel) data and partly because of the spread of transmission infection disease. To cope with this correlated property, we resort to the adoption of random-effect approach expressed as a linear mixed model and used in a longitudinal follow-up study.

The model form is modified from the equation (4-24) and expressed as follows.

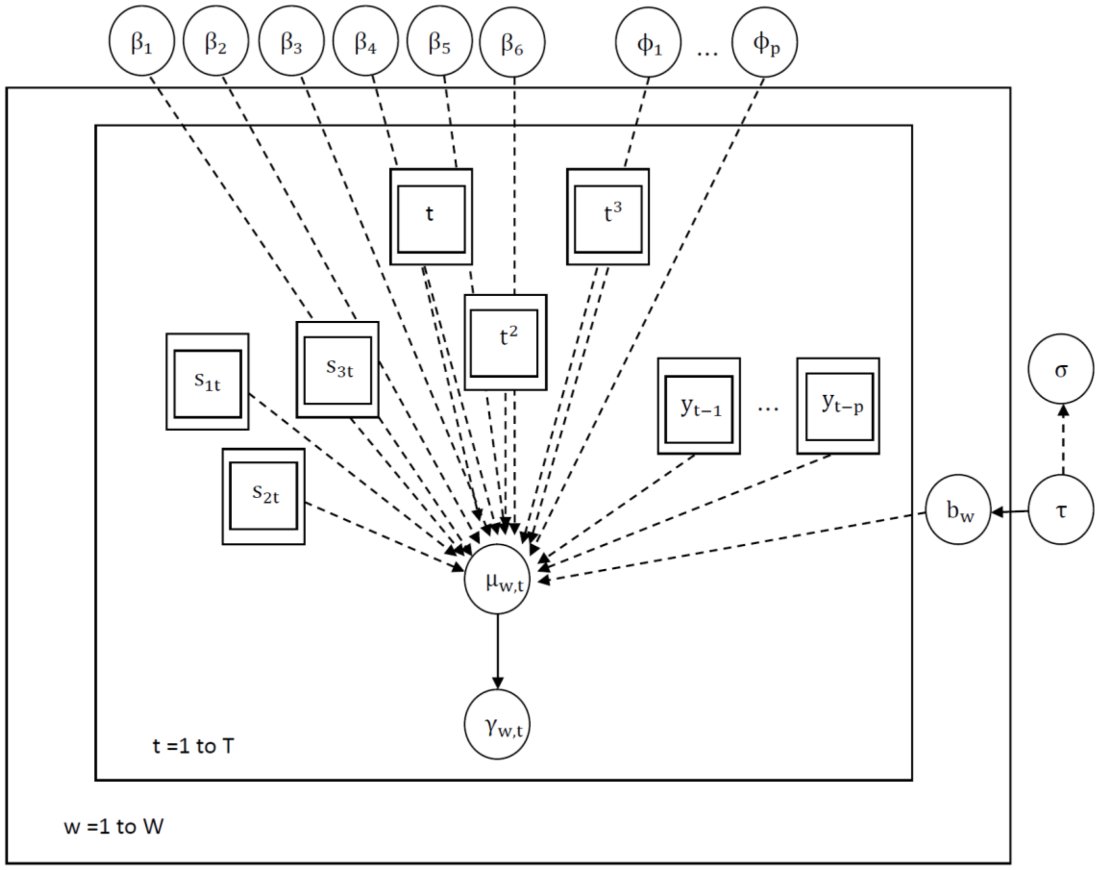
$$\operatorname{logit} \mu_t = \beta_{0k} + \beta_1 S_1 + \beta_2 S_2 + \beta_3 S_3 + \beta_4 f(t) + \beta_5 X + \phi_1 y_{t-1} + \phi_2 y_{t-2} + \cdots + \phi_\beta y_{t-p} u_t - \theta_1 u_{t-1} - \theta_2 u_{t-2} - \cdots - \theta_p u_{t-p} \quad (4\text{-}26)$$

$$\beta_{0k} \sim N(0, \sigma_k^2)$$

k represent department (hierarchy) or site of infection.

This model is often so-called random-intercept model in a classical mixed model.

Doodle



4.5 Estimation of parameters

There are two main methods to estimate the parameters of generalized time series model and dynamic linear model, including maximum likelihood method and Bayesian approach.

4.5.1 Maximum Likelihood Estimate (MLEs)

We can specify the probability distribution of the data given the states and parameters for the observation equation and specify the probability distribution of the state conditional on the previous state in the previous time point in the process equation. The maximum likelihood estimates (MLE) of the parameters can be obtained provided data and initial state available. However, in some situations, in nonlinear and non-Gaussian distributions, MLE is not easily feasible.

4.5.2 Bayesian Markov chain Monte Carlo methods

In Bayesian inference, the posterior distributions of the parameters are often analytically intractable in that it is difficult to derive in closed form summaries of the posterior. To deal with this problem, one of the methods is to resort to simulation methods. Complicated computational problems also arise in the condition of non-linear distributions. Bayesian simulation-based methods such as Markov chain Monte Carlo (MCMC) approach with Gibbs sampling and Metropolis-Hasting algorithm for Bayesian dynamic models.

Markov Chain Monte Carlo (MCMC) Method[75]

The MCMC method is to generate stationary distribution underpinning the Markov chain model for which the parameter θ in the time j +1 follows the transition kernel $K(\theta \mid \theta^{(j)})$, indicating that the distribution of parameters in the time j +1 is only dependent on the distribution of parameter θ in time j. According to the theory of Markov chain, the Markov chain under regular situations may reach the equilibrium and independent of initial distribution after a long run of transitions. This implies that if a stationary distribution, $S(\theta)$, can be identified one can infer if θ_j comes from $S(\theta)$. θ_{j+1} also comes from $S(\theta)$.

Gibbs Sampler

The posterior distribution for the random effect model consists of all parameters involved, β_1-β_5, ϕ_1-ϕ_p, θ_1-θ_p, τ_b is denoted by

$p(\theta \mid y) = p(\beta_1\text{-}\beta_5, \phi_1\text{-}\phi_p, \theta_1\text{-}\theta_p, \tau_b \mid y)$ ------ (1)

The Gibbs sampler is a method of estimating these marginal posterior distributions.

The procedure is as follows.

Suppose θ is k-dimension denoted by

$\theta = \{\beta_1\text{-}\beta_5, \phi_1\text{-}\phi_p, \theta_1\text{-}\theta_p, \tau\}$

1) Assign starting value

$\theta^0 = \{\beta_1^{(0)}, \ldots, \theta_p^{(0)}, \tau^{(0)}\}$

2) Step 1: Update β_1 by sampling

$\beta_1^{(1)} \sim P\{\beta_1 \mid \beta_2^{(0)}, \ldots, \theta_p^{(0)}, \tau^{(0)}\}$

3) Step 2: Update β_2 by sampling

$\beta_2^{(1)} \sim P\{\beta_2 \mid \beta_1^{(1)}, \beta_3^{(0)},..., \theta_p^{(0)}, \tau^{(0)} \}$

4) Step 3: Update β_3 by sampling

$\beta_3^{(1)} \sim P\{\beta_3 | \beta_1^{(1)}, \beta_2^{(1)}, \beta_4^{(1)} ... , \theta_p^{(0)}, \tau^{(0)} \}$

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4) Step *k*: Update τ by sampling

$\tau^{(1)} \sim P\{\tau \mid \beta_1^{(1)}, \beta_2^{(1)}, \beta_4^{(1)} ... , \theta_p^{(1)} \}$

This completes one iteration of the Gibbs sampler, which yields a new realization for θ which is given by $\beta_1^{(1)}, \beta_2^{(1)}, \beta_3^{(1)} ... , \theta_p^{(1)}, \tau^{(1)}$. The above procedure is then repeated to get a second realization $\beta_1^{(2)}, \beta_2^{(2)}, \beta_3^{(2)} ... , \theta_p^{(2)}, \tau^{(2)}$. This can be obtained by sampling $\beta_1^{(2)}$ from the full conditional probability of β_1

$P\{\beta_1 \mid \beta_2^{(1)}, \beta_3^{(1)},..., \theta_p^{(1)}, \tau^{(1)} \}$

Next, $\beta_2^{(2)}$ is sampled from the full conditional probability:

$P\{\beta_2 \mid \beta_1^{(2)}, \beta_3^{(1)},..., \theta_p^{(1)}, \tau^{(1)} \}$

This process continues until $\tau^{(2)}$ is sampled from the full conditional probability:

$P\{\tau \mid \beta_1^{(2)}, \beta_2^{(2)},... , \theta_p^{(2)} \}$

This completes the second iteration.

This whole process is repeated for *r* iterations. The final iteration yields the realization $\beta_1^{(r)}, \beta_2^{(r)},..., \theta_p^{(r)}, \tau^{(r)}$. Geman and Geman show that, for very large values of r, the distribution of the sample $\beta_1^{(r)}, \beta_2^{(r)},..., \theta_p^{(r)}, \tau^{(r)}$ becomes close to the marginal posterior distribution of $\beta_1, \beta_2,..., \theta_p, \tau$.

In addition to marginal posterior density, disease prediction using the Bayesian approach needs predictive distribution.

The fundamental idea of getting predictive distribution is that given the observed data r one can integrate out relevant regression parameters to get predictive distribution, $P(\mu^{new}|\mu)$, which is given by

$$p(\mu^{new}|\mu) = \int p(\mu^{new}|\theta, \mu) p(\theta|\mu) d\theta$$

However, like marginal posterior density, to integrate out relevant parameters requires high-dimension integration. Again, the MCMC method is tailored for such an intractable computation.

4.5.3 Model selection for Poisson autoregressive model

Akaike's information criterion (AIC) was used for model selection in the Poisson autoregressive model [76]. The last selected model were based on minimizing AIC. Additionally, the residuals of the models were checked whether there were autocorrelations by Ljung-Box statistics methods and any patterns by residual plots [77]. Model selection for Bayesian dynamic linear model was based deviance information criteria (DIC).

Chapter 5 Results

5.1 Basic results

A total of 552,233 admissions were registered during the period from 1 January, 1994 to 31 December, 2013. 6,776 (1.2%) admissions were excluded either because information on variables (date of birth or department of admission) were unavailable (n=254) or the admission was indicated for a health check-up or consultations only (n=6522). Therefore, 545,457 admissions from 315,209 patients with 4,210,609 patient-days were available for analysis in this study. Of these, there were 10,117 patients with healthcare-associated infection and 20,221 cultures were identified. There were 2,965 deaths ascertained within 30 days after the onset of HAIs (Figure 5.1.1). Figure 6 shows the incidence rates of HAI by calendar year. The median length of stay for HAI patients was 35 days (IQR: 22-58 days, range:1-4,033 days). The median length of stay was 5 days (IQR: 3-8) for non-HAI patients. Males accounted for 52.29% of cases (8,450 episodes) with a median age of 68.00 years (IQR: 54.73-76.94); and females accounted for 47.71% of cases (7,711 episodes) and had a median age of 71.94 years (IQR: 60.92-80.25).

The HAIs cohort was systematically collected between 1994 and 2013 that was continued in a 921-bed teaching medical center hospital in Taipei. Total admissions was about 25,000-28,000 every year. There was no substantial change in the hospitalized admission by year. The healthcare-associated infectious (HAI) cases among those admissions were around 900-1,200 by year (Table 1). The range of HAIs incidence rates of were about 2.86-5.16 per 1000 patient-days for every calendar year. The trend of overall HAI incidence between 1994 and 2013 showed obvious decline, especially in the last two years (see Table 5.1.1). The detail statistical results were demonstrated in Table 5.1.2. The incidence rate of HAI in male was slight higher compared with female. Regarding the admission department, the highest HAI incidence rate was revealed in Department of Oncology, followed by GI, Pediatric, and Chest. The Incidence rates were different from seasons. The HAI incidence rate in summer was higher than others. The incidence rate was highest for urinary tract infections (1.59 episodes per 1,000 patient-days), followed by bacteremia (1.09), pneumonia (0.72), and surgical site infection (0.45).

In multi-variable Poisson model in evaluating the causes of incidence rate, age was a significant factor. The relative risk was highest in the age group of over 80 years old. The lowest risk age group was between 20 to 29 years old. Male patients had higher relative risk of contracting HAIs than female patients. Emergency department staying had higher incidence risk of HAIs compared to other departments.

Patients admitted as an emergency had a higher risk of HAIs compared to those admitted from outpatient departments. After adjusting for age, gender, and the department of hospitalization, patient admission type (outpatient or emergency) and sites of infection were still associated with HAIs incidence (Table 5.1.3).

5.2 Decomposition method with Generalized Linear Time-series Model among selected infection sites and species

Based on Table 5.1.3, we focused on four infection sites and the two species of Gram (-) based on the longitudinal follow-up for the incidence of HAI from 1994 to 2013.

(A) Overall HAI incidence

The longitudinal follow-up for the incidence of HAI from 1994 to 2013 was shown in Figure 5.2.1. The monthly time series of the HAIs count was shown in Figure 5.2.4. Seasonality was noted in the HAIs incidence. The incidence was higher in the summer and spring than that in the winter ($p<0.0001$) (Table 5.2.1). The relative risk was higher in the summer than in the winter. Figure 5.2.5 is the time series after de-seasonalization of the HAI, and there were five outliers noted in this figure. After deleting the outliers, there was a significant third degree polynomial trend (Table 5.2.2). The autoregression analysis for the de-seasonalized and de-trend time series revealed lacking of autoregressive order and white noise (Table 5.2.3).

(B) Bacteremia incidence

The monthly time series of the healthcare-associated bacteremia count was shown in Figure 5.2.7. Seasonality was noted. The incidence was higher in the summer and spring than that in the winter ($p<0.0001$) (Table 5.2.4). The relative risk was 19% higher in the summer than in the winter, and 16% higher in the spring than in the winter. Figure 5.2.8 is the time series after de-seasonalization of the HAI bacteremia, and there were five possible outliers noted in this figure. After deleting the outliers, there was a significant linear trend (Table 5.2.5). The analysis for the de-seasonalized and de-trend time series revealed lacking of autoregressive order (Table 5.2.6).

(C) Pneumonia incidence

The monthly time series of the healthcare-associated pneumonia count was shown in Figure 5.2.10. Although the univariate seasonal variation analysis was not significant, the incidence tended to be higher in the summer than in the winter (Table 5.2.7). Figure 5.2.11 is the time series after de-seasonalization of the HAI pneumonia, and there were three outliers noted in this figure. After deleting the outliers, there was a significant linear trend (Table 5.2.8). The analysis for the de-seasonalized and de-trend time series revealed second-order autoregressive pattern (Table 5.2.9).

(D) Surgical site infection incidence (SSI)

The monthly time series of the healthcare-associated SSI count was shown in Figure 5.2.13. Seasonality was noted. The incidence was higher in the summer and spring than that in the winter ($p=0.0029$) (Table 5.2.10). The relative risk was 20% higher in the summer than in the winter, and 24% higher in the spring than in the winter. Figure 5.2.14 was the time series after de-seasonalization of the healthcare-associated SSI, and there were five outliers noted in this figure. After deleting the outliers, there was a significant linear trend ($p<0.0001$) (Table 5.2.11). There was lacking of autoregressive pattern for the de-seasonalized and de-trend time series (Table 5.2.12).

(E) Urinary tract infection incidence (UTI)

The monthly time series of the healthcare-associated UTI count was shown in Figure 5.2.16. Seasonality was noted. The incidence was higher in the summer and spring than that in the winter ($p<0.0001$) (Table 5.2.13). The relative risk was 16% higher in the summer than in the winter, and 11% higher in the spring than in the winter. Figure 5.2.17 was the time series after de-seasonalization of the healthcare-associated UTI, and there were four outliers noted in this figure. After deleting the outliers, there was a significant third degree polynomial trend (Table 5.2.14). The analysis for the de-seasonalized and de-trend time series revealed fourth-order autoregressive pattern (Table 5.2.15).

(F) *E. coli* Bacteremia incidence

The monthly time series of the healthcare-associated *E. coli* bacteremia count was shown in Figure 5.2.18. Seasonality was not significant (Table 5.2.16). Figure 5.2.19 was the time series after de-seasonalization of the HAI *E. coli* bacteremia, and there were four outliers noted in this figure. After deleting the outliers, there was a significant quadratic trend (Table 5.2.17). The autoregression analysis for the de-seasonalized and de-trend time series revealed second-order autoregressive pattern (Table 5.2.18).

(G) *P. aeruginosa* Bacteremia incidence

The monthly time series of the healthcare-associated *P. aeruginosa* bacteremia count was shown in Figure 5.2.20. Seasonal variation was not significant (Table 5.2.19). Figure 5.2.21 is the time series after de-seasonalization of the HAI *P. aeruginosa* bacteremia, and there were four outliers noted in this figure. Despite deleting the outliers, there was no significant trend (Table 5.2.20). The autoregression analysis for the de-seasonalized and de-trend time series revealed lacking of autoregressive pattern (Table 5.2.21).

Autoregressive integrated moving-average model (ARIMA)

The traditional ARIMA time series analysis for the original overall HAI incidence revealed an order one moving average after one differencing of the original incidence time series. The model for bacteremia, pneumonia, and surgical site infections incidence was ARIMA (0,1,1). The ARIMA model for UTI was ARIMA (1.0.2).

In the bacteremia, the E. coli incidence shows no significant autoregressive or moving average order. In *P. aeruginosa* incidence, both the order two autoregressive and moving average order were significant, the absolute value of the higher order was small than that of the low order are also shown in (Table 5.2.22, Table 5.2.23).

5.3 Generalized Time-series Model with covariates, seasonality, time trend, and autoregressive order: A MLE approach

(A) Overall HAI incidence

In the multi-variable analysis, we adjusted covariates of age, gender, and admission department. We also adjusted seasonal factor, third-degree polynomial trend effect and autoregressive order one. Under the assumption of normal distribution, the result showed negative of Hessian and the model was not stable. Thus, we adjusted age, gender, season, third-degree polynomial trend effect and autoregressive order one. After adjustment, the incidence of overall incidence had third-degree polynomial trend and autoregressive order one pattern (Table 5.3.1). In the Poisson time series model, it revealed the over-dispersion shown in the deviance. Thus we applied negative binomial distribution to fit the data, the seasonal factor result became not significant. Although third-degree polynomial trend effect was significant in all three model forms, the regression coefficients were very small (Table 5.3.1-5.3.3).

(B) Bacteremia

In the multi-variable analysis of bacteremia incidence, the linear trend was significant after adjusting the age, gender, and seasonal effect. The autoregressive order and seasonal effect was not significant (Table 5.3.4). The seasonal factor was not significant in both Poisson and negative binomial model, either. The linear trend was obvious in three models. The autoregressive order one was significant in Poisson and negative binomial model, but not in the normal distribution model (Table 5.3.4-5.3.6).

(C) Pneumonia

In the multi-variable analysis of pneumonia incidence, the autoregressive order two effect was significant after adjusting the age, gender, trend and seasonal effect. The autoregressive order was significant, whereas the seasonal and trend effect were not (Table 5.3.7). The negative binomial model results on the seasonal effects, trend, and autoregressive pattern was similar with those in the normal distribution model (Table 5.3.7, Table 5.3.9).

(D) Surgical site infections

In the multi-variable analysis of surgical site infection incidence, the linear trend was significant after adjusting the age, gender, and seasonal effect. The autoregressive order and seasonal effect was not significant (Table 5.3.10). In both Poisson and negative binomial model, the results of seasonal effects, linear trend, and autoregressive order one agreed with those in the normal model (Table 5.3.11, Table 5.3.12).

(E) Urinary tract infections

The seasonal effect was not significant in the urinary tract HAIs. The third-degree polynomial trend was shown in all three distribution model forms (Table 5.3.13, Table 5.3.14, and Table 5.3.15). The autoregressive order three was significant in Poisson and negative binomial model.

(F) *E. coli* bacteremia

In the multi-variable analysis of *E. coli* bacteremia incidence, the seasonal effect, trend, and autoregressive order were not significant after adjusting the age and gender (Table 5.3.16). However, in the Poisson and negative binomial model, they revealed quadratic trend effects (Table 5.3.17, Table 5.3.18).

(G) *P. aeruginosa* bacteremia

After adjusting covariates of age and gender, the seasonal effect, trend effect, and autoregressive order were not significant in all three distribution models (Table 5.3.19, Table 5.3.20, and Table 5.3.21).

5.4 Bayesian dynamic linear model

In the Bayesian dynamic time linear model, the model assumed normal distribution assumption. The age was a dichotomous variable, with a variable of 50-years-old versus those below 50.

(A) Overall HAI incidence

It revealed first order autoregressive pattern after adjusting seasonal effect, trend effect, age and gender. The seasonal and trend effect was not significant. As compared with the result of non-Bayesian time series model, in which the significant third-polynomial trend became insignificant in the Bayesian analysis. The seasonal effect results were similar (Table 5.4.1).

(B) Bacteremia

The first-order autoregressive pattern was still significant after adjusting age, gender, trend, and seasonal factors. The trend effect was not significant (Table 47).

(C) Pneumonia

There was a significant second-order autoregressive pattern in the Bayesian analysis after adjusting age, gender, and seasonal effect. The trend and seasonal effect were not significant (Table 5.4.3).

(D) Surgical site infections

There was a significant first-order autoregressive pattern shown in the Table 54. In the multi-variable Bayesian analysis, there was no seasonal effect. After adjusting the seasonal effect, the linear trend became significant, though the regression coefficient was very small (Table 5.4.4).

(E) Urinary tract infections

The autoregressive pattern was fourth-order in the urinary tract HAI. The seasonal and trend effect were not significant (Table 5.4.5).

(F) *E. coli* bacteremia

The seasonal effect was not significant in the model after adjust the age, gender, trend and autocorrelations. It revealed third-order autoregressive pattern and linear trend in the adjusted model (Table 5.4.6).

(G) *P. aeruginosa* bacteremia

There was a third-order autoregressive pattern and linear trend in the multi-variable Bayesian analysis. The seasonal effect was not significant (Table 5.4.7).

5.5 Bayesian Autoregressive Moving Average model

1. Bayesian autoregressive model

   (1) HAIs

Table 5.5.1 shows the estimated regression coefficients with Bayesian autoregressive model incorporating time trend and seasonal variation in the model but without considering any other non time-series covariates for overall HAI. In the model of first order autoregressive, summer, spring, and autumn had higher risk of HAI than winter. The estimated regression coefficients were 0.133 (0.081-0.186), 0.14 (0.082-0.199), 0.092 (0.039-0.146) for spring, summer, and autumn, respectively. The first autoregressive order was statistically significant (0.45(0.46-0.63)). Linear time trend significantly decreased with time. When higher orders of autoregressive terms were considered, the effects of seasons were similar. However, time trend effect became insignificant in the second, third, and fourth order autoregressive model. In Table 5.5.1, fourth-order autoregressive term was not statistically significant.

The trigonometric function was used as an alternative for seasonal variation

(Table 5.5.2). The regression coefficient for the series of autoregressive models was close to their counterparts in Table 5.5.1. The results still support that the fourth-order of autoregressive terms was not suggested.

The results of Bayesian autoregressive model incorporating time trend, seasonal variation, and non time-series covariates (age and gender) for overall HAI were shown in Table 5.5.3. The regressive coefficients for season and time trend effect did not changed a lot. For the first autoregressive term, the regression coefficient became smaller (0.275±0.019) than that in Table 5.5.1 (0.545±0.042). Younger patients had significantly less HAIs than the elder patients aged over 70. The estimated regression coefficients were -2.069 (95% CI: -2.145- -1.991) and -1.195 (95% CI: -1.248- -1.143) for age under 40 and age between 40 and 69, respectively. Male had significantly larger HAI counts than female. The estimated coefficient was 0.086 (95% CI: 0.042-0.131).

This thesis further considers cubic form of time trend in the first order autoregressive model (Table 5.5.4). Such model did not change much of the estimated results for age, gender, and season. The regression coefficient of the first autoregressive became smaller (0.223±0.02) than that in Table 5.5.3 (0.275±0.019). Regarding time trend, linear trend became insignificant, but both quadratic and cubic terms were statistically significant.

The cubic time trend model of first-order autoregressive model (Table 5.5.4) was further extended to cubic time trend model of third-order autoregressive model (Table 5.5.5). The effects of age, gender, season, and time trend were similar in the two models. All first-, second-, and third-order of autoregressive were statistically significant (Table 5.5.5). The third-order autoregressive model had smaller DIC (7491.98) than that in the first-order autoregressive model (7599.01). With cubic form of time trend, the autoregressive of first, second, third, and fourth-order were all statistically significant with DIC of 7482.3 (Table 5.5.6).

(2) UTI

The estimated results of the Bayesian autoregressive model incorporating time trend and seasonal variation in the model but without considering any other non time-series covariates for UTI were shown in Table 5.5.7. In the model of first order autoregressive, summer, spring, and autumn had higher risk of UTI than winter. The estimated regression coefficients were 0.135 (0.050-0.220), 0.186 (0.090-0.277), 0.109 (0.022-0.194) for spring, summer, and autumn, respectively. The first autoregressive order was statistically significant (0.51 (95% CI: 0.42-0.59)). Linear time trend was positive and statistically significant. When higher orders of autoregressive terms were concerned, the effects of seasons were similar. However, time trend effect was only significant in the second-order autoregressive model but not in the third and fourth order autoregressive model. The same as overall HAI, the fourth-order autoregressive term was not statistically significant for UTI.

The estimated results of using trigonometric seasonal variation for UTI are shown in Table 5.5.8. The regression coefficient for the series of autoregressive models was similar to their counterparts in Table 5.5.7, except that linear time trend was consistently insignificant in all the four models in Table 5.5.7. The results still supported that the fourth-order of autoregressive terms was not suggested.

The results of Bayesian autoregressive model incorporating time trend in cubic form, seasonal variation, and non time-series covariates (age and gender) for UTI are shown in Table 5.5.9. The regressive coefficients for seasonal variation did not were similar. The linear time trend became significant. The magnitude of autoregressive terms was half of that in Table 5.5.7. Table 5.5.10 shows the results with fourth-order of autoregressive terms. Younger patients had significantly less UTI than the elder patients aged over 70. The estimated regression coefficients were -2.866 (-3.072- -2.674) and -1.526 (-1.644- -1.406) for age under 40 and age between 40 and 69, respectively. Male had significantly larger UTI counts than female. The estimated coefficient was -0.247 (95% CI: -0.331- -0.161).

(3) *E. coli.* bacteremia

The estimated results of the Bayesian autoregressive model incorporating time trend and seasonal variation in the model but without considering any other non time-series covariates for *E. coli*. bacteremia infections are shown in Table 5.5.11. In the model of first order autoregressive, seasons did not have statistically significant effects. The first autoregressive order was statistically significant (0.246 (95% CI: 0.117-0.377)). Linear time trend was insignificant. When higher orders of autoregressive terms were concerned, the effects of seasons and time trend were similar. However, higher order of autoregressive were insignificant.

The estimated results of using trigonometric seasonal variation for *E. coli*. bacteremia infection are shown in Table 5.5.12. The regression coefficient for the series of autoregressive models and linear time trend were similar to their counterparts in Table 5.5.11.

The results of Bayesian autoregressive model incorporating time trend in quadratic form, seasonal variation, and non time-series covariates (age and gender) for *E. coli*. bacteremia infection are shown in Table 5.5.13. The regressive coefficients for seasonal variation, linear time trend, and first-order autoregressive were similar. Younger patients had significantly less *E. coli*. bacteremia infection than the elder patients aged over 70. The estimated regression coefficients were -2.861 (-3.716- -2.217) and -1.109 (-1.474- -0.815) for age under 40 and age between 40 and 69, respectively. Male had higher *E. coli*. bacteremia infection counts than female. The estimated coefficient was 0.106 (95% CI: -0.140-0.349) (p>0.05).

The results with second-order autoregressive terms of Bayesian autoregressive model incorporating time trend in quadratic form, seasonal variation, and non time-series covariates (age and gender) for *E. coli*. bacteremia infection are shown in Table 5.5.14. The effects for all covariates were similar to those in Table 5.5.12. The second order autoregressive was not significant.

(4) *P. aeruginosa* bacteremia

The estimated results of the Bayesian autoregressive model incorporating time trend and seasonal variation in the model but without considering any other non time-series covariates for *P. aeruginosa* bacteremia infections were shown in Table 5.5.15. The same as observed in *E coli* bacteremia infection, seasons did not have statistically significant effects in the model of first order autoregressive. The first autoregressive order was also insignificant (0.079 (95% CI: -0.097-0.258)). Linear time trend was decreasing. When higher orders of autoregressive terms were concerned, the effects of seasons and time trend were similar. All the autoregressive terms were not statistically significant.

The estimated results of using trigonometric seasonal variation for P. aeruginosa bacteremia infection are shown in Table 5.5.16. The regression coefficient for the series of autoregressive models and linear time trend were similar to their counterparts in Table 5.5.15.

The results of Bayesian autoregressive model incorporating time trend in quadratic form, seasonal variation, and non time-series covariates (age and gender) for *P. aeruginosa* bacteremia infection are shown in Table 5.5.17. The regressive coefficients for seasonal variation, linear time trend, and first-order autoregressive were similar. Younger patients had significantly less P. aeruginosa bacteremia infection than the elder patients aged over 70. The estimated regression coefficients were -2.417 (-3.577- -1.626) and -1.025 (-1.603- -0.640) for age under 40 and age between 40 and 69, respectively. Male had higher *P. aeruginosa* bacteremia infection counts than female. The estimated coefficient was 0.426 (95% CI: 0.134-0.793).

The results with third-order autoregressive terms of Bayesian autoregressive model incorporating time trend in quadratic form, seasonal variation, and non time-series covariates (age and gender) for *P. aeruginosa* bacteremia infection are shown in Table 5.5.18. The effects for all covariates were similar to those in Table 5.5.17. The third order autoregressive was statistically significant.

2. Bayesian moving average model

(1) HAIs

Table 5.5.19 shows the estimated regression coefficients with Bayesian moving-average model incorporating third-degree polynomial trend and seasonal variation in the model but without considering any other non time-series covariates for overall HAI. For seasonal factors, counts of HAIs shows the higher increase in spring and summer than winter, but was not statistically significant. The estimated regression coefficients were 0.077 (-0.179-0.340), 0.091 (-0.180-0.357), -0.017 (-0.295-0.249) for spring, summer, and autumn, respectively. The first order moving average was significant (0.143(0.009-0.27)).

This thesis further adjusted non time-series covariates (age and gender) (Table

5.5.20). Compared with the elder patients aged over 70, the estimated regression coefficients were -2.085 (-2.152- -2.017) and -1.203 (-1.248- -1.155) for age under 40 and age between 40 and 69, respectively. Male was more likely to have the HAIs than female. The estimated coefficient was 0.091 (0.054-0.128). The model adjusting with age and gender results on the seasonal factor, trend, and first order moving average were similar with the previous model without adjusting age and gender.

(2) UTI

Table 5.5.21shows the estimated regression coefficients with Bayesian moving-average model incorporating third-degree polynomial trend and seasonal variation in the model but without considering any other non time-series covariates for UTI. For seasonal factors, counts of UTI was higher in spring, summer, autumn than in winter. The estimated regression coefficients were 0.105 (0.023-0.172), 0.158 (0.089-0.232), 0.106 (0.032-0.174) for spring, summer, and autumn, respectively. The result shows the statistically significant (0.209(0.123-0.298)) for the effect of first order moving average on the counts of UTI.

Table 5.5.22 shows the extended model adjusting age and gender. Male was less likely to have the counts of UTI than female. The model adjusting with age and gender results on the seasonal factor, trend, and first order moving average were similar with the previous model without adjusting age and gender.

(3) *E. coli.* bacteremia

Table 5.5.23 shows the estimated regression coefficients with Bayesian moving-average model incorporating third-degree polynomial trend and seasonal variation in the model but without considering any other non time-series covariates for E coli bacteremia infection. The result shows the no statistically significance for the effects of seasonal factors, first order moving average on the counts of *E.coli.* bacteremia. The 0.391 (0.152-0.686) of estimated coefficient shows that male was more likely to have the *E. coli*. bacteremia than female. The model adjusting with age and gender results on the seasonal factor, trend, and first order moving average were similar with the previous model without adjusting age and gender (Table 5.5.24).

(4) *P. aeruginosa* bacteremia

Table 5.5.25 the estimated regression coefficients with Bayesian moving-average model incorporating third-degree polynomial trend and seasonal variation in the model but without considering any other non time-series covariates for *P. aeruginosa* bacteremia infection. The result shows there was lacking of statistical significance for the effects of seasonal factors, first order moving average on the counts of *P. aeruginosa* bacteremia. The results with further adjustment for age and gender were similar with the previous model without adjusting age and gender (Table 5.5.26).

3. Bayesian autoregressive moving average model

(1) HAIs

Table 5.5.27 shows the estimated regression coefficients with Bayesian first order autoregressive and first-order moving-average (ARIMA (1,1)) model incorporating third-degree polynomial trend and seasonal variation in the model but without considering any other non time-series covariates for overall HAI. For seasonal factors, the counts of HAIs shows the remarkable increase in spring and summer than winter. The less increase in autumn and the negative linear trend were found in the model. The joint effect of the first autoregressive order and the first order moving average on the counts of HAIs were statistically significant. Table 5.5.28 shows the extended model with adjusting age and gender. The model adjusting with age and gender results on the seasonal factor, trend, and first autoregressive order were similar with the previous model without adjusting age and gender. However, the first order moving average was negative associated with the counts of HAI. The estimated coefficient was -0.221(-0.422- -0.017).

Table 5.5.30 shows the Bayesian ARIMA (2,2) model adjusting for age, gender, , seasonal factors, and linear time trend for overall HAI. The joint effects of age, gender, seasonal factor, and linear time trend on the counts of HAIs were statistically significant. The first and second autoregressive orders were statistically significant associated with the counts of HAI. The first order moving average was negative associated with the counts of HAI, but the second order moving average was not statistically significant.

Table 5.5.31 shows the Bayesian ARIMA (3,1) model adjusting for age, gender, , seasonal factors, and linear time trend for overall HAI. The joint effects of age, gender, and seasonal factor on the counts of HAIs are statistically significant. The first, second, and third autoregressive orders were statistically significant associated with the counts of HAI. The first order moving average was negative associated with the counts of HAI.

(2) UTI

Table 5.5.32 shows the Bayesian ARIMA (1,1) model adjusting for seasonal factors, and linear time trend for UTI. For seasonal factors, the counts of UTI was higher in spring and summer than winter. The less increase in autumn and the positive linear trend were found in the model. The joint effect of the first autoregressive order and the first order moving average on the counts of HAIs were statistically significant. Table 5.5.33 shows the ARIMA(1,1) model adjusting for age and gender for UTI. The model adjusting for age and gender results on the seasonal factor, trend, and first autoregressive order were similar with the previous model without adjusting age and gender. However, the first order moving average was negative associated with the counts of HAI. The estimated coefficient was -0.196(-0.623- -0.134).

Table 5.5.34 shows the Bayesian ARIMA (2,2) model adjusting for seasonal factors, and linear time trend for UTI. The first and second order moving average were not statistical significant. Table 5.5.35 shows the extended model with adjusting age and gender. The joint effects of age, gender, seasonal factor, and linear time trend on the counts of UTI were statistically significant. The first and second autoregressive orders were statistically significant associated with the counts of UTI. Both of the first and second order moving average were not statistical significant.

(3) *E. coli.* bacteremia

Table 5.5.36 shows the Bayesian ARIMA (1,1) model adjusting for seasonal factors, and linear time trend for *E. coli.* bacteremia infection. For seasonal factors, the counts of *E. coli.* bacteremia shows the slightly high in spring and summer. The effect of the first auto regressive order on the counts of HAIs was statistically significant. However, the first order moving average was not statistically significant to be the associated with the counts of *E. coli*. bacteremia. The estimated coefficient was 0.041(-0.943- 0.946).

Table 5.5.37 shows the extended model with adjusting age and gender. The model adjusting with age and gender results on the seasonal factor, trend, and first order autoregressive moving average were similar with the previous model without adjusting age and gender.

Table 5.5.38 shows the Bayesian ARIMA (2,2) model adjusting for seasonal factors, and linear time trend for *E. coli.* bacteremia infection. The first and second order moving average were not statistical significant.

(4) *P. aeruginosa* bacteremia

Table 5.5.39 shows the Bayesian ARIMA (1,1) model adjusting for seasonal factors, and linear time trend for *E. coli.* bacteremia infection for *P. aeruginosa* bacteremia infection. The counts of *P. aeruginosa* bacteremia infection was high in summer. But the seasonal factors were not statistically significant. The effects of the first autoregressive moving average orders on the counts of *P. aeruginosa* bacteremia were not statistically significant.

Table 5.5.40 shows the extended model with adjusting age and gender. The model adjusting with age and gender results on the seasonal factor, trend, and first order autoregressive moving average are similar with the previous model without adjusting age and gender.

Table 5.5.41 shows the Bayesian ARIMA (2,2) model adjusting for seasonal factors, and linear time trend for *E. coli.* bacteremia infection for *P. aeruginosa* bacteremia. The first and second autoregressive moving average orders were not statistical significant.

5.6 The effect of the intervention programs for HAI control in the Bayesian generalized time series model

Based on the longitudinal follow-up for the HAI incident count, we estimated the effects of different intervention programs with Bayesian Poisson linear ARIMA model. Table 5.6.1 shows the estimated results with linear trend effect and autoregressive order one. The regression coefficients for CDC/TJCHA and bundle care were both statistically significantly less than zero, revealing a protective effect with relative risks (RRs) of 0.76 (95% Credible Interval (CI): 0.66-0.87)) and 0.62 (95% CI: 0.54-0.72) for CDC/TJCHA and bundle care, respectively. The linear trend effect was insignificant but the autoregressive order one was significant.

After adjusting for age and gender, it was still insignificant for linear trend effect and significant for the autoregressive order one. Patients aged less than 40 (RR=0.13, 95% CI: 0.12-0.14) and 40-59 years (RR=0.30, 95% CI: 0.29-0.32) had smaller risk for HAIs compared to those aged elder than 70 years. The age and gender-adjusted effects of intervention program were similar to those in the crude model, RR=0.76 (95% CI: 0.68-0.86) for CDC/TJCHA and 0.62 (95% CI: 0.55-0.70) for bundle care. The tracking plot for the MCMC models shows that a good convergence for this model.

If we took a six-month period for the buffering time for the intervention taking effect, the effect of this lagged intervention effect is shown in Table 5.6.2. Although the regression coefficients of time trend and autoregressive order one move toward the null hypothesis, it was still no significant time trend effect but had significant autoregressive effect. For the lagged 6-month intervention effect, CDC/TJCHA (RR=0.67, 95% CI: 0.58-0.77) and bundle care (RR=0.65, 95% C: 0.57-0.74) remained significant. Their counterparts in the age and gender-adjusted model were similar (RR=0.66 (95% CI: 0.58-0.76) for CDC/TJCHA and 0.65 (95% CI: 0.58-0.73) for bundle care).

When we considered both with and without time-lagged intervention in the same model, it was still insignificant for trend effect and significant for autoregressive order one regardless of whether age and gender were adjusted (Table 5.6.3). After adjusting for age and gender, the effects of both with and without lagged six-month CDC/TJCHA and bundle care were statistically effective. In this model, the RR of HAI for concurrent CDC/TJCHA and bundle care were 0.85 (95% CI: 0.73-0.98) and 0.60 (95% CI: 0.51-0.72), and the lagged six-month RR were 0.68 (95% CI: 0.58-0.80) and 0.63 (95% CI: 0.55-0.71). Note that from previous results, we found the results with and without adjustment for age and gender were similar, so that we presented only the results with age and gender adjustment thereafter.

When autoregressive order two was taken into account, both first- and second-order autoregressive pattern were statistically significant in the model for the effect of concurrent intervention programs for HAI. CDC/TJCHA and bundle care remained statistically significant (Table 5.6.4).

If there considered third-order autoregressive pattern, all three autoregressive terms were statistically significant. Interestingly, linear trend effect became statistically significant. The concurrent intervention programs of CDC/TJCHA (RR=0.74, 95% CI: 0.63-0.87) and bundle care (RR=0.61, 95% CI: 0.52-0.71) remained statistically significant (Table 5.6.5). The tracking plots on the relevant parameters were shown in (Table 5.6.5a).

In a third-order autoregressive and first-order moving average model (Table 5.6.6), the moving-average term was not statistically significant. The results for intervention programs were similar to previous third-order autoregressive model.

When it was lagged six-month intervention programs were considered in the three-order autoregressive and linear trend effect time series model, the linear trend was not statistically significant. For the effect of intervention program, the lagged six-month intervention programs of CDC/TJCHA (RR=0.64, 95% CI: 0.54-0.75) and bundle care (RR=0.65, 95% CI: 0.55-0.76) were statistically significant (Table 5.6.7).

The results of the generalized time-series model considered both concurrent and lagged six-month intervention programs were shown in Table 5.6.8. In this model, linear trend effect was insignificant, but all three autoregressive order terms were statistically significant. As far as the intervention effects were concerned, the RR of HAI for concurrent CDC/TJCHA and bundle care were 0.83 (95% CI: 0.70-0.99) and

0.57 (95% CI: 0.46-0.70), and the lagged six-month RR were 0.65 (95% CI: 0.53-0.79) and 0.62 (95% CI: 0.53-0.73).

5.7 The effect of the intervention programs for HAI control in the Bayesian generalized linear mixed ARIMA model

As far as the heterogeneity across infection site, department, and pathogens were concerned, a series of Bayesian GLIMMIX-AR(1) models were conducted. Table 5.7.1 shows the results of random effect on the infection site. It was shown that the random effect term was highest for UTI, and followed by Bacteremia, pneumonia, and SSI. The standard deviation for the random effect term was 0.638 (±0.245). The results for age, gender, season, trend effect, and autoregressive order one were similar to their counterparts of the fixed effect model in previous sections. In this model, the RRs of HAI for CDC/TJCHA and bundle care were 0.75 (95% CI: 0.66-0.86) and 0.63 (95% CI: 0.56-0.71), respectively.

For the Bayesian GLIMMIX-AR(1) model with random effect on departments, the random effect term was highest for surgical department, followed by Departments of nephrology, chest, and GI, and lowest in pediatric and ER. The standard deviation for the random effect term was 1.216 (±0.266). In this model, the hygiene was statistically significant (RR=0.90, 95% CI: 0.83-0.99). The RRs of HAI control for

CDC/TJCHA and bundle care were 0.74 (95% CI: 0.65-0.84) and 0.60 (95% CI: 0.54-0.69), respectively. (Table 5.7.2)

For the Bayesian GLIMMIX-AR(1) model with random effect on pathogens, the random effect term was highest for Gram-negative, followed by Gram-positive, fungi, and lowest in anaerobic. The standard deviation for the random effect term was 1.449 (±0.495). In this model, the hygiene was statistically significant (RR=0.91, 95% CI: 0.84-0.98). The RRs of HAI control for CDC/TJCHA and bundle care were 0.75 (95% CI: 0.67-0.84) and 0.62 (95% CI: 0.55-0.69), respectively. (Table 5.7.3)

The interaction terms were further considered in the Bayesian GLIMMIX-AR model in order to exam the effect of intervention program for different infection sites, departments, and pathogens. For the random effect on infection site, we successfully obtained the posterior distribution of the effects of two intervention programs of interests, CDC/TJCHA and bundle care, for different infection sites (Table 5.7.4). The CDC/TJCHA and bundle care did not work on pneumonia. The most striking effect of CDC/TJCHA was for SSI (RR=0.63, 95% CI: 0.46-0.85) and bacteremia (RR=0.64, 95% CI: 0.52-0.80), and followed by UTI (RR=0.84, 95% CI: 0.70-1.00) (others was not in discussion). The bundle care had similar effect on SSI (RR=0.56, 95% CI: 0.44-0.72), UTI (RR=0.62, 95% CI: 0.53-0.72), and bacteremia (RR=0.63, 95% CI: 0.53-

0.75).

Table 5.7.5 shows the results of interaction for intervention programs and departments. The CDC/TJCHA and bundle care did not work in oncology department. The most striking effect of CDC/TJCHA was for ER (RR=0.06, 95% CI: 0.00-0.56). For GI, cardiovascular, chest, and neurology, the RRs of CDC/TJCHA on HAI control were around 0.6-0.7 ($p<0.05$). In surgical department, the CDC/TJCHA had significant effect on HAI (RR=0.74, 95% CI: 0.62-0.90). The effects were not statistically significant in the Department of Pediatric, Nephrology, and Infection. The RR was statistically larger than one in the Department of Oncology (RR=1.46, 95%: 1.02-2.07). The bundle care was most effective in the Department of Infection (RR=0.24, 95% CI: 0.15-0.37), followed by Chest (RR=0.34, 95% CI: 0.26-0.46), ER (RR=0.43, 95% CI: 0.30-0.62), Cardiovascular (RR=0.49, 95% CI: 0.34-0.69), Neurology (RR=0.56, 95% CI: 0.43-0.74), Nephrology (RR=0.53, 95% CI: 0.42-0.67), GI (RR=0.58, 95% CI: 0.45-0.73), and Surgical (RR=0.66, 95% CI: 0.56-0.77). Note that the RRs were statistically significantly larger than one in the Department of Pediatric (RR=0.45, 95% 0.04-0.85) and Oncology (RR=1.61, 95% CI: 1.24-2.09).

Table 5.7.6 shows the results of interaction for intervention programs and pathogens. The most striking effect of CDC/TJCHA was for anaerobic (RR=0.35, 95% CI: 0.13-0.78). It could reduce around 30% HAI for both Gram-positive and Gram-negative. The effect on fungi was small and not statistically significant (RR=0.95, 95% CI: 0.76-1.17). For bundle care, the most striking effect was still for anaerobic (RR=0.18, 95% CI: 0.09-0.37). The second one was for fungi (RR=0.48, 95% CI: 0.39-0.58). For Gram-positive and negative, the RR of bundle care was 0.66 (95% CI: 0.56-0.78) and 0.69 (95% CI: 0.62-0.78), respectively.

5.8 Forecasting for time series data on HAIs

Based on the estimated parameters of Bayesian ARIMA model, the counts of HAIs were predicted and were compared with the observed ones. Figure 5.8.1 shows the predicted curve compared with the observed with AR(1) model. Figure 5.8.2 shows the predicted curve compared with the observed with ARMA (3.1) model. It can be clearly seen that the latter one forecast more accurately than the former. This is due to the inclusion of more past values and moving-average parameters. Figure 5.8.3 shows the projection of HAIs counts after 2005 based on the posterior distribution estimated by the empirical data before 2005 (before intervention). This predicted curve is the creation of pseudo-control curve used for the reference group for evaluation of the efficacy of intervention programs. This can account for why this predicted curve was higher than the observed curve (period for intervention program). Note that 95% confidence interval was also built for the purpose of monitoring the evolution of HAIs.

5.9 Estimated and Predicted Reduction of HAI counts

The Bayesian generalized time series model enables this thesis to assess the HAI count reduction after the introduction of different intervention programs. As mentioned in the Chapter 3, we are interested in the evaluation of the efficacy of a series of intervention programs. The first evaluation was based on before and after comparison. We calculated the estimated mean for HAI count in the same length of the period before the introduction of intervention programs. It can be shown that the difference of HAI counts between observed and estimated was 129.7 for hygiene+CDC/TJCHA and 643.4 for hygiene+CDC/TJCHA+bundle care, resulting in the relative effect of 14.4% and 31.1% reduction. If it is the lagged 6-month intervention effect included in the trained model, the hygiene+CDC/TJCHA and hygiene+CDC/TJCHA+bundle care could reduce 274.9 (30.2%) and 508.5 (30.7%) HAI counts (Table 5.9.1).

The second was based on a pseudo-randomized controlled study design. We mimicked the control arm in a randomized controlled trial by sampling the predictive distribution for HAI counts based on the posterior distribution whose parameters was trained based on data before the inception of HAI preventing programs, 2005. It can be shown that the predicted HAI reduction was 40.4 for hygiene+CDC/TJCHA and 283.4.4 for hygiene+CDC/TJCHA+bundle care, resulting in the relative effect of 5% and 17% reduction. If it is the lagged 6-month intervention effect included in the trained model, the hygiene+CDC/TJCHA and hygiene+CDC/TJCHA+bundle care could 118.5 (15.3%) and 223.4 (16.3%) HAI counts (Table 5.9.2).

Chapter 6 Discussion

6.1 Summary of findings

The thesis makes great contribution to monitoring and assessing long-term evolution of HAIs for the surveillance of long-term time series data of HAIs and the quantification of the effect of intervention on time trend of HAIs with the application of both the conventional statistical method and the classical time-series method (such as de-seasonalized and de-trend analysis) and by the development of a novel Bayesian generalized linear mixed model.

There are two main series of major findings presented here regarding the practical aspect of the surveillance of HAIs and the methodological development shown as follows.

6.1.1 Surveillance of time-series HAIs and the efficacy of intervention

1. **Heterogeneity affecting long-term time series of HAIs**

(1) The elderly males are more likely to be susceptible to HAIs than the young female

using demographic features.

(2) The most frequent infection sites are UTI and bacteremia and there is much variation of HAIs across departments.

(3) The findings on the properties of time-series data include the much preponderance in summer but less in winter seasons, decreasing time trends with linear and non-linear (quadratic and cubic) pattern, the consideration of autoregressive orders depending on the site of infection and pathogens.

2. Efficacy of intervention

(1) Around 26% and 36% reduction resulting from CDC/TJCHA and Bundle care program, respectively, after 2010 were estimated with adjustment for age, gender, time trend, seasonal variation, and third-order of autoregressive order. However, there was a 10% non-significant reduction for hygiene program and lacking of significant benefit for PCDA.

(2) The 36% reduction resulting from time lag (6 months) of either CDC/TJCHA or Bundle care program after 2010 was estimated with adjustment for age, gender, time trend, seasonal variation, and autoregressive order.

(3) The similar findings on (1) were found when random-effects considering the

hierarchical structure of department, infection site, and pathogen were allowed.

(4) The results of efficacy of CDC/TJCHA and Bundle care varied with site of infection. CDC/TJCHA was conducive to 36% reduction in HAIs for bacteremia and SSI, 16% for UTI, 81% for others but there was lacking of any benefit for pneumonia. Bundle care was conducive to 37% reduction in HAIs for bacteremia, 44% for SSI, 38% for UTI, 88% for others but only 3%for pneumonia.

(5) The results of efficacy of CDC/TJCHA and Bundle care largely varied with departments. The reduction in HAIs for CDC/TJCHA was the greatest in emergency department (almost 94%) and the least in pediatrics (7%). There was lacking any benefit for oncology. The reduction in HAIs for Bundle care was the greatest in infection department (almost 77%) and the least in surgical (34%). There was lacking any benefit for oncology and pediatric department.

(6) The results of efficacy of CDC/TJCHA and Bundle care largely varied with pathogens. The reduction in HAIs with CDC/TJCHA was the greatest for anaerobic pathogen (65%), followed by Gram-positive (31%) and Gram-negative (30%), but smallest for Fungi pathogen (5%). There was lacking of any benefit for other pathogens. The reduction in HAIs with Bundle care was greatest for others (91%), followed by anaerobic pathogen (82%), by Fungi (52%), Gram-positive

(34%), and Gram-negative (31%).

6.1.2 Methodological development

There are two parts pertaining to the novelty of methodology presented in this thesis, the development of a Bayesian generalized linear mixed ARIMA model and the model-based design for evaluation of the efficacy of intervention dispensing with the randomized controlled trial.

1. We developed a generalized linear mixed effect ARIMA model by combining the generalized linear mixed model widely used in longitudinal follow-up study and ARIMA model widely used in economic studies. It can be useful for monitoring the episodes of HAIs by projecting time-series-featuring HAIs with the relevant parameters estimated by Bayesian approach making allowance for both properties of heterogeneity and time series components.
2. We have devised a time-series model-based design to evaluate the efficacy of intervention associated with HAIs in the absence of randomized controlled trial. Such a time-series model-based design is very flexible in the evaluation of any kind of evaluation of intervention in association with HAIs without needing a randomized controlled trial design.

6.2 Clinical usefulness for HAI

It is very meaningful to have a better understanding of how these three components implicated in time-series analysis are responsible for HAI. Elucidating seasonal variation makes contribution to guiding the policy for the containment of HAI and the deployment of manpower and resources in nosocomial infection control. Moreover, deciphering seasonal variation in association with each specific HAI also provide a new insight into to the role of microorganism played in endogeneous and exogeneous infection associated with HAI.

The results of time trend can reveal the evolution of each HAI with time. For example, urinary tract infection has shown a cubic trend. This finding suggests a complex pattern for its growth over the past decade. Bacteremia has shown a declining linear trend. This may imply the yield of prophylactic prevention resulting from the containment of nosocomial infection.

Although autoregressive orders are symbolic of correlations the order has a significant implication for giving a clue to the transmission of infectious disease the nearer the order it is the more likely to have the spread of infectious disease.

Finally, the integration of three components together with covariates such as age and gender can do a good prediction for occurrence of each infection site and the species of HAI. We can use 95% confidence interval for building up the surveillance of HAI in nosocomial infection.

Non-time series analysis

By calculating person years and counts of HAI, the overall incidence rate in our study was 3.82 per 1,000 patient-days. The continuing interventions were to increase the intensity of staff education and the density of hand hygiene stands. The incidence rate was shown to decrease since 2008. The lowered incidence was found in urinary tract, surgical site, and bacteremia, but not in pneumonia. This finding was similar with Haley and Rioux's study that surveillance and policy change could effectively reduce some HAIs incidence, [8,9] however, the surveillance effect varies for different sites of infection.[7] There was the possibility that factors other than this measure might have helped reduce the incidence during this period of time, in particular, reinforcement of the national infection control program and audit being promoted by the Taiwan joint commission on hospital accreditation in recent years. Our multi-variables regression analysis shows that the department of hospitalization and age had significant effect on the incidence. These findings were consistent with other studies.[78-80]

We also identified four sites of infection responsible for the majority of HAI, including bacteremia, pneumonia, surgical site infection, and urinary tract infection. Of species, gram negative species is more likely to have HAI compared with gram positive ones as shown in Table 5.7.6.

Time-series analysis

To assess the impact of seasonality, time trend, and autoregressive order on the counts of HAI by four sites and the two species, *Escherichia coli* and *Pseudomonas aeruginosa* in bacteremia, this is the first study to use a decomposition method to dissect these three components of time-series model with a discrete time generalized linear model, with emphasis on a Poisson distribution. We started from a de-seasoning process after considering seasonal variation by using a Poisson distribution. We then fitted the residual values to various forms of polynomial time trends with a linear regression model. The residual values after time trend further fitted the order of autoregressive terms. After decomposition method, seasonal variation, the form of polynomial time trend, and the order of autoregressive terms were determined to implement time series model with the incorporation of three components with adjustment for age and gender for different sites of infection and also species.

We found the impacts of three components on each site of infection and the two species are very heterogeneous. The majority of infection sites except pneumonia are indicative of seasonal variation with higher incidence rate in summer season but lower in the winter season. Certain infection site showed a linear time trend whereas some showed a non-linear time trend, either quadratic or cubic. In a similar vein, different sites of infection and species had also different orders of autoregressive terms.

6.3 Comparison with previous studies

In 2014, Cohen et al. combined 650-tertiary care hospital and 220-bed community hospital electronic medical record to investigate the infection rate difference by gender and age[81]. The HAIs were ascertained using computerized algorithms according to ICD-9-CM codes. After adjusting for the patients' characteristics and hospital stay factors, the women significantly had lower propensity of having community-associated bloodstream infection, healthcare-associated bloodstream infections, and surgical site infection with adjusted ORs 0.85(95%CI: 0.77, 0.93), 0.82(95%CI: 0.74, 0.91), and 0.78(95%CI: 0.68, 0.91), respectively. This results were especially significantly in young adults (age 17-49), but were contrary to young children (<12 year-old) and elder (>70 year-old) (Cohen et al., 2013). Klein et al. explore the relationship between patient age and type of bacteria strain[82]. The significant differences with healthcare-associated-MRSA (HA-MRSA)–related hospitalizations being more common in elder patients. We also found the similar finding in the relationship between patient age and HAIs. The counts of HAIs was increased by patient age. In 2013, Uçkay reported the UTI infection based on nationwide prevalent survey demonstrated the risk of prior exposure of urinary catheter use was significantly high with OR=3.9 (95%CI: 2.6, 5.9) and higher UTI infection rate in female (OR=2.1, 95%CI: 1.4, 3.1) compared with male[83]. However, this study focused on those who were absent from urinary catheterisation (UC) use still showed the significant risk of being UTI in female (OR=3.3, 95%CI: 1.7, 6.5). This study revealed the UC use could not be competent to explain the major cause of UTI and the gender propensity of UTI infection was striking different from other HAI infection[83]. Gender difference is also found for different type of HAIs in this thesis. We found a 1.3 fold increased risk of UTI infection in female.

Seasonal variation has been demonstrated in other studies. Perencevich et al. reported a 17% increase in the monthly rates of infection caused by *P. aeruginosa* and *A. baumannii* during the summer months. The 13%-15% of increase in the counts of

HAIs is also found in our study. Mermel et al. also observed the seasonal variability in patients in tropical climates[84]. They found a two to three-fold increased incidence of MRSA infections in pediatric patients during the second two quarters over the last decade. Data from USA show the significant seasonality in incidence with Community-associated MRSA peaking in the late summer and hospital-associated MRSA peaking in the winter[82]. In our hospital, the new employment, including intern and new nurses, was largely in summer. Thus, the implication of seasonal effects was not only meteorologically but also the surrogate of the events which happened in the corresponding season. This was also found in Fernandz-Perez et al study. They found that the medical strike and new employment was associated with the increase of cumulative incidence, while the prevention program and personnel training was associated with decease[43].

The results of 26% reduction from CDC/TJCHA for overall HAI were shown in this thesis. This effect varied with infection site: 36% for bacteremia and SSI, 16% for UTI, but no benefit of pneumonia. The remarkable results for bacteremia were consistent with the decreasing of healthcare-associated *Staphylococcus aureus* bloodstream infections by 17-28% in Australia[48] and methicillin-resistant

Staphylococcus aureus bacteremia for discharging patients in 24-month follow up from 0.05% to 0.02% in Grayson et al's study [50]. The hygiene-based programs also reduce the central line-associated blood stream infection in neonatal intensive care unit from 4.4 per 1000 to zero in Dumpa et al's study [49]. The Turkey study also showed a significant reduction of hand hygiene program for bacteremia in adult ICU.

This thesis showed that the hygiene-based approach had no benefit for pneumonia. One hand hygiene program in Turkey also showed that their ventilator-associated pneumonia rate remained stable after the initiation of the prevention program (RR=0.88, p=0.574).

The results of this thesis showed that the bundle care was conducive to 37% reduction in HAIs for bacteremia, 44% for SSI, 38% for UTI, but only 3% (p >0.05) for pneumonia. Cheng et al also found that the introduction of catheter-associated UTI bundle not only reduce the HAI for UTI but also bacteremia and overall HAI [53]. They suggested that the decline might due to the culture and clinical practice change in the whole environment. Different from this thesis, Cheng's study also showed a reduction of HAI for ventilator-associated pneumonia from3.69 to 2.90 per 1000 ventilator days, whereas this thesis found showed no significant benefit for pneumonia from the bundle care. Moreover, the explanations of these interventions effects might partly due to the cumulative effects of the previous interventions.

6.4 Strength of Bayesian GLIMMIX-ARIMA Model

The unique characteristics of the methodology on time-series model is the adoption of Bayesian directed acyclic graphic (DAG) approach in combination with ARIMA time-series model with generalized linear mixed model underpinning. The is the first study, to the best of our knowledge, to develop Bayesian generalized linear mixed (GLIMMIX) ARIMA model to apply it to long-term time series data on HAIs. There are several advantages and novelties of the proposed Bayesian GLIMMIX-ARMA). Frist, it is possible to dispense with the stationary and the invertible condition imposed on AR and MA process in contrast to the classical AR (1) and MA (1), for example, process that requires the absolute value of regression coefficients of AR and MA less than 1. Relaxing these constraints is similar to the application of Bayesian approach to explosive and non-explosive cases (Zellner 1996) and also close to monitoring the proportion of value of regression coefficients exceeding the stationary bound and testing stationarity without necessarily imposing it a priori (Naylor and Marriot 1996). Second, it can reduce the heterogeneity and raise the high likelihood of reaching stationarity and invertibility by including other covariates beyond the components of time series data. For example, the inclusion of age and gender to explain the observed heterogeneity can reduce the magnitude of regression coefficients of autoregressive order and moving-average as shown in the Table 5.5.1 without and Table 5.5.3 including age and gender as two covariates. Third, the proposed Bayesian approach can also accommodate the hierarchical data structure that are fraught with correlated property by introducing random effect (random intercept) into the model to cope with this issue. Fourth, the most flexibility of proposing Bayesian approach is to project the occurrence of HAIs based on the estimates of posterior distributions with and without adjusting for covariates. Finally

6.5 Limitations

While this study benefits from the large sample size and longitudinal time trend decomposition analysis and Bayesian dynamic linear model, there are some limitations that are noteworthy. First, the database was obtained from the electronic hospital registration and infection control system. The initial electronic database lack individual antibiotics dosing documentation and disease severity index for non-intensive care unit patients, which might affect the exact relative risk estimates.

Secondly, this study was a metropolitan teaching hospital-based study, the generalization of specific results such as relative risk or intervention efficacy to other levels of healthcare institutions may be limited. Further study was needed for the external validation. Third, the HAI definition was modified in 2008 during the study period of twenty years, and the inclusion criteria was changed accordingly by the hospital central infection committee. The absolute incidence and the absolute interventions efficacy might be affected, especially in urinary tract infection and bacteremia. Their monthly representation was still useful for evaluating trends. Fourth, we did not include covariates such as patient comorbidities into the model. The most related covariates was departments of admission and infection sites, which represented part of major comorbidities of the patients in this study. In the time series study, the autoregressive order was the proxy for the history information unavailable. Fifth, the follow-up time for the intervention evaluation may be short, especially for Bundle care intervention. Finally, the model fitting diagnostics were not done, further studies may be needed.

In conclusion, my thesis here developed a novel Bayesian generalized linear mixed ARMA model to monitor and evaluate the long-term time series on monthly frequencies of HAIs in association with the impact of a set of interventions, the effects of time trend, seasonal variation, autoregressive order and innovation (moving average), and personal characteristics (age and gender) taking in account hierarchical correlated data property. This approach can be easily applied to forecasting the outcome of long-term time-series data and can be used for evaluation of the efficacy of intervention programs in the absence of randomized controlled trial design.

TABLES

Table 5.1. 1 Incidence rate by calendar year

Year	patient-days	HAI count number	Incidence rate	95%CI
1994	223113	901	4.04	(3.77, 4.30)
1995	240468	1193	4.96	(4.68, 5.24)
1996	251118	1295	5.16	(4.88, 5.44)
1997	245854	1123	4.57	(4.30, 4.83)
1998	244453	1108	4.53	(4.27, 4.80)
1999	248542	1109	4.46	(4.20, 4.72)
2000	247713	1061	4.28	(4.03, 4.54)
2001	261645	993	3.8	(3.56, 4.03)
2002	259001	1117	4.31	(4.06, 4.57)
2003	291580	1095	3.76	(3.53, 3.98)
2004	270502	1086	4.01	(3.78, 4.25)
2005	234963	1074	4.57	(4.3, 4.84)
2006	241628	1110	4.59	(4.32, 4.86)
2007	279113	1211	4.34	(4.09, 4.58)
2008	218678	960	4.39	(4.11, 4.67)
2009	217437	958	4.41	(4.13, 4.68)
2010	222534	888	3.99	(3.73, 4.25)
2011	234007	674	2.88	(2.66, 3.10)
2012	237930	695	2.92	(2.70, 3.14)
2013	226422	648	2.86	(2.64, 3.08)

Table 5.1. 2 The incidence rate of HAI by different factors and microbes

Variable	Classification	Incidence rate (95% CI)
Age	0-9	1.27(1.14, 1.41)
	10-19	1.62(1.38, 1.85)
	20-29	1.06(0.96, 1.16)
	30-39	1.51(1.39, 1.62)
	40-49	3.12(2.96, 3.28)
	50-59	3.62(3.48, 3.77)
	60-69	5.09(4.93, 5.24)
	70-79	6.76(6.58, 6.94)
	>=80	9.14(8.85, 9.42)
Gender	Female	4.22(4.13, 4.30)
	Male	4.35(4.26, 4.43)
Department	CV	3.61(3.38, 3.84)
	Chest	7.52(7.21, 7.83)
	Neurology	5.98(5.69, 6.26)
	Pediatric	1.33(1.18, 1.48)
	Nephrology	7.31(7.02, 7.61)
	Infection	6.90(6.45, 7.35)
	GI	6.39(6.11, 6.67)
	Oncology	7.72(7.18, 8.25)
	Emergency	8.75(7.17, 10.33)
	Surgical	3.30(3.22, 3.38)
	Other	2.00(1.87, 2.13)
Season	Spring	4.46(4.33, 4.58)
	Summer	4.57(4.44, 4.70)
	Autumn	4.22(4.10, 4.34)
	Winter	3.91(3.79, 4.02)
Infection site	Bacteremia	1.12(1.09, 1.15)
	RTI	0.72(0.69, 0.74)
	SSI	0.47(0.45, 0.49)
	UTI	1.63(1.59, 1.67)
	GI	0.04(0.04, 0.05)
	SST	0.09(0.08, 0.09)
	EENT	0.02(0.02, 0.03)
	Other	0.19(0.18, 0.20)

SSI: surgical site infection; UTI: urinary tract infection; GI: gastrointestinal system; SST: skin and soft tissue; EENT: eye, ear, nose, throat, or mouth infection

Table 5.1. 3 Univariate and multi-variable analysis for HAIs incidence

Variable	Classification	Univariate analysis		Multi-variable analysis	
		RR(95%CI)	p-value	aRR(95%CI)	p-value
Age at admission	0-9 / >=80	0.14(0.13, 0.16)	<0.0001	0.16(0.13, 0.21)	<0.0001
	10-19 / >=80	0.18(0.16, 0.21)		0.23(0.19, 0.26)	
	20-29 / >=80	0.12(0.11, 0.13)		0.15(0.14, 0.17)	
	30-39 / >=80	0.16(0.15, 0.18)		0.22(0.20, 0.23)	
	40-49 / >=80	0.34(0.32, 0.36)		0.42(0.40, 0.45)	
	50-59 / >=80	0.40(0.39, 0.42)		0.49(0.47, 0.52)	
	60-69 / >=80	0.57(0.54, 0.59)		0.62(0.60, 0.65)	
	70-79 / >=80	0.76(0.73, 0.79)		0.83(0.80, 0.87)	
Gender	Male / Female	1.04(1.01, 1.07)	0.004	1.06(1.03, 1.09)	<0.0001
Department	CV / Neurology	0.58(0.54, 0.63)	<0.0001	0.54(0.50, 0.58)	<0.0001
	Chest / Neurology	1.20(1.12, 1.27)		0.90(0.84, 0.95)	
	Pediatric / Neurology	1.21(1.14, 1.29)		1.01(0.95, 1.08)	
	Nephrology / Neurology	1.09(1.01, 1.18)		0.85(0.78, 0.92)	
	Infection / Neurology	1.05(0.99, 1.12)		1.00(0.94, 1.07)	
	GI / Neurology	1.31(1.21, 1.42)		1.47(1.36, 1.59)	
	Oncology / Neurology	1.40(1.17, 1.69)		1.05(0.87, 1.26)	
	Emergency / Neurology	0.58(0.54, 0.63)		0.54(0.50, 0.58)	
	Surgical / Neurology	0.55(0.52, 0.57)		0.76(0.72, 0.80)	
	Others / Neurology	0.32(0.29, 0.34)		0.45(0.41, 0.48)	
Admission type	Emergency/ OPD	2.17(2.11, 2.23)	<0.0001	1.60(1.55, 1.65)	<0.0001
Infection site	Bacteremia / SSI	2.40(2.28, 2.52)	<0.0001	2.40(2.28, 2.52)	<0.0001
	PNEU / SSI	1.57(1.49, 1.66)		1.57(1.49, 1.66)	
	UTI / SSI	3.49(3.33, 3.66)		3.49(3.33, 3.66)	
	GI / SSI	0.09(0.08, 0.11)		0.09(0.08, 0.11)	
	SST / SSI	0.18(0.16, 0.20)		0.18(0.16, 0.20)	
	EENT / SSI	0.05(0.04, 0.06)		0.05(0.04, 0.06)	
	Others / SSI	0.38(0.35, 0.42)		0.39(0.36, 0.42)	

CV: cardiovascular, GI: Gastrointestinal unit, PNEU: pneumonia, SSI: surgical site infection, UTI: urinary tract infection, SST: skin and soft tissue, EENT: eye, ear, nose, throat, or mouth

Table 5.2. 1 The seasonal effect on HAIs incidence (univariate analysis)

Season	RR	95% CI		p value
Spring /Winter	1.13	1.09	1.18	<.0001
Summer /Winter	1.16	1.11	1.21	
Autumn /Winter	1.07	1.03	1.12	

Table 5.2. 2 Time trend analysis with de-seasonalized HAIs

Method	Model	Trend	Estimate	SD	R^2	p value
Original	Model a	Linear	2.790E-03	1.660E-03	0.0362	0.0941
		Quadratic	-2.341E-05	1.239E-05		0.0602
		Cubic	-5.777E-07	2.183E-07		0.0087
	Model b	Linear	-1.210E-03	6.868E-04	0.0091	0.0785
		Quadratic	-1.475E-05	1.212E-05		0.2250
	Model c	Linear	-1.070E-03	6.767E-04	0.0069	0.1165
Excluding Outliers*	Model a	Linear	2.610E-03	1.690E-03	0.0365	0.1241
		Quadratic	-2.287E-05	1.259E-05		0.0707
		Cubic	-5.660E-07	2.221E-07		0.0115
	Model b	Linear	-1.320E-03	7.007E-04	0.0111	0.0605
		Quadratic	-1.466E-05	1.233E-05		0.2357
	Model c	Linear	-1.180E-03	6.916E-04	0.0091	0.0884

Model a: time trend analysis using residual for linear, quadratic, and cubic

Model b: time trend analysis using residual for linear, and quadratic

Model c: time trend analysis using residual for linear

*excluding outliers : May-95, Jun-96, Feb-97, Dec-99, Nov-00

Table 5.2. 3 De-seasonalization and de-trend time series of HAI incidence

Autoregressive	Coefficient	SD	p value
AR(1)	-0.0982	0.0688	0.1532
AR(2)	0.0775	0.0683	0.2565
AR(3)	0.1068	0.0682	0.1175
AR(4)	0.0307	0.0678	0.6506
AR(1)	-0.0846	0.0686	0.2174
AR(2)	0.0819	0.0686	0.2321
AR(3)	0.1254	0.0678	0.0644
AR(1)	-0.0735	0.0689	0.2860
AR(2)	0.0833	0.0681	0.2214
AR(1)	-0.0794	0.0679	0.2426

Table 5.2. 4 The seasonal effect on bacteremia HAIs incidence (univariate analysis)

Season	RR	95% CI		p value
Spring /Winter	1.16	1.07	1.25	<.0001
Summer /Winter	1.19	1.10	1.29	
Autumn /Winter	1.08	1.00	1.17	

Table 5.2. 5 Time trend analysis with de-seasonalized residual for bacteremia HAIs

Method	Model	Trend	Estimate	SD	R^2	p value
Original	Model a	Linear	3.920E-03	2.160E-03	0.0397	0.0710
		Quadratic	-3.485E-05	1.618E-05		0.0324
		Cubic	-7.838E-07	2.850E-07		0.0065
	Model b	Linear	-1.500E-03	8.977E-04	0.0101	0.0953
		Quadratic	-2.310E-05	1.584E-05		0.1464
	Model c	Linear	-1.270E-03	8.859E-04	0.0049	0.1521
Excluding Outliers*	Model a	Linear	2.430E-03	2.180E-03	0.0341	0.2650
		Quadratic	-1.448E-05	1.617E-05		0.3713
		Cubic	2.134E-08	2.878E-07		0.9410
	Model b	Linear	2.580E-03	8.851E-04	0.0388	0.0040
		Quadratic	-1.476E-05	1.568E-05		0.3476
	Model c	Linear	2.700E-03	8.749E-04	0.0393	0.0023

Model a: time trend analysis using residual for linear, quadratic, and cubic

Model b: time trend analysis using residual for linear, and quadratic

Model c: time trend analysis using residual for linear

*excluding outliers : May-95, Jun-96, Feb-97, Dec-99, Nov-00

Table 5.2. 6 Bacteremia HAI incidence time series after de-seasonalization and de-

trend

Autoregressive	Coefficient	SD	p value
AR(1)	0.0582	0.0693	0.4012
AR(2)	0.0478	0.0688	0.4870
AR(3)	0.1122	0.0687	0.1023
AR(4)	-0.0736	0.0688	0.2850
AR(1)	0.0461	0.0687	0.5025
AR(2)	0.0465	0.0687	0.4987
AR(3)	0.1057	0.0685	0.1229
AR(1)	0.0482	0.0690	0.4851
AR(2)	0.0582	0.0689	0.3977
AR(1)	0.0470	0.0688	0.4941

Table 5.2. 7 The seasonal effect on pneumonia HAIs incidence (univariate analysis)

Season	RR	95% CI		p value
Spring /Winter	1.03	0.93	1.13	0.0897
Summer /Winter	1.12	1.02	1.24	
Autumn /Winter	1.09	0.98	1.20	

Table 5.2. 8 Time trend analysis with de-seasonalized residual for pneumonia HAIs

Method	Model	Trend	Estimate	SD	R^2	p value
Original	Model a	Linear	2.590E-03	2.130E-03	0.0369	0.2240
		Quadratic	-1.413E-05	1.589E-05		0.3747
		Cubic	4.453E-09	2.825E-07		0.9874
	Model b	Linear	2.620E-03	8.654E-04	0.0414	0.0027
		Quadratic	-1.420E-05	1.538E-05		0.3570
	Model c	Linear	2.750E-03	8.538E-04	0.0421	0.0015
Excluding Outliers*	Model a	Linear	3.070E-03	2.140E-03	0.0421	0.1526
		Quadratic	-1.377E-05	1.590E-05		0.3875
		Cubic	-3.984E-08	2.829E-07		0.8882
	Model b	Linear	2.790E-03	8.683E-04	0.0466	0.0015
		Quadratic	-1.323E-05	1.539E-05		0.3910
	Model c	Linear	2.910E-03	8.564E-04	0.0478	0.0008

Model a: time trend analysis using residual for linear, quadratic, and cubic

Model b: time trend analysis using residual for linear, and quadratic

Model c: time trend analysis using residual for linear

*excluding outliers: Jul-03, Apr-08, Nov-08

Table 5.2. 9 Pneumonia HAI incidence time series after de-seasonalization and de-trend

Autoregressive	Coefficient	SD	p value
AR(1)	0.1174	0.0691	0.0895
AR(2)	0.1671	0.0693	0.0158
AR(3)	0.1099	0.0692	0.1125
AR(4)	-0.0701	0.0694	0.3124
AR(1)	0.1108	0.0688	0.1072
AR(2)	0.1561	0.0684	0.0225
AR(3)	0.1025	0.0688	0.1367
AR(1)	0.1284	0.068	0.0591
AR(2)	0.1695	0.0681	0.0127
AR(1)	0.1546	0.068	0.023

Table 5.2. 10 The seasonal effect on SSI HAIs incidence (univariate analysis)

Season	RR	95% CI		p value
Spring /Winter	1.24	1.10	1.40	0.0029
Summer /Winter	1.20	1.06	1.36	
Autumn /Winter	1.10	0.97	1.25	

Table 5.2. 11 Time trend analysis with de-seasonalized residual for SSI HAIs

Method	Model	Trend	Estimate	SD	R^2	p value
Original	Model a	Linear	-2.920E-03	2.280E-03	0.1214	0.2018
		Quadratic	-6.460E-06	1.698E-05		0.7042
		Cubic	-3.195E-07	2.997E-07		0.2877
	Model b	Linear	-5.140E-03	9.299E-04	0.1209	<.0001
		Quadratic	-1.600E-06	1.636E-05		0.9221
	Model c	Linear	-5.120E-03	9.138E-04	0.1250	<.0001
Excluding Outliers*	Model a	Linear	-3.400E-03	2.320E-03	0.1312	0.1433
		Quadratic	-4.780E-06	1.715E-05		0.7808
		Cubic	-2.863E-07	3.033E-07		0.3463
	Model b	Linear	-5.400E-03	9.439E-04	0.1317	<.0001
		Quadratic	-5.668E-07	1.655E-05		0.9727
	Model c	Linear	-5.390E-03	9.292E-04	0.1359	<.0001

SSI: surgical site infection

Model a: time trend analysis using residual for linear, quadratic, and cubic

Model b: time trend analysis using residual for linear, and quadratic

Model c: time trend analysis using residual for linear

*excluding outliers:

Table 5.2. 12 SSI HAIs incidence time series after de-seasonalization and de-trend

Autoregressive	Coefficient	SD	p value
AR(1)	0.125	0.0696	0.0728
AR(2)	0.0286	0.0701	0.6837
AR(3)	-0.0352	0.0701	0.6160
AR(4)	-0.0778	0.0696	0.2637
AR(1)	0.1287	0.0696	0.0646
AR(2)	0.0263	0.0702	0.7080
AR(3)	-0.0452	0.0696	0.5164
AR(1)	0.1275	0.0695	0.0666
AR(2)	0.0205	0.0695	0.7678
AR(1)	0.1302	0.0688	0.0583

Table 5.2. 13 The seasonal effect on urinary tract HAIs incidence (univariate analysis)

Season	RR	95% CI		p value
Spring /Winter	1.11	1.04	1.18	<0.0001
Summer /Winter	1.16	1.09	1.24	
Autumn /Winter	1.04	0.97	1.11	

Table 5.2. 14 Time trend analysis with de-seasonalized residual for UTI HAIs

Method	Model	Trend	Estimate	SD	R^2	p value
Original	Model a	Linear	6.330E-03	1.850E-03	0.0517	0.0007
		Quadratic	-2.600E-05	1.384E-05		0.0617
		Cubic	-9.053E-07	2.438E-07		0.0003
	Model b	Linear	6.705E-05	7.787E-04	-0.0052	0.9315
		Quadratic	-1.242E-05	1.374E-05		0.3672
	Model c	Linear	1.913E-04	7.662E-04	-0.0044	0.8031
Excluding Outliers*	Model a	Linear	6.260E-03	1.880E-03	0.0502	0.001
		Quadratic	-2.530E-05	1.403E-05		0.0727
		Cubic	-9.036E-07	2.473E-07		0.0003
	Model b	Linear	-1.418E-05	7.933E-04	-0.0059	0.9858
		Quadratic	-1.201E-05	1.394E-05		0.3901
	Model c	Linear	9.803E-05	7.820E-04	-0.0047	0.9004

Model a: time trend analysis using residual for linear, quadratic, and cubic

Model b: time trend analysis using residual for linear, and quadratic

Model c: time trend analysis using residual for linear

*excluding outliers : May-95, Jun-96, Feb-97, Dec-99

Table 5.2. 15 UTI HAI incidence time series after de-seasonalization and de-trend

Autoregressive	Coefficient	SD	p value
AR(1)	0.0748	0.0686	0.2755
AR(2)	0.1033	0.0683	0.1304
AR(3)	0.0416	0.0683	0.5424
AR(4)	-0.1408	0.0682	0.0389
AR(1)	0.0652	0.0688	0.3431
AR(2)	0.0922	0.0686	0.1793
AR(3)	0.0347	0.0687	0.6138
AR(1)	0.066	0.0688	0.3370
AR(2)	0.0903	0.0687	0.1886
AR(1)	0.0735	0.0687	0.2842

Table 5.2. 16 The seasonal effect on *E.coli* HAIs incidence (univariate analysis)

Season	RR	95% CI		p value
Spring /Winter	1.10	0.85	A1.43	0.7962
Summer /Winter	1.08	0.83	1.39	
Autumn /Winter	1.14	0.88	1.47	

Table 5.2. 17 Time trend analysis with de-seasonalized residual for *E.coli* HAIs

Method	Model	Trend	Estimate	SD	R^2	p value
Original	Model a	Linear	1.099E+00	8.453E-01	0.0760	0.9958
		Quadratic	1.078E+00	8.335E-01		<.0001
		Cubic	1.136E+00	8.796E-01		0.6073
	Model b	Linear	-1.610E-03	1.530E-03	0.0799	0.2943
		Quadratic	-1.088E-04	2.606E-05		<.0001
	Model c	Linear	8.710E-05	1.540E-03	-0.0056	0.9550
Excluding Outliers*	Model a	Linear	-4.585E-05	3.590E-03	0.0746	0.9898
		Quadratic	-1.139E-04	2.835E-05		<.0001
		Cubic	-2.418E-07	4.936E-07		0.6249
	Model b	Linear	-1.630E-03	1.560E-03	0.0787	0.2973
		Quadratic	-1.091E-04	2.655E-05		<.0001
	Model c	Linear	1.339E-05	1.570E-03	-0.0058	0.9932

Model a: time trend analysis using residual for linear, quadratic, and cubic

Model b: time trend analysis using residual for linear, and quadratic

Model c: time trend analysis using residual for linear

*excluding outliers: May-95, Feb-97, Dec-99, Apr-00

Table 5.2. 18 *E. coli* bacteremia HAI incidence time series after de-seasonalization and de-trend

Autoregressive	Coefficient	SD	p value
AR(1)	-0.0266	0.0755	0.7242
AR(2)	-0.1758	0.0753	0.0196
AR(3)	0.0791	0.0755	0.2948
AR(4)	-0.0536	0.0723	0.4582
AR(1)	-0.0385	0.076	0.6126
AR(2)	-0.1713	0.0751	0.0225
AR(3)	0.0376	0.0729	0.6065
AR(1)	-0.0431	0.075	0.5660
AR(2)	-0.1547	0.072	0.0315
AR(1)	-0.0302	0.0727	0.6778

Table 5.2. 19 The seasonal effect on *Pseudomonas aeruginosa* HAIs incidence

Season	RR	95% CI		p value
Spring /Winter	0.94	0.67	1.31	0.9171
Summer /Winter	1.05	0.76	1.47	
Autumn /Winter	1.01	0.73	1.40	

Table 5.2. 20 Time trend analysis with de-seasonalized *Pseudomonas aeruginosa* bacteremia HAIs

Method	Model	Trend	Estimate	SD	R^2	p value
Original	Model a	Linear	-1.650E-03	4.210E-03	-0.0033	0.696
		Quadratic	-2.140E-05	3.358E-05		0.5249
		Cubic	-1.793E-07	5.796E-07		0.7575
	Model b	Linear	-2.820E-03	1.830E-03	0.0025	0.1255
		Quadratic	-1.815E-05	3.180E-05		0.5690
	Model c	Linear	-2.540E-03	1.760E-03	0.0069	0.1509
Excluding Outliers*	Model a	Linear	-1.770E-03	4.310E-03	-0.0021	0.6811
		Quadratic	-1.877E-05	3.410E-05		0.5828
		Cubic	-1.873E-07	5.911E-07		0.7517
	Model b	Linear	-3.000E-03	1.870E-03	0.0038	0.11
		Quadratic	-1.553E-05	3.243E-05		0.6328
	Model c	Linear	-2.770E-03	1.800E-03	0.0089	0.1256

Model a: time trend analysis using residual for linear, quadratic, and cubic

Model b: time trend analysis using residual for linear, and quadratic

Model c: time trend analysis using residual for linear

*excluding outliers: May-95, Sep-96, Dec-99, Jan-00

Table 5.2. 21 *P. aeruginosa* HAI incidence time series after de-seasonalization and de-trend

Autoregressive	Coefficient	SD	p value
AR(1)	0.1270	0.0685	0.0635
AR(2)	-0.0036	0.0684	0.9578
AR(3)	-0.1402	0.0686	0.0409
AR(4)	0.1186	0.0687	0.0842
AR(1)	0.1192	0.0687	0.0827
AR(2)	-0.0050	0.0692	0.9428
AR(3)	-0.1201	0.0688	0.0809
AR(1)	0.1202	0.0691	0.0819
AR(2)	-0.0162	0.069	0.8144
AR(1)	0.1179	0.0683	0.0846

Table 5.2. 22 ARMA model for the HAI infection sites

Outcome	Model	Effect	Estimate	S.E.	p-value
All Infection	ARMA(1,1)	Mean	0.0042	0.0035	0.2294
		MA(1)	0.9040	0.0445	<.0001
		AR(1)	1.0000	0.0165	<.0001
Bacteremia	ARMA(1,1)	Mean	-0.0003	0.0012	0.812
		MA(1)	0.8398	0.0564	<.0001
		AR(1)	0.9823	0.0277	<.0001
Pneumonia	ARMA(2,1)	Mean	-0.0002	0.0004	0.7157
		MA(1)	0.5444	0.2268	0.0172
		AR(1)	0.8462	0.2384	0.0005
		AR(2)	-0.0237	0.1356	0.8616
SSI	ARMA(1,1)	Mean	0.0017	0.0007	0.0147
		MA(1)	0.9472	0.0282	<.0001
		AR(1)	1.0000	0.0060	<.0001
UTI	ARMA(4,1)	Mean	0.0001	0.0014	0.9401
		MA(1)	0.8139	0.1412	<.0001
		AR(1)	0.8885	0.1577	<.0001
		AR(2)	0.2082	0.0932	0.0265
		AR(3)	-0.1301	0.1021	0.204
		AR(4)	0.0012	0.0878	0.9891

Table 5.2. 23 ARMA model for the bacteremia species

Outcome	Model	Effect	Estimate	S.E.	p-value
E. coli	ARMA(1,1)	Mean	4.24E-08	5.38E-05	0.9994
		MA(1)	-0.5227	0.5101	0.3066
		AR(1)	-0.4318	0.5393	0.4243
P. aeruginosa	ARMA(3,2)	Mean	3.81E-06	3.88E-05	0.9219
		MA(1)	-1.2203	0.0094	<.0001
		MA(2)	-0.9983	0.0102	<.0001
		AR(1)	-1.0610	0.0705	<.0001
		AR(2)	-0.8077	0.0855	<.0001
		AR(3)	0.0442	0.0711	0.5347

Table 5.3. 1 The adjusted time series model for HAIs incidence (normal distribution)

Parameter	**Level**	**Estimate**	**S.E.**	**Chisq**	**p-value**
Season	Spring/Winter	0.0101	0.0168	1.16	0.7619
	Summer/Winter	0.0174	0.0168		
	Autumn/Winter	0.0131	0.0170		
Time trend	Linear	2.6649E-05	0.0002	0.01	0.9104
	Quadratic	-5.1747E-06	1.7619E-06	8.62	0.0033
	Cubic	-1.1630E-07	3.1100E-08	13.93	0.0002
Autocorrelations	AR (1)	-0.0347	0.0055	39.40	<.0001
Age	0-9 / >=80	-0.9433	0.0257	2639.75	<.0001
	10-19 / >=80	-0.9245	0.0257		
	20-29 / >=80	-0.9346	0.0257		
	30-39 / >=80	-0.8989	0.0256		
	40-49 / >=80	-0.7309	0.0255		
	50-59 / >=80	-0.6117	0.0254		
	60-69 / >=80	-0.4370	0.0253		
	70-79 / >=80	-0.2422	0.0252		
Gender	Male / Female	0.0250	0.0119	4.43	0.0354

Table 5.3. 2 The adjusted Poisson model for HAIs incidence

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	0.0381	0.0212	11.4	0.0097
	Summer/Winter	0.0710	0.0213		
	Autumn/Winter	0.0477	0.0218		
Time trend	Linear	7.4737E-04	0.000296757	6.34	0.0118
	Quadratic	-1.6703E-05	2.3646E-06	50.61	<.0001
	Cubic	-3.4250E-07	4.05E-08	71.48	<.0001
Autocorrelations	AR (1)	8.7558E-04	0.0004	6.05	0.0139
Age	0-9 / >=80	-2.0160	0.0591	6508.2	<.0001
	10-19 / >=80	-1.7863	0.0783		
	20-29 / >=80	-2.1405	0.0531		
	30-39 / >=80	-1.8330	0.0420		
	40-49 / >=80	-1.1082	0.0309		
	50-59 / >=80	-0.8066	0.0262		
	60-69 / >=80	-0.5360	0.0229		
	70-79 / >=80	-0.2868	0.0214		
Gender	Male / Female	0.0301	0.0149	4.1	0.043

Table 5.3. 3 The adjusted negative binominal model for HAIs incidence

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	0.0446	0.0319	4.23	0.2379
	Summer/Winter	0.0628	0.0318		
	Autumn/Winter	0.0480	0.0324		
Time trend	Linear	6.3281E-04	4.4455E-04	2.02	0.1548
	Quadratic	-1.5758E-05	3.5092E-06	20.01	<.0001
	Cubic	-3.5340E-07	6.07E-08	33.68	<.0001
Autocorrelations	AR (1)	7.5456E-04	0.0005	1.95	0.1629
Age	0-9 / >=80	-2.0345	0.0658	2481.32	<.0001
	10-19 / >=80	-1.8159	0.0842		
	20-29 / >=80	-2.1219	0.061		
	30-39 / >=80	-1.8335	0.0510		
	40-49 / >=80	-1.1325	0.0421		
	50-59 / >=80	-0.8336	0.0387		
	60-69 / >=80	-0.5421	0.0364		
	70-79 / >=80	-0.2803	0.0355		
Gender	Male / Female	0.1063	0.0225	22.68	<.0001

Table 5.3. 4 The adjusted time series model for HAIs bacteremia incidence (normal distribution)

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	0.0989	0.0675	4.91	0.1785
	Summer/Winter	0.1175	0.067		
	Autumn/Winter	0.0084	0.068		
Time trend	Linear	-1.30E-03	0.0004	11.18	0.0008
Autocorrelations	AR (1)	-1.28E-02	0.0203	0.4	0.5263
Age	0-9 / >=80	-1.7992	0.1054	546.83	<.0001
	10-19 / >=80	-1.9445	0.1059		
	20-29 / >=80	-1.8778	0.1067		
	30-39 / >=80	-1.7759	0.1057		
	40-49 / >=80	-1.3476	0.1031		
	50-59 / >=80	-1.0596	0.1017		
	60-69 / >=80	-0.7646	0.101		
	70-79 / >=80	-0.4505	0.1007		
Gender	Male / Female	0.249	0.0474	27.43	<.0001

Table 5.3. 5 The adjusted Poisson model for bacteremia HAIs incidence

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	0.0561	0.0415	3.9	0.2726
	Summer/Winter	0.0744	0.0417		
	Autumn/Winter	0.0226	0.0428		
Time trend	Linear	-1.1876E-03	0.0002	23.22	<.0001
Autocorrelations	AR (1)	9.2969E-03	0.0019	22.73	<.0001
Age	0-9 / >=80	-1.5271	0.0994	1346.41	<.0001
	10-19 / >=80	-1.7659	0.1619		
	20-29 / >=80	-2.0728	0.1099		
	30-39 / >=80	-1.5756	0.0801		
	40-49 / >=80	-0.8296	0.059		
	50-59 / >=80	-0.5143	0.0506		
	60-69 / >=80	-0.3509	0.0461		
	70-79 / >=80	-0.1959	0.0442		
Gender	Male / Female	0.1724	0.0292	35.04	<.0001

Table 5.3. 6 The adjusted negative binominal model for bacteremia HAIs incidence

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	0.0681	0.0499	2.79	0.4255
	Summer/Winter	0.0745	0.0499		
	Autumn/Winter	0.0368	0.0511		
Time trend	Linear	-1.3145E-03	0.0003	19.36	<.0001
Autocorrelations	AR (1)	9.3852E-03	0.0024	15.57	<.0001
Age	0-9 / >=80	-1.5427	0.1048	976.92	<.0001
	10-19 / >=80	-1.7821	0.1658		
	20-29 / >=80	-2.0857	0.1153		
	30-39 / >=80	-1.5854	0.0866		
	40-49 / >=80	-0.8448	0.0675		
	50-59 / >=80	-0.5323	0.0603		
	60-69 / >=80	-0.3626	0.0565		
	70-79 / >=80	-0.2019	0.055		
Gender	Male / Female	0.1940	0.0351	30.76	<.0001

Table 5.3. 7 The adjusted time series model for HAIs pneumonia incidence (normal distribution)

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	-0.0149	0.0865	4.19	0.2417
	Summer/Winter	0.1442	0.0865		
	Autumn/Winter	0.0608	0.0864		
Time trend	Linear	0.0003	0.0005	0.37	0.5437
Autocorrelations	AR (1)	0.0535	0.0293	3.32	0.0682
	AR (2)	0.0868	0.0282	9.44	0.0021
Age	0-9 / >=80	-1.2312	0.1444	131.08	<.0001
	10-19 / >=80	-1.1855	0.1394		
	20-29 / >=80	-1.1703	0.1430		
	30-39 / >=80	-1.1051	0.1427		
	40-49 / >=80	-0.8034	0.1385		
	50-59 / >=80	-0.7408	0.1361		
	60-69 / >=80	-0.4200	0.1333		
	70-79 / >=80	-0.2320	0.1303		
Gender	Male / Female	0.3217	0.0623	26.47	<.0001

Table 5.3. 8 The adjusted Poisson model for pneumonia HAIs incidence

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	-0.0156	0.0515	10.19	0.0170
	Summer/Winter	0.1110	0.0511		
	Autumn/Winter	0.1022	0.0508		
Time trend	Linear	1.4807E-03	0.0003	6.34	0.0118
Autocorrelations	AR (1)	2.2691E-02	0.0031	53.11	<.0001
	AR (2)	0.0003	0.0029	0.01	0.9296
Age	0-9 / >=80	-3.0450	0.2269	1316.81	<.0001
	10-19 / >=80	-1.6101	0.1713		
	20-29 / >=80	-2.3704	0.1395		
	30-39 / >=80	-1.9751	0.1102		
	40-49 / >=80	-1.1961	0.0757		
	50-59 / >=80	-1.0075	0.0634		
	60-69 / >=80	-0.6025	0.0546		
	70-79 / >=80	-0.3327	0.0511		
Gender	Male / Female	0.4891	0.0374	177.03	<.0001

Table 5.3. 9 The adjusted negative binominal model for pneumonia HAIs incidence

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	-0.0441	0.0692	1.04	0.7909
	Summer/Winter	0.0101	0.0683		
	Autumn/Winter	0.0210	0.0679		
Time trend	Linear	5.8614E-04	0.0004	2.07	0.1499
Autocorrelations	AR (1)	1.9548E-02	0.0041	22.21	<.0001
	AR (2)	0.0112	0.0042	7.07	0.0078
Age	0-9 / >=80	-3.0691	0.2332	890.61	<.0001
	10-19 / >=80	-1.6525	0.1804		
	20-29 / >=80	-2.4019	0.1562		
	30-39 / >=80	-2.0246	0.122		
	40-49 / >=80	-1.2525	0.0924		
	50-59 / >=80	-0.9384	0.0826		
	60-69 / >=80	-0.5987	0.0756		
	70-79 / >=80	-0.2694	0.0727		
Gender	Male / Female	0.5422	0.0491	121.82	<.0001

Table 5.3. 10 The adjusted time series model for SSI HAIs incidence (normal distribution)

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	0.0733	0.0587	3.49	0.3217
	Summer/Winter	-0.0243	0.0583		
	Autumn/Winter	-0.0090	0.0591		
Time trend	Linear	-0.0023	0.0003	47.29	<.0001
Autocorrelations	AR (1)	-0.0250	0.0207	1.46	0.2271
Age	0-9 / >=80	-0.1007	0.0866	59.19	<.0001
	10-19 / >=80	-0.1380	0.0866		
	20-29 / >=80	0.0781	0.0866		
	30-39 / >=80	0.0141	0.0866		
	40-49 / >=80	0.2998	0.0867		
	50-59 / >=80	0.1597	0.0868		
	60-69 / >=80	0.2930	0.0868		
	70-79 / >=80	0.2812	0.0868		
Gender	Male / Female	0.1737	0.0409	17.97	<.0001

Table 5.3. 11 The adjusted Poisson model for SSI HAIs incidence

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	0.0904	0.0652	2.11	0.5508
	Summer/Winter	0.0321	0.0662		
	Autumn/Winter	0.0332	0.0669		
Time trend	Linear	-3.3693E-03	0.0004	65.21	<.0001
Autocorrelations	AR (1)	6.6174E-03	0.0048	1.92	0.1659
Age	0-9 / >=80	-0.5651	0.1625	172.00	<.0001
	10-19 / >=80	-0.1660	0.1893		
	20-29 / >=80	-0.1050	0.1275		
	30-39 / >=80	0.0023	0.1165		
	40-49 / >=80	0.5188	0.1031		
	50-59 / >=80	0.4849	0.1006		
	60-69 / >=80	0.5461	0.0968		
	70-79 / >=80	0.4720	0.0975		
Gender	Male / Female	0.3457	0.046	57.48	<.0001

Table 5.3. 12 The adjusted negative binominal model for SSI HAIs incidence

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	0.1171	0.0947	1.91	0.5913
	Summer/Winter	0.0163	0.0945		
	Autumn/Winter	0.0439	0.0956		
Time trend	Linear	-4.1034E-03	0.0006	46.35	<.0001
Autocorrelations	AR (1)	4.0409E-03	0.0072	0.31	0.5752
Age	0-9 / >=80	-0.6135	0.1861	104.71	<.0001
	10-19 / >=80	-0.2015	0.2125		
	20-29 / >=80	-0.0956	0.156		
	30-39 / >=80	-0.0522	0.1467		
	40-49 / >=80	0.4787	0.1357		
	50-59 / >=80	0.4467	0.1336		
	60-69 / >=80	0.5307	0.1306		
	70-79 / >=80	0.5239	0.1309		
Gender	Male / Female	0.3664	0.0656	31.1	<.0001

Table 5.3. 13 The adjusted time series model for UTI HAIs incidence (normal distribution)

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	0.1220	0.1202	4.36	0.2251
	Summer/Winter	0.1772	0.1188		
	Autumn/Winter	-0.0321	0.1203		
Time trend	Linear	0.0034	0.0017	3.98	0.0461
	Quadratic	-2.9E-05	1.24E-05	5.66	0.0174
	Cubic	-6.4E-07	2.27E-07	7.96	0.0048
Autocorrelations	AR (1)	0.1322	0.0289	20.77	<.0001
	AR (2)	0.1619	0.0288	31.14	<.0001
Age	0-9 / >=80	-3.1555	0.2410	207.86	<.0001
	10-19 / >=80	-3.0777	0.2372		
	20-29 / >=80	-2.9591	0.2386		
	30-39 / >=80	-2.9870	0.2362		
	40-49 / >=80	-2.6401	0.2260		
	50-59 / >=80	-2.3370	0.2152		
	60-69 / >=80	-1.7265	0.2000		
	70-79 / >=80	-1.0525	0.1839		
Gender	Male / Female	-0.2974	0.0858	11.96	0.0005

Table 5.3. 14 The adjusted Poisson model for UTI HAIs incidence

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	0.0459	0.035	6.73	0.0810
	Summer/Winter	0.0800	0.0347		
	Autumn/Winter	0.0114	0.0353		
Time trend	Linear	3.0828E-03	0.0005	33.8	<.0001
	Quadratic	-9.1979E-06	4E-06	5.6	0.0182
	Cubic	-5.4700E-07	7E-08	53.1	<.0001
Autocorrelations	AR (1)	1.5313E-03	0.0012	1.59	0.2068
	AR (2)	6.8500E-03	0.0013	27.54	<.0001
	AR (3)	3.2731E-03	0.0012	7.16	0.0075
	AR (4)	-8.7871E-04	0.0012	0.51	0.4786
Age	0-9 / >=80	-3.3635	0.1639	4514.43	<.0001
	10-19 / >=80	-2.4827	0.1619		
	20-29 / >=80	-2.8583	0.1037		
	30-39 / >=80	-2.6382	0.0846		
	40-49 / >=80	-1.7270	0.0564		
	50-59 / >=80	-1.2960	0.0441		
	60-69 / >=80	-0.8317	0.0356		
	70-79 / >=80	-0.4244	0.0314		
Gender	Male / Female	-0.3802	0.0246	243.64	0.043

Table 5.3. 15 The adjusted negative binominal model for UTI HAIs incidence

Parameter	**Level**	**Estimate**	**S.E.**	**Chisq**	**p-value**
Season	Spring/Winter	0.0431	0.0448	4.89	0.1801
	Summer/Winter	0.0891	0.0441		
	Autumn/Winter	0.0154	0.0447		
Time trend	Linear	2.5617E-03	0.0007	14.4	0.0001
	Quadratic	-7.4606E-06	5E-06	2.3	0.1321
	Cubic	-4.7140E-07	9E-08	24.4	<.0001
Autocorrelations	AR (1)	2.2398E-03	0.0015	2.13	0.1447
	AR (2)	6.5026E-03	0.0017	14.91	0.0001
	AR (3)	3.8568E-03	0.0016	6.09	0.0136
	AR (4)	-4.3736E-04	0.0016	0.08	0.7823
Age	0-9 / >=80	-3.3546	0.1665	2279.11	<.0001
	10-19 / >=80	-2.4891	0.1649		
	20-29 / >=80	-2.8400	0.1086		
	30-39 / >=80	-2.6124	0.0899		
	40-49 / >=80	-1.7259	0.0636		
	50-59 / >=80	-1.2828	0.053		
	60-69 / >=80	-0.8228	0.0459		
	70-79 / >=80	-0.4138	0.043		
Gender	Male / Female	-0.3424	0.0312	112.19	<.0001

Table 5.3. 16 The adjusted time series model for *E. coli* bacteremia incidence (normal distribution)

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	-0.0022	0.0018	2.62	0.4537
	Summer/Winter	0.0001	0.0017		
	Autumn/Winter	-0.0015	0.0017		
Time trend	Linear	-6.33E-06	1.071E-05	0.35	0.5543
	Quadratic	-2.95E-07	1.822E-07	2.63	0.1052
Autocorrelations	AR (1)	-0.0037	0.0057	0.42	0.5161
	AR (2)	-0.0098	0.0057	2.91	0.0882
Age	0-9 / >=80	-0.0215	0.0026	162.15	<.0001
	10-19 / >=80	-0.0183	0.0026		
	20-29 / >=80	-0.0214	0.0026		
	30-39 / >=80	-0.0173	0.0026		
	40-49 / >=80	-0.0148	0.0026		
	50-59 / >=80	-0.0039	0.0026		
	60-69 / >=80	-0.0048	0.0026		
	70-79 / >=80	-0.0074	0.0026		
Gender	Male / Female	-0.0004	0.0012	0.13	0.7134

Table 5.3. 17 The adjusted Poisson model for *E. coli* bacteremia incidence

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	-0.0842	0.1410	0.41	0.9374
	Summer/Winter	-0.0641	0.1343		
	Autumn/Winter	-0.0346	0.1338		
Time trend	Linear	-3.6820E-04	0.0009	0.17	0.6796
	Quadratic	-3.7440E-05	2E-05	5.31	0.0212
Autocorrelations	AR (1)	4.4086E-03	0.0116	0.14	0.7046
	AR (2)	-6.0608E-03	0.0124	0.24	0.6232
Age	0-9 / >=80	-2.7629	0.5881	176.89	<.0001
	10-19 / >=80	-1.6736	0.5127		
	20-29 / >=80	-3.1753	0.5883		
	30-39 / >=80	-1.3836	0.2407		
	40-49 / >=80	-1.0075	0.2046		
	50-59 / >=80	-0.2228	0.1533		
	60-69 / >=80	-0.2118	0.1459		
	70-79 / >=80	-0.3529	0.1487		
Gender	Male / Female	-0.0197	0.0943	0.04	0.8346

Table 5.3. 18 The adjusted negative binominal model for *E. coli* bacteremia incidence

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	-0.0845	0.1443		
	Summer/Winter	-0.0643	0.1371		
	Autumn/Winter	-0.0316	0.1370		
Time trend	Linear	-4.4002E-04	0.0009	0.23	0.6288
	Quadratic	-3.7640E-05	2E-05	5.16	0.0232
Autocorrelations	AR (1)	5.1253E-03	0.0118	0.19	0.6651
	AR (2)	-5.0240E-03	0.0126	0.16	0.6898
Age	0-9 / >=80	-2.7695	0.5889		<.0001
	10-19 / >=80	-1.6805	0.5138		
	20-29 / >=80	-3.1796	0.5893		
	30-39 / >=80	-1.3888	0.2428		
	40-49 / >=80	-1.0146	0.2071		
	50-59 / >=80	-0.2155	0.1567		
	60-69 / >=80	-0.2158	0.1494		
	70-79 / >=80	-0.3557	0.1521		
Gender	Male / Female	-0.0123	0.0964	0.02	0.8985

Table 5.3. 19 The adjusted time series model for *P. aeruginosa* bacteremia incidence (normal distribution)

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	-0.0008	0.0016	0.66	0.8816
	Summer/Winter	-0.0003	0.0016		
	Autumn/Winter	0.0005	0.0016		
Time trend	Linear	-1.21E-05	9.506E-06	1.61	0.2042
Autocorrelations	AR (1)	-0.0075	0.0065	1.32	0.2513
	AR (2)	0.0016	0.0064	0.07	0.7985
	AR (3)	-0.0061	0.0063	0.95	0.3304
Age	0-9 / >=80	-0.0051	0.0024	44.47	<.0001
	10-19 / >=80	-0.0070	0.0024		
	20-29 / >=80	-0.0087	0.0024		
	30-39 / >=80	-0.0066	0.0024		
	40-49 / >=80	-0.0032	0.0024		
	50-59 / >=80	0.0003	0.0024		
	60-69 / >=80	0.0020	0.0024		
	70-79 / >=80	0.0011	0.0024		
Gender	Male / Female	0.0011	0.0011	0.93	0.3350

Table 5.3. 20 The adjusted Poisson model for *P. aeruginosa* bacteremia incidence

Parameter	Level	Estimate	S.E.	Chisq	p-value
Season	Spring/Winter	-0.0439	0.1812	0.48	0.9235
	Summer/Winter	0.0598	0.1765		
	Autumn/Winter	0.0565	0.1772		
Time trend	Linear	1.2384E-06	0.0012	0.00	0.9992
Autocorrelation	AR (1)	1.2172E-02	0.0154	0.6	0.4388
	AR (2)	-2.0591E-02	0.0209	0.99	0.3209
	AR (3)	-2.1787E-02	0.0185	1.44	0.2300
Age	0-9 / >=80	-0.8970	0.3946	57.86	<.0001
	10-19 / >=80	-1.4612	0.729		
	20-29 / >=80	-1.6790	0.481		
	30-39 / >=80	-1.0368	0.3378		
	40-49 / >=80	-0.4493	0.269		
	50-59 / >=80	-0.1242	0.2281		
	60-69 / >=80	0.1955	0.2134		
	70-79 / >=80	0.1019	0.2146		
Gender	Male / Female	0.1886	0.1254	2.28	0.1312

Table 5.3. 21 The adjusted negative binominal model for *P. aeruginosa* bacteremia incidence

Parameter	**Level**	**Estimate**	**S.E.**	**Chisq**	**p-value**
Season	Spring/Winter	-0.0830	0.1876	0.50	0.9200
	Summer/Winter	0.0239	0.1820		
	Autumn/Winter	0.0257	0.1817		
Time trend	Linear	-2.6561E-04	0.0013	0.04	0.8355
Autocorrelation	AR (1)	1.0440E-02	0.0159	0.42	0.5170
	AR (2)	-2.2382E-02	0.0213	1.12	0.2892
	AR (3)	-2.0616E-02	0.0186	1.27	0.2592
Age	0-9 / >=80	-0.8992	0.3958		
	10-19 / >=80	-1.4668	0.7298		
	20-29 / >=80	-1.6831	0.4821		
	30-39 / >=80	-1.0384	0.3391		
	40-49 / >=80	-0.4520	0.2707		
	50-59 / >=80	-0.0786	0.2346		
	60-69 / >=80	0.1910	0.2155		
	70-79 / >=80	0.0989	0.2168		
Gender	Male / Female	0.2007	0.1272	2.51	0.1129

Table 5.4. 1 Posterior summary, forecasts AR2 model with age, gender, seasonal factor, AR, and time trend in HAIs

Parameter	Level	Mean	SD	95% CI	
	Intercept	0.0016	0.0010	-0.0002	0.0035
Autocorrelations	AR(1)	0.4879	0.0151	0.4587	0.5173
Time trend	Linear	5.29E-07	1.45E-05	-2.80E-05	2.90E-05
	Quadratic	-4.33E-08	1.04E-07	-2.40E-07	1.63E-07
	Cubic	-2.30E-09	1.88E-09	-6.00E-09	1.41E-09
Age	50+/ 0-50	0.0075	0.0007	0.0060	0.0090
Gender	Male / Female	-2.93E-05	7.22E-04	-1.40E-03	1.40E-03
Season	Spring/Winter	3.61E-04	1.01E-03	-1.61E-03	2.35E-03
	Summer/Winter	4.12E-04	1.02E-03	-1.61E-03	2.42E-03
	Autumn/Winter	-1.75E-05	1.02E-03	-2.01E-03	1.99E-03

Table 5.4. 2 Posterior summary, forecasts AR2 model with age, gender, seasonal factor, AR, and time trend in bacteremia

Parameter	Level	Mean	SD	95% CI	
	Intercept	7.73E-05	1.79E-04	-2.80E-04	4.22E-04
Autocorrelations	AR(1)	4.46E-01	1.74E-02	4.11E-01	4.80E-01
Time trend	Linear	-5.87E-08	1.16E-06	-2.30E-06	2.26E-06
Age	50+/ 0-50	1.64E-03	1.53E-04	1.35E-03	1.95E-03
Gender	Male / Female	5.17E-04	1.46E-04	2.33E-04	8.01E-04
Season	Spring/Winter	-8.15E-05	2.08E-04	-4.90E-04	3.23E-04
	Summer/Winter	-3.52E-05	2.06E-04	-4.50E-04	3.66E-04
	Autumn/Winter	1.00E-05	2.07E-04	-4.00E-04	4.19E-04

Table 5.4. 3 Posterior summary, forecasts AR2 model with age, gender, seasonal factor, AR, and time trend in pneumonia

Parameter	Level	Mean	SD	95% CI	
	Intercept	7.73E-05	1.79E-04	-2.80E-04	4.22E-04
Autocorrelations	AR(1)	4.46E-01	1.74E-02	4.11E-01	4.80E-01
	AR(2)	-9.96E-02	1.72E-02	-1.33E-01	-6.54E-02
Time trend	Linear	-5.87E-08	1.16E-06	-2.30E-06	2.26E-06
Age	50+/ 0-50	1.53E-04	1.54E-06	1.64E-03	3.00E+03
Gender	Male / Female	5.17E-04	1.46E-04	2.33E-04	8.01E-04
Season	Spring/Winter	-8.15E-05	2.08E-04	-4.90E-04	3.23E-04
	Summer/Winter	-3.52E-05	2.06E-04	-4.50E-04	3.66E-04
	Autumn/Winter	1.00E-05	2.07E-04	-4.00E-04	4.19E-04

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Table 5.4. 4 Posterior summary, forecasts AR2 model with age, gender, seasonal factor, AR, and time trend in SSI

Parameter	Level	Mean	SD	95% CI	
	Intercept	2.84E-04	1.32E-04	2.68E-05	5.38E-04
Autocorrelations	AR(1)	2.90E-01	1.71E-02	2.56E-01	3.23E-01
Time trend	Linear	-4.40E-06	8.64E-07	-6.10E-06	-2.70E-06
Age	50+/ 0-50	6.40E-04	1.07E-04	4.30E-04	8.54E-04
Gender	Male / Female	2.94E-04	1.06E-04	8.82E-05	5.06E-04
Season	Spring/Winter	1.40E-04	1.51E-04	-1.55E-04	4.37E-04
	Summer/Winter	7.82E-05	1.50E-04	-2.19E-04	3.72E-04
	Autumn/Winter	4.77E-05	1.49E-04	-2.45E-04	3.40E-04

Table 5.4. 5 Posterior summary, forecasts AR2 model with age, gender, seasonal factor, AR, and time trend in UTI

Parameter	Level	Mean	SD	95% CI	
	Intercept	1.29E-03	4.11E-06	4.91E-04	2.09E-03
Autocorrelations	AR(1)	4.76E-01	1.73E-02	1.74E-04	4.76E-01
	AR(2)	3.40E-02	1.85E-02	1.64E-04	3.40E-02
	AR(3)	-3.25E-01	1.83E-02	1.89E-04	-3.25E-01
	AR(4)	1.13E-02	1.71E-02	1.77E-04	1.13E-02
Time trend	Linear	8.42E-06	6.09E-06	5.81E-08	8.41E-06
	Quadratic	-1.90E-08	4.35E-08	5.15E-10	-1.90E-08
Age	50+/ 0-50	5.32E-03	3.41E-04	4.65E-03	5.99E-03
Gender	Male / Female	-1.44E-03	3.05E-04	-2.03E-03	-8.40E-04
Season	Spring/Winter	2.02E-04	4.31E-04	-6.20E-04	1.05E-03
	Summer/Winter	2.86E-04	4.21E-04	-5.40E-04	1.11E-03
	Autumn/Winter	-6.20E-05	4.27E-04	-9.10E-04	7.78E-04

Table 5.4. 6 Posterior summary, forecasts AR2 model with age, gender, seasonal factor, AR, and time trend in *E. coli* bacteremia

Parameter	Level	Mean	SD	95% CI	
	Intercept	8.52E-04	4.34E-04	4.20E-07	1.72E-03
Autocorrelations	AR(1)	4.54E-01	1.56E-02	4.23E-01	4.84E-01
	AR(2)	6.80E-06	6.47E-06	-5.70E-06	1.98E-05
Time trend	Linear	-9.90E-09	4.63E-08	-1.00E-07	8.14E-08
	Quadratic	-1.60E-09	8.53E-10	-3.20E-09	9.54E-11
Age	50+/ 0-50	3.60E-03	3.40E-04	2.94E-03	4.27E-03
Gender	Male / Female	-9.80E-04	3.19E-04	-1.61E-03	-3.60E-04
Season	Spring/Winter	1.47E-04	4.56E-04	-7.40E-04	1.05E-03
	Summer/Winter	2.03E-04	4.55E-04	-6.90E-04	1.10E-03
	Autumn/Winter	-1.40E-05	4.53E-04	-9.20E-04	8.63E-04

Table 5.4. 7 Posterior summary, forecasts AR2 model with age, gender, seasonal factor, AR, and time trend in *Pseudomonas aeruginosa* bacteremia

Parameter	Level	Mean	SD	95% CI	
	Intercept	2.62E-05	3.72E-07	-5.60E-05	2.57E-05
Autocorrelations	AR(1)	1.54E-01	2.56E-04	9.99E-02	1.54E-01
	AR(2)	2.04E-02	2.72E-04	-3.41E-02	2.08E-02
	AR(3)	-9.01E-02	3.07E-04	-1.44E-01	-8.99E-02
Time trend	Linear	-3.50E-07	2.68E-09	-8.90E-07	-3.50E-07
Age	50+/ 0-50	1.84E-04	3.47E-07	1.15E-04	2.52E-04
Gender	Male / Female	3.46E-05	3.22E-07	-3.20E-05	1.02E-04
Season	Spring/Winter	-2.90E-06	5.00E-07	-9.80E-05	9.36E-05
	Summer/Winter	8.44E-06	4.82E-07	-8.70E-05	1.04E-04
	Autumn/Winter	1.04E-05	4.89E-07	-8.60E-05	1.04E-04

Table 5.5. 1 Estimated regression coefficients with Bayesian autoregressive model with time trend and seasonal variation for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Season	Spring / Winter	0.133(0.027)	0.081	0.186	1885.6
	Summer / Winter	0.140(0.030)	0.082	0.199	
	Autumn / Winter	0.092(0.028)	0.039	0.146	
Time trend	Linear	-7.6E-4(2.5E-0.4)	-1.25E-3	-2.49E-04	
Autocorrelations	AR(1)	0.545(0.042)	0.46	0.63	
Season	Spring / Winter	0.115(0.024)	0.068	0.162	1852.7
	Summer / Winter	0.115(0.027)	0.062	0.169	
	Autumn / Winter	0.096(0.024)	0.048	0.144	
Time trend	Linear	-3.5E-4(8.0E-4)	-0.00117	9.91E-04	
Autocorrelations	AR(1)	0.392(0.052)	0.293	0.501	
	AR(2)	0.301(0.055)	0.202	0.423	
Season	Spring / Winter	0.104(0.021)	0.063	0.144	1870.2
	Summer / Winter	0.106(0.024)	0.059	0.155	
	Autumn / Winter	0.091(0.021)	0.050	0.133	
Time trend	Linear	0.003(0.003)	-0.002	0.012	
Autocorrelations	AR(1)	0.399(0.056)	0.291	0.507	
	AR(2)	0.314(0.057)	0.199	0.423	
	AR(3)	0.244(0.054)	0.133	0.347	
Season	Spring / Winter	0.105(0.020)	0.066	0.145	1841.2
	Summer / Winter	0.109(0.023)	0.064	0.156	
	Autumn / Winter	0.094(0.021)	0.053	0.135	
Time trend	Linear	0.004(0.004)	-0.004	0.013	
Autocorrelations	AR(1)	0.383(0.053)	0.278	0.487	
	AR(2)	0.290(0.054)	0.181	0.396	
	AR(3)	0.215(0.055)	0.108	0.321	
	AR(4)	0.088(0.05)	-0.011	0.188	

Table 5.5. 2 Estimated regression coefficients with Bayesian autoregressive model with time trend and trigonometric seasonal variation for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Trigonometric	Cos(2πt/12)	-0.049(0.018)	-0.084	-0.013	1897.54
	Cos(4πt/12)	-0.026(0.013)	-0.051	-0.001	
	Sin(2πt/12)	-0.038(0.018)	-0.075	-0.002	
	Sin(4πt/12)	-0.029(0.013)	-0.055	-0.005	
Time trend	Linear	-7.95E-04(2.48E-04)	-0.001	0.000	
Autocorrelations	AR(1)	0.526(0.041)	0.447	0.608	
Trigonometric	Cos(2πt/12)	-0.047(0.016)	-8E-02	-1E-02	1857.87
	Cos(4πt/12)	-0.024(0.01)	-4E-02	-5E-03	
	Sin(2πt/12)	-0.036(0.016)	-7E-02	-3E-03	
	Sin(4πt/12)	-0.028(0.01)	-5E-02	-9E-03	
Time trend	Linear	-3.49E-04(6.86E-04)	-1E-03	1E-03	
Autocorrelations	AR(1)	0.377(0.051)	3E-01	5E-01	
	AR(2)	0.318(0.054)	2E-01	4E-01	
Trigonometric	Cos(2πt/12)	-0.041(0.012)	-0.066	-0.016	1845.79
	Cos(4πt/12)	-0.023(0.008)	-0.038	-0.007	
	Sin(2πt/12)	-0.031(0.013)	-0.056	-0.006	
	Sin(4πt/12)	-0.025(0.008)	-0.041	-0.008	
Time trend	Linear	0.003(0.003)	-0.002	0.011	
Autocorrelations	AR(1)	0.375(0.052)	0.273	0.475	
	AR(2)	0.337(0.053)	0.231	0.437	
	AR(3)	0.248(0.052)	0.139	0.347	
Trigonometric	Cos(2πt/12)	-0.041(0.012)	-0.065	-0.017	1846.14
	Cos(4πt/12)	-0.022(0.008)	-0.038	-0.006	
	Sin(2πt/12)	-0.031(0.012)	-0.055	-0.007	
	Sin(4πt/12)	-0.025(0.008)	-0.041	-0.008	
Time trend	Linear	0.004(0.004)	2.964	5.167	
Autocorrelations	AR(1)	0.365(0.052)	0.259	0.462	
	AR(2)	0.313(0.05)	0.210	0.413	
	AR(3)	0.222(0.051)	0.126	0.323	
	AR(4)	0.07(0.052)	-0.035	0.169	

Table 5.5. 3 Estimated regression coefficients with Bayesian first-order autoregressive model with linear time trend, seasonal variation, and non time-series covariates for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Age	<40 / 70+	-2.069(0.039)	-2.145	-1.991	7703.14
	40-69 / 70+	-1.195(0.027)	-1.248	-1.143	
Gender	Male / Female	0.087(0.022)	0.042	0.131	
Season	Spring / Winter	0.111(0.025)	0.062	0.158	
	Summer / Winter	0.124(0.026)	0.072	0.175	
	Autumn / Winter	0.099(0.025)	0.049	0.148	
Time trend	Linear	-0.001(0)	-0.001	-0.001	
Autocorrelations	AR(1)	0.275(0.019)	0.236	0.312	

Table 5.5. 4 Estimated regression coefficients with Bayesian first-order autoregressive model with cubic time trend, seasonal variation, and non time-series covariates for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Age	<40 / 70+	-2.071(0.037)	-2.145	-1.999	7599.01
	40-69 / 70+	-1.197(0.025)	-1.247	-1.148	
Gender	Male / Female	0.088(0.02)	0.047	0.128	
Season	Spring / Winter	0.105(0.026)	0.056	0.156	
	Summer / Winter	0.12(0.026)	0.068	0.172	
	Autumn / Winter	0.1(0.026)	0.052	0.151	
Time trend	Linear	1.15E-04(3.71E-04)	-6.29E-04	8.47E-04	
	Quadratic	-2.51E-05(2.43E-06)	-2.98E-05	-2.03E-05	
	Cubic	-1.33E-07(4.09E-08)	-2.13E-07	-5.11E-08	
Autocorrelations	AR(1)	0.223(0.02)	0.185	0.262	

Table 5.5. 5 Estimated regression coefficients with Bayesian third-order autoregressive model with cubic time trend, seasonal variation, and non time-series covariates for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Age	<40 / 70+	-1.996(0.051)	-2.096	-1.895	7491.98
	40-69 / 70+	-1.165(0.035)	-1.233	-1.096	
Gender	Male / Female	0.084(0.028)	0.029	0.139	
Season	Spring / Winter	0.106(0.023)	0.062	0.150	
	Summer / Winter	0.114(0.026)	0.065	0.164	
	Autumn / Winter	0.101(0.023)	0.056	0.148	
Time trend	Linear	0.0001(0.00048)	-0.001	0.001	
	Quadratic	-2.64E-05(3.32E-06)	-3.3E-05	-2.0E-05	
	Cubic	-9.5E-08(5.2E-08)	-1.9E-07	1.3E-08	
Autocorrelations	AR(1)	0.158(0.021)	0.117	0.199	
	AR(2)	0.164(0.021)	0.123	0.204	
	AR(3)	0.113(0.021)	0.072	0.153	

Table 5.5. 6 Estimated regression coefficients with Bayesian fourth-order autoregressive model with cubic time trend, seasonal variation, and non time-series covariates for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Age	<40 / 70+	-1.971(0.056)	-2.08	-1.859	7482.37
	40-69 / 70+	-1.156(0.038)	-1.233	-1.082	
Gender	Male / Female	0.083(0.03)	0.022	0.142	
Season	Spring / Winter	0.108(0.022)	0.066	0.15	
	Summer / Winter	0.119(0.024)	0.073	0.167	
	Autumn / Winter	0.105(0.022)	0.062	0.15	
Time trend	Linear	-0.00023(0.0005)	2.00E-05	0.001	
	Quadratic	-27.13(3.468)	-33.9	-20.35	
	Cubic	-0.075(0.056)	-0.182	0.036	
Autocorrelations	AR(1)	0.152(0.021)	0.111	0.192	
	AR(2)	0.151(0.022)	0.108	0.194	
	AR(3)	0.101(0.021)	0.06	0.143	
	AR(4)	0.073(0.021)	0.033	0.112	

Table 5.5. 7 Estimated regression coefficients with Bayesian autoregressive model with time trend and seasonal variation for UTI

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Season	Spring / Winter	0.135(0.043)	0.0495	0.2198	1630.59
	Summer / Winter	0.186(0.047)	0.090	0.277	
	Autumn / Winter	0.109(0.044)	0.022	0.194	
Time trend	Linear	3.14E-04(3.82E-04)	0.000	0.001	
Autocorrelations	AR(1)	0.508(0.044)	0.423	0.593	
Season	Spring / Winter	0.102(0.001)	0.030	0.175	1587.16
	Summer / Winter	0.151(0.001)	0.068	0.235	
	Autumn / Winter	0.093(0.001)	0.017	0.171	
Time trend	Linear	6.38E-04(6.83E-06)	0.000	0.002	
Autocorrelations	AR(1)	0.335(0.001)	0.236	0.437	
	AR(2)	0.346(0.001)	0.245	0.447	
Season	Spring / Winter	0.097(0.001)	0.031	0.163	1573.3
	Summer / Winter	0.148(0.001)	0.075	0.226	
	Autumn / Winter	0.092(0.001)	0.026	0.160	
Time trend	Linear	1.37E-03(4.14E-05)	-0.00035	5.11E-03	
Autocorrelations	AR(1)	0.273(0.001)	0.167	0.382	
	AR(2)	0.284(0.001)	0.172	0.397	
	AR(3)	0.224(0.001)	0.116	0.335	
Season	Spring / Winter	0.097(0.033)	0.033	0.162	1574.39
	Summer / Winter	0.149(0.038)	0.075	0.223	
	Autumn / Winter	0.092(0.033)	0.028	0.159	
Time trend	Linear	0.002(0.003)	-0.00033	7.61E-03	
Autocorrelations	AR(1)	0.261(0.058)	0.149	0.376	
	AR(2)	0.277(0.058)	0.164	0.389	
	AR(3)	0.217(0.058)	0.103	0.331	
	AR(4)	0.064(0.056)	-0.047	0.174	

Table 5.5. 8 Estimated regression coefficients with Bayesian autoregressive model with time trend and trigonometric seasonal variation for UTI

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Trigonometric	Cos(2πt/12)	-0.064(0.029)	-0.119	-0.007	1641.23
	Cos(4πt/12)	-0.021(0.021)	-0.061	0.021	
	Sin(2πt/12)	-0.035(0.028)	-0.090	0.021	
	Sin(4πt/12)	-0.007(0.021)	-0.046	0.034	
Time trend	Linear	3.04e-04(3.69e-04)	-3.98E-04	0.001038	
Autocorrelations	AR(1)	0.497(0.043)	0.410	0.581	
Trigonometric	Cos(2πt/12)	-0.064(0.025)	-0.113	-0.016	1592.56
	Cos(4πt/12)	-0.02(0.015)	-0.050	0.010	
	Sin(2πt/12)	-0.034(0.025)	-0.083	0.016	
	Sin(4πt/12)	-0.004(0.016)	-0.034	0.027	
Time trend	Linear	0.001(0.001)	-4.78E-04	0.001921	
Autocorrelations	AR(1)	0.326(0.049)	0.233	0.424	
	AR(2)	0.356(0.051)	0.255	0.453	
Trigonometric	Cos(2πt/12)	-0.06(0.02)	-0.101	-0.019	1577.92
	Cos(4πt/12)	-0.019(0.013)	-0.045	0.007	
	Sin(2πt/12)	-0.034(0.02)	-0.073	0.006	
	Sin(4πt/12)	-0.003(0.014)	-0.029	0.024	
Time trend	Linear	0.002(0.003)	-3.22E-04	0.006658	
Autocorrelations	AR(1)	0.259(0.055)	0.154	0.366	
	AR(2)	0.299(0.057)	0.188	0.414	
	AR(3)	0.232(0.059)	0.118	0.356	
Trigonometric	Cos(2πt/12)	-0.059(0.02)	-0.098	-0.021	1578.9
	Cos(4πt/12)	-0.019(0.013)	-0.045	0.007	
	Sin(2πt/12)	-0.034(0.02)	-0.073	0.005	
	Sin(4πt/12)	-0.003(0.013)	-0.030	0.023	
Time trend	Linear	0.002(0.003)	-2.53E-04	0.009069	
Autocorrelations	AR(1)	0.248(0.055)	0.140	0.358	
	AR(2)	0.295(0.056)	0.187	0.405	
	AR(3)	0.221(0.058)	0.110	0.335	
	AR(4)	0.05(0.056)	-0.059	0.164	

Table 5.5. 9 Estimated regression coefficients with Bayesian first-order autoregressive model with cubic time trend, seasonal variation, and non time-series covariates for UTI

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Age	<40 / 70+	-2.767(0.07)	-2.903	-2.631	5406.360
	40-69 / 70+	-1.578(0.041)	-1.658	-1.497	
Gender	Male / Female	-0.269(0.031)	-0.329	-0.209	
Season	Spring / Winter	0.092(0.039)	0.018	0.170	
	Summer / Winter	0.151(0.04)	0.076	0.230	
	Autumn / Winter	0.1(0.039)	0.024	0.177	
Time trend	Linear	0.004(0.001)	0.003	0.005	
	Quadratic	-30.14(3.717)	-37.540	-22.950	
	Cubic	-0.418(0.061)	-0.541	-0.304	
AR	AR(1)	0.162(0.027)	0.109	0.215	

Table 5.5. 10 Estimated regression coefficients with Bayesian fourth-order autoregressive model with cubic time trend, seasonal variation, and non time-series covariates for UTI

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Age	<40 / 70+	-2.866(0.101)	-3.072	-2.674	5366.58
	40-69 / 70+	-1.526(0.06)	-1.644	-1.406	
Gender	Male / Female	-0.247(0.043)	-0.3307	-0.1605	
Season	Spring / Winter	0.092(0.035)	0.0240	0.1608	
	Summer / Winter	0.148(0.038)	0.0745	0.2218	
	Autumn / Winter	0.098(0.036)	0.0269	0.1670	
Time trend	Linear	0.003(0.001)	0.0017	0.0047	
	Quadratic	-3.1E-05(5.3E-06)	-4.1E-05	-2.1E-05	
	Cubic	3.6E-07(8.2E-08)	-5.1E-07	-1.9E-07	
Autocorrelations	AR(1)	0.122(0.028)	0.0678	0.1770	
	AR(2)	0.108(0.028)	0.0534	0.1622	
	AR(3)	0.116(0.028)	0.0604	0.1704	
	AR(4)	0.064(0.028)	0.0099	0.1183	

Table 5.5. 11 Estimated regression coefficients with Bayesian autoregressive model with time trend and seasonal variation for *E. coli.* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Season	Spring / Winter	0.098(0.003)	-0.178	0.370	842.77
	Summer / Winter	0.097(0.003)	-0.191	0.379	
	Autumn / Winter	-0.042(0.003)	-0.324	0.239	
Time trend	Linear	-0.002(0)	-0.0035	5.98E-05	
Autocorrelations	AR(1)	0.246(0.001)	0.117	0.377	
Season	Spring / Winter	0.134(0.138)	-0.139	0.410	843.53
	Summer / Winter	0.109(0.15)	-0.181	0.406	
	Autumn / Winter	-0.026(0.145)	-0.311	0.260	
Time trend	Linear	-0.002(0.001)	-0.004	0.000	
Autocorrelations	AR(1)	0.228(0.068)	0.095	0.364	
	AR(2)	0.085(0.066)	-0.046	0.217	
Season	Spring / Winter	0.118(0.135)	-0.149	0.385	844.63
	Summer / Winter	0.103(0.147)	-0.183	0.397	
	Autumn / Winter	-0.026(0.139)	-0.301	0.246	
Time trend	Linear	-0.002(0.001)	-0.004	0.000	
Autocorrelations	AR(1)	0.224(0.068)	0.091	0.358	
	AR(2)	0.069(0.068)	-0.064	0.201	
	AR(3)	0.068(0.067)	-0.060	0.200	
Season	Spring / Winter	0.105(0.131)	-0.156	0.359	844.57
	Summer / Winter	0.099(0.138)	-0.162	0.372	
	Autumn / Winter	-0.004(0.135)	-0.267	0.257	
Time trend	Linear	-0.002(0.001)	-0.004	0.001	
Autocorrelations	AR(1)	0.217(0.068)	0.086	0.347	
	AR(2)	0.061(0.068)	-0.073	0.194	
	AR(3)	0.045(0.068)	-0.088	0.178	
	AR(4)	0.103(0.069)	-0.031	0.238	

Table 5.5. 12 Estimated regression coefficients with Bayesian autoregressive model with time trend and trigonometric seasonal variation for *E. coli.* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Trigonometric	Cos(2πt/12)	-0.011(0.081)	-0.169	0.148	845.234
	Cos(4πt/12)	-0.044(0.069)	-0.178	0.092	
	Sin(2πt/12)	-0.051(0.08)	-0.207	0.109	
	Sin(4πt/12)	-0.025(0.07)	-0.165	0.111	
Time trend	Linear	-0.002(0.001)	-0.004	0.000	
Autocorrelations	AR(1)	0.24(0.066)	0.112	0.369	
Trigonometric	Cos(2πt/12)	-0.011(0.081)	-0.168	0.147	846.08
	Cos(4πt/12)	-0.043(0.066)	-0.169	0.086	
	Sin(2πt/12)	-0.051(0.08)	-0.206	0.111	
	Sin(4πt/12)	-0.025(0.066)	-0.154	0.106	
Time trend	Linear	-0.002(0.001)	-0.004	0.000	
Autocorrelations	AR(1)	0.224(0.067)	0.095	0.358	
	AR(2)	0.073(0.065)	-0.056	0.203	
Trigonometric	Cos(2πt/12)	-0.011(0.078)	-0.1655	0.1387	846.953
	Cos(4πt/12)	-0.042(0.063)	-0.1642	0.08126	
	Sin(2πt/12)	-0.051(0.079)	-0.2062	0.108	
	Sin(4πt/12)	-0.024(0.062)	-0.1455	0.0953	
Time trend	Linear	-0.002(0.001)	-0.00375	4.40E-04	
Autocorrelations	AR(1)	0.219(0.066)	0.090	0.350	
	AR(2)	0.06(0.068)	-0.075	0.190	
	AR(3)	0.069(0.066)	-0.062	0.200	
Trigonometric	Cos(2πt/12)	-0.015(0.072)	-0.155	0.127	846.635
	Cos(4πt/12)	-0.041(0.062)	-0.162	0.080	
	Sin(2πt/12)	-0.052(0.072)	-0.189	0.091	
	Sin(4πt/12)	-0.022(0.062)	-0.144	0.098	
Time trend	Linear	-0.002(0.001)	-0.004	0.001	
Autocorrelations	AR(1)	0.213(0.067)	0.083	0.342	
	AR(2)	0.056(0.067)	-0.073	0.189	
	AR(3)	0.042(0.069)	-0.089	0.176	
	AR(4)	0.109(0.068)	-0.023	0.244	

Table 5.5. 13 Estimated regression coefficients with Bayesian first-order autoregressive model with quadratic time trend, seasonal variation, and non time-series covariates for *E. coli.* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Age	<40 / 70+	-2.861(0.38)	-3.716	-2.217	1942.82
	40-69 / 70+	-1.109(0.167)	-1.474	-0.815	
Gender	Male / Female	0.106(0.122)	-0.140	0.349	
Season	Spring / Winter	0.098(0.141)	-0.178	0.379	
	Summer / Winter	0.097(0.149)	-0.194	0.390	
	Autumn / Winter	-0.021(0.146)	-0.307	0.265	
Time trend	Linear	-0.003(0.001)	-0.00497	-8.12E-04	
	Quadratic	-7.8E-05(1.7E-05)	-1.1E-04	-4.7E-05	
AR	AR(1)	0.243(0.09)	0.064	0.418	

Table 5.5. 14 Estimated regression coefficients with Bayesian second-order autoregressive model with quadratic time trend, seasonal variation, and non time-series covariates for *E. coli.* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Age	<40 / 70+	-3.11(0.599)	-4.586	-2.218	1945.21
	40-69 / 70+	-1.19(0.237)	-1.753	-0.812	
Gender	Male / Female	0.118(0.137)	-0.142	0.397	
Season	Spring / Winter	0.108(0.14)	-0.169	0.383	
	Summer / Winter	0.096(0.151)	-0.202	0.393	
	Autumn / Winter	-0.018(0.146)	-0.306	0.268	
Time trend	Linear	-0.003(0.001)	-0.0056	-8.91E-04	
	Quadratic	-83.08(20.97)	-130.2	-48.0	
Autocorrelations	AR(1)	0.242(0.089)	0.066	0.410	
	AR(2)	0.056(0.093)	-0.131	0.237	

Table 5.5. 15 Estimated regression coefficients with Bayesian autoregressive model with time trend and seasonal variation for *P. aeruginosa* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Season	Spring / Winter	-0.194(0.181)	-0.56	0.16	691.791
	Summer / Winter	0.128(0.171)	-0.20	0.46	
	Autumn / Winter	0.097(0.168)	-0.23	0.43	
Time trend	Linear	-0.002(0.001)	-0.004	0.000	
Autocorrelations	AR(1)	0.079(0.09)	-0.097	0.258	
Season	Spring / Winter	-0.198(0.181)	-0.550	0.149	693.289
	Summer / Winter	0.12(0.172)	-0.213	0.463	
	Autumn / Winter	0.106(0.167)	-0.218	0.433	
Time trend	Linear	-0.002(0.001)	-0.004	0.000	
Autocorrelations	AR(1)	0.077(0.09)	-0.097	0.253	
	AR(2)	0.085(0.089)	-0.088	0.261	
Season	Spring / Winter	-0.198(0.178)	-0.551	0.146	695.076
	Summer / Winter	0.114(0.17)	-0.217	0.453	
	Autumn / Winter	0.107(0.165)	-0.213	0.439	
Time trend	Linear	-0.002(0.001)	-0.00448	1.71E-04	
Autocorrelations	AR(1)	0.075(0.09)	-0.101	0.253	
	AR(2)	0.087(0.09)	-0.088	0.266	
	AR(3)	0.057(0.09)	-0.118	0.235	
Season	Spring / Winter	-0.199(0.003)	-0.554	0.140	697.161
	Summer / Winter	0.11(0.003)	-0.230	0.445	
	Autumn / Winter	0.1(0.003)	-0.214	0.427	
Time trend	Linear	-0.002(0)	-0.005	0.000	
Autocorrelations	AR(1)	0.078(0.001)	-0.106	0.252	
	AR(2)	0.082(0.001)	-0.096	0.260	
	AR(3)	0.055(0.001)	-0.121	0.233	
	AR(4)	0.017(0.001)	-0.164	0.195	

Table 5.5. 16 Estimated regression coefficients with Bayesian autoregressive model with time trend and trigonometric seasonal variation for *P. aeruginosa* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Trigonometric	Cos(2πt/12)	-0.002(0.088)	-0.173	0.174	695.401
	Cos(4πt/12)	0.071(0.084)	-0.089	0.235	
	Sin(2πt/12)	-0.11(0.091)	-0.285	0.073	
	Sin(4πt/12)	0.021(0.086)	-0.148	0.189	
Time trend	Linear	-0.002(0.001)	-0.004	0.000	
Autocorrelations	AR(1)	0.074(0.091)	-0.103	0.254	
Trigonometric	Cos(2πt/12)	0(0.091)	-0.176	0.178	696.967
	Cos(4πt/12)	0.068(0.082)	-0.093	0.230	
	Sin(2πt/12)	-0.112(0.095)	-0.296	0.073	
	Sin(4πt/12)	0.02(0.081)	-0.137	0.182	
Time trend	Linear	-0.002(0.001)	-0.00415	-1.05E-04	
Autocorrelations	AR(1)	0.071(0.09)	-0.102	0.252	
	AR(2)	0.078(0.089)	-0.097	0.253	
Trigonometric	Cos(2πt/12)	0(0.089)	-0.173	0.175	698.79
	Cos(4πt/12)	0.068(0.08)	-0.084	0.228	
	Sin(2πt/12)	-0.112(0.091)	-0.296	0.064	
	Sin(4πt/12)	0.022(0.078)	-0.130	0.177	
Time trend	Linear	-0.002(0.001)	-0.004	1.12E-04	
Autocorrelations	AR(1)	0.07(0.091)	-0.106	0.250	
	AR(2)	0.077(0.09)	-0.101	0.253	
	AR(3)	0.047(0.091)	-0.125	0.227	
Trigonometric	Cos(2πt/12)	0.003(0.089)	-0.171	0.179	700.745
	Cos(4πt/12)	0.069(0.078)	-0.083	0.225	
	Sin(2πt/12)	-0.109(0.091)	-0.288	0.073	
	Sin(4πt/12)	0.022(0.079)	-0.131	0.181	
Time trend	Linear	-0.002(0.001)	-0.004	0.000	
Autocorrelations	AR(1)	0.071(0.091)	-0.106	0.244	
	AR(2)	0.075(0.09)	-0.100	0.252	
	AR(3)	0.046(0.091)	-0.136	0.222	
	AR(4)	0.024(0.089)	-0.145	0.198	

Table 5.5. 17 Estimated regression coefficients with Bayesian first-order autoregressive model with linear time trend, seasonal variation, and non time-series covariates for *P. aeruginosa* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Age	<40 / 70+	-2.417(0.52)	-3.577	-1.626	1451.66
	40-69 / 70+	-1.025(0.25)	-1.603	-0.6403	
Gender	Male / Female	0.426(0.168)	0.1342	0.7934	
Season	Spring / Winter	-0.212(0.192)	-0.5952	0.1471	
	Summer / Winter	0.144(0.181)	-0.2061	0.5002	
	Autumn / Winter	0.117(0.176)	-0.2178	0.4663	
Time trend	Linear	-0.002(0.001)	-0.005031	-2.68E-04	
AR	AR(1)	0.188(0.156)	-0.1293	0.4712	

Table 5.5. 18 Estimated regression coefficients with Bayesian third-order autoregressive model with linear time trend, seasonal variation, and non time-series covariates for *P. aeruginosa* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Age	<40 / 70+	-3.804(0.815)	-4.954	-2.110	1472.37
	40-69 / 70+	-1.634(0.459)	-2.612	-0.833	
Gender	Male / Female	0.678(0.311)	0.167	1.376	
Season	Spring / Winter	-0.237(0.168)	-0.577	0.081	
	Summer / Winter	0.029(0.174)	-0.306	0.374	
	Autumn / Winter	0.073(0.154)	-0.223	0.385	
Time trend	Linear	-0.004(0.002)	-0.009	-0.001	
Autocorrelations	AR(1)	0.137(0.129)	-0.124	0.386	
	AR(2)	0.115(0.123)	-0.146	0.347	
	AR(3)	0.26(0.12)	0.021	0.487	

Table 5.5. 19 Estimated regression coefficients with Bayesian first-order moving-average model with cubic time trend and seasonal variation for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Season	Spring / Winter	0.077(0.133)	-0.179	0.340	823.939
	Summer / Winter	0.091(0.137)	-0.180	0.357	
	Autumn / Winter	-0.017(0.143)	-0.295	0.249	
Time trend	Linear	-0.002(0.002)	-0.006	0.002	
	Quadratic	-6.49-05(1.33E-05)	-9.42E-05	-3.82E-05	
	Cubic	2.70E-08(2.24E-07)	-4.22E-07	4.51E-07	
MA	MA(1)	0.143(0.066)	0.009	0.270	

Table 5.5. 20 Estimated regression coefficients with Bayesian first-order moving-average model with cubic time trend and seasonal variation, and non time-series covariates for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%	DIC
Age	<40 / 70+	-2.085(0.034)	-2.152	-2.017	7632.15
	40-69 / 70+	-1.203(0.024)	-1.248	-1.155	
Gender	Male / Female	0.091(0.019)	0.054	0.128	
Season	Spring / Winter	0.103(0.024)	0.058	0.15	
	Summer / Winter	0.12(0.025)	0.073	0.165	
	Autumn / Winter	0.104(0.024)	0.057	0.147	
Time trend	Linear	2.10E-04(3.38E-04)	0	0.001	
	Quadratic	-2.5E-05(2.2E-06)	-2.92E-05	-2.04E-05	
	Cubic	-1.4E-07(3.7E-08)	-2.16E-07	-7.30E-08	
MA	MA(1)	0.166(0.017)	0.132	0.198	

Table 5.5. 21 Estimated regression coefficients with Bayesian first-order moving-average model with cubic time trend and seasonal variation for UTI

Parameter	Level	Estimate (SD)	2.50%	97.50%
Season	Spring / Winter	0.105(0.038)	0.023	0.172
	Summer / Winter	0.158(0.037)	0.089	0.232
	Autumn / Winter	0.106(0.038)	0.032	0.174
Time trend	Linear	0.004(0.001)	0.003	0.005
	Quadratic	-3.0E-05(3.8E-06)	-3.81E-02	-2.33E-02
	Cubic	-4.1E-07(6.2E-08)	-5.33E-04	-3.00E-04
MA	MA(1)	0.209(0.044)	0.123	0.298

Table 5.5. 22 Estimated regression coefficients with Bayesian first-order moving-average model with cubic time trend and seasonal variation, and non time-series covariates for UTI

Parameter	Level	Estimate (SD)	2.50%	97.50%
Age	<40 / 70+	-2.752(0.061)	-2.860	-2.637
	40-69 / 70+	-1.587(0.037)	-1.655	-1.514
Gender	Male / Female	-0.275(0.028)	-0.328	-0.221
Season	Spring / Winter	0.09(0.036)	0.017	0.155
	Summer / Winter	0.15(0.037)	0.078	0.222
	Autumn / Winter	0.101(0.037)	0.030	0.173
Time trend	Linear	0.004(0.001)	0.003	0.005
	Quadratic	-3.0E-05(3.4E-06)	-3.70E-02	-2.37E-02
	Cubic	-4.3E-07(5.6E-08)	-5.36E-04	-3.23E-04
MA	MA(1)	0.13(0.024)	0.083	0.179

Table 5.5. 23 Estimated regression coefficients with Bayesian first-order moving-average model with cubic time trend and seasonal variation for *E. coli.* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%
Season	Spring / Winter	0.093(0.136)	-0.164	0.369
	Summer / Winter	0.11(0.132)	-0.16	0.376
	Autumn / Winter	-0.001(0.143)	-0.28	0.277
Time trend	Linear	-0.002(0.002)	-0.006	0.002
	Quadratic	-6.4E-05(1.3E-5)	-9.27E-02	-3.97E-02
	Cubic	9E-09(2.3E-07)	-5.04E-04	4.45E-04
MA	MA(1)	0.14(0.067)	0.003	0.269

Table 5.5. 24 Estimated regression coefficients with Bayesian first-order moving-average model with cubic time trend, seasonal variation, and non time-series covariates for *E. coli* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%
Age	<40 / 70+	-2.652(0.249)	-3.136	-2.173
	40-69 / 70+	-1.044(0.14)	-1.322	-0.78
Gender	Male / Female	0.09(0.112)	-0.155	0.297
Season	Spring / Winter	0.081(0.137)	-0.184	0.37
	Summer / Winter	0.093(0.139)	-0.151	0.378
	Autumn / Winter	-0.021(0.135)	-0.272	0.239
Time trend	Linear	-0.002(0.002)	-0.006	0.001
	Quadratic	-7.4E-05(1.4E-05)	-1.03E-04	-4.96E-05
	Cubic	-2.2E-08(2.1E-07)	-3.72E-07	4.27E-07
MA	MA(1)	0.219(0.077)	0.071	0.364

Table 5.5. 25 Estimated regression coefficients with Bayesian first-order moving-average model with cubic time trend and seasonal variation for *P. aeruginosa* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%
Season	Spring / Winter	-0.235(0.177)	-0.574	0.113
	Summer / Winter	0.096(0.163)	-0.211	0.42
	Autumn / Winter	0.074(0.165)	-0.243	0.4
Time trend	Linear	0.001(0.002)	-0.003	0.005
	Quadratic	-4.4E-05(1.4E-05)	-7.49E-05	-1.99E-05
	Cubic	-3.9E-07(2.3E-07)	-8.55E-07	2.8E-08
MA	MA(1)	0.041(0.083)	-0.117	0.2

Table 5.5. 26 Estimated regression coefficients with Bayesian first-order moving-average model with cubic time trend, seasonal variation and non time-series covariates for *P. aeruginosa* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%
Age	<40 / 70+	-2.191(0.322)	-2.837	-1.612
	40-69 / 70+	-0.938(0.161)	-1.266	-0.641
Gender	Male / Female	0.391(0.141)	0.152	0.686
Season	Spring / Winter	-0.222(0.194)	-0.62	0.162
	Summer / Winter	0.126(0.193)	-0.234	0.537
	Autumn / Winter	0.105(0.177)	-0.228	0.476
Time trend	Linear	0.001(0.003)	-0.004	0.006
	Quadratic	-4.8E-05(1.8E-05)	-8.28E-05	-1.36E-05
	Cubic	-4.6E-07(2.8E-07)	-9.71E-07	5.3E-08
MA	MA(1)	0.141(0.134)	-0.126	0.396

Table 5.5. 27 Estimated regression coefficients with Bayesian ARIMA(1,1) model with linear time trend and seasonal variation for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%
Season	Spring / Winter	0.135(0.024)	0.088	0.1823
	Summer / Winter	0.122(0.027)	0.071	0.1746
	Autumn / Winter	0.085(0.024)	0.040	0.1306
Time trend	Linear	-9.99E-05(3.05E-04)	-6.81E-04	5.20E-04
AR	AR(1)	0.677(0.042)	0.594	0.7572
MA	MA(1)	0.824(0.127)	0.524	0.9937

Table 5.5. 28 Estimated regression coefficients with Bayesian ARIMA(1,1) model with linear time trend, seasonal variation and non time-series covariates for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%
Age	<40 / 70+	-2.091(0.03)	-2.150	-2.031
	40-69 / 70+	-1.212(0.023)	-1.256	-1.166
Gender	Male / Female	0.161(0.022)	0.120	0.204
Season	Spring / Winter	0.125(0.023)	0.080	0.168
	Summer / Winter	0.141(0.024)	0.093	0.190
	Autumn / Winter	0.115(0.022)	0.070	0.159
Time trend	Linear	-0.001(0)	-0.001	-0.001
AR	AR(1)	0.192(0.032)	0.128	0.255
MA	MA(1)	-0.211(0.102)	-0.422	-0.017

Table 5.5. 29 Estimated regression coefficients with Bayesian ARIMA(2,2) model with linear time trend and seasonal variation for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%
Season	Spring / Winter	0.108(0.021)	0.068	0.149
	Summer / Winter	0.112(0.022)	0.069	0.155
	Autumn / Winter	0.093(0.02)	0.054	0.132
Time trend	Linear	-6.15E-04(4.08E-04)	-1.38E-03	2.32E-04
AR	AR(1)	0.43(0.076)	0.302	0.596
	AR(2)	0.354(0.082)	0.175	0.489
MA	MA(1)	0.43(0.369)	-0.408	0.967
	MA(2)	0.501(0.331)	-0.214	0.977

Table 5.5. 30 Estimated regression coefficients with Bayesian ARIMA(2,2) model with linear time trend, seasonal variation and non time-series covariates for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%
Age	<40 / 70+	-2.057(0.037)	-2.127	-1.982
	40-69 / 70+	-1.196(0.028)	-1.250	-1.141
Gender	Male / Female	0.158(0.027)	0.105	0.209
Season	Spring / Winter	0.12(0.022)	0.078	0.161
	Summer / Winter	0.13(0.024)	0.082	0.177
	Autumn / Winter	0.11(0.023)	0.065	0.154
Time trend	Linear	-0.001(0)	-0.001	-0.001
AR	AR(1)	0.13(0.028)	0.074	0.184
	AR(2)	0.199(0.036)	0.131	0.266
MA	MA(1)	-0.476(0.256)	-0.978	-0.100
	MA(2)	-0.001(0.202)	-0.350	0.457

Table 5.5. 31 Estimated regression coefficients with Bayesian ARIMA(3,1) model with cubic time trend, seasonal variation and non time-series covariates for HAIs

Parameter	Level	Estimate (SD)	2.50%	97.50%
Age	<40 / 70+	-2.025(0.041)	-2.103	-1.944
	40-69 / 70+	-1.184(0.031)	-1.245	-1.123
Gender	Male / Female	0.151(0.027)	0.099	0.202
Season	Spring / Winter	0.117(0.02)	0.078	0.156
	Summer / Winter	0.131(0.022)	0.087	0.173
	Autumn / Winter	0.111(0.02)	0.073	0.15
Time trend	Linear	-9.25E-04(2.44E-04)	-0.001	0
	Quadratic	-1.6E-05(3.3E-06)	-2.21E-05	-8.91E-06
	Cubic	-3.7E-08(3.7E-08)	-1.12E-07	3.60E-08
Autocorrelations	AR(1)	0.099(0.028)	0.05	0.159
	AR(2)	0.183(0.018)	0.148	0.218
	AR(3)	0.122(0.017)	0.09	0.155
MA	MA(1)	-0.484(0.206)	-0.934	-0.139

Table 5.5. 32 Estimated regression coefficients with Bayesian ARIMA(1,1) model with linear time trend and seasonal variation for UTI

Parameter	Level	Estimate (SD)	2.50%	97.50%
Season	Spring / Winter	0.135(0.039)	0.059	0.210
	Summer / Winter	0.161(0.043)	0.077	0.243
	Autumn / Winter	0.099(0.038)	0.024	0.172
Time trend	Linear	0.00138(0.00041)	0.001	0.002
AR	AR(1)	0.615(0.048)	0.524	0.709
MA	MA(1)	0.836(0.126)	0.528	0.994

Table 5.5. 33 Estimated regression coefficients with Bayesian ARIMA(1,1) model with linear time trend, seasonal variation and non time-series covariates for UTI

Parameter	Level	Estimate (SD)	2.50%	97.50%
Age	<40 / 70+	-2.773(0.056)	-2.887	-2.667
	40-69 / 70+	-1.571(0.034)	-1.638	-1.503
Gender	Male / Female	-0.218(0.029)	-0.274	-0.162
Season	Spring / Winter	0.11(0.035)	0.042	0.178
	Summer / Winter	0.179(0.037)	0.108	0.253
	Autumn / Winter	0.119(0.035)	0.053	0.188
Time trend	Linear	5.66E-05(2.04E-04)	-0.0003	0.0005
AR	AR(1)	0.181(0.045)	0.093	0.271
MA	MA(1)	-0.196(0.185)	-0.623	0.134

Table 5.5. 34 Estimated regression coefficients with Bayesian ARIMA(2,2) model with linear time trend and seasonal variation for UTI

Parameter	Level	Estimate (SD)	2.50%	97.50%
Season	Spring / Winter	0.095(0.031)	0.033	0.156
	Summer / Winter	0.147(0.035)	0.078	0.216
	Autumn / Winter	0.092(0.031)	0.031	0.154
Time trend	Linear	4.30E-04(6.11E-04)	-8.04E-04	0.001648
AR	AR(1)	0.339(0.065)	0.236	0.499
	AR(2)	0.433(0.072)	0.260	0.547
MA	MA(1)	0.296(0.417)	-0.592	0.956
	MA(2)	0.623(0.314)	-0.171	0.988

Table 5.5. 35 Estimated regression coefficients with Bayesian ARIMA(2,2) model with linear time trend, seasonal variation and non time-series covariates for UTI

Parameter	Level	Estimate (SD)	2.50%	97.50%
Age	<40 / 70+	-2.854(0.077)	-3.013	-2.713
	40-69 / 70+	-1.546(0.042)	-1.627	-1.462
Gender	Male / Female	-0.216(0.036)	-0.287	-0.145
Season	Spring / Winter	0.1(0.033)	0.038	0.166
	Summer / Winter	0.167(0.036)	0.097	0.238
	Autumn / Winter	0.112(0.033)	0.047	0.177
Time trend	Linear	1.07E-04(2.53E-04)	0.000	0.001
AR	AR(1)	0.158(0.041)	0.077	0.241
	AR(2)	0.192(0.049)	0.096	0.278
MA	MA(1)	-0.319(0.35)	-0.965	0.394
	MA(2)	0.092(0.372)	-0.666	0.880

Table 5.5. 36 Estimated regression coefficients with Bayesian ARIMA(1,1) model with linear time trend and seasonal variation for *E. coli.* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%
Season	Spring / Winter	0.061(0.104)	-0.144	0.260
	Summer / Winter	0.081(0.11)	-0.141	0.294
	Autumn / Winter	-0.029(0.107)	-0.240	0.177
Time trend	Linear	-0.001(0.001)	-0.002327	4.48E-04
AR	AR(1)	0.243(0.052)	0.143	0.348
MA	MA(1)	0.041(0.569)	-0.943	0.946

Table 5.5. 37 Estimated regression coefficients with Bayesian ARIMA(1,1) model with linear time trend, seasonal variation and non time-series covariates for *E. coli.* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%
Age	<40 / 70+	-3.055(0.383)	-3.939	-2.421
	40-69 / 70+	-1.185(0.158)	-1.543	-0.913
Gender	Male / Female	0.12(0.096)	-0.066	0.314
Season	Spring / Winter	0.104(0.105)	-0.100	0.313
	Summer / Winter	0.117(0.111)	-0.106	0.342
	Autumn / Winter	-0.036(0.109)	-0.250	0.179
Time trend	Linear	-0.002(0.001)	-0.004	-0.001
AR	AR(1)	0.3(0.087)	0.132	0.477
MA	MA(1)	0.15(0.587)	-0.947	0.967

Table 5.5. 38 Estimated regression coefficients with Bayesian ARIMA(2,2) model with linear time trend, seasonal variation and non time-series covariates for *E. coli.* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%
Season	Spring / Winter	0.124(0.099)	-0.073	0.319
	Summer / Winter	0.107(0.107)	-0.105	0.322
	Autumn / Winter	-0.031(0.103)	-0.238	0.177
Time trend	Linear	-0.002(0.001)	-0.003	-4.16E-04
AR	AR(1)	0.229(0.054)	0.121	0.336
	AR(2)	0.075(0.052)	-0.027	0.178
MA	MA(1)	-0.012(0.557)	-0.945	0.940
	MA(2)	0.082(0.539)	-0.919	0.950

Table 5.5. 39 Estimated regression coefficients with Bayesian ARIMA(1,1) model with linear time trend and seasonal variation for *P. aeruginosa* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%
Season	Spring / Winter	-0.22(0.131)	-0.475	0.033
	Summer / Winter	0.147(0.12)	-0.094	0.382
	Autumn / Winter	0.027(0.123)	-0.211	0.270
Time trend	Linear	-0.001(0.001)	-0.002	0.000
AR	AR(1)	0.063(0.072)	-0.076	0.203
MA	MA(1)	0.053(0.553)	-0.941	0.947

Table 5.5. 40 Estimated regression coefficients with Bayesian ARIMA(1,1) model with linear time trend, seasonal variation and non time-series covariates for *P. aeruginosa* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%
Age	<40 / 70+	-2.17(0.295)	-2.840	-1.675
	40-69 / 70+	-0.929(0.144)	-1.247	-0.678
Gender	Male / Female	0.389(0.101)	0.204	0.598
Season	Spring / Winter	-0.191(0.131)	-0.457	0.069
	Summer / Winter	0.133(0.125)	-0.105	0.376
	Autumn / Winter	0.104(0.121)	-0.134	0.338
Time trend	Linear	-0.002(0.001)	-0.004	-0.001
AR	AR(1)	0.106(0.11)	-0.112	0.327
MA	MA(1)	0.042(0.569)	-0.942	0.958

Table 5.5. 41 Estimated regression coefficients with Bayesian ARIMA(2,2) model with linear time trend and seasonal variation for *P. aeruginosa* bacteremia

Parameter	Level	Estimate (SD)	2.50%	97.50%
Season	Spring / Winter	-0.197(0.128)	-0.445	0.059
	Summer / Winter	0.116(0.120)	-0.124	0.352
	Autumn / Winter	0.094(0.119)	-0.138	0.328
Time trend	Linear	-0.002(0.001)	-0.004	-0.001
AR	AR(1)	0.058(0.067)	-0.073	0.189
	AR(2)	0.057(0.067)	-0.076	0.189
MA	MA(1)	0.040(0.568)	-0.946	0.945
	MA(2)	-0.018(0.568)	-0.953	0.943

Table 5.6. 1 The generalized AR(1) model for HAIs with concurrent intervention programs

Parameter	Level	Estimate (SD)	95% CI	
Crude model				
Season	Spring / Winter	0.110 (0.026)	0.060	0.162
	Summer / Winter	0.128 (0.028)	0.074	0.183
	Autumn / Winter	0.102 (0.026)	0.050	0.154
Time trend	Linear	5.81E-04 (3.57E-04)	-1.42E-04	0.001
Autocorrelations	AR(1)	0.321 (0.052)	0.220	0.424
Interventions	PDCA	0.030 (0.047)	-0.061	0.120
	Hygiene	-0.067 (0.050)	-0.164	0.034
	CDC/TJCHA	-0.275 (0.072)	-0.417	-0.137
	Bundle	-0.474 (0.069)	-0.611	-0.332
Age-gender adjusted model				
Age	<40 / 70+	-2.073 (0.037)	-2.146	-2.002
	40-69 / 70+	-1.198 (0.025)	-1.247	-1.149
Gender	Male / Female	0.088 (0.020)	0.049	0.128
Season	Spring / Winter	0.102 (0.025)	0.054	0.154
	Summer / Winter	0.124 (0.026)	0.073	0.177
	Autumn / Winter	0.105 (0.025)	0.057	0.157
Time trend	Linear	5.60E-04(3.22E-04)	-7.77E-05	1.17E-03
Autocorrelations	AR(1)	0.216 (0.020)	0.176	0.254
Interventions	PDCA	0.036 (0.040)	-0.042	0.116
	Hygiene	-0.067 (0.045)	-0.153	0.023
	CDC/TJCHA	-0.271 (0.064)	-0.393	-0.146
	Bundle	-0.475 (0.061)	-0.592	-0.355

DIC: (Crude model) 1831.40, (Adjusted model) 7599.91

Table 5.6. 2 The generalized AR(1) model for HAIs with time lagged 6-month

intervention programs

Parameter	Level	Estimate (SD)	95% CI	
Crude model				
Season	Spring / Winter	0.111 (0.025)	0.061	0.161
	Summer / Winter	0.120 (0.027)	0.068	0.172
	Autumn / Winter	0.092 (0.026)	0.042	0.141
Time trend	Linear	3.14E-04 (3.28E-04)	-3.11E-04	9.74E-04
Autocorrelations	AR(1)	0.288 (0.051)	0.187	0.386
Interventions	PDCA(lag6)	0.118 (0.043)	0.036	0.203
	Hygiene(lag6)	-0.075 (0.048)	-0.172	0.019
	CDC/TJCHA(lag6)	-0.400 (0.073)	-0.542	-0.258
	Bundle(lag6)	-0.425 (0.067)	-0.558	-0.296
Age-gender adjusted model				
Age	<40 / 70+	-2.073 (0.036)	-2.144	-2.001
	40-69 / 70+	-1.198 (0.025)	-1.245	-1.151
Gender	Male / Female	0.088 (0.020)	0.049	0.127
Season	Spring / Winter	0.106 (0.025)	0.058	0.155
	Summer / Winter	0.116 (0.026)	0.065	0.165
	Autumn / Winter	0.092 (0.025)	0.045	0.140
Time trend	Linear	3.41E-04 (2.96E-04)	-2.18E-04	9.28E-04
Autocorrelations	AR(1)	0.211 (0.020)	0.171	0.250
Interventions	PDCA(lag6)	0.115 (0.039)	0.035	0.191
	Hygiene(lag6)	-0.082 (0.043)	-0.165	0.002
	CDC/TJCHA(lag6)	-0.409 (0.066)	-0.545	-0.279
	Bundle(lag6)	-0.429 (0.060)	-0.547	-0.316

DIC: (Crude model) 1813.31, (Adjusted model) 7579.42

Table 5.6. 3 The generalized AR(1) model for HAIs with concurrent and time lagged

6-month intervention programs

Parameter	Level	Estimate (SD)	95% CI	
Crude model				
Season	Spring / Winter	0.109 (0.026)	0.060	0.158
	Summer / Winter	0.129 (0.028)	0.074	0.183
	Autumn / Winter	0.102 (0.026)	0.051	0.154
Time trend	Linear	5.96E-04 (3.60E-04)	-9.68E-05	1.32E-03
Autocorrelations	AR(1)	0.284 (0.054)	0.178	0.391
Interventions	PDCA	-0.141 (0.072)	-0.287	-0.001
	PDCA(lag6)	0.09 (0.05)	-0.009	0.184
	Hygiene	0.073 (0.069)	-0.064	0.206
	Hygiene(lag6)	-0.102 (0.053)	-0.207	0.001
	CDC/TJCHA	-0.17 (0.082)	-0.333	-0.013
	CDC/TJCHA(lag6)	-0.401 (0.09)	-0.580	-0.228
	Bundle	-0.498 (0.096)	-0.685	-0.311
	Bundle(lag6)	-0.476 (0.071)	-0.618	-0.341
Age-gender adjusted model				
Age	<40 / 70+	-2.074 (0.036)	-2.144	-2.001
	40-69 / 70+	-1.197 (0.025)	-1.246	-1.149
Gender	Male / Female	0.088 (0.020)	0.050	0.127
Season	Spring / Winter	0.104 (0.025)	0.055	0.153
	Summer / Winter	0.124 (0.026)	0.073	0.175
	Autumn / Winter	0.103 (0.026)	0.053	0.152
Time trend	Linear	5.51E-04 (3.25E-04)	-6.36E-05	0.001
Autocorrelations	AR(1)	0.209 (0.020)	0.170	0.247
Interventions	PDCA	-0.132 (0.066)	-0.263	-0.003
	PDCA(lag6)	0.094 (0.044)	0.010	0.181

Hygiene	0.082 (0.063)	-0.041	0.205
Hygiene(lag6)	-0.099 (0.047)	-0.193	-0.007
CDC/TJCHA	-0.166 (0.076)	-0.316	-0.021
CDC/TJCHA(lag6)	-0.389 (0.082)	-0.551	-0.229
Bundle	-0.503 (0.089)	-0.674	-0.334
Bundle(lag6)	-0.467 (0.065)	-0.595	-0.343

DIC: (Crude model) 1816.28, (Adjusted model) 7581.50

Table 5.6. 4 The generalized AR(2) model for HAIs with concurrent intervention programs

Parameter	Level	Estimate (SD)	95% CI	
Age	<40 / 70+	-2.033 (0.044)	-2.119	-1.945
	40-69 / 70+	-1.182 (0.031)	-1.242	-1.121
Gender	Male / Female	0.086 (0.024)	0.037	0.133
Season	Spring / Winter	0.105 (0.024)	0.058	0.153
	Summer / Winter	0.120 (0.026)	0.067	0.170
	Autumn / Winter	0.105 (0.024)	0.055	0.152
Time trend	Linear	6.55E-04 (3.89E-04)	-8.72E-05	1.43E-03
Autocorrelations	AR(1)	0.174 (0.02)	0.134	0.214
	AR(2)	0.180 (0.02)	0.141	0.220
Interventions	PDCA	0.022 (0.049)	-0.078	0.118
	Hygiene	-0.079 (0.055)	-0.191	0.029
	CDC/TJCHA	-0.280 (0.077)	-0.431	-0.129
	Bundle	-0.478 (0.073)	-0.623	-0.337

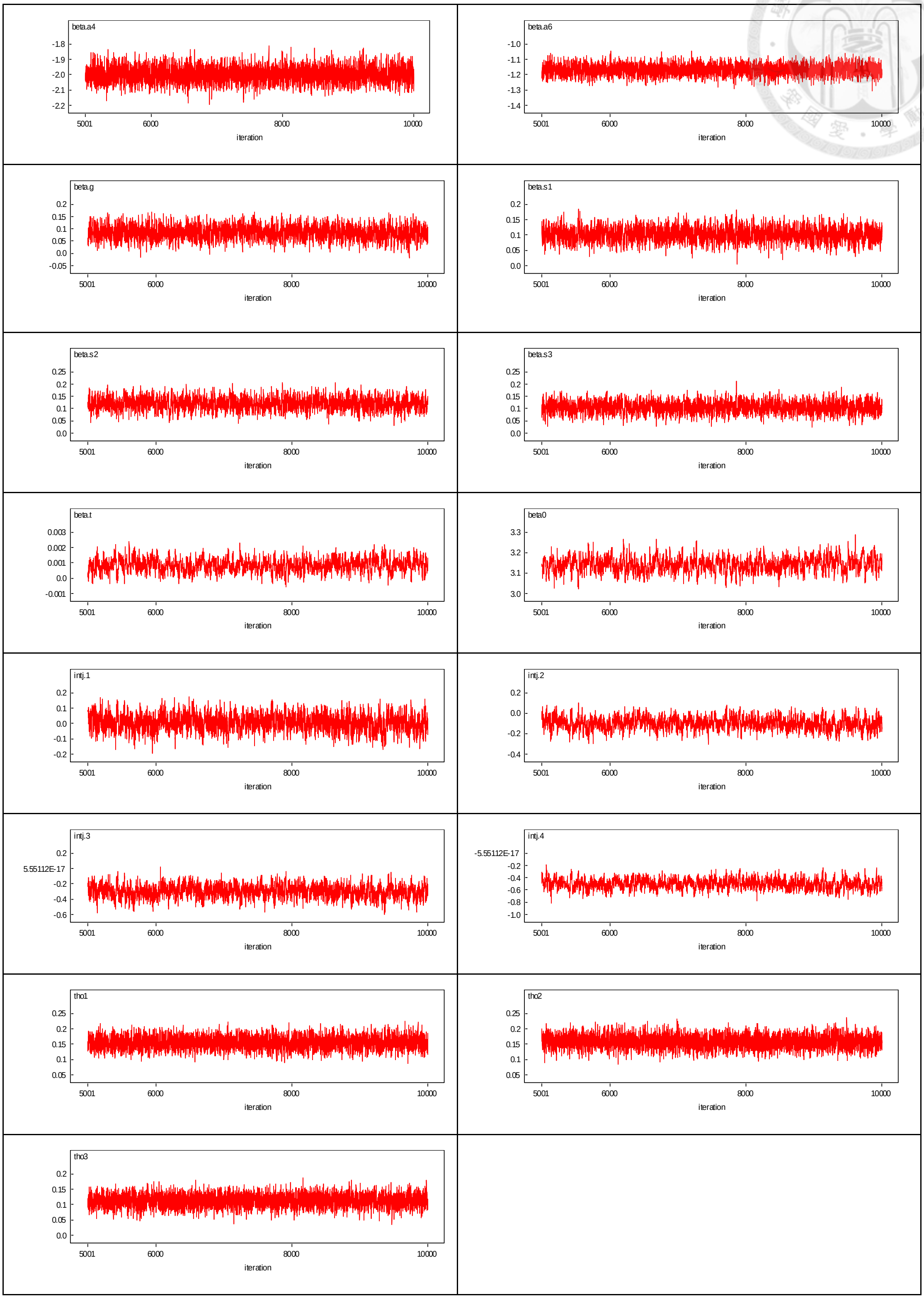
DIC:7525.40

Table 5.6. 5 The generalized AR(3) model for HAIs with concurrent intervention programs

Parameter	Level	Estimate (SD)	95% CI	
Age	<40 / 70+	-2 (0.051)	-2.098	-1.898
	40-69 / 70+	-1.169 (0.035)	-1.237	-1.101
Gender	Male / Female	0.085 (0.027)	0.031	0.140
Season	Spring / Winter	0.102 (0.023)	0.058	0.148
	Summer / Winter	0.120 (0.025)	0.072	0.169
	Autumn / Winter	0.106 (0.024)	0.060	0.151
Time trend	Linear	8.44E-04 (4.23E-04)	1.79E-05	0.002
Autocorrelations	AR(1)	0.155 (0.020)	1.15E-01	0.195
	AR(2)	0.158 (0.021)	1.16E-01	0.200
	AR(3)	0.112 (0.021)	7.25E-02	0.153
Interventions	PDCA	0.006 (0.053)	-0.100	0.111
	Hygiene	-0.100 (0.059)	-0.217	0.016
	CDC/TJCHA	-0.299 (0.081)	-0.462	-0.139
	Bundle	-0.502 (0.080)	-0.658	-0.346

DIC:7498.66

Table 5.6.5a Tracking plots



tho1:AR(1), tho2:AR(2), tho3:AR(3), beta0:intercept, beta.t:linear trend
beta.a4:age <40 / 70+, beta.a6: age 40-69 / 70+, betea.g:gender

beta.s1: Spring / Winter, beta.s2: Summer / Winter, beta.s3: Autumn / Winter
intj.1:PDCA intervention, intj.2: intervention Hygiene, intj.3:CDC/TJCHA
intj.4:Bundle intervention

Table 5.6. 6 The generalized ARIMA(3,1) model for HAIs with concurrent intervention programs

Parameter	Level	Estimate (SD)	95% CI	
Age	<40 / 70+	-2.028(0.037)	-2.1	-1.955
	40-69 / 70+	-1.185(0.028)	-1.24	-1.13
Gender	Male / Female	0.142(0.026)	0.091	0.194
Season	Spring / Winter	0.109(0.02)	0.07	0.149
	Summer / Winter	0.129(0.022)	0.086	0.175
	Autumn / Winter	0.113(0.02)	0.075	0.151
Time trend	Linear	0.00037(0.0004)	3.00E-05	0.001
Autocorrelations	AR(1)	0.109(0.031)	0.05	0.169
	AR(2)	0.161(0.017)	0.128	0.195
	AR(3)	0.109(0.016)	0.078	0.141
MA	MA(1)	-0.308(0.201)	-0.799	0.01
Interventions	PDCA	0.012(0.048)	-0.08	0.105
	Hygiene	-0.069(0.054)	-0.173	0.037
	CDC/TJCHA	-0.223(0.073)	-0.366	-0.079
	Bundle	-0.44(0.072)	-0.579	-0.293

Table 5.6. 7 The generalized AR(3) model for HAIs with time lagged 6-month intervention programs

Parameter	Level	Estimate (SD)	95% CI	
Age	<40 / 70+	-2.004 (0.049)	-2.102	-1.902
	40-69 / 70+	-1.169 (0.034)	-1.235	-1.103
Gender	Male / Female	0.085 (0.027)	0.032	0.137
Season	Spring / Winter	0.107 (0.022)	0.062	0.150
	Summer / Winter	0.111 (0.025)	0.063	0.159
	Autumn / Winter	0.093 (0.023)	0.048	0.138
Time trend	Linear	5.51E-04 (3.98E-04)	-2.40E-04	1.34E-03
Autocorrelations	AR(1)	0.151 (0.021)	0.110	0.191
	AR(2)	0.157 (0.021)	0.116	0.198
	AR(3)	0.107 (0.020)	0.067	0.148
Interventions	PDCA(lag6)	0.097 (0.050)	-0.001	0.196
	Hygiene(lag6)	-0.104 (0.058)	-0.219	0.009
	CDC/TJCHA(lag6)	-0.448 (0.085)	-0.618	-0.286
	Bundle(lag6)	-0.438 (0.079)	-0.589	-0.281

DIC:7843.35

Table 5.6. 8 The generalized AR(3) model for HAIs with concurrent and time lagged 6-month intervention programs

Parameter	Level	Estimate (SD)	95% CI	
Age	<40 / 70+	-2.005 (0.050)	-2.103	-1.906
	40-69 / 70+	-1.169 (0.034)	-1.235	-1.101
Gender	Male / Female	0.086 (0.027)	0.031	0.139
Season	Spring / Winter	0.106 (0.022)	0.063	0.150
	Summer / Winter	0.122 (0.025)	0.071	0.169
	Autumn / Winter	0.105 (0.023)	0.058	0.150
Time trend	Linear	7.80E-04 (4.10E-04)	-3.18E-05	0.002
Autocorrelations	AR(1)	0.150 (0.021)	1.08E-01	0.191
	AR(2)	0.157 (0.021)	1.15E-01	0.200
	AR(3)	0.108 (0.021)	6.71E-02	0.149
Interventions	PDCA	-0.118 (0.074)	-0.266	0.026
	PDCA(lag6)	0.076 (0.057)	-0.035	0.188
	Hygiene	0.047 (0.074)	-0.100	0.195
	Hygiene(lag6)	-0.120 (0.061)	-0.238	0.004
	CDC/TJCHA	-0.189 (0.089)	-0.363	-0.014
	CDC/TJCHA(lag6)	-0.434 (0.098)	-0.627	-0.237
	Bundle	-0.561 (0.104)	-0.769	-0.358
	Bundle(lag6)	-0.483 (0.081)	-0.638	-0.320

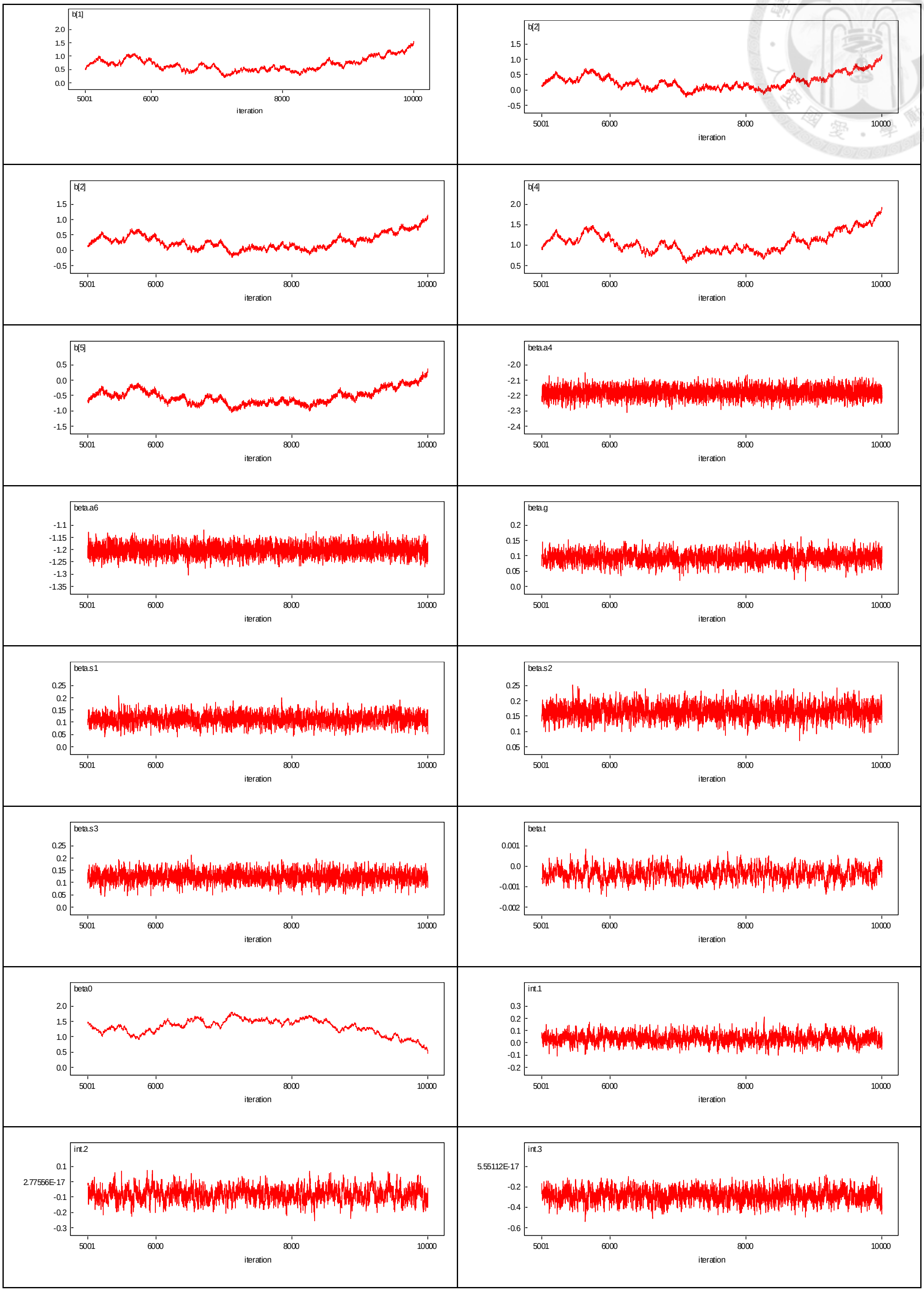
DIC:7486.38

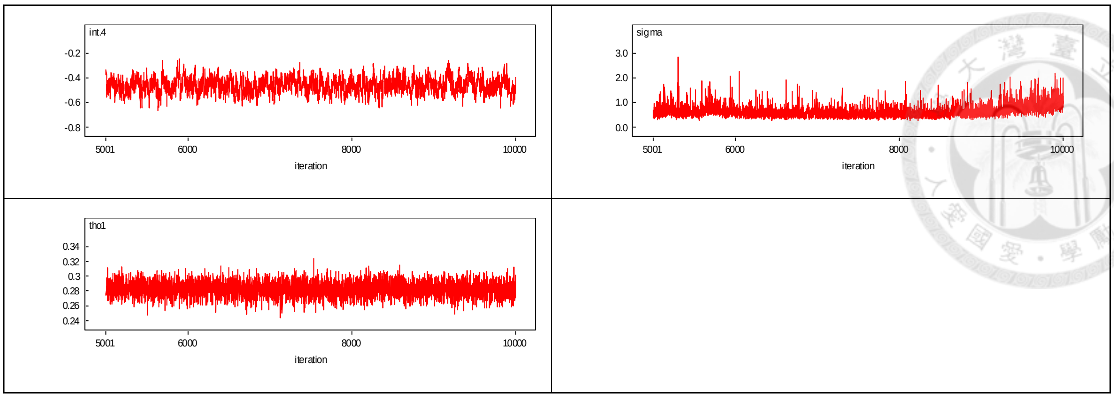
Table 5.7. 1 The Bayesian GLIMMIX-AR(1) model for HAIs with intervention programs and random effect on infection site

Parameter	Level	Estimate (SD)	95% CI	
Random effect				
Infection sites	Bacteremia	0.693 (0.247)	0.310	1.226
	Pneumonia	0.282 (0.247)	-0.101	0.822
	SSI	-0.13 (0.248)	-0.512	0.410
	UTI	1.071 (0.247)	0.689	1.602
	Others	-0.533 (0.248)	-0.912	0.007
sigma		0.638 (0.245)	0.344	1.294
Fixed effect				
Age	<40 / 70+	-2.18 (0.035)	-2.248	-2.111
	40-69 / 70+	-1.201 (0.024)	-1.248	-1.154
Gender	Male / Female	0.094 (0.019)	0.057	0.130
Season	Spring / Winter	0.113 (0.023)	0.068	0.157
	Summer / Winter	0.165 (0.024)	0.119	0.211
	Autumn / Winter	0.124 (0.023)	0.080	0.171
Interventions	PDCA	0.035 (0.041)	-0.042	0.116
	Hygiene	-0.081 (0.045)	-0.168	0.007
	CDC/TJCHA	-0.285 (0.066)	-0.414	-0.155
	Bundle	-0.463 (0.060)	-0.580	-0.347
Time trend	Linear	-3.63×10^{-4} (3.14×10^{-4})	-0.001	2.52×10^{-4}
Autocorrelations	AR(1)	0.283 (0.010)	0.263	0.302

DIC: 27248.20

Table 5.7.1a Tracking plots





tho1:AR(1), beta0:intercept, beta.t: linear trend

beta.a4:age <40 / 70+, beta.a6: age 40-69 / 70+

beta.s1: Spring / Winter, beta.s2: Summer / Winter, beta.s3: Autumn / Winter

b[1]:bacteremia, b[2]:pneumonia, b[3]:SSI, b[4]:UTI, b[5]:others

intj.1:PDCA intervention, intj.2: intervention Hygiene, intj.3:CDC/TJCHA

intj.4:Bundle intervention

Table 5.7. 2 The Bayesian GLIMMIX-AR(1) model for HAIs with intervention programs and random effect on random departments

Parameter	Level	Estimate (SD)	95% CI	
Random effect				
Department	Cardiovascular	-0.161 (0.267)	-0.618	0.352
	Chest	0.747 (0.265)	0.298	1.253
	Neurology	0.472 (0.266)	0.018	0.979
	Pediatric	-1.307 (0.273)	-1.771	-0.778
	Nephrology	0.876 (0.265)	0.422	1.380
	Infection	-0.262 (0.268)	-0.722	0.254
	Gastrointestinal	0.689 (0.265)	0.235	1.196
	Oncology	-0.182 (0.267)	-0.637	0.334
	Surgical	1.924 (0.264)	1.473	2.429
	Emergency	-2.939 (0.293)	-3.482	-2.366
	Others	-0.224 (0.27)	-0.688	0.299
sigma		1.216 (0.266)	0.824	1.852
Fixed effect				
Age	<40 / 70+	-2.382 (0.039)	-2.459	-2.306
	40-69 / 70+	-1.314 (0.026)	-1.366	-1.263
Gender	Male / Female	0.091 (0.021)	0.050	0.133
Season	Spring / Winter	0.11 (0.023)	0.065	0.154
	Summer / Winter	0.172 (0.024)	0.126	0.218
	Autumn / Winter	0.131 (0.023)	0.085	0.177
Interventions	PDCA	0.03 (0.041)	-0.049	0.109
	Hygiene	-0.1 (0.046)	-0.189	-0.008
	CDC/TJCHA	-0.306 (0.067)	-0.436	-0.170
	Bundle	-0.503 (0.063)	-0.625	-0.374
Time trend	Linear	-3.19×10^{-4} (3.25×10^{-4})	-0.001	3.00×10^{-4}
Autocorrelations	AR(1)	0.31 (0.01)	0.292	0.329

DIC:39934.5

Table 5.7. 3 The Bayesian GLIMMIX-AR(1) model for HAIs with intervention programs and random effect on pathogens)

Parameter	Level	Estimate (SD)	95% CI	
Random effect				
Pathogens	Gram-positive	-0.029 (0.477)	-0.789	1.087
	Gram-negative	1.082 (0.476)	0.320	2.198
	Anaerobic	-2.687 (0.482)	-3.444	-1.588
	Fungi	-0.301 (0.477)	-1.063	0.810
	Others	-1.496 (0.478)	-2.256	-0.387
sigma		1.449 (0.495)	0.812	2.720
Fixed effect				
Age	<40 / 70+	-2.131 (0.032)	-2.193	-2.069
	40-69 / 70+	-1.202 (0.022)	-1.244	-1.161
Gender	Male / Female	0.086 (0.017)	0.051	0.120
Season	Spring / Winter	0.111 (0.022)	0.067	0.154
	Summer / Winter	0.162 (0.023)	0.118	0.206
	Autumn / Winter	0.133 (0.022)	0.091	0.175
Interventions	PDCA	0.031 (0.036)	-0.038	0.103
	Hygiene	-0.093 (0.039)	-0.171	-0.018
	CDC/TJCHA	-0.289 (0.057)	-0.403	-0.175
	Bundle	-0.486 (0.054)	-0.590	-0.378
Time trend	Linear	$-1.98\times10^{-4}(2.75\times10^{-4})$	-0.001	3.41×10^{-4}
Autocorrelations	AR(1)	0.184 (0.013)	0.159	0.210

DIC: 21560.60

Table 5.7. 4 The Bayesian GLIMMIX-AR(1) model for HAIs with intervention programs and random effect on infection site allowing interaction

Parameter	Level	Estimate (SD)	95% CI	
Random effect				
Infection sites	Bacteremia	0.634 (0.272)	0.146	1.254
	Pneumonia	0.155 (0.271)	-0.338	0.764
	SSI	-0.179 (0.270)	-0.667	0.434
	UTI	1.004 (0.270)	0.515	1.614
	Others	-0.491 (0.270)	-0.981	0.113
sigma		0.601 (0.230)	0.324	1.182
Fixed effect				
Age	<40 / 70+	-2.173 (0.034)	-2.239	-2.106
	40-69 / 70+	-1.200 (0.024)	-1.244	-1.153
Gender	Male / Female	0.093 (0.020)	0.054	0.130
Season	Spring / Winter	0.114 (0.022)	0.070	0.157
	Summer / Winter	0.167 (0.023)	0.120	0.212
	Autumn / Winter	0.126 (0.022)	0.083	0.169
Time trend	Linear	-3.5×10^{-4} (3.3×10^{-4})	-1.0×10^{-3}	2.82×10^{-4}
Autocorrelations	AR (1)	0.274 (0.010)	0.255	0.294
Interaction				
CDC/TJCHA	Bacteremia	-0.441 (0.112)	-0.657	-0.223
	Pneumonia	0.072 (0.108)	-0.140	0.285
	SSI	-0.464 (0.156)	-0.774	-0.167
	UTI	-0.177 (0.088)	-0.350	-0.003
	Others	-1.684 (0.302)	-2.314	-1.115
Bundle care	Bacteremia	-0.459 (0.087)	-0.632	-0.292
	Pneumonia	-0.029 (0.089)	-0.201	0.146
	SSI	-0.577 (0.122)	-0.810	-0.335
	UTI	-0.477 (0.077)	-0.630	-0.326
	Others	-2.117 (0.228)	-2.579	-1.689

DIC: 27110.1

Table 5.7. 5 The Bayesian GLIMMIX-AR(1) model for HAIs with intervention programs and random effect on department allowing interaction

Parameter	Level	Estimate (SD)	95% CI	
Random effect				
Department	Cardiovascular	-0.223 (0.307)	-0.709	0.436
	Chest	0.698 (0.308)	0.226	1.371
	Neurology	0.396 (0.308)	-0.074	1.062
	Pediatric	-1.521 (0.318)	-2.025	-0.850
	Nephrology	0.795 (0.308)	0.328	1.469
	Infection	-0.293 (0.310)	-0.774	0.383
	Gastrointestinal	0.616 (0.308)	0.143	1.285
	Oncology	-0.439 (0.312)	-0.923	0.232
	Surgical	1.827 (0.308)	1.358	2.504
	Emergency	-2.934 (0.334)	-3.493	-2.239
	Others	-0.289 (0.311)	-0.775	0.381
sigma		1.227 (0.272)	0.837	1.861
Fixed effect				
Age	<40 / 70+	-2.370 (0.038)	-2.446	-2.294
	40-69 / 70+	-1.307 (0.025)	-1.356	-1.258
Gender	Male / Female	0.091 (0.020)	0.053	0.130
Season	Spring / Winter	0.110 (0.023)	0.066	0.154
	Summer / Winter	0.172 (0.024)	0.124	0.217
	Autumn / Winter	0.132 (0.023)	0.086	0.177
Time trend	Linear	-2.83×10^{-4} (3.24×10^{-4})	-9.3×10^{-4}	3.5×10^{-4}
Autocorrelations	AR (1)	0.303 (0.010)	0.285	0.322
Interaction				
CDC/TJCHA	Cardiovascular	-0.466 (0.239)	-0.934	-0.017
	Chest	-0.396 (0.162)	-0.727	-0.089
	Neurology	-0.473 (0.185)	-0.843	-0.113

	Pediatric	-0.070 (0.351)	-0.805	0.584
	Nephrology	-0.271 (0.147)	-0.565	0.012
	Infection	-0.270 (0.222)	-0.718	0.161
	Gastrointestinal	-0.643 (0.178)	-1.002	-0.311
	Oncology	0.379 (0.183)	0.018	0.726
	Surgical	-0.298 (0.094)	-0.480	-0.109
	Emergency	-2.840 (1.374)	-5.895	-0.574
	Others	-0.225 (0.223)	-0.682	0.193
Bundle care	Cardiovascular	-0.704 (0.181)	-1.067	-0.375
	Chest	-1.065 (0.142)	-1.353	-0.783
	Neurology	-0.571 (0.136)	-0.844	-0.305
	Pediatric	0.451 (0.207)	0.042	0.849
	Nephrology	-0.632 (0.121)	-0.871	-0.398
	Infection	-1.435 (0.234)	-1.923	-1.004
	Gastrointestinal	-0.546 (0.122)	-0.790	-0.314
	Oncology	0.476 (0.133)	0.217	0.739
	Surgical	-0.413 (0.080)	-0.571	-0.259
	Emergency	-0.833 (0.181)	-1.193	-0.486
	Others	-0.833 (0.181)	-1.193	-0.486

DIC: 39831.2

Table 5.7. 6 The Bayesian GLIMMIX-AR(1) model for HAIs with intervention programs and random effect on pathogens site allowing interaction

Parameter	Level	Estimate (SD)	95% CI	
Random effect				
Pathogens	Gram-positive	0.245 (0.183)	0.036	0.876
	Gram-negative	1.351 (0.182)	1.145	1.986
	Anaerobic	-2.315 (0.194)	-2.574	-1.698
	Fungi	-0.017 (0.184)	-0.229	0.615
	Others	-1.157 (0.186)	-1.380	-0.529
sigma		1.274 (0.430)	0.742	2.385
Fixed effect				
Age	<40 / 70+	-2.129 (0.031)	-2.191	-2.068
	40-69 / 70+	-1.202 (0.021)	-1.245	-1.161
Gender	Male / Female	0.085 (0.017)	0.050	0.119
Season	Spring / Winter	0.110 (0.022)	0.068	0.154
	Summer / Winter	0.162 (0.023)	0.118	0.208
	Autumn / Winter	0.133 (0.022)	0.090	0.177
Time trend	Linear	-1.9×10^{-4} (2.8×10^{-4})	-7.5×10^{-4}	3.7×10^{-4}
Autocorrelations	AR (1)	0.180 (0.013)	0.155	0.205
Interaction				
CDC/TJCHA	Gram-positive	-0.375 (0.108)	-0.588	-0.167
	Gram-negative	-0.356 (0.069)	-0.489	-0.219
	Anaerobic	-1.047 (0.444)	-2.005	-0.254
	Fungi	-0.056 (0.107)	-0.269	0.153
	Others	0.035 (0.168)	-0.301	0.357
Bundle care	Gram-positive	-0.423 (0.084)	-0.580	-0.253
	Gram-negative	-0.364 (0.058)	-0.478	-0.251
	Anaerobic	-1.689 (0.366)	-2.456	-1.007
	Fungi	-0.739 (0.100)	-0.940	-0.546
	Others	-2.398 (0.309)	-3.022	-1.818

DIC: 21457.40

Table 5.9. 1 Counts of predicted and observed HAIs during the period of interventions

Intervention	Observed	Prediction	Number of HAIs reduction	Observed (lagged)	Prediction (lagged)	Number of HAIs reduction
Hygiene+CDC/TJCHA	772	812.4(401,1303)	40.4(-371,531)	635	753.5(360,1221)	118.5(-275,586)
Hygiene+CDC/TJCHA+Bundle	1422	1705.4(813,2772)	283.4(-609,1350)	1150	1373.4(659,2231)	223.4(-491,1081)

Predicted by the trained data from 1994 to June, 2005. AR(1) linear trend, age, and gender adjusted model.

Table 5.9. 2 Counts of estimated and observed HAIs during the period of interventions

Intervention	Observed	Estimated	Number of HAIs reduction	Observed (lagged)	Estimated (lagged)	Number of HAIs reduction
Hygiene+CDC/TJCHA	772	901.7(862.3,942.7)	129.7(90.3,170.7)	635	909.9(869.4,952.0)	274.9(234.4,317)
Hygiene+CDC/TJCHA+Bundle	1422	2065.4(1971.9,2162.6)	643.4(549.9,740.6)	1150	1658.5(1583.7,1736.1)	508.5(433.7,586.1)

Estimated by the trained data from 1994 to June, 2005. AR(3) linear trend, age, and gender adjusted model.

Figure 3.3 1 Study design of the healthcare-associated infection analysis

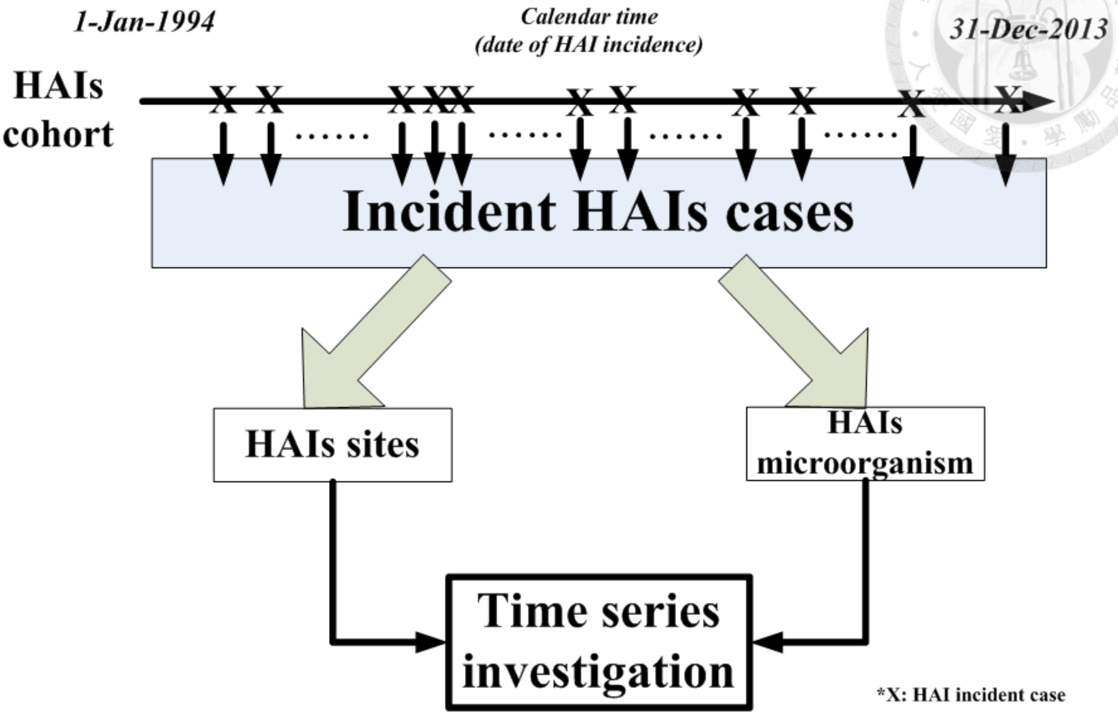


Figure 4.1. 1 Autoregressive time series model

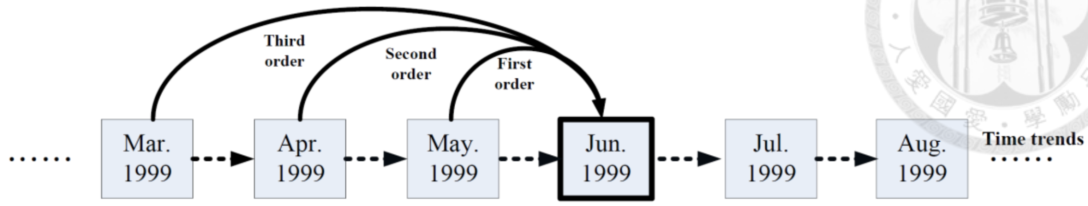


Figure 4.1. 2 Autoregressive model with lagged covariates

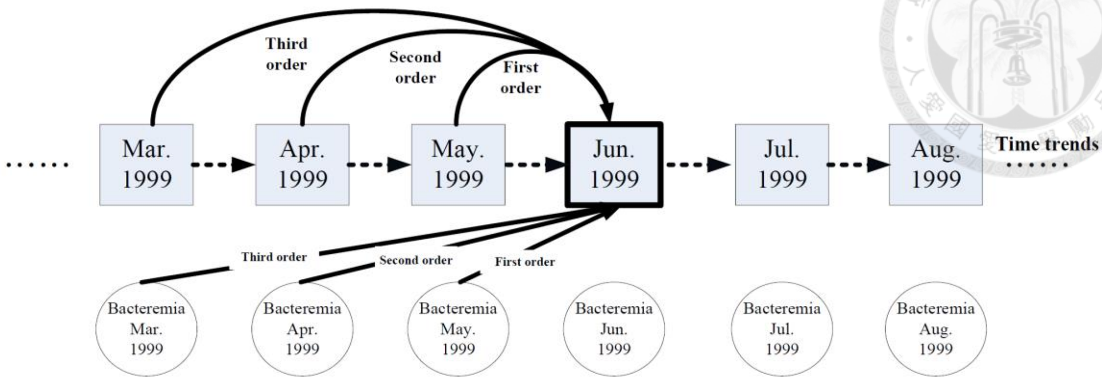


Figure 5.1. 1 Number of admission patients, episodes of healthcare-associated infections and deaths between 1994 and 2013 in SKMH, Taipei, Taiwan.

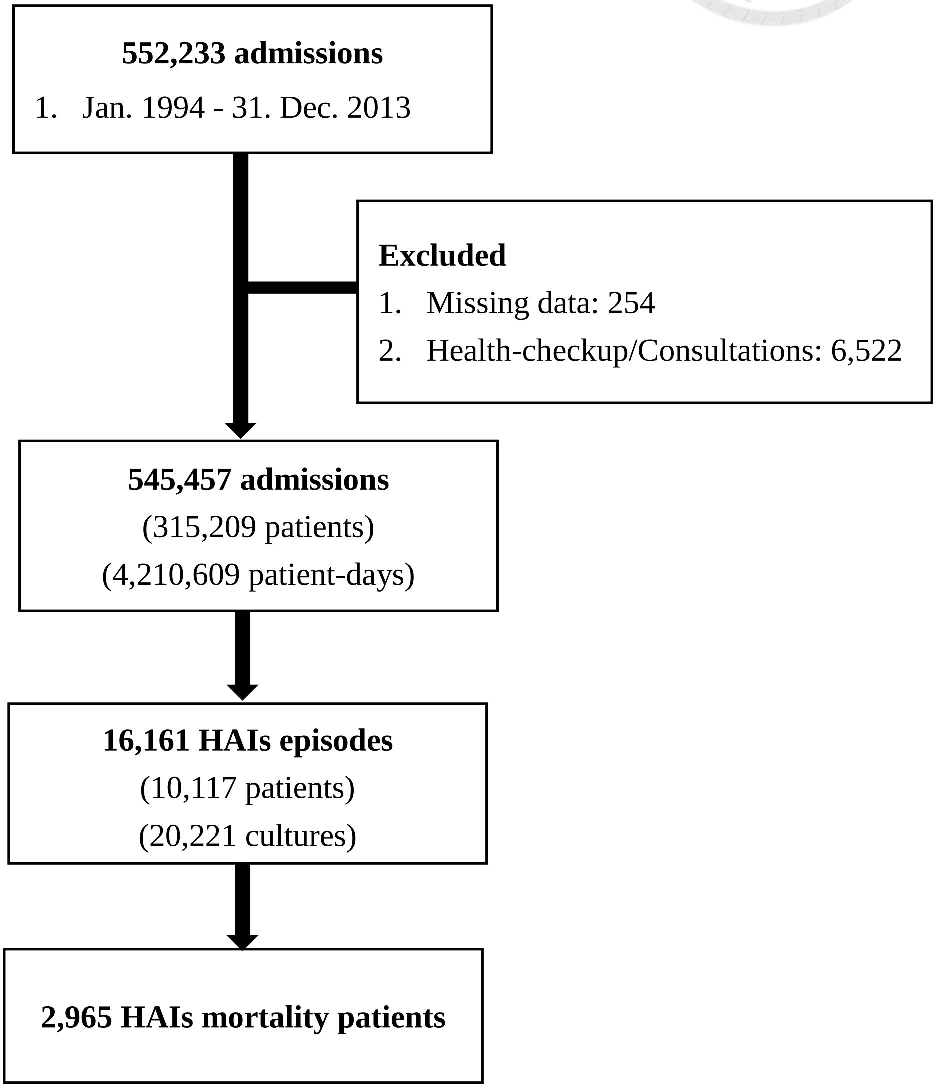
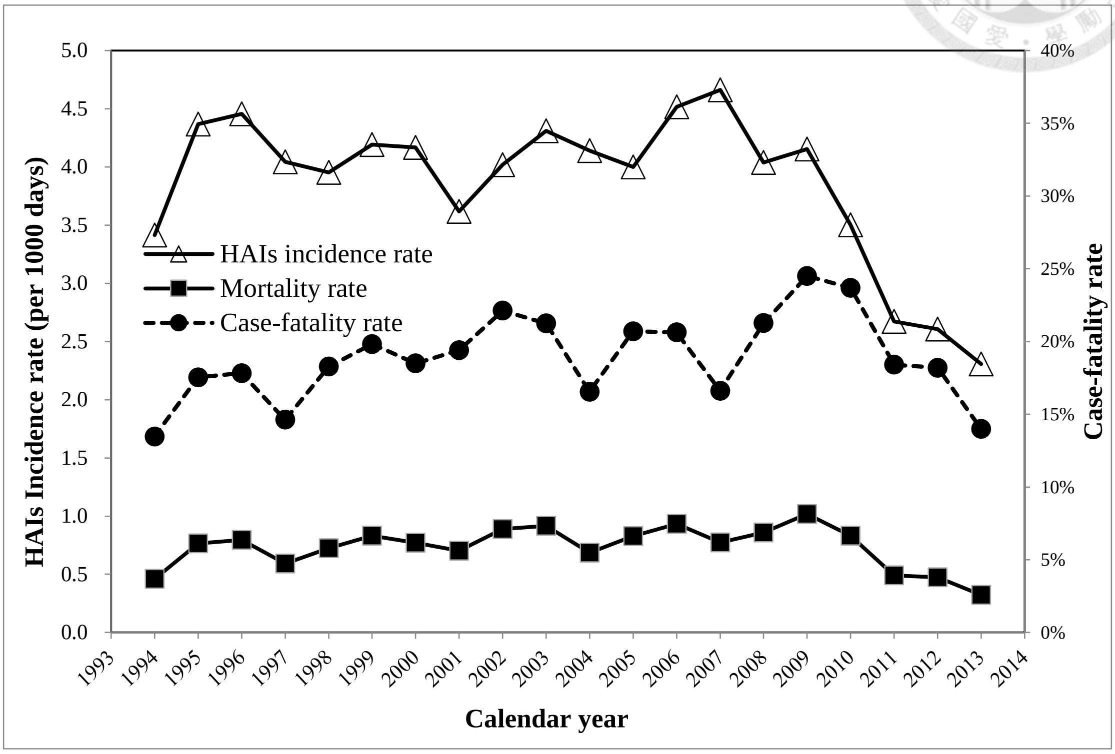


Figure 5.1. 2 HAI incidence, case-fatality, and mortality (1994-2013)



Note. Modified from Shen et al thesis.

Figure5.2. 1 The long-term trend of HAIs incidence (1994-2013)

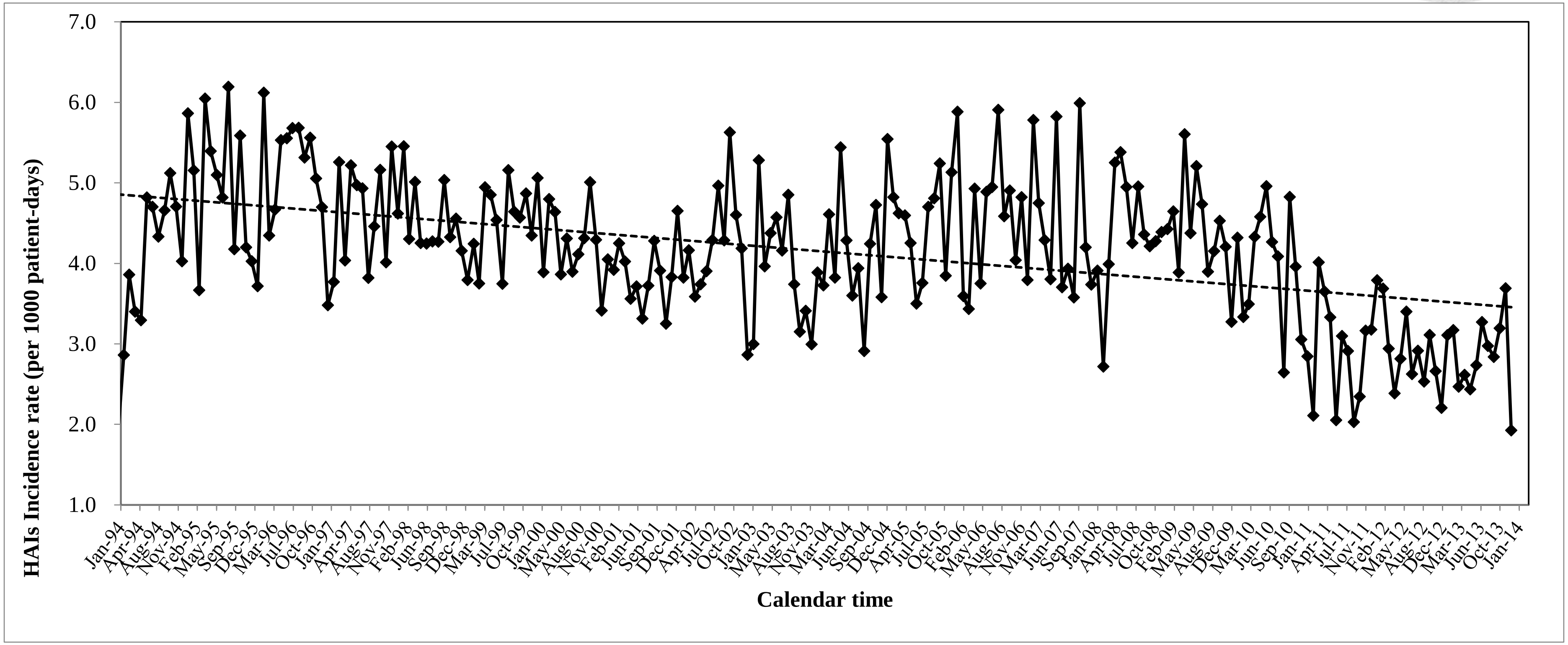


Figure5.2. 2 The long-term HAIs incidence rate by infection site

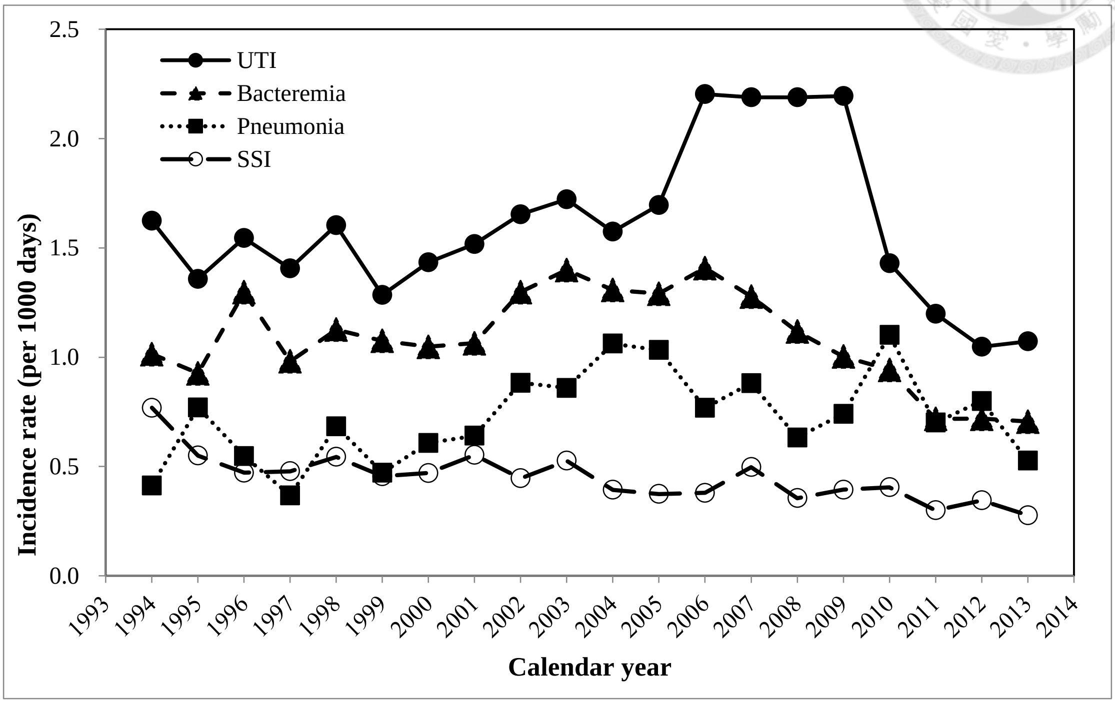


Figure5.2. 3 The long-term HAIs incidence rate of different subtype

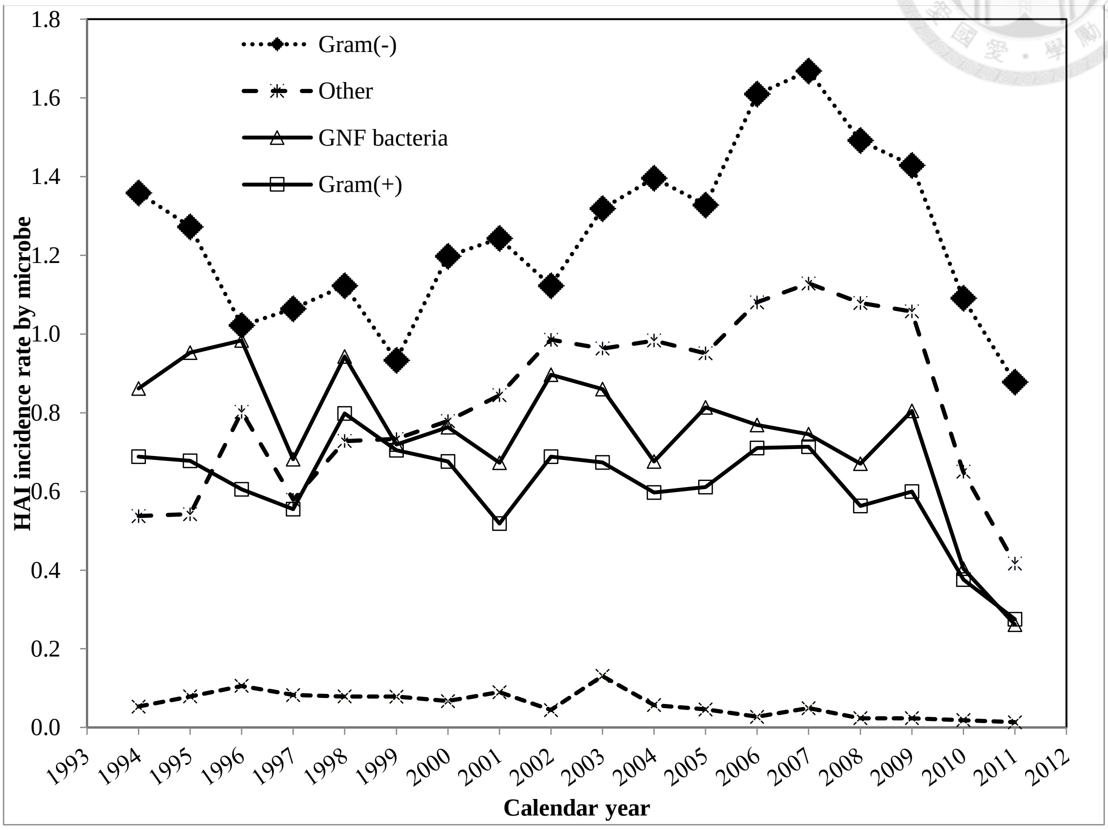


Figure5.2. 4 Time series of overall HAI count

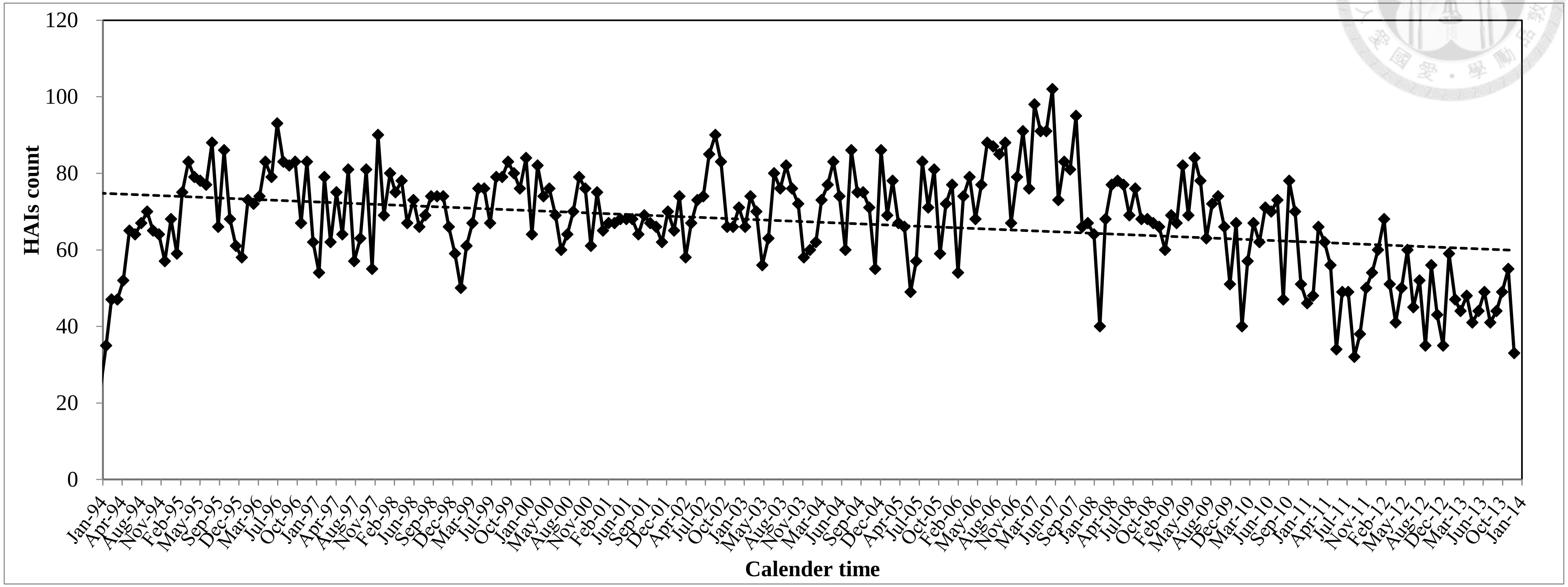


Figure5.2. 5 Time series of de-seasonalized overall HAI count

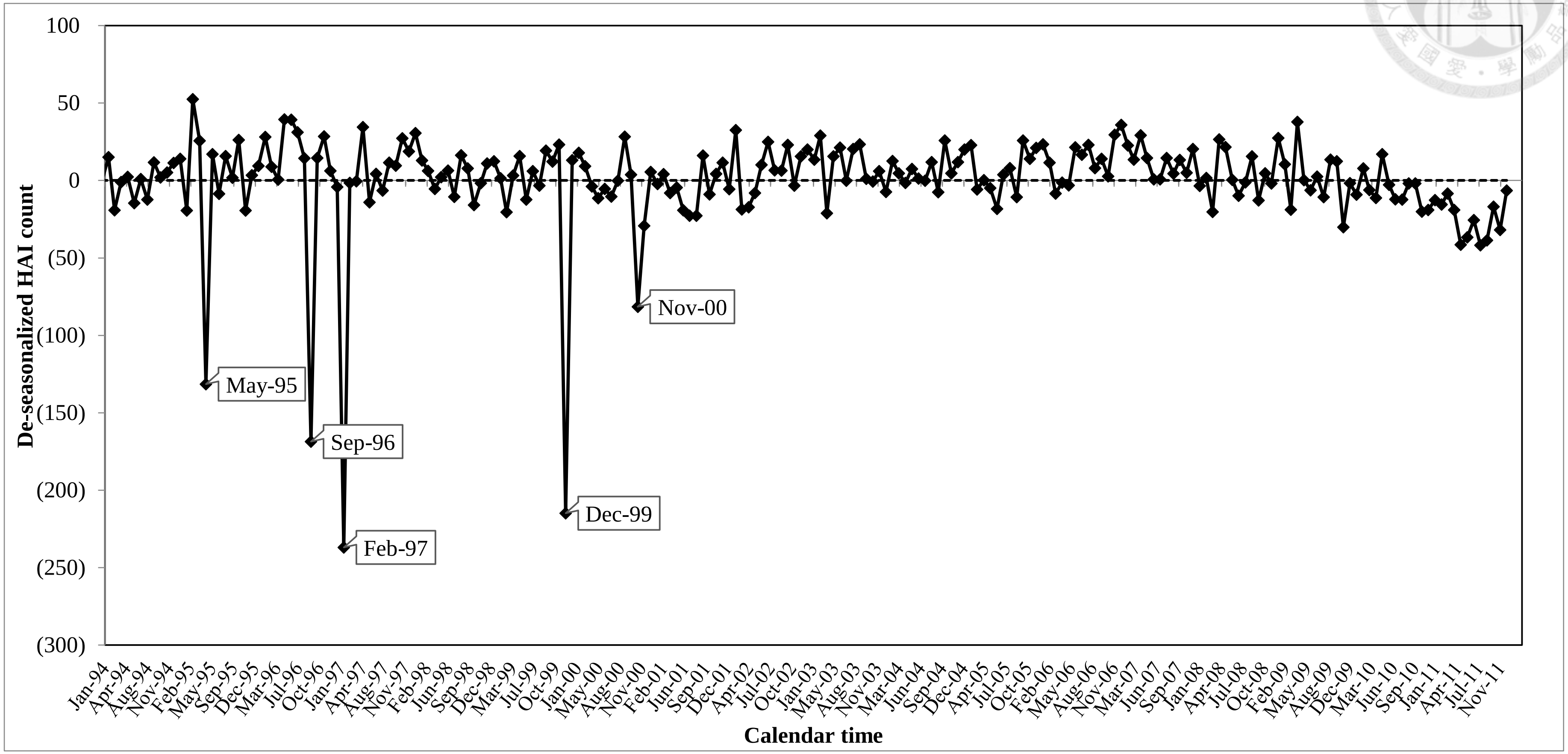


Figure5.2. 6 The long-term trend of HAI incidence of bacteremia (1994-2013)

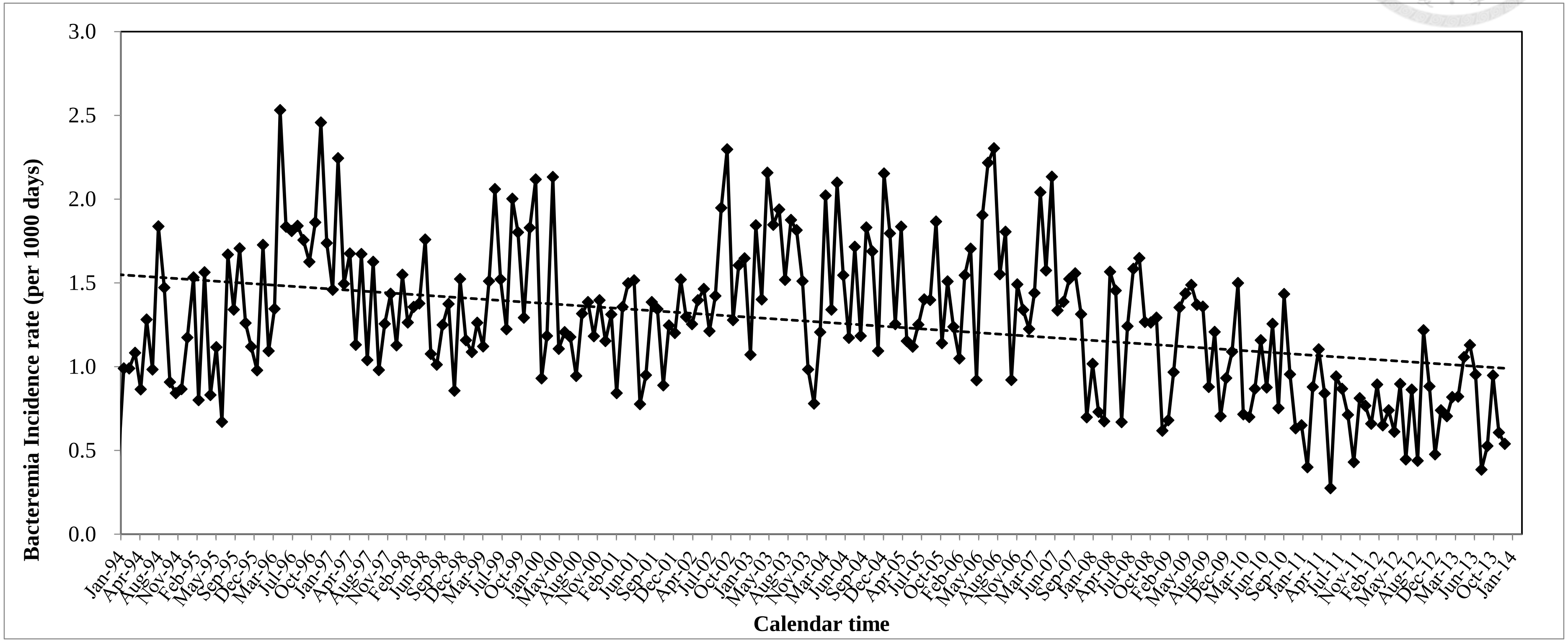


Figure5.2. 7 Time series of HAI bacteremia count

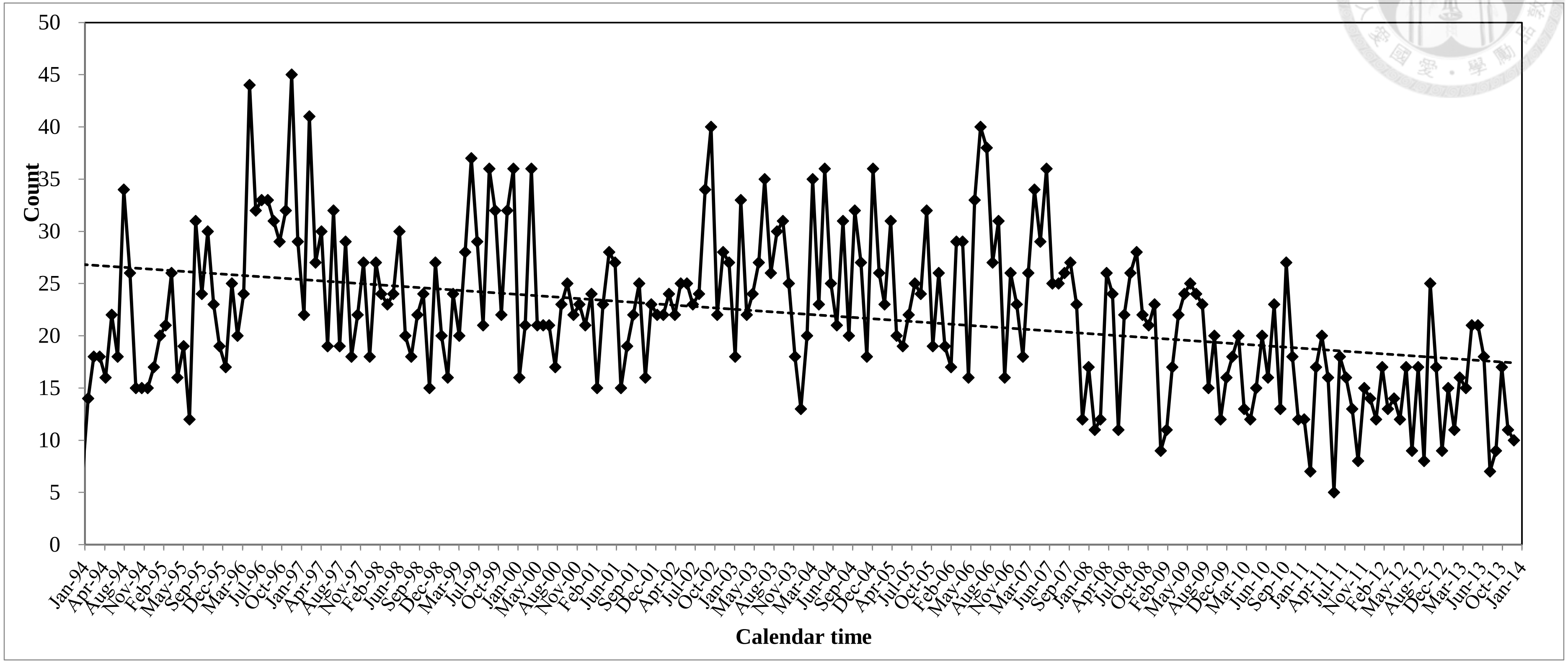


Figure5.2. 8 Time series of de-seasonalized bacteremia count

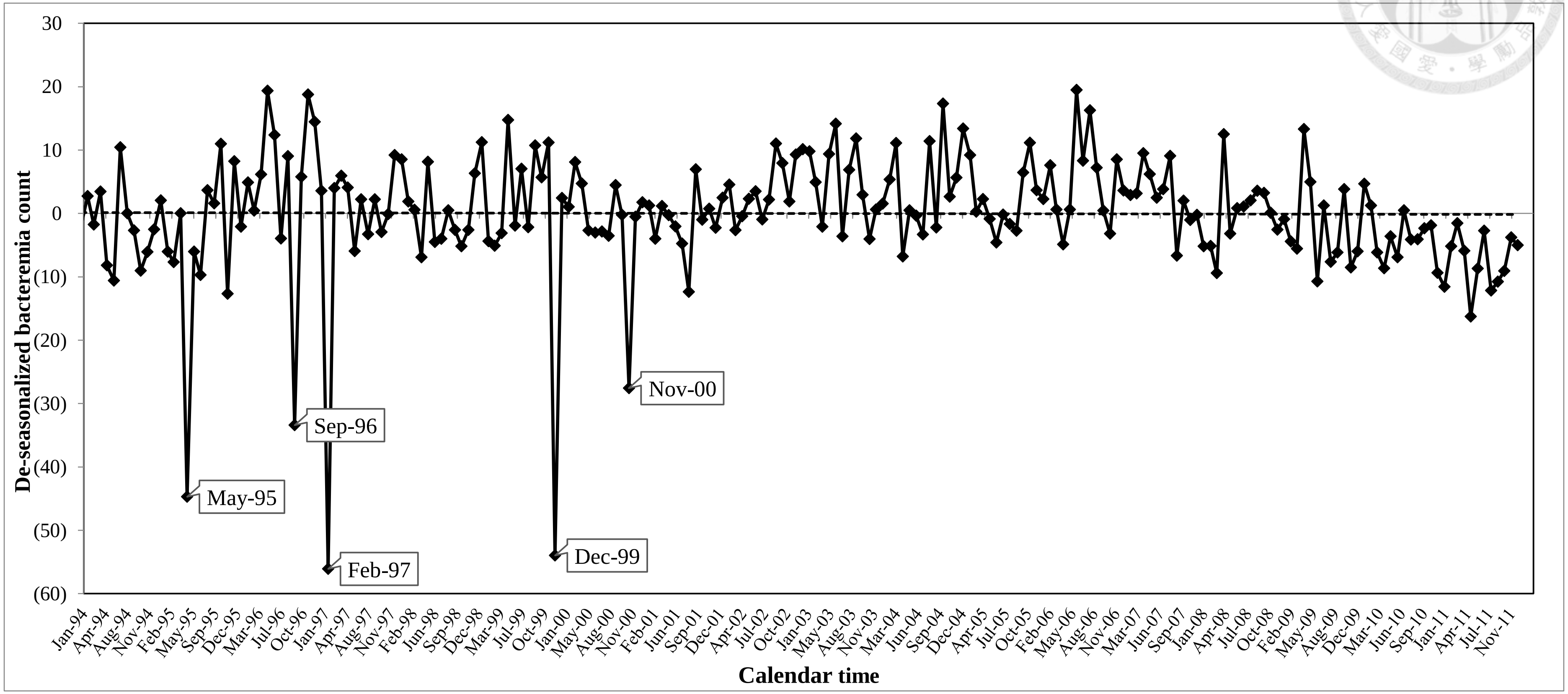


Figure5.2. 9 The long-term trend of HAI incidence of pneumonia (1994-2013)

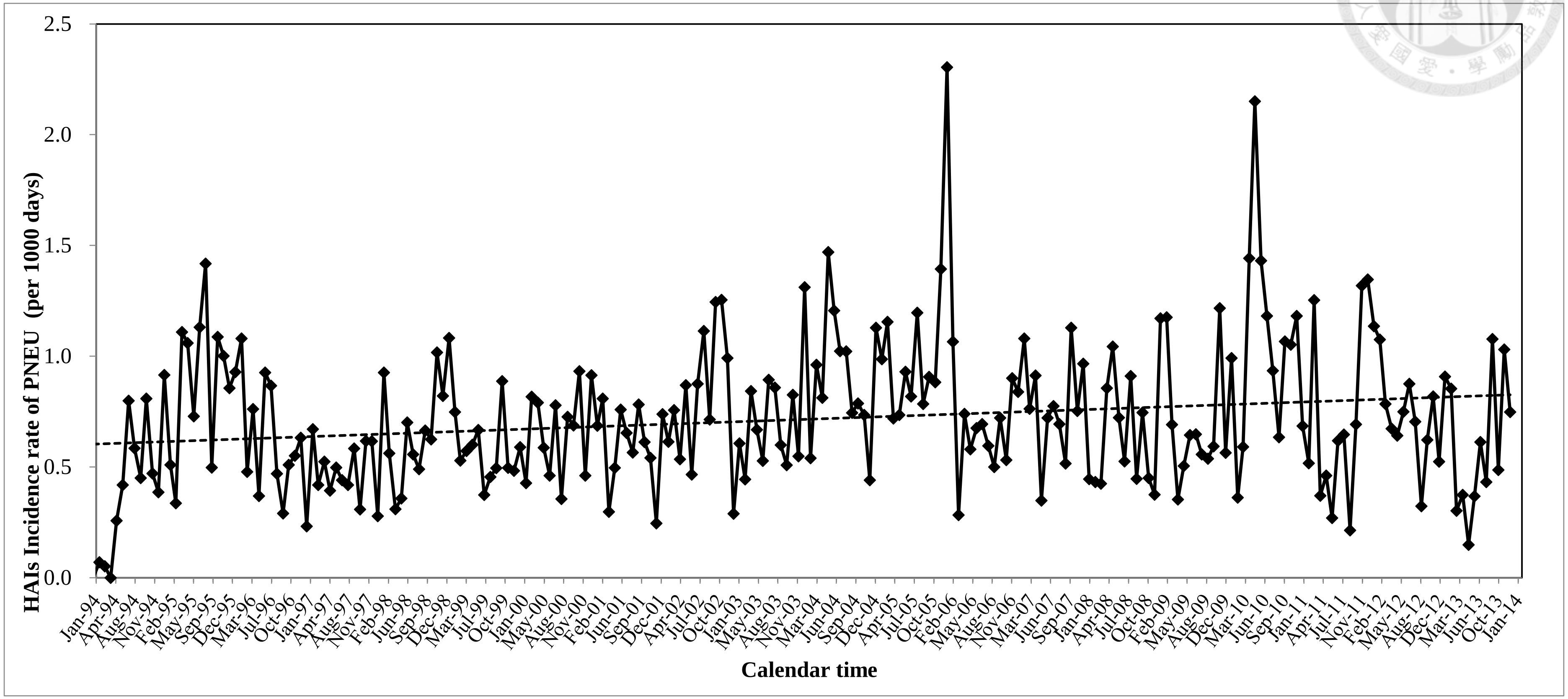


Figure5.2. 10 Time series of HAI pneumonia count

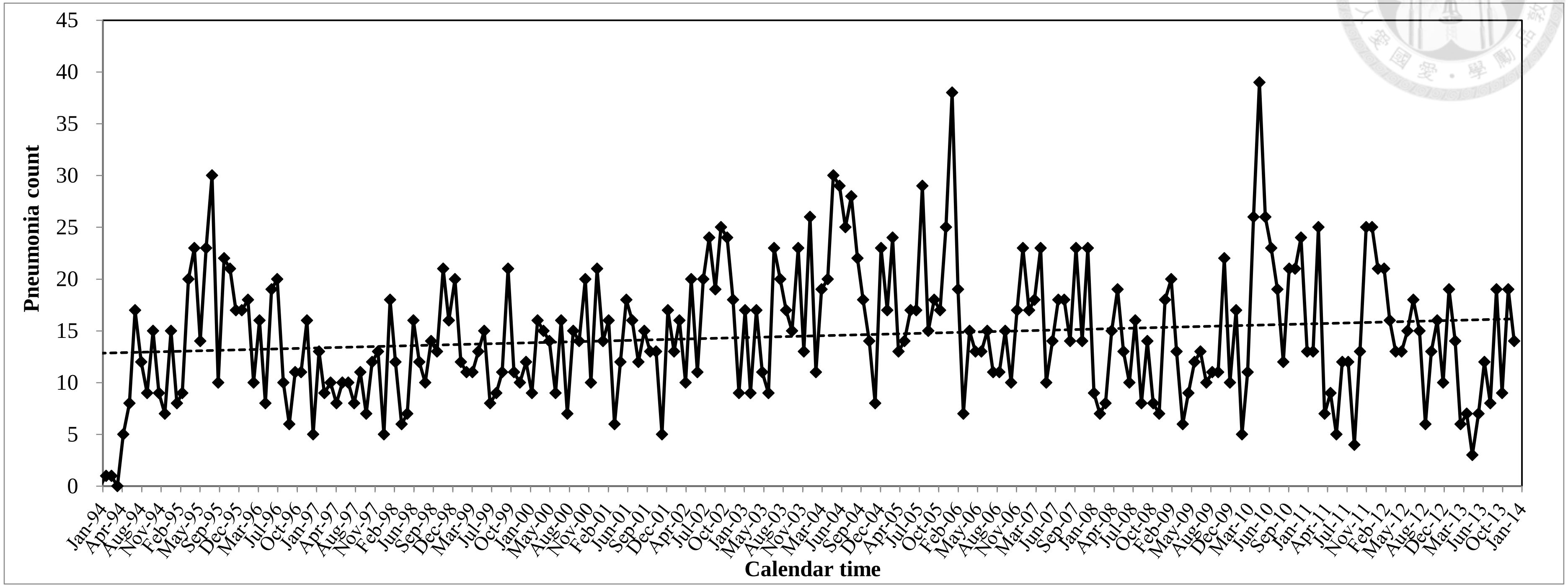


Figure5.2. 11 Time series of de-seasonalized pneumonia count

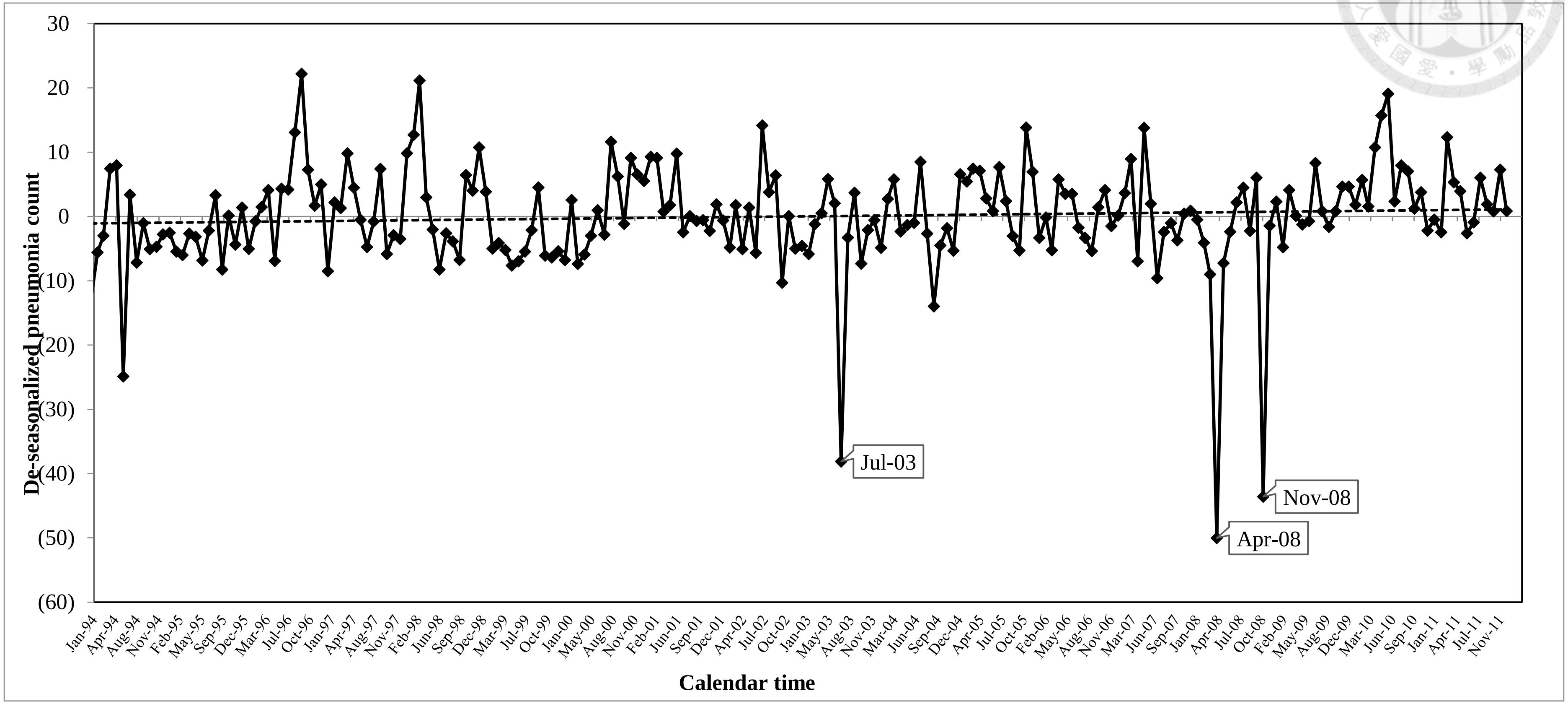


Figure5.2. 12 The long-term trend of HAIs incidence of SSI (1994-2013)

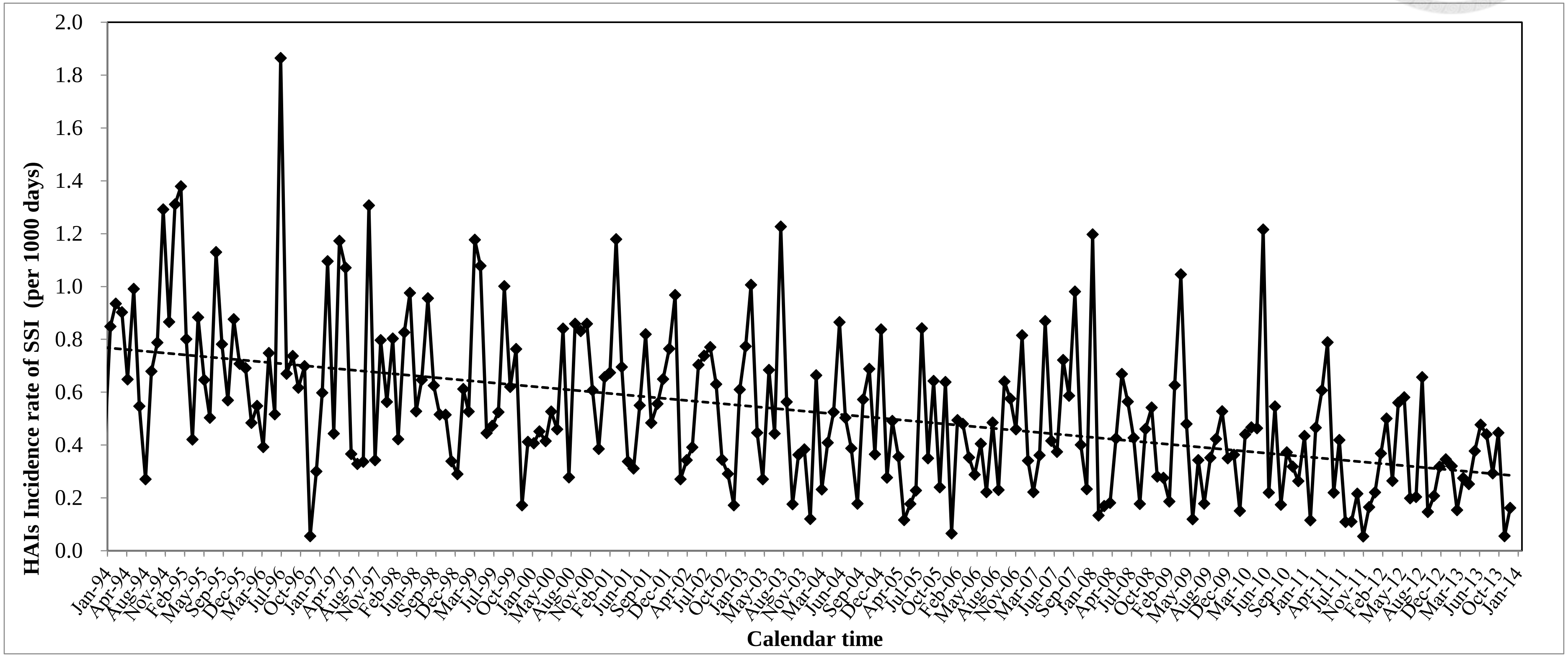


Figure5.2. 13 Time series of HAI of SSI count

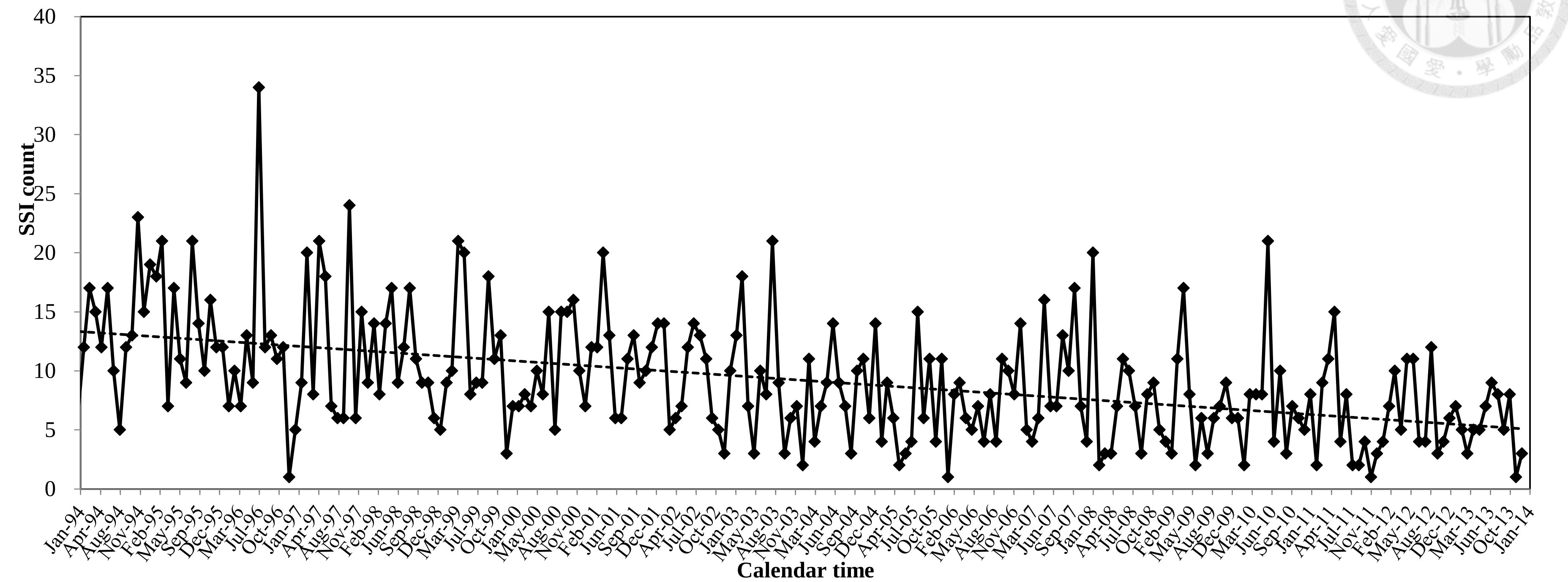


Figure5.2. 14 Time series of de-seasonalized SSI (surgical site infection) count

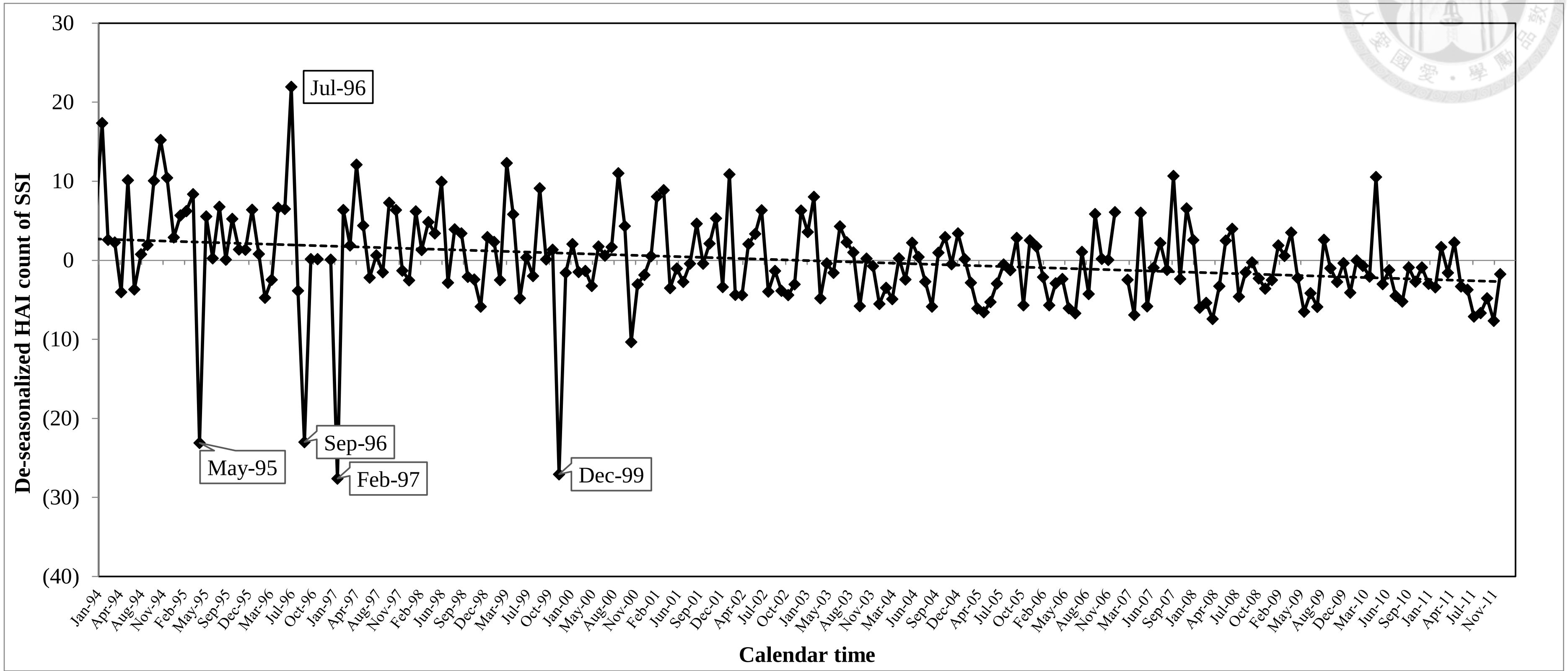


Figure5.2. 15 The long-term trend of HAIs incidence of UTI (1994-2013)

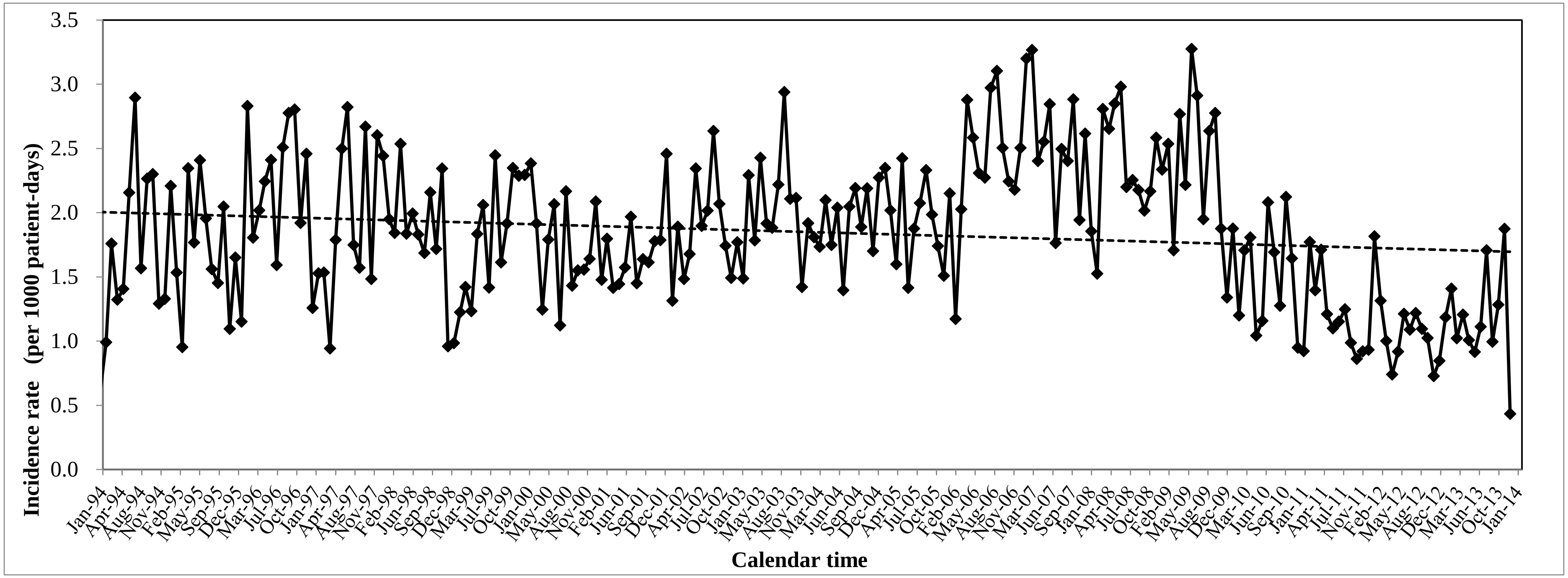


Figure5.2. 16 Time series of HAI of UTI count

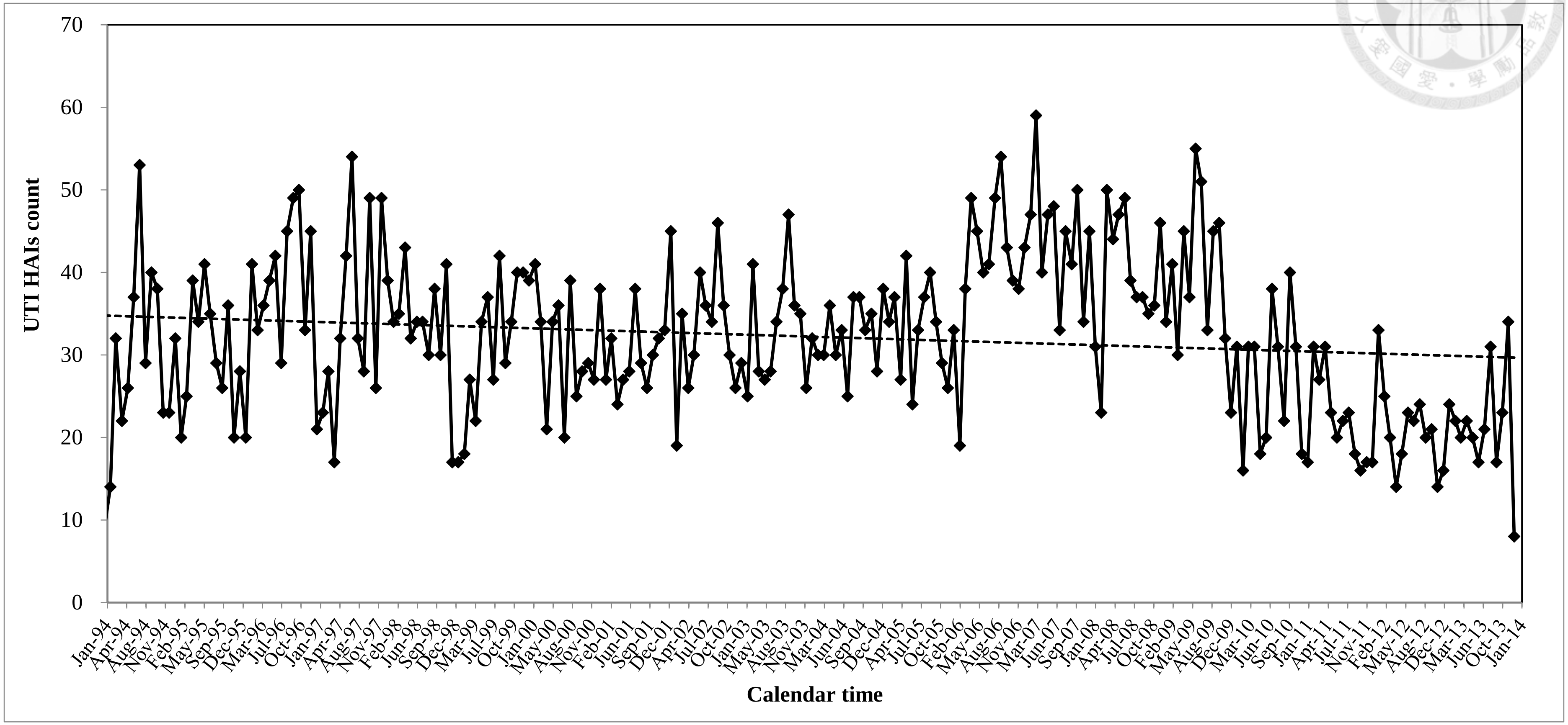


Figure5.2. 17 Time series of de-seasonalized UTI (urinary tract infection) count

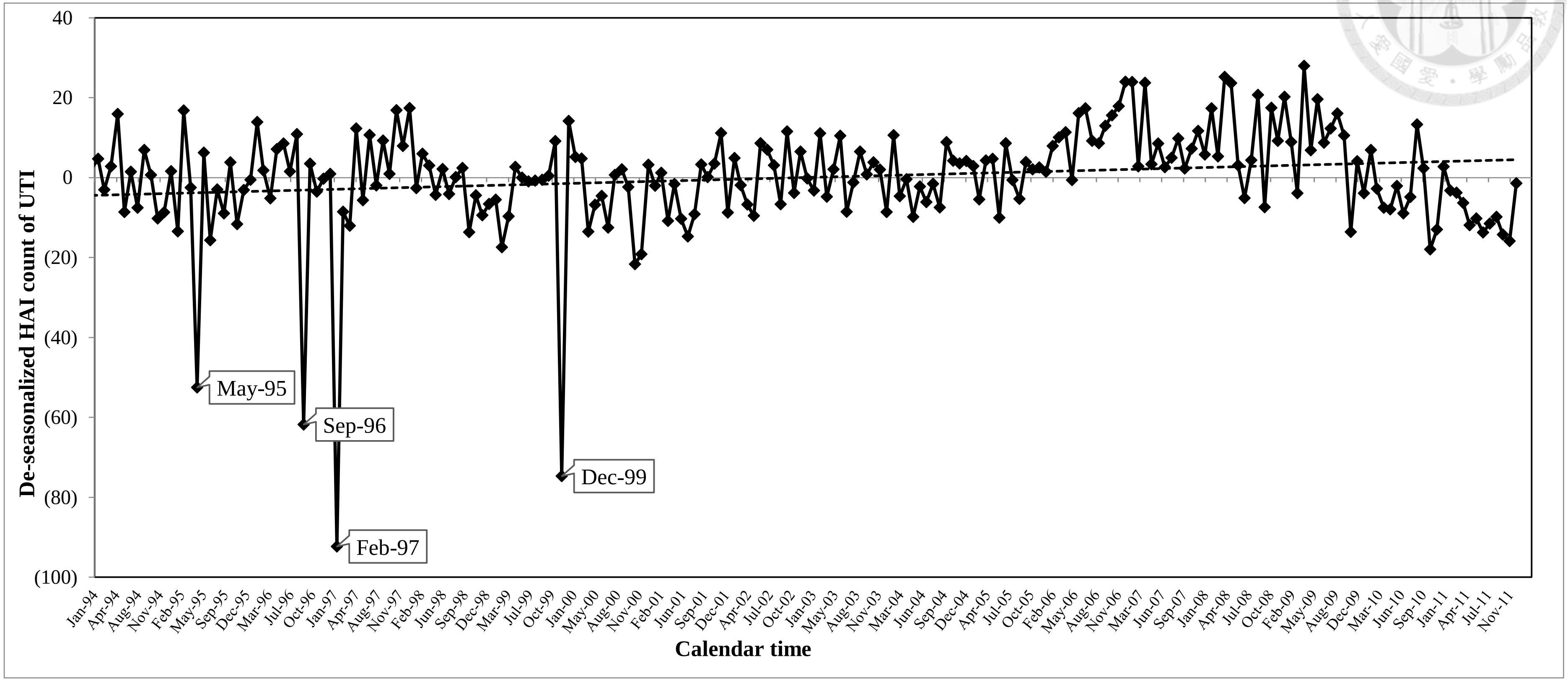


Figure5.2. 18 Time series of overall HAI *E. coli* bacteremia count

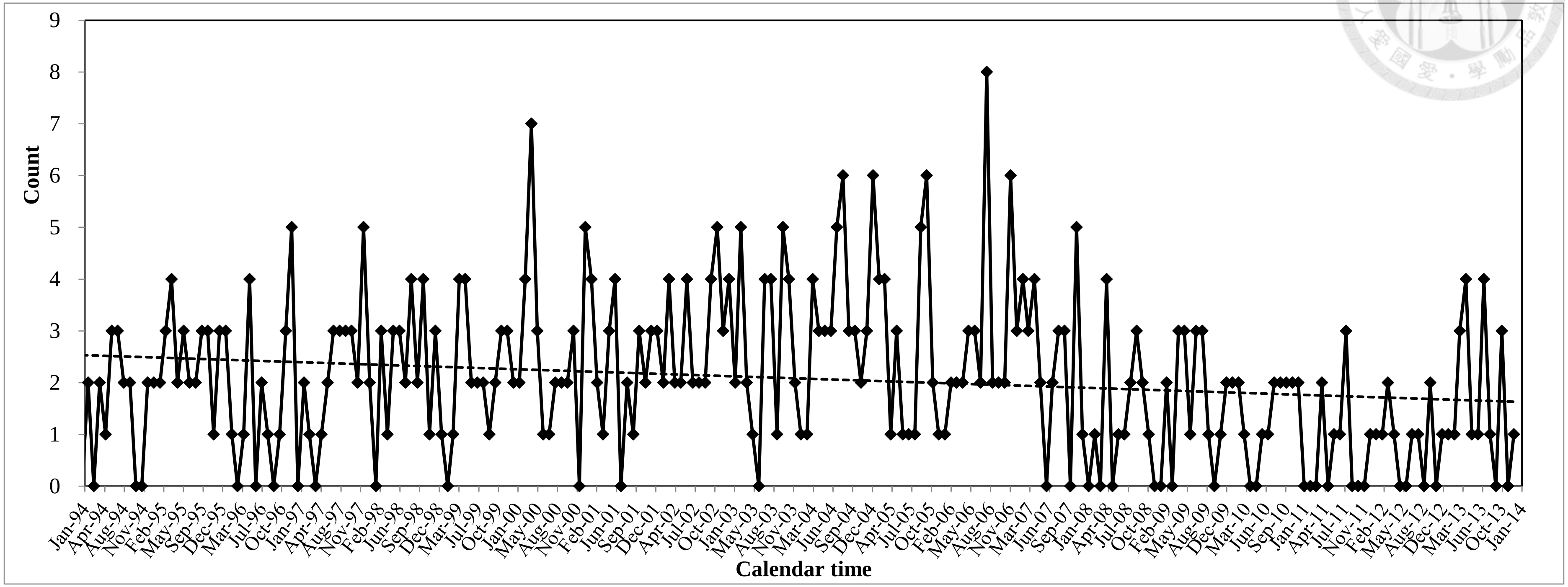


Figure5.2. 19 Time series of de-seasonalized *E. coli* bacteremia count

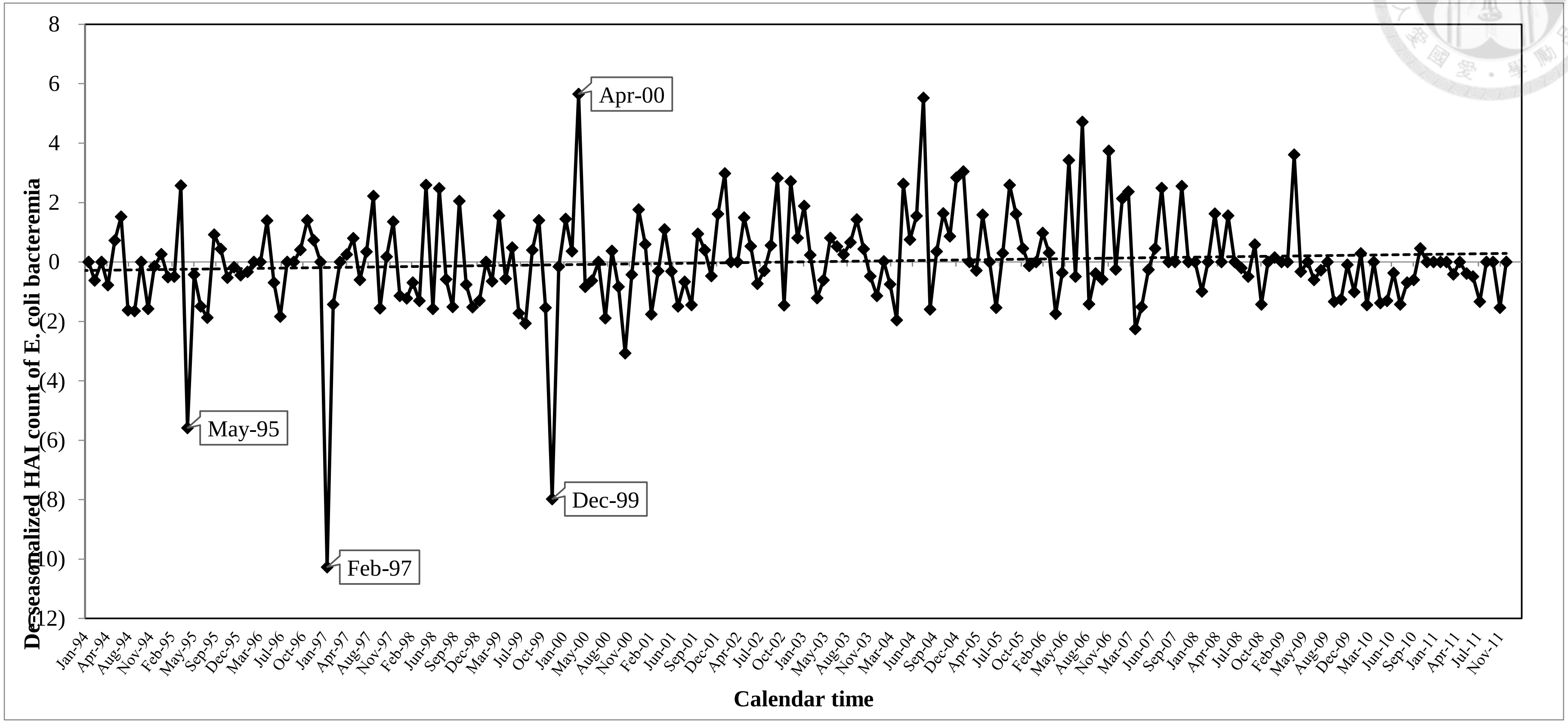


Figure5.2. 20 Time series of *Pseudomonas aeruginosa* bacteremia HAI count

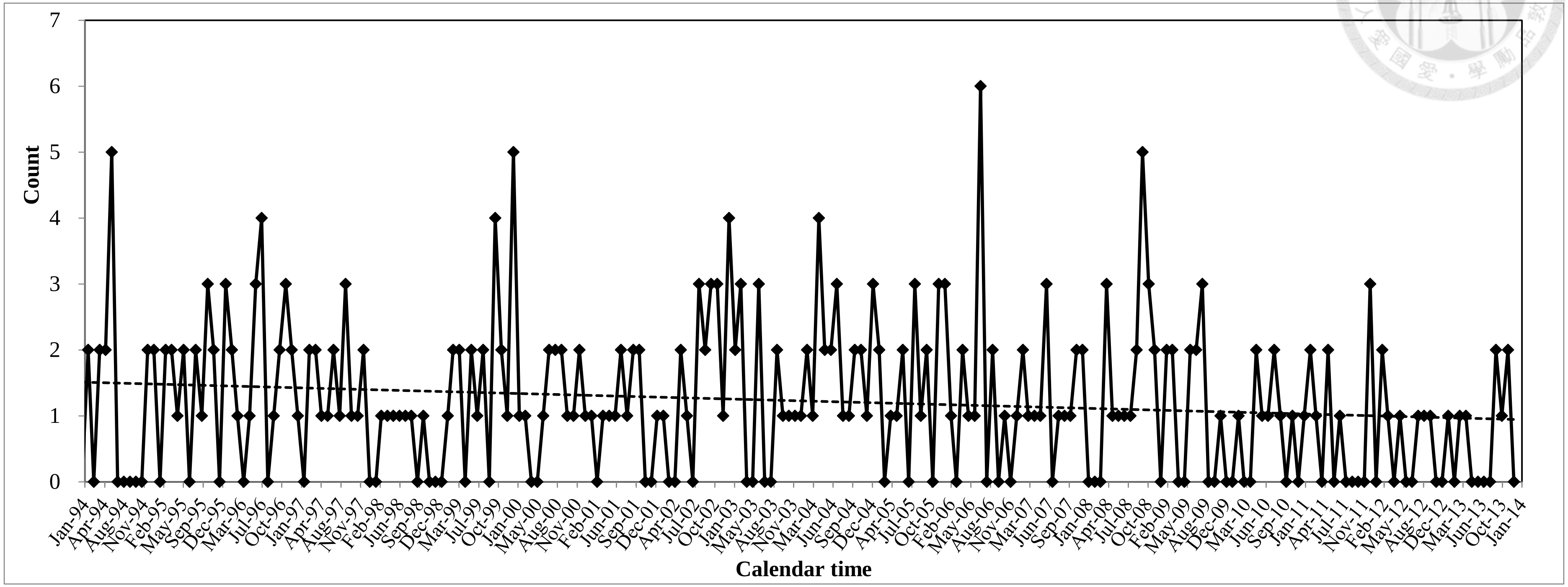


Figure5.2. 21 Time series of de-seasonalized *Pseudomonas aeruginosa* bacteremia count

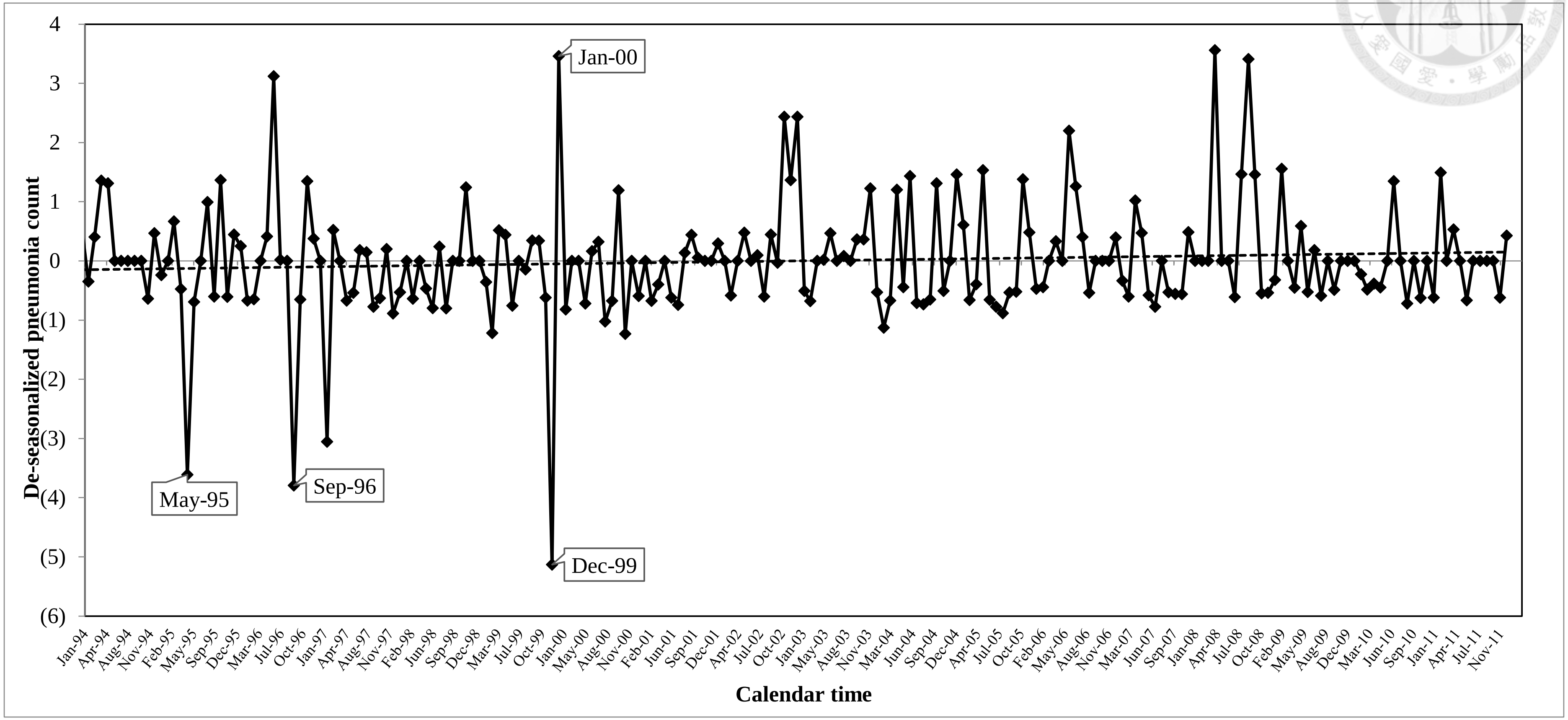
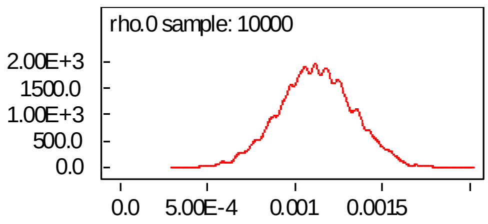
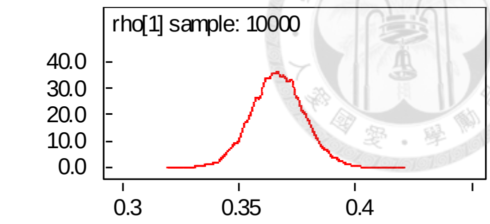


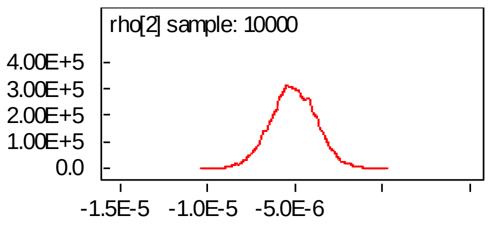
Figure 5.4. 1 Bayesian approach results: density



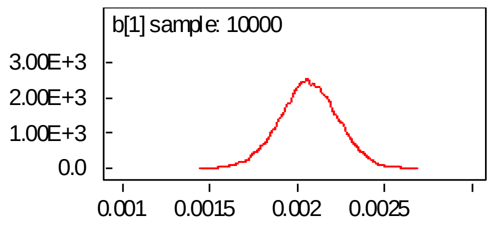
rho.0 intercept



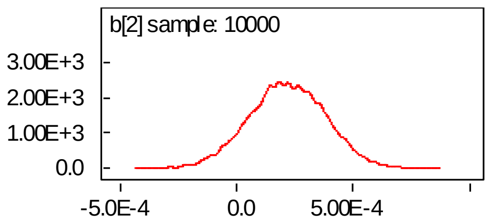
rho[1]:AR(1)



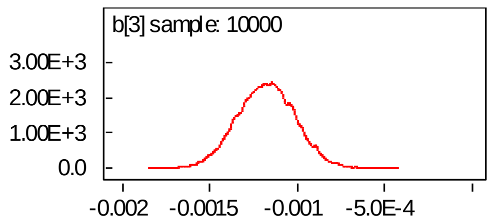
rho[2]:AR(2)



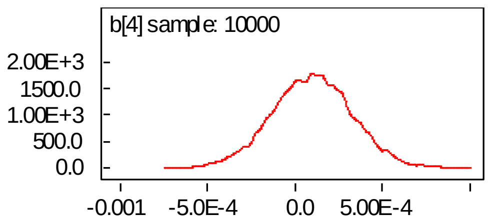
b[1]:age



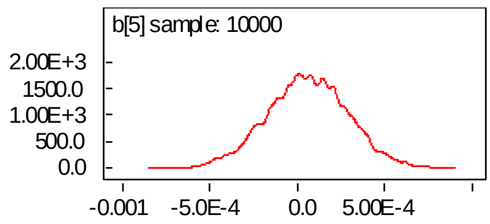
b[2]:gender



b[3]]:



b[4]:spring/winter



b[5]:summer/winter

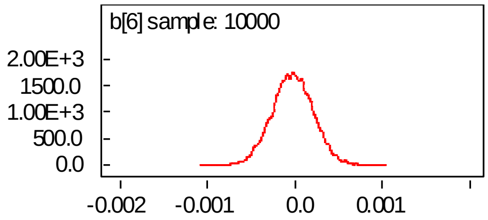
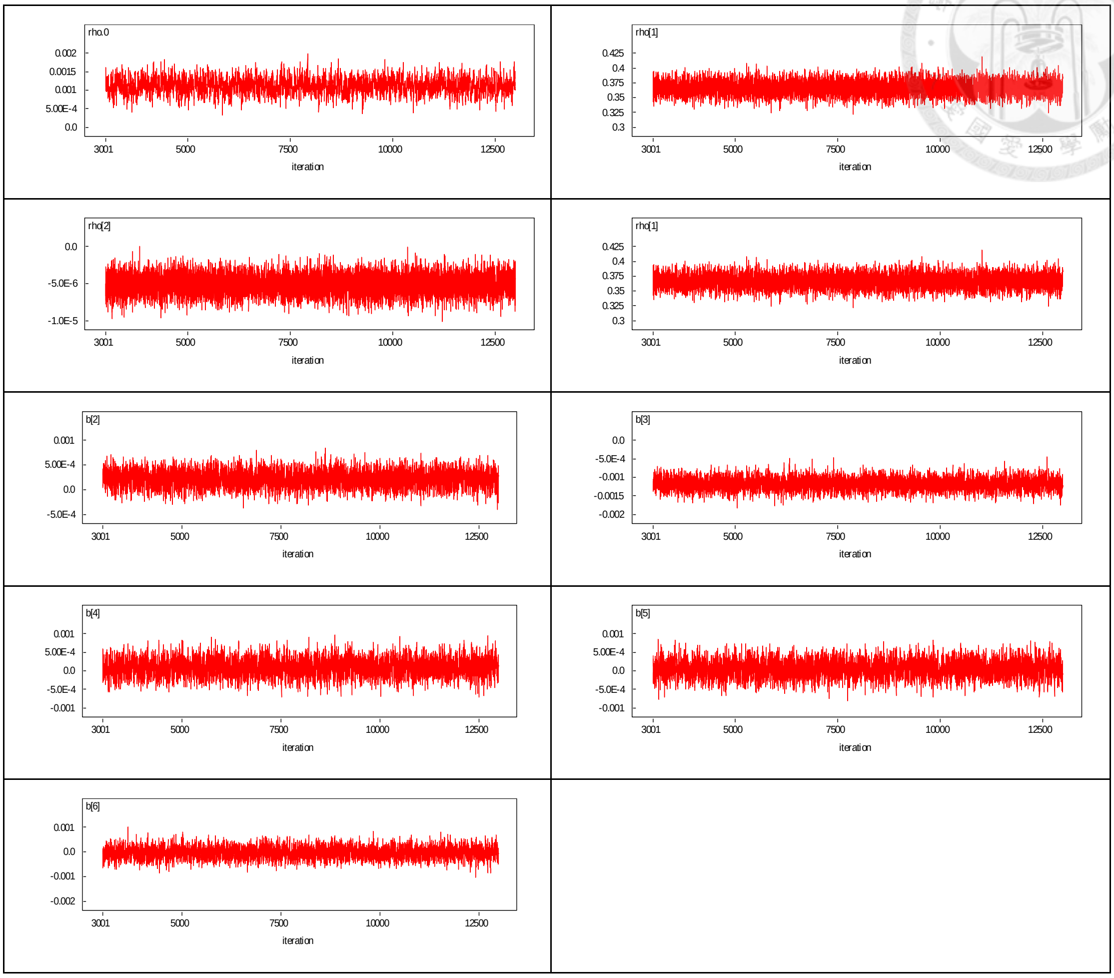
 b[6]:autumn/winter	

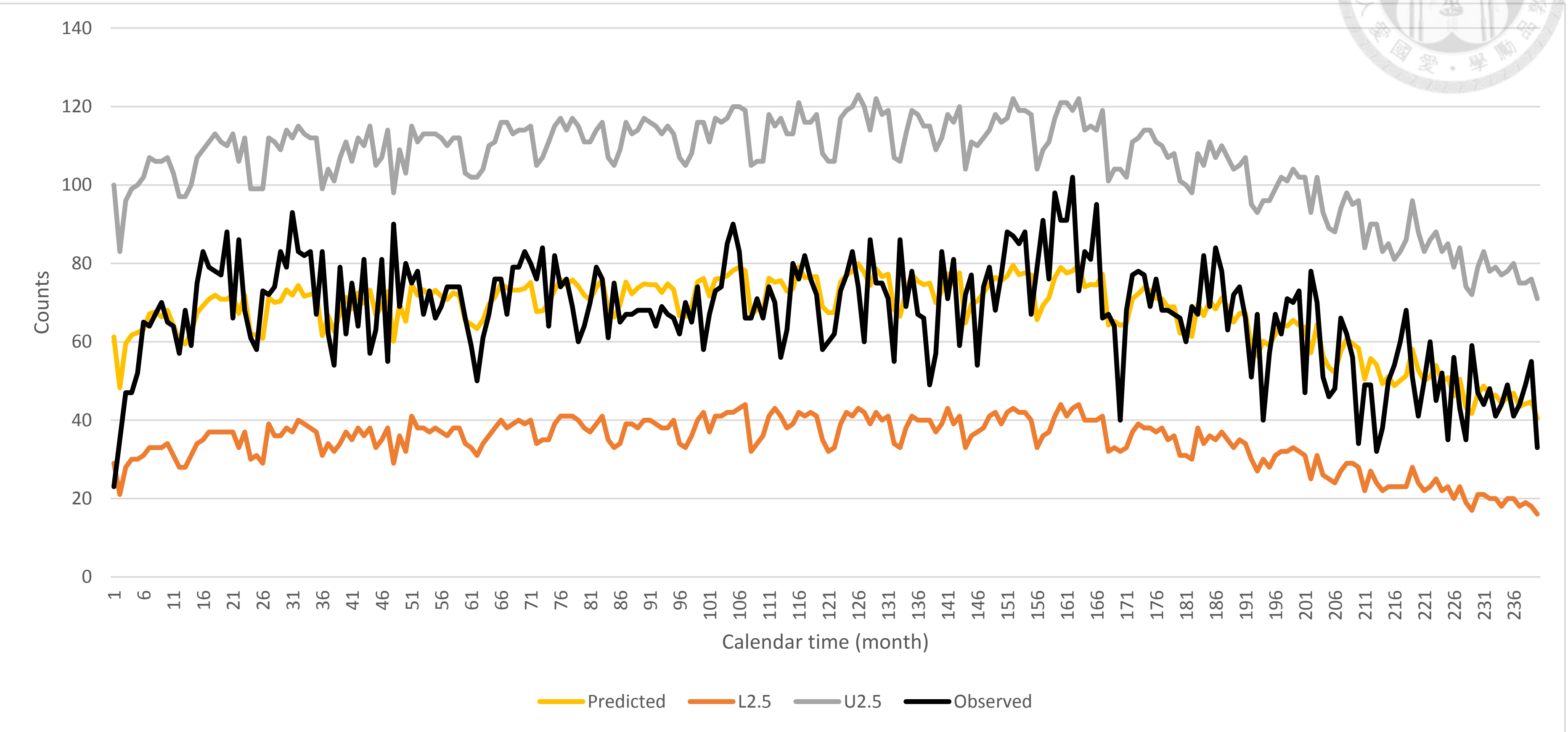
Figure 5.4. 2 Bayesian approach, tracking plot



rho.0 intercept, rho[1]:AR(1), rho[2]:AR(2), b[1]:age, b[2]:gender,

b[4]:spring/winter, b[5]:summer/winter, b[6]:autumn/winter

Figure 5.8. 1 Prediction of overall HAI (cubic trend, AR(1), and covariates adjusted) with 95%CI



AR(1), season, cubic trend, and covariates (age/gender) adjusted prediction (data trained till Dec. 2013)

Figure 5.8. 2 Prediction of overall HAI (cubic trend, ARMA (3,1), and covariates adjusted) with 95%CI

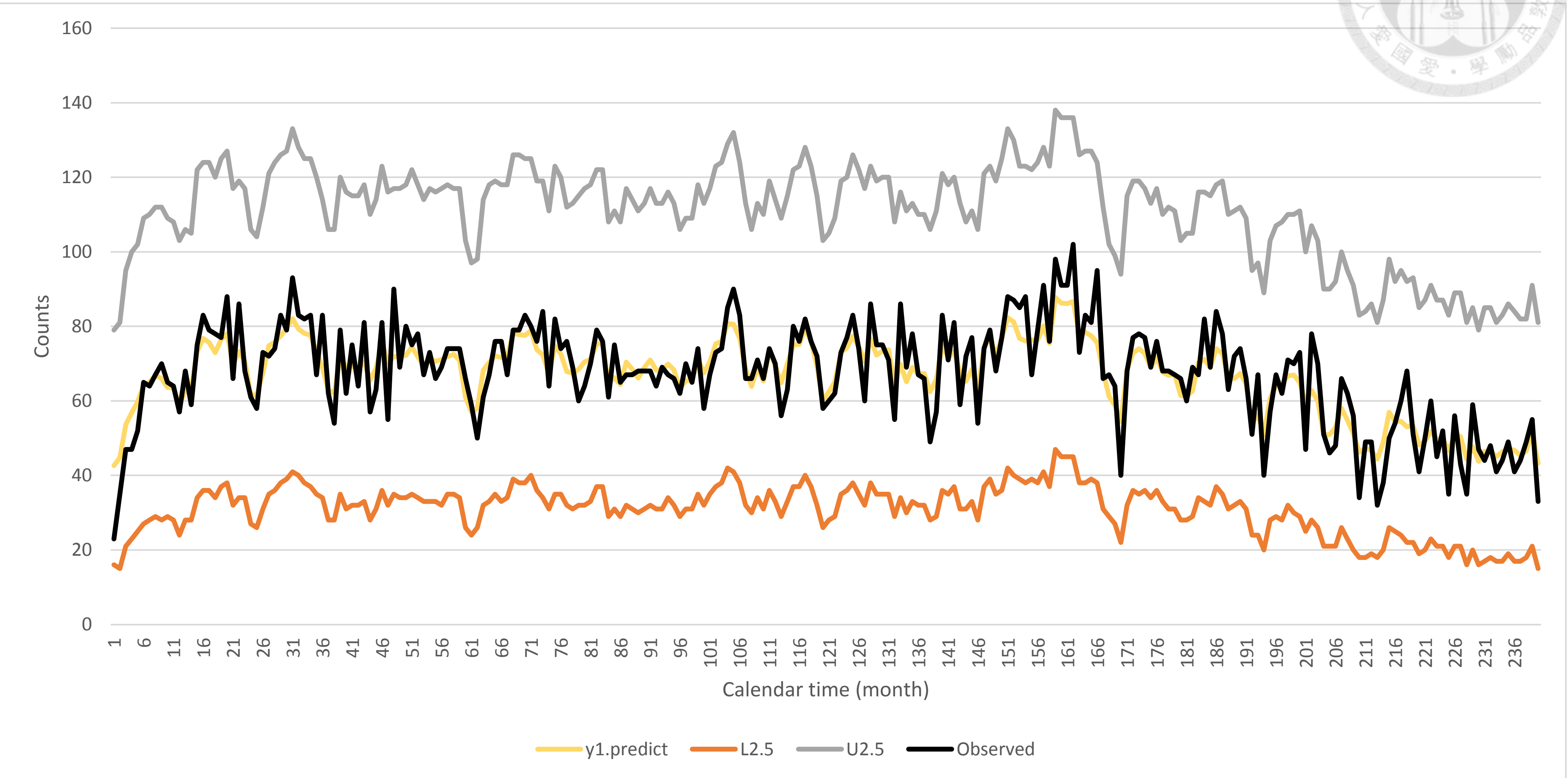
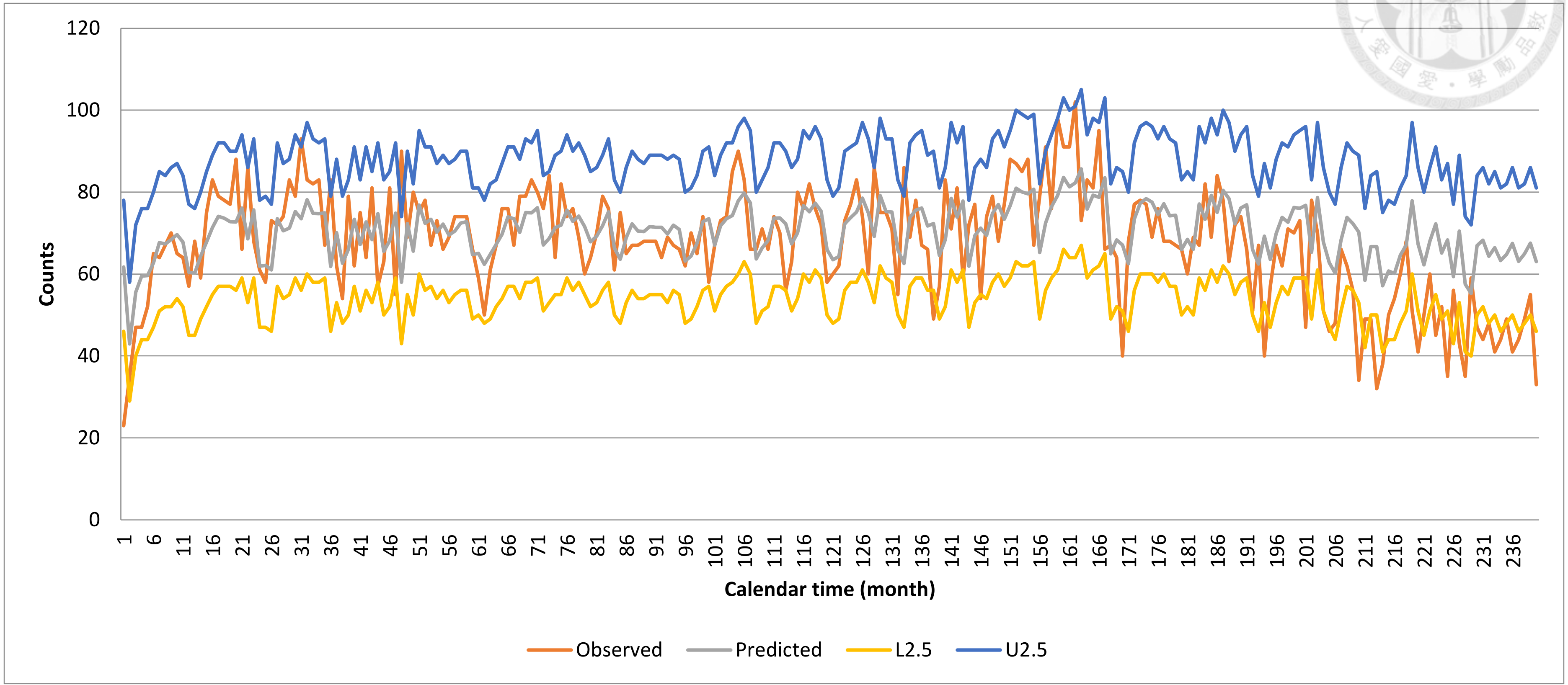


Figure 5.8. 3 Prediction of overall HAI count with 95% CI



AR(1), season and linear trend adjusted prediction (data trained till June, 2005)

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