The Impact of Legislative Measures for Infection Control on Healthcare Quality and Hospital Utilization

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The Impact of Legislative Measures for Infection Control on Healthcare Quality and Hospital Utilization

A Dissertation

Submitted to the Department of Public Health

and the Graduate School of Yonsei University

in partial fulfillment of the

requirements for the degree of

Doctor of Philosophy in Public Health

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June 2024

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Acknowledgement

Without the extensive support and guidance of numerous individuals throughout my graduate school journey, I find it difficult to envision myself completing this dissertation. I am deeply grateful to each person who has profoundly influenced me during my time on this academic path.

First of all, I would like to express my sincere gratitude to my dissertation advisor, Dr. Eun-Cheol Park, for his indispensable guidance, support, and encouragement throughout the entire research process. His expertise, patience, and unwavering commitment to excellence have been instrumental in shaping this study. Since the beginning of the program, his perceptive insights into healthcare policies and the broader landscape of Public Health have consistently made me realize and appreciate by the depth of this academic field. Being granted the opportunity to join Ph.D. program in Professor Park's lab was profoundly an honor for me, and his wise guidance has been pivotal in navigating this scholarly journey.

I am sincerely grateful to Professor Chung Mo Nam, whose passionate introduction to biostatistics has been astounding. Recognizing him as the foremost scholar in the field, it was a privilege to attend his classes and seek his guidance on statistical matters. I deeply appreciate his generous investment of time in discussing the methods for this dissertation and assisting me through statistical challenges.

I am deeply thankful to Professor Sung-In Jang for his valuable feedback and guidance, serving as a supportive mentor for students. He not only demonstrated exceptional leadership in research group projects but also provided insightful teaching in research methodologies. His meticulous instructions on various research aspects ensured my success, and his example illustrated the proper attitude and stress management skills essential for researchers, particularly during challenging times.

I am grateful to Professor Jae Yong Shin for his dedication to offering students exposure to diverse research methods and projects. He strives to create an environment where students can concentrate on their research, and ensures they have the necessary resources. Participating in one of his projects was an honor for me. I gained valuable insights not only into the subject matter but also into his diligent approach to task management.

I would like to convey my appreciation to Professor Suk Yong Jang, whose support in instructing me on qualitative approaches in health policy and management, as well as guiding me through government-sponsored research group projects, has facilitated my academic growth. Not only an exceptional professor, but also a compassionate mentor, encouraged me through my academic journey in the program.

Thank you to all my seniors and colleagues at the Department of Public Health: Jieun Jang, Wonjeong Chae, Junhyun Kwon, Hin Moi Youn, Hyeon Ji Lee, Doo Woong Lee, Wonjeong Jeong, Jae Hong Joo, Seung Hoon Kim, Bich Na Jang, Soo Hyun Kang,

Sung Hoon Jeong, Minah Park, Kyungduk Hurh, Hyun Kyu Kim, Fatima Nari, Shinetsetseg Oyuntuya, Natalia Nebrobkova, Yun Hwa Jung, Jinhyun Kim, Yun Seo Jang, Ye Seul Jang, Dan Bi Kim, Ji Su Ko, Jae Hyeok Lim, MinJeong Joo, Cho Rong Kim, Ah Jung Ko, Su Min Park and Se Mi Park. For four years we took classes together, prepared presentations, and discussed our theses. I will always be immensely grateful to my colleagues for sharing their time and their concerns with me.

Special thanks to Hye Jin Joo, Yu Shin Park, and Il Yun for supporting me academically and in my school life throughout my studies. Your presence and support will always be fondly remembered as an integral part of my time in graduate school. Adding to the expressions of gratitude, I would like to give a shout out to Dr. Joo for the warm welcome and guidance given in my early days of graduate school and continuing to this day.

I owe immense gratitude to my family for their unwavering love, encouragement, and understanding throughout this challenging journey. Their steadfast support and faith in my abilities have been the pillars of my strength and motivation. Above all, I want to express my deepest thanks to my parents, Dr. Kim and Ryu, who are the most compassionate and devoted individuals I know. I am deeply indebted to you for all that you have done for me. I cannot imagine completing this course without your support. To my beloved husband, thank you for bringing joy even the toughest days. I am truly blessed to have you as my lifelong partner, and I eagerly anticipate our future together. Additionally, to my big brother, my lifelong mentor, thank you for the comfort

and guidance you always provide. Last but not least, my in-laws who always supported my career and was understanding and loving for who I am. I look forward for our time together and forth.

I wish to express my sincere gratitude to all my extended family and friends who have supported me in completing my graduate studies. Your support is remembered and cherished.

Lastly, I would like to thank all the participants who generously volunteered their time and shared their insights for this study. Their contributions are invaluable, and this research would not have been possible without their cooperation and participation.

June 2024

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ABSTRACT

The Impact of Legislative Measures for Infection Control on Healthcare Quality and Hospital Utilization

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Background: The enactment of the Patient Safety Act in 2016 and subsequent amendments to the Medical Service Act in South Korea aimed to enhance infection control measures in healthcare institutions. These legislative measures were introduced to address the increasing concern over patient safety and infection control. This study investigates the impact of these legislative measures on healthcare quality and hospital utilization, providing a comprehensive analysis of their effectiveness across different types and sizes of hospitals.

Methods: Data were obtained from the National Health Insurance Service National Sample Cohort (NHIS-NSC) for the period from 2013 to 2019. The study employed an interrupted time series (ITS) design with segmented regression to analyze the change in

level and trends before and after the interventions. Key outcome variables included the use of restricted antibiotics, the incidence of healthcare associated infections, length of hospital stay, and total medical expenditure. The analysis included multiple hospital types: tertiary hospitals, general hospitals, hospitals, and non-applicable hospitals. Statistical models were adjusted for potential confounders, including patient demographics and hospital characteristics. In order to minimize the possible bias of performing ITS, ITS reporting guidelines were employed and Generalized Estimating Equations(GEE) were used for statistical method, which is the recognized method for accounting for clustering and repeated longitudinal observation.

Results: The implementation of the Patient Safety Act, amendment of the Medical Service Act and subsequent infection control regulations resulted in reductions in use of restricted antibiotics and healthcare associated infections. For instance, in tertiary hospitals, the trend change after the second intervention showed a statistically significant reduction in the use of restricted antibiotics(Trend change after second intervention: $Exp(\beta_5)=0.9666$, p=0.0005). The mean incidence of healthcare associated infections decreased following the first intervention in hospitals(Trend change after first intervention: $Exp(\beta_3)=0.9897$, p=0.04). Additionally, the length of hospital stays decreased across all hospital types, yet the total medical expenditure increased in hospitals and non-applicable hospitals gradually(Trend change after first intervention at hospital: $Exp(\beta_3)=1.0023$, p=0.0081, Trend change after first intervention at non-

applicable hospital: Exp(β_3)=1.0030, p=<.0001, Exp(β_5)=1.0083, p=<.0001,). In a segmented regression models stratified by levels of financial incentive for infection control, level 1 and 2 showed significant decrease in use of restricted antibiotics(Trend change after first intervention at grade 1: Exp(β_3)=0.5101,p<.0001 and trend change after second intervention at grade 2: Exp(β_5)=0.9715, p=0.0002).

Conclusion: The legislative measures for infection control have led to enhanced healthcare quality and more efficient hospital utilization. General hospitals and tertiary hospitals exhibited more pronounced improvements than smaller hospitals, suggesting that larger institutions may have more resources to effectively implement and benefit from these legislative measures. The effects varied by hospital size, suggesting the need for tailored policy approaches to maximize the benefits of infection control regulations. Continuous evaluation and adaptation of these policies are crucial to sustaining improvements in patient safety and healthcare quality. This study underscores the importance of government-led initiatives in driving improvements in healthcare systems and highlights the need for ongoing support and resources for smaller hospitals to achieve similar outcomes.

Keywords: infection control, patient safety, healthcare quality, infection control regulation, healthcare utilization

I. Introduction

1. Background

The significance of quality of care has become increasingly recognized within the realm of healthcare provision subsequent to the establishment of foundational patient health facilitated by advancements in medical care. The significance of quality of care is tantamount to the advancements in technical capabilities within the field of medical practice in healthcare.[1] Types of quality of care could vary; it includes patient safety, patient experience, and end of life care, etc. Among them especially, patient safety is directly connected to the health outcome of patients and widely applicable to everyone who use healthcare.[2] Patient safety can be divided into smaller units. Instances of inadvertent errors committed by healthcare personnel, lapses in infection control protocols, or occurrences stemming from patient inattentiveness exemplify components pertinent to patient safety. In contrast to errors directly attributed to human actions posing threats to patient safety, instances of infection control challenges often arise with greater inevitability, albeit accompanied by relatively clearer and discernible preventive measures.[3]

Infection control is a fundamental aspect of medical practice, yet in situations involving significant external threats or a surge in healthcare associated infections, the

establishment of a central administrative system or entity becomes imperative. A dedicated task force should be convened to investigate such cases and develop effective solutions and preventive measures for infection management. The central task force not only investigates instances of infection but also reconstructs the entire hospital system to proactively prevent future infections[4]. Their responsibilities encompass infection surveillance, the establishment and revision of infection control guidelines, staff training and more.

In 2010, a devastating medication error tragically affected a 7-year-old cancer patient due to an error by healthcare personnel in Korea.[5] This incident garnered widespread attention and societal concern, prompting legislative action following advocacy efforts by the grieving families. This resulted in the enactment of the Patient Safety Act in 2015, marking a pivotal moment where awareness of patient safety extended beyond healthcare facilities to the broader public sphere. Patient safety was subsequently assessed to qualify for incentives or to adhere to the fundamental criteria of government evaluations. Infection control emerged as an essential aspect of patient safety measurement, underscoring its significance within the realm of hospital quality care.[6]

Following the enactment of the Patient Safety Act, major amendments were made to the Medical Service Act pertaining to infection control. While legal regulations regarding infection control were already in place, revisions were implemented concerning the scope of hospitals required to adhere to these regulations as legal mandates. Previously, the target for regulation was hospitals and general hospitals with over 200 beds, as well as medical institutions operating intensive care units(ICU) regardless of the bed counts. However, with

the revision, the applicability of the law was extended to include local hospitals with over 150 beds and general hospitals with over 100 beds. Moreover, the number of obligatory infection control practitioner was differentially distributed per bed counts of the institution.[7]

Korea's healthcare delivery system comprises primary clinics, secondary small and medium hospitals, general hospitals, and tertiary hospitals. Despite this arrangement, patients typically favor tertiary hospitals over smaller hospitals.[8] There is an institutional mechanism to regulate reckless visits to tertiary hospitals such as higher medical service fee and imposing extra fees if medical treatment request is not suggested from smaller medical institutions, but the excess visit still continues.[9] This preference risk compromising care quality in smaller medical institutions due to impairment of sustaining and developing for better quality of care. For example, government-funded incentives and certification evaluations beside the regular insurance fee tend to benefit larger hospitals, creating financial challenges for smaller ones.[10,11] A stratified approach is essential for effective healthcare delivery, ensuring that tertiary hospitals can prioritize emergencies and severe illnesses while smaller hospitals provide remaining care.

Several studies have explored the impact of infection control within hospitals, focusing either on individual institutions or taking a narrow, detailed approach to the system. Some have examined the implementation of infection control measures by infection control practitioners and subsequent outcomes, while others have analyzed the placement of infection control personnel within institutions and its effect on health outcomes. It is

imperative to examine infection control regulations from a broader perspective. Such regulations that are particularly applied universally across hospitals in Korea gives the opportunity to understanding how various sizes of hospitals adapt to these regulations and their impact on outcomes.

2. Study Objective

This study aims to examine the effect of the series of legislative changes regulating infection control in hospitals on healthcare quality and utilization. In particular, this study will observe how different types of hospital in size have impact on the quality of care regarding infection control and related healthcare utilization. The results of this finding will suggest insight to evaluate how the enactments were effective and how differently the regulation was adapted to various sizes of hospitals and see the effectiveness.

Details of the study objectives are as follows:

(1) To investigate the difference in prescription in restricted antibiotics for patients and amount of the antibiotics using days of therapy before and after the laws regulating infection control initiation in hospitals.

(2) To investigate the difference in diagnosis of healthcare associated infection: Urinary tract infection, pneumonia, sepsis, pseudomembranous colitis during the hospital stay

(3) To investigate the difference in healthcare utilization related to infection control by total days of hospitalization and total health expenditure per episodes

II. Literature Review

1. Quality of care model – The Systems Engineering Initiative for Patient Safety(SEIPS) model

The evaluation of the healthcare system was conducted using indicators that measure its adequacy in terms of structure, process, and outcome, which was a model created by Avedis Donabedian in 1966.[12] There are several methods to measure the quality of care in medical institutions, but most of the frameworks have the same base of structure, which trace back to Donabedian model. Subsequently, this study adopted Avedis Donabedian's model as the research model.[13] Each element that consists the quality of healthcare are important, and usually the measurement is performed in process and outcome. According to this model, the contextual intricacies of the Patient Safety Act and amendments to the Medical Services Act concerning infection control could be analyzed in fragmented segments, and examine how the legislative intent aimed to improve the quality of care through amendments in the stages of the model.

The structure part represents factors that have an important influence on maintaining the quality of service and primarily refers to the human, material, and financial resources required to provide services.[14] The process refers to all activities required to

deliver care and reflects how the system works to achieve desired outcomes. Therefore, a process that does not affect the results is meaningless.[15] The outcomes concern the impact on the patient and whether the ultimate goal has been achieved. The outcome indicators are the final products of the service, mainly referring to changes in health status. Examples include reduced mortality, length of stay, adverse incidents, emergency hospitalizations, and patient experience.[16]

Although the content of the Patient Safety Act and the amendments to the Medical Services Act concerning infection control differ, their essence is similar. Both legislations mandate the assignment of dedicated personnel and regulate the number of the personnel based on the hospital size, estimated by the number of beds. There are accompanying incentives for the establishment and operation of related committees, but the ultimate aim of these laws is to create a task force within hospitals led by dedicated personnel, who are committed to patient safety and infection control, thus fostering a hospital-wide culture of safety and effective infection management.[14]

To observe the effectiveness of dedicated personnel, the systems engineering initiative for patient safety model(SEIPS) can be adopted as a research model.[17] SEIPS, an integrated concept of structure-process-outcome(SPO) model by Donabedian in 1988 and work system model of Smith and Carayon in 2006, is the model notably expands and emphasizes the structure component, asserting that not only are the SPO components interconnected, but there are also interactions among the elements within the structure itself. At the center of the SEIPS model lies the work system, which encompasses various

elements such as individuals, tasks, tools and technologies, the physical environment, and organizational conditions. This framework facilitates a comprehensive and nuanced analysis that remains adaptable, allowing for the exploration of a broad spectrum of patient safety issues.[18] Assigning a dedicated employee to each specific area is anticipated to enhance the process component of the model within the hospital care setting.[19] This research is conducted with the foundational premise of this theory. Should the work system be devoid of barriers and with supplementary inputs to facilitate coherent interactions, it is anticipated that there will be a favorable influence on process indicators, ultimately culminating in positive outcomes.[20]

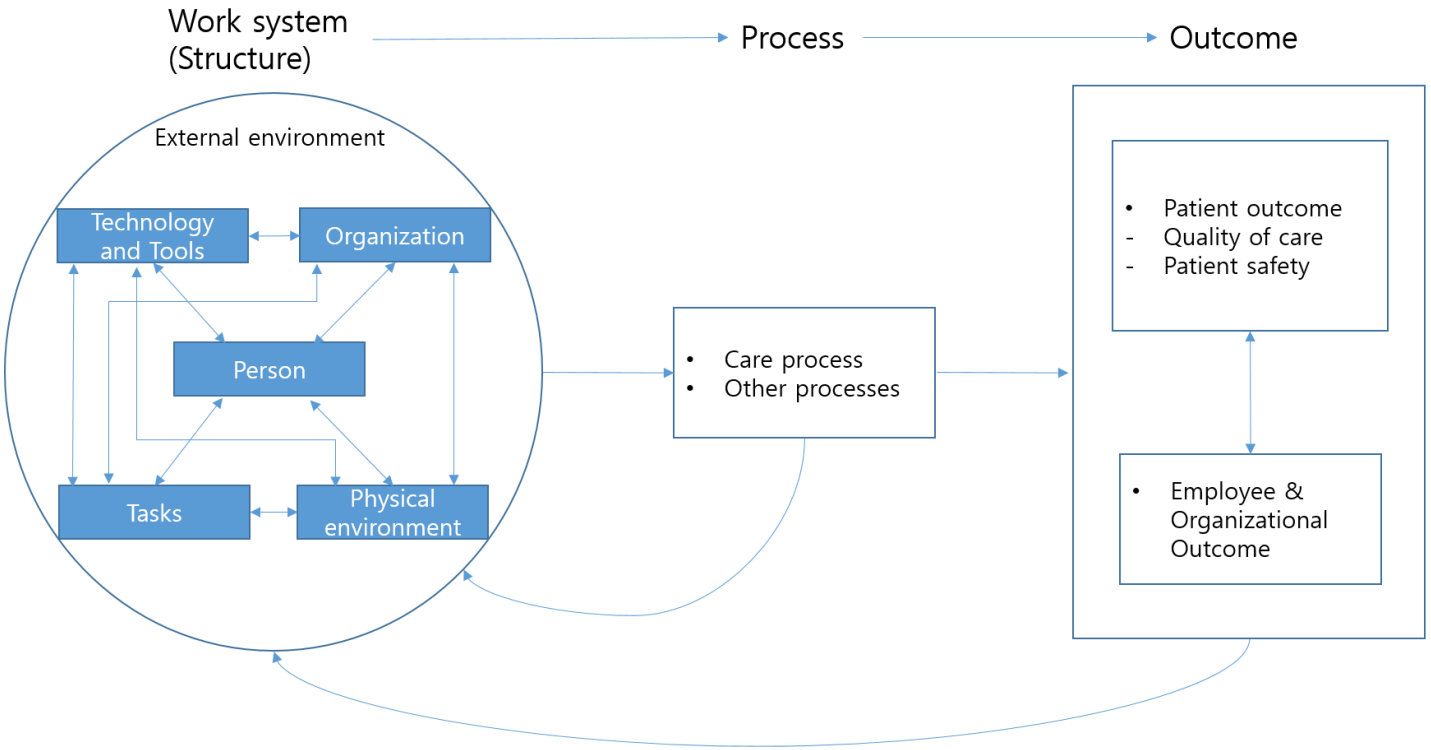

Figure 1. Systems Engineering Initiative for Patient Safety(SEIPS) Model

Source: Carayon P. Human factors of complex sociotechnical systems. Applied ergonomics 2006;37:525-35.

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2. Policy background: Patient Safety Act

The World Health Organization(WHO) defines patient safety as 'the absence of preventable harm to patients during the health care process and the reduction of the possibility of health-related harm to the lowest acceptable level'.[21] The publication of a report by the American Academy of Medicine titled "To Err is Human: Building a Safer Health System" was critical milestone for the issue of patient safety to emerge as a major policy agenda in the health care field at the time.[22] Patient safety has become a global concern as the WHO adopted a resolution at the World Health Assembly in 2002 urging member countries to pay close attention to patient safety, and accordingly launched a patient safety program called the World Alliance for Patient Safety in 2004. In 2003, Agency for Healthcare Research and Quality(AHRQ) published "Guide to Patient Safety Indicators", which is used until today, updated every year with relevant indicators added.[23,24]

Several countries have legislated the Patients safety context starting in the early 2000s. In United Kingdom, an independent organization called the National Patient Safety Agency was established and divided into an organization in charge of reporting and analysis and an organization in charge of improvement activities in 2001.[25] Denmark was the first to enact legislation in 2003, and to establish the world's first nationwide medical accident reporting system.[26] In the United States, The Patient Safety and Quality Improvement Act

was signed into law in 2005. This legislation aims to directly and systematically address patient safety and by establishing a new national medical error reporting system and providing federal privilege for data collection.[27] Japan in 1999 through 2009, basic patient safety system was established that included the creation of a patient safety division(embedded in law under Medical Service Act article 6) and an incident-reporting system ran by the government from the perspective of systems error rather than individual responsibility.[28]

Patient Safety Act in Korea has been enacted in January 2015 and implemented in August of 2016. The Patient Safety was implemented in detail as a law, enforcement ordinance, and enforcement regulations consisting of a total of 19 articles.[29] Among the matters specified in the law, the role of health care institutions is to establish and operate a patient safety committee that establishes and implements plans, and assign dedicated personnel in charge of patient safety. In 2016 when the legislation was first implemented, general hospitals with more than 100 beds and local hospitals with more than 200 beds were required to have one assigned personnel, and general hospitals with more than 500 beds were to have at least two people in demand. Personnel dedicated to patient safety do not perform any other work, but only task related to patient safety.[5,30] Following the enactment of the legislation, there was a subsequent rise in reports of patient safety incidents over the ensuing years. While the majority of these reports were made by dedicated patient safety personnel, the involvement of other individuals, including healthcare workers and others, suggests an integration of patient safety education and

awareness into the prevailing culture.[31]

Table 1. Comprehensive overview of legislative measures addressed in this study

Features	Patient Safety Act	Medical Service Act (amendment regarding infection control)
Enactment and enforcement date	February, 2015 August, 2016	June, 2016 October, 2018
Content	**Assignment of dedicated personnel for patient safety** - At least one dedicated personnel for hospitals with 200 or more beds - At least one dedicated personnel for general hospitals with 100 to less than 500 beds - At least two dedicated personnel for general hospitals with 500 or more beds - Dedicated personnel must be individuals who have worked in healthcare institutions for at least five years after obtaining a medical license **Establishment of a Patient Safety Committee** - General hospitals or hospitals with 200 or more beds must establish and operate - The committee is responsible for formulating and implementing plans to prevent the recurrence of patient safety incidents - The committee is responsible for appointing and assigning dedicated personnel for patient safety, and participate in establishing patient safety system in the institution	**Assignment of dedicated personnel for infection control** - At least one dedicated personnel for hospitals with 150 or more beds - At least one dedicated personnel for general hospitals - Dedicated personnel should be either physicians or nurses, or individuals whom the director of the medical institution acknowledges as possessing substantial expertise and experience in the field of infection management **Establishment of an Infection Control Committee** - Hospitals with 150 or more beds or general hospitals must establish and operate - The committee is responsible for formulating and implementing plans to prevent the recurrence of healthcare associated infections - The committee is responsible for appointing and assigning dedicated personnel for infection control, and participate in establishing infection control system in the institution

* The content above contains the provisions of the law as it was enacted at the time, which may differ from the current law.

3. Policy background: Infection control related legislations

Healthcare associated infection is a major issue of patient safety. It complicates a significant proportion of patient care deliveries, adds to the burden of resource use, and contributes to unexpected deaths.[32] The concept of infection control predates the introduction of quality healthcare standards. It constitutes a significant component of patient safety, prompting numerous endeavors over time to mitigate or prevent its occurrence.[33]

United States infection control is primarily regulated at the federal level by agencies such as the Centers for Disease Control and Prevention(CDC), the Food and Drug Administration(FDA), and the Occupational Safety and Health Administration(OSHA). These agencies develop guidelines, standards, and recommendations for infection control practices in various healthcare settings. However, there is no legal binds in these guidelines provided by multiple governmental institutions[34]. Rather, individual state governments have their own regulations regarding infection control. In the United Kingdom(UK), infection control oversight is multifaceted, notably the National Health Services(NHS) and the Care Quality Commission(CQC) serving as the apex authority for care standards, ensuring adherence to infection control protocols among healthcare providers[35]. Japan has “Infectious Disease Control Law(IDCL)”, which provides the legal framework for preventing the spread of infectious diseases, including healthcare-associated infections.

The IDCL specifies measures for disease surveillance, reporting, quarantine, and outbreak response. It also outlines the responsibilities of healthcare facilities, healthcare workers, and public health authorities in managing infectious diseases.[36-38]

In Korea, legislation concerning healthcare-associated infections is governed by Articles 43 and 46 of the Medical Service Act, and the infection-related legal contents to be addressed in this study are included within the Medical Services Act.[39,40] Regulations concerning infection prevention and control have undergone several revisions over an extended period, often involving minor adjustments. Among numerous revisions, the significance of the 2016 amendment lies in its mandate for hospitals to allocate infection control personnel proportional to their size. Prior to the revisions, only the medical institutions equipped with intensive care units were mandated to employ specialized staff and maintain an infection control task force within the medical facilities. Moreover, it is an important feature that starting in 2016 revision, staffing and deployment standards for personnel performing infection control duties in the infection control division was specified.[6] Dedicated personnel should be either physicians or nurses, or individuals whom the director of the medical institution acknowledges as possessing substantial expertise and experience in the field of infection management.[41] Before the modifications, only requirements for the educational attainment of dedicated staff in infection control was stated.[40]

Table 2. Article 43 Enforcement Rule of Medical Service Act revision over time

Timeline	Law revision
2008.04.11	Pursuant to Article 47 (1) of the Act, the head of a general hospital with 300 or more beds must establish and operate an infection response committee (hereinafter referred to as the "Committee") to prevent hospital infections.
2012.08.02	Pursuant to Article 47 (1) of the Act, the head of a hospital (applicable only to cases with 200 or more beds) and general hospitals that operate intensive care units shall consult with the Infection Control Committee (hereinafter referred to as the "Committee") to prevent hospital-acquired infections. A management office must be established and operated.
2016.10.06	In Article 47 (1) of the Act, "hospital-level medical institutions of a certain size or larger as prescribed by Ordinance of the Ministry of Health and Welfare" refers to medical institutions classified as follows: 1. Period until March 31, 2017: General hospitals and medical institutions with more than 200 beds that operate intensive care units 2. Period from April 1, 2017 to September 30, 2018: General hospitals and hospitals with more than 200 beds 3. Period from October 1, 2018: General hospitals and hospitals with more than 150 beds
2021.06.30	In Article 47 (1) of the Act, "hospital-level medical institution of a certain size or larger as prescribed by Ordinance of the Ministry of Health and Welfare" refers to a hospital-level medical institution with 100 or more beds.

4. Prior studies on regulations in patient safety and infection control

There have been few studies that have macro-evaluated the effectiveness of regulations governing infection control or patient safety. Therefore, studies that addressed the mechanisms by which each element of the law, as implemented, produced positive outcomes were selectively sought. Specifically, studies were identified that demonstrate the beneficial impacts associated with the legal mandates for staffing and the establishment and operation of relevant committees.

Several studies examining human factors in healthcare suggest that human resources can significantly impact patient care processes. Enhancing individual capabilities and ensuring job quality can ultimately influence patient outcomes.[15,42] A few studies written by the actual hands-on workers, practitioners, emphasize the importance of related education to dedicated personnel.[41,43] The authors discuss that a concurrent enactment of multiple laws concerning patient safety and infection control has led to the establishment of numerous roles for specialists in these fields. They particularly highlight the necessity for smaller hospitals to prioritize the training of these dedicated personnel.

Moreover, there are existing studies related to the establishment and operation of committees concerning patient safety or infection control. These studies report positive patient outcomes as a result of regular discussions on related topics within small groups in wards.[44] Additionally, research using interviews as a methodology has shown that even

healthcare professionals within the same field benefit significantly from listening to and communicating with those in different areas.[45] Commonly, these studies indicate that such committee activities not only benefit the committee members but also contribute to the development of a culture of patient safety throughout the hospital.[45-47]

Beyond statutory requirements, research has also explored the effects of ancillary elements introduced by legislative implementation. The enactment of the law provides for specific fees, and scholarly investigations have examined the positive outcomes associated with these financial allocations.[37,48] Moreover, eligibility for these fees requires compliance with criteria that extend beyond legal mandates, including certification. Research has been conducted examining patient outcomes in relation to certification status. The standards set by the Joint Commission International(JCI) focus on improving quality and ensuring patient safety, which includes better management of antibiotics. As a result, the use of restricted antibiotics dropped by about 14% from one phase of the program to the next.[49] A study indicated that resource allocation towards infection control in preparation for certification facilitated an enhanced focus on this area in the medical institution, subsequently improving the quality of infection management.[38]

5. Theoretical model for the study

With the law revisions and policy implementation about infection control by the government, infection control practitioner will be placed in each medical institution, and infection control committee is required to be operated and have regular meetings about the internal infection control system and cases or programs. Significance of infection control in the hospital and safety culture will be embedded. This will lead to improved health outcome of hospitalized patients and changes in healthcare utilization among inpatients by reducing the length of stay and decrease in medical expenditure. Restricted antibiotics prescription will be reduced by the stewardship of infection control professional, and healthcare associated infection will be likely to decrease, for the process indicators will be improved by the profession and the hospital in total. Lastly, the improved health outcome of hospitalized patients will lead to avoidable outpatient or emergency department visit reduction, and overall better health outcome for the population and removing unnecessary healthcare utilization.

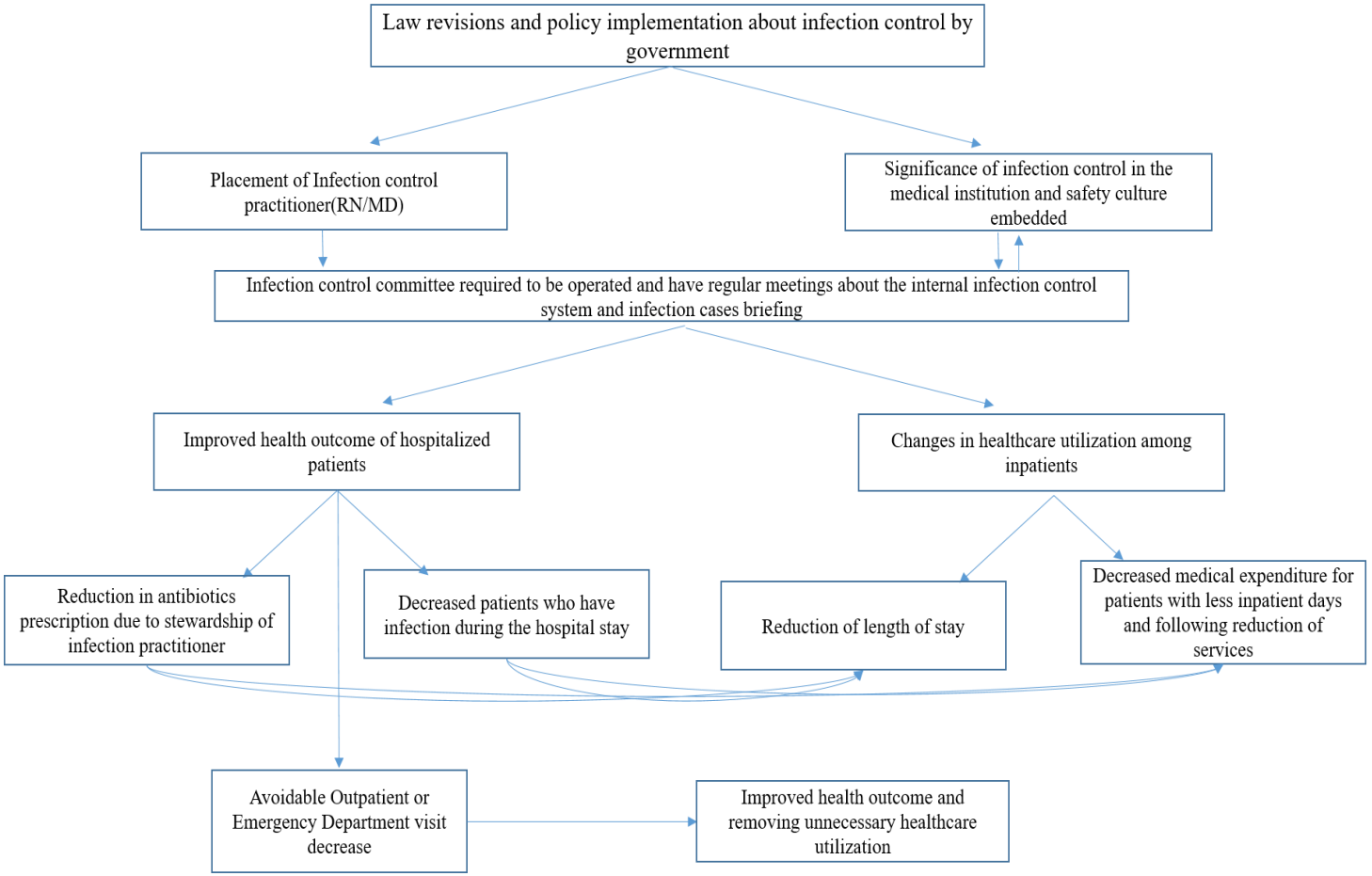

Figure 2. Theoretical Model

III. Material and Methods

1. Data and Study Population

The data in this study were obtained from the National Health Insurance Service National Sample Cohort(NHIS-NSC) for years 2002 through 2019. The NHIS-NSC data include a sample of 2.2% of 48,222,537 Korean individuals in 2006 using stratified random sampling by age, sex, and health insurance premium, and observed from 2002 to 2019. Records of years 2002 through 2005 were included using the exclusive individual identification number given to insurance eligible individuals in 2006 retrospectively. These data were constructed to provide representative information regarding Korean citizens' utilization of health insurance and health examinations for policy makers and public health research. The NHIS-NSC records patients' claim data into four categories: insurance eligibility, medical institutions' data, health examination data, and medical treatments which include diagnosis codes, medications, and treatments.

In the total data of 3,972,318 hospitalizations, episodes of patients who transferred from other medical institutions, who could have experienced healthcare associated infection in the previous medical institution, and those who were hospitalized for less than

two days, and lastly, those who have infectious disease as their primary diagnosis were excluded, leaving 1,125,189 claims. Moreover, for comparable data composed of acute care hospitals, only the episodes from tertiary, general hospitals and local hospitals were included in the study. There are cases where several claims are made in one episode of hospitalization, when there are divided payments and longer hospital stays. By sorting out the episodes that are divided in several claims even though it was the same one-episode, downsized the data. Therefore, after leaving the first claim of each episode, the data consisted 657,784 episodes. In the final phase of data preparation, the temporal scope of the investigation was confined to the period between May 2013 and December 2019. Throughout this timeframe, instances that did not fall within these parameters were excluded, as were any data points lacking in covariate information. Consequently, the dataset was refined to include a total of 614,127 episodes for subsequent analysis, as depicted in Figure 3.

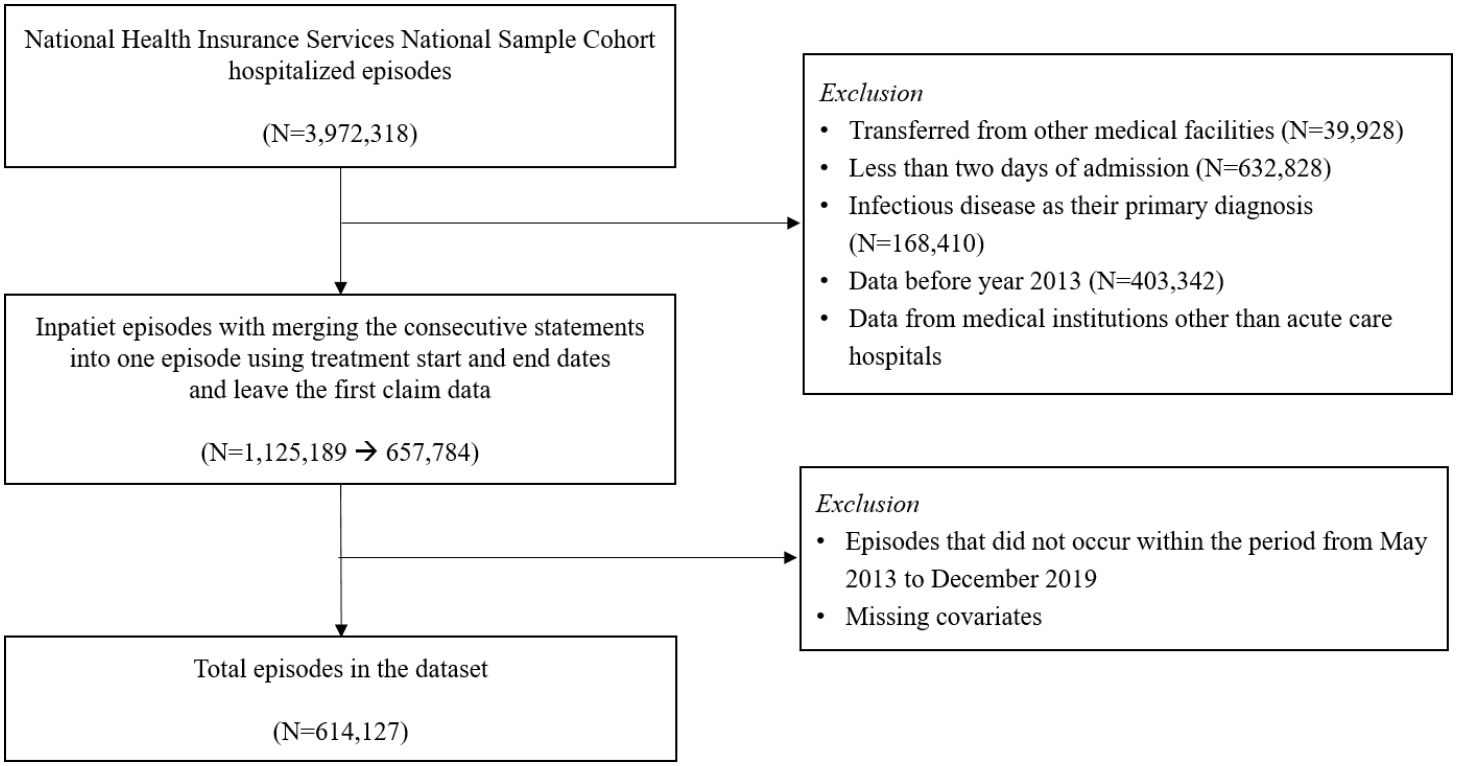

Figure 3. Flowchart of study episodes selection

2. Definition of Variables

1) Dependent Variables

The dependent variables in this study encompass two primary domains: healthcare outcomes and healthcare utilization. First, healthcare outcomes are delineated by several indicators including healthcare associated infections such as urinary tract infection, pneumonia, sepsis, pseudomembranous colitis, and the administration of restricted multi-resistant antibiotics, and the duration of antibiotic therapy using restricted antibiotics. A healthcare associated infection is categorized based on diagnoses identified by specific ICD-10 codes recorded as sub-diagnoses during hospitalization.[50-54] Restricted antibiotics refer to certain antimicrobial drugs that have limitations placed on their use in medical settings. These restrictions are implemented to combat the growing issue of antibiotics resistance, and they are mostly consisted of multi resistant antibiotics. The occurrence of infections or the administration of antibiotics is quantified as a binary variable, whereas the extent of antibiotic treatment is quantified as a count variable. These parameters serve to assess infection-related health outcomes, particularly those attributable to in-hospital infection control measures. Secondly, healthcare utilization is assessed through the aggregated duration of hospital stays and the total medical expenses throughout each hospital stays. To ensure a precise evaluation of medical expenditures that accounts for

inflationary effects, the total medical expenses are adjusted using an annual relative value scale conversion factor.

Table 3. Claim codes for restricted antibiotics and healthcare associated infection

Variables		Claim code
Restricted antibiotics	Glycopeptide (Teicoplanin, Vancomycin)	“247203BIJ”, “247205BIJ”, “247204BIJ”, “478300BIJ”, “247206BIJ”, 234901BIJ”, “234903BIJ”, “234902BIJ”
	Oxazolidinones (Linezolid)	“412930BIJ”, “412901ATB”, “412903ATB”
	Glycylcyclines (Tigecycline)	"495301BIJ",
	Polymyxin (Colistin)	"484201BIJ"
	Carbapenem (Imipenem, Ertapenem, Doripenem, Meropenem)	"190702BIJ", "190703BIJ", "190704BIJ", "447701BIJ", "329400BIJ", "329300BIJ", "472900BIJ", "593201BIJ",
Healthcare Associated Infection	Urinary tract infection	"N30" "N10" "N11" "N12" "N13" "N15" "N16" "N390" "O088"
	Pneumonia	"J13" "J14" "J15" "J16" "J18"
	Sepsis	"A021" "A207" "A227" "A241" "A267" "A327"A40"
	Pseudomembranous Colitis	“A047”

*KCD diagnosis codes and pharmaceutical claim codes are extracted from the medical history database

There are many multi resistant antibiotics in use, but not every antibiotics use should be restricted and watched. WHO published a report on surveillance of antibiotic consumption in 2018 and renewing annually, reporting the need for a standardized approach to measuring antimicrobial consumption. According to this guideline, the AWaRe(access, watch, reserve) classification provides an appropriate framework for target setting, especially with respect to the use of antibiotics, and can be included as an indicator for monitoring and evaluation.[21] Even though WHO publish the AWaRe classification, because patient groups are different and there are variations in races, there is no golden standard list of restricted antibiotics worldwide. Thus, each medical institution independently establishes and implements its own guidelines. Consequently, although certain antibiotics are commonly identified in prior research on restricted antibiotics, there is no complete uniformity across all studies. The research was conducted by defining and identifying antibiotics that were most commonly appeared across studies as restricted antibiotics.[37,55-58]

2) Exposure Variable

The variable of interest in this research pertains to the enactment of the Patient Safety Act in year 2016 and other infection control related policies implemented at the time, and the revision to the Medical Service Act concerning infection control in healthcare facilities in year 2018. In the year 2016, a variety of policies pertaining to infection control were instituted. However, the most emblematic of these was the enactment of The Patient Safety Act, which also represented the earliest related intervention of that year. Thus, the month in which this Act was implemented was designated as the first intervention point in the study. The Patient Safety Act was passed in February 2015 and came into effect in August 2016, while the modifications to the Medical Service Act regarding infection control were approved in June 2016 and implemented in October 2018. This study utilized monthly data intervals, identifying August 2016 and October 2018 as the respective intervention points. Data collection was terminated on December 31, 2019, 14 months subsequent to the second intervention. The interval spanning the first and second interventions was 22 months. In alignment with the stipulations of the interrupted time series design, which mandates that the baseline period surpasses subsequent periods to verify the initial trend, the initial phase was prolonged to be 1.5 times the length of the period succeeding the first intervention. Consequently, the dataset commenced in May 2013, 33 months preceding the initial intervention. Over the 80-month period analyzed, the

coding for the first intervention variable remained at “0” through the initial 33 months, thereafter transitioning to “1”. In a parallel manner, the second intervention variable maintained a “0” code through the 66th month, subsequently changing to “1” through to the conclusion of the study period.

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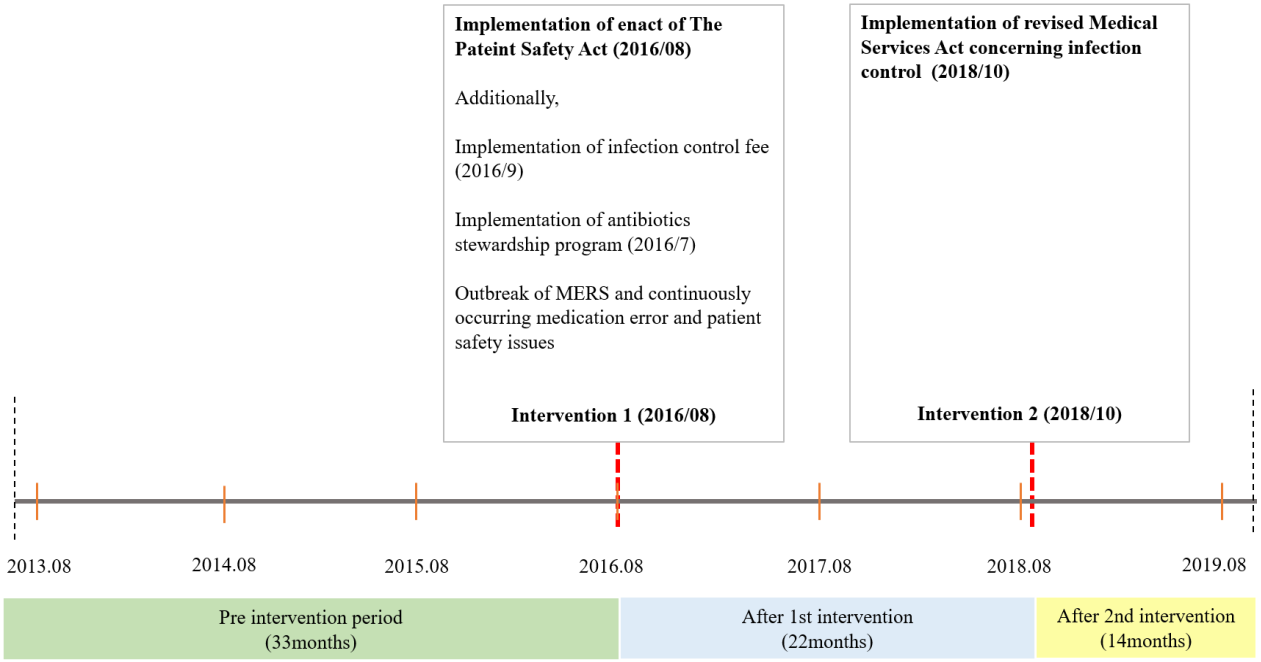


Figure 4. Schematic diagram of the study

3) Independent Variables

The independent variables of this study were age grouped in 10 years(<19, 19-29, 30-39, 40-49, 50-59, 60-69, ≥70), gender (men or women), income level in deciles(none, low 30%, middle 40%, and high 30%), health insurance type(employee insurance, regional insurance, or medical aid), region(capital(Seoul and Kyunggi), metropolitan, other), disability status(present, not present), surgical procedure during the hospital stay(yes, no), invasive treatment during the hospital stay(central catheter, ventilation/tracheotomy, none), region of the medical institution(capital(Seoul and Kyunggi), metropolitan, other), primary diagnosis category(Muscoloskeletal system and connective tissue, Injury/other consequences of external causes, digestive system, respiratory system, neoplasm, circulatory system, else), type of hospital(tertiary, general, and hospital, non-applicable hospital), number of doctor counts in each types of hospitals in quartiles, nurse staffing level in claim code(levels 0 through 7), Charlson comorbidity index(0, 1, 2, 3 or above), process after hospitalization treatment(outpatient follow-up, transfer, deceased, discharged), and seasonality(spring, summer, autumn, winter).

Types of hospitals were grouped in tertiary hospital, general hospital, hospital, and non-applicable hospital. In the healthcare delivery system of Korea, there are tertiary hospitals, general hospitals, and hospitals in that order. Specialty hospitals or public

hospitals are classified as hospital-level institutions. This study includes acute care hospitals, encompassing tertiary hospitals, general hospitals, and hospitals. However, hospitals with fewer than 100 beds are not subject to the Patient Safety Act or the Medical Services Act concerning infection control. Therefore, these hospitals are grouped separately as the non-applicable group.[59] Charlson comorbidity index(CCI) score is an index for assessing the patients' comorbidities for use in longitudinal studies using administrative data. All covariates were adjusted for the analyses.

Table 4. Description of covariates for the analysis

Variables		Description
Individual factors	Age	<19, 19-29, 30-39, 40-49, 50-59, 60-69, ≥70
	Gender	Men, women
	Region	Capital(Seoul and Kyunggi), Metropolitan, other
	Income	0, Low 30%, middle 40%, high 30%
	Health insurance type	Employee insurance, regional insurance, or medical aid
	Seasonality	Spring, summer, fall, winter
Individual factors related to health	Primary diagnosis category (ICD-10)	Muscoloskeletal system and connective tissue(M00-M99), Injury/other consequences of external causes(S00-T98), digestive system(K00-K93), respiratory system(J00-J99), neoplasm(C00-D48), circulatory system(I00-I99), else
	Disability	Yes, no
	Charlson Comorbidity Index	0, 1, 2, ≥3
	Surgical procedure received during the stay	Yes, no
	Received invasive treatment	Treatment of central venous catheter, tracheostomy /artificial ventilation, none
	Process after the hospitalization treatment	Outpatient follow-up, transfer, deceased, discharged
Hospital related factors	Region of the medical institution	Capital(Seoul and Kyunggi), Metropolitan, other
	Number of doctors available	Divided into quartiles by each type of hospitals
	Nurse staffing level	0,1,2,3,4,5,6,7
	Hospital type	Tertiary hospital, general hospital, hospital, non-applicable hospital

3. Statistical methods

To examine the distribution of the general characteristics of study population, chi-squared test was performed. General characteristics were presented as frequencies and percentages. Then, descriptive statistics on all dependent variables were reported as means and standard deviations.[60,61]

To investigate the effect of each intervention, two intervention single interrupted time-series(ITS) with segmented regression at individual episode levels were performed. ITS models are likely to be used for evaluating public health interventions, particularly those introduced at a population level over a specific period of time. ITS models have been increasingly used quasi-experimental study designs.[62] By the repeatedly measured before the policy, pre-policy is determined, and then assesses the change at the policy implementation point and the post-policy trend.[63] By setting the pre-policy trend as counterfactual value, effect of post policy is evaluated. The evaluation of a policy' effect is measured by examining changes in the level and trend following the policy implementation.[21,62]

Generalized Estimating Equation(GEE) was used as the statistical method for the ITS design. The GEE model adjusts for time-related changes and correlations among repeated measurements in longitudinal study designs, making it suitable for marginal estimates with non-linear link functions.[64] In analysis exploring differences in the duration

of restricted antibiotics use, log link with zero-inflated negative binomial distribution was employed due to high incidence of zero counts in the use of restricted antibiotics.[65,66] Moreover, for outcome variables that are binary, binomial distribution and logit link was employed, whereas count outcome variable, such as length of stay, Poisson distribution and flog link was used. To address the uneven dispersion in the distribution of the variable, the Gamma distribution and log link function were applied to total medical expenditure.[67]

Due to inherent sensitivity of the ITS design, it is advisable to adhere strictly to reporting guidelines to ensure its safe application. Although there is no universally accepted protocol currently serving as the golden standard, ongoing developments are being made in this area. Common recommendations found in ITS reporting guideline protocols include the following: autocorrelation, where data points collected in close temporal proximity are correlated; nonstationary or secular trends, which involve consistent increases or decreases in the data over time regardless of any intervention; seasonality or cyclic patterns; outliers; other interventions occurring within the data series; and sample size.[60,68-71] To adhere to ITS reporting guidelines, correlation was assessed using the Durbin-Watson test, and non-stationarity was addressed with the augmented Dickey-Fuller test. Seasonality was incorporated as a covariate in the analysis.

The following equation for ITS using Generalized Estimating Equation(GEE) was used for the analysis:[72]

$$g(E(Y_{it})) = \beta_0 + B_1 x \text{Time}_{it} + \beta_2 x \text{Intervention1}_{it} + \beta_3 x \text{Time after intervention1}_{it} + \beta_4 x \text{intervention2}_{it} + \beta_5 x \text{Time after intervention2}_{it} + \boldsymbol{v}' x_{it}$$

g: link function

E: expectation

Y: dependent variables

i: individual

t: time period

Time: time variable from February 2013 as 1

Intervention1: dummy variable that is assigned "1" if time is after the first intervention

Intervention2: dummy variable that is assigned "1" if time is after the second intervention

Time after intervention: dummy variable that is assigned "0" if during intervention period, and "1" assigned at the start of intervention, added every 1 month

x_{it}: covariates (age group, gender, region, income level, health insurance type, seasonality, primary diagnosis category, disability status, surgical procedure during the hospital stay, Charlson Comorbidity Index score, region of the medical institution, invasive treatment,

process after the hospitalization, nurse staffing level, number of doctors)

In all analyses, the estimated coefficients were converted to exponentials as Exp(β). This is to demonstrate the trend and changes in dependent variables on the original scale, and subsequently, the model coefficients were to be interpreted multiplicatively. All statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA). A p-value of less than 0.05 was considered to indicate statistical significance.

4. Ethics Statement

This study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Yonsei University Health System(IRB number: 4-2023-1157). Informed consent was waived, for the NHIS-NSC data does not contain any personally identifiable information.

IV. Results

1. General characteristics of the study episodes

Following table present the results of the general characteristics of the study participants, divided according to the time point: pre intervention, during intervention 1 and 2, and post intervention 2. The final episodes included in the study was 614,127 and Pre-intervention included 322,776(52.6%) episodes, intervention 1 through 2 189,979(30.9%), and post-intervention 2 period 101,372(16.5%) episodes. There was no outstanding value of frequency in the table, throughout the different time periods. The table is divided into three sections vertically, which are individual factors, individual factors associated with health, and hospital related ones. Patients with primary diagnosis of musculoskeletal system and connective tissue and injury, poisoning and certain other consequences of external causes were almost 30%. More than half of the patient episodes were discharged(88.7%) and almost half of the patient episodes were CCI score of 0(43.5%). The patient episodes encompassed individuals who were hospitalized during the study period, but were characterized by a relatively healthy condition.

Table 5. General characteristics of the study episodes divided into pre-intervention, intervention 1, and intervention 2

Characteristics	Total		Pre-intervention		Intervention 1		Intervention 2		
	N	%	N	%	N	%	N	%	P-value
	614,127	**100.0**	**322,776**	**52.6**	**189,979**	**30.9**	**101,372**	**16.5**	
Individual factors									
Sex									0.0544
Men	286585	46.7	150214	52.4	88771	31.0	47600	16.6	
Women	327542	53.3	172562	52.7	101208	30.9	53772	16.4	
Age									<.0001
<19	104448	17.0	57575	55.1	30970	29.7	15903	15.2	
20-29	47552	7.7	25234	53.1	14736	31.0	7582	15.9	
30-39	72216	11.8	40468	56.0	21117	29.2	10631	14.7	
40-49	75147	12.2	40285	53.6	22976	30.6	11886	15.8	
50-59	103999	16.9	54896	52.8	32508	31.3	16595	16.0	
60-69	89927	14.6	43306	48.2	29204	32.5	17417	19.4	
>=70	120838	19.7	61012	50.5	38468	31.8	21358	17.7	
Social Health Insurance type									<.0001
Work sponsored	416262	67.8	216472	52.0	130142	31.3	69648	16.7	
Regional	171215	27.9	91838	53.6	51830	30.3	27547	16.1	
Medical aid	26650	4.3	14466	54.3	8007	30.0	4177	15.7	
Income(10th decile)									<.0001
0	36723	6.0	18566	50.6	11837	32.2	6320	17.2	

1 (1,2,3) lower 30%	123926	20.2	64398	52.0	38373	31.0	21155	17.1	
2 (4,5,6,7) mid 40%	219572	35.8	117084	53.3	67411	30.7	35077	16.0	
3 (8,9,10) high 30%	233906	38.1	122728	52.5	72358	30.9	38820	16.6	
Disability									0.0222
yes	56069	9.1	29172	52.0	17599	31.4	9298	16.6	
no	558058	90.9	293604	52.6	172380	30.9	92074	16.5	
Region									0.0085
Capital(Seoul, Kyunggi)	223573	36.4	117903	52.7	68875	30.8	36795	16.5	
Metropolitan	167498	27.3	87771	52.4	51698	30.9	28029	16.7	
Rural	223056	36.3	117102	52.5	69406	31.1	36548	16.4	
Health related individual factors									
Main diagnosis (by ICD-10 code categories)									<.0001
Muscoloskeletal system and connective tissue (M00-M99)	99830	16.3	50749	50.8	31228	31.3	17853	17.9	
Injury, poisoning and certain other consequences of external causes(S00-T98)	90571	14.7	47048	51.9	28672	31.7	14851	16.4	
Digestive system(K00-K93)	58771	9.6	29747	50.6	18712	31.8	10312	17.5	
Respiratory system(J00-J99)	56416	9.2	30198	53.5	16958	30.1	9260	16.4	
Neoplasm(C00-D48)	48407	7.9	25405	52.5	14843	30.7	8159	16.9	
Circulatory system(I00-I99)	43609	7.1	24091	55.2	12664	29.0	6854	15.7	
Else	216523	35.3	115538	53.4	66902	30.9	34083	15.7	
Surgical procedure during the stay at hospital									<.0001
yes	261570	42.6	136553	52.2	81001	31.0	44016	16.8	
no	352557	57.4	186223	52.8	108978	30.9	57356	16.3	

Seasonality									<.0001
1~3	148033	24.1	81936	55.3	44094	29.8	22003	14.9	
4~6	165226	26.9	97668	59.1	45022	27.2	22536	13.6	
7~9	151113	24.6	68174	45.1	55310	36.6	27629	18.3	
10~12	149755	24.4	74998	50.1	45553	30.4	29204	19.5	
CCI									<.0001
0	266925	43.5	138662	51.9	83308	31.2	44955	16.8	
1	161442	26.3	84850	52.6	50096	31.0	26496	16.4	
2	76448	12.4	39825	52.1	23626	30.9	12997	17.0	
3<	109312	17.8	59439	54.4	32949	30.1	16924	15.5	
Invasive treatment									<.0001
central catheter	8768	1.4	4390	50.1	2829	32.3	1549	17.7	
ventilation or tracheotomy	6510	1.1	3424	52.6	2045	31.4	1041	16.0	
none	598849	97.5	314962	52.6	185105	30.9	98782	16.5	
Result of treatment									<.0001
Outpatient follow-up? Continue?	57340	9.3	32110	56.0	16770	29.2	8460	14.8	
Transfer	7700	1.3	3796	49.3	2465	32.0	1439	18.7	
Dead	4212	0.7	2221	52.7	1338	31.8	653	15.5	
Discharged	544875	88.7	284649	52.2	169406	31.1	90820	16.7	
Hospital related factors									
Region of Medical institution									<.0001
Capital(Seoul, Kyunggi)	249101	40.6	130003	52.2	77361	31.1	41737	16.8	
Metropolitan	192077	31.3	100995	52.6	58972	30.7	32110	16.7	

Rural	172949	28.2	91778	53.1	53646	31.0	27525	15.9	
Number of doctors available (Quartile by types of medical institutions)									<.0001
Q1	173268	28.2	93389	53.9	53196	30.7	26683	15.4	
Q2	142542	23.2	74610	52.3	43873	30.8	24059	16.9	
Q3	153045	24.9	81829	53.5	46400	30.3	24816	16.2	
Q4	145272	23.7	72948	50.2	46510	32.0	25814	17.8	
Nurse staffing level (1~7)									<.0001
0 (not receiving the fee)	114232	18.6	45745	40.0	40849	35.8	27638	24.2	
1	66602	10.8	24424	36.7	22631	34.0	19547	29.3	
2	124239	20.2	66259	53.3	39467	31.8	18513	14.9	
3	91063	14.8	57486	63.1	23250	25.5	10327	11.3	
4	30854	5.0	17914	58.1	9063	29.4	3877	12.6	
5	20973	3.4	11776	56.1	6614	31.5	2583	12.3	
6	51482	8.4	33054	64.2	13075	25.4	5353	10.4	
7	114682	18.7	66118	57.7	35030	30.5	13534	11.8	
Hospital type									<.0001
Tertiary hospital	130663	21.3	68765	52.6	40792	31.2	21106	16.2	
General hospital	230850	37.6	120414	52.2	71473	31.0	38963	16.9	
Hospital	57863	9.4	32259	55.8	17286	29.9	8318	14.4	
Non-applicable hospital	194751	31.7	101338	52.0	60428	31.0	32985	16.9	

*The pre intervention 1 period: May 2013 through July 2016
The intervention 1 and intervention 2 period: August 2016 through September 2018
The post intervention 2 period: October 2018 through December 2019

Table 6. Unadjusted differences in dependent variables during the study period

	Pre-intervention	Intervention 1	Intervention 2	Difference
	(Mean±SD)	(Mean±SD)	(Mean±SD)	(unadjusted, from pre intervention to intervention 2)
	Tertiary hospital			
Restricted antibiotics use	0.067±0.250	0.058±0.233	0.046±0.209	-0.021
Hospital associated infections during the stay	0.041±0.198	0.035±0.183	0.033±0.177	-0.008
Length of stay(LOS) in days	16.165±29.664	13.217±24.448	10.270±15.960	-5.895
Health expenditure in KRW	3,059,702.29±4566817.08	3,853,285.18±5711756.84	4,437,871.96±6491534.71	1,378,169.67
	General hospital			
Restricted antibiotics use	0.037±0.188	0.032±0.176	0.027±0.161	-0.01
Hospital associated infections during the stay	0.072±0.258	0.062±0.241	0.060±0.237	-0.012
Length of stay(LOS) in days	16.768±36.010	12.774±23.278	9.977±14.661	-6.791
Health expenditure in KRW	1,907,768.68±2749287.77	2,366,540.67±3367182.41	2,880,665.51±3916951.13	972,896.83
	Hospital			
Restricted antibiotics use	0.015±0.120	0.015±0.120	0.015±0.120	0
Hospital associated infections during the stay	0.060±0.237	0.062±0.241	0.063±0.243	0.003
Length of stay(LOS) in days	22.806±76.646	19.386±56.690	14.014±29.303	-8.792
Health expenditure in KRW	1,353,124.99±1708457.42	1,621,316.73±2055688.34	1,866,530.45±2181051.63	513,405.46

	Non-applicable hospital			
Restricted antibiotics use	0.005±0.068	0.005±0.074	0.005±0.069	0
Hospital associated infections during the stay	0.039±0.194	0.046±0.209	0.049±0.216	0.01
Length of stay(LOS) in days	13.864±54.735	11.365±34.756	9.031±18.410	-4.833
Health expenditure in KRW	987,849.677±1217823.83	1,154,033.12±1431318.63	1,375,343.6±1669156.11	387,493.92

* The pre intervention 1 period: May 2013 through July 2016
The intervention 1 and intervention 2 period: August 2016 through September 2018
The post intervention 2 period: October 2018 through December 2019

The table above shows the unadjusted differences in mean and standard deviation of dependent variables by different hospital types during each sections of the study period. Except health expenditure, every category, which are restricted antibiotics use, healthcare associated infection, and total hospital days, have decreasing trend in tertiary and general hospitals when comparing the mean values of baseline period and post second intervention. Length of hospital stay decreased in all types of hospitals, and hospitals had the greatest decreasing days(-8.792 days).

2. Effect of legislations on healthcare outcome and utilization

1) Effect of legislations on healthcare outcome

Infection related outcomes were whether restricted multi-resistant antibiotics were prescribed and whether the patient episode had infectious disease as a secondary diagnosis during the hospital stay. The results from interrupted time series(ITS) analysis during multiple intervention periods are presented in table 6, 7 and figure 4, 5. There was a decreasing trend change in tertiary hospital after 2nd intervention in use of restricted antibiotics, and estimated coefficient was statistically significant(Trend change after second intervention: $Exp(\beta_5)=0.9666$, $p=0.0005$). The estimated coefficients showed decrease in trend change after each intervention in tertiary and general hospital, but the values were statistically insignificant. The graph illustrates this decreasing pattern, indicating that general hospitals and tertiary hospitals exhibit a greater degree of change compared to hospitals during the interventions. The mean incidence of healthcare associated infections, defined as instances where UTI, sepsis, or pneumonia, or pseudomembranous colitis were diagnosed as secondary or ancillary during the hospitalization, decreased following the 1st intervention, among the episodes from hospitals(Trend change after first intervention: $Exp(\beta_3)=0.9897$, $p=0.04$). According to the graph(figure 5), compared to other hospital types, non-applicable hospital seem to have continuous increasing trend. Tertiary hospital, on the other hand, shows a decreasing trend

overall.

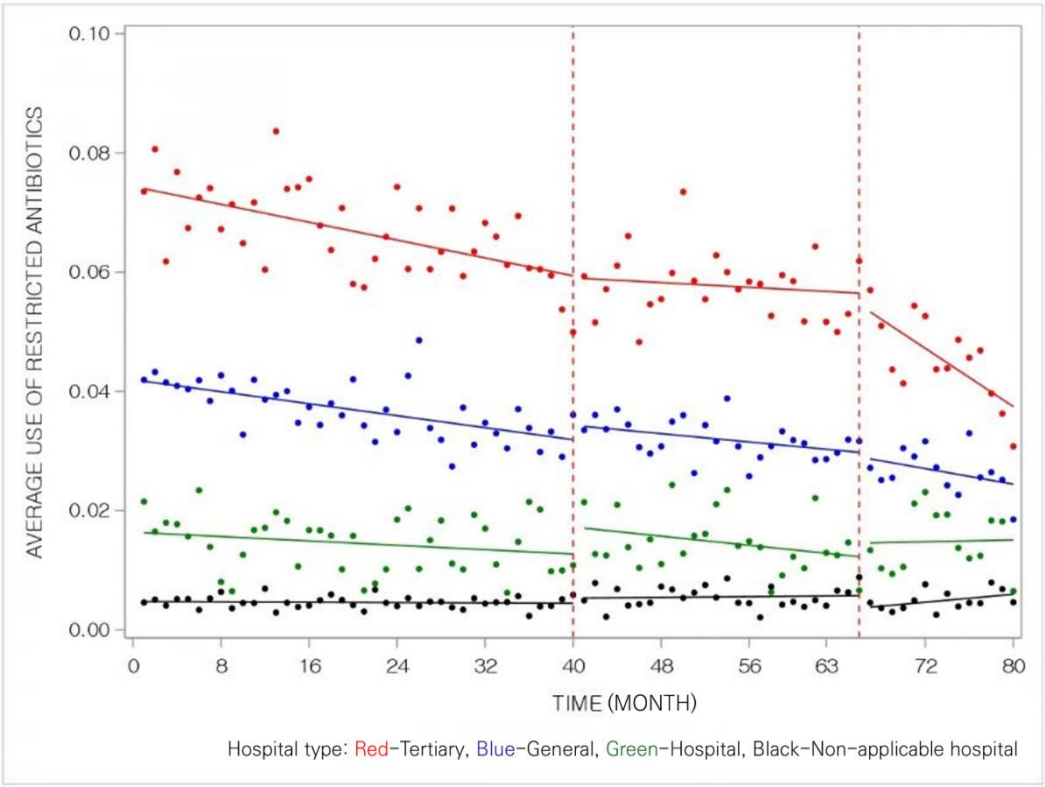


Figure 5. Three segmented ITS segmented regression parameter estimates for average use of restricted antibiotics

*1st intervention: August 2016, 2nd intervention: October 2018

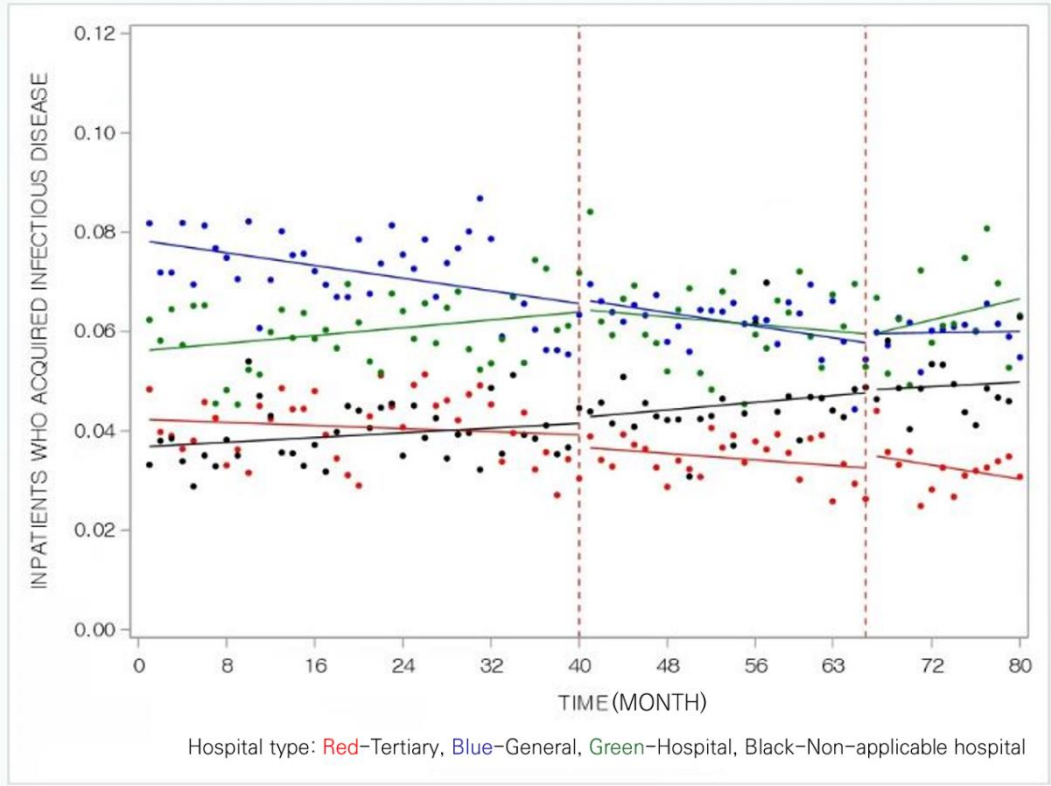


Figure 6. Three segmented ITS segmented regression parameter estimates for average healthcare associated infections

*1st intervention: August 2016, 2nd intervention: October 2018

Table 7. Segmented regression model results: Parameter estimates, standard errors, and p-values for the use of restricted antibiotics

Parameter	Exp(β)	Exp(SE(β))	95% Confidence interval		P-value
Use of restricted antibiotics					
Tertiary Hospital					
Intercept β0	0.0202	1.1967	0.0142	0.0287	<.0001
Baseline trend β1	0.9944	1.0014	0.9916	0.9972	<.0001
Level change after 1st intervention β2	0.9612	1.0608	0.8562	1.0791	0.5022
Trend change after 1st intervention β3	0.9999	1.0035	0.9931	1.0067	0.9738
Level change after 2nd intervention β4	1.0486	1.0923	0.8820	1.2468	0.5906
Trend change after 2nd intervention β5	0.9666	1.0098	0.9482	0.9853	0.0005
General Hospital					
Intercept β0	0.0115	1.1801	0.0083	0.0160	<.0001
Baseline trend β1	0.9942	1.0014	0.9914	0.9970	<.0001
Level change after 1st intervention β2	1.0346	1.0624	0.9188	1.1650	0.5744
Trend change after 1st intervention β3	0.9962	1.0036	0.9893	1.0033	0.2925
Level change after 2nd intervention β4	1.0118	1.0950	0.8469	1.2089	0.8973
Trend change after 2nd intervention β5	0.9887	1.0099	0.9698	1.0079	0.2469
Hospital					
Intercept β0	0.0049	1.7074	0.0017	0.0141	<.0001
Baseline trend β1	0.9958	1.0043	0.9875	1.0041	0.3188
Level change after 1st intervention β2	1.4493	1.1872	1.0353	2.0287	0.0306
Trend change after 1st intervention β3	0.9805	1.0105	0.9608	1.0007	0.0581
Level change after 2nd intervention β4	1.3558	1.3045	0.8053	2.2826	0.2521
Trend change after 2nd intervention β5	1.0243	1.0283	0.9699	1.0818	0.3895
Non-applicable hospital					
Intercept β0	0.0023	1.5264	0.0010	0.0053	<.0001
Baseline trend β1	1.0014	1.0041	0.9934	1.0095	0.7287
Level change after 1st intervention β2	1.1002	1.1664	0.8137	1.4875	0.535

Trend change after 1st intervention β3	1.0001	1.0088	0.9830	1.0175	0.9951
Level change after 2nd intervention β4	0.7303	1.2452	0.4751	1.1224	0.1518
Trend change after 2nd intervention β5	1.0164	1.0228	0.9727	1.0622	0.4683

Table 8. Segmented regression model results: Parameter estimates, standard errors, and p-values for the healthcare associated infection

Parameter	Exp(β)	Exp(SE(β))	95% Confidence interval		P-value
Healthcare Associated Infection					
Tertiary Hospital					
Intercept β0	0.0317	1.2416	0.0208	0.0485	<.0001
Baseline trend β1	0.9984	1.0018	0.9949	1.0019	0.3619
Level change after 1st intervention β2	0.9650	1.0771	0.8343	1.1163	0.6315
Trend change after 1st intervention β3	0.9965	1.0044	0.9880	1.0052	0.4332
Level change after 2nd intervention β4	1.1367	1.1168	0.9153	1.4117	0.2464
Trend change after 2nd intervention β5	0.9881	1.0121	0.9651	1.0116	0.3161
General Hospital					
Intercept β0	0.1145	1.1105	0.0932	0.1405	<.0001
Baseline trend β1	0.9972	1.0010	0.9952	0.9992	0.0055
Level change after 1st intervention β2	0.9790	1.0436	0.9004	1.0646	0.6202
Trend change after 1st intervention β3	1.0003	1.0026	0.9953	1.0053	0.9017
Level change after 2nd intervention β4	1.0460	1.0653	0.9239	1.1844	0.4771
Trend change after 2nd intervention β5	1.0073	1.0067	0.9942	1.0205	0.2754
Hospital					
Intercept β0	0.0856	1.2213	0.0579	0.1267	<.0001
Baseline trend β1	1.0055	1.0021	1.0013	1.0096	0.0103
Level change after 1st intervention β2	0.9883	1.0893	0.8358	1.1686	0.8904
Trend change after 1st intervention β3	0.9897	1.0051	0.9798	0.9995	0.04
Level change after 2nd intervention β4	1.0479	1.1343	0.8186	1.3416	0.7102
Trend change after 2nd intervention β5	1.0128	0.0132	0.9869	1.0394	0.3356

Non-applicable hospital					
Intercept β0	0.0533	1.1433	0.0410	0.0694	<.0001
Baseline trend β1	1.0037	1.0015	1.0008	1.0066	0.0117
Level change after 1st intervention β2	0.9763	1.0571	0.8756	1.0885	0.6656
Trend change after 1st intervention β3	1.0025	1.0032	0.9962	1.0088	0.4338
Level change after 2nd intervention β4	0.9036	1.0772	0.7810	1.0454	0.1728
Trend change after 2nd intervention β5	0.9963	1.0078	0.9813	1.0117	0.6382

2) Effect of legislations on subcategories of healthcare outcome

For further subcategory of quality control measures for infection management, days of therapy of restricted multi resistant antibiotics and hospital associated infection as urinary tract infection, pneumonia, sepsis and pseudomembranous colitis were analyzed. In tertiary and hospital, sepsis was shown to have decreasing trend after 1st intervention (Trend change after 1st intervention at tertiary: $Exp(\beta_3)=0.9842$, $p=0.0404$, Trend change after 1st intervention at hospital: $Exp(\beta_3)=0.9775$, $p=0.045$). According to the graph, even though not significant in the estimated coefficients, UTI seems to have decreasing trend overall in tertiary hospitals. Pseudomembranous colitis is rare cases in smaller hospitals like hospitals or non-applicable hospitals, resulting in figures with steady trend over the study period. The amount of restricted antibiotics use measured by days of therapy, did not show any statistically significant estimated coefficient. However, in graph, the overall trend seems to go down, and especially in tertiary hospitals.

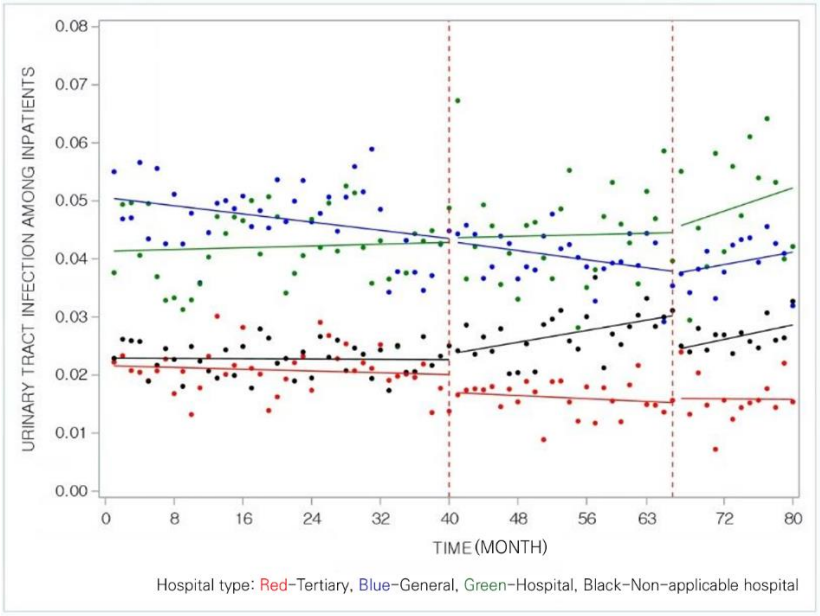


Figure 7. Results of interrupted time series analyses of changes in urinary tract infection as subgroup

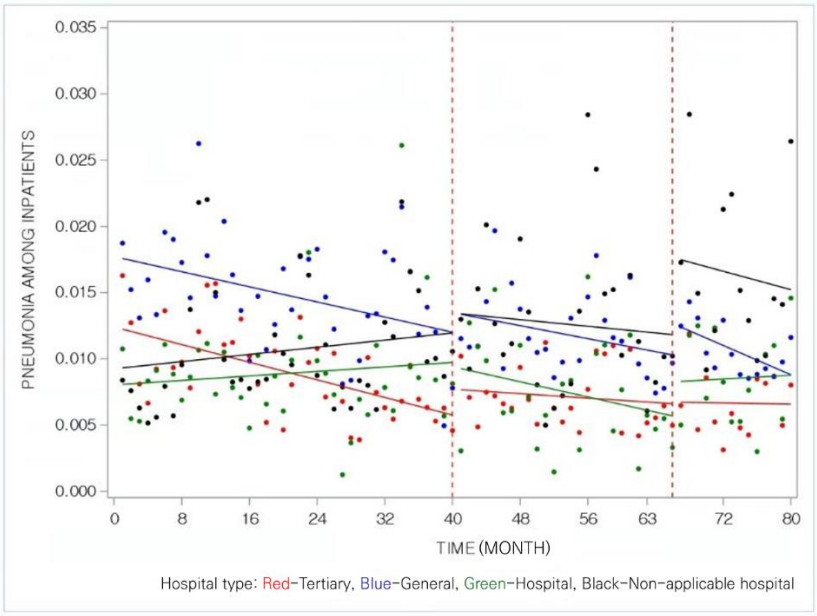


Figure 8. Results of interrupted time series analyses of changes in pneumonia as subgroup

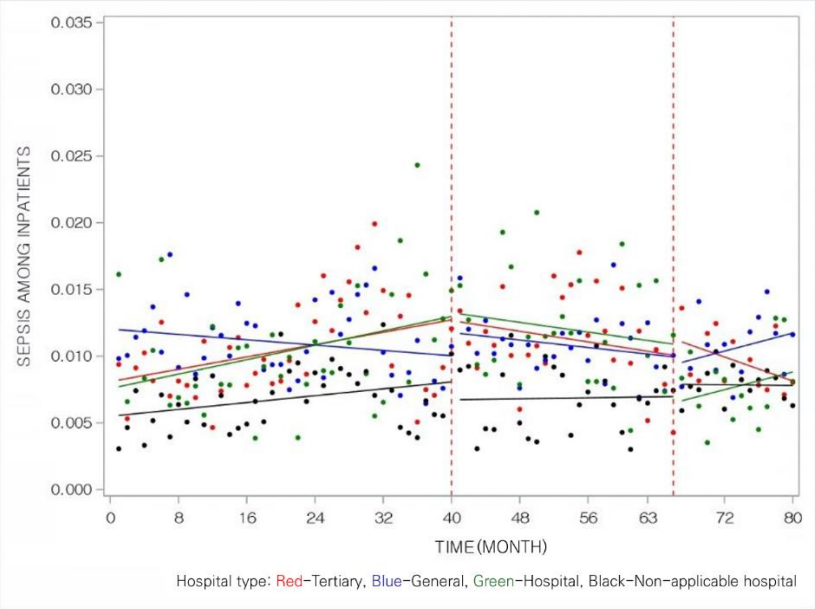


Figure 9. Results of interrupted time series analyses of changes in sepsis as subgroup

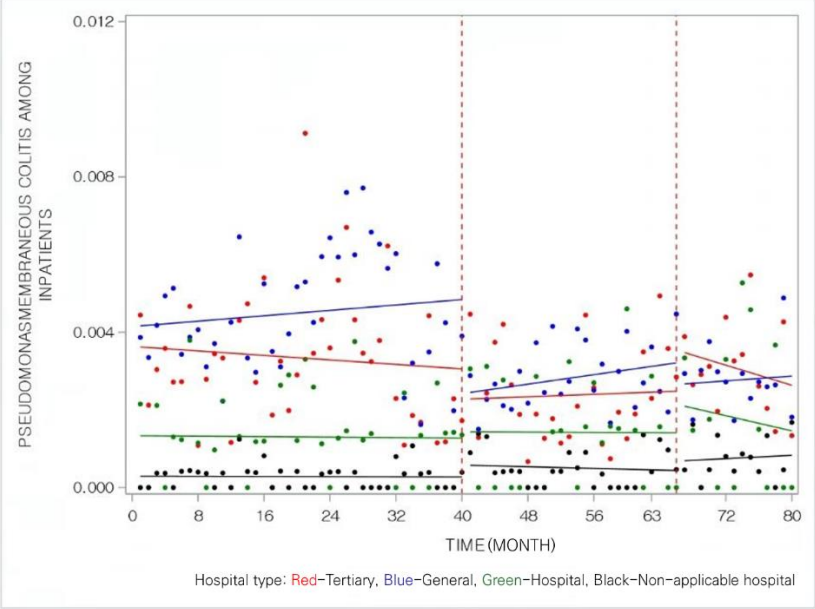


Figure 10. Results of interrupted time series analyses of changes in pseudomembranous colitis as subgroup

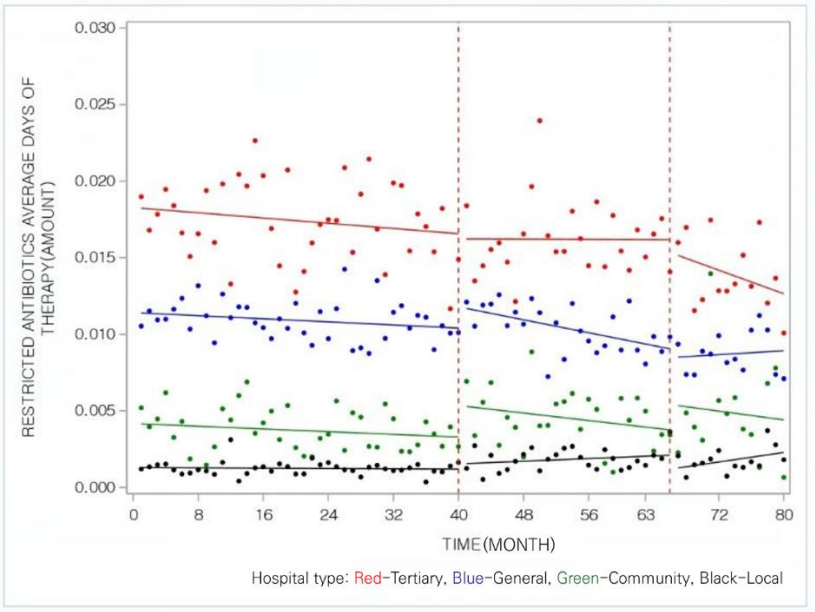


Figure 11. Results of interrupted time series analyses of changes in restricted antibiotics days of therapy as subgroup

*1st intervention: August 2016, 2nd intervention: October 2018

Table 9. Segmented regression model estimates for mean monthly infections of UTI and pneumonia per episode over time

Parameter	Exp(β)	Exp(SE(β))	95% Confidence interval		P-value	Exp(β)	Exp(SE(β))	95% Confidence interval		P-value
	Urinary Tract Infection					Pneumonia				
Tertiary Hospital										
Intercept β0	0.0206	1.3633	0.0112	0.0378	<.0001	0.0018	1.6605	0.0007	0.0048	<.0001
Baseline trend β1	1.0007	1.0024	0.9960	1.0054	0.7747	0.9794	1.0038	0.9722	0.9868	<.0001
Level change after 1st intervention β2	0.8354	1.1099	0.6809	1.0249	0.0846	1.4758	1.1768	1.0727	2.0303	0.0168
Trend change after 1st intervention β3	0.9956	1.0063	0.9835	1.0079	0.4842	1.0106	1.0097	0.9915	1.0299	0.2772
Level change after 2nd intervention β4	1.0762	1.1732	0.7869	1.4717	0.6458	1.1183	1.2766	0.6929	1.8047	0.647
Trend change after 2nd intervention β5	0.9983	1.0172	0.9653	1.0324	0.9224	0.9986	1.0268	0.9482	1.0518	0.959
General Hospital										
Intercept β0	0.0806	1.1377	0.0626	0.1038	<.0001	0.0062	1.2481	0.0040	0.0095	<.0001
Baseline trend β1	0.9978	1.0012	0.9954	1.0002	0.073	0.9916	1.0023	0.9872	0.9960	0.0002
Level change after 1st intervention β2	0.9466	1.0530	0.8556	1.0473	0.2872	1.1076	1.0999	0.9191	1.3350	0.2832
Trend change after 1st intervention β3	1.0004	1.0031	0.9943	1.0064	0.9077	1.0042	1.0058	0.9928	1.0156	0.4729
Level change after 2nd intervention β4	1.0132	1.0797	0.8718	1.1776	0.8643	1.0704	1.1552	0.8066	1.4202	0.6377
Trend change after 2nd intervention β5	1.0146	1.0080	0.9989	1.0307	0.0688	0.9897	1.0158	0.9595	1.0206	0.5084

Hospital										
Intercept β0	0.0661	1.2728	0.0412	0.1060	<.0001	0.0020	1.6621	0.0008	0.0055	<.0001
Baseline trend β1	1.0044	1.0025	0.9995	1.0093	0.0754	1.0048	1.0057	0.9937	1.0161	0.3952
Level change after 1st intervention β2	1.0029	1.1057	0.8237	1.2213	0.9767	0.7806	1.2655	0.4920	1.2385	0.2929
Trend change after 1st intervention β3	0.9924	1.0059	0.9810	1.0040	0.197	0.9920	1.0148	0.9639	1.0210	0.5844
Level change after 2nd intervention β4	1.1381	1.1541	0.8595	1.5071	0.3663	1.1694	1.4144	0.5927	2.3071	0.6517
Trend change after 2nd intervention β5	1.0054	1.0150	0.9765	1.0353	0.7166	1.0342	1.0353	0.9661	1.1071	0.3337
Non-applicable hospital										
Intercept β0	0.0298	1.1844	0.0214	0.0415	<.0001	0.0025	1.3842	0.0013	0.0048	<.0001
Baseline trend β1	1.0016	1.0019	0.9979	1.0052	0.3952	1.0036	1.0028	0.9981	1.0092	0.1938
Level change after 1st intervention β2	1.0093	1.0736	0.8783	1.1600	0.8958	1.0481	1.1092	0.8555	1.2842	0.6499
Trend change after 1st intervention β3	1.0083	1.0040	1.0004	1.0163	0.0389	0.9968	1.0062	0.9848	1.0089	0.607
Level change after 2nd intervention β4	0.7965	1.1015	0.6590	0.9628	0.0187	1.0942	1.1430	0.8419	1.4219	0.5011
Trend change after 2nd intervention β5	0.9951	1.0103	0.9754	1.0152	0.6299	1.0046	1.0139	0.9779	1.0321	0.7361

Table 10. Segmented regression model estimates for mean monthly infections of sepsis and pseudomembranous colitis per episode over time

Parameter	Exp(β)	Exp(SE(β))	95% Confidence interval		P-value	Exp(β)	Exp(SE(β))	95% Confidence interval		P-value
	Sepsis					Pseudomembranous colitis				
Tertiary Hospital										
Intercept β0	0.0092	1.4835	0.0042	0.0199	<.0001	0.0001	2.2603	0.0000	0.0006	<.0001
Baseline trend β1	1.0089	1.0035	1.0020	1.0160	0.0117	0.9993	1.0059	0.9878	1.0109	0.8992
Level change after 1st intervention β2	0.9986	1.1407	0.7717	1.2924	0.9916	0.8285	1.2971	0.4976	1.3795	0.4695
Trend change after 1st intervention β3	0.9842	1.0078	0.9694	0.9993	0.0404	1.0029	1.0155	0.9731	1.0337	0.8518
Level change after 2nd intervention β4	1.2044	1.2088	0.8306	1.7467	0.3266	1.5414	1.4148	0.7808	3.0429	0.2124
Trend change after 2nd intervention β5	0.9761	1.0211	0.9370	1.0168	0.2453	0.9738	1.0372	0.9066	1.0459	0.4665
General Hospital										
Intercept β0	0.0182	1.2866	0.0111	0.0298	<.0001	0.0044	1.4911	0.0020	0.0095	<.0001
Baseline trend β1	0.9987	1.0026	0.9937	1.0037	0.619	1.0075	1.0038	0.9999	1.0151	0.0519
Level change after 1st intervention β2	1.1358	1.1064	0.9317	1.3846	0.2077	0.4978	1.2027	0.3467	0.7148	0.0002
Trend change after 1st intervention β3	0.9961	1.0059	0.9846	1.0078	0.5154	1.0047	1.0111	0.9832	1.0268	0.669

Level change after 2nd intervention β4	1.0217	1.1587	0.7655	1.3636	0.8842	0.7323	1.3306	0.4184	1.2817	0.2754
Trend change after 2nd intervention β5	1.0061	1.0155	0.9762	1.0370	0.6904	1.0259	1.0300	0.9680	1.0872	0.388
Hospital										
Intercept β0	0.0047	1.6568	0.0017	0.0126	<.0001	0.0013	3.2095	0.0001	0.0126	<.0001
Baseline trend β1	1.0118	1.0050	1.0018	1.0218	0.0203	1.0043	1.0135	0.9781	1.0311	0.7514
Level change after 1st intervention β2	1.0923	1.2074	0.7550	1.5804	0.6393	1.0491	1.7100	0.3665	3.0024	0.9289
Trend change after 1st intervention β3	0.9775	1.0115	0.9559	0.9995	0.045	0.9852	1.0318	0.9265	1.0476	0.6339
Level change after 2nd intervention β4	0.7635	1.3935	0.3984	1.4630	0.416	2.2008	1.9820	0.5757	8.4115	0.2489
Trend change after 2nd intervention β5	1.0190	1.0369	0.9492	1.0938	0.6031	0.9712	1.0744	0.8437	1.1178	0.6837
Non-applicable hospital										
Intercept β0	0.0059	1.3786	0.0032	0.0112	<.0001	0.0010	3.2236	0.0001	0.0102	<.0001
Baseline trend β1	1.0086	1.0034	1.0020	1.0153	0.0104	1.0017	1.0164	0.9703	1.0342	0.9158
Level change after 1st intervention β2	0.8208	1.1389	0.6360	1.0593	0.1291	1.7582	1.7158	0.6102	5.0657	0.2959
Trend change after 1st intervention β3	0.9920	1.0077	0.9772	1.0071	0.3004	0.9915	1.0306	0.9347	1.0518	0.7778

Level change after 2nd intervention β4	1.1011	1.1904	0.7824	1.5496	0.5807	1.7857	1.7803	0.5765	5.5306	0.3148
Trend change after 2nd intervention β5	0.9964	1.0184	0.9616	1.0325	0.8429	1.0019	1.0581	0.8968	1.1193	0.9733

Table 11. Segmented regression model estimates for mean monthly days of restricted antibiotic therapy per episode over time

Parameter	Exp(β)	Exp(SE(β))	95% Confidence interval		P-value
Days of Therapy(DoT) of restricted antibiotics					
Tertiary Hospital					
Intercept β0	0.0066	1.3461	0.0037	0.0118	<.0001
Baseline trend β1	0.9986	1.0026	0.9936	1.0036	0.5803
Level change after 1st intervention β2	1.0097	1.1093	0.8241	1.2374	0.9252
Trend change after 1st intervention β3	0.9973	1.0061	0.9855	1.0091	0.6515
Level change after 2nd intervention β4	1.0536	1.1639	0.7825	1.4186	0.7307
Trend change after 2nd intervention β5	0.9833	1.0167	0.9518	1.0158	0.3112
General Hospital					
Intercept β0	0.0035	1.3459	0.0020	0.0063	<.0001
Baseline trend β1	0.9992	1.0030	0.9934	1.0050	0.7821
Level change after 1st intervention β2	1.0971	1.1065	0.8997	1.3379	0.3599
Trend change after 1st intervention β3	0.9916	1.0061	0.9799	1.0036	0.1711
Level change after 2nd intervention β4	0.9201	1.1643	0.6828	1.2397	0.5841

Trend change after 2nd intervention β5	1.0163	1.0161	0.9849	1.0489	0.3108
Hospital					
Intercept β0	0.0010	3.3542	0.0001	0.0111	<.0001
Baseline trend β1	0.9971	1.0083	0.9811	1.0135	0.7307
Level change after 1st intervention β2	1.7395	1.3645	0.9460	3.1986	0.0748
Trend change after 1st intervention β3	0.9822	1.0188	0.9471	1.0186	0.3333
Level change after 2nd intervention β4	1.7971	1.8147	0.5589	5.7777	0.3253
Trend change after 2nd intervention β5	1.0007	1.0737	0.8705	1.1504	0.9921
Non-applicable hospital					
Intercept β0	0.0009	2.1270	0.0002	0.0040	<.0001
Baseline trend β1	1.0007	1.0077	0.9856	1.0160	0.928
Level change after 1st intervention β2	1.1852	1.3190	0.6887	2.0393	0.5396
Trend change after 1st intervention β3	1.0125	1.0154	0.9827	1.0432	0.4175
Level change after 2nd intervention β4	0.6609	1.4361	0.3251	1.3433	0.2524
Trend change after 2nd intervention β5	1.0172	1.0375	0.9464	1.0934	0.6421

3) Effect of legislations on healthcare utilization

Change in healthcare utilization is investigated to evaluate the effect of the enactment of The Patient Safety Act and law revision in Medical Service Act concerning infection control. Total days of stay in hospital showed decreasing immediate change and trend during the two intervention periods in every types of hospitals. Trend change after 2nd intervention was shown in every hospital types, and all estimated coefficients were statistically significant.(Trend change after second intervention at tertiary: $Exp(\beta_5)=0.9691$, p=<.0001, at general: $Exp(\beta_5)=0.9812$, p=<.0001, at hospital: $Exp(\beta_5)=0.9638$, p=<.0001, at non-applicable hospital: $Exp(\beta_5)=0.9709$, p=<.0001) It is more obvious with the graph; overall trend, not only the intervention hospitals, but also non-applicable hospital have decreasing total days at hospital. It is possible that there is another history effect regarding length of stay. Au contraire, health expenditure increased during the study period, and the estimate coefficients were statistically significant(Level change after second intervention at tertiary: $Exp(\beta_4)=1.0509$, p=0.0008, at general: $Exp(\beta_4)=1.0652$, p=<.0001, Trend change after first intervention at hospital: $Exp(\beta_3)=1.0023$, p=0.0081, non-applicable hospital: $Exp(\beta_3)=1.003$, p=<.0001, Trend change after second intervention: $Exp(\beta_5)=1.0083$, p=<.0001). Medical expense would have another effect that caused the increase, since non-applicable hospital also showed the same increasing trend. Nevertheless, trend change after 2nd intervention in tertiary hospital showed decreasing trend and the estimated coefficients were statistically significant, and is shown as in the

graph.(Trend change after second intervention: Exp(β_5)=0.9939, p=0.0001)

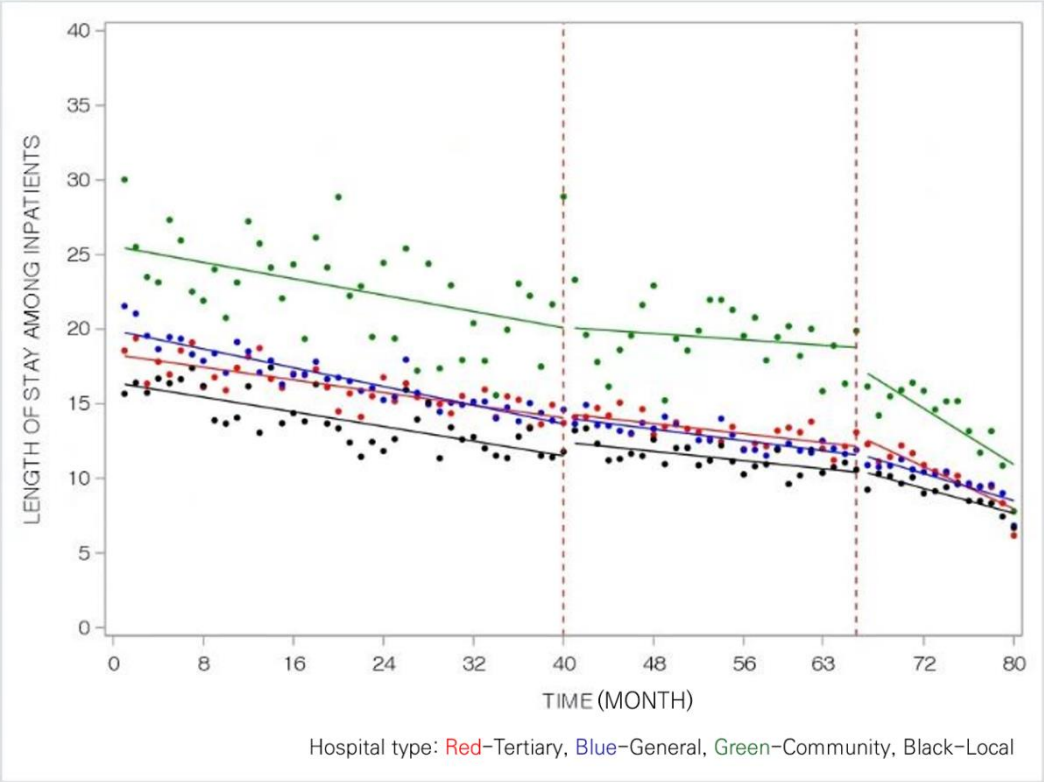


Figure 12. Three segmented ITS regression parameter estimates for length of stay

*1st intervention: August 2016, 2nd intervention: October 2018

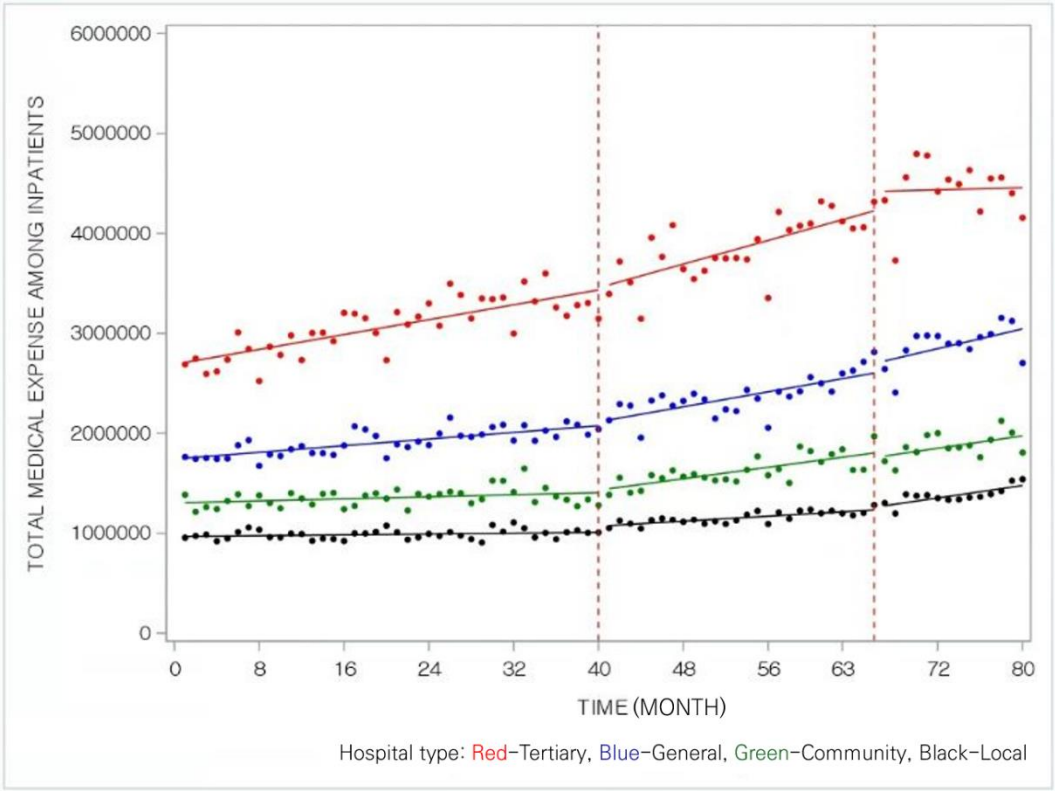


Figure 13. Three segmented ITS regression parameter estimates for total medical expenditure

**1st intervention: August 2016, 2nd intervention: October 2018

Table 12. Segmented regression model results: Parameter estimates, standard errors, and p-values for the length of stay

Parameter	Exp(β)	Exp(SE(β))	95% Confidence interval		P-value
Length of Stay					
Tertiary Hospital					
Intercept β0	4.6293	1.0112	4.5294	4.7313	<.0001
Baseline trend β1	0.9941	1.0001	0.9940	0.9943	<.0001
Level change after 1st intervention β2	0.9803	1.0035	0.9735	0.9871	<.0001
Trend change after 1st intervention β3	0.9978	1.0002	0.9973	0.9982	<.0001
Level change after 2nd intervention β4	1.0991	1.0055	1.0874	1.1109	<.0001
Trend change after 2nd intervention β5	0.9691	1.0006	0.9679	0.9703	<.0001
General Hospital					
Intercept β0	10.2954	1.0070	10.1553	10.4385	<.0001
Baseline trend β1	0.9929	1.0001	0.9928	0.9931	<.0001
Level change after 1st intervention β2	0.9967	1.0027	0.9914	1.0020	0.2264
Trend change after 1st intervention β3	0.9963	1.0002	0.9960	0.9966	<.0001
Level change after 2nd intervention β4	1.0445	1.0043	1.0356	1.0533	<.0001
Trend change after 2nd intervention β5	0.9812	1.0005	0.9802	0.9821	<.0001
Hospital					
Intercept β0	21.1576	1.0116	20.6827	21.6412	<.0001
Baseline trend β1	0.9957	1.0001	0.9955	0.9959	<.0001
Level change after 1st intervention β2	0.9771	1.0045	0.9685	0.9857	<.0001
Trend change after 1st intervention β3	0.9997	1.0003	0.9992	1.0002	0.2899
Level change after 2nd intervention β4	0.9939	1.0074	0.9796	1.0083	0.4066
Trend change after 2nd intervention β5	0.9638	1.0008	0.9621	0.9653	<.0001
Non-applicable hospital					
Intercept β0	7.5867	1.0081	7.4670	7.7083	<.0001
Baseline trend β1	0.9947	1.0001	0.9945	0.9948	<.0001
Level change after 1st intervention β2	1.0270	1.0032	1.0205	1.0336	<.0001

Trend change after 1st intervention β3	0.9980	1.0002	0.9976	0.9984	<.0001
Level change after 2nd intervention β4	1.1408	1.0050	1.1296	1.1519	<.0001
Trend change after 2nd intervention β5	0.9709	1.0005	0.9699	0.9720	<.0001

Table 13. Segmented regression model results: Parameter estimates, standard errors, and p-values for the total medical expenditure

Parameter	Exp(β)	Exp(SE(β))	95% Confidence interval		P-value
Total Medical expenditure					
Tertiary Hospital					
Intercept β0	1975041.5617	1.0309	1860954.3398	2096122.9876	<.0001
Baseline trend β1	1.0063	1.0003	1.0057	1.0068	<.0001
Level change after 1st intervention β2	0.9940	1.0106	0.9738	1.0146	0.5645
Trend change after 1st intervention β3	1.0006	1.0006	0.9994	1.0018	0.3493
Level change after 2nd intervention β4	1.0509	1.0149	1.0207	1.0818	0.0008
Trend change after 2nd intervention β5	0.9939	1.0016	0.9908	0.9970	0.0001
General Hospital					
Intercept β0	1565631.7897	1.0194	1507857.0068	1625620.2610	<.0001
Baseline trend β1	1.0051	1.0002	1.0047	1.0054	<.0001
Level change after 1st intervention β2	0.9898	1.0075	0.9754	1.0044	0.1689
Trend change after 1st intervention β3	1.0001	1.0004	0.9993	1.0010	0.7906
Level change after 2nd intervention β4	1.0652	1.0109	1.0430	1.0881	<.0001
Trend change after 2nd intervention β5	1.0000	1.0012	0.9977	1.0022	0.9786
Hospital					
Intercept β0	1687738.4577	1.0368	1572535.7472	1811380.8266	<.0001
Baseline trend β1	1.0025	1.0004	1.0017	1.0032	<.0001
Level change after 1st intervention β2	0.9811	1.0148	0.9531	1.0097	0.1933

Trend change after 1st intervention β3	1.0023	1.0009	1.0006	1.0040	0.0081
Level change after 2nd intervention β4	0.9712	1.0220	0.9307	1.0135	0.1795
Trend change after 2nd intervention β5	1.0019	1.0023	0.9974	1.0065	0.4102
Non-applicable hospital					
Intercept β0	1378215.3561	1.0216	1321661.2156	1437189.4593	<.0001
Baseline trend β1	1.0013	1.0002	1.0008	1.0017	<.0001
Level change after 1st intervention β2	1.0155	1.0083	0.9991	1.0323	0.0644
Trend change after 1st intervention β3	1.0030	1.0005	1.0020	1.0039	<.0001
Level change after 2nd intervention β4	1.0063	1.0118	0.9835	1.0295	0.5902
Trend change after 2nd intervention β5	1.0083	1.0012	1.0059	1.0108	<.0001

4) Effect of legislations on healthcare outcome and utilization stratified by levels of financial incentives for infection prevention and management

By dividing the study sample into levels of financial incentives for infection prevention and management in hospitals, exact interrupted time series analyses were performed. In grade 1, which is the highest grade in the incentive system, the level change after 1st intervention and trend change after 2nd intervention in the use of restricted antibiotics were shown in estimated coefficients(Trend change after first intervention in grade 1: Exp(β_3)=0.5101, p=<.0001, Exp (β_5)=0.9715, p=0.0002). Moreover, there was a great level decrease in grade 2 as well, which was also statistically significant(Trend change after first intervention in grade 2: Exp(β_3)$_{=0.4981,}$ p=<.0001). These trends are more apparent with the graphs. There is a sudden level drop in grade 1 and 2 in the average use of restricted antibiotics after intervention 1. Moreover, even though statistically not significant, graph show that healthcare associated infection decreased right after intervention 1 in hospitals that are grade 1 and 2.

Table 14. Parameter estimate, standard errors and p-values from the segmented regression models stratified by levels of financial incentive for infection control

Parameter	Exp(β)	Exp(SE(β))	95% Confidence interval		P-value	Exp(β)	Exp(SE(β))	95% Confidence interval		P-value
	Use of Restricted Antibiotics					Disease during the hospital stay				
No grade										
Intercept β0	0.0813	1.1498	0.0619	0.1070	<.0001	0.1464	1.0741	0.1272	0.1684	<.0001
Baseline trend β1	0.9901	1.0012	0.9880	0.9924	<.0001	0.9999	1.0007	0.9985	1.0014	0.9003
Level change after 1st intervention β2	1.1366	1.0678	0.9995	1.2925	0.051	1.0575	1.0350	0.9886	1.1311	0.1039
Trend change after 1st intervention β3	0.9998	1.0042	0.9916	1.0079	0.9582	1.0038	1.0021	0.9998	1.0079	0.0654
Level change after 2nd intervention β4	0.8261	1.1331	0.6466	1.0555	0.1265	0.9254	1.0562	0.8313	1.0302	0.157
Trend change after 2nd intervention β5	1.0175	1.0135	0.9909	1.0446	0.1986	1.0090	1.0058	0.9976	1.0207	0.1221
Grade 3										
Intercept β0	0.4915	2.2862	0.0972	2.4851	0.3903	0.2783	1.9782	0.0731	1.0599	0.0608
Baseline trend β1	0.9974	1.0115	0.9753	1.0200	0.8192	0.9956	1.0115	0.9753	1.0200	0.6783
Level change after 1st intervention β2	1.0127	1.4911	0.4629	2.2155	0.9748	1.0970	1.4435	0.5342	2.2526	0.8009
Trend change after 1st intervention β3	0.9970	1.0218	0.9557	1.0400	0.8888	0.9893	1.0205	0.9506	1.0294	0.5943
Level change after 2nd intervention β4	0.5415	1.4917	0.2473	1.1857	0.125	1.9365	1.3719	1.0421	3.5984	0.0366
Trend change after 2nd intervention β5	0.9583	1.0385	0.8896	1.0318	0.2578	0.9622	1.0277	0.9121	1.0151	0.1581

Grade2										
Intercept β0	0.0778	2.0842	0.0185	0.3283	0.0005	0.2422	1.7809	0.0782	0.7507	0.014
Baseline trend β1	0.9990	1.0050	0.9892	1.0088	0.8366	0.9927	1.0063	0.0000	1.0050	0.2432
Level change after 1st intervention β2	0.4981	1.1623	0.3710	0.6688	<.0001	1.0105	1.1938	0.7141	0.6995	0.9534
Trend change after 1st intervention β3	0.9856	1.0089	0.9685	1.0029	0.1031	1.0110	1.0095	0.9922	1.0300	0.2553
Level change after 2nd intervention β4	1.0809	1.2660	0.6807	1.7162	0.7416	1.2511	1.2132	0.8566	1.8272	0.2465
Trend change after 2nd intervention β5	1.0026	1.0286	0.9487	1.0596	0.9275	1.0268	1.0219	0.9841	1.0713	0.2228
Grade1										
Intercept β0	0.1622	1.5605	0.0678	0.3879	<.0001	0.1444	1.4386	0.0708	0.2945	<.0001
Baseline trend β1	0.9940	1.0019	0.9902	0.9977	0.0018	1.0028	1.0027	0.9975	1.0080	0.2995
Level change after 1st intervention β2	0.5101	1.0628	0.4527	0.5748	<.0001	0.8689	1.0758	0.7531	1.0027	0.0545
Trend change after 1st intervention β3	0.9979	1.0033	0.9914	1.0044	0.5317	0.9932	1.0039	0.9857	1.0008	0.0788
Level change after 2nd intervention β4	1.0987	1.0749	0.9537	1.2657	0.1924	1.1185	1.0747	0.9713	1.2881	0.1197
Trend change after 2nd intervention β5	0.9715	1.0079	0.9567	0.9866	0.0002	0.9951	1.0075	0.9805	1.0099	0.5183

Parameter	Exp(β)	Exp (SE(β))	95% Confidence interval		P-value	Exp(β)	Exp (SE(β))	95% Confidence interval		P-value
	Length of stay					Total Medical Expenditure				
No grade										
Intercept β0	30.0091	1.0046	29.7372	30.2834	<.0001	3100890.8527	1.0134	3021004.6512	3183207.8367	<.0001
Baseline trend β1	0.9925	1.0000	0.9926	0.9926	<.0001	1.0031	1.0001	1.0028	1.0033	<.0001
Level change after 1st intervention β2	1.0847	1.0021	1.0803	1.0893	<.0001	0.9305	1.0059	0.9199	0.9413	<.0001
Trend change after 1st intervention β3	1.0032	1.0001	1.0029	1.0034	<.0001	0.9988	1.0004	0.9981	0.9995	0.0009
Level change after 2nd intervention β4	1.0590	1.0037	1.0514	1.0666	<.0001	1.0082	1.0094	0.9899	1.0271	0.3817
Trend change after 2nd intervention β5	0.9744	1.0004	0.9737	0.9752	<.0001	1.0042	1.0010	1.0022	1.0062	<.0001
Grade 3										
Intercept β0	137.4005	1.0338	128.7407	146.6428	<.0001	3086042.2417	1.1193	2474378.9668	3849292.7958	<.0001
Baseline trend β1	0.9888	1.0004	0.9881	0.9895	<.0001	1.0018	1.0020	0.9979	1.0057	0.3624
Level change after 1st intervention β2	0.8920	1.0149	0.8666	0.9182	<.0001	0.9752	1.0728	0.8497	1.1193	0.7211
Trend change after 1st intervention β3	1.0086	1.0008	1.0070	1.0103	<.0001	1.0113	1.0038	1.0037	1.0188	0.0033
Level change after 2nd intervention β4	0.6020	1.0153	0.5844	0.6201	<.0001	0.9340	1.0565	0.8385	1.0403	0.2144

Trend change after 2nd intervention β5	0.9326	1.0015	0.9298	0.9353	<.0001	0.9845	1.0049	0.9751	0.9940	0.0014
Grade2										
Intercept β0	105.9111	1.0274	100.4540	111.6646	<.0001	1999684.5478	1.1222	1595025.0509	2506755.8874	<.0001
Baseline trend β1	0.9904	1.0002	0.9900	0.9908	<.0001	1.0106	1.0011	1.0083	1.0128	<.0001
Level change after 1st intervention β2	0.5364	1.0075	0.5286	0.5444	<.0001	0.8738	1.0307	0.8236	0.9271	<.0001
Trend change after 1st intervention β3	0.9972	1.0005	0.9963	0.9981	<.0001	0.9922	1.0016	0.9891	0.9954	<.0001
Level change after 2nd intervention β4	1.0983	1.0130	1.0709	1.1265	<.0001	1.0604	1.0361	0.9891	1.1367	0.0991
Trend change after 2nd intervention β5	0.9809	1.0016	0.9778	0.9839	<.0001	0.9923	1.0042	0.9843	1.0005	0.0654
Grade1										
Intercept β0	108.4186	1.0142	105.4567	111.4527	<.0001	3343403.9745	1.0597	2984073.8838	3745628.5576	<.0001
Baseline trend β1	0.9918	1.0001	0.9916	0.9920	<.0001	1.0094	1.0004	1.0086	1.0104	<.0001
Level change after 1st intervention β2	0.5223	1.0032	0.5190	0.5256	<.0001	0.8916	1.0121	0.8710	0.9128	<.0001
Trend change after 1st intervention β3	1.0004	1.0002	1.0000	1.0007	0.0399	0.9963	1.0006	0.9951	0.9975	<.0001

Level change after 2nd intervention β4	1.0597	1.0041	1.0513	1.0683	<.0001	1.0667	1.0112	1.0438	1.0901	<.0001
Trend change after 2nd intervention β5	0.9756	1.0005	0.9747	0.9765	<.0001	0.9971	1.0012	0.9948	0.9994	0.0118

V. Discussion

1. Discussion of the method

Effect of Patient Safety Act legislation and law revision in Medical Service Act with respect to infection prevention and control in medical institutions was evaluated in this study. This study utilized segmented regression within a multiple interrupted time series design, leveraging the National health insurance data from South Korea. This data source and methodological approach introduced both strengths and limitations to the research.

In this study investigating the effect of two legislations enacted and implemented in two different time periods, segmented regression for an interrupted time series study involving multiple intervention was used. Usually, when the two time points are set as the time point of legislation and implementation of a law, in between time is omitted as the lag time. Nevertheless, in this model, which is a three-segmented model, all data were included during the roll-out.[73] When modeling segmented regression model specifying more than one change point, or in the effects of an intervention that was implemented and later withdrawn, this method was used in previous studies.[70] ITS design is particularly effective in accommodating certain unique aspects of the interventions under investigation, such as differing lengths of intervention rollout periods and delayed effects within the population

being studied.[70,74] To investigate the two interventions at once, the ITS design is the most suitable methodology available.

This study included the effect of Patient Safety Act legislation and law revision in Medical Service Act with respect to infection prevention and control in medical institutions for all kinds of diseases, not limited to specific disease type. Previous studies have generally limited the target population to patients diagnosed with certain diseases[75,76]. ITS analysis is a study design used for evaluating the effectiveness of healthcare interventions implemented at a specific, clearly defined time point on a population level.[60] Considering the legislation was applied to all medical institutions with certain size, it was necessary to analyze the impact on all patients, regardless of the severity and type of illness. Given that Korea has achieved universal coverage of health insurance and a single payer system, this study included all policy target populations.[77]

Although this study was implemented with a universal data and complex method of investigating the differences of two independent legislations over time, certain limitations lie upon. Even though this research was exploring quality of care, no process indicator was assessed. The national health claims data do not include any process indicator, such as the exact time or date of intake or injection of antibiotics or hand hygiene status or use of prophylactic antibiotics. The process indicators that infection control professionals manage include catheter-associated urinary tract infection prevention, surgical site infection prevention, and more.[78] The interventions carried out by infection control

professionals primarily involve the implementation of appropriate process indicators, which are expected to lead to improved outcome indicators.[79-81]

Nonetheless, sensitivity analysis was conducted to account for different time periods. Comparison of the outcome variables pre intervention and post 2nd intervention was performed as a sensitivity analysis. Additional analysis is comprehensively detailed in Appendix.

Another limitation of this study is the potential underreporting and neglect of numerous cases of healthcare-associated infections in patient diagnoses. This underreporting would be primarily due to a financial incentive program in Korea, which bases reimbursement on infection control performance in medical institutions. The criteria for reimbursing infection prevention and control fees include the establishment of an infection control headquarter, the presence of dedicated personnel, and results of hospital certification by the Health Insurance Review and Assessment Service according to type, participation in the National Healthcare-associated Infections Surveillance System operated by the Korea Disease Control and Prevention Agency, and the execution of infection control activities.[82] Consequently, data specifically collected for infection control research should be utilized when investigating this topic in the future.

The ITS design is a robust study design for evaluating the effects of policies, yet it has several limitations. Firstly, various statistical methods can be applied, each potentially yielding different results, which thoughtful consideration should accompany when using the design. The data, often collected over short, regular intervals can suffer from bias issues

such as autocorrelation and non-stationarity. Lastly, to accurately determine causality, the inclusion of a control group is essential.

When designing an ITS study and analyzing the data, several critical characteristics must be taken into account. According to several ITS protocols, certain methodological issues must be considered or tested, including autocorrelation, nonstationary, and seasonality.[83,84] Therefore, in this study, autocorrelation was assessed by Durbin-Watson statistic, and the static value was almost 2(all above 1.9 for the four dependent variables), showing that there is no autocorrelation in all dependent variables analyzed in the research.[85] For the nonstationary, augmented Dickey-Fuller test was performed. As a result, p values for rho and tau were very small(all 0.0001 or smaller), which indicates that time series is stationary. Ensuring stationarity is crucial for reliable regression, for statistical properties, such as mean, variance, and autocorrelation, are constant regardless of time.[86] Lastly, seasonality was adjusted as covariates and therefore accounted. Neglecting to address these issues can result in biased outcomes.

The use of multiple intervention time points in ITS design is a subject of debate. Many studies addressing multiple treatment periods highlight the overarching correlation structure involved.[87] Consequently, other research utilizing three-segment measures has undergone rigorous autocorrelation review employing various testing methods, such as the Cumby-Huizinga general test and Newey-West standard errors.[88] Additionally, multilevel regression models were utilized to account for the clustering of observations within time periods.[89] In this study, correlation was tested through Durbin Watson statistic, and was

confirmed that no autocorrelation was found. Additionally, general estimating equations(GEE) were employed, a recognized method for accounting for clustering and repeated longitudinal observations.[90] GEE is particularly effective in correcting for autocorrelation in repeatedly collected outcomes within facilities, thereby preventing the underestimation of standard errors for time-dependent predictors.[91] Future studies should employ mixed-effects models, such as multilevel ITS to conduct similar study.

Despite these limitations, this study was meaningful trying to explore the differences of baseline level and trend to each legislation time points. Furthermore, utilizing population-based data in Korea to assess the legislative impact on all medical institutions is of considerable importance.

2. Discussion of the results

In this study, effect of newly legislated Patient Safety Act and revision of Medical Service Act about infection control on healthcare outcomes associated with infection control and healthcare utilization for inpatients was examined. As a result, the total days spent in hospitals for inpatient episodes decreased in trend throughout the two interventions and total expenditure throughout the study period increased constantly, regardless of the type of hospital. Moreover, use of restricted antibiotics in the tertiary hospitals have decreased after 2nd intervention in trend. In the tertiary hospital, sepsis decreased in trend after the 1st intervention. The general hospital showed significant effect size of decrease in pseudomembranous colitis immediately after the 1st intervention. Lastly, stratified by the grade level in receiving financial incentive for infection prevention and management, episodes from the hospitals that have 1st or 2nd grade showed compelling decrease in level after 1st intervention in use of restricted antibiotics.

Following the implementation of the Patient Safety Act in 2016, numerous policies and programs related to patient safety and infection control have been developed and enforced. These include the newly introduced provisions related to infection control in Healthcare Institution Accreditation,[92] the Antibiotic Resistance Management Program,[93] and the Infection Prevention and Control financial incentive policy[48]. The heightened focus on patient safety and infection control were largely driven by the increased social awareness and concern regarding patient safety issue that emerged prominently.

The Antimicrobial Stewardship Programme(ASP), which is a component of the National Antibiotic Resistance Management Program, encompasses a range of multidisciplinary initiatives aimed at ensuring the appropriate use of antimicrobials. Its objectives are to achieve optimal clinical outcomes, prevent adverse effects associated with antimicrobial use, reduce hospital costs, and curb the development of antimicrobial resistance.[94] Enhancing ASPs is a key component of the Korean National Action Plan on Antimicrobial Resistance 2016-2020.[95] Compared to smaller hospitals, tertiary hospitals have strength in these program, because of the power for the hospitals to lead the program with sufficient resources.[93,96] As of 2021, a study that identified the national status of ASPs found that small to medium sized Korean hospitals are not implementing such programs, but aware of the program and its usefulness.[97] Furthermore, since 2018, the Korea Institute for Healthcare Accreditation requires that for accreditation, acute care hospitals should have management systems for antibiotics, such as antimicrobial management committees.[98]

For effective infection control, dedicated personnel (such as infection control doctors and nurses), facilities and equipment (such as isolation rooms and pressure differential systems), and various consumables (such as hand sanitizers, disposable personal protective equipment, and environmental disinfectants) are necessary. Thus, hospitals need to secure and execute a budget that includes labor costs and more for appropriate infection control activities.[99] Prior to 2016, South Korea's health insurance system did not effectively provide compensation for this. However, with the introduction of the infection prevention and management fee as a reimbursable item under health

insurance, major hospitals began to establish comprehensive infection control infrastructures. This fee has significantly transformed the landscape of infection control management in South Korea.[82] The fee, ranging from 1650 to 4060 KRW per patient per day, is applicable under certain conditions, such as creating infection prevention and control teams, recruiting professionals for infection control, certifying medical institutions, participating in nationwide infection monitoring, and implementing infection control measures.[100] Due to this impact of reimbursement, results in this study by sorting the hospitals into level of receiving fees showed apparent difference among the grade levels in healthcare outcome.[101]

One of the results that was not in accordance with the hypothesis was the increase in total medical expenditure. Previous studies on medical expenditure trends in Korea have shown a consistent increase, which has raised significant concerns. Several factors contribute to this trend, one of which is the rise in pharmaceutical costs, which surged by 38.5% from 2011 to 2020. In 2020, Korea ranked third in pharmaceutical expenditure per capita and had the highest share of pharmaceutical expenditure among the 19 Organisation for Economics Co-operation and Development(OECD) countries studied.[102] Additionally, there is a direct correlation between population aging and healthcare expenditure. The proportion of medical expenses for the population aged 65 years and over out of total healthcare expenditure increased from 17.7% in 2001 to 34.4% in 2012. Korea is anticipated to face severe challenges with escalating healthcare costs due to its rapidly aging population, with the rate of increase outpacing that of Japan.[103]

Decrease in length of stay aligned with the hypothesis. Nevertheless, the overall decreasing trend may show other causes of the decrease, not only because of the laws and policy implementations regarding infection control. Similar to the reason of medical expenditure increase, the decrease in length of stay is associated with many causes. Implementation of Diagnosis Related Groups(DRG) payment system had an impact on length of stay. This payment system had a predefined compensation structure for specific groups of diseases, thus early discharge of patients was a strategy to prevent financial losses for hospitals.[103] Since healthcare providers were required to treat patients within a set budget, a clinical pathway(CP) was developed as a guideline for each medical service, functioning like a recipe for surgeries. Following CP would lessen the complications and most patients would be able to get discharged as planned.[104,105]

Furthermore, the use of a multidisciplinary team approach in patient treatment also impacts the length of hospital stay. There was a research on comparison of multidisciplinary initiative to the regular treatment, and the result showed decreasing length of stay in acute care surgery patients is possible without adding a significant burden to healthcare providers when performed multidisciplinary team approach.[106]

Improved post-acute care facilities and home based care programs also affected the decrease in length of stay. Discharge planning, which is now commonly planned in healthcare facilities for high risk populations, could be helpful for the patients to be discharged without delay, but still get the treatment elsewhere or at home. As this field area advances, the overall length of stay could decrease further. [107]

Quality assessment of Health Insurance Review and Assessment Service of Korea(HIRA) is an annual evaluation that determines the reimbursement rates based on the performance of specific critera.[108] Korea operates a single-payer health insurance system, which is mandatory for all citizens. In 2014, HIRA started assessing the length of inpatient stays as a criterion for reimbursing hospitals. This move was controversial due to the absence of adjustments for patient condition severity in the assessment.[108] Since reimbursement is tied to these evaluations, hospitals might have expedited patient discharges to increase bed occupancy rates.[108]

The Patient Safety Act, the amendments to medical laws concerning infection control, introduction of new provisions related to infection control in the Healthcare Institution Accreditation, the Antibiotic Resistance Management Program, and the Infection Prevention and Control Fee are all designed with a unified objective and are largely interconnected in their systems and concepts. These measures were implemented around the same period and target similar groups, making it challenging to analyze them in isolation. For future studies, to eliminate the history effect of policies related to patient safety or infection control, it is essential to collect detailed data and maintain a micro-level focus during the design phase.

VI. Conclusion

This study identified the effectiveness of legislation of The Patient Safety Act and revision of the Medical Service Act concerning infection control to health outcome and utilization related to infection. Series of legislations to control patient safety, especially infection prevention, was effective on length of stay for inpatients in both interventions an in all types of hospitals. Marginal reduction in the use of restricted antibiotics was observed in larger hospitals.

Through the results of this study, law imposition was proven to be effective, and parts that need additional effort has been revealed. Present results could provide support in reinforcing the law and also accommodate government support for the small hospitals. Furthermore, such information may be valuable for reforming of other management systems when applying to all types of hospitals.

Abbreviations

ICU – Intensive Care Unit

SEIPS – Systems Engineering Initiative for Patient Safety

SPO – Structure-process-outcomes model

WHO – World Health Organization

AHRQ – Agency for Healthcare Research and Quality

CDC – Centers for Disease Control and Prevention

FDA – Food and Drug Administration

OSHA – Occupational Safety and Health Administration

UK – United Kingdom

NHS – National Health Services

CQC – Care Quality Commission

IDCL – Infectious Disease Control Law

JCI – Joint Commission International

NHIS-NSC – National Health Insurance Service National Sample Cohort

ICD - International Classification of Diseases

CCI – Charlson Comorbidity Index

ITS – Interrupted Time Series

GEE – Generalized Estimating Equation

IRB – International Review Board

ASP – Antimicrobial Stewardship Programme

OECD – Organisation for Economic Co-operation and Development

DRG - Diagnosis Related Groups

CP – Clinical Pathway

HIRA – Health Insurance Review and Assessment Service of Korea

References

1. Campbell SM, Roland MO, Buetow SA. Defining quality of care. Social science & medicine 2000;51:1611-25.
2. Mitchell PH. Defining patient safety and quality care. Patient safety and quality: An evidence-based handbook for nurses 2008.
3. Reed D, Kemmerly SA. Infection control and prevention: a review of hospital-acquired infections and the economic implications. Ochsner Journal 2009;9:27-31.
4. Bjerke NB, Fabrey LJ, Johnson CB, Bennet G, Schollenberger D, Jacobsen D, et al. Job analysis 1992: infection control practitioner. American Journal of Infection Control 1993;21:51-7.
5. Ock M, Kim JH, Lee S-i. A legal framework for improving patient safety in Korea. Health Policy and Management 2015;25:174-84.
6. Choi JS. Changes of the core competency of infection control nurses in accordance with the new law supporting infection control manpower. Korean Journal of Healthcare-Associated Infection Control and Prevention 2019;24:35-42.
7. Korean Law No. [Medical Service Act Enforcement Regulation]. (2016). Article 43.
8. Park E-C. Strategies for improving healthcare delivery system in Korea. Health Insurance Review & Assessment Service Research 2021;1:9-15.
9. Han D, Kim B, Lee Y, Bae S, Kwon S. An Evaluative Analysis of the Referral System for Insurance Patients. Journal of Preventive Medicine and Public Health 1991;24:485-95.
10. Park E-C, Jang S-I. The diagnosis of healthcare policy problems in Korea. Journal of the Korean Medical Association/Taehan Uisa Hyophoe Chi 2012;55.
11. Han D-S. A revisit to policy agenda concerned with the distortion of functional differentiation among health care providers. Health Policy and Management 2010;20:1-18.
12. Blumenthal D. Quality of care—what is it? : Mass Medical Soc; 1996. p.891-4.
13. Donabedian A. Evaluating the quality of medical care. The Milbank memorial fund quarterly 1966;44:166-206.
14. Braun BI, Chitavi SO, Suzuki H, Soyemi CA, Puig-Asensio M. Culture of safety: impact on improvement in infection prevention process and outcomes. Current infectious disease reports 2020;22:1-41.
15. Yanke E, Zellmer C, Van Hoof S, Moriarty H, Carayon P, Safdar N. Understanding the current state of infection prevention to prevent Clostridium difficile infection: a human factors and systems engineering approach. American journal of infection control 2015;43:241-7.
16. Donabedian A. Evaluating the quality of medical care. The Milbank Quarterly 2005;83:691.
17. Carayon P. Human factors of complex sociotechnical systems. Applied ergonomics 2006;37:525-35.

18. Lumley C, Ellis A, Ritchings S, Venes T, Ede J. Using the Systems Engineering Initiative for Patient Safety (SEIPS) model to describe critical care nursing during the SARS-CoV-2 pandemic (2020). Nursing in critical care 2020;25:203.
19. Clayton JL, Miller KJ. Professional and regulatory infection control guidelines: collaboration to promote patient safety. AORN journal 2017;106:201-10.
20. Kwan W-M, Mok C-K, Kwok Y-T, Ling H, Lam H-W, Law T-H, et al. Using the Systems Engineering Initiative for Patient Safety (SEIPS) model to describe the planning and management of the COVID-19 pandemic in Hong Kong. International Journal for Quality in Health Care 2021;33:mzab042.
21. World Health Organization: Patient Safety. Available at: https://www.who.int/news-room/fact-sheets/detail/patient-safety
22. Kohn L, Corrigan J, Donaldson M. Institute of Medicine. To err is human: building a safer health system. Washington, DC: National Academy Press; 2000.
23. Indicators AQ. Guide to patient safety indicators. Rockville, MD: Agency for Healthcare Research and Quality 2003.
24. Giese A, Khanam R, Nghiem S, Staines A, Rosemann T, Boes S, et al. Assessing the excess costs of the in-hospital adverse events covered by the AHRQ's Patient Safety Indicators in Switzerland. Plos one 2024;19:e0285285.
25. Clarkson PJ, Buckle P, Coleman R, Stubbs D, Ward J, Jarrett J, et al. Design for patient safety: a review of the effectiveness of design in the UK health service. Journal of Engineering Design 2004;15:123-40.
26. Kim J, Lee M. A Comparative Study on the Patient Safety Law: Korea, USA and Denmark.
27. Levy F, Mareniss D, Iacovelli C, Howard J. The patient safety and quality improvement act of 2005: preventing error and promoting patient safety. The Journal of Legal Medicine 2010;31:397-422.
28. Hirose M. Is patient safety sufficient in Japan? Differences in patient safety between Japan and the United States–Learning from the United States. Journal of Hospital Administration 2016;5:1-13.
29. Korean Law No. [Patient Safety Act]. (2016). Article 1-19.
30. Kim Y-M. Application of patient safety indicators using Korean national hospital discharge In-depth injury survey. Journal of the Korea Academia-industrial cooperation society 2013;14:2293-303.
31. Shin S, Won M. Trend analysis of patient safety incidents and their associated factors in korea using national patient safety report data (2017~ 2019). International Journal of Environmental Research and Public Health 2021;18:8482.
32. Pittet D. Infection control and quality health care in the new millenium. American journal of infection control 2005;33:258-67.
33. Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchman SD, et al. Guideline for infection control in healthcare personnel, 1998. Infection Control & Hospital Epidemiology 1998;19:407-63.
34. Burke JP. Infection control-a problem for patient safety. New England Journal of Medicine 2003;348:651-6.

35. Haustein T, Gastmeier P, Holmes A, Lucet J-C, Shannon RP, Pittet D, et al. Use of benchmarking and public reporting for infection control in four high-income countries. The Lancet infectious diseases 2011;11:471-81.
36. Kawabata J, Fukuda H, Morikane K. Effect of participation in a surgical site infection surveillance programme on hospital performance in Japan: a retrospective study. Journal of Hospital Infection 2023.
37. Okubo Y, Nishi A, Uda K, Miyairi I, Michihata N, Kumazawa R, et al. Financial incentives for infection prevention and antimicrobial stewardship to reduce antibiotic use: Japan's nationwide observational study. Journal of Hospital Infection 2023;131:89-98.
38. Sekimoto M, Imanaka Y, Kobayashi H, Okubo T, Kizu J, Kobuse H, et al. Impact of hospital accreditation on infection control programs in teaching hospitals in Japan. American journal of infection control 2008;36:212-9.
39. Korean law No. [Infectious Disease Control and Prevention Act]. (2009). .
40. Medical Services Act. Korean Law; 1973.
41. Kim J-M, Choi Y-S. Awareness and performance about nosocomial infection management; a early stage nurse in small and medium hospitals. Journal of the Korea Academia-Industrial cooperation Society 2018;19:492-500.
42. Carayon P, Wetterneck TB, Rivera-Rodriguez AJ, Hundt AS, Hoonakker P, Holden R, et al. Human factors systems approach to healthcare quality and patient safety. Applied ergonomics 2014;45:14-25.
43. Lee J. The present and future of infection control policy in Korea. Korean Journal of Healthcare-associated Infection Control and Prevention 2020;25:70-8.
44. Lamming L, Montague J, Crosswaite K, Faisal M, McDonach E, Mohammed MA, et al. Fidelity and the impact of patient safety huddles on teamwork and safety culture: an evaluation of the Huddle Up for Safer Healthcare (HUSH) project. BMC Health Services Research 2021;21:1-11.
45. Jeffs L, Abramovich IA, Hayes C, Smith O, Tregunno D, Chan W-H, et al. Implementing an interprofessional patient safety learning initiative: insights from participants, project leads and steering committee members. BMJ Quality & Safety 2013;22:923-30.
46. Piotrowski MM, Saint S, Hinshaw DB. The Safety Case Management Committee: expanding the avenues for addressing patient safety. The Joint Commission journal on quality improvement 2002;28:296-305.
47. Weaver SJ, Lubomksi LH, Wilson RF, Pfoh ER, Martinez KA, Dy SM. Promoting a culture of safety as a patient safety strategy: a systematic review. Annals of internal medicine 2013;158:369-74.
48. Park YS, Kim SY, Kim H, Jang S-Y, Park E-C. Impact of financial incentives for infection prevention and management on antibiotic use: A Korea National Health Insurance cohort study. Journal of Infection and Public Health 2024;17:362-9.
49. Song P, Li W, Zhou Q. An outpatient antibacterial stewardship intervention during the journey to JCI accreditation. BMC Pharmacology and Toxicology 2014;15:1-9.

50. Kim SH. Association between nurse staffing level and medical-related infections in surgical patients: Yonsei University Graduate School; 2022.
51. Emmerson A, Enstone J, Griffin M, Kelsey M, Smyth E. The Second National Prevalence Survey of infection in hospitals—overview of the results. Journal of hospital infection 1996;32:175-90.
52. Fernando SA, Gray TJ, Gottlieb T. Healthcare-acquired infections: prevention strategies. Internal medicine journal 2017;47:1341-51.
53. Gilmartin HM, Sousa KH. Testing the Quality Health Outcomes Model applied to infection prevention in hospitals. Quality Management in Healthcare 2016;25:149-61.
54. Haque M, Sartelli M, McKimm J, Bakar MA. Health care-associated infections–an overview. Infection and drug resistance 2018:2321-33.
55. Jang W, Hwang H, Jo H-u, Cha Y-H, Kim B. Effect of discontinuation of an antimicrobial stewardship programme on the antibiotic usage pattern. Clinical Microbiology and Infection 2021;27:1860. e1-. e5.
56. Tarcea Bizo P, Dumitras D, Popa A. Evaluation of restricted antibiotic use in a hospital in Romania. International journal of clinical pharmacy 2015;37:452-6.
57. Mahmoudi L, Sepasian A, Firouzabadi D, Akbari A. The impact of an antibiotic stewardship program on the consumption of specific antimicrobials and their cost burden: a hospital-wide intervention. Risk Management and Healthcare Policy 2020:1701-9.
58. Eljaaly K, Elarabi S, Alshehri S, Nix DE. Impact of requiring re-authorization of restricted antibiotics on day 3 of therapy. Journal of Antimicrobial Chemotherapy 2018;73:527-30.
59. Oh YH. Establishment of Healthcare Delivery System through Improvement of Health Insurance System. Health Policy and Management 2019;29:248-61.
60. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. International journal of epidemiology 2017;46:348-55.
61. Linden A. Conducting interrupted time-series analysis for single-and multiple-group comparisons. The Stata Journal 2015;15:480-500.
62. Sheingold S, Bir A. Evaluation for health policy and health care: a contemporary data-driven approach: SAGE Publications; 2019.
63. Zorn CJ. Generalized estimating equation models for correlated data: A review with applications. American Journal of Political Science 2001:470-90.
64. Fitzmaurice GM, Laird NM, Ware JH. Applied longitudinal analysis: John Wiley & Sons; 2012.
65. Ridout M, Hinde J, Demétrio CG. A score test for testing a zero-inflated Poisson regression model against zero-inflated negative binomial alternatives. Biometrics 2001;57:219-23.
66. Lee DW, Jang J, Choi D-W, Jang S-I, Park E-C. The effect of shifting medical coverage from National Health Insurance to Medical Aid type I and type II on health care utilization and out-of-pocket spending in South Korea. BMC health

services research 2020;20:1-10.
67. Blough DK, Ramsey SD. Using generalized linear models to assess medical care costs. Health Services and Outcomes Research Methodology 2000;1:185-202.
68. Hudson J, Fielding S, Ramsay CR. Methodology and reporting characteristics of studies using interrupted time series design in healthcare. BMC medical research methodology 2019;19:1-7.
69. Jandoc R, Burden AM, Mamdani M, Lévesque LE, Cadarette SM. Interrupted time series analysis in drug utilization research is increasing: systematic review and recommendations. Journal of clinical epidemiology 2015;68:950-6.
70. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. Journal of clinical pharmacy and therapeutics 2002;27:299-309.
71. Nguyen P-Y, Turner S, Korevaar E, Forbes A, Page MJ, McKenzie JE. Investigation of reporting bias in interrupted time series (ITS) studies: a study protocol. F1000Research 2024;13:153.
72. Taljaard M, McKenzie JE, Ramsay CR, Grimshaw JM. The use of segmented regression in analysing interrupted time series studies: an example in pre-hospital ambulance care. Implementation Science 2014;9:1-4.
73. Habib N, Steyn PS, Boydell V, Cordero JP, Nguyen MH, Thwin SS, et al. The use of segmented regression for evaluation of an interrupted time series study involving complex intervention: the CaPSAI project experience. Health Services and Outcomes Research Methodology 2021;21:188-205.
74. Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE. Interrupted time series designs in health technology assessment: lessons from two systematic reviews of behavior change strategies. International journal of technology assessment in health care 2003;19:613-23.
75. shin Park Y, Kim H, Jang S-Y, Park E-C. Trends in private caregiving cost after implementing a comprehensive nursing service covered by national health insurance: Interrupted time series. International Journal of Nursing Studies 2024;152:104689.
76. Park YS, Song IS, Jang SY, Nam CM, Park EC. Impact of Cardiac Rehabilitation Health Insurance Coverage on Cardiac Rehabilitation Use in Korea Using an Interrupted Time Series. Journal of the American Heart Association 2024;13:e031395.
77. Kwon S. Thirty years of national health insurance in South Korea: lessons for achieving universal health care coverage. Health policy and planning 2009;24:63-71.
78. Promotion NCfEaZIDUSDoHQ. CDC's Core Infection Prevention and Control Practices for Safe Healthcare Delivery in All Settings. Available at: https://stacks.cdc.gov/view/cdc/134781 [Accessed June 2024]
79. Dawson S. The role of the infection control link nurse. Journal of Hospital Infection 2003;54:251-7.
80. Peter D, Meng M, Kugler C, Mattner F. Strategies to promote infection prevention

and control in acute care hospitals with the help of infection control link nurses: a systematic literature review. American journal of infection control 2018;46:207-16.
81. Perry C. The infection control nurse in England—past, present and future. British Journal of Infection Control 2005;6:18-21.
82. Eom JS. What is the fee for infection prevention and control? current status and prospect. The Korean Journal of Medicine 2022;97:199-203.
83. Lagarde M. How to do (or not to do)… Assessing the impact of a policy change with routine longitudinal data. Health policy and planning 2012;27:76-83.
84. Bero L, Deane K, Eccles M, Grimshaw J, Gruen R, Mayhew A, et al. Cochrane Effective Practice and Organisation of Care Review Group (Cochrane Group Module). The Cochrane Library 2009.
85. Durbin J, Watson GS. Testing for serial correlation in least squares regression. III. Biometrika 1971;58:1-19.
86. Dickey DA, Fuller WA. Distribution of the estimators for autoregressive time series with a unit root. Journal of the American statistical association 1979;74:427-31.
87. Cruz M, Bender M, Ombao H. A robust interrupted time series model for analyzing complex health care intervention data. Statistics in medicine 2017;36:4660-76.
88. MacBride-Stewart S, Marwick C, Houston N, Watt I, Patton A, Guthrie B. Evaluation of a complex intervention to improve primary care prescribing: a phase IV segmented regression interrupted time series analysis. British Journal of General Practice 2017;67:e352-e60.
89. Kontopantelis E, Doran T, Springate DA, Buchan I, Reeves D. Regression based quasi-experimental approach when randomisation is not an option: interrupted time series analysis. bmj 2015;350.
90. Hanley JA, Negassa A, Edwardes MDd, Forrester JE. Statistical analysis of correlated data using generalized estimating equations: an orientation. American journal of epidemiology 2003;157:364-75.
91. Ansari F, Gray K, Nathwani D, Phillips G, Ogston S, Ramsay C, et al. Outcomes of an intervention to improve hospital antibiotic prescribing: interrupted time series with segmented regression analysis. Journal of Antimicrobial Chemotherapy 2003;52:842-8.
92. Jeong S-Y, Oh H-S, Chun H-K. Analysis of the status of infection controls after application of the healthcare accreditation system. The Korean journal of health service management 2015;9:33-49.
93. Shin DH, Kim H-S, Heo E, Shin M-j, Kim N-H, Lee H, et al. Stepwise expansion of antimicrobial stewardship programs and its impact on antibiotic use and resistance rates at a tertiary care hospital in Korea. Microbiology spectrum 2022;10:e00335-22.
94. MacDougall C, Polk RE. Antimicrobial stewardship programs in health care systems. Clinical microbiology reviews 2005;18:638-56.
95. Ryu S. The new Korean action plan for containment of antimicrobial resistance. Journal of global antimicrobial resistance 2017;8:70-3.

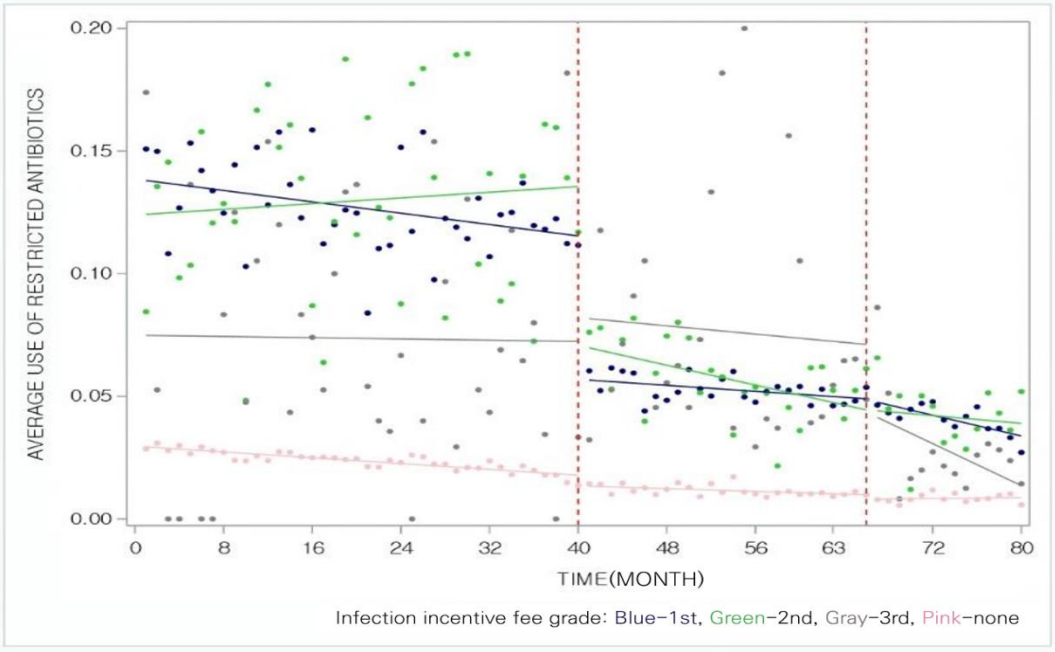
96. Cheong HS, Park K-H, Kim HB, Kim S-W, Kim B, Moon C, et al. Core elements for implementing antimicrobial stewardship programs in Korean general hospitals. Infection & Chemotherapy 2022;54:637.
97. Kim B, Kim J, Kim S-w, Pai H. A survey of antimicrobial stewardship programs in Korea, 2015. Journal of Korean medical science 2016;31:1553-9.
98. Oh HS, Chung HW, Kim JS, Cho SI. National survey of the status of infection surveillance and control programs in acute care hospitals with more than 300 beds in the Republic of Korea. American journal of infection control 2006;34:223-33.
99. Yoon YK, Lee SE, Seo BS, Kim HJ, Kim JH, Yang KS, et al. Current status of personnel and infrastructure resources for infection prevention and control programs in the Republic of Korea: A national survey. American Journal of Infection Control 2016;44:e189-e93.
100. Lee J. The present and future of infection control policy in Korea. 2020.
101. Haley RW, White JW, Culver DH, Hughes JM. The financial incentive for hospitals to prevent nosocomial infections under the prospective payment system: an empirical determination from a nationally representative sample. Jama 1987;257:1611-4.
102. Kim Y, Chae J, Shin S, Jo G, Shin J, Kim B, et al. Trends in National Pharmaceutical Expenditure in Korea during 2011-2020. Infection & Chemotherapy 2023;55:237.
103. Hyun KR, Kang S, Lee S. Population aging and healthcare expenditure in Korea. Health economics 2016;25:1239-51.
104. Geissler A, Scheller-Kreinsen D, Quentin W, Group E. Do diagnosis-related groups appropriately explain variations in costs and length of stay of hip replacement? A comparative assessment of DRG systems across 10 European countries. Health Economics 2012;21:103-15.
105. Rotter T, Kugler J, Koch R, Gothe H, Twork S, van Oostrum JM, et al. A systematic review and meta-analysis of the effects of clinical pathways on length of stay, hospital costs and patient outcomes. BMC health services research 2008;8:1-15.
106. DePesa CD, El Hechi MW, McKenzie R, Waak K, Woodis L, Chang Y, et al. A multidisciplinary approach to decreasing length of stay in acute care surgery patients. Journal of Advanced Nursing 2020;76:1364-70.
107. Siddique SM, Tipton K, Leas B, Greysen SR, Mull NK, Lane-Fall M, et al. Interventions to reduce hospital length of stay in high-risk populations: a systematic review. JAMA network open 2021;4:e2125846-e.
108. Kim J-H, Kim A-K. A quality assessment of meta-analyses of nursing in South Korea. Journal of Korean Academy of Nursing 2013;43:736-45.

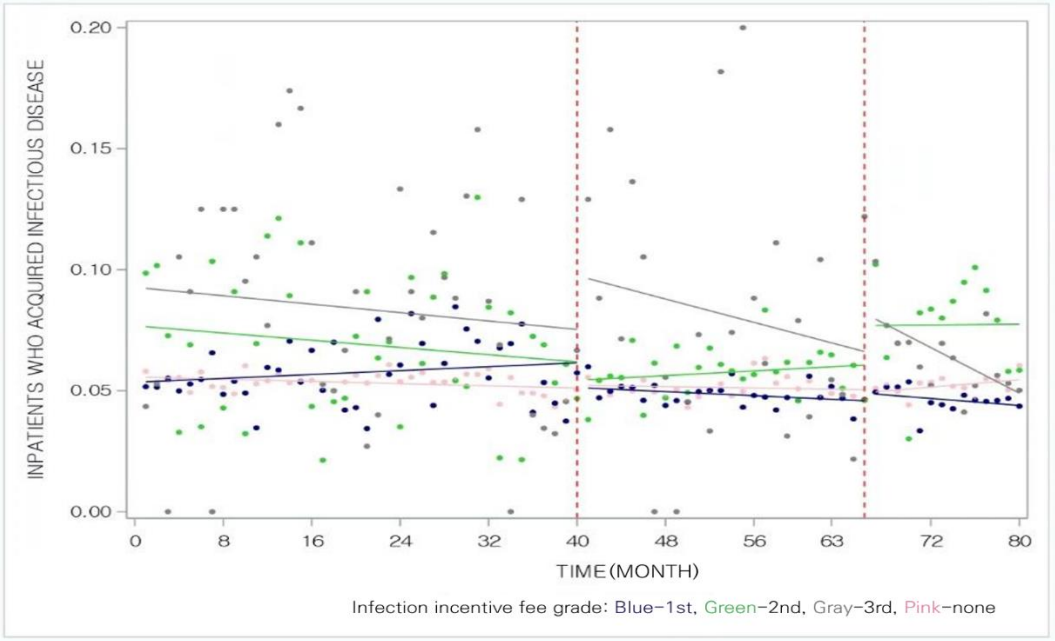
Appendix

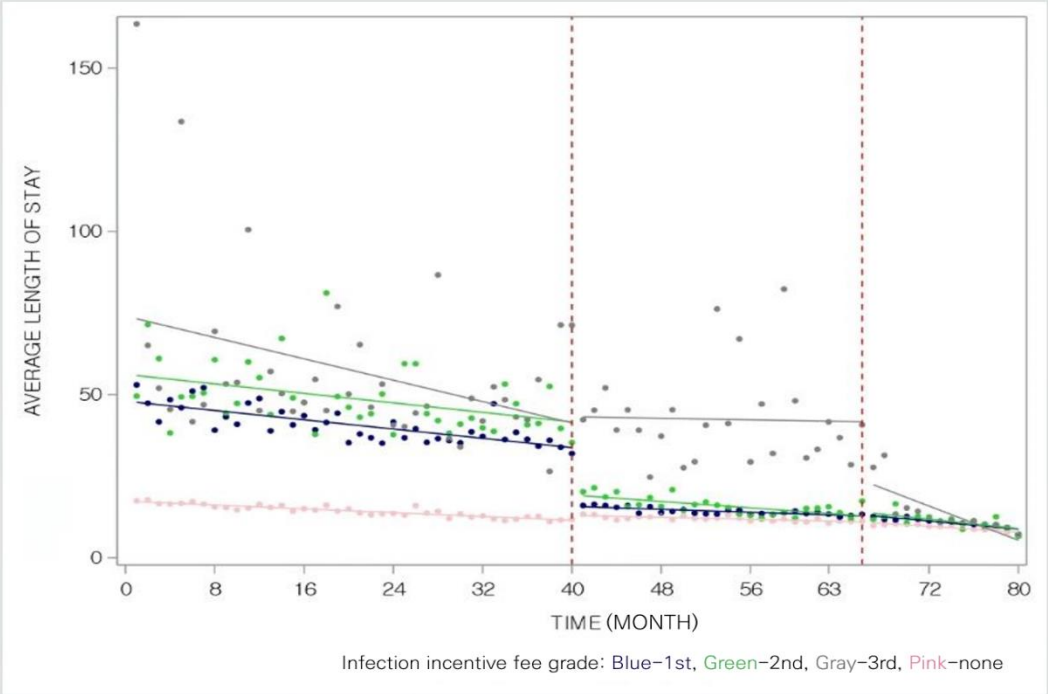
Appendix 1. Weighted index applied to calculate CCI score

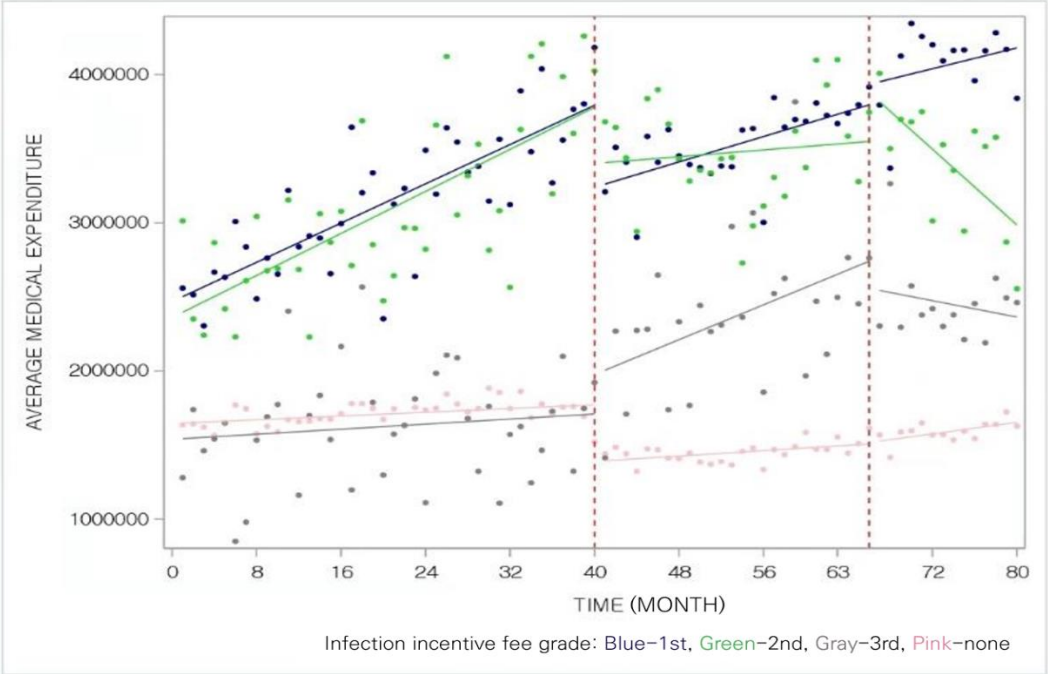
Conditions	Assigned weights for each condition
Myocardial infarction	1
Congestive heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic pulmonary disease	1
Connective tissue disease	1
Ulcer disease	1
Mild liver disease	1
Diabetes	1
Hemiplegia	2
Moderate or severe renal disease	2
Diabetes with end organ damage	2
Any tumor	2
Leukemia / lymphoma	2
Moderate or severe liver disease	3
Metastatic solid tumor	6
AIDS	6

Appendix 2. Result of ITS analysis on healthcare outcomes and utilization stratified by the financial incentive levels of infection control

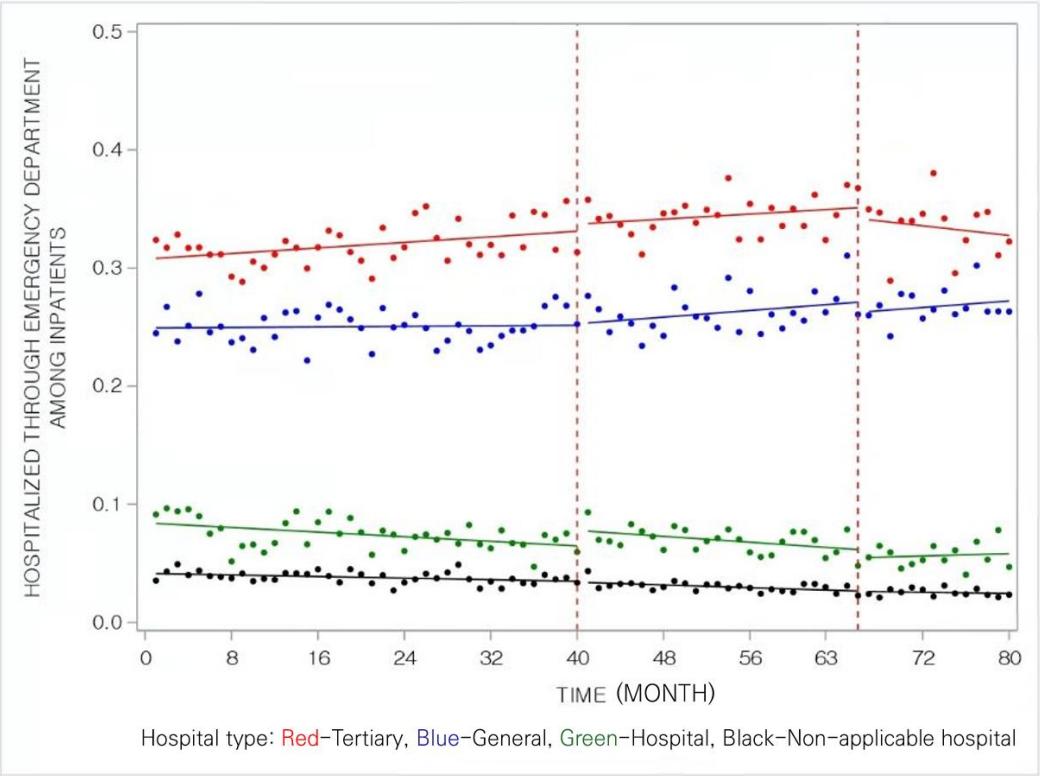








Appendix 3. Result of ITS analysis on admission through emergency department during the intervention periods (Outcome control)



Parameter	Exp(β)	Exp(SE(β))	95% Confidence interval		P-value
Hospitalization through Emergency Room (Outcome control)					
Tertiary Hospital					
Intercept β0	0.1111	1.1112	0.0903	0.1365	<.0001
Baseline trend β1	1.0003	1.0008	0.9987	1.0020	0.6948
Level change after 1st intervention β2	0.9751	1.0349	0.9116	1.0429	0.462
Trend change after 1st intervention β3	1.0023	1.0020	0.9983	1.0062	0.2573
Level change after 2nd intervention β4	0.9777	1.0502	0.8883	1.0761	0.6444
Trend change after 2nd intervention β5	0.9964	1.0052	0.9863	1.0066	0.4861

General Hospital					
Intercept β0	0.4177	1.0682	0.3670	0.4754	<.0001
Baseline trend β1	0.9990	1.0006	0.9978	1.0003	0.1357
Level change after 1st intervention β2	0.9936	1.0265	0.9439	1.0459	0.8072
Trend change after 1st intervention β3	1.0027	1.0015	0.9997	1.0057	0.0796
Level change after 2nd intervention β4	1.0025	1.0381	0.9316	1.0787	0.9472
Trend change after 2nd intervention β5	0.9975	1.0040	0.9898	1.0053	0.5293
Hospital					
Intercept β0	0.0799	1.2056	0.0554	0.1152	<.0001
Baseline trend β1	0.9935	1.0020	0.9897	0.9973	0.0009
Level change after 1st intervention β2	1.1774	1.0840	1.0052	1.3791	0.043
Trend change after 1st intervention β3	0.9997	1.0048	0.9903	1.0092	0.9533
Level change after 2nd intervention β4	0.9608	1.1373	0.7465	1.2364	0.7558
Trend change after 2nd intervention β5	1.0121	1.0138	0.9852	1.0396	0.3818
Non-applicable hospital					
Intercept β0	0.1383	1.1790	0.1001	0.1910	<.0001
Baseline trend β1	0.9954	1.0016	0.9922	0.9985	0.004
Level change after 1st intervention β2	0.9800	1.0698	0.8586	1.1187	0.7652
Trend change after 1st intervention β3	0.9975	1.0041	0.9897	1.0055	0.5435
Level change after 2nd intervention β4	1.1606	1.1098	0.9461	1.4235	0.1532
Trend change after 2nd intervention β5	0.9947	1.0114	0.9731	1.0169	0.6399

Appendix 4. Results of subgroup analysis stratified by health related individual factors in all hospitals

Variables	Restricted antibiotics use				Healthcare associated infection			
	Exp(β_2) (*p*-value)	**Exp(β_3) (*p*-value)**	**Exp(β_4) (*p*-value)**	**Exp(β_5) (*p*-value)**	**Exp(β_2) (*p*-value)**	**Exp(β_3) (*p*-value)**	**Exp(β_4) (*p*-value)**	**Exp(β_5) (*p*-value)**
Surgical procedure during the stay								
Yes	0.989 (0.8364)	0.999 (0.7750)	1.080 (0.3234)	0.972 (0.0007)	0.952 (0.3267)	0.997 (0.3611)	0.997 (0.9646)	1.001 (0.9169)
No	1.101 (0.0971)	**0.990 (0.0040)**	0.935 (0.4688)	0.999 (0.9495)	0.981 (0.5826)	1.002 (0.3979)	1.033 (0.5260)	1.003 (0.5585)
Disability status								
Yes	0.933 (0.4034)	1.000 (0.9746)	0.963 (0.7552)	0.986 (0.3005)	0.960 (0.5803)	0.996 (0.4195)	1.087 (0.4380)	0.998 (0.8288)
No	1.072 (0.1224)	**0.994 (0.0247)**	1.037 (0.5878)	**0.982 (0.0152)**	0.977 (0.4634)	1.001 (0.5014)	1.004 (0.9255)	1.003 (0.4722)
CCI								
0	1.016 (0.8559)	**0.983 (0.0012)**	1.342 (0.0220)	0.978 (0.1058)	1.002 (0.9678)	0.998 (0.5960)	1.109 (0.1501)	1.000 (0.9720)
1	1.197 (0.0384)	0.997 (0.4960)	0.907 (0.4515)	0.992 (0.5515)	0.919 (0.1171)	1.003 (0.3150)	0.931 (0.3574)	1.010 (0.2222)
2	1.038 (0.6981)	1.000 (0.9776)	0.997 (0.9825)	**0.961 (0.0151)**	1.037 (0.6377)	0.998 (0.6650)	0.874 (0.2466)	1.027 (0.0256)
3	0.980 (0.7326)	0.998 (0.5764)	0.946 (0.5430)	0.991 (0.3516)	0.978 (0.6929)	1.001 (0.6931)	1.077 (0.3645)	0.985 (0.0830)

Treatment result								
Continue	1.135	0.992	1.128	**0.975**	0.950	0.997	1.057	1.012
	(0.1075)	(0.0922)	(0.2901)	**(0.0360)**	(0.5266)	(0.5158)	(0.6305)	(0.2940)
Transfer	0.828	1.020	1.048	0.959	0.849	1.019	0.857	0.975
	(0.3905)	(0.1096)	(0.8651)	(0.1550)	(0.4360)	(0.1166)	(0.5842)	(0.4030)
Deceased	1.246	1.010	1.171	0.951	1.877	**0.973**	1.427	1.062
	(0.2687)	(0.3523)	(0.5533)	(0.0957)	(0.0013)	**(0.0168)**	(0.2010)	(0.0452)
Discharge	1.000	**0.994**	0.961	0.990	0.967	1.001	1.009	1.000
	(0.9960)	**(0.0239)**	(0.5960)	(0.2205)	(0.2932)	(0.5346)	(0.8515)	(0.9463)
Invasive treatment								
Central catheter	1.213	0.995	1.193	0.977	1.241	1.001	0.987	1.008
	(0.0957)	(0.4520)	(0.2791)	(0.1910)	(0.1163)	(0.9245)	(0.5023)	(0.7013)
Ventilation or tracheostomy	0.965	1.016	1.263	**0.924**	1.165	0.983	1.402	0.999
	(0.8222)	(0.0726)	(0.2625)	**(0.0006)**	(0.4166)	(0.1047)	(0.1916)	(0.9622)
None	1.033	**0.994**	0.971	0.991	0.961	1.001	1.014	1.003
	(0.4593)	**(0.0117)**	(0.6583)	(0.1950)	(0.1795)	(0.6441)	(0.7392)	(0.5639)
Primary diagnosis (by ICD-10 code categories)								
Muscoloskeletal system and connective tissue(M00-M99)	1.117	1.000	1.067	0.991	0.984	0.996	0.941	1.008
	(0.3642)	(0.9846)	(0.6845)	(0.5740)	(0.8512)	(0.4388)	(0.6274)	(0.5325)
Injury, poisoning and certain other consequences of external causes(S00-T98)	1.116	0.999	1.024	0.965	0.917	0.996	1.113	0.988
	(0.3934)	(0.8437)	(0.9004)	(0.0819)	(0.3237)	(0.4371)	(0.3954)	(0.3596)
Digestive system(K00-K93)	1.034	0.987	1.204	0.979	0.980	1.002	0.914	1.019
	(0.7930)	(0.0776)	(0.3293)	(0.3077)	(0.8544)	(0.7541)	(0.5685)	(0.2630)

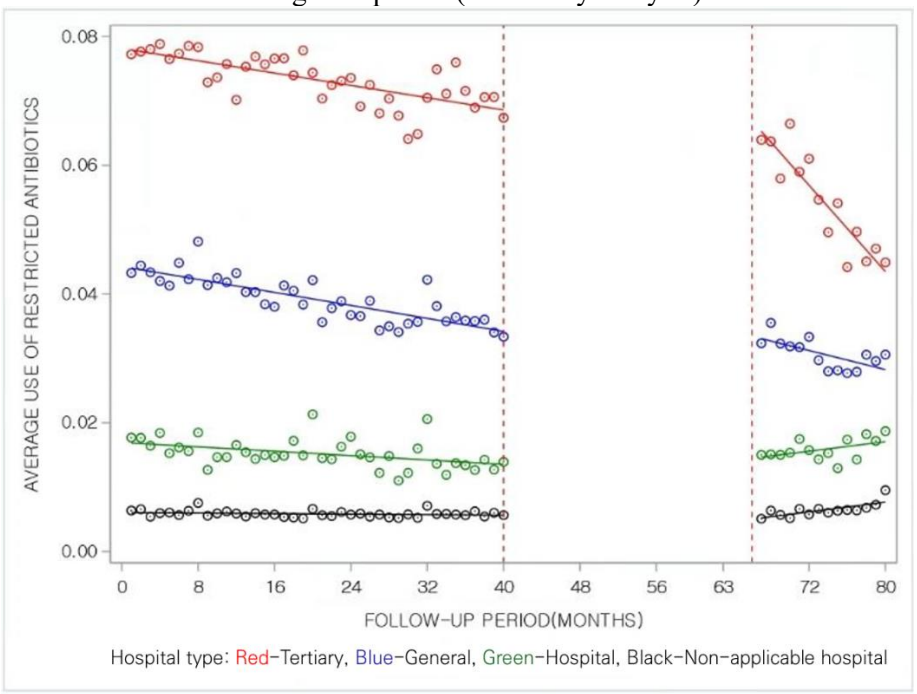
Respiratory system(J00-J99)	1.192	**0.979**	1.047	1.032	1.048	1.006	1.003	0.995
	(0.2596)	**(0.0263)**	(0.8436)	(0.2000)	(0.4813)	(0.1175)	(0.9742)	(0.6249)
Neoplasm(C00-D48)	1.038	0.998	0.958	**0.965**	0.910	1.003	1.043	1.016
	(0.6526)	(0.6434)	(0.7283)	**(0.0110)**	(0.3815)	(0.6791)	(0.7776)	(0.3101)
Circulatory system(I00-I99)	0.899	0.999	1.021	0.974	1.049	1.005	1.027	0.992
	(0.3460)	(0.9279)	(0.8998)	(0.1578)	(0.6527)	(0.4260)	(0.8618)	(0.6460)
Else	1.011	**0.991**	1.067	0.989	0.967	0.999	1.047	1.002
	(0.8827)	**(0.0356)**	(0.5854)	(0.3986)	(0.4797)	(0.6144)	(0.5092)	(0.7532)

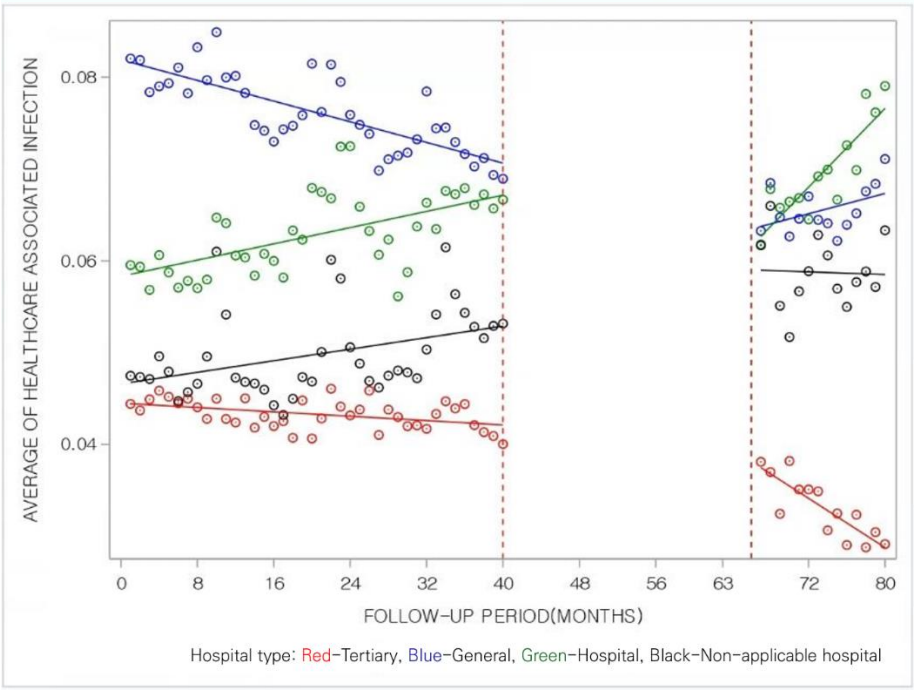
Variables	**Length of Stay**				**Medical Expenditure**			
	Exp(β_2) (*p*-value)	**Exp(β_3) (*p*-value)**	**Exp(β_4) (*p*-value)**	**Exp(β_5) (*p*-value)**	**Exp(β_2) (*p*-value)**	**Exp(β_3) (*p*-value)**	**Exp(β_4) (*p*-value)**	**Exp(β_5) (*p*-value)**
Surgical procedure during the stay								
Yes	**0.972**	**0.996**	1.030	**0.981**	**0.972**	1.000	1.018	0.999
	<.0001	**<.0001**	<.0001	**<.0001**	**<.0001**	(0.2944)	(0.0731)	(0.4272)
No	1.012	1.000	1.085	**0.969**	1.019	1.000	1.060	1.001
	<.0001	(0.9136)	<.0001	**<.0001**	(0.0029)	(0.6783)	<.0001	(0.2686)
Disability status								
Yes	**0.991**	**0.997**	1.086	**0.958**	0.991	**0.998**	1.007	1.002
	(0.0189)	**<.0001**	<.0001	**<.0001**	(0.5723)	**(0.0346)**	(0.7603)	(0.4548)
No	1.006	1.000	1.055	**0.977**	0.999	1.000	1.044	1.000
	(0.0021)	(0.3388)	<.0001	**<.0001**	(0.8444)	(0.3060)	<.0001	(0.6955)
CCI								

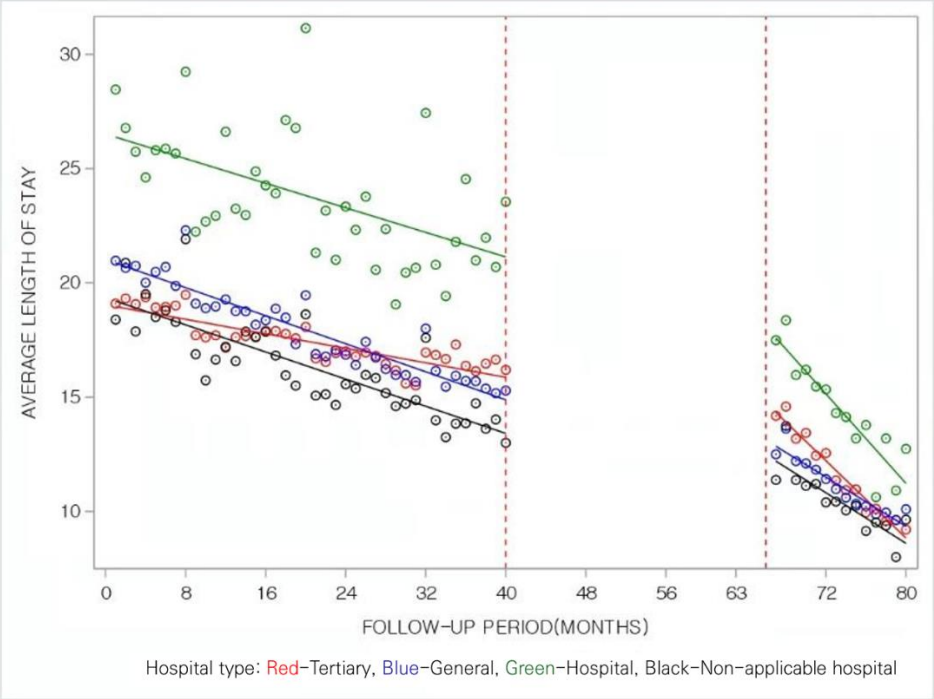
0	1.027	1.000	1.029	**0.980**	0.989	1.001	1.038	1.001
	<.0001	(0.3368)	<.0001	**<.0001**	(0.1341)	(0.0955)	(0.0006)	(0.3665)
1	1.000	1.002	1.026	**0.980**	1.017	1.000	1.046	1.001
	(0.9182)	<.0001	<.0001	**<.0001**	(0.0660)	(0.4456)	(0.0006)	(0.7267)
2	1.013	**0.997**	1.124	**0.968**	1.000	0.999	1.070	0.998
	(0.0023)	**<.0001**	<.0001	**<.0001**	(0.9925)	(0.3717)	(0.0003)	(0.2109)
3	**0.986**	**0.998**	1.100	**0.964**	0.993	**0.999**	1.019	0.999
	<.0001	**<.0001**	<.0001	**<.0001**	(0.5490)	**(0.0324)**	(0.2484)	(0.5957)
Treatment result								
Continue	1.000	**0.998**	1.163	**0.944**	1.002	**0.998**	1.068	0.997
	(0.9917)	**<.0001**	<.0001	**<.0001**	(0.8838)	**(0.0183)**	(0.0050)	(0.2204)
Transfer	**0.981**	**0.991**	1.079	**0.981**	0.938	0.998	0.965	1.001
	(0.1786)	**<.0001**	(0.0002)	**<.0001**	(0.1255)	(0.5085)	(0.5383)	(0.8129)
Deceased	1.003	1.006	**0.899**	1.003	1.096	0.999	0.923	1.011
	(0.8831)	<.0001	**(0.0005)**	(0.4709)	(0.1891)	(0.8236)	(0.4105)	(0.3295)
Discharge	1.009	**0.999**	1.031	**0.984**	0.997	1.000	1.039	1.000
	<.0001	**<.0001**	<.0001	**<.0001**	(0.5663)	(0.3399)	<.0001	(0.7028)
Invasive treatment								
Central catheter	**0.979**	**0.998**	1.062	**0.957**	1.062	0.999	1.006	1.001
	(0.0046)	**<.0001**	<.0001	**<.0001**	(0.1185)	(0.6101)	(0.9049)	(0.9301)
Ventilation or tracheostomy	1.096	1.000	0.995	**0.970**	1.047	0.999	1.001	1.000
	<.0001	(0.9024)	(0.7491)	**<.0001**	(0.3281)	(0.7139)	(0.9924)	(0.9472)
None	1.004	1.000	1.060	**0.975**	0.998	1.000	1.042	1.000

	(0.0216)	<.0001	<.0001	**<.0001**	(0.6104)	(0.9142)	<.0001	(0.8900)
Primary diagnosis (by ICD-10 code categories)								
Muscoloskeletal system and connective tissue(M00-M99)	1.036	1.001	1.005	**0.986**	1.063	1.001	1.012	1.006
	<.0001	<.0001	(0.4418)	**<.0001**	<.0001	(0.0864)	(0.4287)	(0.0004)
Injury, poisoning and certain other consequences of external causes(S00-T98)	0.996	**0.999**	1.092	**0.980**	**0.977**	1.002	1.016	0.998
	(0.3761)	**<.0001**	<.0001	**<.0001**	**(0.0294)**	(0.0006)	(0.2998)	(0.1627)
Digestive system(K00-K93)	1.078	**0.932**	1.069	**0.984**	1.019	1.001	1.046	**0.995**
	<.0001	**<.0001**	<.0001	**<.0001**	(0.2274)	(0.1865)	(0.0409)	**(0.0433)**
Respiratory system(J00-J99)	1.083	**0.993**	1.125	**0.984**	0.992	**0.996**	1.072	1.008
	<.0001	**<.0001**	<.0001	**<.0001**	(0.5262)	**<.0001**	(0.0001)	<.0001
Neoplasm(C00-D48)	**0.924**	**0.996**	1.121	**0.955**	**0.931**	1.000	1.011	**0.994**
	<.0001	**<.0001**	<.0001	**<.0001**	**<.0001**	(0.8900)	(0.6407)	**(0.0156)**
Circulatory system(I00-I99)	**0.915**	**0.998**	1.047	**0.963**	0.992	**0.998**	1.063	0.996
	<.0001	**<.0001**	<.0001	**<.0001**	(0.6362)	**(0.0395)**	(0.0109)	(0.1341)
Else	1.027	**0.999**	1.057	**0.970**	0.991	1.000	1.079	1.001
	<.0001	**<.0001**	<.0001	**<.0001**	(0.2775)	(0.7733)	<.0001	(0.3008)

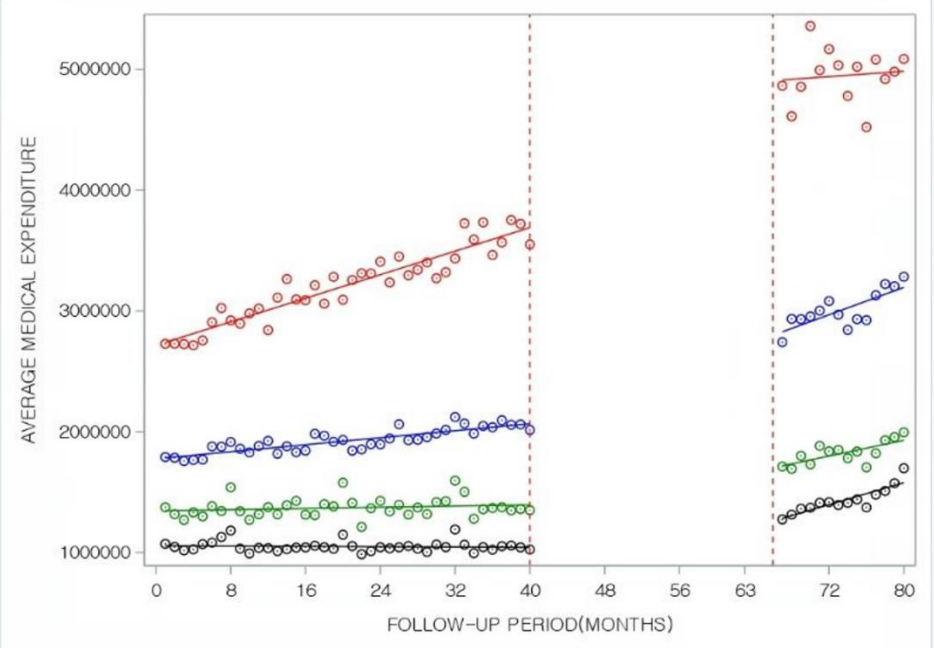
Appendix 5. Two segmented ITS regression parameter estimates for healthcare outcomes and utilization controlling time period (Sensitivity analysis)







Hospital type: Red-Tertiary, Blue-General, Green-Hospital, Black-Non-applicable hospital



Hospital type: Red-Tertiary, Blue-General, Green-Hospital, Black-Non-applicable hospital

Parameter	Exp(β)	Exp(SE (β))	95% Confidence interval		P-value	Exp(β)	Exp(SE (β))	95% Confidence interval		P-value
	Use of restricted antibiotics					Healthcare associated infection				
Tertiary Hospital										
Intercept β0	0.0248	1.2275	0.0166	0.0371	<.0001	0.0319	1.2761	0.0198	0.0514	<.0001
Baseline trend β1	0.9940	1.0014	0.9913	0.9968	<.0001	0.9982	1.0018	0.9947	1.0016	0.3016
Level change after intervention β2	0.9883	1.1052	0.8124	1.2023	0.906	0.9937	1.1321	0.7791	1.2674	0.9594
Trend change after intervention β3	0.9702	1.0093	0.9527	0.9879	0.001	0.9861	1.0115	0.9644	1.0083	0.219
General Hospital										
Intercept β0	0.0131	1.2188	0.0089	0.0193	<.0001	0.1280	1.1320	0.1003	0.1632	<.0001
Baseline trend β1	0.9938	1.0014	0.9910	0.9967	<.0001	0.9971	1.0010	0.9951	0.9990	0.0038
Level change after intervention β2	0.9159	1.1089	0.7479	1.1215	0.3953	1.0219	1.0743	0.8879	1.1763	0.7618
Trend change after intervention β3	0.9889	1.0093	0.9710	1.0070	0.2269	1.0112	1.0063	0.9988	1.0237	0.0764
Local Hospital										
Intercept β0	0.0040	1.8210	0.0012	0.0131	<.0001	0.1050	1.2662	0.0661	0.1667	<.0001
Baseline trend β1	0.9950	1.0043	0.9867	1.0034	0.2473	1.0051	1.0021	1.0009	1.0093	0.017
Level change after intervention β2	1.1151	1.3488	0.6203	2.0043	0.7158	0.7715	1.1566	0.5801	1.0261	0.0746
Trend change after intervention β3	1.0149	1.0258	0.9655	1.0668	0.5605	1.0094	1.0125	0.9853	1.0343	0.4457
Non-applicable hospital										
Intercept β0	0.0015	1.6849	0.0005	0.0042	<.0001	0.0467	1.1768	0.0340	0.0643	<.0001
Baseline trend β1	1.0006	1.0041	0.9925	1.0086	0.8899	1.0034	1.0015	1.0005	1.0062	0.0207
Level change after intervention β2	0.7709	1.3077	0.4556	1.3042	0.3321	0.9617	1.0955	0.8042	1.1498	0.6677

Trend change after intervention β3	1.0258	1.0214	0.9840	1.0694	0.2303	0.9969	1.0074	0.9826	1.0114	0.6726
	Length of stay					**Total medical expenditure**				
Tertiary Hospital										
Intercept β0	4.5227	1.0127	4.4128	4.6353	<.0001	2065122.2839	1.0361	1926470.2492	2213974.7777	<.0001
Baseline trend β1	0.9939	1.0001	0.9937	0.9940	<.0001	1.0061	1.0003	1.0056	1.0066	<.0001
Level change after intervention β2	1.0073	1.0061	0.9954	1.0194	0.2294	1.0563	1.0176	1.0209	1.0931	0.0016
Trend change after intervention β3	0.9687	1.0006	0.9676	0.9699	<.0001	0.9958	1.0015	0.9929	0.9988	0.0051
General Hospital										
Intercept β0	10.1716	1.0083	10.0082	10.3388	<.0001	1652665.5050	1.0234	1579628.1039	1729079.9427	<.0001
Baseline trend β1	0.9928	1.0001	0.9927	0.9929	<.0001	1.0049	1.0002	1.0046	1.0053	<.0001
Level change after intervention β2	0.9256	1.0048	0.9170	0.9343	<.0001	1.0536	1.0127	1.0279	1.0800	<.0001
Trend change after intervention β3	0.9793	1.0005	0.9784	0.9802	<.0001	1.0019	1.0011	0.9998	1.0041	0.0786
Local Hospital										
Intercept β0	21.1492	1.0139	20.5837	21.7301	<.0001	1716846.9536	1.0434	1579470.1490	1865985.7058	<.0001
Baseline trend β1	0.9956	1.0001	0.9954	0.9958	<.0001	1.0024	1.0004	1.0017	1.0031	<.0001
Level change after intervention β2	0.9396	1.0081	0.9249	0.9546	<.0001	1.0183	1.0253	0.9697	1.0693	0.4681
Trend change after intervention β3	0.9668	1.0008	0.9653	0.9683	<.0001	1.0022	1.0020	0.9984	1.0061	0.0182
Non-applicable hospital										

Intercept β0	8.3537	1.0097	8.1956	8.5148	<.0001	1358647.1229	1.0259	1292385.1208	1428449.2882	<.0001
Baseline trend β1	0.9944	1.0001	0.9943	0.9946	<.0001	1.0012	1.0002	1.0008	1.0016	<.0001
Level change after intervention β2	1.0786	1.0056	1.0669	1.0905	<.0001	1.1062	1.0138	1.0770	1.1362	<.0001
Trend change after intervention β3	0.9740	1.0005	0.9731	0.9750	<.0001	1.0121	1.0011	1.0098	1.0144	<.0001

Korean Abstract(국문요약)

감염 관리를 위한 일련의 법적 조치와 병원의 의료 질 및 이용에 미치는 영향

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김수영

배경: 의료기관에서 감염관리를 강화하는 것을 목적으로 2016년 환자안전법이 제정되고 이후 의료법이 개정되었다. 이러한 입법 조치는 환자안전과 의료기관의 감염 관리에 대한 우려가 증가함에 따라 도입되었다. 본 연구는 이러한 입법 조치가 의료의 질과 의료기관 이용에 미치는 영향을 조사하여, 다양한 유형 및 규모의 병원에서 그 효과성을 종합적으로 분석하였다.

방법: 이 연구는 2013년부터 2019년까지의 국민건강보험공단 국민표본코호트(NHIS-NSC) 자료를 활용하였다. 두개의 개입 지점을 포함한 단절적 시계열 분석(ITS) 디자인과 분절 회귀 분석을 사용하여 환자안전법 및 후속 의료법 개정의 시행 효과를 평가했다. 주요 결과 변수로는 제한 항생제의 사용, 의료 관련 감염 발생, 입원기간, 총 의료비용이 포함되었다. 분석은 상급종합병원, 종합병원, 병원 및 규모가 작아 정책 개입이 반영되지 않은 비적용 병원으로 계층화하여 시행되었고, 환자의 인구통계학적 특성과 병원 특성을 포함한 잠재적 혼란변수들을 보정변수로 포함하여 진행했다. 단절적 시계열 분석을 수행함에 있어 발생할 수 있는 편향을 최소화하기 위해 보고 지침을 적용하고, 군집과 반복적 종단 관찰을 고려하는 방법 중 하나인 일반화 추정 방정식을 통계적 방

법으로 사용했다.

결과: 환자안전법의 시행 및 이후 개정된 의료법은 제한 항생제의 사용 감소와 의료 관련 감염의 감소에 기여했다. 상급종합병원에서는 의료법 개정 후 제한 항생제 사용에 대한 추세 변화가 통계적으로 유의미한 감소를 보였다(두번째 개입 후 추세 변화: Exp(β_5)=0.9666, p=0.0005). 병원에서의 의료 관련 감염 발생은 첫번째 개입 후 감소하였다(첫 번째 개입 후 추세 변화: Exp(β_3)=0.9897, p=0.04). 또한, 모든 병원 유형에서 입원기간은 감소했지만, 병원과 정책 비적용 병원에서의 총 의료비용은 점진적으로 증가하였다(병원에서 첫 번째 개입 후 추세 변화: Exp(β_3)=1.0023, p=0.0081, 비적용 병원에서 첫 번째 개입 후 추세 변화: Exp(β_3)=1.0030, p=<.0001, Exp(β_5)=1.0083, p=<.0001). 감염 관리에 대한 재정적 인센티브 수준별로 분류한 분절 회귀 모델에서는 1급과 2급에서 제한 항생제 사용 감소가 유의하게 나타났다(1급에서 첫 번째 개입 후 추세 변화: Exp(β_3)=0.5101,p<.0001, 2급에서 두 번째 개입 후 추세 변화: Exp(β_5)=0.9715, p=0.0002).

결론: 감염 관리를 위한 입법 조치는 의료의 질 향상과 보다 효율적인 의료기관 이용을 도출했다. 상급종합병원과 종합병원은 작은 병원보다 더 두드러진 개선을 보였으며, 이는 규모가 큰 기관이 이러한 입법 조치를 효과적으로 시행하고 혜택을 받을 수 있는 자원이 더 많음을 시사한다. 효과는 의료기관 크기에 따라 달려졌으며, 감염 관리 규정의 이점을 극대화하기 위한 맞춤형 정책 접근이 필요함을 시사한다. 이러한 정책의 지속적인 평가와 수용은 환자안전 및 의료 질 개선을 향상시키는 데에 중요하다. 이 연구는 의료 체계의 개선을 이끄는 정부 주도의 노력의 중요성을 강조하며, 비슷한 결과를 달성하기 위해 작은 병원에 대한 지속적인 지원과 자원의 필요성을 강조한다.

핵심어: 감염관리, 환자안전, 의료 질, 감염관리 규정, 의료기관 이용