Impact of Coronavirus Disease 2019 Pandemic on Management and Healthcare Utilization of Patients with Dementia

Kyungduk Hurh

The Graduate School

Yonsei University

Department of Public Health

Impact of Coronavirus Disease 2019 Pandemic on Management and Healthcare Utilization of Patients with Dementia

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

Kyungduk Hurh

December 2023

This certifies that the dissertation of ***Kyungduk Hurh*** is approved.

_____

Eun- Cheol Park: Thesis Supervisor

_____

Chung Mo Nam: Thesis Committee Member #1

_____

Jaeyong Shin: Thesis Committee Member #2

_____

Suk-Yong Jang: Thesis Committee Member #3

_____

Seung Hoon Kim: Thesis Committee Member #4

The Graduate School

Yonsei University

December 2023

Acknowledgments

I want to express my heartfelt thanks to everyone who has provided their support and encouragement throughout my PhD journey. Their assistance has been indispensable in achieving the successful completion of this program.

First of all, I would like to convey my profound appreciation to Professor Eun-Cheol Park, my supervisor. He has provided me with unwavering mentorship and assistance as both an esteemed educator and a distinguished scholar. Professor Park's exceptional insights and foresight in the field of preventive medicine and public health have consistently left me in awe and have proven to be an indispensable resource in my journey as a public health practitioner. His emphasis on the role of a genuine scholar and mentor (有學有心), one who provides guidance and walks the path alongside colleagues, has significantly influenced my perception of my forthcoming professional endeavors.

I am also grateful for Professor Chung Mo Nam, who has imparted to me the significance of biostatistics as a formidable instrument in health policy analysis during my doctoral program. His remarkable expertise and dedication to the field of biostatistics, coupled with his sincere care for his students, serve as qualities I aspire to emulate.

I would also like to extend my gratitude to Professor Suk-Yong Jang, who served as my dissertation advisor during my doctoral program. His unwavering commitment to

offering relevant guidance and going the extra mile for me has left an indelible mark on my academic journey. His expertise and mentorship have significantly contributed to the success of my research.

I am also thankful to Professor Jaeyong Shin for his invaluable feedback and suggestions. His insightful advice and personal anecdotes about the research experience have not only enriched my academic work but have also broadened my perspective on life.

I would also like to express my gratitude to Professor Seung Hoon Kim for his support throughout my doctoral journey. Once a colleague, now a mentor, he has consistently provided me with guidance and direction on the path I should take. His influence has played a pivotal role in my growth and development as a researcher.

I would like to express my deep gratitude to Professor Sung-In Jang for his unwavering support throughout my doctoral program. His remarkable empathy not only validated my perspectives but also served as a fundamental pillar for the continued advancement of my research. Professor Jang also afforded me numerous opportunities that significantly expanded my exposure to health policy, particularly in the realm of healthcare workforce policy. It has been a privilege to work alongside him and benefit from his guidance and mentorship.

Thank you to all my seniors and colleagues at the Department of Public Health: Jieun Jang, Dong-Woo Choi, Wonjeong Chae, Junhyun Kwon, Hin Moi Yoon, Doo Woong Lee, Hyeon Ji Lee, Jae Hong Joo, Wonjeong Jeong, Soo Hyun Kang, Hye Jin Joo, Sung

Hoon Jeong, Selin Kim, Bich Na Jang, Fatima Nari, Minah Park, Hyunkyu Kim, Eun-ji Kim, Jinhyun Kim, Yoon Sik Park, Il Yun, Soo Young Kim, Yoo Shin Park, Yun Hwa Jeong, Yun Seo Jang, Ye Seul Jang, Dan Bi Kim, Ji su Ko, Jae Hyeok Lim, Min Jeong, Joo Shinetsetseg Oyuntuya, and Nataliya Nerobkova. 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. I would also like to extend my gratitude to Professor Kyu-Ri Kim, who taught me a great deal about research methods and statistics during my early semesters.

Above all, I would like to thank my wife You-Na Sung, who is the love of my life and spiritual mentor. I would not have been able to complete this program without her sacrifice. I will never forget her unwavering trust and support for me. I also thank my daughter Yoonje Hurh, who always welcomes me warmly even though I haven't been able to spend much time with her while completing this work. Last but certainly not least, I would like to express my gratitude to my mom and dad, who believed in me and have waited patiently while I focused on completing this program.

December 2023

Kyungduk Hurh

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Impact of Coronavirus Disease 2019 Pandemic on Management and Healthcare Utilization of Patients with Dementia

Kyungduk Hurh

Dept. of Public Health

The Graduate School

Yonsei University

Background:

The aging population in South Korea has led to a rapid increase in the number of elderly patients with dementia. Concurrently, concerns have been raised globally about the negative impact of the Coronavirus Disease 2019 (COVID-19) pandemic on the management, medical access, and mental health of patients with dementia. This study aims to analyze the impact of the COVID-19 pandemic on the management and healthcare utilization of patients with dementia in South Korea.

Methods:

For this study, we utilized the customized database provided by the National Health Insurance Service of South Korea as the data source. The study population consisted of patients with dementia aged 60 and above from February 1, 2016, to October 31, 2021. Final sample comprising 9,821,803 observations for medication analyses and 11,358,180 observations for healthcare utilization analyses, extracted at three-month intervals for each patient with dementia. The primary dependent variables of the study encompassed surrogate indicators of dementia management, specifically the prescription of antipsychotic drugs that could be prescribed in the event of non-pharmacological intervention failure for behavioral psychological symptoms of dementia. Additionally, the study included the duration and the number of antipsychotic drug prescriptions, as well as adherence to anti-dementia medications, as surrogate indicators for the dementia management. Furthermore, healthcare utilization-related dependent variables, the likelihood of emergency room visits, the number of outpatient visits, likelihood of hospitalization, and the number of days hospitalized were included. To evaluate the association between COVID-19 pandemic and relative change in dependent variables, interrupted time series analysis with segmented regression was performed.

Results:

Following the COVID-19 pandemic, there was a relative increase of 1.5% ($p<.001$), 3.2% ($p<.001$), and 0.4% ($p<.001$) every three months in the likelihood, duration, and the number

of antipsychotic drug prescriptions, respectively. Compared to the pre-pandemic period, the likelihood of antipsychotic drug prescription in patients with dementia was 1.6% lower ($p<.001$) in the first 3 months after COVID-19, but increased by 4.1% at 10–12 months and 8.9% at 19–21 months, indicating a dose-dependent response for the elapsed time after COVID-19 pandemic. Patients with good adherence to anti-dementia medication showed a gradual increase of 0.5% ($p<.001$) every three months post-COVID-19 compared to pre-pandemic period. Healthcare utilization related outcomes, the likelihood of emergency room visits, the number of outpatient visits, the likelihood of hospitalization, and the number of days hospitalized showed short-term reductions of -21.1%, -13.7%, -13.0%, and -3.8%, respectively, immediately following the COVID-19 outbreak and subsequent recovery during pandemic.

Conclusions: The COVID-19 pandemic was associated with an increase in antipsychotic drug prescriptions for patients with dementia, with a higher likelihood observed as the post-pandemic duration lengthened. Healthcare utilization in patients with dementia exhibited a pattern of initial decline followed by gradual recovery after COVID-19 pandemic. To prepare for future similar infectious disease crises, mental health support, non-pharmacological interventions, caregiving, and prescribing guidelines tailored for patients with dementia should be developed to provide qualitatively improved medical services.

Key words: dementia; antipsychotics; Coronavirus Disease 19; healthcare utilization; Interrupted time series study

I. Introduction

1. Background

The portion of the elderly population in South Korea is increasing at an unprecedented rate globally, with the country on the verge of entering a super -aged society where individuals aged 65 and older account for over 20% of the entire population.[1]

Dementia is one of the most common geriatric diseases, and in line with the increasing elderly population, the number of patients with dementia in South Korea is also on the rise. Korean National Institute of Dementia (NID) estimated that among the population aged 65 or older in 2021, the number of patients with dementia was approximately 890,000 and the prevalence of dementia was 10.4%.[2] Dementia imposes physical, psychological, and socio-economic burdens not only on patients with dementia but also on caregivers, such as family members. In particular, behavioral and psychological symptoms of dementia (BPSD) are known to be one of the major causes of increased burden of care and hospitalization of patients with dementia. [3-5] For the management of BPSD, antipsychotic drug are often used off-label. However, adverse effects including increased risk of mortality,[6-10] cerebrovascular events,[11-15] myocardial infarction,[16,17] arrhythmia,[18] falls,[19-21] pneumonia,[22-24] metabolic effects[25,26] and extrapyramidal symptoms[27] were reported regarding

antipsychotics use in older patients with dementia. The US Food and Drug Administration (FDA) does not authorize antipsychotic drug for the purpose of managing BPSD in older adults.[28,29] Other clinical guidelines recommend attempting antipsychotic drug for BPSD management only when non-pharmacological interventions and alternative approaches have proven unsuccessful, and when the benefits are deemed to outweigh the risks.[30]

Meanwhile, the Korean government, recognizing the challenges posed by the increase in patients with dementia, had undertaken a national-level effort by establishing a comprehensive dementia management plan. The plan aimed to address dementia through various initiatives, including prevention, early detection, and the management and treatment of patients with dementia. For instance, community dementia centers was established to implement cognitive rehabilitation programs, support groups, education, and other activities for dementia patients.[31]

However, the public health measures implemented in response to the Coronavirus Disease 2019 (COVID-19) pandemic, which began in early 2020, had a profound impact on the lives of patients with dementia. Gathering restrictions and the closure of public facilities had disrupted the daily lives of individuals and affected their social activities and interpersonal relationships.[32,33] Moreover, national and societal attention and efforts had been focused on preventing the spread of infection, leading to a relative decrease in support for patients with dementia compared to before.[34] In this context, concerns had been raised about the exacerbation of BPSD and increased use of antipsychotics drugs in patients with

dementia due to reduced activity, discontinuation of social support and assistance programs, decreased access to medical services, and increase in caregiver burden after COVID-19 outbreak. [35]

Previous studies had observed an increase in psychiatric symptoms such as depressive mood, anxiety, insomnia, and stress in the general population after COVID-19, attributed to social isolation.[36-39] The COVID-19 lockdown measures was related to additional cognitive decline among dementia patients.[40-42] Additionally, a reduction in healthcare utilization and delays in disease diagnosis and treatment had been reported due to concerns about infection and quarantine measures.[43] Given that patients with dementia are typically elderly, face challenges in self-care, and require caregiving, they may be particularly vulnerable to the effects of COVID-19 lockdown.[44,45] Dementia was identified as a significant risk factor for COVID-19 and an increase in all-cause mortality had been observed in patients with dementia during COVID-19 pandemic periods.[46-49]

Furthermore, studies reported an increase in the use of antipsychotic drug in elderly patients with dementia during the early stages of COVID-19.[50,51] However, these studies had limitations such as short observation periods, lack of comparison groups, and small sample sizes. Subsequent large-scale observational studies utilizing two different samples showed conflicting results regarding the increase in antipsychotic drug prescriptions following COVID-19.[52,53]

Therefore, the primary objective of this study is to investigate the impact of the

COVID-19 pandemic on the prescription of antipsychotic drug in older adults with dementia, addressing limitations identified in previous research. In this study, we aim to investigate the prescription of antipsychotic drug in patients with dementia before and after the COVID-19 pandemic on an individual level, using customized data from the Korean National Health Insurance Service (NHIS), which encompassed 50% of entire patients with dementia in South Korea. Furthermore, to comprehensively analyze the impact of COVID-19 on dementia management, additional analyses for adherence to anti-dementia medication and healthcare utilizations were conducted. The findings of this study might help understanding how healthcare providers adapted their approach to the management of dementia in response to the COVID-19 pandemic and infection control policies, which can be instrumental in shaping dementia policies for future public health disasters.

2. Study Objectives

This study aims to evaluate the effects of COVID-19 pandemic on management and healthcare utilizations of dementia patients. We analyzed surrogate indicators of dementia management discernible from health insurance claims data, focusing on the antipsychotic drug prescriptions, adherence to anti-dementia medications among older individuals with dementia before and after the onset of COVID-19 pandemic.

The specific study objectives are as follows:

(1) To investigate whether the COVID-19 pandemic was associated with changes in antipsychotic drug prescriptions (likelihood of prescription, the duration of prescriptions, and the total number of prescriptions) among patients with dementia.

(2) To investigate whether the COVID-19 pandemic was associated with changes in adherence to anti-dementia medications among patients with dementia.

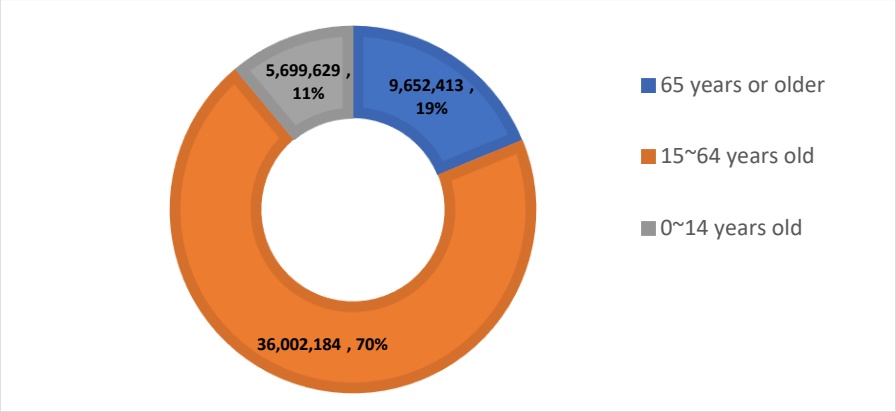
(3) To investigate whether the COVID-19 pandemic was associated with changes in healthcare utilization (the likelihood of ER visits, the number of outpatient visits, the likelihood of hospitalization, and the number of days hospitalized) of patients with dementia.

II. Literature Review

1. Dementia Status of South Korea

1) Rapid-Aging Korea

South Korea is experiencing an unprecedented rapid aging of population, driven by the increase in life expectancy associated with economic growth, and recent low birth rates. In 2023, the elderly population aged 65 or older in South Korea reached 9,652,413, accounting for 18.8% of the total population. The proportion of elderly population is expected to increase to 20.6% by 2025, indicating that South Korea will enter the super-aged society (Figure 1).[54]

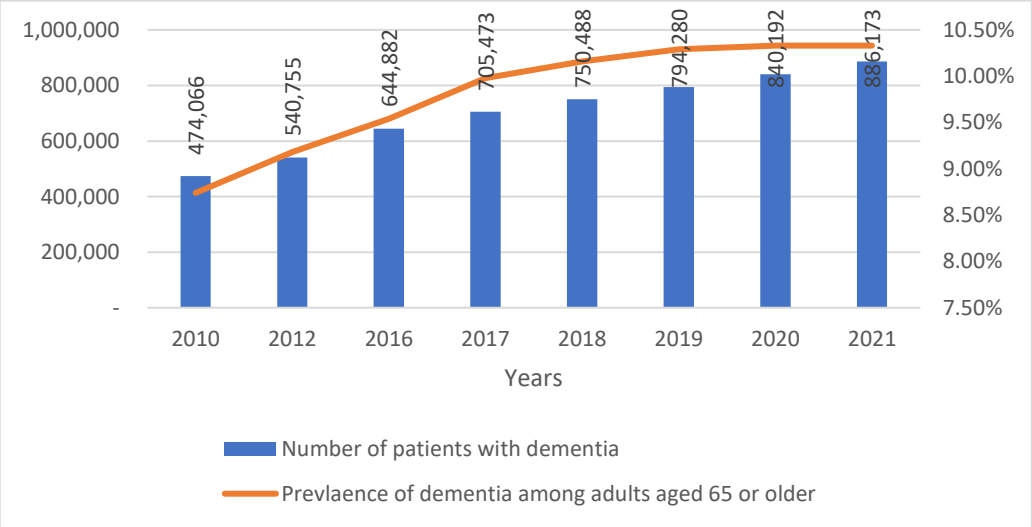


Source: Statistic Korea, Registered population of South Korea

Figure 1. Population composition in South Korea, 2023

2) Prevalence and Trends of Dementia in South Korea

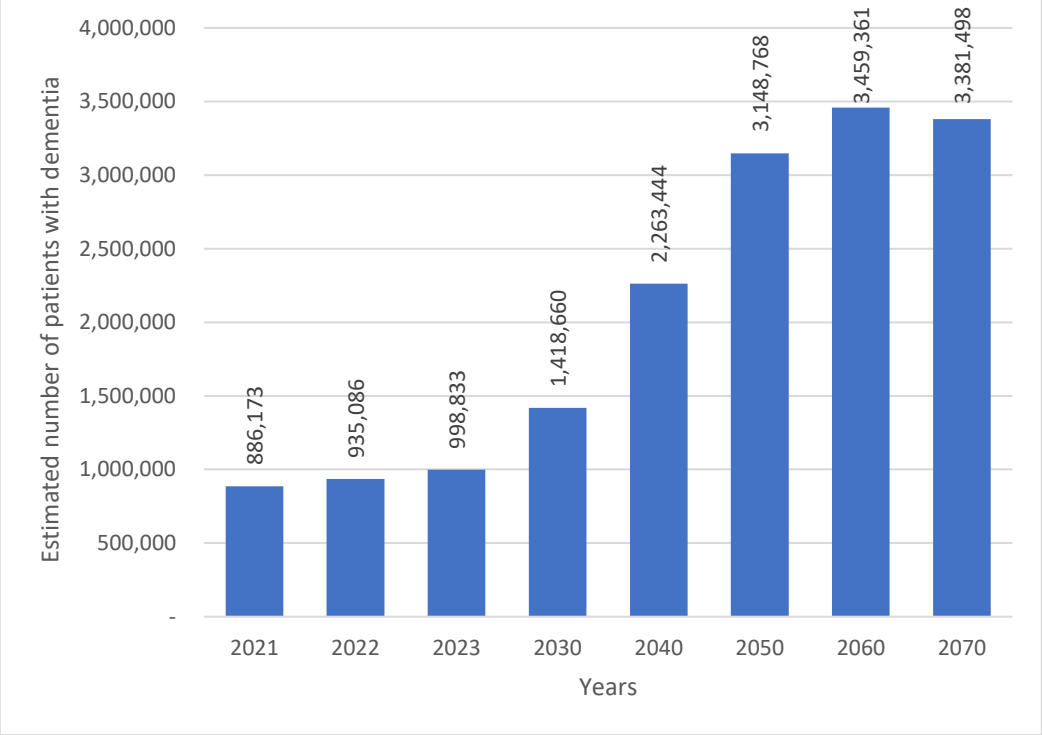
In tandem with the rapid increase in the elderly population in South Korea, there was also a substantial surge in the number of patients with dementia, an age-related condition. According to a nationwide dementia epidemiological study conducted by the Ministry of Health and Welfare (MOHW) and the NID in South Korea, the number of patients with dementia rose nearly twofold from 474,066 in 2010 to 886,173 in 2021.[55] Moreover, owing to the increase in life expectancy, there was a growing trend in the prevalence of dementia among the elderly population. The prevalence of patients with dementia among individuals aged 65 and older in South Korea was estimated at 8.74% in 2010, which has steadily increased to 9.54% in 2016 and further to 10.33% in 2021 (Figure 2).[56]



Source: National institute of Dementia, 2016 Nationwide Survey on the Dementia Epidemiology of Korea; Korean Ministry of Health and Welfare, 2012 Nationwide Survey on the Dementia Prevalence of Korea

Figure 2. Number and prevalence of patients with dementia in South Korea

If the current trend continues, it is anticipated that the number of patients with dementia aged 65 and older in South Korea will surpass 2 million by 2040 and exceed 3 million by 2050.[56] Subsequently, the growth in the number of patients with dementia may attenuate due to population decline resulting from low birth rates. However, the overall prevalence rate relative to the total population is projected to increase sharply, with patients with dementia comprising approximately 9.0% of the entire South Korean population by the year 2070 (Figure 3).[56,57]



Source: National institute of Dementia, 2016 Nationwide Survey on the Dementia Epidemiology of Korea; Statistics Korea, Population Dashboard 2023

Figure 3. Projection of number of patients with dementia in South Korea

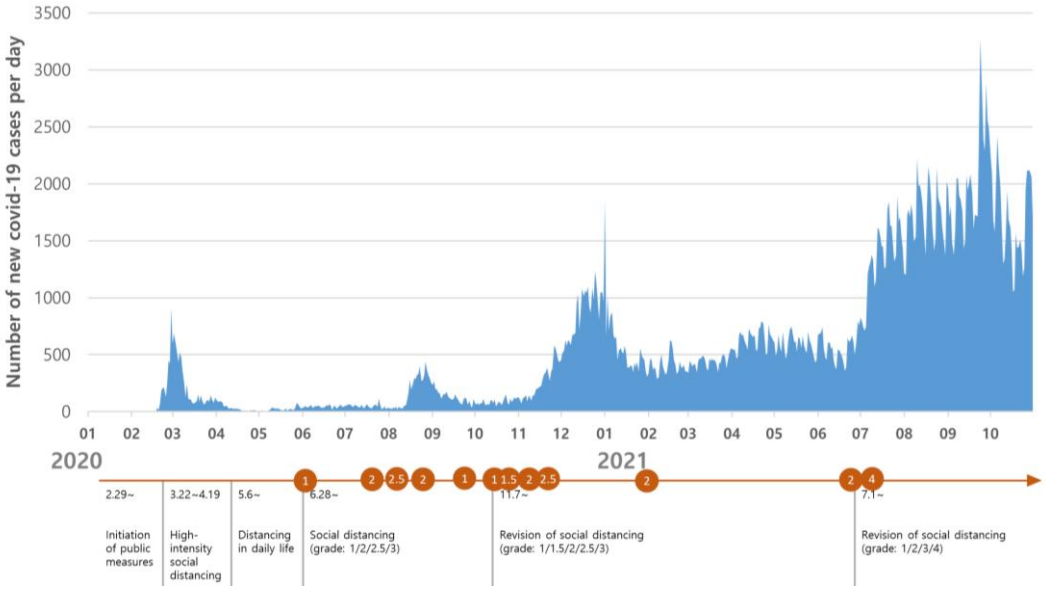
2. COVID-19 Outbreak and Public Health Interventions (Implementation of Social Distancing) in South Korea throughout 2020 and 2021

Building on the experience of the 2015 Middle East Respiratory Syndrome (MERS) outbreak, South Korean government implemented a centralized epidemic control policy from the early stages of the COVID-19 pandemic. During the MERS outbreak, hospital-acquired infections, predominantly among hospitalized patients and healthcare workers, expanded into the community through visitors.[58,59]

Following the first case of COVID-19 in January 20, 2020, there were subsequent outbreaks in religious facilities in February 2020 and in clubs and logistics centers in May 2020. Consequently, the South Korean government emphasized identifying close contacts of infected individuals and isolating them, along with imposing usage restrictions on high-risk facilities and public spaces prone to group infections.[58,59] In April 2020, measures were implemented to restrict the operation of religious facilities, indoor sports facilities, entertainment venues, academies, and tutoring centers. Moreover, long-term care hospitals (LTCHs), which handle the majority of hospitalization services for patients with dementia, also faced restrictions, including visitation limits, restrictions on outings, and the discontinuation of external programs.[58,59]

As the scale of COVID-19 infections began to decrease, the intensity of epidemic

control measures was eased in May 2020, transitioning to a more relaxed approach known as "distancing in daily life".[58,59] From the mid-2020 onward, the government systematically refined its epidemic control policies, implementing a phased approach to social distancing based on the scale of the outbreak. The social distancing measures included operational restrictions on multi-use facilities, the suspension of events, and the discontinuation of gatherings.[58,59] In August 2020, a resurgence of infections, particularly in the metropolitan area, was observed, notably linked to group infections in political rallies. In response, the South Korean government, starting from November 2020, fine-tuned its social distancing measures to address the specific circumstances. However, as the COVID-19 pandemic persisted, with vulnerable facilities such as LTCHs and prisons experiencing outbreaks in the winter of 2020, a shift in social distancing measures occurred.[59] Taking into account public fatigue and the national vaccination status, a policy overhaul aimed at minimizing business closures and restrictions was implemented from the mid-2021.[59] Figure 4 illustrates the change in daily COVID-19 cases and grade of “social distancing”, the infection control policy of South Korea.

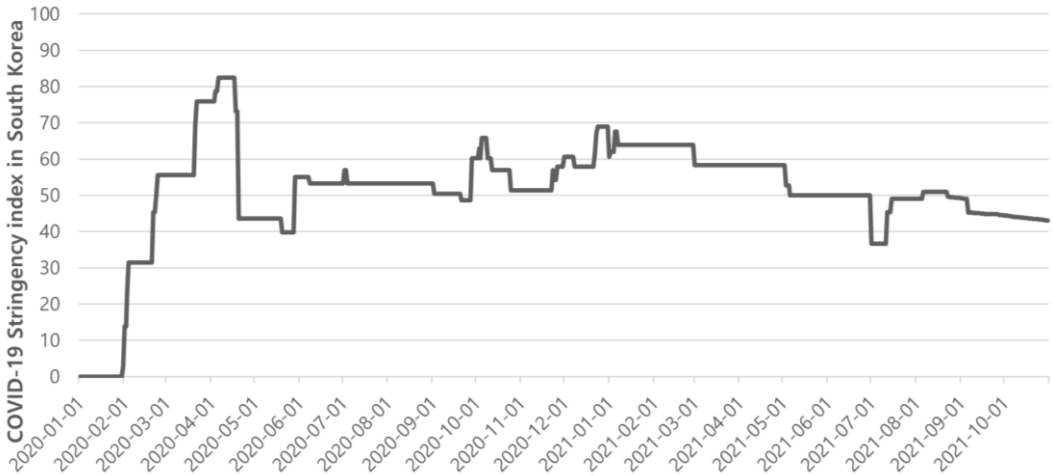


Source: Our world in data, Coronavirus Pandemic (COVID-19)

Korea Disease Control and Prevention Agency, Coronavirus Disease-19

Figure 4. Change in COVID-19 cases and grade of ‘Social distancing’ in South Korea

The fluctuations in the intensity of South Korea's public measures from 2020 to 2021 were also reflected in the COVID-19 Stringency Index, generated using the Oxford COVID-19 Government Response Tracker.60 The COVID-19 Stringency Index for South Korea exhibited a peak ranging from 70 to 80 points in April 2020, followed by a dynamic pattern fluctuating between 30 and 70 points in response to changes in government epidemic control policies (Figure 5).[61]



Source: Our world in data, Coronavirus Pandemic (COVID-19)

Figure 5. COVID-19 stringency index in South Korea

3. Dementia Management, BPSD and Antipsychotic drug Prescriptions during COVID-19 Pandemic

Since the early stages of the COVID-19 pandemic, experts had expressed concerns about the potential negative impact of public health measures and COVID-19 on the management and health of patients with dementia.[62-65] Patients with dementia might face limitations in accessing accurate information related to the COVID-19 pandemic. Due to difficulties in understanding or remembering public health measures, there were concerns about the increased risk of COVID-19 infection and complications among patients with dementia.[64] Moreover, many patients with dementia reside in long-term care facilities or live alone or with spouses. The transition to remote services and the reduction of in-person support services due to epidemic control measures might increase the loneliness and isolation of patients with dementia who rely on social support for human relationships.[62,63]

Furthermore, measures such as visitation bans, reduced group activities, and isolation of infected individuals could exacerbate the isolation of patients with dementia residing in long-term care facilities, leading to increased stress and anxiety. The decrease in opportunities for facility use and social support could contribute to the fatigue and exhaustion of family members and caregivers of patients with dementia. Previous studies had primarily assessed the impact of the COVID-19 pandemic on patients with dementia

in two aspects: first, exploring the association between dementia and the increase in COVID-19 infections and mortality, and second, investigating the impact of the COVID-19 pandemic on the management of patients with dementia, including mental health (cognitive function, neuropsychiatric symptoms, antipsychotic drug prescriptions), caregiver burden, and overall mortality.

1) BPSD among Patients with Dementia during COVID-19 Pandemic

Many studies conducted in the early stages of the COVID-19 pandemic had found that patients with dementia were experiencing a worsening of neuropsychiatric symptoms compared to the pre-pandemic period. A study conducted in mid-2020 in Italy through telephone surveys revealed that more than half of the participants reported the onset or worsening of BPSD after the lockdown.[62] Subsequent research, utilizing data from various countries worldwide, observed an increase in BPSD in dementia patients following the pandemic. Studies using data from Brazil,[66] Italy,[66] four countries (Australia, Germany, Spain, and Netherlands),[51] and Norway[50] reported an association between the COVID-19 pandemic and an increase in BPSD. These studies commonly reported a link between the COVID-19 pandemic and symptoms of depressive mood and anxiety.[35] Additionally, a deterioration in various areas of neuropsychiatric symptoms, including apathy, psychosis, delusion, aggression, agitation, and irritability, was identified.[50,66] Moreover, studies have found that social isolation were associated with more pronounced BPSD among patients

with dementia.[67] The neuropsychiatric symptoms appear to be exacerbated with and longer periods of social restrictions.[37,68]

2) COVID-19 Pandemic and Antipsychotic drug Prescriptions in Patients with Dementia

The increase in BPSD in patients with dementia related to the COVID-19 pandemic might also lead to an escalation in the prescription of antipsychotic drug. A study using data from England's National Health Service showed that the prevalence of patients with dementia being prescribed antipsychotic drug increased by 4.4% to 6.95% during March to May 2020 compared with the corresponding months in 2018.[69] Another study primarily relying on data from the United States indicated a growth in the prevalence of dementia patients with antipsychotic drug prescriptions, increased from 14.7% in 2019 to 16.4% in the year 2020.[70] A study conducted in Argentina reported a 20% increase in the use of antipsychotic drug among patients with dementia during the COVID-19 pandemic period, based on surveys.[71] In a Dutch study, the use of antipsychotic drug among patients with dementia showed insignificant variation within the range of 21.0% to 22.9% from February to August 2020.[72] However, these early studies had limitations, including the absence of pre-COVID-19 data, short observation periods, small sample sizes, and reliance on self-reporting methods to assess the antipsychotic drug prescriptions.

Subsequent large-scale study using data from the United States, the United Kingdom,

Germany, France, Italy, and South Korea reported an increase in the prescription rates of antipsychotic drug in all countries following COVID-19 pandemic.[52] However, the direction of changes in the antipsychotic drug prescription before and after COVID-19 pandemic varied across datasets in the study. For instance, in the United States, using the IBM Market Scan Medicare Supplemental and Coordination of Benefits Database, the antipsychotic drug prescription increased 1.4 times immediately after COVID-19 pandemic compared to the pre-pandemic period, followed by a relative monthly decline of 0.6%. In contrast, the US Open Claims Data indicated a 0.9-fold decrease immediately after COVID-19 pandemic with a subsequent increase in trend of 0.3%, compared to the pre-pandemic period. Additionally, in the case of South Korea, the data for study was limited to patients with dementia admitted to two hospitals, posing representative limitations. Data from Kangwon National University Hospital showed a nearly twofold increase in the use of antipsychotic drug for patients with dementia in April to June 2020 compared to the same months in 2019. However, patients with dementia admitted to Ajou University Hospital did not exhibit significant change.[52] On the other hand, in the most recent study utilizing data from Wales, United Kingdom, a slight increase in the antipsychotic drug prescriptions among patients with dementia after COVID-19 pandemic was observed. However, the authors concluded that there was an existing upward trend in prescription rates before COVID-19 pandemic, starting from mid-2019, and the absolute difference in antipsychotic drug prescriptions before and after COVID-19 was small, suggesting no apparent association between the pandemic and antipsychotic drug prescriptions.[53]

4. Healthcare Utilizations among Patients with dementia during the COVID-19 Pandemic

Previous studies consistently reported a common decrease in healthcare utilization during the COVID-19 pandemic, regardless of the characteristics of countries or study participants. A repeated cross-sectional study in Canada during the initial six months of the COVID-19 pandemic found a reduction in hospital visits and new admissions to long-term care facilities for individuals aged 65 and older with dementia, Parkinson's disease, or the general elderly population compared to the same period in the previous year.[43] According to research in Singapore, consultations for doctor among middle-aged and older adults decreased by 30% during the initial three months of the COVID-19 pandemic.[73] Similarly, in the United States, outpatient visits decreased by 20–80%, and ER visits and hospitalizations showed reductions of up to 30%.[74,75] Overall, the decrease in healthcare utilization occurred universally across both high-income and low- to middle-income countries, irrespective of the severity of COVID-19 incidence. This reduction extended beyond routine healthcare services such as chronic disease management or preventive vaccinations and was also observed in the treatment of emergency conditions like myocardial infarction or cerebrovascular diseases.[76]

In South Korea, early studies based on self-report surveys revealed that approximately 73% of participants avoided healthcare utilization after the onset of COVID-19 pandemic,

with no significant differences based on underlying health conditions.[77] Additionally, among individuals aged 60 and above, the likelihood of delaying non-urgent medical conditions or chronic disease consultations was lower compared to younger adults, although the potential for delaying emergency medical conditions remained relatively high.[78] Subsequent studies in South Korea employed a time series analysis to evaluate healthcare utilization before and after COVID-19 pandemic. Among Korean older adults aged 65-84, healthcare utilization for acute upper respiratory infections decreased by approximately 20% during the first six months of the COVID-19 pandemic. However, there was no significant change observed in healthcare utilization for chronic conditions.[79] Also, outpatient visits, emergency room visits, and hospitalizations for mental health conditions showed a decreasing trend after COVID-19 pandemic.[80]

5. Theoretical Model for Changes in Dementia Management after COVID-19 Pandemic

The purpose of this study is to analyze the impact of COVID-19 pandemic and subsequent public measures on the management of patients with dementia. In this research, we examined surrogate indicators for dementia management, specifically the prescription of antipsychotic drug and adherence to dementia medications. The increased loneliness and reduced social support due to social restrictions, coupled with limited medical access, might exacerbate cognitive decline and BPSD of patients with dementia. Additionally, patients with dementia might face challenges in understanding and complying with preventive measures due to cognitive impairment, potentially leading to an increased risk of COVID-19 infection, morbidity, and mortality. Consequently, the burden on caregivers might increase, compounded by reduced access to medical resources due to social restrictions, ultimately contributing to an escalation in the prescription of antipsychotic drug in patients with dementia (Figure 6).

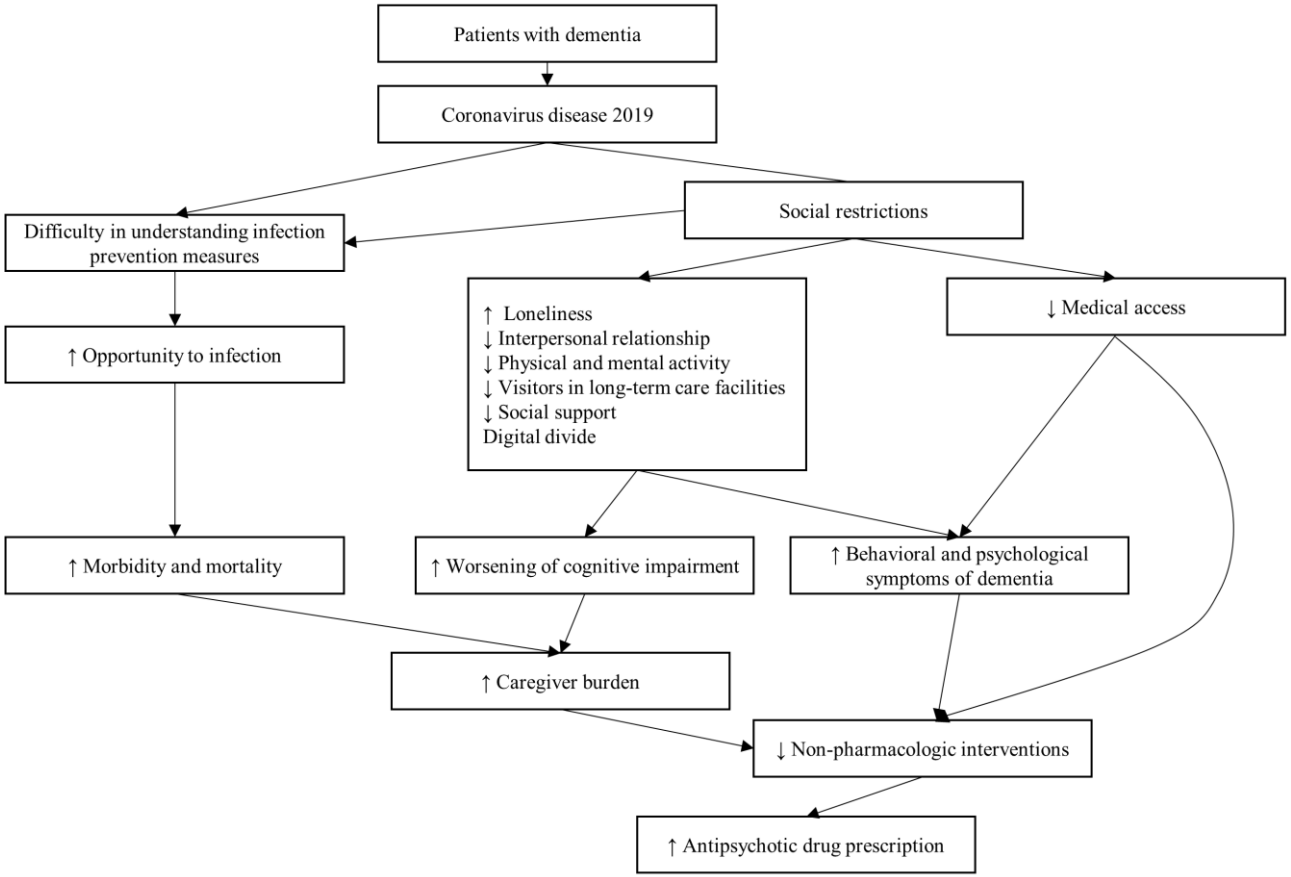


Figure 6. Conceptual model for changes in dementia management after COVID-19 pandemic

III. Material and Methods

1. Data Source and Study Population

We used data for 2010–2021 from the Korean National Health Insurance Database (NHID). The data were formed by Korea National Health Insurance Service (NHIS), which covers 97% of the South Korean population (approximately 50 million) for research purpose. Since the NHIS also manages the healthcare claims of the remaining 3% of the Korean population, the medical aid program beneficiaries, the NHIS database contains the medical records of the almost all Korean population. The data includes anonymized participant information (demographics, healthcare utilizations, and prescription records). All participants were followed up until their loss of eligibility due to death or emigration.[81]

The data for the study included 1,198,577 individuals aged ≥60 years and with medical claims for any type of dementia (ICD-10 codes F00, F01, F02, F03, G30, G3100, G3182) between January 1, 2010 to December 31, 2021, the 50% simple random sample of total patients with dementia. The subjects of the study were patients with dementia aged 60 years or older between February 1, 2016 and October 31, 2021. For analysis, only medical records from the date of dementia diagnosis (first claim for dementia) were used. The observations with missing covariates were excluded from the study.

South Korean LTCHs operate under a per-diem reimbursement system, which could result in omissions of drugs that do not receive compensation based on claims in our dataset. Specifically, from November 1, 2019, the antipsychotic drug prescription was included as one of the patient classification criteria for LTCH per-diem reimbursement, which might introduce increased imbalance in the claim data compared to the preceding period.[82] Therefore, in the present study, periods during which patients with dementia were hospitalized in LTCHs were excluded from the analysis when evaluating medications.

Among all participants, 305,835 individuals without medical records after February 1, 2016, and 16,2584 individuals diagnosed with dementia after Oct 31, 2021 were excluded, resulting in a total of 876,158 eligible patients with dementia for the study. Subsequently, 12,070,271 observations for every 3-months of selected participants were extracted from February 1, 2016 to October 31, 2021. After excluding 712,090 observations with missing covariates, the sample for evaluating healthcare utilizations included a total of 11,358,180 observations of patients with dementia over the 24 time-interval of study periods. Finally, 1,536,377 observations of dementia patients hospitalized in LTCHs throughout each time unit were excluded, the sample for evaluating medications included 9,821,803 observations (Figure 7).

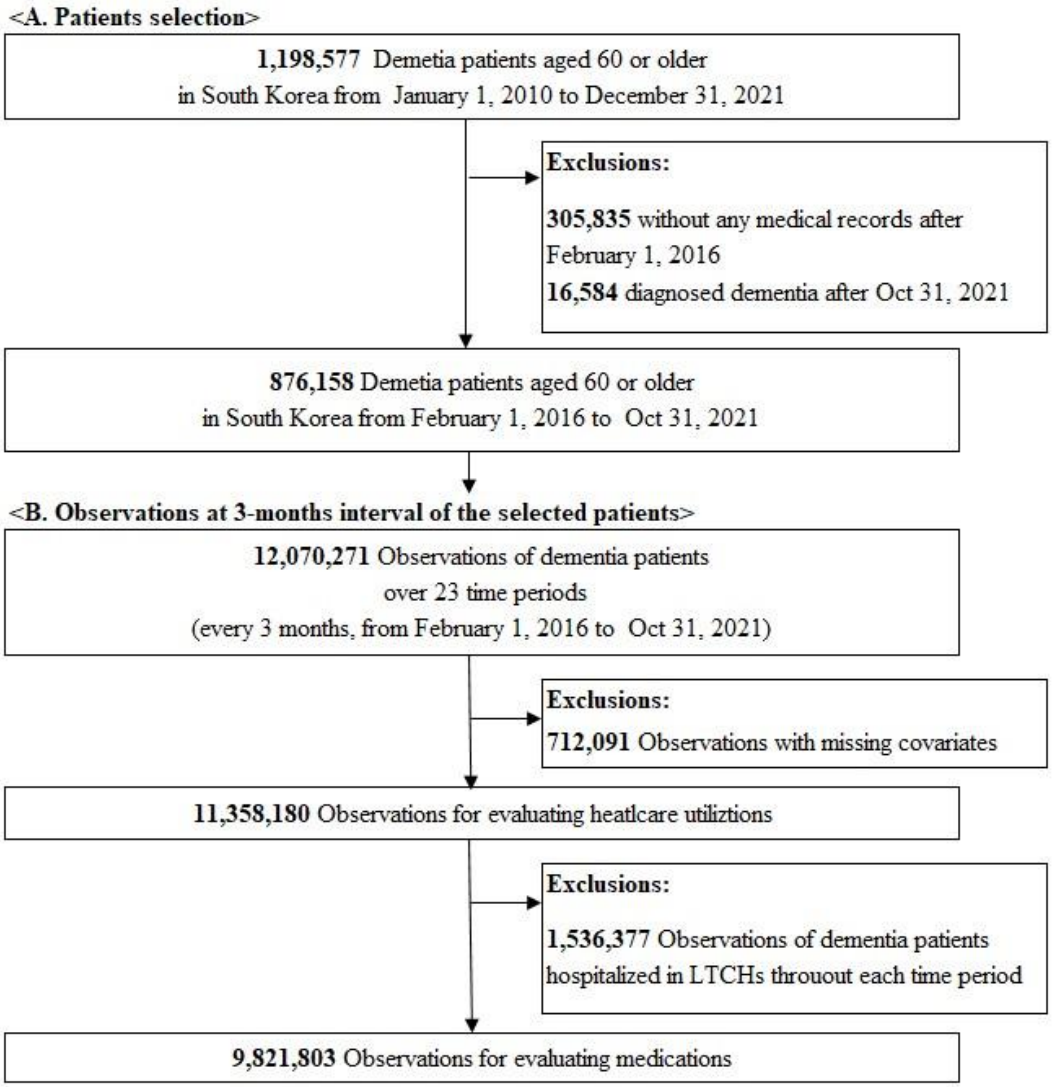


Figure 7. Flowchart of the study sample selection

Abbreviations: LTCHs, Long-Term Care Hospitals

2. Definition of Variables

1) Dependent Variables

The primary dependent variable of the study served as a surrogate indicator for dementia management was the patients with antipsychotics prescriptions at each time interval (3-months scale). All antipsychotic drug covered by Korean NHI during the study period (chlorpromazine, clozapine, haloperidol, levomepromazine, molindone, olanzapine, perphenazine, pimozide, risperidone, thiothixene, quetiapine, amisulpride, aripiprazole, ziprasidone, paliperidone) were included as study outcomes.[83] Other indicators regarding the antipsychotic drug prescription, the duration of prescription and the number of prescriptions were also included as dependent variables.

In addition, proportion of patients with good adherence for anti-dementia medications (donepezil, rivastigmine, galantamine, memantine) was included as an another surrogate indicator for dementia management.[84] The adherence to anti-dementia medications was calculated using the Proportion of Days Covered (PDC).[85,86] PDC was computed by dividing the duration of prescription for each time unit by the observation period for every individual. PDC ranges from 0 (no prescription of anti-dementia medication) is received to 1 (the anti-dementia medication covers the entire observation period). Anti-dementia medications prescribed beyond the time unit were considered as being utilized in the subsequent time unit.[85,86]

Dependent variables related to healthcare utilization were the patients with ER visits, numbers of outpatient visits, the patients with hospitalization, and the number of days hospitalized. The details of the dependent variables are summarized in the Table 1.

Table 1. Definition of dependent variables

Category			Definition
Surrogate indicators for dementia management	Antipsychotics	Patients of antipsychotics prescriptions	Whether dementia patients received at least one prescription of antipsychotics during each time unit.
		No. of days with antipsychotics prescriptions	The number of days covered by antipsychotics during each time unit (within the limits of the observation period).
		No. of prescriptions	Frequency of daily prescriptions × Quantity of each prescription× Days of prescription (including any periods beyond the observation period)
	Patients with good adherence to anti-dementia medications		Patients with PDC≥0.8 to anti-dementia medications.
Healthcare Utilizations	Patients with ER visits		Whether dementia patients had at least one ER visits during each time unit
	No. of outpatient visits		Sum of the number of outpatient visits during each time unit
	Patients with hospitalization		Whether dementia patients had at least one hospitalization during each time unit
	No. of days hospitalized		Sum of the days of admission during each time unit, ranges 0 to observation periods

Abbreviations: No, Number; ER, Emergency Room

2) Variable of Interest

The variable of interest in the study was the COVID-19 outbreak in South Korea and the began of subsequent containment policy. The first COVID-19 case in South Korea occurred on January 20, 2020, and from early February 2020, a 'social distancing' campaign was initiated. The official start of government epidemic control policies was on February 29, 2020, and the stringency index indicates that public measures began in early February 2020.[58,59] Overall, this study divided the period before and after the onset of COVID-19 outbreak in Korea using February 1, 2020, as a reference point.

A binary intervention variable indicating before and after COVID-19 pandemic (February 1, 2020) was included to estimate level change. A continuous time variable as a 3-month interval, centered to February 1, 2020, was included to estimate baseline slope of outcome variables. The interaction between binary intervention variable and time variable was incorporated in the model to estimate slope change after the COVID-19 pandemic.

3) Independent Variables

The independent variables included sex (male or female), age (continuous variable), residential area (Seoul, metropolitan, urban, or rural), household income levels (quintiles), health insurance type(local subscriber, employee-based, or medical aid program), registered disability (yes or no), Charlson comorbidity index (CCI: ≤1, 2, 3 or over), years after dementia diagnosis (<1, 1–4, 5 or over), continuous time dummy variable (as 3-months scale), seasonal effect (based on each 3-month time unit), and the offset variable to account for individual-specific observation periods. To calculated CCI score, individuals were classified having comorbid conditions if they had at least two outpatient visits or one admission for corresponding disease in the 2 years preceding each time unit. Table 2 displays the weights used for calculating the CCI score.[87]

Table 2. Weights for calculating Charlson comorbidity index score

Comorbid conditions	Weights
Myocardial infarction	1
Congestive heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic pulmonary disease	1
Connective tissue disease	1
Peptic ulcer disease	1
Mild liver disease	1
Diabetes	1
Hemiplegia	2
Moderate or severe renal disease	2
Diabetes with chronic complications	2
Cancer without metastases	2
Lukemia / lymphoma	2
Moderate or severe liver disease	3
Metastatic cancer	6
AIDS/HIV	6

3. Statistical Methods

Data were analyzed between July and November 2023. The Chi-square and T-test were used to evaluate general characteristics of patients with dementia before and after COVID-19 pandemic. We performed an interrupted time series (ITS) analysis to compare the longitudinal changes of dependent variables among patients with dementia before and after COVID-19 pandemic, using an individual-level claim data. The ITS method is commonly employed to evaluate the effects of policy implementation. The model utilizes segmented regression with three temporal variables to estimate the pre-intervention slope, level change at the time of intervention, and post-intervention slope change. In this study, we designated the onset of the COVID-19 pandemic and the subsequent introduction of government epidemic control policies as the intervention.[88,89]

The unit of analysis was a person-quarter (every 3 months). For each dependent variable, the analysis was performed separately. We used generalized estimating equation (GEE) model with logit link and binomial distributions with a robust error variance to estimate marginal relationship between the COVID-19 pandemic and binary dependent variables (the patients with antipsychotic drug prescriptions, the patients with good adherence to anti-dementia medications, the patients with ER visits, and the patients with hospitalization). To analyze the countable dependent variables (the duration of antipsychotic drug prescriptions, the number of antipsychotic drug prescriptions, the

number of outpatient visits, and the number of days hospitalized), log link and the Poisson distributions was utilized. An autoregressive working correlation matrix was used to account for repeated measures within participants over time.

The commencement date of the COVID-19 pandemic was set as February 1, 2020. The pre-pandemic period was defined as the February 1, 2016 to the January 31, 2020 and the post- implementation period was defined as the February 1, 2020 to the October 31, 2021. We adjusted temporal trends of outcomes by using a continuous time variable with 3-months scale. We also controlled the potential seasonality of study outcomes, based on each time unit.

The interrupted time series model used in this study is as follows, for patient *i* at time *t*:

$$g(E[Y_{it}]) = \beta_0 + \beta_1 * Time_t + \beta_2 * Post_t + \beta_3 * Time_t * Post_t + \phi_q * Season_q + \lambda_v * X_{vit}$$

g: link function;

E: Expectation;

Y_{it}: dependent variable;

$Time_t$: a continuous time variable in 3-months interval, centered at the last pre-intervention time unit;

$Post_t$: an indicator which assigns 1 if time falls within the post-pandemic periods;

$Season_q$: an indicator for season based on calendar quarter;

X_{vit}: the individual-level covariates (sex, age, residential area, household income levels, registered disability, insurance type, CCI, and years after dementia diagnosis);

In this model, the interpretations of each regression coefficient are as follows: β0 represents the estimates of the baseline level of the dependent variables. β1 represents the estimate of the baseline slope of the dependent variables. β2 is the estimate of the level change in the dependent variables immediately following the pandemic. β3 is the estimate of the slope change in the dependent variables after pandemic. The sum of β1 and β3 denotes the slope of the dependent variables following the post-pandemic periods.[89]

The additional analyses were performed to identify whether the stringency of public measure or duration after pandemic was related to antipsychotic drug prescriptions of patients with dementia. Instead of binary intervention variable and interaction term, government stringency index (rescaled by 5-point) and nominal time variables (1–3, 4–6, 7–9, 10–12, 13–15, 16–18, and 19–21 months after the COVID-19 pandemic) were included for the analyses. Finally, we performed subgroup analyses with the purpose of evaluating the relationship between primary dependent variable (the patients with antipsychotic drug prescriptions) and the COVID-19 pandemic according to type of medical services (outpatient or inpatient). Two-sided p-values <0.05 were considered statistically significant. All analyses were performed using SAS Enterprise Guide software (version 7.1; SAS Institute, Cary, NC, USA).

4. Ethics Statement

This study was reviewed and approved by the Institutional Review Board of Yonsei University's Health System in accordance with the principles of the Declaration of Helsinki (IRB no. 4-2022-1394). Furthermore, as the NHID, the data for this study did not contain personally identifiable information, the informed consent requirement was exempted.

IV. Results

1. Impact of COVID-19 Pandemic on Dementia Management: Antipsychotic Drug Prescriptions and Adherence to Anti-dementia Medications

1) Participants Characteristics

The final sample to evaluate antipsychotic drug prescriptions comprised 9,821,803 observations of patients with dementia over 24 time-periods (every 3-months), with 6,243,936 and 3,577,867 observations in before and after COVID-19 pandemic, respectively. The mean age was 79.6 years (SD, 8.0 years) and 80.5 (SD, 7.9 years) in before and after COVID-19 pandemic, respectively. There was a higher proportion of observations with 5 or more years from dementia diagnosis in post-pandemic group (30.3%), compared to pre-pandemic group (24.9%). Demographics of study participants were exhibited in Table 3.

Table 3. Participants characteristics (to evaluate medications)[a]

Characteristics	Total	Pre-pandemic[b]	Post-pandemic[b]	*p*-value
	n=9,821,803	n=6,243,936	n=3,577,867	
Sex (N, %)				
Male	3,017,562 (30.7)	1,907,541 (30.6)	1,110,021 (31.0)	<0.001
Female	6,804,241 (69.3)	4,336,395 (69.4)	2,467,846 (69.0)	
Age, years (mean, SD)	79.9 ±8.0	79.6 ±8.0	80.5 ±7.9	<0.001
Residential area (N, %)				
Seoul	1,416,673 (14.4)	906,929 (14.5)	509,744 (14.2)	<0.001
Metropolitans	1,971,578 (20.1)	1,251,784 (20.0)	719,794 (20.1)	
Urban	4,574,899 (46.6)	2,898,877 (46.4)	1,676,022 (46.8)	
Rural	1,858,653 (18.9)	1,186,346 (19.0)	672,307 (18.8)	
Household income, quintiles (N, %)				
1st (lowest)	2,862,170 (29.1)	1,795,816 (28.8)	1,066,354 (29.8)	<0.001
2nd	848,290 (8.6)	527,976 (8.5)	320,314 (9.0)	
3rd	1,134,551 (11.6)	706,929 (11.3)	427,622 (12.0)	
4th	1,119,215 (11.4)	730,087 (11.7)	389,128 (10.9)	
5th (highest)	3,857,577 (39.3)	2,483,128 (39.8)	1,374,449 (38.4)	
Health insurance type (N, %)				
Local subscriber	2,662,004 (27.1)	1,631,156 (26.1)	1,030,848 (28.8)	<0.001
Employee-based	5,808,578 (59.1)	3,744,847 (60.0)	2,063,731 (57.7)	
Medical aid program	1,351,221 (13.8)	867,933 (13.9)	483,288 (13.5)	
Registered disability (N, %)				
Yes	7,208,033 (73.4)	4,597,115 (73.6)	2,610,918 (73.0)	<0.001
No	2,613,770 (26.6)	1,646,821 (26.4)	966,949 (27.0)	
CCI (N, %)				
0 – 1	3,745,485 (38.1)	2,300,047 (36.8)	1,445,438 (40.4)	<0.001
2	2,621,814 (26.7)	1,685,873 (27.0)	935,941 (26.2)	
3 or over	3,454,504 (35.2)	2,258,016 (36.2)	1,196,488 (33.4)	
Years after dementia diagnosis (N, %)				
< 1	2,307,090 (23.5)	1,580,664 (25.3)	726,426 (20.3)	<0.001
1– 4	4,874,860 (49.6)	3,108,368 (49.8)	1,766,492 (49.4)	
5 or over	2,639,853 (26.9)	1,554,904 (24.9)	1,084,949 (30.3)	

Abbreviations: CCI, Charlson Comorbidity Index

[a]The numbers represent observations from study participants at 3-month intervals.

[b]The pre- and post-pandemic period were defined as February 1, 2016, through January 31, 2020 and February 1, 2020 through October 31, 2021

2) Unadjusted Changes in Antipsychotic drug Prescriptions and Adherence to Anti-dementia Medication before and after COVID-19 Pandemic

Table 4 present the unadjusted changes in the medications including the patients with antipsychotic drug prescriptions, the primary outcome of the study, among patients with dementia before and after COVID-19 pandemic. After COVID-19 pandemic, increases in patients with antipsychotic drug prescription (0.69 to 0.72 per a person-year, 5.3%), in the duration of antipsychotic drug prescriptions (51.86 to 57.03 per a person- year, 10.0%), the numbers of prescription (72.39 to 84.59 per a person-year, 16.9%) were observed. The proportion of patients with good adherence to anti-dementia medication showed slight increase (1.71 to 1.76 per a person- year, 2.5%) after the COVID-19 pandemic.

Table 4. Unadjusted changes in medications before and after COVID-19 pandemic[a]

Variables	Pre-pandemic[b] (1,491,955 Person-years)		Post-pandemic[b] (866,084 Person-years)		Unadjusted Change, %
	Number	Crude IR[c]	Number	Crude IR[c]	
Antipsychotic drug prescriptions					
A. Patients with prescription	1,026,165	0.69	627,008	0.72	5.3
B. Duration of prescription	77,370,303	51.86	49,391,221	57.03	10.0
C. Numbers of prescription	108,002,312	72.39	73,260,002	84.59	16.9
Patients with good anti-dementia medication adherence (PDC≥0.8)	2,556,695	1.71	1,521,766	1.76	2.5

Abbreviations: COVID-19, Coronavirus Disease 2019; IR, Incidence Rate; PDC, Proportion of Days Covered

[a]The numbers represent observations from study participants at 3-month intervals.

[b]The pre- and post-pandemic period were defined as February 1, 2016, through January 31, 2020 and February 1, 2020 through October 31, 2021

[c]Per person-years

3) Results of ITS Analysis for Antipsychotic drug Prescriptions and Adherence to Anti-dementia Medication

Figure 8 illustrates the results of ITS analysis regarding antipsychotic drug prescriptions and adherence to anti-dementia medication among patients with dementia aged 60 or older. The increases in slopes were observed in patients with the likelihood of being prescribed with antipsychotic drug, the duration of antipsychotic drug prescription, and the patients with good adherence to anti-dementia medication after the COVID-19 pandemic, as compared to the pre-pandemic period. The number of antipsychotics prescription showed an immediate increase after the pandemic, followed by a slight upward trend.

Table 5 presents the results of ITS analysis, illustrating the pre-pandemic trend, level change, slope change, and post-pandemic trend for each outcome variable. The likelihood of being prescribed with antipsychotic drug and the duration of prescription after the COVID-19 pandemic were immediately decreased by -2.7% (estimate, 0.973; 95% CI, 0.967-0.979; $P < .001$), and -1.8 % (estimate, 0.982; 95% CI, 0.976-0.987; $P < .001$), respectively, but the trends were significantly increased during the post-pandemic periods, compared to pre-pandemic periods. The trend of likelihood of receiving antipsychotic drug and the duration of prescription increased relatively by 1.5% (estimate, 1.015; 95% CI, 1.013-1.017; $P < .001$) and 3.2% (estimate, 1.015; 95% CI, 1.013-1.017; $P < .001$), respectively, compared with pre-pandemic trends. Compared to pre-pandemic, the number of antipsychotic prescription exhibited an immediate increase of 2.7% (estimate, 1.027; 95%

CI, 1.019-1.034; P < .001) following the pandemic, along with an increase in trend by 0.4% per 3-months (estimate, 1.004; 95% CI, 1.002-1.006; P < .001).

Patients with good adherence to anti-dementia medication showed immediate decrease of -1.5% (estimate, 0.985; 95% CI, 0.983-0.988; P < .001) following the pandemic, along with an increase in trend by 0.5% per 3-months (estimate, 1.005; 95% CI, 1.005-1.006; P < .001).

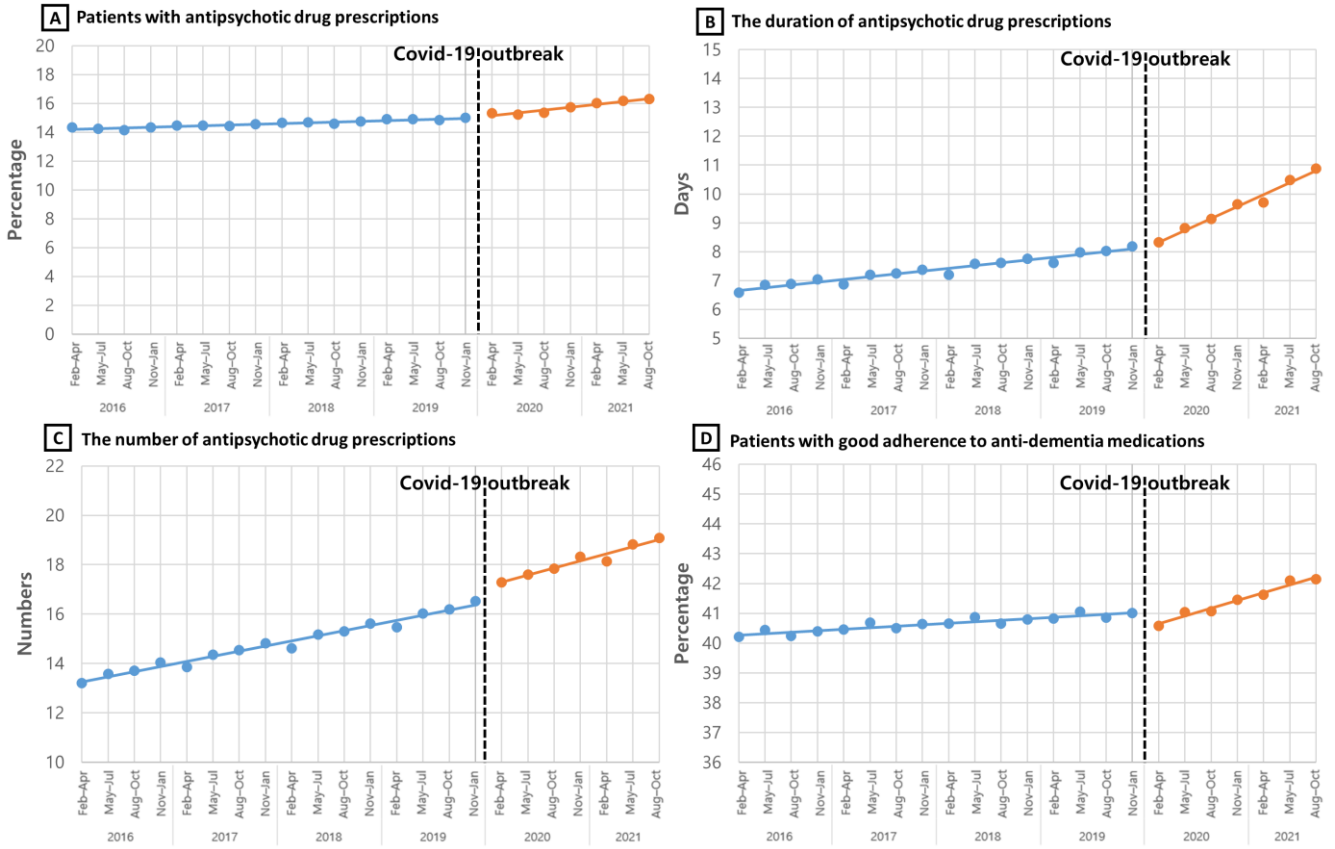


Figure 8. Results of interrupted time series analyses of changes in antipsychotic drug prescriptions and adherence to anti-dementia medications among patients with dementia

Table 5. Results of ITS analysis for antipsychotic drug prescriptions and adherence to anti-dementia medication[a]

	Exp(β)	95% CI	*P*-value
Antipsychotic drug prescriptions			
A. Likelihood of prescription			
Baseline trend	1.000	(0.999 – 1.001)	0.496
Level change after pandemic	0.973	(0.967 – 0.979)	<.001
Slope change after pandemic	1.015	(1.013 – 1.017)	<.001
Follow-up outcome trend	1.015	(1.014 – 1.017)	<.001
B. Duration of prescriptions			
Baseline trend	1.011	(1.010 – 1.013)	<.001
Level change after pandemic	0.982	(0.976 – 0.987)	<.001
Slope change after pandemic	1.032	(1.029 – 1.034)	<.001
Follow-up outcome trend	1.055	(1.052 – 1.057)	<.001
C. Numbers of prescriptions			
Baseline trend	1.011	(1.010 – 1.012)	<.001
Level change after pandemic	1.027	(1.019 – 1.034)	<.001
Slope change after pandemic	1.004	(1.002 – 1.006)	0.001
Follow-up outcome trend	1.015	(1.013 – 1.017)	<.001
Patients with good adherence for anti-dementia medications (PDC≥0.8)			
Baseline trend	1.000	(1.000 – 1.001)	0.037
Level change after pandemic	0.985	(0.983 – 0.988)	<.001
Slope change after pandemic	1.006	(1.005 – 1.006)	<.001
Follow-up outcome trend	1.006	(1.005 – 1.006)	<.001

Abbreviations: ITS, Interrupted Time Series; PDC, Proportion of Days Covered

[a]The pre- and post-pandemic period were defined as February 1, 2016, through January 31, 2020 and February 1, 2020 through October 31, 2021

4) The Association between the Stringency of Public Measures, the Elapsed Period after COVID-19 Pandemic, and the Antipsychotic drug Prescription.

The likelihood of being prescribed with antipsychotic drug had demonstrated a dose-response relationship with elapsed period after the COVID-19 pandemic. For instance, compared to pre-pandemic period, the likelihood of receiving antipsychotic prescriptions was -1.6% (estimate, 0.984; 95% CI, 0.978-0.991; P < .001) lower, 4.1% (estimate, 1.041; 95% CI, 1.031-1.046; P < .001) and 8.9% (estimate, 1.089; 95% CI, 1.075-1.103; P < .001) higher during the first 3 months, 10–12 months, and 19–21 months after COVID-19 pandemic. In the same analysis, the baseline trend for antipsychotic drug prescriptions before COVID-19 remained unchanged (estimate, 1.000; 95% CI, 0.999-1.001; P=0668). However, the likelihood of antipsychotic drug prescription after the COVID-19 pandemic decreased by -0.01% (estimate, 0.999; 95% CI, 0.998-0.999; P < .001) for every 5 scores of stringency index (Table 6).

Table 6. The association between the stringency of public measures, the elapsed time after pandemic, and the antipsychotic drug prescriptions[a]

	Exp(β)	95% CI	*P*-value
Patients with antipsychotic drug prescriptions			
A. The COVID-19 stringency index[b]			
Baseline outcome trend	1.004	(1.004 – 1.005)	<.001
Stringency index (rescaled)	0.999	(0.998 – 0.999)	<.001
B. Elapsed time after COVID-19 pandemic			
Baseline outcome trend	1.000	(0.999 – 1.001)	0.668
1 – 3 months	0.984	(0.978 – 0.991)	<.001
4 – 6 months	1.038	(1.030 – 1.046)	<.001
7 – 9 months	1.046	(1.036 – 1.055)	<.001
10 – 12 months	1.041	(1.031 – 1.046)	<.001
13 – 15 months	1.060	(1.048 – 1.073)	<.001
16 – 18 months	1.073	(1.060 – 1.086)	<.001
19 – 21 months	1.089	(1.075 – 1.103)	<.001

Abbreviations: COVID-19, Coronavirus disease-19

[a]The pre- and post-pandemic period were defined as February 1, 2016, through January 31, 2020 and February 1, 2020 through October 31, 2021

[b]The COVID-19 stringency index was rescaled to 5-point increments

5) The Association between the Antipsychotic drug Prescriptions and COVID-19 Pandemic in Outpatient and Inpatient Settings

Table 7 exhibits the association between the antipsychotic drug prescriptions and COVID-19 pandemic in outpatient and inpatient settings. The likelihood of being prescribed antipsychotic drug in outpatient clinic showed relative increase in slope by 1.7% (estimate, 1.017; 95% CI, 1.015-1.019; P < .001) after immediate level change by -3.0% (estimate, 1.017; 95% CI, 1.015-1.019; P < .001) following the COVID-19 pandemic. The likelihood of receiving antipsychotic drug in hospitalized patients with dementia showed immediate level change by 4.6% (estimate, 1.046; 95% CI, 1.003-1.090; P < .001) and subsequent slope change by -1.0% (estimate, 0.990; 95% CI, 0.981-0.999; P < .001) after the COVID-19 pandemic. The likelihood of being prescribed with antipsychotic drug among hospitalized patients with dementia showed increasing baseline trend by 0.8% (estimate, 1.008; 95% CI, 1.005-1.010; P < .001) per every 3-monts before the pandemic, but demonstrated stable post-pandemic trend (estimate, 0.997; 95% CI, 0.989-1.006; P =.520).

Table 7. The association between the antipsychotic drug prescriptions and COVID-19 pandemic in outpatient and inpatient settings[a]

	Exp(β)	95% CI	*P*-value
Patients with antipsychotics prescriptions			
A. Outpatient setting			
Baseline trend	1.001	(1.000 - 1.002)	0.049
Level change after pandemic	0.970	(0.964 - 0.976)	<.001
Slope change after pandemic	1.017	(1.015 - 1.019)	<.001
Follow-up outcome trend	1.018	(1.017 - 1.020)	<.001
B. Inpatient setting			
Baseline trend	1.008	(1.005 - 1.010)	<.001
Level change after pandemic	1.046	(1.003 - 1.090)	0.036
Slope change after pandemic	0.990	(0.981 - 0.999)	0.027
Follow-up outcome trend	0.997	(0.989 - 1.006)	0.520

Abbreviations: COVID-19, Coronavirus disease-19
[a]The pre- and post-pandemic period were defined as February 1, 2016, through January 31, 2020 and February 1, 2020 through October 31, 2021

2. Impact of COVID-19 Pandemic on Healthcare Utilizations of Patients with Dementia

1) Participants Characteristics

Table 8 shows the general characteristics of study participants to evaluate healthcare utilizations among patients with dementia. The final sample to evaluate healthcare utilizations comprised 11,358,180 observations of patients with dementia over 24 time-periods (every 3-months), with 7,291,460 and 4,066,720 observations in before and after COVID-19 pandemic, respectively. The mean age was 80.0 years (SD, 8.1 years) and 80.8 (SD, 8.0 years) in before and after COVID-19 pandemic, respectively. There was a higher proportion of observations with 5 or more years from dementia diagnosis in post-pandemic group (31.6%), compared to pre-pandemic group (27.8%).

Table 8. Participants characteristics (to evaluate healthcare utilization)[a]

Characteristics	Total	Pre-pandemic[b]	Post-pandemic[b]	*p*-value
	n=11,358,180	n=7,291,460	n=4,066,720	
Sex (N, %)				
Male	3,415,169 (30.1)	2,174,759 (29.8)	1,240,410 (30.5)	<0.001
Female	7,943,011 (69.9)	5,116,701 (70.2)	2,826,310 (69.5)	
Age, years (mean, SD)	80.3 ±8.1	80.0 ±8.1	80.8 ±8.0	<0.001
Residential area (N, %)				
Seoul	1,551,736 (13.7)	998,721 (13.7)	553,015 (13.6)	<0.001
Metropolitans	2,439,317 (21.5)	1,572,811 (21.6)	866,506 (21.3)	
Urban	5,230,143 (46.0)	3,343,024 (45.8)	1,887,119 (46.4)	
Rural	2,136,984 (18.8)	1,376,904 (18.9)	760,080 (18.7)	
Household income, quintiles (N, %)				
1st (lowest)	3,428,279 (30.2)	2,173,587 (29.8)	1,254,692 (30.9)	<0.001
2nd	972,995 (8.6)	611,957 (8.4)	361,038 (8.9)	
3rd	1,299,814 (11.4)	817,687 (11.2)	482,127 (11.9)	
4th	1,275,406 (11.2)	840,105 (11.5)	435,301 (10.7)	
5th (highest)	4,381,686 (38.6)	2,848,124 (39.1)	1,533,562 (37.7)	
Health insurance type (N, %)				
Local subscriber	3,067,064 (27.0)	1,899,464 (26.1)	1,167,600 (28.7)	<0.001
Employee-based	6,627,567 (58.4)	4,314,608 (59.2)	2,312,959 (56.9)	
Medical aid program	1,663,549 (14.6)	1,077,388 (14.8)	586,161 (14.4)	
Registered disability (N, %)				
Yes	8,259,458 (72.7)	5,321,132 (73.0)	2,938,326 (72.3)	<0.001
No	3,098,722 (27.3)	1,970,328 (27.0)	1,128,394 (27.7)	
CCI (N, %)				
0 – 1	4,366,539 (38.4)	2,715,360 (37.2)	1,651,179 (40.6)	<0.001
2	3,000,218 (26.4)	1,948,108 (26.7)	1,052,110 (25.9)	
3 or over	3,991,423 (35.1)	2,627,992 (36.0)	1,363,431 (33.5)	
Years after dementia diagnosis (N, %)				
< 1	2,589,591 (22.8)	1,790,860 (24.6)	798,731 (19.6)	<0.001
1– 4	5,607,508 (49.4)	3,626,237 (49.7)	1,981,271 (48.7)	
5 or over	3,161,081 (27.8)	1,874,363 (25.7)	1,286,718 (31.6)	

Abbreviations: CCI, Charlson Comorbidity Index

[a]The numbers represent observations from study participants at 3-month intervals.

[b]The pre- and post-pandemic period were defined as February 1, 2016, through January 31, 2020 and February 1, 2020 through October 31, 2021

2) Unadjusted Changes in Healthcare Utilizations among Patients with Dementia before and after COVID-19 Pandemic

Table 9 present the unadjusted changes in the healthcare utilizations among dementia patients after COVID-19 pandemic. After COVID-19 pandemic, all four dependent variables regarding healthcare utilization decreased compared with pre-pandemic period. Specifically, in patients with ER visits (0.16 to 0.13 per a person-year, -17.1%), in the number outpatient visits (32.86 to 31.11 per a person- year, -5.3%), in the patients experienced admission (1.16 to 0.96 per a person-year, -17.1%), and in the number of days hospitalized (65.80 to 54.03 per a person- year, -17.9%) were observed.

Table 9. Unadjusted changes in healthcare utilizations before and after COVID-19 pandemic[a]

Variables	Pre-pandemic[b] (1,764,559 Person-years)		Post-pandemic[b] (991,695 Person-years)		Unadjusted Change, %
	Number	Crude IR[c]	Number	Crude IR[c]	
Health utilizations					
A. Patients with ER visit	283,126	0.16	131,934	0.13	-17.1
B. Number of outpatient visits	57,983,821	32.86	30,849,633	31.11	-5.3
C. Patients with hospitalization	2,050,395	1.16	955,134	0.96	-17.1
D. Number of days hospitalized	116,111,881	65.80	53,585,920	54.03	-17.9

Abbreviations: COVID-19, Coronavirus Disease 2019; IR, Incidence Rate
[a]The numbers represent observations from study participants at 3-month intervals.
[b]The pre- and post-pandemic period were defined as February 1, 2016, through January 31, 2020 and February 1, 2020 through October 31, 2021
[c]Per person-years

3) Results of ITS Analysis for Healthcare Utilizations

Figure 9 exhibits the results of ITS analysis to predict the change in healthcare utilizations before and after COVID-19 pandemic. All four indicators of healthcare utilization showed immediate decrease at the time of COVID-19 pandemic and the subsequent recovery during pandemic period. Additionally, the declining trend observed before the pandemic shifted to an upward trajectory afterward for the likelihood of having ER visits, numbers of outpatient visits, and the number of days hospitalized patients with dementia. However, in the case of the likelihood of being hospitalized, although the pre-pandemic decreasing trend had somewhat mitigated, it still exhibits a continuous decline pattern during pandemic period.

Table 10 shows the results of ITS, the estimated parameters for pre-pandemic trend, level change, slope change, and post-pandemic trend for the healthcare utilizations (the patients with ER visits, numbers of outpatient visits, the patients with hospitalization, and the number of days hospitalized patients with dementia) among patients with dementia. All four healthcare utilization-related dependent variables showed an immediate decrease at the time of COVID-19 pandemic, followed by an increasing trend over the course of the pandemic period. The likelihood of having ER visits, the number outpatient visits, the likelihood of being hospitalized, and the number of days hospitalized after the COVID-19 pandemic were immediately decreased by -22.1% (estimate, 0.779; 95% CI, 0.767-0.791; $P < .001$), -13.7% (estimate, 0.863; 95% CI, 0.861-0.865; $P < .001$), -13.0% (estimate, 0.870; 95% CI, 0.865-0.875; $P < .001$), and -3.8% (estimate, 0.962; 95% CI, 0.956-0.968;

P < .001), respectively. The estimated slope after COVID-19 pandemic were relatively increased by 0.6% (estimate, 1.006 95% CI, 1.003-1.010; P < .001), 2.0% (estimate, 1.020; 95% CI, 1.019-1.020; P < .001), 0.9% (estimate, 1.009; 95% CI, 1.007-1.010; P < .001), and 5.2% (estimate, 1.052; 95% CI, 1.049-1.055; P < .001) for the likelihood of having ER visits, the number outpatient visits, the likelihood of being hospitalized, and the number of days hospitalized, respectively.

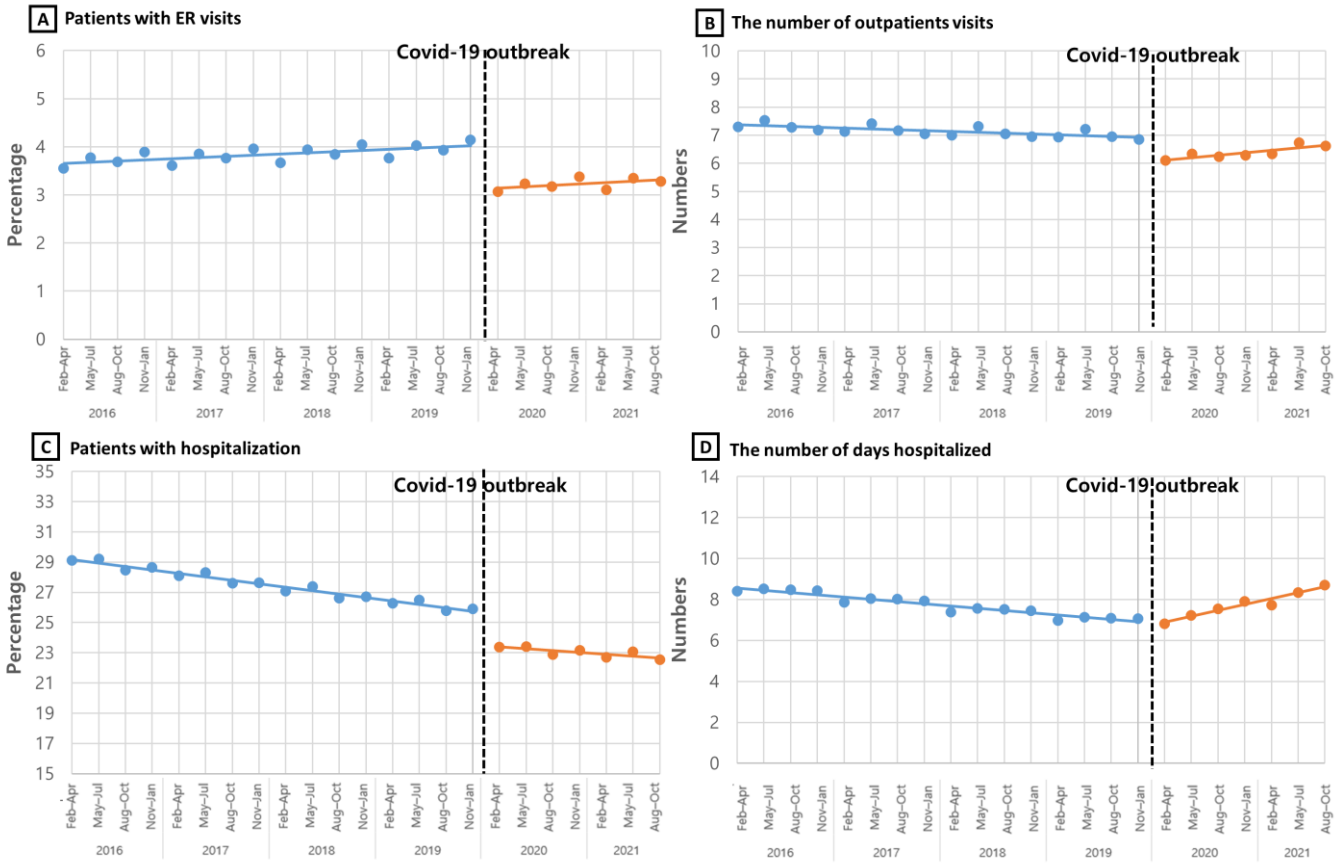


Figure 9. Results of interrupted time series analyses of changes in healthcare utilizations among patients with dementia

Table 10. Results of ITS analysis for healthcare utilizations[a]

	Exp(β)	95% CI	*P*-value
Healthcare utilizations of patients with dementia			
A. Patients with ER visit			
Baseline trend	1.005	(1.004 – 1.006)	<.001
Level change after pandemic	0.779	(0.767 – 0.791)	<.001
Slope change after pandemic	1.006	(1.003 – 1.010)	<.001
Follow-up outcome trend	1.011	(1.008 – 1.014)	<.001
B. Number of outpatient visits			
Baseline trend	0.998	(0.997 – 0.998)	<.001
Level change after pandemic	0.863	(0.861 – 0.865)	<.001
Slope change after pandemic	1.020	(1.019 – 1.020)	<.001
Follow-up outcome trend	1.017	(1.016 – 1.018)	<.001
C. Patients with hospitalization			
Baseline trend	0.986	(0.985 – 0.986)	<.001
Level change after pandemic	0.870	(0.865 – 0.875)	<.001
Slope change after pandemic	1.009	(1.007 – 1.010)	<.001
Follow-up outcome trend	0.994	(0.993 – 0.995)	<.001
D. Number of days hospitalized			
Baseline trend	0.980	(0.979 – 0.982)	<.001
Level change after pandemic	0.962	(0.956 – 0.968)	<.001
Slope change after pandemic	1.052	(1.049 – 1.055)	<.001
Follow-up outcome trend	1.031	(1.029 – 1.033)	<.001

Abbreviations: ITS, Interrupted Time Series; ER, Emergency Room
[a]The pre- and post-pandemic period were defined as February 1, 2016, through January 31, 2020 and February 1, 2020 through October 31, 2021

V. Discussion

1. Discussion of the Study Method

1) Discussion of the Study Method

This study aimed to investigate the impact of the COVID-19 pandemic on the management and healthcare utilizations of patients with dementia aged 60 and above in South Korea. Surrogate indicators for assessing the management of patients with dementia in this study included three variables related to the prescription of antipsychotic drug (likelihood of prescription, the duration of prescriptions, and the number of prescriptions), as well as adherence to anti-dementia medications. Additionally, healthcare utilization variables in the study included the likelihood of ER visits, the number of outpatient visits, the likelihood of hospitalization, and the number of days hospitalized.

For the study, we selected surrogate indicators from health insurance claim data to indirectly assess the management status of patients with dementia. Antipsychotic drug are not officially approved for the treatment of BPSD in patients with dementia.[28,29] However, they are commonly prescribed off-label when non-pharmacological means fail, and the patient exhibits symptoms such as psychosis and aggression, where the benefits outweigh the risks.[30] Previous studies have consistently reported increased social isolation, caregiving burden, and BPSD in patients with dementia after the onset of COVID-

pandemic.[66,68,90] These challenges in dementia management could ultimately lead to an increase in the prescription of antipsychotic drug.[52,69] Furthermore, to assess changes in medical treatment and healthcare accessibility for patients with dementia after the pandemic, variables related to healthcare utilization and adherence to dementia drug prescriptions were included. Moreover, our study utilized data provided by the NHIS, including a 50% random sample of patients with dementia, identified from ICD-10 codes, from 2010 to 2021. Therefore, our study enabled the analysis of a large sized nationwide sample and individual-level observations.

To determine the onset of the COVID-19 pandemic and the subsequent public health measures, we comprehensively considered the number of COVID-19 cases, the stringency index representing the intensity of public measures, and the overall situation in South Korea during the early stages of the outbreak.[60] South Korea experienced early COVID-19 outbreaks and government-driven infection control polices globally.[58,59] Therefore, in our study, we defined February 1, 2020, as the starting point of the COVID-19 pandemic, considering the period between the first COVID-19 case on January 20, 2020, and the official initiation of government infection control policies on February 29, 2020. The ITS method used in this study allows the analysis of changes in dependent variables over time concerning interventions that occurred at specific points. While commonly used to evaluate the effects of policies, it can also be applied to assess the impact of significant events like the COVID-19 pandemic.[88] In South Korea, where the number of patients with dementia is showing a rapid increase over time due to aging population, the characteristics

of participants included in the early and later stages of the study period may differ. Therefore, we utilized individual-level data for statistical analysis to avoid potential ecological fallacy and evaluate the pure impact of the COVID-19 pandemic on the temporal changes of outcome variables.

2) Strengths and Limitations of the Study

This study, using an ITS method, examined the impact of the COVID-19 pandemic on the prescription of antipsychotic drug, adherence to anti-dementia medications and healthcare utilizations among patients with dementia aged 60 or older in South Korea. The data used in our study is derived from customized data provided by the NHI, encompassing 50% of all South Korean dementia patients, which strengthened the study in terms of both representativeness and sample size. Furthermore, we utilized data that includes individual-level variables until October 2021. In addition to encompassing a relatively extended observation period after pandemic compared to similar previous studies, we were able to more accurately discern the impact of COVID-19 on the dependent variables by controlling individual-level variables.[88] In addition, our study went beyond investigating changes in antipsychotic drug usage following the COVID-19 pandemic; We not only analyzed variables such as the duration and the number of antipsychotic drug prescriptions but also comprehensively examined the healthcare utilization and adherence to anti-dementia medication among patients with dementia. This allowed us to assess the management and healthcare utilization status of patients with dementia before and after the pandemic.

However, our study has certain limitations that require careful consideration when interpreting the results. Firstly, assessing the qualitative impact of COVID-19 on patients with dementia posed challenges in the claims data used for the study. The data for the study included variables such as individuals' general characteristics, medical diagnoses

represented as ICD-10 codes, healthcare utilization, and medical expenses. However, the data did not provide insights into crucial aspects of dementia management, such as changes in behaviors, psychological aspects, social activities, and caregiving environments among patients with dementia. While these variables had been well-studied in previous research, our study evaluated prescriptions antipsychotic drug, a variable reflecting the challenges in dementia management, with a nationwide large sample. Secondly, our study focused on evaluating process indicators, such as healthcare utilization and medications, rather than outcome indicators reflecting the health status of patients with dementia. Therefore, it should be clarified through future research that whether the changes in antipsychotic drug prescriptions or healthcare utilization following the COVID-19 pandemic affected the health outcomes of patients with dementia. Third, patients with dementia admitted to LTCHs throughout each time-unit were excluded from the analysis related to medication changes. Given the restrictions on visitation, patients with hospitalized in LTCHs might also have experienced an increased likelihood of antipsychotic drug prescriptions. Therefore, the estimated effect size in our study regarding antipsychotic drug prescriptions might have been underestimated compared to the actual scenario. Lastly, although we used the ITS method and controlled patient-level characteristics to evaluate relative changes in dependent variables, there might still be unmeasured confounding factors or the impact of external factors. Lastly, our study identified patients with dementia and comorbid conditions using ICD-10 codes, which might introduce some inaccuracies due to the inherent limitations of claim codes.

2. Discussion of the Results

The summary of the findings from this study are as follows. First, following the COVID-19 pandemic and subsequent infection control policies, there was a relative upswing in the trend of antipsychotic drug prescriptions (likelihood prescription, the duration of prescriptions, and the number of prescriptions) compared to the pre-pandemic period. In ITS analysis controlling for individual-level variables and seasonality, the prescription of antipsychotic drug for patients with dementia showed no significant change before COVID-19 pandemic. However, following the onset of COVID-19 pandemic, a consistent increasing trend has been observed, indicating a turning point in the prescription of antipsychotic drug for patients with dementia associated with the pandemic. In terms of adherence to anti-dementia medications, there was a slight immediate decrease and relative increasing trend following COVID-19 pandemic compared to the pre-pandemic period although the effect size was not substantial. In additional analysis, the likelihood of antipsychotic drug prescriptions exhibited an increase with the lengthening post-pandemic elapsed period rather than being influenced by the intensity of infection control measures (represented as COVID-19 stringency index). For patients with dementia admitted to hospitals, there was an initial increase in antipsychotic drug prescriptions immediately after COVID-19, followed by a relative decrease in slope during the pandemic period, which differed from the pattern observed in outpatient settings. Lastly, Healthcare utilizations

among patients with dementia, including the likelihood of ER visits, the number of outpatient visits, likelihood of hospitalizations, and the number of days hospitalized, all decreased immediately after the onset of COVID-19. Particularly, the likelihood of ER visits showed a significant decline of 22.1% following the COVID-19.

The decline in healthcare utilization after COVID-19 aligns with findings from previous studies conducted in various countries, including those within South Korea.[43,75,77,79,91] Particularly in the case of South Korea, concerns about healthcare-associated infections following the MERS outbreak might have contributed to a noticeable reduction in healthcare facility visits.[59] Our study, focusing solely on patients with dementia, did not appear to show significant differences compared to research targeting the general older adults in South Korea.[79] Additionally, a results from Canadian study also exhibited no substantial differences in the level of pandemic-related reduction in healthcare utilization among patients with dementia, with Parkinson's disease, and the general elderly population.[43]

Despite the decrease in healthcare utilization, the adherence to anti-dementia medication, showed a slight improvement in post-pandemic compared to the pre-pandemic period. Our findings consistent with other studies using methods such as telephone surveys or claim data, indicating that there was no significant difference in healthcare utilization for chronic conditions among Korean older adults before and after COVID-19.[78,79] This could be interpreted as successful adaptation by healthcare institutions, patients with

dementia, and their caregivers to the government's infection control policies in Korea. However, it is deemed that the impact of the temporary allowance of telemedicine (since March 2020) and remote prescriptions (since December 2020), permitted to prevent the spread of COVID-19 within healthcare institutions, might have contributed to the findings.[92] Particularly, as shown in the Figure 9, from the latter half of 2020, adherence to anti-dementia medication surpassed pre-pandemic levels, suggesting the positive influence of telemedicine on medication adherence.

Our study revealed a gradual increasing trend in the antipsychotic drug prescriptions for patients with dementia after the COVID-19 pandemic. The observed slight decrease in antipsychotic drug prescriptions immediately after COVID-19 could be attributed to the reduction in healthcare utilization or considered an artifact resulting from the analysis methodology. In a study conducted by Luo and colleagues, utilizing data from six countries, a trend of increased prescription rates was observed in Germany in the ITS analysis.[52] However, no significant changes were noted in the United Kingdom, France, and South Korea. Moreover, in Germany, there was a substantial immediate decrease in antipsychotic drug prescriptions after COVID-19 pandemic which differed from the findings in our study. In the two datasets from the United States, contrasting changes in antipsychotics prescription were observed. In the case of US Open Claims, there was a similar trend to our study, with a monthly increase of 0.3% in antipsychotics prescription after COVID-19 pandemic. However, in a time-series analysis conducted by Schnier and colleagues using Wales' data, no significant increase in antipsychotic drug prescriptions

was observed after COVID-19, compared to pre-pandemic periods.[53] The Korean data included in Luo's study only included patients with dementia admitted to two tertiary hospitals in South Korea. Along with lack of representativeness for patients with dementia in South Korea, and the data could be influenced by specific events related to hospital conditions other than COVID-19 pandemic. In terms of other countries, the exact reasons for differences across countries were not clear.[52] Variations in antipsychotic drug prescription practices during the pandemic, differences in the management model for dementia patients, disparities in healthcare systems, and variations in dataset and coding might had played a role in different findings across the countries. For instance, in the Wales study, the rate of patients with dementia receiving antipsychotic drug was 0.12 per person-year, which is one-sixth of the level observed in our study.[53] Therefore, the higher level of healthcare utilization or a relatively lenient prescription practice for antipsychotic drug in patients with dementia in South Korea could also have contributed to the differences in results.

Although it is hard to pinpoint the specific reasons for the increase in antipsychotic drug prescriptions based on our data, it is believed that factors such as the exacerbation of BPSD and a decreased accessibility to care and medical services might have played a role.[35,64,67,93] South Korea implemented government-led containment policies restricting public facility usage early in the COVID-19 pandemic. Moreover, due to the prior experience with MERS, there was heightened public awareness of infectious diseases, leading to active voluntary social distancing campaigns.[59] The capacities of community

dementia centers, which previously provided management, education, and social programs for patients with dementia in each region, were redirected toward infectious disease responses, resulting in a reduction in local resources available for patients with dementia.[2]

Consequently, post-pandemic, patients with dementia in South Korea might have experienced limitations in voluntary or involuntary movement, reduced visits from family members or caregivers, and challenges in non-pharmacological management of BPSD through social activities and programs.[77] Additionally, the significant increase in the number of dementia patients due to aging likely exacerbated the shortage of caregiving and support resources during the pandemic, leading to the worsening of BPSD and the subsequent increase in antipsychotic drug prescriptions.[80] Since early stage of COVID-19 pandemic international dementia experts have urged efforts to mitigate the negative impact of the pandemic and lockdown policies on dementia patients.[62,64] In South Korea, accessibility to anti-dementia medications was maintained through initiatives such as telemedicine and voluntary efforts by the public and healthcare institutions. However, the overall increasing trend in antipsychotic drug prescriptions during the pandemic raises questions about whether non-pharmacological behavioral interventions, caregiving, and mental health support for patients with dementia were sufficient.

Finally, in our results, the increase in antipsychotic drug prescriptions for patients with dementia was seemed to be more associated with the elapsed time post-pandemic than the stringency of containment policies. Increased fatigue among patients, caregivers, and

healthcare institutions due to prolonged restrictions ultimately resulting in an increase in antipsychotic drug prescriptions in patients with dementia. Beyond the results of our study, whether these findings apply uniformly to the health outcomes of patients with dementia, other diseases, and the general population should be explored in future research. Moreover, these results indicate that in future similar infectious disease disaster situations where social distancing measures are prolonged, there may be an urgent need for social and mental support, particularly for vulnerable populations, including patients with dementia.

VII. Conclusion

This study investigated the relative changes in surrogate indicators for dementia management (antipsychotic drugs prescriptions, adherence to anti-dementia medications) and healthcare utilizations among Korean patients with dementia following the COVID-19 pandemic and subsequent public measures. The findings indicate a relative increase in the trend of antipsychotic drug prescriptions for patients with dementia after the COVID-19 pandemic compared to the pre-pandemic period. Following the pandemic, despite the gradual restoration of healthcare accessibility and the maintenance of anti-dementia medication prescription levels, the management of patients with dementia had not completely recovered from the negative impact of the pandemic. Therefore, efforts are needed to enhance qualitative healthcare services for patients with dementia, including caregiving programs, non-pharmacological interventions, mental health support, and guidelines for antipsychotic drug prescriptions. Additionally, our findings underscore the importance of swift intervention by policymakers for vulnerable populations, including patients with dementia, in future infectious disease crises similar to COVID-19.

Abbreviations

NID – National Institute of Dementia

BPSD – Behavioral and Psychological Symptoms of Dementia

FDA – US Food and Drug Administration

COVID-19 – Coronavirus Disease 2019

NHI – National Health Insurance Services

NHID – National Health Insurance Database

ER – Emergency Room

MOHW – Ministry of Health and Welfare

MERS – Middle East Respiratory Syndrome

LTCH – Long-Term Care hospitals

ICD-10 – International Statistical Classification of Diseases and Related Health Problems, 10th revision

CCI – Charlson comorbidity index

ITS – Interrupted Time Series

GEE – Generalized Estimating Equation

References

1. Statistics Korea. Senior Statistics 2022. Available at: https://kostat.go.kr/board.es?mid=a10301060500&bid=10820&act=view&list_no=420896&tag=&nPage=1&ref_bid= [Accessed Oct, 05 2023]
2. National Institute of Dementia. Korean Dementia Observatory 2022. Available at: https://ansim.nid.or.kr/community/pds_view.aspx?bid=257 [Accessed Sep 25 2023]
3. Bessey LJ, Walaszek A. Management of behavioral and psychological symptoms of dementia. Current psychiatry reports 2019;21:1-11.
4. Black W, Almeida OP. A systematic review of the association between the behavioral and psychological symptoms of dementia and burden of care. International psychogeriatrics 2004;16:295-315.
5. Kales HC, Gitlin LN, Lyketsos CG. Assessment and management of behavioral and psychological symptoms of dementia. Bmj 2015;350.
6. Huybrechts KF, Gerhard T, Crystal S, Olfson M, Avorn J, Levin R, et al. Differential risk of death in older residents in nursing homes prescribed specific antipsychotic drug: population based cohort study. Bmj 2012;344.
7. Koponen M, Taipale H, Lavikainen P, Tanskanen A, Tiihonen J, Tolppanen A-M, et al. Risk of mortality associated with antipsychotic monotherapy and

polypharmacy among community-dwelling persons with Alzheimer's disease. Journal of Alzheimer's Disease 2017;56:107-18.

8. Maust DT, Kim HM, Seyfried LS, Chiang C, Kavanagh J, Schneider LS, et al. Antipsychotics, other psychotropics, and the risk of death in patients with dementia: number needed to harm. JAMA psychiatry 2015;72:438-45.
9. Ralph SJ, Espinet AJ. Increased all-cause mortality by antipsychotic drug: updated review and meta-analysis in dementia and general mental health care. Journal of Alzheimer's disease reports 2018;2:1-26.
10. Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. Jama 2005;294:1934-43.
11. Arnott W. RISPERDAL (risperidone) and cerebrovascular adverse events in placebo-controlled dementia trials. Janssen-Ortho Inc.: Santé Canada: Direction générale des produits de santé et des aliments 2002.
12. Douglas IJ, Smeeth L. Exposure to antipsychotics and risk of stroke: self controlled case series study. Bmj 2008;337.
13. Gill SS, Rochon PA, Herrmann N, Lee PE, Sykora K, Gunraj N, et al. Atypical antipsychotic drug and risk of ischaemic stroke: population based retrospective cohort study. Bmj 2005;330:445.
14. Kleijer B, Van Marum R, Egberts A, Jansen P, Knol W, Heerdink E. Risk of cerebrovascular events in elderly users of antipsychotics. Journal of

Psychopharmacology 2009;23:909-14.

15. Sacchetti E, Trifirò G, Caputi A, Turrina C, Spina E, Cricelli C, et al. Risk of stroke with typical and atypical anti-psychotics: a retrospective cohort study including unexposed subjects. Journal of Psychopharmacology 2008;22:39-46.

16. Huang K-L, Fang C-J, Hsu C-C, Wu S-I, Juang JJ, Stewart R. Myocardial infarction risk and antipsychotics use revisited: a meta-analysis of 10 observational studies. Journal of Psychopharmacology 2017;31:1544-55.

17. Pariente A, Fourrier-Réglat A, Ducruet T, Farrington P, Béland S-G, Dartigues J-F, et al. Antipsychotic use and myocardial infarction in older patients with treated dementia. Archives of internal medicine 2012;172:648-53.

18. Wu CS, Tsai YT, Tsai HJ. Antipsychotic drug and the risk of ventricular arrhythmia and/or sudden cardiac death: a nation-wide case-crossover study. Journal of the American Heart Association 2015;4:e001568.

19. Katz IR, Rupnow M, Kozma C, Schneider L. Risperidone and falls in ambulatory nursing home residents with dementia and psychosis or agitation: secondary analysis of a double-blind, placebo-controlled trial. The American journal of geriatric psychiatry 2004;12:499-508.

20. Panel AGSBCUE. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. Journal of the American Geriatrics Society 2023.

21. Schneider LS, Dagerman K, Insel PS. Efficacy and adverse effects of atypical

antipsychotics for dementia: meta-analysis of randomized, placebo-controlled trials. The American Journal of Geriatric Psychiatry 2006;14:191-210.

22. Herzig SJ, LaSalvia MT, Naidus E, Rothberg MB, Zhou W, Gurwitz JH, et al. Antipsychotics and the risk of aspiration pneumonia in individuals hospitalized for nonpsychiatric conditions: a cohort study. Journal of the American Geriatrics Society 2017;65:2580-6.

23. Knol W, Van Marum RJ, Jansen PA, Souverein PC, Schobben AF, Egberts AC. Antipsychotic drug use and risk of pneumonia in elderly people. Journal of the American Geriatrics Society 2008;56:661-6.

24. Trifiro G, Gambassi G, Sen EF, Caputi AP, Bagnardi V, Brea J, et al. Association of community-acquired pneumonia with antipsychotic drug use in elderly patients: a nested case–control study. Annals of internal medicine 2010;152:418-25.

25. Albert SG, Grossberg GT, Thaipisuttikul PJ, Scouby J, Green E. Atypical antipsychotics and the risk of diabetes in an elderly population in long-term care: a retrospective nursing home chart review study. Journal of the American Medical Directors Association 2009;10:115-9.

26. Zheng L, Mack WJ, Dagerman KS, Hsiao JK, Lebowitz BD, Lyketsos CG, et al. Metabolic changes associated with second-generation antipsychotic use in Alzheimer's disease patients: the CATIE-AD study. American Journal of Psychiatry 2009;166:583-90.

27. Shirzadi AA, Ghaemi NS. Side effects of atypical antipsychotics: extrapyramidal symptoms and the metabolic syndrome. Harvard review of psychiatry 2006;14:152-64.

28. Kuehn BM. FDA warns antipsychotic drug may be risky for elderly. Jama 2005;293:2462-.

29. Lenzer J. FDA warns about using antipsychotic drug for dementia. Bmj 2005;330:922.

30. Reus VI, Fochtmann LJ, Eyler AE, Hilty DM, Horvitz-Lennon M, Jibson MD, et al. The American Psychiatric Association practice guideline on the use of antipsychotics to treat agitation or psychosis in patients with dementia. American Journal of Psychiatry 2016;173:543-6.

31. Lee SB. The community dementia reassurance center (chime ansim center) in South Korea. Annals of geriatric medicine and research 2019;23:43.

32. You J. Lessons from South Korea's Covid-19 policy response. The American Review of Public Administration 2020;50:801-8.

33. Choi H, Lim J-S, Lee C-N, Jang J-W, Yi S, Na S, et al. Coronavirus disease 2019 and dementia: the survey for dementia patients in COVID-19 crisis. Dementia and neurocognitive disorders 2021;20:16.

34. Korea Institute for Health And Social Affairs. The Operational Status and Policy Challenges of the Dementia Care Center. Available at: https://www.kihasa.re.kr/publish/regular/hsw/view?seq=49488&volume=49482

[Accessed Sep 25 2023]

35. Soysal P, Smith L, Trott M, Alexopoulos P, Barbagallo M, Tan SG, et al. The Effects of COVID-19 lockdown on neuropsychiatric symptoms in patients with dementia or mild cognitive impairment: A systematic review and meta-analysis. Psychogeriatrics 2022;22:402-12.
36. LeVasseur AL. Effects of social isolation on a long-term care resident with dementia and depression during the COVID-19 pandemic. Geriatric nursing 2021;42:780-1.
37. Manca R, De Marco M, Venneri A. The impact of COVID-19 infection and enforced prolonged social isolation on neuropsychiatric symptoms in older adults with and without dementia: a review. Frontiers in psychiatry 2020;11:585540.
38. Okuno T, Itoshima H, Shin J-h, Morishita T, Kunisawa S, Imanaka Y. Physical restraint of dementia patients in acute care hospitals during the COVID-19 pandemic: A cohort analysis in Japan. PloS one 2021;16:e0260446.
39. Vislapuu M, Angeles RC, Berge LI, Kjerstad E, Gedde MH, Husebo BS. The consequences of COVID-19 lockdown for formal and informal resource utilization among home-dwelling people with dementia: results from the prospective PAN. DEM study. BMC Health Services Research 2021;21:1-12.
40. Ismail II, Kamel WA, Al-Hashel JY. Association of COVID-19 pandemic and rate of cognitive decline in patients with dementia and mild cognitive impairment: a cross-sectional study. Gerontology and Geriatric Medicine

2021;7:23337214211005223.

41. Suárez-González A, Rajagopalan J, Livingston G, Alladi S. The effect of COVID-19 isolation measures on the cognition and mental health of people living with dementia: A rapid systematic review of one year of quantitative evidence. EClinicalMedicine 2021;39.

42. Tondo G, Sarasso B, Serra P, Tesser F, Comi C. The impact of the COVID-19 pandemic on the cognition of people with dementia. International Journal of Environmental Research and Public Health 2021;18:4285.

43. Bronskill SE, Maclagan LC, Maxwell CJ, Iaboni A, Jaakkimainen RL, Marras C, et al. Trends in health service use for Canadian adults with dementia and Parkinson disease during the first wave of the COVID-19 pandemic. JAMA health forum: American Medical Association; 2022. p.e214599-e.

44. Beach B, Steptoe A, Zaninotto P. Depression and anxiety in people with cognitive impairment and dementia during the COVID-19 pandemic: Analysis of the English Longitudinal Study of Ageing. Plos Medicine 2023;20:e1004162.

45. Guterman EL. Addressing Vulnerability and Dementia in the Era of COVID-19. JAMA neurology 2022;79:327-8.

46. Hua CL, Cornell PY, Zimmerman S, Carder P, Thomas KS. Excess mortality among assisted living residents with dementia during the COVID-19 pandemic. Journal of the American Medical Directors Association 2022;23:1743-9. e6.

47. Liu N, Sun J, Wang X, Zhao M, Huang Q, Li H. The impact of dementia on the

clinical outcome of COVID-19: a systematic review and meta-analysis. Journal of Alzheimer's Disease 2020;78:1775-82.

48. Panagiotou OA, Kosar CM, White EM, Bantis LE, Yang X, Santostefano CM, et al. Risk factors associated with all-cause 30-day mortality in nursing home residents with COVID-19. JAMA Internal Medicine 2021;181:439-48.

49. Raknes G, Strøm MS, Sulo G, Øverland S, Roelants M, Juliusson PB. Lockdown and non-COVID-19 deaths: cause-specific mortality during the first wave of the 2020 pandemic in Norway: a population-based register study. BMJ open 2021;11:e050525.

50. Gedde MH, Husebo BS, Vahia IV, Mannseth J, Vislapuu M, Naik M, et al. Impact of COVID-19 restrictions on behavioural and psychological symptoms in home-dwelling people with dementia: a prospective cohort study (PAN. DEM). BMJ open 2022;12:e050628.

51. Wei G, Diehl-Schmid J, Matias-Guiu JA, Pijnenburg Y, Landin-Romero R, Bogaardt H, et al. The effects of the COVID-19 pandemic on neuropsychiatric symptoms in dementia and carer mental health: an international multicentre study. Scientific Reports 2022;12:2418.

52. Luo H, Lau WC, Chai Y, Torre CO, Howard R, Liu KY, et al. Rates of antipsychotic drug prescribing among people living with dementia during the COVID-19 pandemic. JAMA psychiatry 2023;80:211-9.

53. Schnier C, McCarthy A, Morales DR, Akbari A, Sofat R, Dale C, et al.

Antipsychotic drug prescribing and mortality in people with dementia before and during the COVID-19 pandemic: a retrospective cohort study in Wales, UK. The Lancet Healthy Longevity 2023;4:e421-e30.

54. Statistics Korea Registered population of South Korea. Available at: https://kosis.kr/statHtml/statHtml.do?orgId=101&tblId=DT_1B04006&conn_path=I2 [Accessed Oct 11 2023]

55. Korean Ministry of Health and Welfare. 2012 Nationwide Survey on the Dementia Prevalence of Korea. Available [Accessed Nov 29 2023]

56. National institute of Dementia. 2016 Nationwide Survey on the Dementia Epidemiology of Korea. Available [Accessed Nov 29 2023]

57. Statistics Korea. Populatio Dashboard 2023. Available at: https://kosis.kr/visual/populationKorea/PopulationDashBoardMain.do [Accessed Nov 29 2023]

58. Korea Disease Control and Prevention Agency. Coronavirus Disease-19 (COVID-19). Available at: https://ncov.kdca.go.kr/ [Accessed Nov 25 2023]

59. Korean Ministry of Health and Welfare. COVID-19, changes in response to infectious diseases over the past three years. Available [Accessed Nov 17 2023]

60. Hale T, Angrist N, Goldszmidt R, Kira B, Petherick A, Phillips T, et al. A global panel database of pandemic policies (Oxford COVID-19 Government Response Tracker). Nature human behaviour 2021;5:529-38.

61. Edouard Mathieu HR, Lucas Rodés-Guirao, Cameron Appel, Charlie Giattino,

Joe Hasell, Bobbie Macdonald, Saloni Dattani, Diana Beltekian, Esteban Ortiz-Ospina and Max Roser. Coronavirus Pandemic (COVID-19). Published online at OurWorldInData.org 2020.

62. Canevelli M, Valletta M, Blasi MT, Remoli G, Sarti G, Nuti F, et al. Facing dementia during the COVID-19 outbreak. Journal of the American Geriatrics Society 2020;68:1673.

63. Tousi B. Dementia care in the time of COVID-19 pandemic. Journal of Alzheimer's Disease 2020;76:475-9.

64. Wang H, Li T, Barbarino P, Gauthier S, Brodaty H, Molinuevo JL, et al. Dementia care during COVID-19. The Lancet 2020;395:1190-1.

65. Brown EE, Kumar S, Rajji TK, Pollock BG, Mulsant BH. Anticipating and mitigating the impact of the COVID-19 pandemic on Alzheimer's disease and related dementias. The American Journal of Geriatric Psychiatry 2020;28:712-21.

66. Borelli WV, Augustin MC, de Oliveira PBF, Reggiani LC, Bandeira-de-Mello RG, Schumacher-Schuh AF, et al. Neuropsychiatric symptoms in patients with dementia associated with increased psychological distress in caregivers during the COVID-19 pandemic. Journal of Alzheimer's Disease 2021;80:1705-12.

67. Numbers K, Brodaty H. The effects of the COVID-19 pandemic on people with dementia. Nature Reviews Neurology 2021;17:69-70.

68. Simonetti A, Pais C, Jones M, Cipriani MC, Janiri D, Monti L, et al. Neuropsychiatric symptoms in elderly with dementia during COVID-19

pandemic: definition, treatment, and future directions. Frontiers in psychiatry 2020;11:579842.

69. Howard R, Burns A, Schneider L. Antipsychotic prescribing to people with dementia during COVID-19. The Lancet Neurology 2020;19:892.

70. Harrison SL, Buckley BJ, Lane DA, Underhill P, Lip GY. Associations between COVID-19 and 30-day thromboembolic events and mortality in people with dementia receiving antipsychotic medications. Pharmacological research 2021;167:105534.

71. Cohen G, Russo MJ, Campos JA, Allegri RF. COVID-19 epidemic in Argentina: worsening of behavioral symptoms in elderly subjects with dementia living in the community. Frontiers in psychiatry 2020;11:866.

72. Sizoo EM, Thunnissen JA, van Loon AM, Brederveld CL, Timmer H, Hendriks S, et al. The course of neuropsychiatric symptoms and psychotropic drug use in Dutch nursing home patients with dementia during the first wave of COVID-19: A longitudinal cohort study. International journal of geriatric psychiatry 2022;37.

73. Ahn S, Kim S, Koh K. Associations of the COVID-19 pandemic with older individuals' healthcare utilization and self-reported health status: a longitudinal analysis from Singapore. BMC health services research 2022;22:66.

74. Cantor J, Sood N, Bravata DM, Pera M, Whaley C. The impact of the COVID-19 pandemic and policy response on health care utilization: evidence from county-level medical claims and cellphone data. Journal of health economics

2022;82:102581.

75. Xu S, Glenn S, Sy L, Qian L, Hong V, Ryan DS, et al. Impact of the COVID-19 pandemic on health care utilization in a large integrated health care system: retrospective cohort study. Journal of medical Internet research 2021;23:e26558.

76. Roy CM, Bollman EB, Carson LM, Northrop AJ, Jackson EF, Moresky RT. Assessing the indirect effects of COVID-19 on healthcare delivery, utilization and health outcomes: a scoping review. European Journal of Public Health 2021;31:634-40.

77. Lee M, You M. Avoidance of healthcare utilization in South Korea during the coronavirus disease 2019 (COVID-19) pandemic. International journal of environmental research and public health 2021;18:4363.

78. Kang E, Yun J, Hwang S-H, Lee H, Lee JY. The impact of the COVID-19 pandemic in the healthcare utilization in Korea: Analysis of a nationwide survey. Journal of Infection and Public Health 2022;15:915-21.

79. Park K, Byeon J, Yang Y, Cho H. Healthcare utilisation for elderly people at the onset of the COVID-19 pandemic in South Korea. BMC geriatrics 2022;22:395.

80. Kim KH, Lee SM, Hong M, Han K-M, Paik J-W. Changes in mental health service utilization before and during the COVID-19 pandemic: a nationwide database analysis in Korea. Epidemiology and Health 2023;45.

81. Cheol Seong S, Kim Y-Y, Khang Y-H, Heon Park J, Kang H-J, Lee H, et al. Data resource profile: the national health information database of the National Health

Insurance Service in South Korea. International journal of epidemiology 2017;46:799-800.

82. Shin J, Yoon S-J, Ahn H, Yun Y. Effects of Per-diem payment on the duration of hospitalization and medical expenses according to the palliative care demonstration project in Korea. The International journal of health planning and management 2017;32:e206-e17.

83. The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. Available at: https://www.psychiatry.org/psychiatrists/practice/clinical-practice-guidelines [Accessed Dec 02 2023]

84. Rodda J, Carter J. Cholinesterase inhibitors and memantine for symptomatic treatment of dementia. Bmj 2012;344.

85. Dalli LL, Kilkenny MF, Arnet I, Sanfilippo FM, Cummings DM, Kapral MK, et al. Towards better reporting of the proportion of days covered method in cardiovascular medication adherence: A scoping review and new tool TEN-SPIDERS. British Journal of Clinical Pharmacology 2022;88:4427-42.

86. Loucks J, Zuckerman AD, Berni A, Saulles A, Thomas G, Alonzo A. Proportion of days covered as a measure of medication adherence. American Journal of Health-System Pharmacy 2022;79:492-6.

87. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the Charlson comorbidity index predicted in-hospital

mortality. Journal of clinical epidemiology 2004;57:1288-94.

88. Cook TD, Campbell DT, Shadish W. Experimental and quasi-experimental designs for generalized causal inference: Houghton Mifflin Boston, MA; 2002.

89. 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.

90. Rainero I, Bruni AC, Marra C, Cagnin A, Bonanni L, Cupidi C, et al. The impact of COVID-19 quarantine on patients with dementia and family caregivers: A nation-wide survey. Frontiers in aging neuroscience 2021;12:625781.

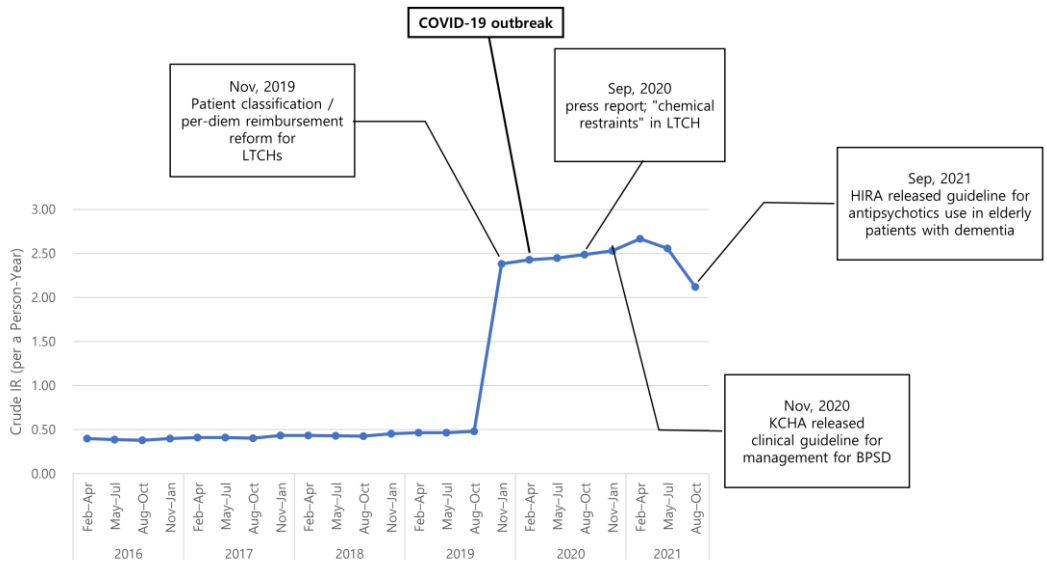
91. Oh J-Y, Cho S-J, Choi J-S. Changes in health care utilization during the COVID-19 pandemic. Health Policy and Management 2021;31:508-17.

92. Ministry of Health and Welfare. Plan to allow tempomrary telemedicine during COVID-19 pandemic. Available at: https://www.mohw.go.kr/board.es?mid=a10501010100&bid=0003 [Accessed Nov 14 2023]

93. Dixon J, Hicks B, Gridley K, Perach R, Baxter K, Birks Y, et al. 'Pushing back': People newly diagnosed with dementia and their experiences of the Covid-19 pandemic restrictions in England. International journal of geriatric psychiatry 2022;37.

Appendix

Appendix 1. Incidence of patients with dementia being prescribed with antipsychotic drugs and related events (potential external effects) in Korean LTCHs



Abbreviations: IR, Incidence Ratio; LTCH, Long-Term Care hospital; HIRA, Health Insurance Review and Assessment Service; COVID-19, Coronavirus Disease 2019; KCHA, Korean Convalescent Hospital Association; BPSD, Behavioral and Psychological Symptoms of Dementia

Appendix 2. Results of subgroup analysis stratified by sex

	Estimates (95% CI)[a]			
	Male	***P*-value**	**Female**	***P*-value**
Patients with antipsychotic drug prescriptions				
Baseline trend	0.998 (0.997 – 1.000)	0.035	1.001 (1.000 – 1.002)	0.043
Level change after pandemic	0.977 (0.966 – 0.987)	<.001	0.971 (0.964 – 0.979)	<.001
Trend change after pandemic	1.012 (1.009 – 1.015)	<.001	1.017 (1.014 – 1.019)	<.001
Follow-up outcome trend	1.010 (1.008 – 1.013)	<.001	1.018 (1.016 – 1.020)	<.001

[a] Estimates were calculated by statistically adjusting for all covariates other than sex

Appendix 3. Results of subgroup analysis stratified by age

	Estimates (95% CI)[a]					
	60 – 69 years	***P*-value**	**70 – 79 years**	***P*-value**	**≥ 80 years**	***P*-value**
Patients with antipsychotic drug prescriptions						
Baseline trend	0.994 (0.991 – 0.997)	<.001	1.000 (0.998 – 1.001)	0.611	1.001 (0.999 – 1.004)	<.001
Level change after pandemic	0.972 (0.953 – 0.991)	0.004	0.973 (0.961 – 0.984)	<.001	0.987 (0.965 – 1.009)	<.001
Trend change after pandemic	1.026 (1.020 – 1.032)	<.001	1.011 (1.008 – 1.014)	<.001	1.005 (1.000 – 1.010)	<.001
Follow-up outcome trend	1.02 (1.015 – 1.025)	<.001	1.011 (1.008 – 1.013)	<.001	1.006 (1.002 – 1.011)	<.001

[a] Estimates were calculated by statistically adjusting for all covariates

Appendix 4. Results of subgroup analysis stratified by household income level

	Estimates (95% CI)[a]									
	Quintile 1 (Lowest)	***P*-value**	**Quintile 2**	***P*-value**	**Quintile 3**	***P*-value**	**Quintile 4**	***P*-value**	**Quintile 5 (Highest)**	***P*-value**
Patients with antipsychotic drug prescriptions										
Baseline trend	1.006 (1.004–1.007)	<.001	1.006 (1.003–1.009)	<.001	1.001 (0.999–1.004)	0.256	1.001 (0.999–1.004)	0.260	1.000 (0.999–1.001)	0.967
Level change after pandemic	0.973 (0.963–0.984)	<.001	0.987 (0.961–1.015)	0.359	0.987 (0.965–1.009)	0.243	0.993 (0.970–1.016)	0.529	0.972 (0.962–0.983)	<.001
Trend change after pandemic	1.012 (1.009–1.015)	<.001	1.001 (0.995–1.008)	0.668	1.005 (1.000–1.010)	0.072	1.006 (1.000–1.012)	0.041	1.009 (1.006–1.012)	<.001
Follow-up outcome trend	1.018 (1.015–1.020)	<.001	1.008 (1.003–1.013)	0.004	1.006 (1.002–1.011)	0.005	1.007 (1.003–1.012)	0.002	1.009 (1.006–1.011)	<.001

[a] Estimates were calculated by statistically adjusting for all covariates other than household income level

Appendix 5. Results of subgroup analysis stratified by years after dementia diagnosis

	Estimates (95% CI)[a]					
	< 1 years	***P*-value**	**1 – 4 years**	***P*-value**	**≥ 5 years**	***P*-value**
Patients with antipsychotic drug prescriptions						
Baseline trend	1.000 (0.998 – 1.002)	0.986	1.004 (1.003 – 1.006)	<.001	1.008 (1.006 – 1.010)	<.001
Level change after pandemic	1.009 (0.991 – 1.028)	0.311	0.964 (0.956 – 0.972)	<.001	0.970 (0.961 – 0.980)	<.001
Trend change after pandemic	1.002 (0.997 – 1.006)	0.455	1.015 (1.012 – 1.018)	<.001	1.012 (1.009 – 1.015)	<.001
Follow-up outcome trend	1.002 (0.998 – 1.006)	0.379	1.019 (1.017 – 1.021)	<.001	1.020 (1.018 – 1.022)	<.001

[a] Estimates were calculated by statistically adjusting for all covariates other than years after dementia diagnosis

Appendix 6. Results of subgroup analysis stratified by Charlson comorbidity index score

	Estimates (95% CI)[a]					
	0 – 1	***P*-value**	**2**	***P*-value**	**3 or over**	***P*-value**
Patients with antipsychotic drug prescriptions						
Baseline trend	1.006 (1.004 – 1.007)	<.001	1.009 (1.007 – 1.011)	<.001	1.008 (1.007 – 1.009)	<.001
Level change after pandemic	0.978 (0.968 – 0.989)	<.001	0.981 (0.967 – 0.996)	0.011	0.983 (0.971 – 0.995)	0.005
Trend change after pandemic	1.015 (1.012 – 1.018)	<.001	1.009 (1.005 – 1.012)	<.001	1.003 (1.000 – 1.006)	0.080
Follow-up outcome trend	1.021 (1.019 – 1.024)	<.001	1.018 (1.015 – 1.021)	<.001	1.011 (1.008 – 1.013)	<.001

[a] Estimates were calculated by statistically adjusting for all covariates other than Charlson comorbidity index score

Korean Abstract (국문 요약)

코로나바이러스감염증-19 유행이

치매 환자의 관리 및 의료 이용에 미치는 영향

연세대학교 일반대학원 보건학과

허경덕

서론: 우리나라는 인구 고령화로 인하여 노인성 질환인 치매 환자의 수도 빠른 속도로 증가하고 있다. 한편 세계적으로 코로나바이러스감염증-19(COVID-19) 유행 및 방역 정책으로 인한 집합금지명령, 면회 제한 조치, 의료 접근성 감소 등이 치매 환자의 관리 및 행동심리증상에 악영향을 미칠 수 있다는 우려가 지속되고 있다. 이러한 배경 속에서 본 연구는 COVID-19 개편이 치매 환자의 관리 및 의료 이용에 미치는 영향에 대하여 분석하고자 한다.

연구방법: 연구를 위한 자료원으로 국민건강보험공단(NHIS)의 맞춤형DB를 사용하였다. 연구 대상은 2016년 2월 1일부터 2021년 10월 31일까지 치매 진단을 받은 60세 이상의 노인이다. 연구를 위해 3개월 간격으로 각 치매 환자의 개인 단위변수가 포함된 관측치를 추출하였다. 최종 연구 대상은 약물 처방 분석을 위한 9,821,803건 및 의료 이용 분석을 위한 11,358,180 건의 관측치를 포함하였다. 연구의 주요 종속변수는 치매 환자 관리의 대리지표로서 행동심리증상의 비약물적 요법 실패 시 처방될 수 있는 항정신병약물의 사용 여부, 사용 일수, 사용 횟수 및 치매 약물에 대한 순응

도가 포함되었다. 또한 의료이용에 관련된 종속 변수로는 응급실 이용 여부, 외래 방문 횟수, 입원 여부 및 입원 일수를 포함하였다. COVID-19 유행에 따른 종속 변수의 변화를 통계적으로 분석하기 위해 단절적 시계열 분석(interrupted time series with segmented regression)이 수행되었다.

연구결과: COVID-19 유행 이후 3개월마다 항정신병약물 처방 가능성, 처방 일수, 처방 횟수는 각각 1.5%(p<.001), 3.2%(p<.001), 0.4%(p<.001)의 상대적인 증가세를 보였다. COVID-19 유행 전과 비교하였을 때, 치매환자의 항정신병약물 처방 가능성은 COVID-19 이후 첫 3개월간은 1.6%(p<.001) 낮았으나, 10–12개월에는 4.1%, 19–21개월에는 8.9% 높아 유행 이후 경과 기간이 길수록 처방 가능성이 높아지는 양상을 보였다. 치매 약물에 좋은 복약 순응도를 가지고 있는 환자는 COVID-19 유행 전과 비교하여, 이후에 매 3개월마다 0.5%(p<.001)씩 증가하는 양상을 보였다. 단절적 시계열 분석 결과 COVID-19 유행 전후로 응급실 방문 여부, 외래 방문 횟수, 입원 여부 및 입원일수는 각각 -21.1%, -13.7%, -13.0%, -3.8%의 단기적인 감소를 보인 후, 매 3개월마다 0.6%, 2.0%, 0.9%, 5.2%씩의 점진적인 증가와 관련이 있었다.

결론: COVID-19 유행은 치매 환자의 항정신병약물 처방 증가와 관련이 있었고, 유행 이후 경과 기간이 길수록 항정신병약물 처방의 가능성이 높았다. 치매 약물에 대한 순응도는 COVID-19 유행 이후 소폭 증가하는 경향이 있었으며, 의료 이용은 유행 시작 직후 감소한 후 서서히 회복되는 양상을 보였다. 향후 유사한 감염병 위기 발생에 대비하여 치매 환자를 위한 정서적 지원, 비약물적 개입, 돌봄 제공 및 약물 처방 가이드라인 등을 마련하여, 질적 측면에서 향상된 의료 서비스를 제공할 수 있도록 준비해야 할 것이다.

제시어: 치매, 항정신병약물, 코로나바이러스-19, 의료이용, 단절적시계열분석