



저작자표시-비영리-변경금지 2.0 대한민국

이용자는 아래의 조건을 따르는 경우에 한하여 자유롭게

- 이 저작물을 복제, 배포, 전송, 전시, 공연 및 방송할 수 있습니다.

다음과 같은 조건을 따라야 합니다:



저작자표시. 귀하는 원저작자를 표시하여야 합니다.



비영리. 귀하는 이 저작물을 영리 목적으로 이용할 수 없습니다.



변경금지. 귀하는 이 저작물을 개작, 변형 또는 가공할 수 없습니다.

- 귀하는, 이 저작물의 재이용이나 배포의 경우, 이 저작물에 적용된 이용허락조건을 명확하게 나타내어야 합니다.
- 저작권자로부터 별도의 허가를 받으면 이러한 조건들은 적용되지 않습니다.

저작권법에 따른 이용자의 권리는 위의 내용에 의하여 영향을 받지 않습니다.

이것은 [이용허락규약\(Legal Code\)](#)을 이해하기 쉽게 요약한 것입니다.

[Disclaimer](#)

Master' s Thesis of Public Health

Excess mortality during the
COVID-19 pandemic in South
Korea: February 2020 through
December 2021

한국의 코로나19 장기화에 따른 초과 사망 분석

August 2023

Graduate School of Public Health
Seoul National University
Public Health Major

Jieun Oh

Excess mortality during the
COVID-19 pandemic in South
Korea: February 2020 through
December 2021

Examiner Ho Kim

Submitting a master's thesis of
Public Health

May 2023

Graduate School of Public Health
Seoul National University
Public Health Major

Jieun Oh

Confirming the master's thesis written by

Jieun Oh

July 2023

Chair Sung-il Cho (Seal)

Vice Chair Woojoo Lee (Seal)

Examiner Ho Kim (Seal)

Abstract

Background: The COVID-19 pandemic has affected the population's mortality due to the risk of infection itself and limited access to healthcare resources. This study aimed to investigate the excess mortality from the first to the second year of the pandemic in South Korea, along with the relevant socioeconomic disparities.

Methods: Daily mortality data for the years 2015–2021 were collected from Statistics Korea. Excess deaths were estimated for two pandemic years (2020–2021) with four sub-periods using a two-stage interrupted time-series analysis. The different patterns of excess death by individual characteristics and places of death were also examined.

Results: From February 18, 2020, to December 31, 2021, there were 9,481 excess deaths (95% eCI: 4,270–14,618), corresponding to the percentage excess of 1.7% (95% eCI: 0.7%–2.6%). The estimated excess death was more evident in the second year (2021; 8,500 excess deaths) compared to the first year (2020; 981 excess deaths), and the Delta period (Jul 7, 2021 to Dec 31, 2021) showed the largest number (11,138 excess deaths). The increase in mortality was more pronounced in males (1.9% excess), people aged 65 or older (2.1% excess), people without a high school education (3.4% excess), and single population (4.5% excess), compared to the total population. Moreover, the increase in excess death was more prominent in the out-of-hospital deaths throughout the pandemic than in the in-hospital deaths.

Conclusions: The results of this study revealed excess mortality during the COVID-19 pandemic 2020–2021 in South Korea and its differentials by sub-periods and individual characteristics. This study provides epidemiological evidence for establishing differentiated public health interventions that can address disproportionate accessibilities to healthcare services in association with socioeconomic disparities and pandemic periods.

Keyword: Excess mortality, COVID-19, Socioeconomic disparity

Student Number: 2021-29601

Table of Contents

Chapter 1. Introduction	1
Chapter 2. Methods	3
2.1. Data	3
2.2. Definition of the pandemic period and its sub-periods	3
2.3. Statistical analysis	4
2.3.1. Two-stage analysis	4
2.3.2 Subgroup analysis	5
2.3.3. Sensitivity analysis.....	6
Chapter 3. Results.....	7
3.1. Excess mortality during the pandemic	7
3.2. Excess mortality by individual characteristic	7
3.3. Excess mortality by place of death	1 2
3.4. Excess mortality by region.....	1 6
3.5. Sensitivity analysis.....	1 8
Chapter 4. Discussion	1 9
Chapter 5. Conclusion	2 5
Bibliography.....	2 6
Supplementary materials.....	2 9
Abstract in Korean	3 8

Tables

Table 1 Number of total deaths, estimated excess deaths, and percentage excess in mortality (with 95% empirical confidence intervals) during the COVID-19 pandemic (February 18, 2020 to December 31, 2021) in Korea.	9
Table 2 Number of total deaths, estimated excess deaths, and percentage excess in mortality (with 95% empirical confidence intervals) during the COVID-19 pandemic (February 18, 2020 to December 31, 2021) in Korea by place of death.	13
Supplementary Table S1. The Quasi-Akaike Information Criterion (QAIC) for the main model and each sensitivity analysis.....	29
Supplementary Table S2. Number of total deaths, estimated excess deaths, and percentage excess in mortality (with 95% empirical confidence intervals) during the year 2020 (February 18, 2020, to December 31, 2020) and the year 2021 (January 1, 2021, to December 31, 2020) in Korea by place of death for each cause.	30
Supplementary Table S3. Number of total deaths, estimated excess deaths, and percentage excess in mortality (with 95% empirical confidence intervals) during the COVID-19 pandemic (February 18, 2020, to December 31, 2021) in Korea by place of death for each cause.....	31
Supplementary Table S4. Percentage excess in mortality (with 95% empirical confidence interval) for the main model and each sensitivity analysis.	32
Supplementary Table S5. Number of total deaths, estimated excess deaths, and percentage excess in mortality (with 95% empirical confidence interval) for the main model and the model adjusted for NPI.....	34

Figures

Fig. 1 Temporal trend in COVID-19 confirmed cases and deaths (a), excess risk (relative risk, RR) with a band corresponding to the 95% eCI (b), and excess risk by sex, age, education level, and marital status (c) during the pandemic period (February 18, 2020–December 31, 2021) in Korea..... 1 1

Fig. 2 Percentage excess in mortality with 95% eCI by place of death across the COVID-19 periods in Korea. 1 5

Fig. 3 Maps of population density (a), percentage excess in mortality during the total pandemic period (b), and percentage excess in mortality stratified by COVID-19 pandemic periods (c) in Korea. 1 7

Supplementary Fig. S1 Temporal trends of total deaths during the study period (2015–2021)..... 3 6

Supplementary Fig. S2 Temporal trends of proportion of influenza-like illness per 1,000 outpatients during the study period (2015–2021)..... 3 7

Chapter 1. Introduction

By December 2021, the World Health Organization (WHO) reported 14.9 million coronavirus disease 2019 (COVID-19) related deaths globally, representing 9.5 million more deaths than those reported as directly attributable to COVID-19 (WHO, 2021). In the first two years of COVID-19 pandemic, South Korea (hereafter, Korea) has experienced several waves of COVID-19 epidemics due to mass infections in healthcare and religious facilities and the Delta variant (Yang et al., 2022).

In response to the pandemic, the Korean government swiftly adopted a comprehensive package of interventions during the early phase of the pandemic, including the active “trace, test, and treat” (Lee et al., 2020), and the counteraction was generally effective in reducing the spread and fatality of COVID-19 (Lee et al., 2020). However, as the pandemic became prolonged and the resultant economic burden increased, the Korean government began to cautiously relax social restrictions (Ministry of Health and Welfare, 2021), and concurrently, the novel variants, such as Delta and Omicron variants, contributed to the exponential increase in confirmed cases and deaths attributable to COVID-19 (Ryu et al., 2022).

In addition, a substantial reduction in healthcare utilization has been reported consistently since the early pandemic (Moynihan et al., 2021). Pressure on healthcare services reduced the less urgent diagnostic and treatment services of COVID-19 (Moynihan et al., 2021), and people were also limited in visiting healthcare facilities with the purpose of general services (Lee & You, 2021). In Korea, concerns about shortages in hospital beds and intensive care units have been

raised repeatedly across the pandemic period, and the shortage issues became more prominent in the Delta period (Kim, 2021). Moreover, the accessibility to healthcare systems was closely associated with socioeconomic status (Patel et al., 2020), and previous studies reported that evident differences in healthcare utilization existed during the pandemic by different sociodemographic statuses and residential areas (Kang et al., 2022; Lee & You, 2021). These results imply that limited access to healthcare resources due to the pandemic might disproportionately affect individuals depending on time and their socioeconomic characteristics.

Excess mortality is defined as the increase in mortality relative to the expected mortality based on historic trends (Karlinsky & Kobak, 2021), and it has been widely used to estimate the comprehensive impacts of the pandemic on deaths (Msemburi et al., 2023). Multiple studies in the early pandemic reported that the impact of COVID-19 on mortality was heterogeneous by sociodemographic characteristics, such as age, sex, race, and income level (Kontopantelis et al., 2022), and suggested that the pandemic exacerbated the pre-existing disparities in mortality (Bambra et al., 2020). Nevertheless, most previous studies were performed in the early phase of the pandemic (i.e., in 2020), and the long-term impacts of the pandemic on deaths associated with socioeconomic disparities were less examined.

Therefore, this study aimed to examine the nationwide excess mortality from the first to the second year of the pandemic in Korea and differential excess mortality by individual characteristics and sub-periods.

Chapter 2. Methods

2.1. Data

Data on deaths were collected from Jan 01, 2015, to Dec 31, 2021, in all 16 regions (“Si” and “Do”) of Korea from Statistics Korea, which included information on the date of death, age, sex, education level, marital status, and underlying causes of death classified with the 10th Revision of the International Classification of Diseases (ICD-10). The daily number of deaths was calculated for all causes (including confirmed COVID-19 deaths) and by individual characteristics: sex, age groups, education level, marital status, places of death, and causes of death (see details in the Subgroup analysis). Furthermore, data on confirmed COVID-19 cases during the study period were collected from Korea Disease Control and Prevention Agency (KDCA), and region-specific daily average temperatures during the study period were obtained from the Korea Meteorological Administration.

2.2. Definition of the pandemic period and its sub-periods

Although the first COVID-19 confirmed case occurred on January 20, 2020, in Korea, this study defined dates from February 18, 2020 (regarded as the epidemic onset date when large-scale outbreaks occurred in Daegu and Gyungbuk) to December 31, 2021, as the pandemic period (Lee et al., 2020).

In addition, to examine the temporal heterogeneities of the pandemic impact, four sub-periods were set according to the criteria in KDCA’s COVID-19 reports (Yang et al., 2022): 1) the first sub-period (February 18, 2020–August 11, 2020) – small outbreaks in limited regions, which mainly occurred due to overseas arrivals;

2) the second sub-period (August 12, 2020– November 12, 2020) – small outbreaks in the metropolitan area; 3) the third sub-period (November 13, 2020– July 6, 2021) – mid-scale outbreaks spread nationwide; and 4) the fourth sub-period (July 7, 2021– December 31, 2021) – the largest outbreaks due to the Delta variant.

2.3. Statistical analysis

2.3.1. Two-stage analysis

The analysis was based on two-stage interrupted time-series analyses to quantify the excess risk of mortality during the COVID-19 pandemic period compared with the pre-pandemic period in Korea, following the methodological approach described in the previous studies (Scortichini et al., 2020).

In the first stage, a quasi-Poisson regression model was conducted for every 16 regions in Korea. To estimate the time-varying risk during the pandemic period (January 20, 2020, to December 31, 2021), the days from the first COVID-19 confirmed case were included in the model, using a constrained quadratic B-spline function with six equally spaced knots; the number of internal knots was determined based on the Quasi-Akaike Information Criterion (QAIC) (see Supplementary Table S1). This function constrains the excess risk starting from null at the initial outbreak date and changing flexibly until the end of the study period. The long-term trends were controlled using a linear term for date, seasonality using cyclic cubic B-spline function with five equally spaced knots for days of the year, and weekly variations using dummy indicators for day of the week. A term for the daily mean temperature was also included using a distributed lag non-linear model, which can consider the non-linear exposure-response and

lag-response association (Gasparrini et al., 2015). A quadratic B-spline was used for exposure-response association with three internal knots set at the 10th, 75th, and 90th percentiles of region-specific temperature readings. The lag-response association was evaluated using a natural cubic B-spline with an intercept and the lag period was set to 0–21 days (Gasparrini, 2014).

In the second stage, the region-specific coefficients of the excess risk were pooled to the nationwide level using a mixed-effects multivariate meta-analysis (Sera et al., 2019). The best linear unbiased prediction (BLUP) was then calculated for each of the 16 regions to stabilize the variability due to the large differences between regions (Gasparrini et al., 2012).

The daily nationwide and region-specific relative risk (RR) of excess mortality was calculated using the pooled estimates and region-specific BLUPs for each day of the outbreak period. The daily number of excess deaths attributable to COVID-19 (hereafter, excess deaths) was computed as $n \times (RR - 1) / RR$, in which n is the number of deaths per day during the pandemic period; to address that COVID-19-related deaths are already included in the number of observed deaths (n), we calculated the excess deaths with this formula, rather than $n \times (RR - 1)$. The daily excess number of deaths was then aggregated by pandemic periods for each of the 16 regions and the whole of Korea. Empirical 95% confidence intervals (eCIs) for the coefficients were calculated using 1000 Montel Carlo simulations.

2.3.2 Subgroup analysis

To examine the disparities of excess mortality and their temporal trends, all analyses were repeated for individual characteristics, places of death, and causes of

death. Death counts were aggregated by sex, age (<65 and ≥ 65 years), education level (\leq middle school, high school, and \geq college), marital status [single, married, and others (divorced or widowed)], and place of death (in-hospital and out-of-hospital). Based on the main category of the ICD-10 code (i.e., the first letter of the code), a total of four causes of death was included in this study: Endocrine, nutritional, and metabolic diseases (E00–E90); Diseases of the circulatory system (I00–I99); Diseases of respiratory system (J00–J99); and Symptoms, signs, and abnormal clinical and laboratory findings (R00–R99). Deaths from COVID-19 (U07.1, U07.2) were included in the all-cause group.

2.3.3. Sensitivity analysis

To evaluate the robustness of main findings, several sensitivity analyses were conducted. More specifically, four and five internal knots were applied in the quadratic B-spline function for days since the first COVID-19 confirmed case, four and six knots were applied for the cyclic cubic B-spline of days of the year, and 14 and 28 days of lag period were applied in the distributed lag nonlinear model. The stringency index from Oxford COVID-19 Government Response Tracker, which proxied for non-pharmaceutical interventions, was also adjusted as linear term in the main model (Hale et al., 2021).

Chapter 3. Results

3.1. Excess mortality during the pandemic

Between February 18, 2020 and December 31, 2021, 579,037 deaths were reported in Korea (Table 1). The 7-day moving averages of COVID-19 confirmed cases and deaths are shown in Fig. 1. The excess deaths were estimated to be 9,481 (95% eCI: 4,270 to 14,618) as compared with the pre-pandemic period, which corresponds to the percentage excess of 1.7% (95% eCI: 0.7 to 2.6%). No noticeable excess was observed in 2020, however, prominent excess was observed in 2021, with a 2.7% (95% eCI: 1.2 to 4.3%) increase of deaths. In addition, the excess death showed different patterns by four sub-periods (Table 1, Fig. 1). During the second sub-period, we found a 3.7% (95% eCI: 2.9 to 4.5%) increase in deaths, whereas the third sub-period showed a negative excess death (-2.0% with eCI: -3.2 to -0.6%). The largest number of excess deaths was observed in the fourth sub-period (Delta period), with 7.5% excess death (95% eCI: 5.7 to 9.4%).

3.2. Excess mortality by individual characteristic

Excess deaths were heterogeneous by socio-demographic characteristics and causes of death (Table 1, Fig. 1). Throughout the pandemic periods, the percentage increase in deaths attributable to the pandemic was more prominent in males (1.9% with eCI: 0.7 to 3.0%), people aged 65 years or older (2.1% with eCI: 0.6 to 3.5%), people without a high school education (3.4% with eCI: 1.3 to 5.5%), and people with single marital status (4.5% with eCI: 2.0 to 6.9%), compared to the total population (1.7%). On the other hand, people with college or higher education

level showed a negative estimate (-4.8% with eCI: -8.2 to -1.1%). Moreover, the impacts of the pandemic on mortality was more pronounced during the Delta variant sub-period (July 7, 2021– December 31, 2021), compared to other sub-periods. Regarding the cause of death, there was an increase in deaths due to endocrine diseases (15.4% with eCI: 3.4 to 27.7%) and ill-defined causes (18.1% with eCI: 11.4 to 24.8%), whereas there was an decrease in deaths due to respiratory diseases (-16.2% with eCI: -20.8 to -11.9%).

Table 1 Number of total deaths, estimated excess deaths, and percentage excess in mortality (with 95% empirical confidence intervals) during the COVID-19 pandemic (February 18, 2020 to December 31, 2021) in Korea.

		Total deaths	Excess deaths	Percentage excess
Total		579,037	9,481 (4,270 to 14,618)	1.7 (0.7 to 2.6)
Period	2020	261,382	981 (-634 to 2,573)	0.4 (-0.2 to 1.0)
	2021	317,655	8,500 (3,820 to 13,052)	2.7 (1.2 to 4.3)
	Period 1 (2020.2.18–2020.8.11)	141,392	-376 (-1,720 to 991)	-0.3 (-1.2 to 0.7)
	Period 2 (2020.8.12–2020.11.12)	77,934	2,766 (2,181 to 3,337)	3.7 (2.9 to 4.5)
	Period 3 (2020.11.13–2021.7.6)	199,499	-4,046 (-6,602 to -1,145)	-2.0 (-3.2 to -0.6)
	Period 4 (2021.7.7–2021.12.31) (Delta period)	160,212	11,138 (8,573 to 13,767)	7.5 (5.7 to 9.4)
Sex	Males	314,012	5,741 (2,231 to 9,232)	1.9 (0.7 to 3.0)
	Females	265,025	3,769 (-1,745 to 9,468)	1.4 (-0.7 to 3.7)
Age	<65	124,529	-347 (-3,165 to 2,125)	-0.3 (-2.5 to 1.7)
	≥65	454,508	9,206 (2,587 to 15,582)	2.1 (0.6 to 3.5)
Education	≤Middle school	343,276	11,174 (4,269 to 17,856)	3.4 (1.3 to 5.5)
	High school	125,349	-49 (-1,720 to 1,622)	0.0 (-1.4 to 1.3)
	≥College	76,452	-3,829 (-6,856 to -889)	-4.8 (-8.2 to -1.1)
Marital status	Single	46,593	2,023 (907 to 2,997)	4.5 (2.0 to 6.9)
	Married	260,842	3,606 (947 to 6,503)	1.4 (0.4 to 2.6)
	Others (divorced/widowed)	270,691	3,876 (-1,631 to 8,864)	1.5 (-0.6 to 3.4)
Causes	Endocrine diseases	19,101	2,550 (620 to 4,145)	15.4 (3.4 to 27.7)
	Circulatory diseases	115,690	1,378 (-2,461 to 5,025)	1.2 (-2.1 to 4.5)

Respiratory diseases	66,641	-12,912 (-17,530 to -8,961)	-16.2 (-20.8 to -11.9)
Ill-defined causes	65,374	10,021 (6,682 to 13,006)	18.1 (11.4 to 24.8)

Note: The total pandemic period was from February 18, 2020 to December 31, 2021. The period of 2020 was from February 18, 2020 to December 31, 2020. The period of 2021 was from January 1, 2021 to December 31, 2021. Abbreviations: Endocrine diseases=Endocrine, nutritional and metabolic diseases, Circulatory diseases=Diseases of circulatory system, Respiratory diseases=Diseases of respiratory system, Ill-defined causes=Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified.

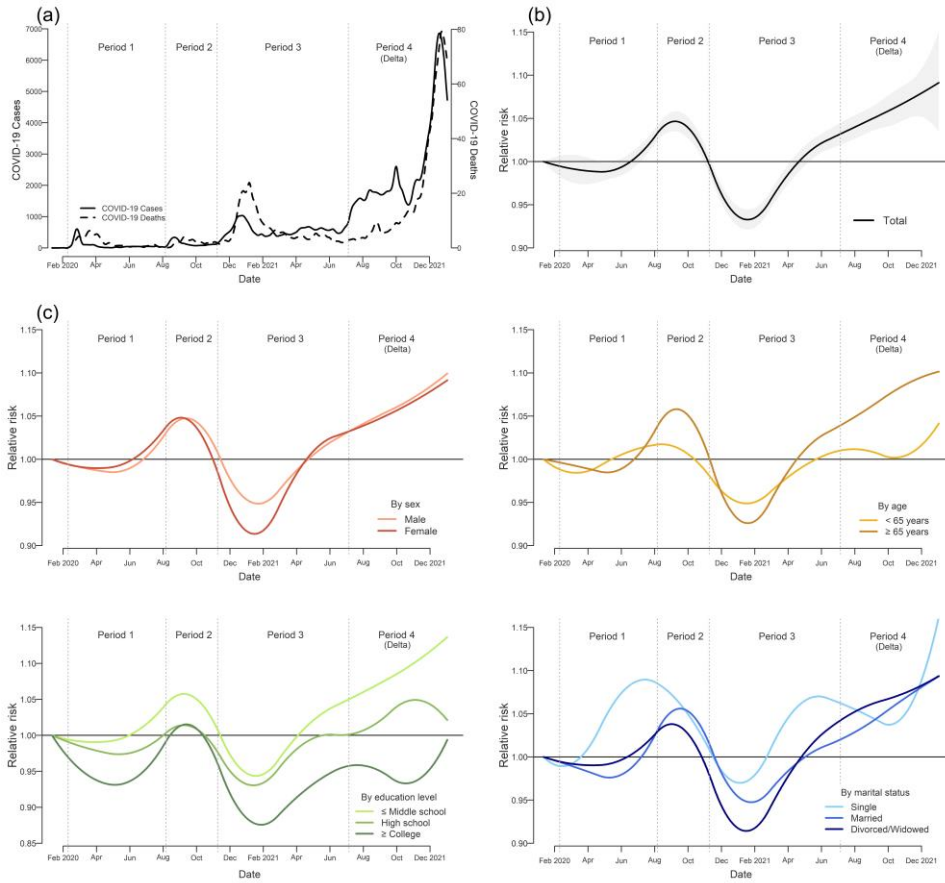


Fig. 1 Temporal trend in COVID-19 confirmed cases and deaths (a), excess risk (relative risk, RR) with a band corresponding to the 95% eCI (b), and excess risk by sex, age, education level, and marital status (c) during the pandemic period (February 18, 2020–December 31, 2021) in Korea.

3.3. Excess mortality by place of death

Excess deaths during the pandemic differed by the place of death (Table 2, Fig. 2) and were more evident in out-of-hospital deaths than in in-hospital deaths. Excess in-hospital mortality showed a decrease of 2.5% (95% eCI: 1.8–3.2%); however, an increase in out-of-hospital mortality was more prominent with 16.1% excess (95% eCI: 15.2–16.8%). In addition, the excess out-of-hospital deaths consistently increased throughout the entire study period, whereas excess in-hospital deaths was positive only in the Delta sub-period. This pattern associated with the place of death was more pronounced in people aged 65 or older, people without high school education, and divorced/widowed people, compared to the total population. In addition, the excess out-of-hospital mortality was more evident in deaths from endocrine diseases and ill-defined causes during the total pandemic period, especially in 2021 (see Supplementary Table S2 and S3).

Table 2 Number of total deaths, estimated excess deaths, and percentage excess in mortality (with 95% empirical confidence intervals) during the COVID-19 pandemic (February 18, 2020 to December 31, 2021) in Korea by place of death.

		In-hospital deaths			Out-of-hospital deaths		
		Total deaths	Excess deaths	Percentage excess	Total deaths	Excess deaths	Percentage excess
Total		434,563	-11,312 (-14,460 to -8,018)	-2.5 (-3.2 to -1.8)	144,474	20,045 (19,081 to 20,819)	16.1 (15.2 to 16.8)
Period	2020	197,011	-6,123 (-8,457 to -3,618)	-3.0 (-4.1 to -1.8)	64,371	6,857 (4,960 to 8,867)	11.9 (8.3 to 16.0)
	2021	237,552	-5,189 (-7,530 to -2,600)	-2.1 (-3.1 to -1.1)	80,103	13,189 (11,715 to 14,644)	19.7 (17.1 to 22.4)
	Period 1 (2020.2.18–2020.8.11)	107,120	-3,321 (-5,006 to -1,556)	-3.0 (-4.5 to -1.4)	34,272	2,836 (1,654 to 4,012)	9.0 (5.1 to 13.3)
	Period 2 (2020.8.12–2020.11.12)	58,700	-27 (-602 to 525)	0.0 (-1.0 to 0.9)	19,234	2,724 (2,117 to 3,350)	16.5 (12.4 to 21.1)
	Period 3 (2020.11.13–2021.7.6)	148,016	-11,282 (-13,299 to -9,115)	-7.1 (-8.2 to -5.8)	51,483	6,947 (6,132 to 7,779)	15.6 (13.5 to 17.8)
	Period 4 (2021.7.7–2021.12.31) (Delta period)	120,727	3,319 (1,680 to 4,930)	2.8 (1.4 to 4.3)	39,485	7,539 (6,578 to 8,485)	23.6 (20 to 27.4)
Sex	Males	233,271	-4,215 (-9,070 to 584)	-1.8 (-3.7 to 0.3)	80,741	9,613 (7,284 to 11,857)	13.5 (9.9 to 17.2)
	Females	201,292	-7,073 (-10,941 to -3,382)	-3.4 (-5.2 to -1.7)	63,733	10,452 (8,608 to 12,253)	19.6 (15.6 to 23.8)
Age	<65	83,515	-810 (-2,666 to 948)	-1.0 (-3.1 to 1.1)	41,014	458 (-1,098 to 1,759)	1.1 (-2.6 to 4.5)
	≥65	351,048	-11,365 (-16,828 to -6,157)	-3.1 (-4.6 to -1.7)	103,460	19,579 (16,836 to 22,141)	23.3 (19.4 to 27.2)
Education level	≤Middle school	261,542	-4,617 (-12,197 to 1,731)	-1.7 (-4.5 to 0.7)	81,734	15,045 (11,972 to 17,789)	22.6 (17.2 to 27.8)
	High school	92,390	-2,498 (-3,772 to -1,276)	-2.6 (-3.9 to -1.4)	32,959	2,392 (567 to 4,178)	7.8 (1.8 to 14.5)
	≥College	56,324	-4,559 (-5,919 to -3,294)	-7.5 (-9.5 to -5.5)	20,128	695 (-290 to 1,525)	3.6 (-1.4 to 8.2)
Marital status	Single	27,846	981 (-80 to 1,911)	3.7 (-0.3 to 7.4)	18,747	1,044 (-596 to 2,420)	5.9 (-3.1 to 14.8)
	Married	204,166	-5,668 (-8,753 to -2,765)	-2.7 (-4.1 to -1.3)	56,676	8,780 (7,933 to 9,584)	18.3 (16.3 to 20.4)

Others (divorced/widowed)	201,927	-6,536 (-9,340 to -3,587)	-3.1 (-4.4 to -1.7)	68,764	10,052 (7,390 to 12,391)	17.1 (12.0 to 22.0)
---------------------------	---------	---------------------------	---------------------	--------	--------------------------	---------------------

Note: The total pandemic period was from February 18, 2020 to December 31, 2021. The period of 2020 was from February 18, 2020 to December 31, 2020. The period of 2021 was from January 1, 2021 to December 31, 2021.

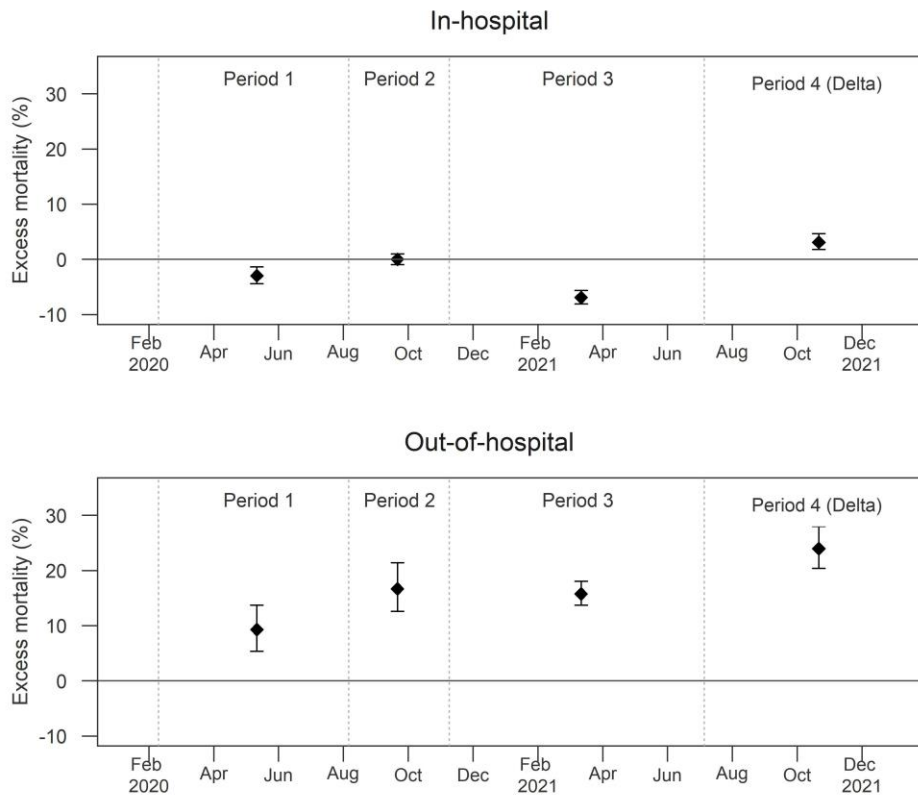


Fig. 2 Percentage excess in mortality with 95% eCI by place of death across the COVID-19 periods in Korea.

3.4. Excess mortality by region

The spatial distribution of excess deaths has changed over the pandemic periods (Fig. 3). In general, metropolitan areas (i.e. areas with high population density) showed greater excess deaths, except for the early sub-period (Period 1), and in particular, substantial increases in mortality were observed nationally during the Delta period, with a marked increase in metropolitan areas.

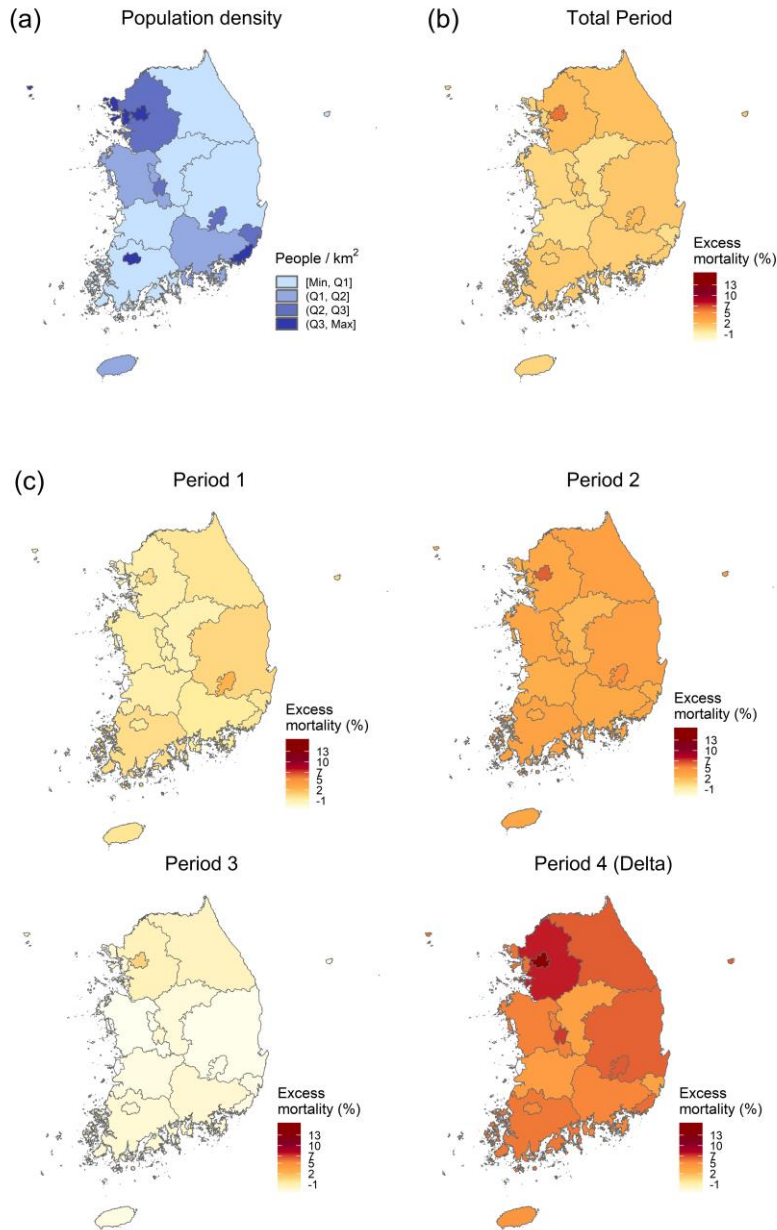


Fig. 3 Maps of population density (a), percentage excess in mortality during the total pandemic period (b), and percentage excess in mortality stratified by COVID-19 pandemic periods (c) in Korea.

Population density (people per km²) is based on 2021. The total pandemic period was from February 18, 2020, to December 31, 2021. The four sub-periods were defined as period 1 (February 18, 2020–August 11, 2020), period 2 (August 12, 2020–November 12, 2020), period 3 (November 13, 2020–July 6, 2021), and period 4 (July 7, 2021–December 31, 2021).

3.5. Sensitivity analysis

Sensitivity analyses were performed to assess whether these findings were generally consistent with the modelling specifications; the sensitivity results showed the robustness of main results (see Supplementary Table S4 and S5).

Chapter 4. Discussion

This study examined the long-term excess mortality due to the COVID-19 pandemic in Korea from February 18, 2020 to December 31, 2021, which is the second pandemic year. There was no noticeable change in mortality in 2020; however, prominent excess was observed in 2021, especially in the Delta variant period. Throughout the study period, compared to the total population, the excess deaths were more pronounced in the elderly (people aged 65 or older), people without high school education, and single populations, who could be interpreted as vulnerable populations, and in deaths from endocrine diseases and ill-defined diseases. In addition, out-of-hospital deaths were persistently elevated throughout the pandemic periods, while in-hospital deaths did not show the consistently increasing pattern.

Excess mortality attributable to COVID-19 has been reported in many countries during the pandemic period in 2020–2021 (Karlinsky & Kobak, 2021; Levitt et al., 2022). Previous studies have investigated excess mortality during the pandemic in Korea and reported up to 7,529 excess deaths in 2020–2021 (Levitt et al., 2022; Wang et al., 2022). However, although the trajectory of the pandemic in Korea differed from that in most other countries (Yeoh et al., 2021), they did not consider the variations across the periods. In addition, the differential risks of COVID-19-related deaths have been less examined within the long-term period. Therefore, the author believes that this study, which captured the temporal trends of the pandemic period with socioeconomic patterns, can provide more comprehensive information about the impact of COVID-19 on mortality.

This study investigated that the impact of COVID-19 on mortality varied across the pandemic periods. Early in the pandemic, Korea's pandemic management strategies were identified to be effective (Lee et al., 2020). Likewise, no prominent change in deaths was found in 2020 in Korea, which is consistent with previous studies (Oh et al., 2022; Shin et al., 2021). Meanwhile, the mortality was estimated to have decreased during the third sub-period (November 13, 2020–July 6, 2021). It reflects the fact that the trend in total deaths during the period was lower than in the previous period (Supplementary Fig. S1). This displacement in excess mortality may be related to the onset of vaccination against COVID-19, which was prioritized for vulnerable subgroups from January 2021 (Kwon & Oh, 2022). Also, the Korean government continued its efforts to maintain a stable number of hospital beds for COVID-19 patient treatment during the third sub-period (Ministry of Health and Welfare, 2021) and began to prepare a shift toward more sustainable COVID-19 response strategies to ensure the coexistence with COVID-19 rather than strict containment strategies (Ministry of Culture, Sports and Tourism, 2020). Thus, the author cautiously speculates that during the third sub-period, the impact of the pandemic was generally controllable and the collateral damage of COVID-19 to public health and society could be mitigated, resulting in a reduction in overall mortality.

As the pandemic went on for more than a year and a half, many countries decided to adopt a “living with COVID-19” policy (Smith-Spark, 2021), and the Korean government implemented the COVID-19 response system with a gradual return to normal from November 2021. However, as the Delta variant became dominant, the scale of the outbreak increased significantly and spread nationwide,

followed by a surge of COVID-19 cases and deaths. This study also investigated pronounced excess mortality across Korea in this fourth sub-period (July 7, 2021–December 31, 2021). These increases in direct and indirect deaths from COVID-19 could be partly explained by the overload of healthcare systems in Korea related to the spread of the Delta variant. The high fatality rate of Delta variation and the rapid increase in COVID-19 patients triggered a shortage of critical care beds (Ministry of Health and Welfare, 2021), and concerns were raised that medical resources were rapidly depleting in the densely populated capital city and nearby metropolitan areas (Ministry of Health and Welfare, 2021).

This study found that the impact of the pandemic on mortality was heterogeneous in accordance with sex, age group, education level, and marital status, and this disparity was evident in the Delta variant period. First, an increase in mortality was observed in males, but not in females. This result supports existing literature that reported higher COVID-19-related mortality among males compared to females (Nielsen et al., 2021). Also, this study found that an increase in mortality was pronounced in those aged 65 years or older. It was widely reported that mortality due to COVID-19 was much higher in older adults, and older adults who have certain comorbidities may have a greater risk of infection and worse health outcomes (Shahid et al., 2020). Although a previous study on early pandemic excess mortality in Korea reported a noticeably decreased mortality in older adults in 2020 (Kim et al., 2022), this study, which extended the study period to 2021, identified increased mortality among older adults, particularly in Delta period. This result may imply that the risk of the infection itself and the delayed medical services during the Delta period may have affected the elderly more seriously than

general population.

One of main findings in this study was that excess deaths due to the pandemic were more prominent in those with low educational levels and single populations. Previous studies have reported that people with low education level (i.e., a proxy for low socioeconomic status) generally have worse health outcomes (Ross & Wu, 1995), and they were more likely to experience delays in medical visits for chronic diseases during the pandemic as compared with highly educated people (Kang et al., 2022). Single people are also likely to have worse health status than married people, although there is no consensus on whether marriage has a protective effect against adverse health outcomes (Drefahl, 2012). During the pandemic, they might face more threats to health including reduced necessary care, financial insecurity, and disrupted social relationships (Hearne, 2022). Moreover, these results highlight a probable ‘syndemic’, describing the coexistence of multiple health problems that significantly affect the overall health status of a population within the context of social conditions, in relation to COVID-19 (Horton, 2020; McGowan & Bambra, 2022). Social deprivation might result in multiple, interacting, and additive adverse risk factors for COVID-19-related mortality (McGowan & Bambra, 2022).

This study also found that those who died out of hospital increased persistently throughout the pandemic period, and its sociodemographic pattern was generally consistent with that found in overall deaths (i.e., a higher excess mortality in those aged 65 year or older and those without high school education). Interestingly, this increase in out-of-hospital deaths was prominent in deaths from endocrine diseases and ill-defined causes. Although further investigation is needed, this result implicates the possibility that the pandemic can negatively affect

consistent care for patients with chronic endocrine diseases and reduce healthcare utilization among older adults at the end of life, which may have resulted in reporting of less well-defined causes of death on the death certificate. In particular, the large number of out-of-hospital deaths in 2021 and the Delta variant period implies that limited access to critical care may have contributed to this rise. Therefore, the author carefully surmises that the increased number of out-of-hospital deaths may have been related to the collateral effects of COVID-19 on healthcare utilization and access.

Some limitations of the study should be acknowledged. First, this study could not take into account information concerning seasonal influenza activity and other potential confounders, which can affect the relationship between COVID-19 and mortality, due to data unavailability. More specifically, the temporal trend of influenza changed prominently during COVID-19 (see Supplementary Fig. S2); however, because the influenza activity data was aggregated weekly and for the whole nation, it was not included in this study. Future studies should consider how the influenza activity can be controlled in the model. Second, the methodology of this study is limited to draw causal inference due to the observational nature of the study design. Thus, further study should be conducted with more elaborate data and robust methods for counterfactual analysis. Finally, even though the robustness of findings were observed using various modelling specifications, it should be noted that estimated of excess mortality may vary by different methodologies. Despite these drawbacks, a notable strength of this study is that it was conducted within longer observations of the pandemic period in 2020–2021, which can update the evaluation of excess mortality for a longer period. In addition, the analysis is

stratified by pandemic period and individual characteristics, thus offering a comprehensive information on the impact of the COVID-19 on mortality in Korea.

Chapter 5. Conclusion

In conclusion, the results of this study revealed excess mortality in Korea during the COVID-19 pandemic period 2020–2021 and its differentials by sub-periods and individual characteristics. This study provides epidemiological evidence for public health interventions to address disproportionate access to medical care in association with socioeconomic status and pandemic periods in the era living with COVID-19.

Bibliography

- Bambra, C., Riordan, R., Ford, J., & Matthews, F. (2020). The COVID-19 pandemic and health inequalities. *J Epidemiol Community Health*, *74*(11), 964-968.
- Drefahl, S. (2012). Do the married really live longer? The role of cohabitation and socioeconomic status. *Journal of marriage and family*, *74*(3), 462-475.
- Gasparrini, A. (2014). Modeling exposure–lag–response associations with distributed lag non-linear models. *Statistics in Medicine*, *33*(5), 881-899.
- Gasparrini, A., Armstrong, B., & Kenward, M. G. (2012). Multivariate meta-analysis for non-linear and other multi-parameter associations. *Statistics in Medicine*, *31*(29), 3821-3839.
- Gasparrini, A., Guo, Y., Hashizume, M., Lavigne, E., Zanobetti, A., Schwartz, J., Tobias, A., Tong, S., Rocklöv, J., & Forsberg, B. (2015). Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *The Lancet*, *386*(9991), 369-375.
- Hale, T., Angrist, N., Goldszmidt, R., Kira, B., Petherick, A., Phillips, T., Webster, S., Cameron-Blake, E., Hallas, L., Majumdar, S., & Tatlow, H. (2021). A global panel database of pandemic policies (Oxford COVID-19 Government Response Tracker). *Nature Human Behaviour*, *5*(4), 529-538.
- Hearne, B. N. (2022). Psychological distress across intersections of race/ethnicity, gender, and marital status during the COVID-19 pandemic. *Ethnicity & Health*, *27*(8), 1932-1951.
- Horton, R. (2020). Offline: COVID-19 is not a pandemic. *The Lancet*, *396*(10255), 874.
- Kang, E., Yun, J., Hwang, S.-H., Lee, H., & Lee, J. Y. (2022). The impact of the COVID-19 pandemic in the healthcare utilization in Korea: Analysis of a nationwide survey. *Journal of Infection and Public Health*, *15*(8), 915-921.
- Karlinsky, A., & Kobak, D. (2021). Tracking excess mortality across countries during the COVID-19 pandemic with the World Mortality Dataset. *Elife*, *10*, e69336.
- Kim, A. (2021, December 23). *Hospital overload: Korea orders 210 COVID-19 patients to leave ICUs.* The Korea Herald. <https://www.koreaherald.com/view.php?ud=20211223000654>
- Kim, J.-H., Kim, S., Park, E., & Kim, C.-y. (2022). Inequitable distribution of excess mortality during the COVID-19 pandemic in Korea, 2020. *Epidemiology and health*, *44*, e2022081.
- Kontopantelis, E., Mamas, M. A., Webb, R. T., Castro, A., Rutter, M. K., Gale, C. P., Ashcroft, D. M., Pierce, M., Abel, K. M., & Price, G. (2022). Excess years of life lost to COVID-19 and other causes of death by sex, neighbourhood deprivation, and region in England and Wales during 2020: A registry-based study. *PLoS Medicine*, *19*(2), e1003904.
- Kwon, S. L., & Oh, J. (2022). COVID-19 vaccination program in South Korea: a long journey toward a new normal. *Health policy and technology*, *11*(2), 100601.
- Lee, M., & You, M. (2021). Avoidance of healthcare utilization in South Korea during the coronavirus disease 2019 (COVID-19) pandemic. *International Journal of Environmental Research and Public Health*, *18*(8), 4363.

- Lee, W., Hwang, S.-S., Song, I., Park, C., Kim, H., Song, I.-K., Choi, H. M., Prifti, K., Kwon, Y., Kim, J., Oh, S., Yang, J., Cha, M., Kim, Y., Bell, M. L., & Kim, H. (2020). COVID-19 in South Korea: epidemiological and spatiotemporal patterns of the spread and the role of aggressive diagnostic tests in the early phase. *International journal of epidemiology*, 49(4), 1106-1116.
- Levitt, M., Zonta, F., & Ioannidis, J. P. (2022). Comparison of pandemic excess mortality in 2020–2021 across different empirical calculations. *Environmental Research*, 213, 113754.
- McGowan, V. J., & Bambra, C. (2022). COVID-19 mortality and deprivation: pandemic, syndemic, and endemic health inequalities. *The Lancet Public Health*, 7(11), e966-e975.
- Ministry of Culture, Sports and Tourism. (2020, November 1). [Press Release] COVID-19 Central Disaster and Safety Countermeasure Headquarters (11.1). <https://www.korea.kr/briefing/pressReleaseView.do?newsId=156418593#pressRelease>
- Ministry of Health and Welfare. (2021, April 28). *Social Gatherings Banned at Entertainment Facilities in Greater Seoul and Other Level 2 Regions*. http://mohw.go.kr/eng/nw/nw0101vw.jsp?PAR_MENU_ID=1007&MENU_ID=100701&page=1&CONT_SEQ=365458
- Ministry of Health and Welfare. (2021, November 29). *Roadmap for Gradual Recovery to a New Normal*. https://www.mohw.go.kr/eng/nw/nw0101vw.jsp?PAR_MENU_ID=1007&MENU_ID=100701&page=1&CONT_SEQ=368629&SEARCHKEY=TITLE&SEARCHVALUE=gradual
- Ministry of Health and Welfare. (2021, December 9). *Measures to eliminate waiting for hospital beds in the metropolitan area (11.24)*. https://www.mohw.go.kr/eng/nw/nw0101vw.jsp?PAR_MENU_ID=1007&MENU_ID=100701&page=9&CONT_SEQ=368837
- Ministry of Health and Welfare. (2021, December 27). *Plans for securing and operating additional hospital beds to speed up crisis recovery (12.22)*. https://www.mohw.go.kr/eng/nw/nw0101vw.jsp?PAR_MENU_ID=1007&MENU_ID=100701&page=9&CONT_SEQ=369110
- Moynihan, R., Sanders, S., Michaleff, Z. A., Scott, A. M., Clark, J., To, E. J., Jones, M., Kitchener, E., Fox, M., & Johansson, M. (2021). Impact of COVID-19 pandemic on utilisation of healthcare services: a systematic review. *BMJ open*, 11(3), e045343.
- Msemburi, W., Karlinsky, A., Knutson, V., Aleshin-Guendel, S., Chatterji, S., & Wakefield, J. (2023). The WHO estimates of excess mortality associated with the COVID-19 pandemic. *Nature*, 613(7942), 130-137.
- Nielsen, J., Nørgaard, S. K., Lanzieri, G., Vestergaard, L. S., & Moelbak, K. (2021). Sex-differences in COVID-19 associated excess mortality is not exceptional for the COVID-19 pandemic. *Scientific reports*, 11(1), 20815.
- Oh, J., Min, J., Kang, C., Kim, E., Lee, J. P., Kim, H., & Lee, W. (2022). Excess mortality and the COVID-19 pandemic: causes of death and social inequalities. *BMC public health*, 22(1), 2293.
- Patel, J. A., Nielsen, F., Badiani, A. A., Assi, S., Unadkat, V., Patel, B., Ravindrane, R., &

- Wardle, H. (2020). Poverty, inequality and COVID-19: the forgotten vulnerable. *Public health, 183*, 110.
- Ross, C. E., & Wu, C.-I. (1995). The links between education and health. *American sociological review, 719-745*.
- Ryu, S., Han, C., Kim, D., Tsang, T. K., Cowling, B. J., & Lee, S. (2022). Association between the Relaxation of Public Health and Social Measures and Transmission of the SARS-CoV-2 Omicron Variant in South Korea. *JAMA network open, 5(8)*, e2225665-e2225665.
- Scortichini, M., Schneider dos Santos, R., De'Donato, F., De Sario, M., Michelozzi, P., Davoli, M., Masselot, P., Sera, F., & Gasparrini, A. (2020). Excess mortality during the COVID-19 outbreak in Italy: a two-stage interrupted time-series analysis. *International journal of epidemiology, 49(6)*, 1909-1917.
- Sera, F., Armstrong, B., Blangiardo, M., & Gasparrini, A. (2019). An extended mixed-effects framework for meta-analysis. *Statistics in Medicine, 38(29)*, 5429-5444.
- Shahid, Z., Kalayanamitra, R., McClafferty, B., Kepko, D., Ramgobin, D., Patel, R., Aggarwal, C. S., Vunnam, R., Sahu, N., & Bhatt, D. (2020). COVID-19 and older adults: what we know. *Journal of the American Geriatrics Society, 68(5)*, 926-929.
- Shin, M. S., Sim, B., Jang, W. M., & Lee, J. Y. (2021). Estimation of excess all-cause mortality during COVID-19 pandemic in Korea. *Journal of Korean medical science, 36(39)*.
- Smith-Spark, L. (2021, September 16). *Here are 5 countries that are opening up and living with Covid*. CNN. <https://edition.cnn.com/2021/09/16/world/covid-countries-opening-up-cmd-intl/index.html>
- Wang, H., Paulson, K. R., Pease, S. A., Watson, S., Comfort, H., Zheng, P., Aravkin, A. Y., Bisignano, C., Barber, R. M., & Alam, T. (2022). Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020–21. *The Lancet, 399(10334)*, 1513-1536.
- WHO. (2022). *Global excess deaths associated with COVID-19, January 2020 - December 2021*. <https://www.who.int/data/stories/global-excess-deaths-associated-with-covid-19-january-2020-december-2021>
- Yang, S.-C., Jang, J.-H., Park, S.-Y., Ahn, S.-H., Kim, S.-S., Park, S.-B., Ryu, B.-Y., Lee, S.-Y., Shin, E.-J., & Kim, N.-Y. (2022). COVID-19 outbreak report from January 20, 2020 to January 19, 2022 in the Republic of Korea. *Public Health Weekly Report, 15(13)*, 796-805.
- Yeoh, E. K., Chong, K. C., Chiew, C. J., Lee, V. J., Ng, C. W., Hashimoto, H., Kwon, S., Wang, W., Chau, N. N. S., & Yam, C. H. K. (2021). Assessing the impact of non-pharmaceutical interventions on the transmissibility and severity of COVID-19 during the first five months in the Western Pacific Region. *One Health, 12*, 100213.

Supplementary materials

Supplementary Table S1. The Quasi-Akaike Information Criterion (QAIC) for the main model and each sensitivity analysis.

Region	The number of knots in the quadratic B-spline function for days from the first COVID-19 confirmed case			
	Main	4	5	7
Korea	26176.1	26235.0	26270.8	26222.0
Seoul	19685.43	19699.5	19696.66	19693.81
Busan	17786.9	17787.13	17793.98	17786.24
Daegu	16679.02	16699.31	16700.77	16670.73
Incheon	16652.81	16648.17	16650.65	16653.82
Gwangju	14918.47	14916.94	14919.18	14922.5
Daejeon	14987.5	14991.03	14990.19	14988.91
Ulsan	13915.49	13912.65	13915.09	13918.73
Gyeonggi	20488.47	20492.7	20491.29	20495.93
Gangwon	16165.76	16167.25	16170.91	16172.18
Chungbuk	15910.17	15907.51	15910.72	15913.55
Chungnam	17063.87	17063.88	17071.41	17065.52
Jeonbuk	16714.33	16715.68	16725.47	16722.26
Jeonnam	17119.03	17119.59	17119.63	17122.2
Gyungbuk	17931.97	17942.6	17942.35	17939.23
Gyungnam	17927.88	17922.83	17931.06	17926.93
Jeju	13003.49	13009.23	13013.09	13009.74

Supplementary Table S2. Number of total deaths, estimated excess deaths, and percentage excess in mortality (with 95% empirical confidence intervals) during the COVID-19 pandemic (February 18, 2020, to December 31, 2021) in Korea by place of death for each cause.

	Total deaths	Excess deaths	Percentage excess
In-hospital	434,563	-11,312 (-14,460 to -8,018)	-2.5 (-3.2 to -1.8)
Endocrine diseases	13,540	1,288 (-157 to 2,637)	10.5 (-1.1 to 24.2)
Circulatory diseases	87,578	-2,419 (-6,130 to 1,188)	-2.7 (-6.5 to 1.4)
Respiratory diseases	60,769	-13,014 (-17,451 to -9,109)	-17.6 (-22.3 to -13)
Ill-defined causes	20,471	2,204 (-528 to 4,692)	12.1 (-2.5 to 29.7)
Out-hospital	144,474	20,045 (19,081 to 20,819)	16.1 (15.2 to 16.8)
Endocrine diseases	5,561	1,269 (482 to 1,840)	29.6 (9.5 to 49.5)
Circulatory diseases	28,112	3,657 (1,429 to 5,522)	15.0 (5.4 to 24.4)
Respiratory diseases	5,872	-203 (-809 to 325)	-3.3 (-12.1 to 5.9)
Ill-defined causes	44,903	7,153 (4,172 to 9,644)	18.9 (10.2 to 27.4)

Abbreviations: Endocrine diseases=Endocrine, nutritional and metabolic diseases, Circulatory diseases=Diseases of circulatory system, Respiratory diseases=Diseases of respiratory system, Ill-defined causes=Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified.

Supplementary Table S3. Number of total deaths, estimated excess deaths, and percentage excess in mortality (with 95% empirical confidence intervals) during the year 2020 (February 18, 2020, to December 31, 2020) and the year 2021 (January 1, 2021, to December 31, 2020) in Korea by place of death for each cause.

	2020			2021		
	Total deaths	Excess deaths	Percentage excess	Total deaths	Excess deaths	Percentage excess
Total	261,382	981 (-634 to 2,573)	0.4 (-0.2 to 1.0)	317,655	8,500 (3,820 to 13,052)	2.7 (1.2 to 4.3)
Endocrine diseases	8,577	816 (124 to 1,351)	10.5 (1.5 to 18.7)	10,524	1,734 (380 to 2,827)	19.7 (3.7 to 36.7)
Circulatory diseases	53,325	658 (-1,229 to 2,476)	1.2 (-2.3 to 4.9)	62,365	720 (-1,234 to 2,594)	1.2 (-1.9 to 4.3)
Respiratory diseases	29,815	-4,800 (-6,536 to -3,222)	-13.9 (-18 to -9.8)	36,826	-8,113 (-11,213 to -5,514)	-18.1 (-23.3 to -13.0)
Ill-defined causes	27,548	2,707 (1,225 to 4,200)	10.9 (4.7 to 18)	37,826	7,314 (5,025 to 9,565)	24 (15.3 to 33.8)
In-hospital	197,011	-6,123 (-8,457 to -3,618)	-3 (-4.1 to -1.8)	237,552	-5,189 (-7,530 to -2,600)	-2.1 (-3.1 to -1.1)
Endocrine diseases	6,184	424 (-205 to 1,015)	7.4 (-3.2 to 19.6)	7,356	864 (-72 to 1,686)	13.3 (-1.0 to 29.7)
Circulatory diseases	40,490	-915 (-2,980 to 1,105)	-2.2 (-6.9 to 2.8)	47,088	-1,504 (-3,607 to 571)	-3.1 (-7.1 to 1.2)
Respiratory diseases	27,183	-4,788 (-6,442 to -3,258)	-15 (-19.2 to -10.7)	33,586	-8,226 (-11,428 to -5,465)	-19.7 (-25.4 to -14)
Ill-defined causes	8,210	314 (-661 to 1,208)	4 (-7.4 to 17.3)	12,261	1,890 (85 to 3,468)	18.2 (0.7 to 39.4)
Out-hospital	64,371	6,857 (4,960 to 8,867)	11.9 (8.3 to 16)	80,103	13,189 (11,715 to 14,644)	19.7 (17.1 to 22.4)
Endocrine diseases	2,393	399 (71 to 656)	20 (3.1 to 37.7)	3,168	870 (386 to 1,224)	37.9 (13.9 to 63)
Circulatory diseases	12,835	1,527 (344 to 2,614)	13.5 (2.8 to 25.6)	15,277	2,130 (716 to 3,379)	16.2 (4.9 to 28.4)
Respiratory diseases	2,632	-116 (-427 to 141)	-4.2 (-14.0 to 5.7)	3,240	-87 (-507 to 246)	-2.6 (-13.5 to 8.2)
Ill-defined causes	19,338	2,194 (869 to 3,337)	12.8 (4.7 to 20.9)	25,565	4,958 (2,965 to 6,667)	24.1 (13.1 to 35.3)

Note: The total pandemic period was from February 18, 2020 to December 31, 2021. The period of 2020 was from February 18, 2020 to December 31, 2020. The period of 2021 was from January 1, 2021 to December 31, 2021. Abbreviations: Endocrine diseases=Endocrine, nutritional and metabolic diseases, Circulatory diseases=Diseases of circulatory system, Respiratory diseases=Diseases of respiratory system, Ill-defined causes=Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified.

Supplementary Table S4. Percentage excess in mortality (with 95% empirical confidence interval) for the main model and each sensitivity analysis.

		Main	Sensitivity analysis					
			The number of knots in the quadratic B-spline function for days from the first COVID-19 confirmed case		The number of knots in cyclic B-spline function for days of the year		The days of lag period in distributed lag non-linear model	
			4	5	4	6	14	28
Total		1.7 (0.7 to 2.6)	1.5 (0.8 to 2.2)	1.5 (0.1 to 2.9)	1.7 (0.6 to 2.8)	1.7 (0.2 to 3.2)	1.4 (0.8 to 2.1)	1.9 (0.9 to 2.9)
Period	2020	0.4 (-0.2 to 1.0)	0.0 (-0.5 to 0.6)	0.1 (-0.9 to 1.2)	0.4 (-0.5 to 1.2)	0.3 (-0.8 to 1.6)	0.1 (-0.5 to 0.7)	0.6 (-0.1 to 1.4)
	2021	2.7 (1.2 to 4.3)	2.8 (1.5 to 4)	2.6 (0.7 to 4.5)	2.8 (1.2 to 4.5)	2.8 (0.7 to 4.8)	2.5 (1.5 to 3.6)	3.0 (1.4 to 4.6)
	Period 1	-0.3 (-1.2 to 0.7)	-0.1 (-0.9 to 0.8)	-0.1 (-1.4 to 1.2)	-0.3 (-1.3 to 0.8)	-0.3 (-1.8 to 1.2)	-0.6 (-1.6 to 0.4)	0.1 (-1 to 1.1)
	Period 2	3.7 (2.9 to 4.5)	2.2 (1.4 to 3)	1.6 (0.5 to 2.9)	3.6 (2.7 to 4.7)	3.6 (2.1 to 5.4)	3.5 (2.7 to 4.3)	3.9 (2.9 to 4.9)
	Period 3	-2.0 (-3.2 to -0.6)	-1.8 (-3 to -0.7)	-1.8 (-3.3 to -0.3)	-2.0 (-3.3 to -0.5)	-2 (-3.5 to -0.4)	-2.3 (-3.3 to -1.2)	-1.7 (-3 to -0.3)
	Period 4	7.5 (5.7 to 9.4)	7.3 (5.7 to 8.9)	7.4 (4.7 to 10.2)	7.5 (5.5 to 9.9)	7.6 (4.7 to 10.7)	7.4 (6.1 to 8.7)	7.6 (5.6 to 9.7)
Sex	Males	1.9 (0.7 to 3.0)	1.7 (0.4 to 3)	1.7 (0.5 to 3.0)	1.9 (0.7 to 3.2)	1.9 (0.6 to 3.2)	1.6 (0.4 to 2.9)	2.1 (1.0 to 3.3)
	Females	1.4 (-0.7 to 3.7)	1.3 (-0.4 to 2.9)	1.2 (-0.1 to 2.5)	1.4 (-0.7 to 3.9)	1.4 (0.1 to 2.9)	1.2 (-0.7 to 3.2)	1.7 (-0.3 to 3.9)
Age	<65	-0.3 (-2.5 to 1.7)	-0.3 (-2.0 to 1.4)	-0.3 (-2.5 to 1.6)	-0.3 (-2.6 to 1.9)	-0.3 (-2.5 to 1.7)	-0.5 (-2.5 to 1.3)	-0.2 (-2.3 to 1.7)
	≥65	2.1 (0.6 to 3.5)	1.9 (0.7 to 3.1)	1.8 (0.6 to 3.1)	2.1 (0.7 to 3.4)	2.1 (0.7 to 3.4)	1.8 (0.4 to 3.2)	2.4 (1.0 to 3.7)
Education	≤Middle school	3.4 (1.3 to 5.5)	3.2 (1.0 to 5.3)	3.2 (1.2 to 5.0)	3.4 (1.6 to 5.1)	3.4 (2.2 to 4.5)	3.1 (1.1 to 5.1)	3.7 (2.6 to 4.8)
	High school	0.0 (-1.4 to 1.3)	-0.2 (-2.4 to 2.3)	-0.2 (-1.3 to 0.9)	0.0 (-2.1 to 2.2)	0.0 (-1.9 to 2.0)	-0.3 (-2.4 to 1.8)	0.1 (-1.1 to 1.4)
	≥College	-4.8 (-8.2 to -1.1)	-4.9 (-7.2 to -2.6)	-5 (-8.8 to -1.3)	-4.8 (-8.3 to -1)	-4.8 (-8.2 to -1.1)	-5.0 (-8.4 to -1.4)	-4.7 (-7.8 to -1.3)
Marital status	Single	4.5 (2.0 to 6.9)	4.6 (2.6 to 6.3)	4.4 (2.7 to 6.2)	4.5 (1.5 to 7.4)	4.6 (2.1 to 6.9)	4.4 (2.1 to 6.7)	5.0 (2.4 to 7.4)
	Married	1.4 (0.4 to 2.6)	1.2 (-0.1 to 2.6)	1.2 (-0.1 to 2.6)	1.4 (0.3 to 2.6)	1.4 (0.2 to 2.7)	1.2 (-0.1 to 2.7)	1.6 (0.5 to 2.8)
	Others (divorced/widowed)	1.5 (-0.6 to 3.4)	1.3 (-0.7 to 3.3)	1.3 (0.2 to 2.3)	1.4 (-0.4 to 3.1)	1.4 (-0.8 to 3.5)	1.2 (-1.1 to 3.4)	1.7 (-0.2 to 3.6)
Causes	Endocrine diseases	15.4 (3.4 to 27.7)	15.4 (5.9 to 25.1)	15.4 (3.7 to 26.5)	15.4 (3.5 to 27.6)	15.3 (3.1 to 27.5)	14.9 (3.3 to 26.1)	16.1 (3.9 to 28.7)

Circulatory diseases	1.2 (-2.1 to 4.5)	1.1 (-2.2 to 4.7)	1.0 (-3.5 to 5.4)	1.2 (-2.9 to 5.4)	1.2 (-2 to 4.5)	1.0 (-1.6 to 3.7)	1.6 (-2.8 to 6.1)
Respiratory diseases	-16.2 (-20.8 to -11.9)	-16.5 (-20.7 to -12.5)	-16.8 (-21.1 to -12.6)	-16.2 (-20.7 to -11.9)	-16.2 (-20.5 to -11.9)	-16.7 (-21.1 to -12.5)	-15.7 (-19.4 to -12.1)
Ill-defined causes	18.1 (11.4 to 24.8)	17.9 (11 to 25.5)	17.9 (12.7 to 23.5)	18.1 (12.1 to 24.3)	18.1 (12.4 to 23.9)	18.0 (11.6 to 25.1)	18.3 (10.4 to 26.7)

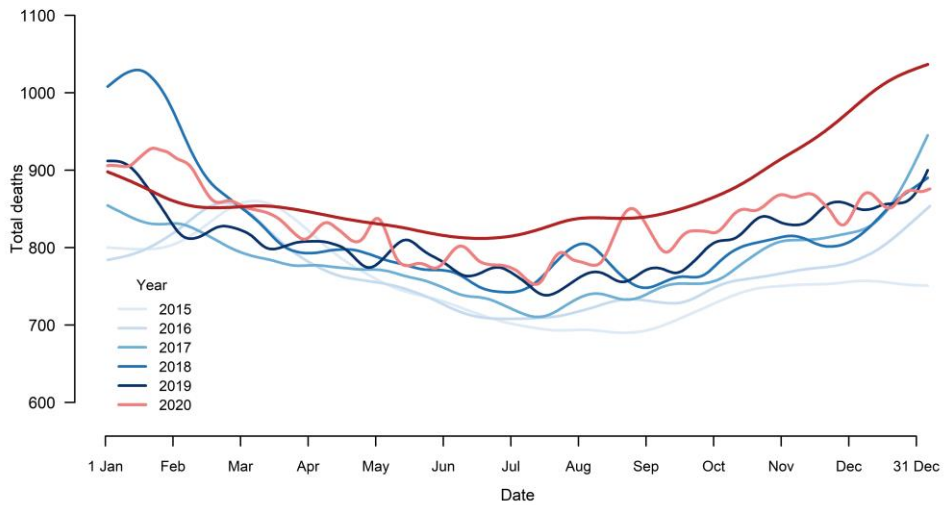
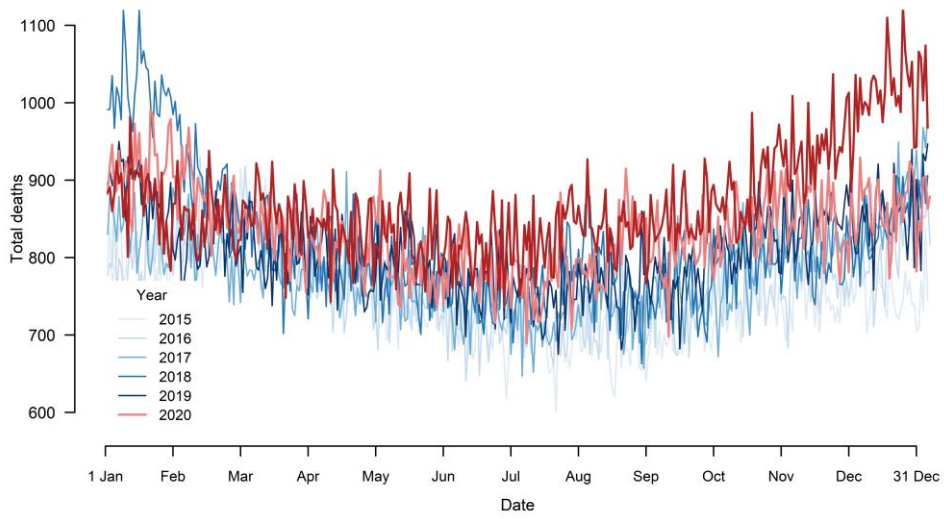
Note: The total pandemic period was from February 18, 2020 to December 31, 2021. The period of 2020 was from February 18, 2020 to December 31, 2020. The period of 2021 was from January 1, 2021 to December 31, 2021. Abbreviations: Endocrine diseases=Endocrine, nutritional and metabolic diseases, Circulatory diseases=Diseases of circulatory system, Respiratory diseases=Diseases of respiratory system, Ill-defined causes=Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified.

Supplementary Table S5. Number of total deaths, estimated excess deaths, and percentage excess in mortality (with 95% empirical confidence interval) for the main model and the model adjusted for NPI.

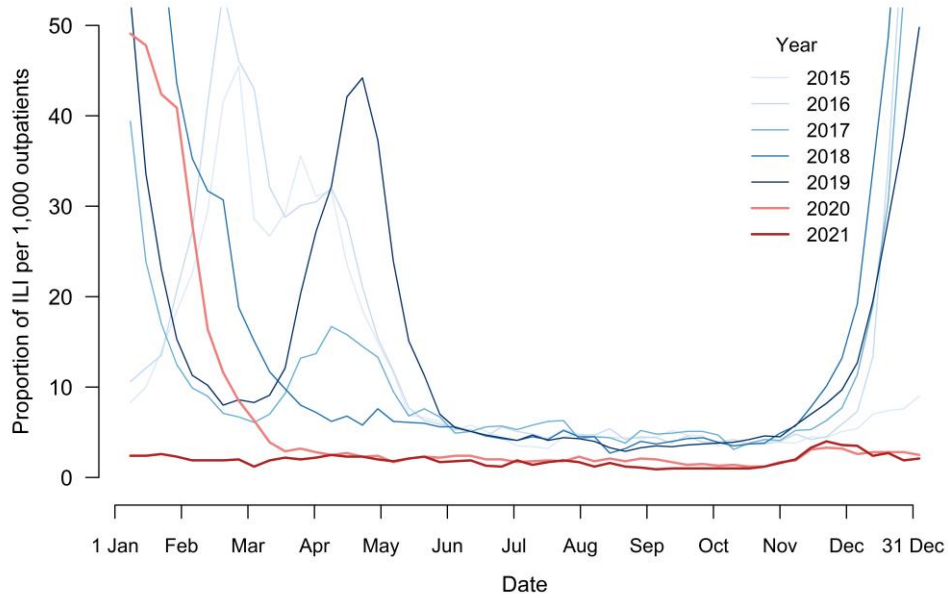
		Total deaths	Main		Adjusted for NPI	
			Excess deaths	Percentage excess	Excess deaths	Percentage excess
Total		579,037	9,481 (4,270 to 14,618)	1.7 (0.7 to 2.6)	9,827 (-9,751 to 27,501)	1.7 (-1.7 to 5.0)
Period	2020	261,382	981 (-634 to 2,573)	0.4 (-0.2 to 1.0)	1,127 (-8,306 to 9,794)	0.4 (-3.1 to 3.9)
	2021	317,655	8,500 (3,820 to 13,052)	2.7 (1.2 to 4.3)	8,700 (-2,348 to 17,941)	2.8 (-0.7 to 6.0)
	Period 1	141,392	-376 (-1,720 to 991)	-0.3 (-1.2 to 0.7)	-303 (-5,940 to 4,789)	-0.2 (-4.0 to 3.5)
	Period 2	77,934	2,766 (2,181 to 3,337)	3.7 (2.9 to 4.5)	2,804 (470 to 5,006)	3.7 (0.6 to 6.9)
	Period 3	199,499	-4,046 (-6,602 to -1,145)	-2.0 (-3.2 to -0.6)	-3,904 (-11,959 to 3,359)	-1.9 (-5.7 to 1.7)
	Period 4	160,212	11,138 (8,573 to 13,767)	7.5 (5.7 to 9.4)	11,230 (6,355 to 16,081)	7.5 (4.1 to 11.2)
Sex	Males	314,012	5,741 (2,231 to 9,232)	1.9 (0.7 to 3.0)	922 (-18,308 to 19,620)	0.3 (-5.5 to 6.7)
	Females	265,025	3,769 (-1,745 to 9,468)	1.4 (-0.7 to 3.7)	8,811 (-8,971 to 26,264)	3.4 (-3.3 to 11)
Age	<65	124,529	-347 (-3,165 to 2,125)	-0.3 (-2.5 to 1.7)	2,247 (-7,606 to 11,460)	1.8 (-5.8 to 10.1)
	≥65	454,508	9,206 (2,587 to 15,582)	2.1 (0.6 to 3.5)	6,537 (-21,312 to 33,941)	1.5 (-4.5 to 8.1)
Education	≤Middle school	343,276	11,174 (4,269 to 17,856)	3.4 (1.3 to 5.5)	12,473 (-9,048 to 33,356)	3.8 (-2.6 to 10.8)
	High school	125,349	-49 (-1,720 to 1,622)	0.0 (-1.4 to 1.3)	-2,370 (-19,324 to 12,488)	-1.9 (-13.4 to 11.1)
	≥College	76,452	-3,829 (-6,856 to -889)	-4.8 (-8.2 to -1.1)	-3,017 (-13,025 to 5,529)	-3.8 (-14.6 to 7.8)
Marital status	Single	46,593	2,023 (907 to 2,997)	4.5 (2.0 to 6.9)	2,772 (-483 to 4,631)	6.3 (-1.0 to 11.0)
	Married	260,842	3,606 (947 to 6,503)	1.4 (0.4 to 2.6)	3,681 (-2,217 to 9,270)	1.4 (-0.8 to 3.7)

	Others (divorced/widowed)	270,691	3,876 (-1,631 to 8,864)	1.5 (-0.6 to 3.4)	3,270 (-22,404 to 27,515)	1.2 (-7.6 to 11.3)
Causes	Endocrine diseases	19,101	2,550 (620 to 4,145)	15.4 (3.4 to 27.7)	2,174 (-1,485 to 4,716)	12.8 (-7.2 to 32.8)
	Circulatory diseases	115,690	1,378 (-2,461 to 5,025)	1.2 (-2.1 to 4.5)	4,227 (-8,447 to 15,393)	3.8 (-6.8 to 15.3)
	Respiratory diseases	66,641	-12,912 (-17,530 to -8,961)	-16.2 (-20.8 to -11.9)	-5,400 (-14,518 to 2,075)	-7.5 (-17.9 to 3.2)
	Ill-defined causes	65,374	10,021 (6,682 to 13,006)	18.1 (11.4 to 24.8)	9,738 (2,024 to 16,718)	17.5 (3.2 to 34.4)

Note: The total pandemic period was from February 18, 2020 to December 31, 2021. The period of 2020 was from February 18, 2020 to December 31, 2020. The period of 2021 was from January 1, 2021 to December 31, 2021. Abbreviations: Endocrine diseases=Endocrine, nutritional and metabolic diseases, Circulatory diseases=Diseases of circulatory system, Respiratory diseases=Diseases of respiratory system, Ill-defined causes=Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified.



Supplementary Fig. S1 Temporal trends of total deaths during the study period (2015–2021)



Supplementary Fig. S2 Temporal trends of proportion of influenza-like illness per 1,000 outpatients during the study period (2015–2021)

국문 초록

한국의 장기화된 코로나19 팬데믹 기간 동안 초과 사망 분석

서울대학교 보건대학원
보건학과 보건학 전공
오 지 은

연구배경: 코로나19는 감염 자체로 인한 위험 뿐만 아니라 의료자원 부족 등 다양한 경로를 통해 인구의 건강에 영향을 미쳤다. 본 연구는 한국에서의 팬데믹 1년차부터 2년차까지의 초과 사망률과 그에 따른 사회경제적 격차를 확인하는 것을 목적으로 한다.

연구방법: 2015년부터 2021년까지 한국의 일일 사망 자료를 한국 통계청에서 수집하였다. 본 연구에서는 2단계 중재 시계열 분석(interrupted time-series analysis)를 통해 2020년부터 2021년까지 각 하위 기간에 대한 초과 사망을 추정하였다. 또한, 개인 특성과 사망 장소에 따른 초과 사망의 패턴을 확인하였다.

연구결과: 2020년 2월 18일부터 2021년 12월 31일까지 9,481명(95% 경험적 신뢰구간: 4,270명-14,618명)의 초과 사망이 발생하였다. 초과 사망의 추정치는 1년차(2020년; 981명)에 비하여 2년차(2021년; 8,500명)에 더 뚜렷하게 나타났으며, 델타 변이 기간(2021.7.7-2021.12.31)에 가장 많은 초과 사망(11,138명)이 발생하였다. 팬데믹 동안 초과 사망은 남성(1.9%), 65세 이상(2.1%), 고등학교 교육을 받지 않은 인구(3.4%), 미혼 인구(4.5%)에서 더욱 크게 나타났다. 또한, 대유행 기간 동안 병원 밖 사망이 일관되게 증가하였다.

결론: 본 연구에서는 2020년부터 2021년까지 코로나19 기간 동안 한국의 초과 사망과 하위기간 및 개인 특성에 따른 차이를 확인하였다. 본 연구의 결과는 팬데믹 기간 동안 사회경제적 격차와 의료 불균형을 해소하기 위한 공중보건 정책의 필요성을 제안하며 자원 배분을 위한 역학적 증거를 제공한다.