Impact of COVID-19 on disease-specific mortality, healthcare resource utilization, and disease burden across a population over 1 billion in 31 countries: an interrupted time-series analysis

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Summary

Background The COVID-19 pandemic disrupted global health and affected chronic disease management. This study quantified the impact of the pandemic on disease-specific measures of health dynamics, such as mortality rates, healthcare resource utilization (HRU), and disease burden.

Methods An interrupted time-series analysis was performed by examining temporal trends across disease categories over two periods: pre-pandemic and pandemic (after January 2020). Monthly mortality data were collected from 31 countries, while monthly HRU and disease burden data were collected from South Korea. We defined primary outcomes as disease-specific mortality rate, number of patients, outpatient visits, days of hospitalization, disease burden, and per capita cost. We used a generalized least squares model with AR (1) residuals and an automated SARIMA model and Benjamini–Hochberg-adjusted q-values were applied for statistical significance ($q < 0.05$).

Findings A significant increase in disease-specific mortality was observed across multiple countries, with circulatory diseases showing the most widespread rise. HRU declined across most disease categories, including reductions in patient numbers, outpatient visits, and hospital stays; however, patient number showed sustained increase in neoplasm and mental disorder. Although changes in total direct medical costs varied by disease, per capita costs initially increased despite a decrease in the number of patients.

Interpretation The pandemic led to increased mortality and disease burden with limited access to healthcare services. Establishing resilient healthcare systems and appropriate public health policies are key to ensure continuity of care during national crises.

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Keywords: COVID-19; Impact; Global health; Healthcare resource utilization; Mortality; Interrupted-time series analysis; Healthcare disruption

Introduction

The rapid global spread of COVID-19 prompted unprecedented public health responses. Governments and health organizations implemented various policies aimed at controlling the virus and mitigating its impact on healthcare systems. These included vaccine and mask mandates, lockdowns, and ensuring hospital vacancy rates, all intended to minimize infection and

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Research in context

Evidence before this study

A search of the PubMed database from its inception to June 17, 2024, was conducted to identify papers published on the impact of COVID-19 on clinical outcomes and healthcare access without language restrictions. The search utilized the following terms: ("impact of COVID-19"[Title] OR "impact of SARS-CoV-2"[Title] OR ("impact"[Title] AND ("COVID-19"[Title] OR "SARS-CoV-2"[Title])) OR (("Change"[Title] OR "pattern"[Title] OR "trend"[Title] OR "influence"[Title]) AND ("COVID-19"[Title] OR "SARS-CoV-2"[Title]))) AND ("mortality"[MeSH Terms] OR "mortality"[Title] OR "death rate"[Title] OR "death"[Title]) AND ("healthcare resource utilization" OR "HRU" OR "healthcare utilization" OR "hospitalization" OR "emergency department visits" OR "economic burden" OR "healthcare costs" OR "cost of illness" OR "healthcare access" OR "access to healthcare" OR "medical accessibility") NOT (opinion[Title] OR editorial[Publication Type] OR letter[Publication Type] OR review[Publication Type]). In total, 199 publications matching our search criteria were identified. Previous studies have explored the impact of COVID-19 on mortality and healthcare access in relation to specific conditions. Of the 106 studies that evaluated the impact of COVID-19 or vaccination, only 24 concurrently examined both healthcare access and mortality in specific non-COVID-19 conditions. None of these studies conducted a long-term, global comparison across multiple diseases. While some research has suggested potential adverse effects of COVID-19 or related policies on healthcare resource utilization (HRU) in comparison with clinical outcomes in non-COVID-19 conditions, these findings were largely based on short-term analyses of specific conditions in localized settings. To address these gaps and arrive at a consolidated and comprehensive conclusion, it is essential to conduct a thorough study assessing HRU, patient burden, and clinical outcomes (e.g., disease-specific mortality) across a range of diseases using long-term (over three years) data from multiple countries.

Added value of this study

To our knowledge, this is the first comprehensive, multi-country quantitative study to evaluate the long-term impact of COVID-19 on disease-specific mortality, HRU and disease burden. By analyzing interrupted time-series data from 31 countries, we identified significant increases in disease-specific mortality, within the circulatory, digestive, and genitourinary systems. These impacts varied by disease and country, underscoring the challenge of universal policy responses. In South Korea, we observed immediate reductions in patient numbers, outpatient visits, and hospital stays across most conditions, with per capita healthcare costs rising despite fewer patients, suggesting possible care delays for more severe cases. These findings highlight the critical need for resilient health systems, capable of maintaining access to essential care during public health emergencies. Our results provide actionable insights for tailoring future pandemic preparedness policies, enhancing surveillance infrastructure, and supporting equitable, disease-specific health strategies.

Implications of all the available evidence

Current evidence indicates a potential correlation between reduced healthcare access and poor clinical outcomes. It demonstrates the quantitative impact of COVID-19 and necessity of public health policies on clinical outcomes and healthcare access for next pandemic. Future public health policies should account for the disease burden and healthcare access of patients, while also considering the broader impact on outcomes for other diseases, particularly during pandemics. As future pandemics are expected to affect patients with chronic diseases, strategic health policies should focus on vulnerable and marginalized patient groups.

COVID-19-related mortality.[1] However, the ethical, financial, and effectiveness concerns surrounding certain interventions have raised questions about their overall suitability.[2] Notably, "medical neglect" arose when policies restricted hospital visits to minimize COVID-19 exposure. These restrictions affected patients requiring regular check-ups, leading to delays in treatment, negative clinical outcomes, and reduced medical access.[3] This underscores the importance of analyzing the broader impact of public health policies on global health outcomes to evaluate their appropriateness and propose better alternatives.

Previous studies have shown that public health policies significantly altered disease dynamics, directly and indirectly impacting on patients' lives. For example, healthcare utilization decreased worldwide.[4] Numerous local studies examined the impact of COVID-19 on mortality and healthcare resource utilization (HRU) across conditions such as cancer, cardiovascular diseases, suicides, traumas or emergencies, tuberculosis, and opioid use disorders.[5–8] Additionally, increased incidence of mental illnesses such as depression and heightened mortality in patients with liver disease have been reported.[9,10] While delayed medical care may have worsened some conditions, patients with COVID-19-like symptoms benefitted from proactive treatment due to symptom overlap with COVID-19. However, studies on the impact of public health policy have primarily focused on short-term, localized effects, thereby limiting their generalizability and providing an incomplete picture of broader, long-term health dynamics.

This study aimed to address these gaps and assess the impact of COVID-19 public health policy on global health dynamics measures, including mortality, healthcare access, and disease burden. Rather than evaluating individual policies across countries, the focus was on examining the broader effects of COVID-19. The specific objectives were: (1) to investigate the impact of COVID-19 on disease-specific mortality across conditions; and (2) to assess the impact of the COVID-19 on healthcare access and disease burden.

Methods

Study design and data sources

Interrupted time series (ITS) analyses were conducted to assess the immediate and long-term impacts of the COVID-19 pandemic on disease-specific mortality, healthcare access, and diseases burden for each disease. Each objective was addressed using a distinct dataset.

For the first objective, we aimed to include mortality data from as many countries as possible to enhance the scope and representativeness of our analysis. Through a comprehensive search, among countries with official statistics, those with publicly accessible and downloadable monthly cause-specific mortality data were prioritized. Initial searches were carried out on the official websites of the Ministry of Health, Bureau of Statistics, or their equivalents in various countries. If no results were obtained from these searches, translated search terms like "cause of death" and "statistics" were used for conducting a more general internet search, including academic documents. The final selection includes countries that not only met criteria for data availability and accessibility but also span diverse geographic regions and income levels, thereby ensuring regional representativeness. As a result, we obtained regional mortality data from the Bureau of Statistics in 31 countries: Australia, Austria, Belgium, Bulgaria, Canada, Croatia, Cyprus, Czechia, Denmark, England, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Japan, Lithuania, Luxembourg, Malta, Republic of Korea, Romania, Scotland, Serbia, Slovakia, Slovenia, Spain, Taiwan and United States. All datasets were transformed into monthly disease-specific mortality counts. To maintain consistency across the country-specific mortality datasets, only data from 2014 onwards were used in the analysis (Supplementary Table S1). Each dataset was standardized into a common format for analysis and comparison, including information such as the month, year, number of deaths, and disease category.

For the second objective, available HRU data was sourced from the official websites of health ministries and national statistics bureaus. Eligibility criteria for disease prevalence and HRU data included: (1) availability on a monthly basis, (2) inclusion of exact patient counts, (3) identification by ICD-10 codes, and (4) coverage of the period from 2019 to 2022. Data were sought from 20 countries; however, only data from Korea met all criteria and was publicly accessible. The Korean HRU data were sourced from an open data portal managed by the Health Insurance Review and Assessment Service (HIRA).[11] HIRA compiles data from reimbursement reviews and assessment under the National Health Insurance Service system, which covers 97.15% of the population (approximately 50 million people in Korea) and provides detailed statistics.[12] Monthly data from January 2010 to January 2023 were collected, including primary and secondary diagnoses for all diseases categorized by the three-character ICD-10 code. The data were categorized by disease type and included the total number of hospital visits, days of hospitalization, and cost incurred in the hospital; the data were further segmented by inpatient and outpatient status.

Outcomes

For the first objective, we defined outcome as the monthly disease-specific mortality rate categorized by cause, including all-cause and external causes across 20 disease groups. For outcomes in the ITS analyses, disease-specific mortality rates per 1000 persons were calculated by dividing the monthly number of deaths by the estimated total population (reported in units of 1000) as of 1 July sourced from the United Nations (Supplementary Table S1). Disease groups were classified into major categories such as infectious disease, neoplasms, and diseases of the circulatory systems, in accordance with the 20 chapter-level classifications of ICD-10, as defined by the World Health Organization (WHO) (Supplementary Table S2).

For the second objective, five categories were defined as healthcare access and disease burden outcomes: number of patients, number of outpatient visits, days of hospitalization, disease burden, and cost per capita. These outcomes were categorized by 18 disease groups to compare healthcare access and disease burden with mortality. The data were derived from monthly aggregate data based on primary or secondary diagnoses from reimbursement claims. The number of patients was defined as the total number of individuals who had at least one outpatient visit or hospitalization. The number of outpatient visits and days of hospitalization were defined as the total number of outpatients claims and the total duration of hospital stay, respectively. The disease burden was defined as the total direct medical cost obtained from national reimbursement claims for each month. Due to data limitations, indirect and non-medical direct costs could not be included in disease burden. Per capita cost was calculated by dividing the total disease-specific direct medical cost by the number of patients in disease category.

For subgroup analyses, we applied more granular disease classifications across all outcomes available. Specifically, disease-specific mortality was analyzed using ICD-10 subchapters, ICD-10-based specific disease categories, and the 113 selected causes of death list in countries where data were available (Supplementary Table S3). For healthcare access and direct medical cost outcomes, subgroup analyses were conducted using 1631 individual three-character ICD-10 codes.

Statistical analysis

ITS analyses were conducted to evaluate the impact of COVID-19 on all outcomes. The ITS models included four variables: a monthly time variable; a COVID-19 dummy variable (0, 1), indicating the period during which the COVID-19 pandemic was active, starting from its onset in January 2020; a time-varying covariate indicating the number of months after the onset of COVID-19 (e.g., COVID-19 margin = 1 in February 2020, 2 in March 2020, etc.); and a categorical month variable to adjust for potential seasonal effects. Separate outcome models were constructed for each cause of death in each country. For disease-specific mortality, the number of time points in the pre-COVID-19 and post-COVID-19 periods varied by country: 12 and 24 months for most European countries (except England and Scotland), 60 and 24 months for Australia and Japan, and 72 and 24 months for the remaining countries (Supplementary Table S1). For healthcare access and disease burden outcomes, 120 months were included in the pre-COVID-19 period and 25 months in the post-COVID-19 period. Preliminary analyses using ordinary least squares detected autocorrelation; hence, generalized least squares (GLS) models with AR1 residual structures were employed. The primary GLS model with AR1 residuals is specified by the following equation:

$$Y_t = \beta_0 + \beta_1 * Time_t + \beta_2 * COVID\text{-}19_t + \beta_3 * COVID\text{-}19\ margin_t + \beta_4 * month_{categorical} + \epsilon_t$$

$$\epsilon_t = \rho * \epsilon_{\{t-1\}} + \eta_t$$

$$\eta_t \sim N\left(0, \sigma_\eta^2\right)$$

$$COVID\text{-}19_t = \begin{cases} 1 & if\ t \geq 2020/01 \\ 0 & otherwise \end{cases}$$

$$COVID\text{-}19\ margin_t = \begin{cases} Time(t)-1 & if\ t \geq 2020/01 \\ 0 & otherwise \end{cases}$$

When the GLS model failed to meet the stationarity assumption based on the Kwiatkowski–Phillips–Schmidt–Shin (KPSS) test, we additionally applied an automated seasonal autoregressive integrated moving average with exogenous regressors (SARIMAX) model, selected via the corrected Akaike Information Criterion, using the same covariates, incorporating KPSS test results to guide model specification. The automated SARIMAX model is specified by the following equation:

$$SARIMAX(p, d, q)(P, D, Q)s:$$
$$\left(1-\sum_{i=1}^{p}\phi_i L^i\right)\left(1-\sum_{j=1}^{P}\Phi_j L^{jS}\right)\nabla^d \nabla_S^D Y_t =$$
$$\left(1+\sum_{k=1}^{q}\theta_k L^k\right)\left(1+\sum_{l=1}^{Q}\Theta_l L^{lS}\right)\epsilon_t + \sum_{m=1}^{3}\gamma_m X_{mt}$$

$$X_{mt} : Covariates\left(time_t, COVID\text{-}19_t, COVID\text{-}19\ margin_t\right)$$

$$L : Lag\ operator\left(L^k Y_t = Y_{t-k}\right)$$

$$\nabla : Differencing\ operator$$

The same ITS equations and models used in the subgroup analyses were applied to examine diseases using more granular disease classifications.

To assess the impact of the pandemic, we applied Benjamini–Hochberg-adjusted q-values to account for multiple comparisons and control the false discovery rate, with statistical significance defined as $q < 0.05$.[13] The COVID-19 dummy variables captured the immediate impact at the onset of the pandemic (i.e., immediate change), whereas the COVID-19 margin variable represented sustained impact over time (i.e., change in slope).

Python version 3.11.7 (Python Software Foundation, Beaverton, OR, USA) and R version 4.3.3 (R Foundation for Statistical Computing, Vienna, Austria) were used for data acquisition, processing, visualization, and statistical analysis.

Ethics

This study was approved by the Institutional Review Board (IRB) at Kyung Hee University (IRB number: KHSIRB-22-406(EA)). All data used in this study were aggregated and fully de-identified, ensuring that no individual patient could be identified. As such, informed consent was not required. The data were publicly available and accessed online.

Role of the funding source

The funding sources played no role in study design, data collection, analysis, interpretation, or writing of the report.

Results

The dataset included data related to 20 disease groups obtained from 31 countries between 2014 and 2022 (Supplementary Fig. S1). In 2022, Bulgaria reported the highest all-cause mortality rate at 17.0909, while Cyprus reported the lowest rate at 5.5394. Neoplasms and circulatory disease were the leading cause of death in all countries. In contrast, deaths attributed to eye and adnexa diseases, ear diseases, and pregnancy complications were lower than that of deaths due to other causes (Supplementary Fig. S1, Supplementary Tables S4 and S5).

Of the 441 ITS models evaluated across 31 countries and 20 disease categories (Fig. 1 and Supplementary Table S6), 27 countries exhibited statistically significant increases in mortality for at least one disease category (only statistically significant results are presented, ordered by the magnitude of the absolute coefficients (Table 1).

For immediate changes following the onset of COVID-19, significant positive coefficients were observed for various diseases and countries. All-cause mortality increased significantly in the United States and Austria. Mortality due to infectious and parasitic diseases (A00–B99) increased in Slovenia; endocrine, nutritional, and endocrine diseases (E00–E88) in Croatia; mental and behavioral disorders (F01–F99) in Luxembourg; and diseases of the nervous system (G00–G98) in Hungary. Circulatory system mortality (I00–I99) increased in Hungary, Lithuania, and Austria, while digestive diseases (K00–K92) showed significant rises in Bulgaria and United States. Genitourinary diseases (N00–N98) increased in Austria, Romania, and Ireland, and symptoms, signs, and abnormal clinical findings not elsewhere classified (R00–R99) showed immediate increases in Serbia, Bulgaria, Czechia, Australia, Hungary, and Ireland. Finally, mortality from external causes (V01–Y89) rose significantly in Estonia, Lithuania, and Ireland.

When assessing changes in slope, a broad spectrum of significant increases was found across countries and diseases (Table 1). All-cause mortality exhibited a sustained rise in Japan, Taiwan, Republic of Korea, and Australia. Infectious diseases (A00–B99) showed upward trends in Republic of Korea, Slovenia, England, United States, and Japan; neoplasms (C00–D48) in Japan and Australia; and diseases of the blood and immune system (D50–D89) in Austria, Bulgaria, Japan, and United States. Endocrine disorders (E00–E88) trended upward in Republic of Korea, and Japan; mental disorders (F01–F99) in Luxembourg, Croatia, and Slovenia; and nervous system diseases (G00–G98) in Malta, Slovakia, and Republic of Korea. Notably, circulatory diseases (I00–I99) saw widespread increases across 12 countries, including Hungary, Lithuania, Austria, Finland, France, Scotland, England, Japan, Australia, Canada, and Republic of Korea. Respiratory diseases (J00–J98) rose in Malta, Hungary, Slovenia, Czechia, Croatia, Lithuania, and Japan; digestive diseases (K00–K92) in Bulgaria, Italy, France, England, Japan, and Republic of Korea; and skin diseases (L00–L98) in England and United States. Musculoskeletal conditions (M00–M99) increased in Republic of Korea, and United States, while genitourinary diseases (N00–N98) rose in Croatia, Ireland, Romania, Italy, and Japan. Perinatal conditions (P00–P96) and congenital malformations (Q00–Q99) showed increases in the United States, and unexplained symptoms (R00–R99) showed increase in Republic of Korea. Additionally, mortality from external causes (V01–Y89) increased in, Slovenia, Hungary, Italy, and Taiwan.

Significant negative coefficients in immediate change were found in three countries (United States, England, and Japan). In the United States, reductions were found for skin diseases (L00–L98), perinatal conditions (P00–P96) and congenital malformations (Q00–Q99), while England showed declines in infectious diseases (A00–B99). Japan was the only country where significant immediate decreases were noted for all-cause mortality as well as for several specific disease categories, including infectious diseases (A00–B99), metabolic disorders (E00–E88), mental disorders (F01–F99), nervous system diseases (G00–G98), circulatory diseases (I00–I99), musculoskeletal conditions (M00–M99), and perinatal conditions (P00–P96).

Subgroup analyses of mortality were also conducted (Supplementary Table S7). Significant increases in at least one disease-specific mortality category were observed in 29 of the 31 countries, with the exceptions of Greece and Iceland. The most commonly impacted category was circulatory system diseases. Mortality related to ischemic heart disease (I20–I25) showed immediate increases in two countries and significant slope changes in seven countries. Additional increases were observed in other cardiovascular conditions, including other heart diseases (I30–I52), and cerebrovascular disease (I60–I69). Several countries also experienced rising mortality trends for acute myocardial infarction (I20–I22) and hypertensive disease (I11, I13). Beyond cardiovascular causes, positive coefficients were observed for deaths due to dementia (F01, F03, G30), diabetes mellitus (E10–E14), respiratory infections such as pneumonia (J12–J18), chronic liver disease (K73–K74), kidney disease (N00–N07, N17–N19, N25–N27), and various infectious diseases.

HRU data pertaining to 18 groups of diseases were analyzed. Respiratory and endocrine diseases were the most prevalent conditions in 2023. Nervous system diseases were associated with the highest number of outpatient visits and the longest days of hospitalization. Neoplasms, followed by digestive diseases, were associated with the highest healthcare costs (Supplementary Fig. S2).

Of the 90 ITS models evaluated across 18 ICD chapter-based disease categories (Fig. 2 and Supplementary Table S8), a significant immediate

a

Immediate Change – America & Asia-pacific

Cause		America		Asia-Pacific			
		Canada	United States	Japan	Korea	Australia	Taiwan
Total	All-cause	0.01132	0.13008	-0.05502	-0.02000	-0.01533	-0.04569
Certain infectious and parasitic diseases	A00-B99		-0.00647	-0.00125	-0.00790		
Neoplasms	C00-D48	-0.00131	-0.00790	-0.00056	0.00110	-0.00020	-0.00169
Diseases of the blood and blood-forming organs and immune mechanism	D50-D89		-0.00052	-0.00015	-0.00004		
Endocrine, nutritional and metabolic diseases	E00-E88		0.00394	-0.00128	0.00002		
Mental and behavioral disorders	F01-F99		-0.00008	-0.00280	-0.00055		
Diseases of the nervous system	G00-G98		-0.00001	-0.00367	-0.00057		
Diseases of the eye and adnexa	H00-H57			0.00000	0.00000		
Diseases of the ear and mastoid process	H60-H93			0.00001	-0.00001		
Diseases of the circulatory system	I00-I99	-0.00392	-0.01101	-0.01498	-0.00341	-0.00217	-0.01017
Diseases of the respiratory system	J00-J98	-0.01068	-0.01616	-0.00829	-0.00551	-0.00400	-0.00385
Diseases of the digestive system	K00-K92		0.00196	-0.00109	0.00031		
Diseases of the skin and subcutaneous tissue	L00-L98		-0.00091	-0.00019	-0.00016		
Diseases of the musculoskeletal system and connective tissue	M00-M99		-0.00046	-0.00077	-0.00006		
Diseases of the genitourinary system	N00-N98		-0.00199	-0.00019	0.00032		
Pregnancy, childbirth and the puerperium	O00-O99		-0.00010	-0.00001	0.00000		
Conditions originating in the perinatal period	P00-P96		-0.00106	0.00000	-0.00008		
Congenital malformations, deformations and chromosomal abnormalities	Q00-Q99		-0.00072	-0.00015	0.00000		
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	R00-R99		-0.00060		-0.00077		
External causes of morbidity and mortality	V01-Y89	0.00089	0.00256		-0.00107		-0.00007

b

Immediate Change – Europe 1

Cause	Europe												
	Austria	Belgium	Bulgaria	Croatia	Cyprus	Czechia	Denmark	England	Estonia	Finland	France	Greece	Hungary
All-cause	0.19136	0.20956	0.57688	0.34683	0.03355	0.12830	0.01903	0.09080	0.01448	-0.01567	0.08055	0.20907	0.43432
A00-B99	0.00216	-0.00563	0.00221	-0.00137	-0.00246	0.00128	0.00384	-0.00218	0.00011	-0.00027	0.00255	0.00085	0.00140
C00-D48	0.00452	-0.00173	0.01712	0.00734	0.01123	0.00592	0.00529	-0.00285	0.00883	0.00143	0.00689	0.01221	0.01386
D50-D89	0.00027	0.00123	0.00160		0.00245	0.00024	-0.00009	0.00005			-0.00014	0.00031	0.00029
E00-E88	0.00394	0.00325	0.00830	0.03014	0.00063	0.00910	-0.00071	-0.00005	0.00230	0.00053	0.00141	0.00025	0.01456
F01-F99	-0.00006	0.00530	0.00092	0.00453	-0.00651	0.00202	-0.00637	-0.00975	0.00166	-0.00197	-0.00169	0.00277	0.00735
G00-G98	0.00439	0.00049	0.00166	0.00727	0.00241	0.00467	0.00037	-0.00139	0.00282	-0.00072	0.00088	-0.00304	0.00567
H00-H57								0.00000					
H60-H93								-0.00002					
I00-I99	0.04987	0.01158	0.23707	0.07441	0.01272	0.05208	0.00513	-0.01039	0.01693	0.01818	0.00652	0.04156	0.13491
J00-J98	0.01981	0.01253	0.06813	0.01630	0.02017	0.02253	0.02044	-0.03053	0.00367	0.00054	0.01166	0.03390	0.02347
K00-K92	0.00344	-0.00259	0.00749	0.00607	-0.00274	0.00277	-0.00002	0.00037	0.00345	0.00515	0.00234	-0.00171	0.00352
L00-L98	-0.00003	0.00019			-0.00158	0.00076	0.00025	-0.00037			-0.00021		-0.00041
M00-M99	0.00070	0.00096		0.00092		-0.00011	-0.00006	-0.00048	-0.00217	-0.00094	0.00051	0.00126	0.00083
N00-N98	0.00599	0.00422	-0.00161	0.00280	0.00210	0.00262	0.00145	-0.00081	-0.00128	0.00020	-0.00021	0.00760	0.00211
O00-O99								0.00002					
P00-P96	0.00070	-0.00064	-0.00051	-0.00029		-0.00016	-0.00028	0.00001		-0.00016	0.00006	-0.00018	-0.00035
Q00-Q99	0.00078	-0.00035	-0.00022	0.00057		0.00101	0.00007	-0.00032		-0.00100	-0.00014	0.00051	0.00044
R00-R99	0.00354	0.00075	0.02511	0.00225	0.00049	0.02046	0.00676	0.00075	0.00219	-0.00119	-0.00275	0.04054	0.00224
V01-Y89	-0.00049	-0.00239	0.00118	-0.00239	-0.00574	0.00359	-0.00314	-0.00150	0.01489	0.00195	-0.00116	0.00026	0.00283

c

Immediate Change – Europe 2

Cause	Europe											
	Iceland	Ireland	Italy	Lithuania	Luxembourg	Malta	Romania	Scotland	Serbia	Slovakia	Slovenia	Spain
All-cause	-0.06674	-0.04712	0.17029	0.32193	0.07762	0.15254	0.31197	0.02274	0.52366	0.11691	0.26684	0.07610
A00-B99		-0.00117	0.00229	0.00417	-0.00204	0.00221	0.00559		0.00263	-0.00394	0.00550	0.00162
C00-D48	-0.02822	-0.00421	0.01445	0.01694	-0.01910	0.00658	0.01840	-0.00164	0.00650	0.02564	0.00133	0.01150
D50-D89		-0.00016	0.00058				0.00000		0.00031			-0.00012
E00-E88		0.00102	0.01132	0.00412	0.00010	0.01485	0.00494		0.01103	0.00273	-0.00099	0.00313
F01-F99	-0.00135	0.00418	0.00303	0.00332	0.01701	0.01772	0.00077		0.00341	0.00504	0.00656	0.00229
G00-G98	-0.00892	-0.00386	0.00719	0.00864	0.00372	0.00682	0.00387		0.01153	0.00173	0.00656	0.00505
H00-H57												
H60-H93												
I00-I99	-0.01216	-0.00453	0.04887	0.16136	0.00147	0.02897	0.18810	-0.00715	0.09815	0.05526	0.02909	0.02107
J00-J98	-0.00152	-0.00675	0.02158	0.01470	0.00550	0.03473	0.04440	-0.03407	0.04719	0.06614	0.01836	0.03897
K00-K92	0.00486	-0.00458	0.00319	0.00808	0.00849	0.01340	0.00375		0.00050	0.00400	0.00635	0.00300
L00-L98		-0.00038	-0.00006	0.00010			-0.00012		-0.00042	-0.00061		0.00036
M00-M99		-0.00055	0.00107	-0.00034			0.00012		0.00008		-0.00080	0.00169
N00-N98		0.00459	0.00290	0.00243	0.00348	-0.00628	0.00461		0.00562	0.00340	0.00282	0.00240
O00-O99												
P00-P96		0.00025	0.00001				0.00000		0.00070	-0.00006		-0.00018
Q00-Q99		-0.00024	0.00024				0.00030		0.00018	0.00008		0.00020
R00-R99		0.00219	0.00367	0.00446	-0.00979		-0.00097		0.08669	0.00193		-0.00438
V01-Y89	-0.00797	0.00894	0.00147	0.01325	-0.00896	0.00301	-0.02134		-0.00089	-0.00281	0.02188	0.00167

Fig. 1: **Impact of COVID-19 on disease-specific mortality across 31 countries.** The impact of COVID-19 on disease-specific mortality within a country is represented: (a–c) show the immediate change and (d–f) show the change in slope with their coefficients. The change in slope represents sustained effects of the pandemic on the following years. Increases are represented by orange, while decreases are represented by green. Darker shades indicate that the data is statistically significant, referring to q-values < 0.05.

d

Change in Slope – America & Asia-pacific

Cause		America		Asia-Pacific			
		Canada	United States	Japan	Korea	Australia	Taiwan
Total	All-cause	0.00200	-0.00090	0.00485	0.00353	0.00264	0.00472
Certain infectious and parasitic diseases	A00-B99		0.00009	0.00008	0.00166		
Neoplasms	C00-D48	0.00020	0.00012	0.00022	0.00004	0.00016	0.00014
Diseases of the blood and blood-forming organs and immune mechanism	D50-D89		0.00001	0.00002	0.00000		
Endocrine, nutritional and metabolic diseases	E00-E88		0.00000	0.00010	0.00023		
Mental and behavioral disorders	F01-F99		0.00289	-0.00002	-0.00002		
Diseases of the nervous system	G00-G98		0.00022	-0.00002	0.00028		
Diseases of the eye and adnexa	H00-H57			0.00000	0.00000		
Diseases of the ear and mastoid process	H60-H93			0.00000	0.00000		
Diseases of the circulatory system	I00-I99	0.00043	0.00020	0.00103	0.00041	0.00057	0.00096
Diseases of the respiratory system	J00-J98	0.00026	0.00017	0.00079	0.00001	0.00012	-0.00010
Diseases of the digestive system	K00-K92		0.00000	0.00012	0.00007		
Diseases of the skin and subcutaneous tissue	L00-L98		0.00001	0.00000	0.00000		
Diseases of the musculoskeletal system and connective tissue	M00-M99		0.00001	0.00000	0.00002		
Diseases of the genitourinary system	N00-N98		0.00003	0.00017	-0.00001		
Pregnancy, childbirth and the puerperium	O00-O99		0.00000	0.00000	0.00000		
Conditions originating in the perinatal period	P00-P96		0.00001	0.00000	0.00000		
Congenital malformations, deformations and chromosomal abnormalities	Q00-Q99		0.00001	0.00000	0.00000		
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	R00-R99		0.00001		0.00071		
External causes of morbidity and mortality	V01-Y89	0.00010	0.00001		0.00010		0.00007

e

Change in Slope – Europe 1

Cause	Europe												
	Austria	Belgium	Bulgaria	Croatia	Cyprus	Czechia	Denmark	England	Estonia	Finland	France	Greece	Hungary
All-cause	0.01611	0.01082	0.04052	0.03095	0.00418	-0.00076	0.00589	-0.00197	0.00508	0.00802	0.00472	0.01975	0.03835
A00-B99	0.00047	0.00018	0.00044	0.00017	0.00025	0.00025	0.00071	0.00018	0.00004	0.00001	0.00044	0.00035	0.00022
C00-D48	0.00034	0.00046	0.00025	0.00128	0.00067	0.00085	0.00111	0.00019	0.00184	-0.00018	0.00116	0.00101	0.00167
D50-D89	0.00024	0.00007	0.00023		0.00018	0.00000	0.00006	0.00000			0.00008	0.00015	0.00007
E00-E88	0.00069	0.00039	0.00042	0.00191	0.00020	0.00039	0.00012	0.00003	-0.00010	0.00009	0.00035	0.00025	0.00103
F01-F99	0.00054	0.00113	0.00002	0.00199	-0.00029	0.00000	-0.00023	-0.00011	0.00020	0.00053	0.00032	-0.00064	0.00102
G00-G98	0.00062	0.00046	0.00035	0.00044	0.00023	0.00043	0.00022	-0.00008	-0.00015	0.00115	0.00056	-0.00077	0.00059
H00-H57								0.00000					
H60-H93								0.00000					
I00-I99	0.00535	0.00335	0.02252	0.00909	0.00062	0.00331	0.00181	0.00123	0.00367	0.00354	0.00225	0.00414	0.01707
J00-J98	0.00219	0.00439	0.00628	0.00365	0.00333	0.00367	0.00374	0.00107	0.00208	0.00088	0.00352	0.00572	0.00569
K00-K92	0.00026	-0.00012	0.00132	0.00098	0.00003	0.00049	-0.00002	0.00021	-0.00010	0.00036	0.00036	0.00018	0.00080
L00-L98	0.00004	0.00012			-0.00015	0.00010	0.00006	0.00002			0.00002		-0.00004
M00-M99	0.00012	0.00013		0.00016		0.00000	0.00002	0.00004	-0.00002	-0.00009	0.00009	0.00008	0.00009
N00-N98	0.00002	0.00046	-0.00038	0.00130	-0.00019	0.00015	0.00016	0.00005	-0.00044	0.00003	0.00005	0.00090	0.00021
O00-O99								0.00000					
P00-P96	0.00007	-0.00006	-0.00006	-0.00004		-0.00001	-0.00004	0.00000		-0.00003	0.00004	-0.00002	-0.00001
Q00-Q99	0.00013	0.00001	-0.00003	-0.00002		0.00012	-0.00003	0.00001		-0.00011	0.00001	0.00004	0.00006
R00-R99	0.00013	0.00062	0.00222	0.00062	0.00007	0.00045	0.00106	0.00014	0.00051	0.00016	0.00100	0.00305	0.00012
V01-Y89	0.00008	0.00005	0.00019	0.00035	-0.00013	0.00061	0.00001	-0.00004	0.00081	0.00032	0.00044	0.00006	0.00088

f

Change in Slope – Europe 2

Cause	Europe											
	Iceland	Ireland	Italy	Lithuania	Luxembourg	Malta	Romania	Scotland	Serbia	Slovakia	Slovenia	Spain
All-cause	-0.00582	-0.00567	0.00726	0.02550	0.00372	0.01758	0.01876	0.00082	0.02252	0.00038	0.01857	-0.00350
A00-B99		-0.00004	0.00067	0.00035	-0.00012	-0.00003	0.00054		0.00027	0.00035	0.00057	0.00031
C00-D48	-0.00285	0.00007	0.00194	0.00145	-0.00107	0.00047	0.00190	0.00004	0.00081	0.00168	0.00056	0.00146
D50-D89		0.00004	0.00008				0.00000		0.00008			0.00000
E00-E88		-0.00015	0.00091	0.00015	0.00053	0.00048	0.00029		0.00072	0.00021	-0.00086	0.00021
F01-F99	-0.00015	0.00071	0.00057	0.00033	0.00206	0.00067	0.00006		0.00033	0.00065	0.00157	0.00085
G00-G98	-0.00112	-0.00040	0.00064	0.00091	0.00027	0.00114	0.00034		0.00074	0.00071	0.00057	0.00060
H00-H57												
H60-H93												
I00-I99	-0.00103	0.00108	0.00553	0.01703	0.00177	0.00543	0.01504	0.00134	0.00910	0.00398	0.00401	0.00276
J00-J98	0.00085	-0.00027	0.00292	0.00329	0.00198	0.00805	0.00434	0.00119	0.00408	0.00502	0.00384	0.00410
K00-K92	0.00060	-0.00042	0.00061	0.00020	0.00043	0.00103	0.00083		0.00058	0.00086	0.00034	0.00058
L00-L98		-0.00004	0.00000	-0.00002			0.00001		-0.00008	-0.00003		0.00004
M00-M99		-0.00006	0.00014	0.00007			0.00002		-0.00004		0.00004	0.00024
N00-N98		0.00068	0.00037	0.00041	0.00032	0.00003	0.00045		0.00089	0.00023	0.00013	0.00026
O00-O99												
P00-P96		0.00001	0.00000				-0.00001		0.00007	0.00001		-0.00001
Q00-Q99		0.00002	0.00002				0.00003		0.00004	0.00007		0.00003
R00-R99		0.00023	0.00066	0.00020	-0.00111		0.00000		0.00263	0.00074		-0.00027
V01-Y89	-0.00196	0.00046	0.00055	0.00115	-0.00098	0.00079	-0.00305		-0.00023	0.00035	0.00321	0.00035

Fig. 1: Continued.

COVID-19					COVID-19 Margin				
Disease	Country	Coefficient	Standard error	Q-value	Disease	Country	Coefficient	Standard error	Q-value
Negative coefficient[a]									
All-cause	Japan	−0.0550	0.0132	0.0011					
A00–B99	England	−0.0022	0.0005	0.0003					
A00–B99	Japan	−0.0012	0.0003	0.0015					
E00–E88	Japan	−0.0013	0.0004	0.0495					
F01–F99	Japan	−0.0028	0.0007	0.0030					
G00–G98	Japan	−0.0037	0.0011	0.0392					
I00–I99	Japan	−0.0150	0.0040	0.0113					
L00–L98	US	−0.0009	0.0001	0.0000					
M00–M99	Japan	−0.0008	0.0002	0.0260					
P00–P96	US	−0.0011	0.0002	0.0002					
Q00–Q99	US	−0.0007	0.0002	0.0112					
Q00–Q99	Japan	−0.0002	0.0000	0.0112					
Positive coefficient[a]									
All-cause	Austria	0.1914	0.0622	0.0431	All-cause	Japan	0.0048	0.0006	0.0000
All-cause	US	0.1301	0.0282	0.0001	All-cause	Taiwan	0.0047	0.0011	0.0000
A00–B99	Slovenia	0.0055	0.0012	0.0010	All-cause	Korea	0.0035	0.0010	0.0007
E00–E88	Croatia	0.0301	0.0097	0.0495	All-cause	Australia	0.0026	0.0008	0.0009
F01–F99	Luxembourg	0.0170	0.0036	0.0010	A00–B99	Korea	0.0017	0.0006	0.0075
G00–G98	Hungary	0.0057	0.0018	0.0392	A00–B99	Slovenia	0.0006	0.0001	0.0004
I00–I99	Lithuania	0.1614	0.0477	0.0187	A00–B99	England	0.0002	0.0000	0.0000
I00–I99	Hungary	0.1349	0.0397	0.0187	A00–B99	US	0.0001	0.0000	0.0046
I00–I99	Austria	0.0499	0.0152	0.0187	A00–B99	Japan	0.0001	0.0000	0.0000
K00–K92	Bulgaria	0.0075	0.0024	0.0437	C00–D48	Japan	0.0002	0.0000	0.0000
K00–K92	US	0.0020	0.0006	0.0306	C00–D48	Australia	0.0002	0.0001	0.0025
N00–N98	Austria	0.0060	0.0016	0.0096	D50–D89	Austria	0.0002	0.0001	0.0058
N00–N98	Romania	0.0046	0.0013	0.0115	D50–D89	Bulgaria	0.0002	0.0001	0.0028
N00–N98	Ireland	0.0046	0.0009	0.0003	D50–D89	Japan	0.0000	0.0000	0.0000
R00–R99	Serbia	0.0867	0.0142	0.0000	D50–D89	US	0.0000	0.0000	0.0001
R00–R99	Bulgaria	0.0251	0.0073	0.0117	E00–E88	Korea	0.0002	0.0000	0.0000
R00–R99	Czechia	0.0205	0.0040	0.0002	E00–E88	Japan	0.0001	0.0000	0.0000
R00–R99	Austria	0.0035	0.0013	0.0397	F01–F99	Luxembourg	0.0021	0.0004	0.0000
R00–R99	Hungary	0.0022	0.0008	0.0251	F01–F99	Croatia	0.0020	0.0006	0.0016
R00–R99	Ireland	0.0022	0.0007	0.0221	F01–F99	Slovenia	0.0016	0.0005	0.0021
V01–Y89	Estonia	0.0149	0.0047	0.0312	G00–G98	Malta	0.0011	0.0003	0.0022
V01–Y89	Lithuania	0.0132	0.0042	0.0312	G00–G98	Slovakia	0.0007	0.0002	0.0032
V01–Y89	Ireland	0.0089	0.0021	0.0036	G00–G98	Korea	0.0003	0.0001	0.0000
					I00–I99	Hungary	0.0171	0.0052	0.0024
					I00–I99	Lithuania	0.0170	0.0061	0.0083
					I00–I99	Austria	0.0054	0.0020	0.0130
					I00–I99	Finland	0.0035	0.0012	0.0056
					I00–I99	France	0.0022	0.0007	0.0043
					I00–I99	Scotland	0.0013	0.0004	0.0015
					I00–I99	England	0.0012	0.0003	0.0002
					I00–I99	Japan	0.0010	0.0002	0.0000
					I00–I99	Taiwan	0.0010	0.0002	0.0000
					I00–I99	Australia	0.0006	0.0001	0.0002
					I00–I99	Canada	0.0004	0.0002	0.0074
					I00–I99	Korea	0.0004	0.0001	0.0060
					J00–J98	Malta	0.0081	0.0023	0.0011
					J00–J98	Hungary	0.0057	0.0015	0.0007
					J00–J98	Slovenia	0.0038	0.0013	0.0060
					J00–J98	Czechia	0.0037	0.0009	0.0003
					J00–J98	Croatia	0.0036	0.0009	0.0002
					J00–J98	Lithuania	0.0033	0.0011	0.0050
					J00–J98	Japan	0.0008	0.0002	0.0023

(Table 1 continues on next page)

COVID-19					COVID-19 Margin				
Disease	Country	Coefficient	Standard error	Q-value	Disease	Country	Coefficient	Standard error	Q-value
(Continued from previous page)									
					K00–K92	Bulgaria	0.0013	0.0003	0.0000
					K00–K92	Italy	0.0006	0.0002	0.0006
					K00–K92	France	0.0004	0.0001	0.0054
					K00–K92	England	0.0002	0.0000	0.0000
					K00–K92	Japan	0.0001	0.0000	0.0000
					K00–K92	Korea	0.0001	0.0000	0.0018
					L00–L98	England	0.0000	0.0000	0.0003
					L00–L98	US	0.0000	0.0000	0.0000
					M00–M99	Korea	0.0000	0.0000	0.0010
					M00–M99	US	0.0000	0.0000	0.0022
					N00–N98	Croatia	0.0013	0.0004	0.0049
					N00–N98	Ireland	0.0007	0.0001	0.0000
					N00–N98	Romania	0.0004	0.0002	0.0069
					N00–N98	Italy	0.0004	0.0001	0.0067
					N00–N98	Japan	0.0002	0.0000	0.0000
					P00–P96	US	0.0000	0.0000	0.0000
					Q00–Q99	US	0.0000	0.0000	0.0008
					R00–R99	Korea	0.0007	0.0001	0.0000
					V01–Y89	Slovenia	0.0032	0.0010	0.0033
					V01–Y89	Hungary	0.0009	0.0003	0.0065
					V01–Y89	Italy	0.0005	0.0001	0.0004
					V01–Y89	Taiwan	0.0001	0.0000	0.0046

The table presents a matrix of statistically significant results from interrupted time series analyses of disease-specific mortality across 31 countries. Only outcomes with significant coefficients ($q < 0.05$) are included. Disease categories are ordered by the absolute magnitude of estimated coefficients within each group. [a]This table presents only the results with q-values less than 0.05.

***Table 1:* Matrix visualization of statistically significant changes in disease-specific mortality across 31 countries.**

Cause	Number of patients		Number of outpatient visits		Days of hospitalization		Total direct medical cost		Per capita cost	
	Immediate change	Change in slope	Immediate change	Change in slope	Immediate change	Change in slope	Immediate change	Change in slope	Immediate change	Change in slope
A00-B99	-282705.1	-3719.9	-372793.5	-5285.9	-34631.7	-1052.9	-22551177.0	294355.0	419.5	340.7
C00-D48	-13973.1	2646.0	-45801.2	1416.2	-46051.3	-4373.7	67501343.5	1590159.2	6753.7	-295.8
D50-D89	-3741.6	281.6	-6533.0	261.4	-1578.5	-114.8	-603435.7	16739.9	463.8	-215.5
E00-E88	-122260.9	4313.7	-1997.2	4221.0	-7425.2	-492.2	808794.7	761639.6	-3319.3	-322.2
F01-F99	-43605.2	4408.1	70697.3	6667.3	-7973.6	-27832.3	-1653620.8	-545253.5	318.4	-31.0
G00-G98	-11052.2	-757.1	-51088.5	-607.7	-72667.3	-34864.7	17607272.2	-2454610.5	4909.9	-49.1
H00-H57	-263160.2	468.7	-302850.2	-1103.2	7381.7	-226.0	27554831.6	708340.6	258.3	5.8
H60-H93	-139478.4	1280.9	-254124.2	1070.6	-8210.7	-355.4	-4043158.4	-412664.9	337.2	-4.9
I00-I99	-11667.3	1012.2	-41577.3	3021.9	-22468.0	-7030.2	19931064.7	944263.8	1090.2	-2.9
J00-J98	-4116445.7	33996.7	-6293897.0	42989.1	-238485.7	-3941.7	-128960011	883655.0	7551.7	-193.7
K00-K92	-427071.6	3183.2	-497768.4	-2231.2	-9569.8	-33.4	10479361.1	716579.8	1880.7	33.4
L00-L98	-91945.0	-4015.7	-120413.7	-8173.6	-8829.9	-644.9	2104841.5	109450.9	379.8	-16.3
M00-M99	-467471.0	726.1	-969716.0	-12280.1	-89021.5	-6426.8	26220728.0	1453739.2	2088.4	-30.1
N00-N98	-62790.6	2146.6	-95461.1	581.6	-17507.6	-1953.1	39756758.7	1168227.8	1189.0	-2.6
O00-O99	-2566.7	-93.0	-1467.3	-373.4	-6771.2	-4.8	-315088.1	-169650.4	9619.7	-296.3
P00-P96	-2376.6	-28.2	-4192.6	-237.4	-3560.4	39.4	-1350276.0	-122697.4	5223.8	-365.7
Q00-Q99	-5132.3	165.6	-9168.6	101.5	-2032.3	-63.0	-1910537.0	20758.3	10006.5	-389.7
R00-R99	-132537.6	6927.7	-176614.8	10202.2	-1886.1	-1241.7	-8350460.0	1715071.1	1176.2	29.5

***Fig. 2:* Impact of COVID-19 on disease-specific healthcare utilization in Republic of Korea.** The impact of COVID-19 on healthcare utilization related to each disease is shown as immediate level changes and slope changes, represented by their respective coefficients. The change in slope represents sustained effects of the pandemic on the following months. Increases are represented by orange, while decreases are represented by green. Darker shades indicate that the data is statistically significant, referring to q-values < 0.05.

decrease was observed in the number of patients and outpatient visit across a range of disease categories. Immediate decrease was observed in the numbers of patients in 13 disease categories including infectious diseases (A00–B99), endocrine diseases (E00–E88), diseases of eye and adnexa (H00–H57), respiratory diseases (J00–J98), digestive diseases (K00–K92), and musculoskeletal diseases (M00–M99), and in number of outpatient visits in eight disease categories. However, an increasing slope in the number of patients was found for changes in neoplasms (C00–D48), mental diseases (F01–F99), congenital malformations (Q00–Q99), and other abnormal symptoms (R00–R99). Days of hospitalization showed an immediate decrease or decreasing slope across more than 12 disease categories.

Disease burden, measured by total direct medical costs, varied by disease category. Immediate increase in disease burden was observed in diseases of neoplasms (C00–D48), nervous systems (G00–G98), diseases of eye and adnexa (H00–H57), circulatory diseases (I00–I99), respiratory diseases (J00-J98), and genitourinary diseases (N00–N98). Among them, disease with eye and adnexa (H00–H57), circulatory diseases (I00–I99) and genitourinary diseases (N00–N98) was also followed by an increasing slope. Endocrine diseases (E00–E88) and musculoskeletal disease (M00–M99) had an increase in slope. On the other hand, per capita costs had an immediate increase in eight disease categories including diseases of nervous system (G00–G98), respiratory diseases (J00–J98), and obstetric conditions (O00–O99). Several diseases showed varied trends between patient numbers and per capita costs. For disease related to eye, adnexa (H00–H57), and ear (H60–H93), respiratory diseases (J00–J98) and musculoskeletal diseases (M00–M99), the number of patients exhibited an immediate decline, accompanied by an increase in per capita costs.

Subgroup analysis of healthcare access and disease burden involved analysis of 1631 ICD-10 codes (Supplementary Table S9), and significant trends were observed across various categories. There was an immediate decline in endocrine diseases, such as hyperparathyroidism (E21), and Cushing's syndrome (E24), while the numbers related to hyperaldosteronism (E26) increased. For Cushing's syndrome, the number of patients and outpatient visits and total direct medical costs showed immediate and prolonged decrease after COVID-19. Mental disorders, particularly bipolar (F31) and eating disorders (F50), exhibited an increasing slope in patient numbers and costs. Digestive diseases such as irritable bowel disease (K58), intestinal disorders (K59) and alcoholic liver diseases (K70) showed an immediate decline, whereas disorders of pancreas (K86) showed an increase in slope. Most conditions under genitourinary diseases including nephritic syndrome (N03) and urethral syndrome (N34) showed an immediate decrease, while menstrual cycle disorders (N91, N92) exhibited an increasing slope.

Discussion

This study analyzed the impact of the COVID-19 pandemic on the mortality across 31 countries and on HRU and disease burden in Korea. Throughout the pandemic, an increasing slope was observed in disease-specific mortality for diseases of the infectious, blood and immune, circulatory, digestive, and respiratory systems. Additionally, mortality related to ischemic heart disease showed an increase in slope, and mortality related to hypertension and diseases of the liver showed an immediate increase.

Immediate post-COVID-onset decreases in HRU were observed across various diseases in Korea. Subsequently, conditions such as neoplasms and mental diseases exhibited a sustained increase. Eye and adnexa, respiratory, digestive, and musculoskeletal diseases showed opposite trends, i.e., decreased patient numbers and increased per capita costs. Furthermore, during the pandemic, HRU for chronic intestinal conditions had decreased, but number of patients for conditions related to the thyroid, liver, bipolar, and menstrual cycle had increased.

Previous studies have examined the impact of COVID-19 on mortality and healthcare access under specific conditions, with a focus on short-term outcomes in localized settings. Most studies suggest that COVID-19 and public health policies have adversely affected healthcare access and clinical outcomes for various non-COVID-19 conditions, primarily in Europe, the United States, and Asia-Pacific regions.[14,15] These studies suggest that limited healthcare access and suboptimal clinical outcomes can be attributed to factors like hospital strain, emphasizing the need for strategies to alleviate the burden on public health systems and healthcare infrastructure.

To our knowledge, this is the first quantitative study to assess the long-term global impact of COVID-19 and public health policies on mortality, HRU, and disease burden across all disease categories. These findings confirm previous evidence and provide new insights into the three-year post-COVID-19 impact across 31 countries, covering all diseases. Significant increases in mortality related to the circulatory, respiratory, and genitourinary systems. Notably, a decrease in the days of hospitalizations in South Korea was observed, which may reflect challenges in healthcare access after the COVID-19 outbreak. This reduction in HRU could potentially be associated with the observed increase in mortality associated with these conditions in South Korea. However, while HRU and disease burden were analyzed solely in South Korea, mortality trends were examined across 31 countries. Extrapolating this relationship to a global scope requires caution. Given that healthcare access was restricted during the initial stages of the pandemic in similar ways in other countries,[16] it is plausible that comparable reductions in HRU occurred worldwide, which may have contributed to observed mortality trends worldwide. A significant increase was observed in patient numbers for various conditions including mood, eating, and sleep disorders,[17] sepsis,[18] menstrual diseases,[19] and hyperaldosteronism.[20] These increases may be attributed to limited access to hospital care, lifestyle and dietary changes resulting from public health measures, reflecting the broader health impacts of the pandemic. Additionally, a rise in the number of liver-related deaths was found,[21] underscoring the need to consider lifestyle changes and the needs of individuals with pre-existing medical conditions while planning for future pandemics. These results highlight the complex interactions between COVID-19, public health policies, and long-term health outcomes, reinforcing the importance of targeted public health strategies in the future.

By integrating mortality data from 31 countries with detailed analyses of HRU and disease burden in South Korea, our study offers several important clinical and policy insights. First, the impact of the COVID-19 pandemic on disease-specific mortality was highly heterogeneous across countries and conditions. This variability highlights the complexity of designing universal, one-size-fits-all policies to mitigate pandemic-related mortality. It underscores the urgent need for robust health governance systems that can reduce uncertainty, accurately capture the impact of public health emergencies, and respond swiftly and effectively. Key components include real-time data surveillance systems, resilient administrative infrastructures, well-trained public health workforce, and evidence-informed policy frameworks. Quantitative analyses with comprehensive interpretation will be crucial for preparing for and managing future pandemics. Given that each country possesses unique healthcare system and disease epidemiology, fostering local expertise in both clinical and health policy domains is critical to ensuring effective, context-sensitive responses to public health challenges. These experts should also serve as liaisons with international organizations to ensure adequate policy implementation and coordination.

Second, our in-depth analysis of HRU trends in South Korea during the pandemic revealed that, overall, outpatient visits and the number of patients declined immediately after the onset of COVID-19. Hospital days showed both immediate and sustained reductions, while per capita healthcare costs increased despite the fall in patient numbers. These patterns suggest that healthcare systems were unable to admit patients with severe conditions, potentially exacerbating disease severity and financial burden during the early phase of the pandemic. When analyzed by disease category, notable trends emerged. For example, infectious and parasitic diseases showed increased mortality accompanied by decreases in patient volume, outpatient visits, hospital days, and disease burden, suggesting reduced care access despite rising disease burden. Endocrine, nutritional, and metabolic diseases experienced increased mortality and reduced patient volume, with sustained increases in outpatient care and overall burden. Diseases of the nervous system exhibited higher mortality and decreased inpatient care, with a corresponding increase in disease burden. Circulatory diseases showed both increased mortality and rising per capita costs. Despite no aggregate HRU decline, subgroup analyses revealed reductions in patient numbers and care for specific ICD-10 three-character codes within this category. Digestive and musculoskeletal diseases also showed increased mortality and decreased HRU, with a concurrent rise in disease burden. For symptoms and signs not elsewhere classified, we observed immediate reductions in HRU and burden followed by sustained increases. Collectively, these results indicate that mortality increases were often accompanied by HRU reductions though the relationship varied by disease. Furthermore, we noted a unique trend in mental and behavioral disorders, where patient numbers initially declined but then rebounded. This may reflect the growing mental health burden associated with the pandemic. These findings point to the clinical importance of maintaining care continuity, especially for chronic and vulnerable populations, during public health crises. Disruptions in managing long-term conditions, such as cardiovascular diseases, diabetes, dementia, and respiratory illnesses, can lead to preventable mortality and increased strain on health systems. While governments prioritizing infectious disease during pandemics is essential, overlooking non-COVID conditions raises ethical concerns and jeopardizes broader public health.

To ensure healthcare resilience, policymakers should consider continuity of care during pandemics to prevent disruptions in chronic disease management. Solutions may include remote monitoring, home-based care, and streamlined medication delivery. Simultaneously, regulatory frameworks for vaccine and treatment development, along with internationally standardized health data, are essential to support real-time decision-making and equitable policy design. Importantly, many countries face persistent shortages of public health professionals, posing a barrier to effective outbreak response. Strengthening the global public health workforce and improving communication among stakeholders are critical priorities. Especially, as pandemics are expected to affect vulnerable patients with chronic diseases, strategic health policies should focus on marginalized patient groups.

Ultimately, results from this study underscore the need for integrated, data-driven, and disease-specific strategies to enhance both health system preparedness and equitable care delivery in future pandemics.

This study is a pioneering investigation into the global health impacts of COVID-19, analyzing national data to reveal patterns in disease-specific mortality across countries. Unlike previous studies focusing on individual diseases, this study explored multiple conditions, illustrating the broader impact and public health policy implications of the pandemic. Extending the analysis beyond immediate effects to include a three-year post-pandemic perspective allowed for the capture of sustained impacts and recovery trends. Additionally, integrating the analyses of disease burden, healthcare access, and clinical outcomes, helped us provide a comprehensive framework for understanding the multifaceted effects of COVID-19. This framework not only informs policy but also contributes to the broader discourse on pandemic response strategies, enhancing our understanding of the global impact of the pandemic.

This study has several limitations. First, in 25 countries, no significant increase in all-cause mortality was observed. Possible explanations include the high rate of early vaccination, strict public health interventions (e.g., lockdowns), and the reallocation of healthcare resources, which may have mitigated excess mortality. Further research is warranted to explore the interplay of these factors across different settings. Second, although our study highlighted possible mechanisms such as delayed medical care and healthcare system strain, other underlying factors, including economic downturns, social disruptions, and pre-existing health system differences, may also have contributed to changes in disease-specific mortality. Given the limitations of available data, we employed ITS analysis as a pragmatic approach; however, future studies incorporating richer datasets and alternative methodological approaches are necessary to comprehensively assess the multifactorial drivers of mortality shifts during the pandemic. For example, while regional variations in policy responses may have existed within some countries, we included most of the nations in our analysis implemented major public health interventions at the national level. Nevertheless, subnational data could have enabled more granular analyses, and future research using regionally stratified healthcare data with appropriate control group and statistical methods may offer additional insights into within-country variations and effectiveness of public health policies in pandemic. Third, the HRU data were derived solely from South Korea, potentially limiting the generalizability of the results. To improve preparedness for future pandemics, incorporating monthly HRU and other relevant medical data into publicly accessible statistical reports is recommended. Additionally, most countries report mortality data annually with broad disease categorizations, complicating variant-specific impact assessments. Furthermore, variations in disease categorization and reporting standards across countries also posed challenges for comparative analyses. Establishing globally standardized and detailed mortality, HRU, and economic data would enable better understanding of disease-specific impacts and strengthen pandemic preparedness. International collaboration is essential to achieve this goal. Further research using monthly clinical and HRU data from diverse countries is needed to assess the long-term impacts of COVID-19 and public health policies, providing robust evidence for decision-making and global pandemic response strategies. Fourth, due to data limitations, we defined “disease burden” based solely on direct medical costs obtained from reimbursement claims. We were unable to capture direct non-medical costs and indirect costs, which are typically included in the full definition of economic burden in health economics. Therefore, caution is needed when interpreting our findings, as they do not represent the total economic impact from either the societal or payer’s perspective. Future research incorporating comprehensive cost components, including direct non-medical and indirect costs, is needed to provide a more complete assessment. Fifth, the ITS model was associated with challenges related to autocorrelation and limited outcome data. To address these limitations, we applied GLS models with AR1 correction and automated SARIMAX models. Finally, as this study focused on high-income countries, the findings may not be generalizable to low-income countries, where the impact of the pandemic may have been more severe.[22]

The COVID-19 pandemic caused significant disruption in global health, leading to shifts in mortality, access to healthcare, and economic burden across diseases. This study provides global insights into the impact of COVID-19, underscoring the urgent need for informed and proactive public health strategies. This research supports the development of policies aimed at not only reducing mortality but also improving the quality of life of patients during future pandemics. With timely interventions and resilient health systems, we can be better prepared for the inevitable challenges of future global health crises.

Contributors
SJ Park, K Choi, and HS Suh were responsible for the study concept and design. M Jang extracted and processed the data inputs and prepared the tables and figures. K Choi, M Jang, and S Kim statistically analyzed the data. K Choi and M Jang wrote the first draft of the paper with assistance from S Kim, SJ Park, and HS Suh. All authors provided their professional inputs to this study. All authors read and approved the final version of the manuscript. K Choi and M Jang verified the data. SJ park and HS Suh had the final responsibility for the decision to submit the paper.

Data sharing statement
Data used in the analysis is freely available online (Supplementary Table S1).

Declaration of interests
We declare that we have not received any financial, human, or other forms of support from any institutions or stakeholders that could influence this research. Furthermore, we declare that there are no conflicts of interest related to research ethics.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2025.103315.

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