

Brief Communication Infectious Diseases, Microbiology & Parasitology



COVID-19 Vaccination Rates in Patients With Chronic Medical Conditions: A Nationwide Cross-Sectional Study

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Received: Aug 20, 2022 Accepted: Sep 20, 2022 Published online: Nov 9, 2022

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ABSTRACT

As most individuals acquire immunity to severe acute respiratory syndrome coronavirus 2, South Korea declared a return to normalcy a few months ago. However, epidemic waves continue because of endlessly emerging variants and waning immunity. Health authorities are focusing on those at high risk of severe coronavirus disease 2019 to minimize damage to public health and the economy. In this regard, we investigated the vaccination rates in patients with various chronic medical conditions by examining the national health insurance claims data and the national immunization registry. We found that patients with chronic medical conditions, especially those of higher severity, such as malignancy, had vaccination rates approximately 10–20% lower than those of the general population. Public health authorities and healthcare providers should try to vaccinate these patients to avoid preventable morbidity and mortality.

Keywords: COVID-19; Vaccination; Immunity; Chronic Disease

Shortly after the report of the first case of coronavirus disease 2019 (COVID-19) in South Korea, 1 various preventive measures were implemented to protect those at a high risk of developing severe COVID-19, especially those admitted to hospitals or long-term care facilities. A high level of social distancing was enforced for 2 years; however, quarantine strategies changed after the end of the large pandemic wave of the omicron variant in early 2022. By mid-April 2022, virtually all restrictions were lifted in the context of adequate population immunity, achieved by a high vaccination rate and previous infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Owing to public fatigue and decoupling between case incidence and mortality, nationwide lockdown or intensive social distancing is unlikely to return. However, in the face of the incessant emergence of highly transmissible immune-escaping variants and waning population immunity, the outbreak of another epidemic is only a matter of time and is likely to cause significant morbidity and mortality in those at a high risk of severe infection. Sublineages of the omicron variant,

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Disclosure

The authors have no potential conflicts of interest to disclose.

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BA.4 and BA.5, have already caused an alarming number of infection.² Hence, we should be prepared to minimize the damage caused by future pandemic waves.

People who visit healthcare institutions because of chronic medical conditions are not only vulnerable to severe infection but are also likely to transmit the virus to other frail patients.^{3,4} In this regard, understanding the immunity level of this population is essential to guiding infection prevention policies. We recently investigated the COVID-19 vaccination rates in individuals hospitalized with chronic medical conditions, which are important risk factors for severe COVID-19 (unpublished data). We found that these patients, especially those with cancer, had lower vaccination rates than the general population of a similar age. Since this was a single-center study, we aimed to determine whether there is a similar pattern at the national level.

We combined the national healthcare claims database operated by the National Health Insurance Service of Korea with the national immunization registry operated by the Korea Disease Control and Prevention Agency. South Korea has universal, single-payer healthcare coverage for all residents. Categories of chronic medical conditions to be examined were selected as previously described elsewhere.⁵ In brief, the diseases of interest with reports of possible association with SARS-CoV-2 in previous epidemiologic studies and those with theoretical concerns for increased risk were selected from the list of International Classification of Diseases and Related Health Problems, 10th edition (ICD-10) mapping tree (Supplementary Table 1). Patients aged ≥ 18 years who visited outpatient clinics at least thrice or were hospitalized at least once with the abovementioned conditions from March 2020 to February 2022 were included in the study. Domestic and overseas vaccination data up to May 31, 2022, were extracted. The vaccine products included in this study are Vaxzevria® (Oxford-AstraZeneca), Comirnaty[®] (Pfizer-BioNTech), Spikevax[®] (Moderna), Nuvaxovid[®] (Novavax), and Jcovden[®] (Janssen). Jcovden[®] as a first dose was considered equivalent to 2 doses of other vaccines. The corresponding statistics up to May 31, 2022, in the general population aged ≥ 18 years were used as comparators. Patients who died before February 28, 2022, when national immunization virtually ended,7 were excluded from the study to minimize immortal time bias.

The number of patients according to the disease category and vaccination status are presented In **Tables 1**, **2**, and **3**. Among the general population, the percentages of those who received at least one dose, at least two doses, and at least 3 doses of a COVID-19 vaccine were 97.3%, 96.5%, and 74.5%, respectively. When divided by age, the third vaccination rate showed a significant difference between age groups (age 60+ years, 89.7%; age 40–59 years, 74.9%; age 18–39 years, 59.1%), in contrast to the first and second vaccination rates.

Several conditions, such as hematological cancer and systemic lupus erythematosus, were associated with vaccination rates lower by \geq 10% than those of the national statistics in all age groups (Tables 1-3). Patients with solid cancers (except thyroid cancer), liver cirrhosis, and chronic renal failure, had lower vaccination rates in all age groups, with greater differences in the younger age groups. Low vaccine acceptance was more prominent in patients with serious and debilitating diseases, such as malignancy, than in those with less serious conditions, such as isolated hypertension. This trend was consistent with our unpublished single-institution data, which revealed lower vaccination rates in patients with malignancies. Among individuals aged \geq 60 years, patients with heart failure, cerebrovascular disease, and dementia had lower vaccination rates than the general population of a similar age (Table 3). In some disease categories, the second and third vaccination rates were far lower in chronically ill patients than in the general population, suggesting that a considerable number actually did not complete the primary series.



Table 1. Coronavirus disease 2019 vaccination rates in patients aged 18-39 years with various chronic medical conditions

Medical conditions	Total number of patients	Number (%) of patients who received		
		First dose	Second dose	Third dose
General population ^a	13,960,039	13,687,067 (98.0%)	13,519,439 (96.8%)	8,249,769 (59.1%)
Endocrinopathy				
Diabetes	132,986	122,316 (92.0%)	106,268 (79.9%)	82,657 (62.2%)
Thyroid disease	154,101	134,521 (87.3%)	126,238 (81.9%)	76,098 (49.4%)
Cardiovascular disease				
Isolated hypertension	189,715	177,197 (93.4%)	144,255 (76.0%)	120,453 (63.5%)
Ischemic heart disease	12,315	10,592 (86.0%)	8,675 (70.4%)	5,860 (47.6%)
Heart failure and cardiomyopathy	6,670	5,527 (82.9%)	4,746 (71.2%)	3,230 (48.4%)
Valvular heart disease	2,026	1,663 (82.1%)	1,522 (75.1%)	954 (47.1%)
Cardiac arrhythmia	23,223	20,117 (86.6%)	17,714 (76.3%)	11,128 (47.9%)
Chronic respiratory disease				
Chronic obstructive pulmonary disease, asthma, or bronchiectasis	129,564	119,884 (92.5%)	110,712 (85.4%)	77,356 (59.7%)
Interstitial lung disease	462	382 (82.7%)	349 (75.5%)	244 (52.8%)
Chronic kidney disease				
Chronic renal failure and end-stage renal disease	10,516	8,909 (84.7%)	8,126 (77.3%)	5,786 (55.0%)
Viral hepatitis and chronic liver disease				
Liver cirrhosis	3,001	2,378 (79.2%)	2,042 (68.0%)	1,410 (47.0%)
Chronic neurological disease				
Parkinsonism and movement disorder	11,667	10,747 (92.1%)	9,858 (84.5%)	6,882 (59.0%)
Alzheimer's disease and degenerative disease	289	253 (87.5%)	235 (81.3%)	190 (65.7%)
Cerebrovascular disease	22,460	19,102 (85.0%)	16,827 (74.9%)	11,472 (51.1%)
(transient ischemic attack, stroke, or cerebral hemorrhage)				
Dementia	183	160 (87.4%)	155 (84.7%)	127 (69.4%)
Malignancy				
Solid organ, except respiratory and thyroid	34,965	29,406 (84.1%)	26,867 (76.8%)	16,536 (47.3%)
Respiratory tract	1,046	819 (78.3%)	746 (71.3%)	454 (43.4%)
Thyroid cancer	47,417	42,548 (89.7%)	` ` ` `	25,344 (53.4%)
Hematological	8,515	6,550 (76.9%)	6,024 (70.7%)	3,434 (40.3%)
Musculoskeletal and rheumatological disease				
Rheumatoid arthritis	11,452	10,186 (88.9%)	9,420 (82.3%)	6,167 (53.9%)
SLE	7,568	6,149 (81.3%)	5,877 (77.7%)	3,633 (48.0%)
Systemic connective tissue disease	31,503	27,308 (86.7%)	24,737 (78.5%)	15,912 (50.5%)
Hematological disease				
Anemia	43,293	39,521 (91.3%)	37,991 (87.8%)	25,693 (59.3%)
Coagulopathy	8,379	6,805 (81.2%)	6,325 (75.5%)	3,644 (43.5%)
Bone marrow dysfunction	5,257	4,502 (85.6%)	4,113 (78.2%)	2,621 (49.9%)
Mental and behavioral disorders				
Mental disorder of substance use	14,437	13,116 (90.8%)	11,734 (81.3%)	7,772 (53.8%)
Schizophrenia	54,655	48,847 (89.4%)	46,481 (85.0%)	35,069 (64.2%)
Mood disorder	376,661	350,527 (93.1%)	330,670 (87.8%)	218,940 (58.1%)
Neurosis	260,071	237,091 (91.2%)	218,182 (83.9%)	140,211 (53.9%)
Personality disorder	9,762	8,724 (89.4%)	8,098 (83.0%)	4,957 (50.8%)
Mental retardation	16,537	15,526 (93.9%)	15,292 (92.5%)	13,601 (82.2%)
Developmental disorder	9,664	8,851 (91.6%)	8,728 (90.3%)	7,523 (77.8%)
Immune deficiency, HIV infection	6,729	6,182 (91.9%)	5,069 (75.3%)	4,035 (60.0%)

SLE = systemic lupus erythematosus, HIV = human immunodeficiency virus.

There are several reasons why patients with chronic medical conditions have low acceptance of COVID-19 vaccination, such as safety concerns, incompatibility with their diseases or treatments, and lack of information.⁸⁻¹⁰ Indeed, there are only a few studies on vaccine efficacy and safety in chronically ill patients. Despite this limitation, public health authorities and academic societies recommend these patients to be vaccinated based on their higher risk of severe and critical COVID-19 and no reports of major safety signals specific to them.¹¹⁻¹⁶ Additionally, while patients with comorbidities develop lower levels of immunity than people without comorbidities after the primary series,¹⁷⁻¹⁹ a third dose significantly increased

 $^{{}^{\}mathrm{a}}$ The vaccination rates for the entire population of the same age group are presented for comparison.



Table 2. Coronavirus disease 2019 vaccination rates in patients aged 40-59 years with various chronic medical conditions

Medical conditions	Total number of patients	Number (%) of patients who received		
		First dose	Second dose	Third dose
General population ^a	16,610,183	16,178,449 (97.4%)	16,064,650 (96.7%)	12,445,902 (74.9%)
Endocrinopathy				
Diabetes	1,104,777	1,061,770 (96.1%)	1,035,336 (93.7%)	897,979 (81.3%)
Thyroid disease	346,572	330,072 (95.2%)	321,808 (92.9%)	258,640 (74.6%)
Cardiovascular disease				
Isolated hypertension	2,320,756	2,253,368 (97.1%)	2,196,938 (94.7%)	1,905,030 (82.1%)
Ischemic heart disease	201,564	189,787 (94.2%)	184,340 (91.5%)	154,601 (76.7%)
Heart failure and cardiomyopathy	44,950	40,842 (90.9%)	39,570 (88.0%)	32,582 (72.5%)
Valvular heart disease	14,489	13,088 (90.3%)	12,721 (87.8%)	10,161 (70.1%)
Cardiac arrhythmia	84,726	78,882 (93.1%)	75,997 (89.7%)	61,425 (72.5%)
Chronic respiratory disease				
Chronic obstructive pulmonary disease, asthma, or bronchiectasis	233,796	222,452 (95.1%)	216,067 (92.4%)	181,369 (77.6%)
Interstitial lung disease	4,265	3,930 (92.1%)	3,796 (89.0%)	3,114 (73.0%)
Chronic kidney disease				
Chronic renal failure and end-stage renal disease	63,289	57,919 (91.5%)	56,503 (89.3%)	48,062 (75.9%)
Viral hepatitis and chronic liver disease				
Liver cirrhosis	44,917	40,348 (89.8%)	39,089 (87.0%)	32,142 (71.6%)
Chronic neurological disease				
Parkinsonism and movement disorder	36,058	34,025 (94.4%)	33,117 (91.8%)	28,015 (77.7%)
Alzheimer's disease and degenerative disease	12,676	12,171 (96.0%)	11,944 (94.2%)	10,798 (85.2%)
Cerebrovascular disease	236,116	219,439 (92.9%)	213,259 (90.3%)	177,656 (75.2%)
(transient ischemic attack, stroke, or cerebral hemorrhage)				
Dementia	7,739	7,124 (92.1%)	6,886 (89.0%)	6,061 (78.3%)
Malignancy				
Solid organ, except respiratory and thyroid	310,952	285,841 (91.9%)	278,567 (89.6%)	220,108 (70.8%)
Respiratory tract	18,137	16,355 (90.2%)	15,857 (87.4%)	12,636 (69.7%)
Thyroid cancer	175,238	168,082 (95.9%)	163,922 (93.5%)	132,968 (75.9%)
Hematological	20,573	17,652 (85.8%)	16,974 (82.5%)	12,862 (62.5%)
Musculoskeletal and rheumatological disease		4	_	
Rheumatoid arthritis	70,006	66,099 (94.4%)	64,643 (92.3%)	53,648 (76.6%)
SLE	11,935	10,506 (88.0%)	10,223 (85.7%)	7,983 (66.9%)
Systemic connective tissue disease	59,207	54,366 (91.8%)	52,620 (88.9%)	42,393 (71.6%)
Hematological disease				
Anemia	111,741	105,156 (94.1%)	102,251 (91.5%)	79,509 (71.2%)
Coagulopathy	11,076	9,541 (86.1%)	9,133 (82.5%)	6,935 (62.6%)
Bone marrow dysfunction	11,081	9,926 (89.6%)	9,578 (86.4%)	7,460 (67.3%)
Mental and behavioral disorders				
Mental disorder of substance use	44,174	40,908 (92.6%)	38,907 (88.1%)	32,350 (73.2%)
Schizophrenia	115,334	103,457 (89.7%)	100,501 (87.1%)	87,916 (76.2%)
Mood disorder	324,552	304,788 (93.9%)	293,988 (90.6%)	238,125 (73.4%)
Neurosis	309,310	288,826 (93.4%)	277,176 (89.6%)	216,474 (70.0%)
Personality disorder	2,990	2,721 (91.0%)	2,556 (85.5%)	2,102 (70.3%)
Mental retardation	9,133	8,676 (95.0%)	8,385 (91.8%)	7,969 (87.3%)
Developmental disorder	550	506 (92.0%)	494 (89.8%)	449 (81.6%)
Immune deficiency, HIV infection	9,027	8,487 (94.0%)	8,152 (90.3%)	7,064 (78.3%)

SLE = systemic lupus erythematosus, HIV = human immunodeficiency virus.

neutralizing antibody titers.^{20,21} On the other hand, some studies revealed that patients with chronic medical conditions were more willing to accept COVID-19 vaccination.^{22,23} Indeed, patients with certain conditions, such as isolated hypertension, that usually do not require intensive treatment, had high vaccination rates. The reasons why patients with serious comorbidities are not vaccinated might have been difficulty in accessing vaccination centers due to treatment schedules or poor conditions. In addition, younger individuals were found to be more vaccine-hesitant in previous studies.^{24,25} This may be due to lower perceived risk of serious illness than that in older individuals or easier access to misinformation that

 $^{{}^{\}mathrm{a}}$ The vaccination rates for the entire population of the same age group are presented for comparison.



Table 3. Coronavirus disease 2019 vaccination rates in patients aged 60-120 years with various chronic medical conditions

Medical conditions	Total number of	Number (%) of patients who received		
	patients	First dose	Second dose	Third dose
General population ^a	13,763,932	13,247,037 (96.4%)	13,175,927 (95.9%)	12,330,726 (89.7%)
Endocrinopathy				
Diabetes	2,178,501	2,081,774 (95.6%)	2,056,853 (94.4%)	1,969,353 (90.4%)
Thyroid disease	298,008	285,221 (95.7%)	281,307 (94.4%)	265,969 (89.2%)
Cardiovascular disease				
Isolated hypertension	4,523,551	4,349,179 (96.1%)	4,299,396 (95.0%)	4,125,595 (91.2%)
Ischemic heart disease	767,647	725,112 (94.5%)	715,789 (93.2%)	680,501 (88.6%)
Heart failure and cardiomyopathy	217,532	196,910 (90.5%)	193,795 (89.1%)	180,898 (83.2%)
Valvular heart disease	53,347	48,482 (90.9%)	47,828 (89.7%)	44,443 (83.3%)
Cardiac arrhythmia	300,179	280,278 (93.4%)	276,444 (92.1%)	261,089 (87.0%)
Chronic respiratory disease				
Chronic obstructive pulmonary disease, asthma, or bronchiectasis	629,713	595,147 (94.5%)	587,652 (93.3%)	560,663 (89.0%)
Interstitial lung disease	28,035	26,038 (92.9%)	25,629 (91.4%)	24,102 (86.0%)
Chronic kidney disease				
Chronic renal failure and end-stage renal disease	208,070	190,435 (91.5%)	187,497 (90.1%)	175,335 (84.3%)
Viral hepatitis and chronic liver disease				
Liver cirrhosis	72,100	66,398 (92.1%)	65,380 (90.7%)	61,032 (84.6%)
Chronic neurological disease				
Parkinsonism and movement disorder	192,720	178,754 (92.8%)	176,225 (91.4%)	166,050 (86.2%)
Alzheimer's disease and degenerative disease	215,397	205,444 (95.4%)	203,152 (94.3%)	194,874 (90.5%)
Cerebrovascular disease	913,833	847,772 (92.8%)	834,538 (91.3%)	781,837 (85.6%)
(transient ischemic attack, stroke, or cerebral hemorrhage)		, ,		, ,
Dementia	572,555	518,576 (90.6%)	508,376 (88.8%)	470,877 (82.2%)
Malignancy				
Solid organ, except respiratory and thyroid	626,246	585,693 (93.5%)	577,160 (92.2%)	537,803 (85.9%)
Respiratory tract	84,926	77,736 (91.5%)	76,371 (89.9%)	69,746 (82.1%)
Thyroid cancer	128,712	124,367 (96.6%)	122,811 (95.4%)	116,708 (90.7%)
Hematological	35,030	30,956 (88.4%)	30,137 (86.0%)	26,560 (75.8%)
Musculoskeletal and rheumatological disease		4	_	
Rheumatoid arthritis	116,500	110,159 (94.6%)	108,614 (93.2%)	102,580 (88.1%)
SLE	5,663	5,085 (89.8%)	4,968 (87.7%)	4,545 (80.3%)
Systemic connective tissue disease	44,901	41,887 (93.3%)	41,156 (91.7%)	38,547 (85.8%)
Hematological disease				
Anemia	89,750	82,354 (91.8%)	80,972 (90.2%)	75,611 (84.2%)
Coagulopathy	17,218	15,592 (90.6%)	15,160 (88.0%)	13,873 (80.6%)
Bone marrow dysfunction	13,216	11,931 (90.3%)	11,623 (87.9%)	10,495 (79.4%)
Mental and behavioral disorders				
Mental disorder of substance use	30,745	28,859 (93.9%)	28,204 (91.7%)	26,137 (85.0%)
Schizophrenia	68,396	61,927 (90.5%)	60,550 (88.5%)	56,080 (82.0%)
Mood disorder	402,792	381,923 (94.8%)	376,434 (93.5%)	356,282 (88.5%)
Neurosis	342,663	325,405 (95.0%)	320,491 (93.5%)	302,389 (88.2%)
Personality disorder	1,537	1,445 (94.0%)	1,420 (92.4%)	1,316 (85.6%)
Mental retardation	2,125	1,999 (94.1%)	1,934 (91.0%)	1,854 (87.2%)
Developmental disorder	234	221 (94.4%)	216 (92.3%)	195 (83.3%)

SLE = systemic lupus erythematosus, HIV = human immunodeficiency virus.

is widespread online. For patients with hematologic diseases, there might have been more specific concerns such as vaccine-induced immune thrombotic thrombocytopenia.

Undoubtedly, public health authorities and healthcare providers should try to raise vaccination rates in these populations as much as possible. Considering the above findings, we suggest several possible ways to do this. For those who wish to be vaccinated but do not have access to vaccination centers, encouraging vaccinations at secondary and tertiary referral centers would be helpful. For example, physicians can check immunization records

 $^{^{\}mathrm{a}}$ The vaccination rates for the entire population of the same age group are presented for comparison.



and administer catch-up vaccinations at the end of acute care. For those who are hesitant, it is essential to provide accurate information regarding COVID-19 and its vaccines and to encourage vaccination. It is physicians who know best about the potential benefits and risks of vaccination related to their patients' diseases and treatments and thus can be trusted the most. In addition, poor immunogenicity is an important factor for low vaccine uptake in patients with severe immunocompromising conditions such as hematological malignancy and solid organ transplantation. Thus, physicians should also actively consider using tixagevimab—cilgavimab, a prophylactic anti-SARS-CoV-2 monoclonal antibody formulation, that will soon be introduced for these high-risk patients. Amid another pandemic of misinformation, we believe that doctors' efforts can improve vaccination rates and maintain patient safety.

This study has several limitations. First, it was based on health insurance claims data; therefore, it was impossible to obtain detailed information on the severity of chronic medical conditions. Moreover, given that health insurance claims data are collected based on diagnostic codes, there might be a possibility of missing information or information bias. However, categories of serious and/or rare diseases, such as malignancies, are reliable, as diagnoses are verified for reimbursement. Second, although this data might be outdated at the time of submission and publication, we believe it is still relevant since the national statistics did not significantly change since March 1, 2022. Third, natural SARS-CoV-2 infections, by which people could develop protective immunity, were not considered in this study, leaving the possibility that people may have higher immunity levels than those assessed using vaccination data alone.

In conclusion, there is a considerable gap between the COVID-19 vaccination rates among patients with chronic medical conditions and those of the general population, especially in younger individuals. Public health authorities and healthcare providers should be aware of this and try to vaccinate these patients to avoid preventable morbidity and mortality.

Ethics statement

This study was approved by the Institutional Review Board (IRB) of the Korea University Guro Hospital with a waiver of informed consent (IRB No: 2021GR0304).

ACKNOWLEDGMENTS

This study used the database of the Korea Disease Control and Prevention Agency and the National Health Insurance Service of Korea for policy and academic research. The research number of this study is KDCA-NHIS-2022-1-448.

SUPPLEMENTARY MATERIAL

Supplementary Table 1

ICD-10 codes for disease category

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