Appendix 1

Potential confounders used in estimating PS.

We considered sociodemographic and clinical factors as potential confounders. We included sex, age (in years), age square and health insurance type at cohort entry for sociodemographic factors. Clinical factors consisted of 20 comorbidities [arrhythmia, asthma, atrial fibrillation, autoimmune disease, chronic lung disease, coronary artery disease, dementia, diabetes mellitus, heart failure, hyperlipidemia, hypertension, immunosuppression (immunosuppression includes HIV, history of organ transplant, transplant rejection, noninfectious enteritis and colitis, ulcerative colitis, and Crohn's disease), kidney disease, liver disease, other cerebrovascular diseases, peripheral vascular disease, pneumonia including tuberculosis, psychiatric disorders, stroke or TIA, thromboembolism] and 12 co-medications uses (acetaminophen, antibacterials, anticoagulants, antidementia, antidepressants, antidiabetics, antiplatelets, antipsychotics, antivirals, anxiolytics, lipid lowering agents including statin, NSAIDs). The working definitions of the clinical factors are described in Table S1; we defined comorbidity variables using in-hospital ICD-10 diagnostic codes, with an index period from 3 years prior (–1,080 d) through the start of the evaluation of exposure (–120 d). When defining malignancy, we additionally employed the expanded benefit coverage codes to minimize false-positive classification. For co-medication use, we used in/out-hospital ATC codes with an index period from –240 to –120 d. To minimize false-positive classification, we used expanded benefit codes in addition to diagnosis codes when defining malignancy.

Table S1 Diagnosis codes based on the Korean Standard Classification of Diseases, 7th Revision or International Classification of Disease, 10th Revision codes, National Procedure codes, and drug codes based on World Health Organization-Anatomical Therapeutic Chemical classification codes

Diagnoses	Codes
Inclusion criteria	
COVID-19 (KCD-7)	B342, B972, Z208, Z290, U18, U181, Z038, Z115, U071, U072
Confirmed (database-specific code)	'Y'
Study endpoints	
All-cause death (database-specific code)	'Y'
ICU admission (NPC)	AH110, AH190-192, AH194, AH195, AH210, AH29-299, AH390-AH396, AH398, AH399, AH501, AJ001, AJ003-011, AJ020, AJ021, AJ031, AJ043-046, AJ100, AJ102, AJ110, AJ112, AJ120, AJ122, AJ130, AJ132, AJ140, AJ142, AJ143, AJ150, AJ152 AJ160, AJ180, AJ190, AJ200, AJ202, AJ210, AJ212, AJ220, AJ222, AJ230, AJ240, AJ242, AJ250, AJ252, AJ260, AJ280, AJ290, AJ300, AJ302, AJ310, AJ312, AJ320, AJ322, AJ330, AJ332, AJ340, AJ342, AJ350, AJ352, AJ360, AJ380, AJ390, AJ500, AJ510, AJ520, AJ530, AJ540, AJ550, AJ560, AJ580, AJ590
Mechanical ventilation use (NPC)	M0850, M0857, M0858, M0860, M5830, M5850-5858, M5860, MM360, MM400
Comorbidities (ICD-10)	
Arrhythmia	I44, I45, I47 (or Anti-arrhythmias drug uses ATC code 'C01B')
Asthma	J45, J46
Atrial fibrillation	I48
Autoimmune disease	
Autoimmune thyroiditis, polyglandular failure, hepatitis	E063, E31, K754
Glomerular disease	N00-N08
Idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia	D693, D59
Intestinal malabsorption, celiac disease	K90
Lupus	L93, M32
Multiple sclerosis, myasthenia gravis	G35, G700
Noninfectious enteritis and colitis, ulcerative colitis, Crohn's disease	K50-K52, R652, R653
Other interstitial pulmonary disease	J84
Psoriasis	L40, L41, M07, M09
Psoriatic arthritis, juvenile rheumatoid arthritis, ankylosis spondylitis	M07, M08, M45
Sarcoidosis	D86, G532, M633 (and Immunosuppressants drug uses ATC codes 'L04A', 'H02', 'P01BA')
Transplanted status, rejection	Z97, T86
Vasculitis	M05
Chronic lung disease	
Bronchiectasis	J47
Chronic obstructive pulmonary disease	J40, J41, J43, J44, E11
Interstitial pulmonary disease	J84
Coronary artery disease	
Atherosclerosis	I70
Coronary artery disease	I20-I25
Dementia	F00-F03, G30, G3100, G3182
Diabetes mellitus	E10-E14
Heart failure	
Heart failure	I110, I50
Valvular heart disease	I34-I37
Hyperlipidemia	E78
Hypertension	I10-I15 (and Anti-hypertensive drug uses ATC codes 'C09A', 'C09B', 'C09C', 'C09D', 'C07', 'C08', 'C03', 'C01D', 'C02A', 'C02B', 'C02C')
Immunosuppression	
HIV	B20-B24
Ulcerative colitis and Crohn's disease	K50-K52
Transplant and failure	T86, Z94
Kidney disease	
Acute kidney failure	N17
CKD	N18, N19
Liver disease	
Chronic liver disease	K70-K77
Viral hepatitis	B15-B19
Malignancy	C00-C97 (and expanded benefit coverage codes 'V027', 'V193', 'V194')
Other cerebrovascular diseases	G46, I65-I69
Peripheral vascular disease	I70-I79
Pneumonia including tuberculosis	
Pneumonia	J12-J18
Tuberculosis	A15-A19
Psychiatric disorders	F04-F99
Stroke or TIA	
Stroke	G45
TIA	I60-I64, G463-G468
Thromboembolism	I26, I63, I74, I801, I802, I803, I809, I82
Study drugs (ATC)	
Immunosuppressants	
Aminoquinolines, chloroquine, hydroxychloroquine	P01BA
Calcineurin inhibitors	L0AD
Corticosteroids	H02
Interleukin Inhibitors	L0AC
Other immunosuppressants	L0AX
Selective immunosuppressants	L0AA
Tumor necrosis factor alpha inhibitors	L0AB
Co-medications (ATC)	
Acetaminophen	N02BE01, N02BE05, N02BE51, N02BE71
Antibacterials	J01
Anticoagulants	B01AA, B01AB, B01AE, B01AF, B01AX
Antidementia	N06D
Antidepressants	N06A
Antidiabetics	A10
Antineoplastic	L01
Antiplatelets	A01AD05, C07FX02, C07FX03, C07FX04, C10BX01, C10BX02, C10BX04, C10BX05, C10BX06, C10BX08, C10BX12, M01BA03, N02AJ02, N02AJ07, N02AJ18, N02BA01, N02BA51, N02BA71, B01AC
Antipsychotics	N05A
Antivirals	J05
Anxiolytics	N05B
Lipid lowering including statin	C10, A10BH51, A10BH52
NSAIDs	M01A

COVID-19, coronavirus disease 2019; KCD-7, Korean Standard Classification of Diseases 7th Revision; ICU, intensive care unit; NPC, national procedure codes; ICD-10, International Classification of Disease 10th Revision; ATC, anatomical therapeutic chemical classification code; CKD, chronic kidney disease; TIA, transient cerebral ischemic attack; NSAIDs, nonsteroidal anti-inflammatory drugs.

Table S2 OR of primary endpoint associated with immunosuppressants use compared with non-use among COVID-19 patients with ≥40 years of age

Characteristic	Number of patients	Cumulative incidence (%)		OR	(95% CI)
		Non-user	User		
All-cause death, ICU admission, mechanical ventilation use					
Confirmed-patients with COVID-19					
Immunosuppressants	4,613	10.0	13.3	1.33	(1.07–1.65)
Corticosteroids	4,597	10.0	13.5	1.34	(1.08–1.65)
Redefining the exposure searching window					
90 days before and including the date of cohort entry					
Immunosuppressants	4,613	9.9	14.2	1.43	(1.15–1.77)
Corticosteroids	4,598	9.9	14.3	1.44	(1.16–1.78)
Hospitalized-patients with COVID-19					
Immunosuppressants	4,349	10.4	13.6	1.32	(1.06–1.63)
Corticosteroids	4,333	10.4	13.8	1.33	(1.07–1.64)
Redefining the exposure searching window					
90 days before and including the date of cohort entry					
Immunosuppressants	4,349	10.3	14.6	1.43	(1.15–1.77)
Corticosteroids	4,334	10.3	14.7	1.44	(1.16–1.79)
Statistical method based on PS (immunosuppressant)					
IPTW with trimming	4,349	10.4	13.6	1.32	(1.06–1.63)
Outcome adjustment model	4,349	10.4	13.6	1.29	(1.05–1.58)
SMR weighting	4,349	10.4	13.6	1.30	(1.03–1.64)
PS matching	4,349	10.4	13.6	1.32	(1.07–1.64)

OR, odds ratio; CI, confidence interval; ICU, intensive care unit; PS, propensity score; IPTW, inverse probability of treatment weighting; SMR, standardized mortality ratio.

Table S3 OR of all-cause death associated with immunosuppressants use compared with non-use among COVID-19 patients with ≥40 years of age

Characteristic	Number of patients	Cumulative incidence (%)		OR	(95% CI)
		Non-user	User		
All-cause death					
Confirmed-patients with COVID-19					
Immunosuppressants	4,613	4.1	6.7	1.67	(1.23–2.26)
Corticosteroids	4,597	4.1	6.8	1.68	(1.24–2.28)
Redefining the exposure searching window					
90 days before and including the date of cohort entry					
Immunosuppressants	4,613	4.0	7.3	1.82	(1.34–2.46)
Corticosteroids	4,598	4.0	7.4	1.83	(1.35–2.47)
Hospitalized-patients with COVID-19					
Immunosuppressants	4,349	4.2	6.7	1.65	(1.21–2.26)
Corticosteroids	4,333	4.2	6.8	1.67	(1.22–2.76)
Redefining the exposure searching window					
90 days before and including the date of cohort entry					
Immunosuppressants	4,349	4.1	7.5	1.85	(1.36–2.52)
Corticosteroids	4,334	4.1	7.6	1.86	(1.37–2.53)
Statistical method based on PS (immunosuppressant)					
IPTW with trimming	4,349	4.2	6.7	1.65	(1.21–2.26)
Outcome adjustment model	4,349	4.2	6.7	1.59	(1.18–2.13)
SMR weighting	4,349	4.2	6.7	1.51	(1.05–2.16)
PS Matching	4,349	4.2	6.7	1.57	(1.14–2.17)

OR, odds ratio; CI, confidence interval; PS, propensity score; IPTW, inverse probability of treatment weighting; SMR, standardized mortality ratio.

Table S4 OR of adverse mechanical ventilation associated with immunosuppressants use compared with non-use among COVID-19 patients with ≥40 years of age

Characteristic	Number of patients	Cumulative incidence (%)		OR	(95% CI)
		Non-user	User		
Mechanical ventilation					
Confirmed-patients with COVID-19					
Immunosuppressants	4,613	2.3	3.6	1.13	(0.77–1.66)
Corticosteroids	4,597	2.3	3.6	1.13	(0.77–1.66)
Redefining the exposure searching window					
90 days before and including the date of cohort entry					
Immunosuppressants	4,613	2.2	3.9	1.37	(0.92–2.02)
Corticosteroids	4,598	2.2	3.9	1.37	(0.93–2.02)
Hospitalized-patients with COVID-19					
Immunosuppressants	4,349	2.4	3.8	1.12	(0.76–1.65)
Corticosteroids	4,333	2.4	3.8	1.13	(0.77–1.65)
Redefining the exposure searching window					
90 days before and including the date of cohort entry					
Immunosuppressants	4,349	2.4	4.1	1.36	(0.92–2.00)
Corticosteroids	4,334	2.4	4.1	1.36	(0.92–2.01)
Statistical method based on PS (immunosuppressant)					
IPTW with trimming	4,349	2.4	3.8	1.12	(0.76–1.65)
Outcome adjustment model	4,349	2.4	3.8	1.20	(0.81–1.77)
SMR weighting	4,349	2.4	3.8	1.27	(0.83–1.92)
PS matching	4,349	2.4	3.8	1.27	(0.84–1.92)

OR, odds ratio; CI, confidence interval; PS, propensity score; IPTW, inverse probability of treatment weighting; SMR, standardized mortality ratio.

Table S5 OR of ICU admission associated with immunosuppressants use among COVID-19 patients with ≥40 years of age

Characteristic	Number of patients	Cumulative incidence (%)		OR	(95% CI)
		Non-user	User		
ICU admission					
Confirmed-patients with COVID-19					
Immunosuppressants	4,613	6.8	8.3	1.12	(0.88–1.44)
Corticosteroids	4,597	6.8	8.4	1.13	(0.88–1.45)
Redefining the exposure searching window					
90 days before and including the date of cohort entry					
Immunosuppressants	4,613	6.7	8.7	1.22	(0.94–1.59)
Corticosteroids	4,598	6.7	8.8	1.23	(0.95–1.60)
Hospitalized-patients with COVID-19					
Immunosuppressants	4,349	7.1	8.7	1.12	(0.87–1.44)
Corticosteroids	4,333	7.1	8.8	1.13	(0.88–1.45)
Redefining the exposure searching window					
90 days before and including the date of cohort entry					
Immunosuppressants	4,349	7.0	9.1	1.21	(0.93–1.57)
Corticosteroids	4,334	7.0	9.2	1.22	(0.94–1.58)
Statistical method based on PS (immunosuppressant)					
IPTW with trimming	4,349	7.1	8.7	1.12	(0.87–1.44)
Outcome adjustment model	4,349	7.1	8.7	1.13	(0.88–1.45)
SMR weighting	4,349	7.1	8.7	1.10	(0.84–1.46)
PS matching	4,349	7.1	8.7	1.14	(0.88–1.47)

OR, odds ratio; ICU, intensive care unit; CI, confidence interval; PS, propensity score; IPTW, inverse probability of treatment weighting; SMR, standardized mortality ratio.