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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Andersen K M, Bates B A, Rashidi E S, et al. Long-term use of immunosuppressive medicines and in-hospital COVID-19 outcomes: a retrospective cohort study using data from the National COVID Cohort Collaborative. *Lancet Rheumatol* 2021; published online Nov 15. https://doi.org/10.1016/S2665-9913(21)00325-8.

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eTable 1. Immunosuppressive Drugs Considered in Exposure Definition

Interleukin inhibitors	daciluzumab, basiliximab, anakinra, rilonacept, ustekinumab, tocilizumab, canakinumab, briakinumab, secukinumab, siltuximab, brodalumab, ixekizumab, sarilumab, sirukumab, guselkumab, tildrakizumab, risankizumab
Janus kinase inhibitors	tofacitinib, baricitinib, upadacitinib
Tumor necrosis factor alpha inhibitors	etanercept, infliximab, afelimomab, adalimumab, certolizumab pegol, golimumab, opinercept
Other selective immunosuppressa-nts	muromonab-cd3, antilymphocyte immunoglobulin (horse), antithmyocyte immunoglobulin (rabbit), sirolimus, leflunomide, alefacept, everolimus, gusperimus, efalizumab, abetimus, natalizumab, abatacept, eculizumab, belimumab, fingolimod, belatacept, teriflunomide, apremilast, vedolizumab, alemtuzumab, begelomab, ocrelizumab, ozanimod, emapalumab, cladribine, imlifidase, siponimod2eclometh, ravulizumab, thalidomide, lenalidomide, pirfenidone, pomalidomide, dimethyl fumarate, darvadstrocel Defined using products cataloged in the WHO Anatomical Therapeutic Chemistry Class L04 “Selective Immunosuppressants” that were not interleukin inhibitors, janus kinase inhibitors, tumor necrosis factor alpha inhibitors or monoclonal antibodies.
Azathioprine	azathioprine
Calcineurin inhibitors	ciclosporin, cyclosporine, tacrolimus, voclosporin
Mycophenolic acid	mycophenolic acid, mycophenolate sodium, mycophenolate mofetil
Anthracyclines	doxorubicin, daunorubicin, epirubicin, aclarubicin, zorubicin, idarubicin, mitoxantrone, pirarubicin, valrubicin, amrubicin, pixantrone
Checkpoint inhibitors	ipilimumab, nivolumab, pembrolizumab, avelumab, atezolizumab, cemiplimab, durvalumab
Cyclophosphamide	cyclophosphamide

Protein kinase inhibitors	imatinib, gefitinib, erlotinib, sunitinib, sorafenib, dasatinib, lapatinib, nilotinib, temsirolimus, everolimus, pazopanib, vandetanib, afatinib, bosutinib, vemurafenib, crizotinib, axitinib, ruxolitinib, ridaforolimus, regorafenib, masitinib, dabrafenib, ponatinib, trametinib, cabozantinib, ibrutinib, ceritinib, lenvatinib, nintedanib, cediranib, palbociclib, tivozanib, osimertinib, alectinib, rociletinib, cobimetinib, midostaurin, olmutinib, binimetinib, ribociclib, brigatinib, lorlatinib, neratinib, encorafenib, dacomitinib, icotinib, abemaciclib, acalabrutinib, quizartinib, larotrectinib, gilteritinib, entrectinib, fedratinib, toceranib
Other cancer therapies	chlorambucil, melphalan, chlormethine, ifosfamide, trofosfamide, prednimustine, bendamustine, busulfan, treosulfan, mannosulfan, thiotepa, triaziquone, carboquone, carmustine, lomustine, semustine, streptozocin, fotemustine, nimustine, ranimustine, uramustine, etoglucid, itobronitol, pipobroman, temozolomide, dacarbazine, methotrexate, raltitrexed, pemetrexed, pralatrexate, mercaptopurine, tioguanine, cladribine, fludarabine, clofarabine, nelarabine, rabacfosadine, cytarabine, fluorouracil, tegafur, carmofur, gemcitabine, capecitabine, azacitidine, decitabine, floxuridine, fluorouracil, tegafur, trifluridine, vinblastine, vincristine, vindesine, vinorelbine, vinflunine, vintafolide, etoposide, teniposide, demecolcine, paclitaxel, docetaxel, paclitaxel poliglumex, cabazitaxel, trabectedin, dactinomycin, bleomycin, plicamycin, mitomycin, ixabepilone, cisplatin, carboplatin, oxaliplatin, satraplatin, polyplatillen, procarbazine, porfimer sodium, methyl aminolevulinate, aminolevulinic acid, temoporfin, efaproxiral, padeliporfin, amsacrine, asparaginase, altretamine, hydroxycarbamide, lonidamine, pentostatin, masoprocol, estramustine, mitoguazone, topotecan, tiazofurine, irinotecan, alitretinoin, mitotane, pegaspargase, bexarotene, arsenic trioxide, denileukin diftitox, bortezomib, anagrelide, oblimersen, sitimagene ceradenovec, vorinostat, romidepsin, omacetaxine mepesuccinate, eribulin, panobinostat, vismodegib, aflibercept, carfilzomib, olaparib, idelalisib, sonidegib, belinostat, ixazomib, talimogene laherparepvec, venetoclax, vosaroxin, niraparib, rucaparib, etirinotecan pegol, plitidepsin, epacadostat, enasidenib, talazoparib, copanlisib, ivosidenib, glasdegib, entinostat, alpelisib, selinexor, tagraxofusp, belotecan, tigilanol tiglate, cytarabine Defined using WHO Anatomical Therapeutic Chemistry Class L01 products that were not anthracyclines, checkpoint inhibitors, cyclophosphamide, or protein kinase inhibitors.
Rituximab	rituximab

Targeted cancer therapies	edrecolomab, trastuzumab, gemtuzumab ozogamicin, cetuximab, bevacizumab, panitumumab, catumaxomab, ofatumumab, brentuximab vedotin, pertuzumab, trastuzumab emtansine, obinutuzumab, dinutuximab beta, blinatumomab, ramucirumab, necitumumab, elotuzumab, daratumumab, mogamulizumab, inotuzumab ozogamicin, olaratumab, bermekimab Defined using monoclonal antibody products in WHO Anatomical Therapeutic Chemistry Class L04 products that were not interleukin, tumor necrosis factor alpha or janus kinase inhibitors.
Oral glucocorticoids	dexamethasone, prednisone, prednisolone, methylprednisolone

eTable 2. Definitions for Variables Included in Propensity Score.

Week of admission	
Contributing data site	
Age at admission	
Sex	As recorded in local electronic health record
Race and ethnicity	Often, self-reported. Operationalized using Census Track designations of Asian, Hispanic or Latinx, non-Hispanic Black, non-Hispanic white, Another race or missing.
Smoking history	Current or former smoker
Body mass index	We used WHO cutpoints to categorize the body mass index (BMI) as underweight, normal weight, overweight, obese or missing. We took the measure closest to the date of, and considered improbable values, which we defined as < 15 kg/m^2 or >70 kg/m^2, as missing data.
Days between COVID-19 diagnosis and hospital admission	
Cardiovascular disease	ICD-10 codes I25.x
Chronic hypertension	ICD-10 codes I10.x
Medications current at the time of admission used to treat risk factors for severe COVID-19 outcomes	
Congestive heart failure	potassium canrenoate, canrenone, eplerenone, metoprolol, sacubitril with valsartan, spironolactone or digoxin

Diabetes	One variable for each of Biguanides (WHO ATC A10BA): phenformin, metformin, buformin Alpha glucosidase inhibitors (WHO ATC A10BF): acarbose, miglitol, voglibose Sulfonylureas (WHO ATC A10BB and A10BC): glibenclamide, chlorpropamide, tolbutamide, glibornuride, tolazamide, carbutamide, glipizide, gliquidone, gliclazide, metahexamide, glisoxepide, glimepiride, acetohexamide, glymidine Thiazolidinediones (WHO ATC A10BG): troglitazone, rosiglitazone, pioglitazone Dipeptidyl peptidase-4 inhibitors (WHO ATC A10BH): sitagliptin, vildagliptin, saxagliptin, alogliptin, linagliptin, gemigliptin, evogliptin Glucagon-like peptide-1 agonists (WHO ATC A10BJ): exenatide, liraglutide, lixisenatide, albiglutide, dulaglutide, semaglutide Sodium-glucose transport protein-2 inhibitors (WHO ATC A10BK): dapagliflozin, canagliflozin, empagliflozin, ertugliflozin, ipraglifozin, sotagliflozin Other oral antidiabetic drugs (WHO ATC A10BX): guar gum, repaglinide, nateglinide, pramlintide, benfluorex, mitiglinide Insulin
Dementia	(WHO ATC N06D) donepezil, galantamine, rivastigmine or memantine

Pulmonary disorders	One variable for each of Short acting beta agonists (WHO ATC R03CC): salbutamol, terbutaline, fenoterol, hexoprenaline, isoetarine, pirbuterol, procaterol, tretoquinol, carbuterol, tulobuterol, bambuterol, clenbuterol Long acting beta agonists (WHO ATC R03AC): bambuterol, clenbuterol, formoterol, indacaterol, olodaterol, salmeterol Inhaled corticosteroids (WHO ATC R03BA): beclometasone, budesonide, flunisolide, betamethasone valerate, fluticasone, triamcinolone acetonide, mometasone, ciclesonide, fluticasone furoate Leukotriene modifiers (WHO ATC R03DC): zafirlukast, pranlukast, montelukast Other drugs for pulmonary disorders (WHO ATC R03): hexoprenaline, tretoquinol, clenbuterol, ipratropium bromide, oxitropium bromide, stramoni, tiotropium bromide, aclidinium bromide, glycopyrronium bromide, umeclidinium bromide, revefenacin, cromoglicic acid, nedocromil, fenspiride, isoprenaline, methoxyphenamine, orciprenaline, fenoterol, hexoprenaline, tretoquinol, reproterol, diprophylline, choline theophyllinate, proxyphylline, theophylline, aminophylline, etamiphylline, theobromine, bamifylline, acefylline piperazine, bufylline, doxofylline, mepyramine theophyllinacetate
Obesity	Orlistat, lorcaserin, phentermine, bupropion with naltrexone, liraglutide
Renal disease	(WHO ATC B03XA, A11CC and V03AE) Erythropoietin, darbepoetin alfa, methoxy polyethylene glycol-epoetin beta, ergocalciferol, dihydrotachysterol, alfacalcidol, calcitriol, sevelamer, lanthanum carbonate, or sucroferric oxyhydroxide

Comorbidities present at admission	Defined using the conditions included in the Charlson Comorbidity Index, using all-available lookback data in the N3C Enclave, which can be as far as January 1, 2018. We used the standard N3C definitions for all conditions, except for HIV where we used the Immunosuppressed Domain Team's definition. Cancer: code set 535274723 Congestive heart failure: 359043664 Dementia: 78746470 Diabetes: 719585646 Diabetes with complications: 403438288 HIV infection: 382527336 Liver disease, mild: 494981955 Liver disease, severe: 248333963 Metastatic cancer: 378462283 Myocardial infarction: 259495957 Paralysis: 489555336 Peptic ulcer disease: 510748896 Pulmonary disorder: 514953976 Peripheral vascular disease: 376881697 Renal disease: 220495690 Rheumatic disease: 765004404 Stroke: 652711186
History of solid organ transplant	Kidney (N3C Enclave code set ID 913892613), liver (204996696), heart (976928531) or lung (335991647). Other less common organ transplants, such as pancreas, were explored but sample size limitations precluded further use.

Drugs were defined using WHO Anatomical Therapeutic Chemical (WHO ATC) class, and diagnoses were defined using ICD-10 codes.

eTable 3. Frequency of Immunosuppressive Drug Classes in Cohort.

	Number of people among the immunosuppressed group (n = 16,494) with drug class current at the time of admission
Rheumatologic drugs	5,366 (33%)
Glucocorticoid with rheumatological condition	4,281 (26%)
Interleukin inhibitors	377 (2%)
Janus kinase inhibitors	85 (1%)
Rituximab with rheumatological condition	132 (1%)
Tumor necrosis factor alpha inhibitors	343 (2%)
Other selective immunosuppressants	994 (6%)
Antimetabolite drugs	4,288 (26%)
Azathioprine	436 (3%)
Calcineurin inhibitors	3,403 (21%)
Mycophenolic acid	2,788 (17%)
Glucocorticoids with solid organ transplant	2,598 (16%)
Cancer therapies	3,569 (22%)
Cyclophosphamide	280 (2%)
Anthracyclines	328 (2%)
Checkpoint inhibitors	159 (1%)
Protein kinase inhibitors	582 (4%)
Other cancer therapies	2,633 (16%)
Targeted cancer therapies	343 (2%)
Rituximab with cancer	186 (1%)
Rituximab without rheumatologic or cancer diagnosis	84 (< 1%)
Glucocorticoid for chronic pulmonary disease	6,828 (42%)

People can be on more than one immunosuppressive drug at a time. Drug categories are defined in eTable 2.

eTable 4. Prevalence of 17 Comorbidities Among Adults Hospitalized with COVID-19.

	Immunosuppressed N = 16,494	Non-immunosuppressed N = 206,081	SMD
Acute myocardial infarction	2,382 (14%)	9,030 (4%)	0.35
Congestive heart failure	4,915 (30%)	20,510 (10%)	0.51
Peripheral vascular disease	3,783 (23%)	15,852 (8%)	0.43
Cerebral vascular accident	3,226 (20%)	15,695 (8%)	0.35
Dementia	827 (5%)	8,426 (4%)	0.04
Pulmonary disease	8,646 (52%)	28,114 (14%)	0.91
Connective tissue disorder	2,827 (17%)	5,975 (3%)	0.49
Peptic ulcer disease	785 (5%)	2,370 (1%)	0.21
Liver disease	3,059 (19%)	10,229 (5%)	0.43
Diabetes	7,728 (47%)	42,928 (21%)	0.57
Diabetes complications	4,569 (28%)	19,305 (9%)	0.49
Paralysis	580 (4%)	2,636 (1%)	0.15
Renal disease	6,397 (39%)	23,375 (11%)	0.67
Cancer	4,465 (27%)	14,168 (7%)	0.56
Metastatic cancer	1,363 (8%)	2,392 (1%)	0.34
Severe liver disease	743 (5%)	2,014 (1%)	0.22
HIV	210 (1%)	1,162 (1%)	0.07

SMD: standardized mean difference, represented as the absolute value.

eTable 5. Laboratory Measures and Vital Signs on Day of Admission, Before and After Propensity Score Matching.

	Before Propensity Score Matching			After Propensity Score Matching		
	Immunosuppressed	Non-immunosuppressed	SMD	Immunosuppressed	Non-immunosuppressed	SMD
Abnormal vital signs in first admitted day						
Fever	537 (8%)	5,672 (10%)	0.04	424 (9%)	1,040 (9%)	0.01
Low mean arterial pressure	22 (1%)	157 (< 1%)	0.02	Fewer than 20 (1%)	35 (< 1%)	0.01
High mean arterial pressure	1,065 (25%)	11,017 (29%)	0.08	814 (25%)	1,962 (26%)	0.01
Low oxygen saturation	968 (14%)	8,932 (16%)	0.05	749 (14%)	2,077 (16%)	0.06
Rapid pulse	1,290 (25%)	10,310 (25%)	0.00	1,039 (26%)	2,230 (23%)	0.05
Rapid breathing	1,610 (26%)	14,851 (27%)	0.02	1,279 (26%)	3,283 (27%)	0.03
Abnormal laboratory measures in first admitted day						
↓ Albumin	2,930 (37%)	35,951 (42%)	0.10	2,280 (37%)	5,608 (39%)	0.05
↑ ALT	2,122 (26%)	32,840 (39%)	0.29	1,721 (27%)	4,614 (31%)	0.09
↑ AST	3,868 (39%)	50,172 (52%)	0.26	3,065 (40%)	7,589 (45%)	0.11
↑ C-reactive protein	2,837 (90%)	30,691 (92%)	0.10	2,243 (90%)	5,341 (91%)	0.05
↑ Creatinine	3,620 (37%)	26,528 (25%)	0.26	2,514 (33%)	5,698 (32%)	0.02
↑ Troponin	2,756 (71%)	22,921 (62%)	0.20	2,109 (69%)	5,006 (68%)	0.04
↑ White blood cells	1,563 (16%)	10,242 (10%)	0.20	1,148 (15%)	1,904 (11%)	0.13
↓ White blood cells	1,479 (15%)	19,763 (19%)	0.09	1,203 (16%)	3,115 (18%)	0.04

ALT: alanine aminotransferase; AST: aspartate aminotransferase; SMD: standardized mean difference, represented as the absolute value. Vital signs and lab values in the table represent individuals with abnormal values above or below referent standard, and the denominator for the proportions exclude persons missing a result. We defined abnormal vital signs within 24 hours of admission (body temperature >38^{0}C, mean arterial pressure < 60mmHg or >100mmHg, oxygen saturation from pulse oximetry < 93%, pulse >99 beats per minute, respiratory rate >22 breaths per minute) and abnormal lab results within 24 hours of admission (albumin < 3.5 g/dL, alanine aminotransferase (ALT) > 35 u/L, C-reactive protein > 8 mg/L, creatinine > 1.3 mg/dL, detectable troponin, white blood cell count < 4 cells per 10^3/uL or > 11 cells per 10^3/uL).[25]

eTable 6. E-Values for Strength of Association Between Immunosuppressive Medication Classes and Clinical Outcomes in COVID.

	E-value	
	Invasive Mechanical Ventilation	In-Hospital Death
Rheumatologic drugs	2.26	1.11
Glucocorticoid with rheumatological condition	1.63	1.25
Interleukin inhibitors	2.30	2.00
Janus kinase inhibitors	2.78	4.19
Rituximab with rheumatological condition	2.37	2.83
Tumor necrosis factor alpha inhibitors	2.04	1.16
Other selective immunosuppressants	2.08	1.46
Antimetabolite drugs	1.85	1.25
Azathioprine	2.50	2.12
Calcineurin inhibitors	2.40	1.32
Mycophenolic acid	1.67	1.39
Glucocorticoids with solid organ transplant	2.66	1.29
Cancer therapies	2.08	1.16
Cyclophosphamide	2.08	1.97
Anthracyclines	3.18	1.69
Checkpoint inhibitors	2.08	2.39
Protein kinase inhibitors	2.17	1.60
Other cancer therapies	1.50	4.58
Targeted cancer therapies	2.30	1.46
Rituximab with cancer	2.00	1.31

The e-value is calculated as HR + sqrt(HR x (HR – 1)), where HR = hazard ratio. In cases where the hazard ratio was less than 1, the inverse of the hazard ratio is used to calculate the e-value.

eTable 7. Hazard ratios and 95% confidence intervals for the association between long-term immunosuppression and invasive mechanical ventilation, by medication class

	Hazard Ratio (95% Confidence Interval) Comparing Immunosuppressed to Non-Immunosuppressed Persons
Rheumatologic drugs	**0.69 (0.57-0.84)**
Glucocorticoid with rheumatological condition	**0.85 (0.75-0.97)**
Interleukin inhibitors	0.68 (0.45-1.02)
Janus kinase inhibitors	0.59 (0.19-1.86)
Rituximab with rheumatological condition	1.50 (0.85-2.64)
Tumor necrosis factor alpha inhibitors	0.74 (0.47-1.18)
Other selective immunosuppressants	**0.73 (0.57-0.93)**
Antimetabolite drugs	**0.79 (0.68-0.92)**
Azathioprine	**0.64 (0.43-0.95)**
Calcineurin inhibitors	**0.66 (0.55-0.78)**
Mycophenolic acid	0.84 (0.70-1.008)
Glucocorticoids with solid organ transplant	**0.61 (0.49-0.77)**
Cancer therapies	**0.73 (0.63-0.85)**
Cyclophosphamide	**0.53 (0.31-0.89)**
Anthracycline	0.73 (0.47-1.14)
Checkpoint inhibitor	0.73 (0.33-1.61)
Protein kinase inhibitors	**0.71 (0.51-0.994)**
Other antineoplastics	**0.75 (0.63-0.88)**
Targeted cancer therapies	0.68 (0.43-1.06)
Rituximab with cancer	0.89 (0.51-1.58)

eTable 8. Hazard ratios and 95% confidence intervals for the association between long-term immunosuppression and in-hospital death, by medication class

	Hazard Ratio (95% Confidence Interval) Comparing Immunosuppressed to Non-Immunosuppressed Persons
Rheumatologic drugs	1.01 (0.86-1.20)
Glucocorticoid with rheumatological condition	0.96 (0.86-1.07)
Interleukin inhibitors	0.75 (0.48-1.17)
Janus kinase inhibitors	**0.42 (0.24-0.73)**
Rituximab with rheumatological condition	**1.72 (1.10-2.69)**
Tumor necrosis factor alpha inhibitors	1.02 (0.61-1.69)
Other selective immunosuppressants	1.11 (0.92-1.35)
Antimetabolite drugs	0.96 (0.83-1.10)
Azathioprine	0.72 (0.48-1.08)
Calcineurin inhibitors	0.94 (0.79-1.11)
Mycophenolic acid	0.92 (0.75-1.12)
Glucocorticoids with solid organ transplant	0.95 (0.74-1.22)
Cancer therapies	1.02 (0.93-1.11)
Cyclophosphamide	1.20 (0.77-1.88)
Anthracycline	1.51 (0.989-2.30)
Checkpoint inhibitor	1.33 (0.82-2.15)
Protein kinase inhibitors	0.86 (0.68-1.09)
Other antineoplastics	1.06 (0.95-1.18)
Targeted cancer therapies	1.11 (0.81-1.52)
Rituximab with cancer	**2.57 (1.86-3.56)**

eTable 9. Results from Sensitivity Analyses.

	Invasive Mechanical Ventilation[1]	In-Hospital Death
Restricting glucocorticoid definition to persons with dose information available	**0.79 (0.69-0.89)**	1.06 (0.95-1.17)
Restricting Cohort to Persons With At Least 1 Prior Encounter With Health System Prior to COVID-19 Hospitalization	0.93 (0.86-1.000)	0.97 (0.91-1.03)
Restricting Cohort to Persons With Minimum 2 Days Length of Stay	**0.89 (0.83-0.96)**	0.97 (0.91-1.03)
Adding Laboratory Measures and Vitals Signs from Day of Admission	0.96 (0.89-1.03)	0.96 (0.90-1.01)
Varying Ventilation Onset Definition to latest date in range[1]	**0.86 (0.80-0.92)**	**--**

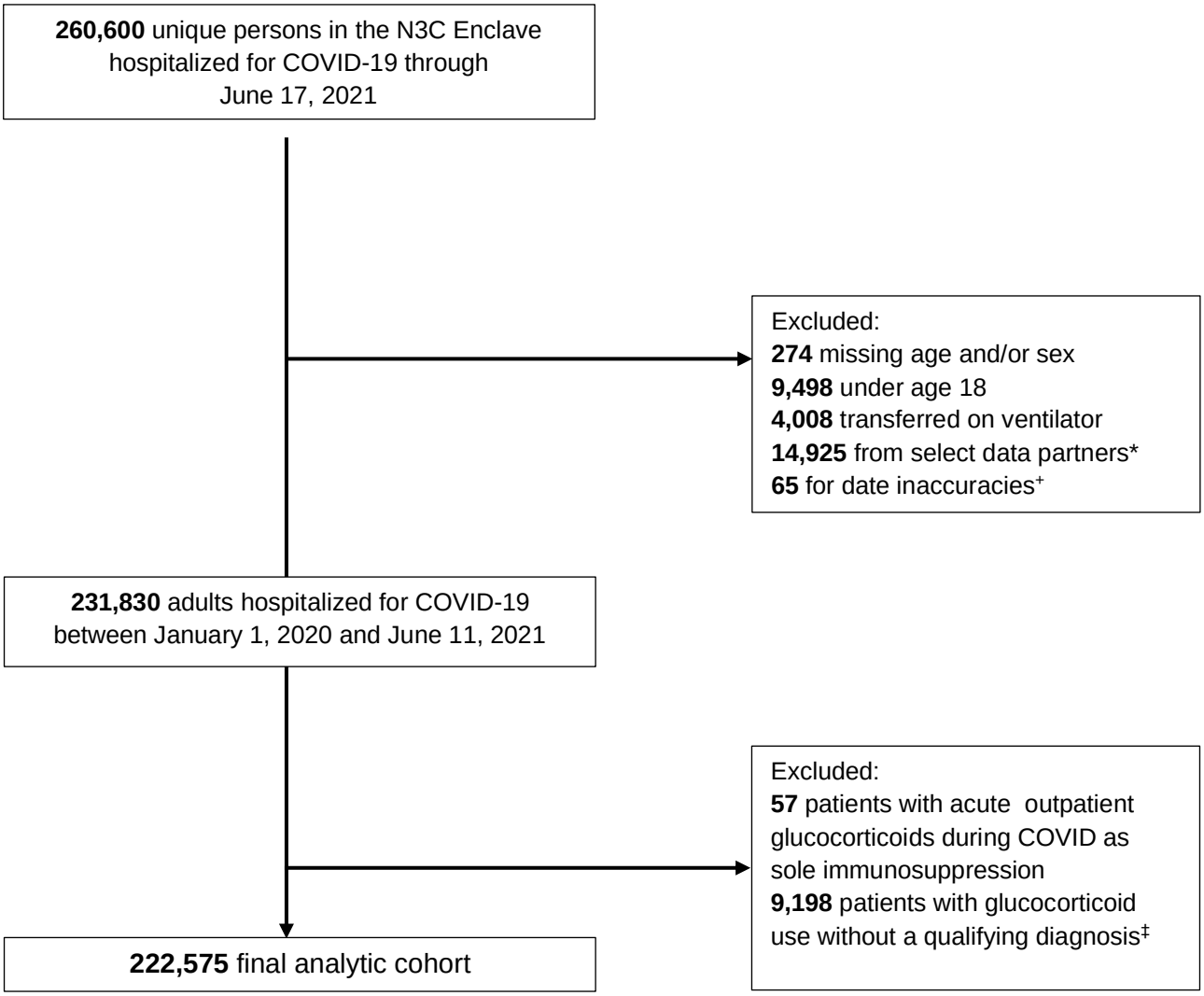
1 For 4% of the cohort, their first code indicating invasive ventilation indicated ventilation placement in the range of 24-96 hours prior. For these people, in this sensitivity analysis, we used 96 hours. For 7% of the cohort, the first code indicating invasive ventilation had been placed “greater than 96 hours”. For these people, in this sensitivity analysis, we used the date of admission as the earliest possible date at risk.

eTable 10. Association Between Chronic Immunosuppression and Clinical Outcomes in COVID, for Race and Ethnicity Groups.

	Hazard Ratio (95% Confidence Interval) Comparing Immunosuppressed to Non-Immunosuppressed Persons	
	Invasive Mechanical Ventilation	In-Hospital Death
Asian	0.72 (0.42-1.24)	0.65 (0.36-1.20)
Hispanic or Latinx	0.95 (0.77-1.18)	1.10 (0.90-1.34)
Non-Hispanic Black	**0.82 (0.70-0.95)**	0.88 (0.76-1.02)
Non-Hispanic white	0.90 (0.82-1.000)	0.97 (0.90-1.04)
Another race*	1.29 (0.45-3.73)	1.28 (0.56-2.91)
Missing or unknown race	**0.68 (0.55-0.84)**	1.02 (0.86-1.21)

*We created the category of “Another race” due to sample size limitations. The category includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and Other.

eFigure 1. Analytic Cohort Derivation.



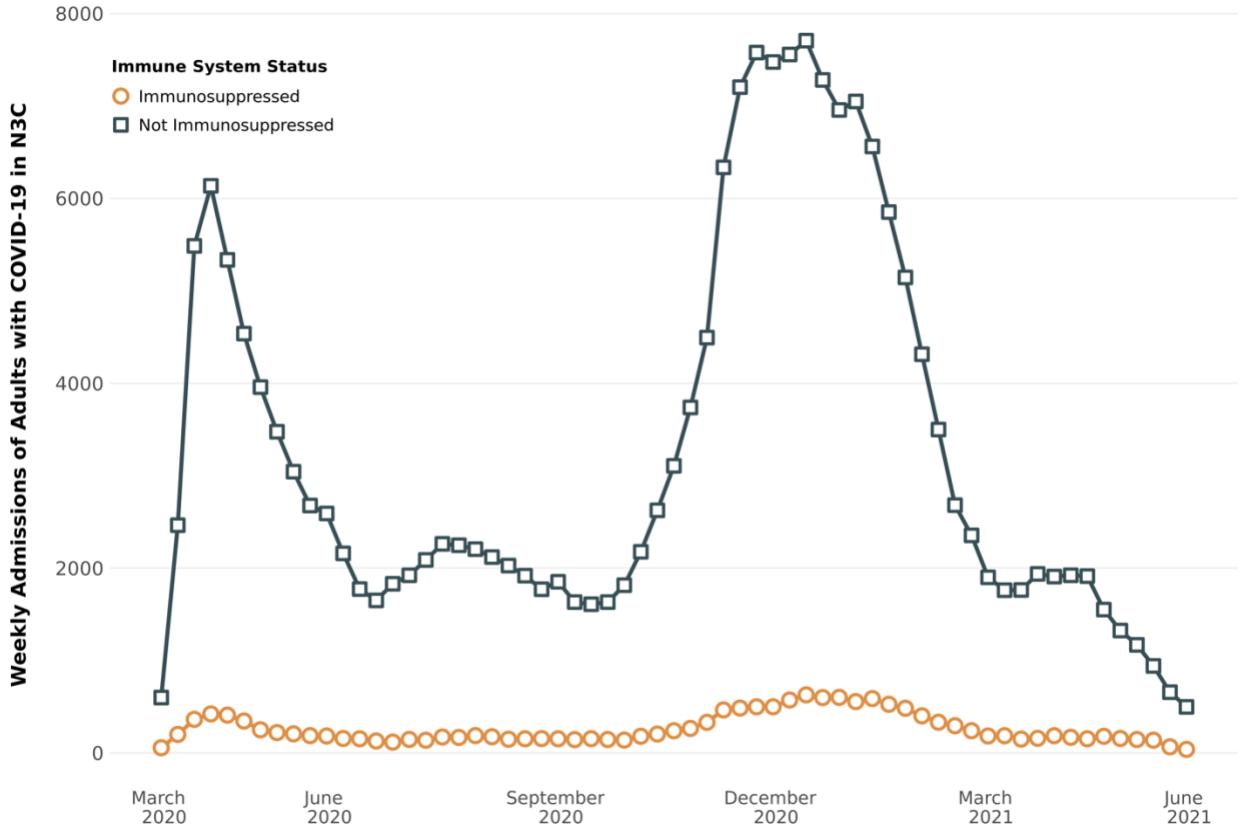
N3C: National COVID Cohort Collaborative.

* In accordance with N3C data quality procedures, we excluded six data partner sites: one with overall data quality concerns, one that shifted dates by up to 90 days before sending data to the N3C, three sites with over 100 hospitalized COVID-positive adults yet zero recorded deaths, and one site with over 100 COVID-positive adults yet zero recorded as receiving invasive mechanical ventilation.

+ Date inaccuracies included persons with a date of COVID diagnosis before January 1, 2020, a date of death before January 1, 2020, or a date of death that preceded date of admission.

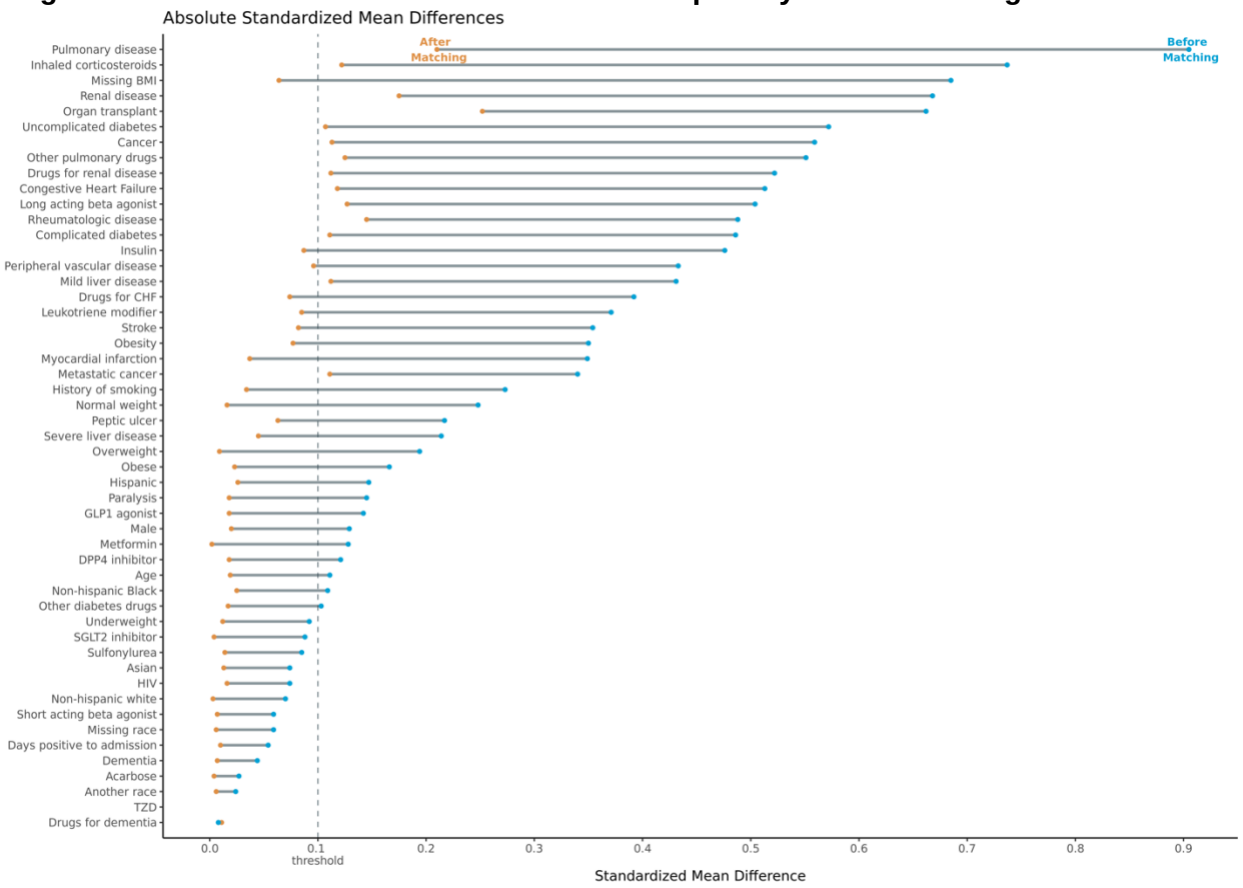
‡ Diagnoses that would suggest chronic glucocorticoid use were psoriasis, ulcerative colitis, rheumatoid arthritis, chronic obstructive pulmonary disease, asthma, systemic lupus erythematosus, vasculitis, ankylosing spondylitis, axial spondyloarthropathy, psoriatic arthritis, or a history of solid organ transplantation.

eFigure 2. Weekly Volume of Admissions in the N3C, March 18, 2020 through June 2, 2021.

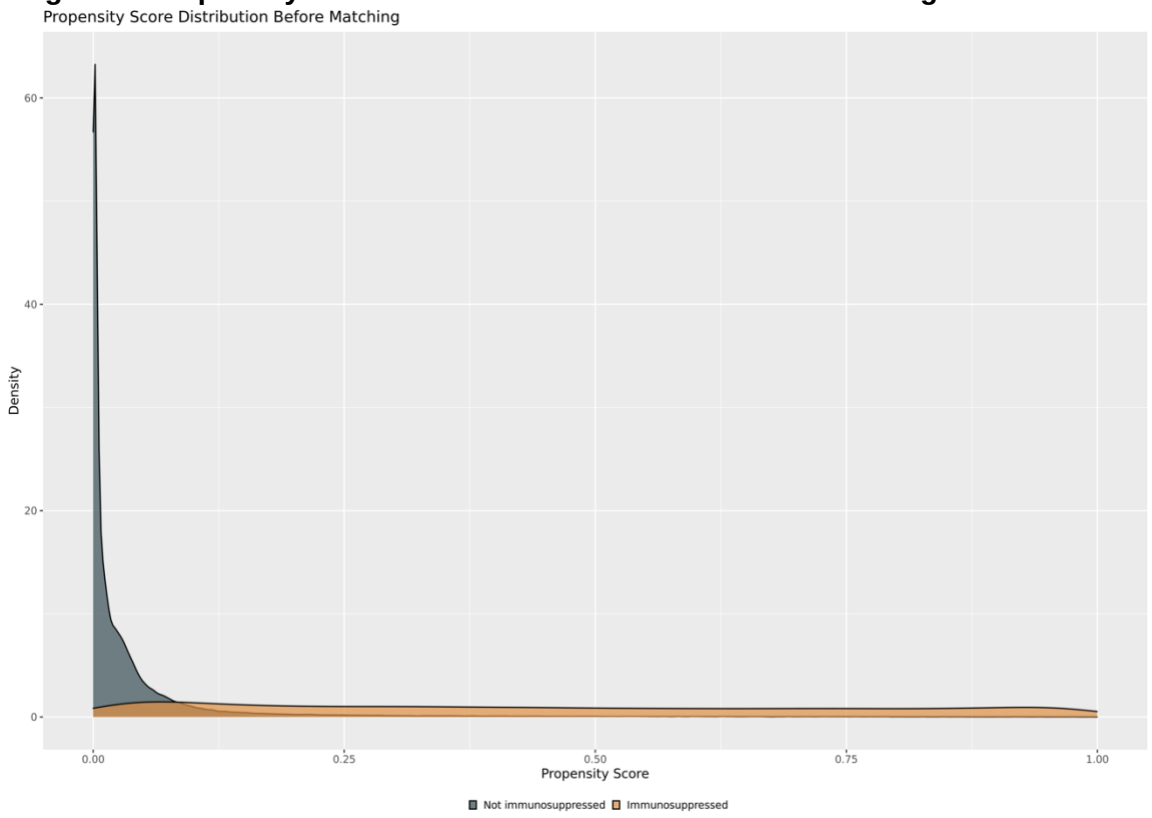


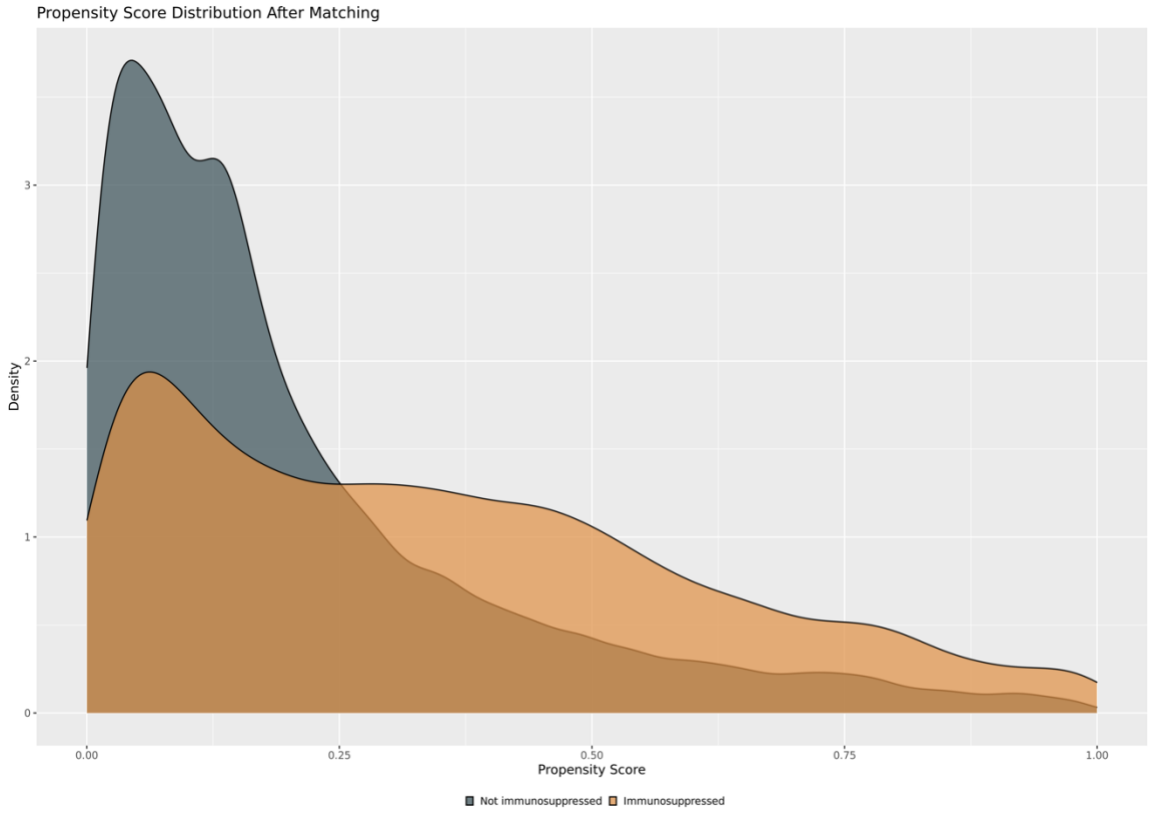
As per N3C data policies, data are suppressed for weeks before March 18, 2020 and after June 2, 2021, as at least one group had 20 or fewer people.

eFigure 3. Covariate Balance Before and After Propensity Score Matching.

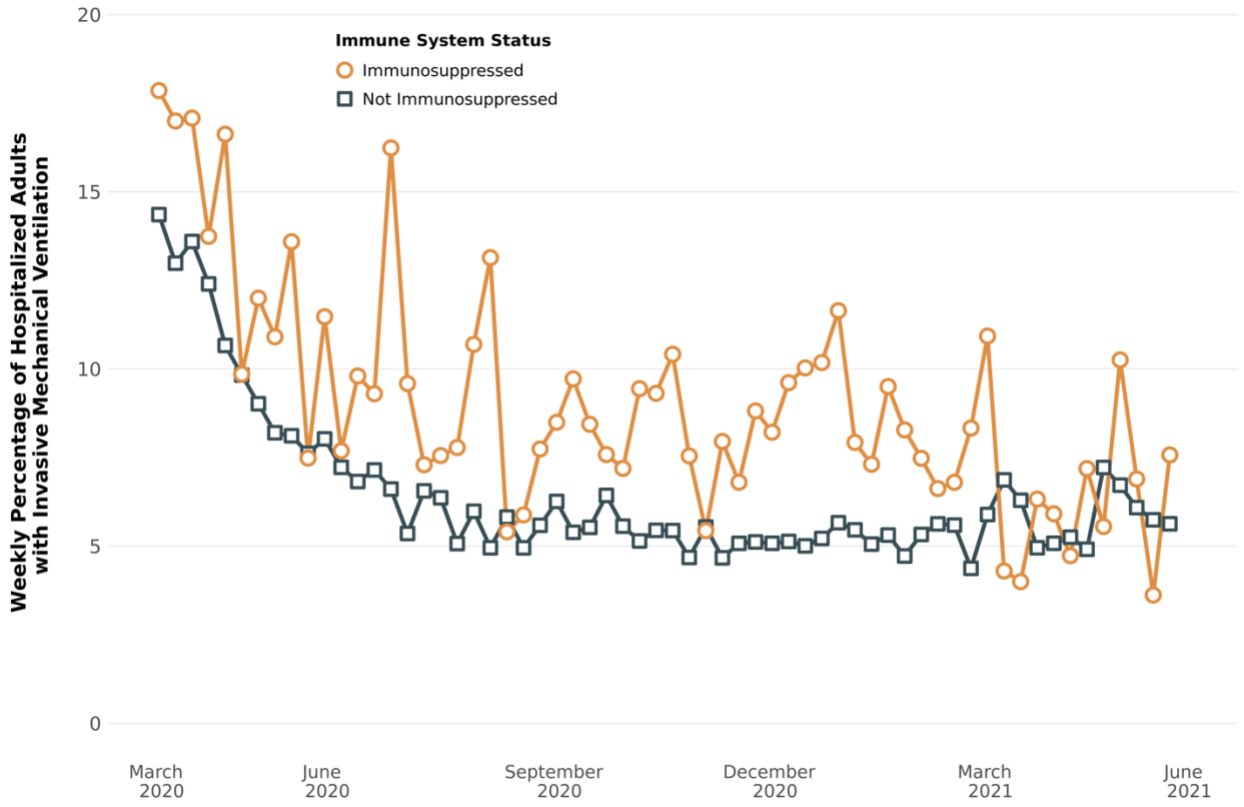


eFigure 4. Propensity Score Distribution Before and After Matching.



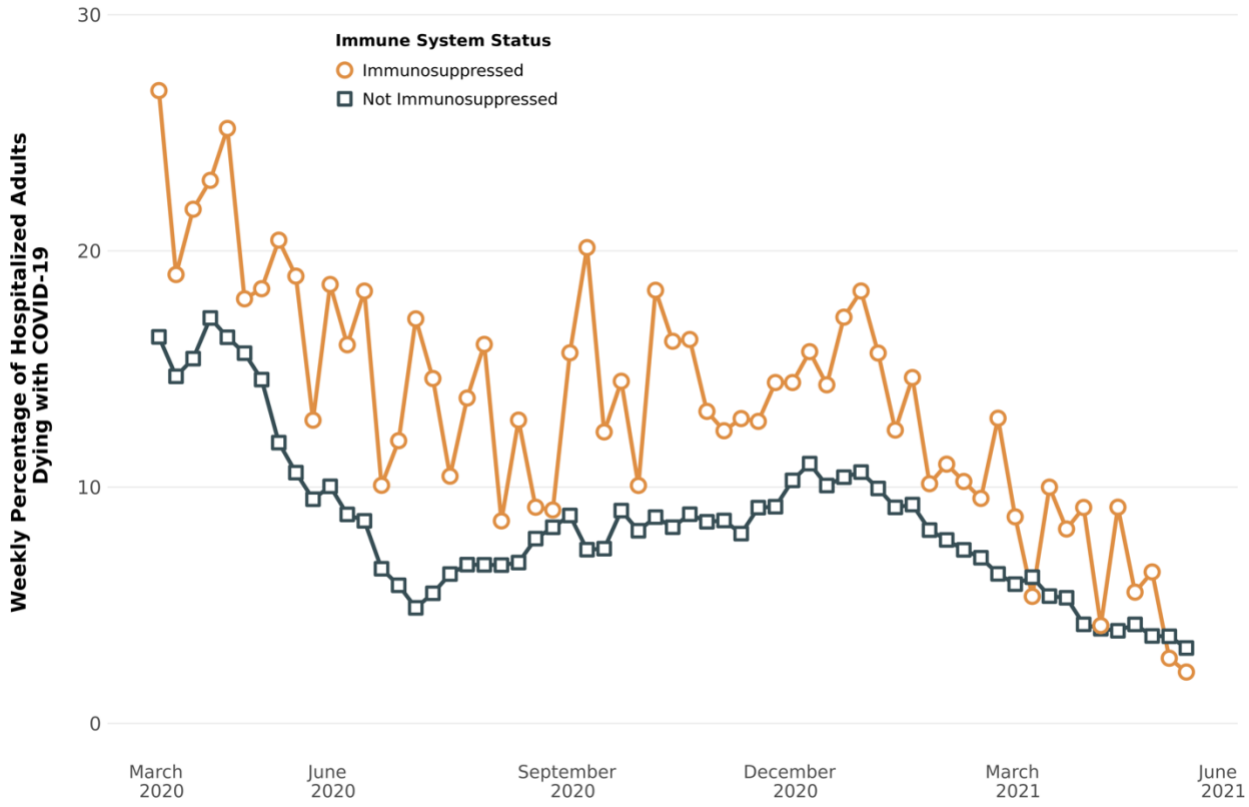


eFigure 5. Weekly Percentage of Hospitalized Adults with Invasive Mechanical Ventilation, by Immune System Status.



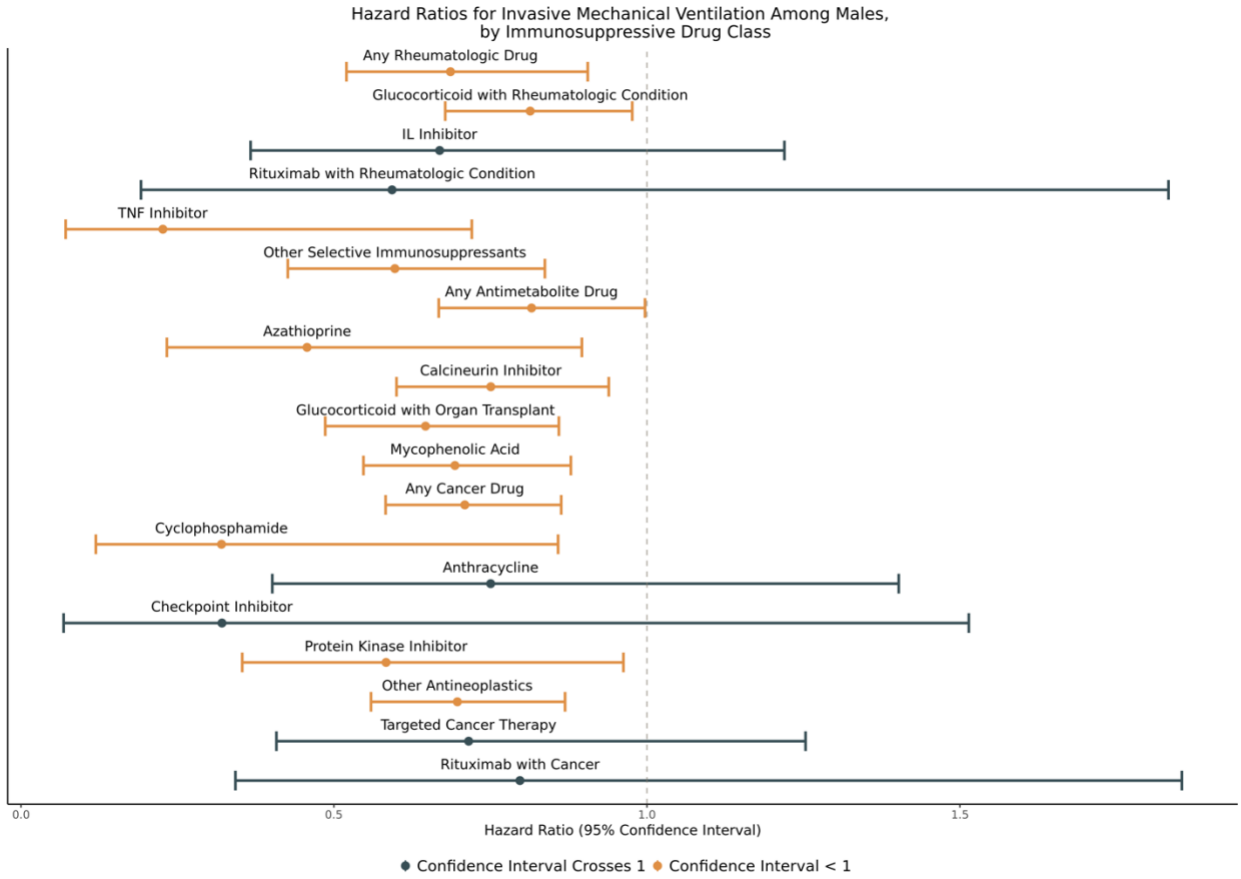
This graph does not present data before March 18, 2020 and after June 2, 2021, where the small number of people at risk may not accurately reflect patterns.

eFigure 6. Weekly Percentage of Hospitalized Adults Dying with COVID-19, by Immune System Status.



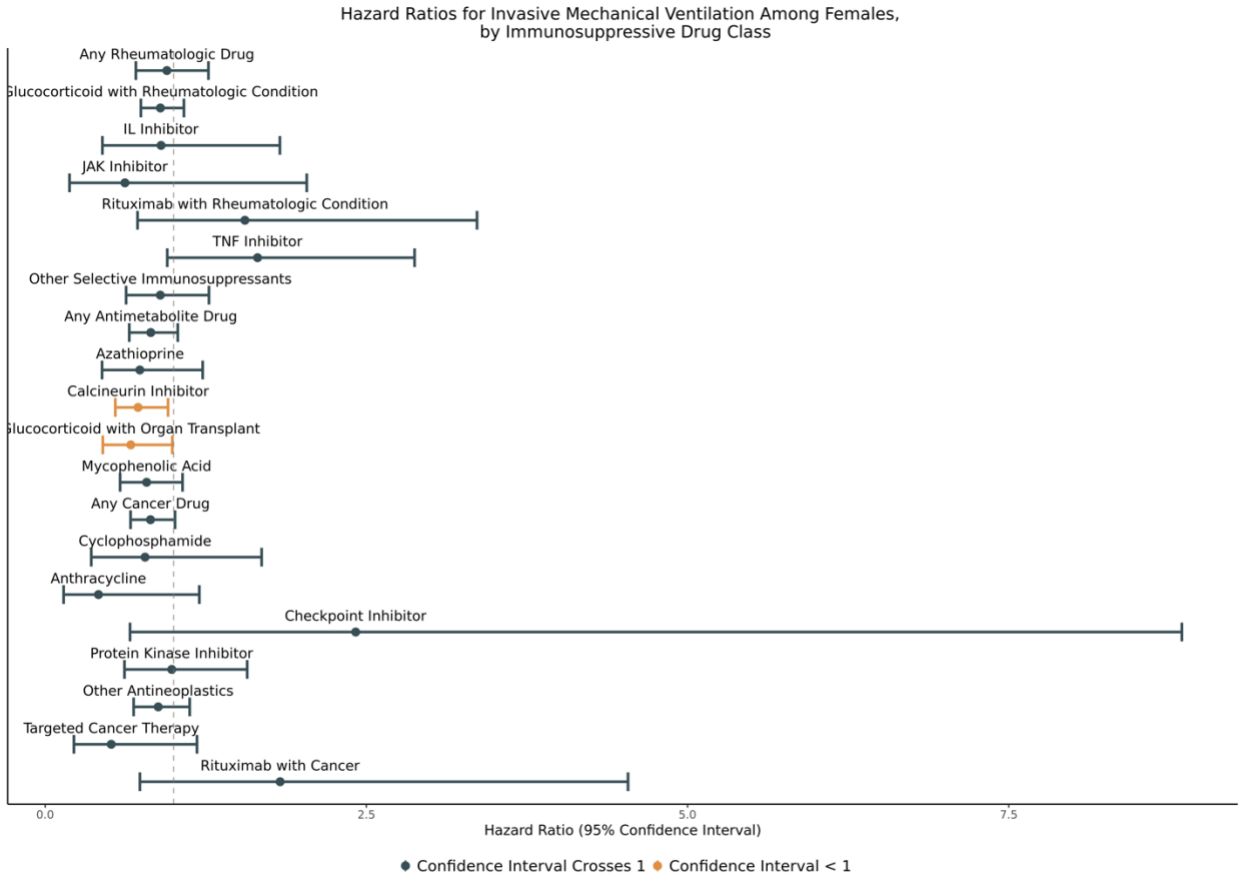
This graph does not present data before March 18, 2020 and after June 2, 2021, where the small number of people at risk may not accurately reflect patterns.

eFigure 7. Association Between Chronic Immunosuppression and Invasive Mechanical Ventilation Among Males, by Medication Classes.

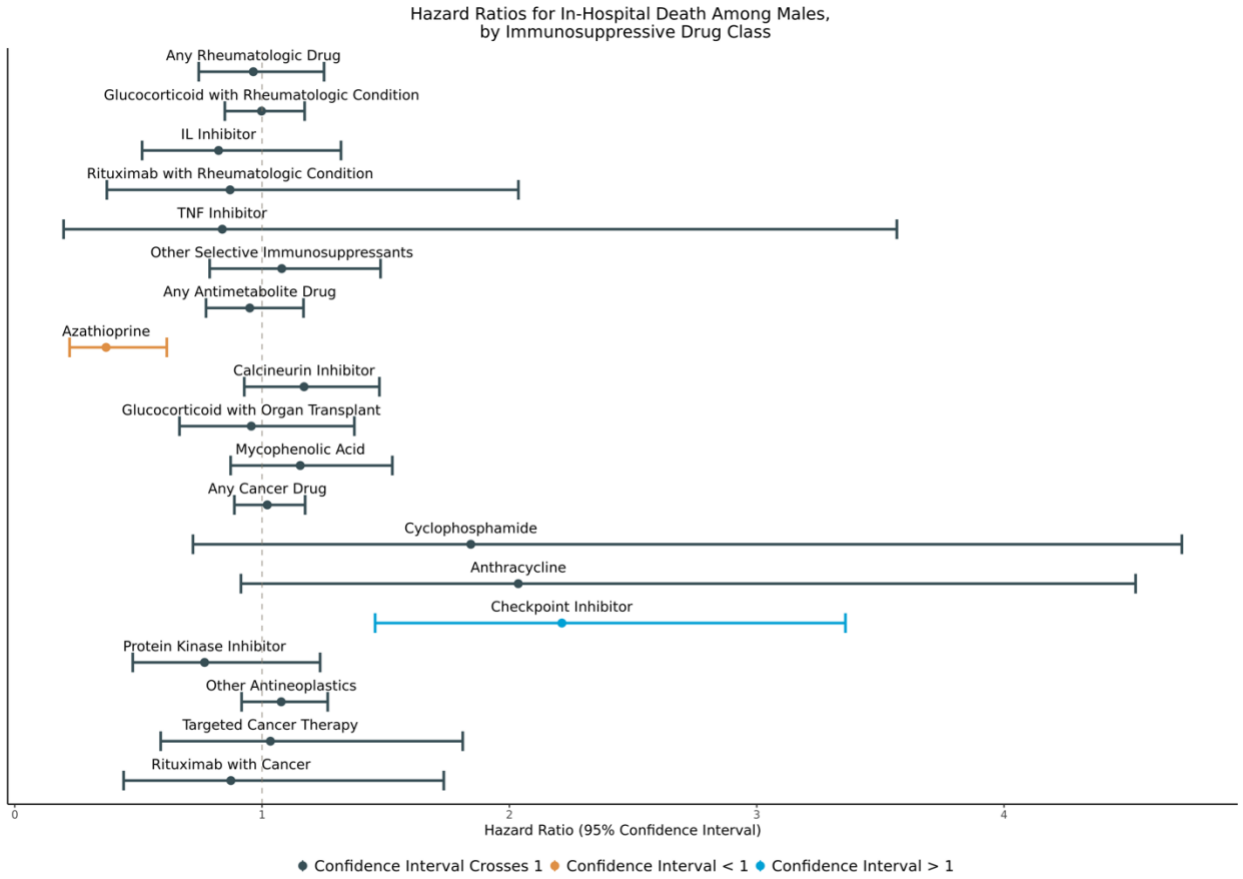


The hazard ratio calculated for janus kinase (JAK) inhibitors was 4.90 (95% confidence interval 0.44-54.97), and is not represented on this plot.

eFigure 8. Association Between Chronic Immunosuppression and Invasive Mechanical Ventilation Among Females, by Medication Classes.

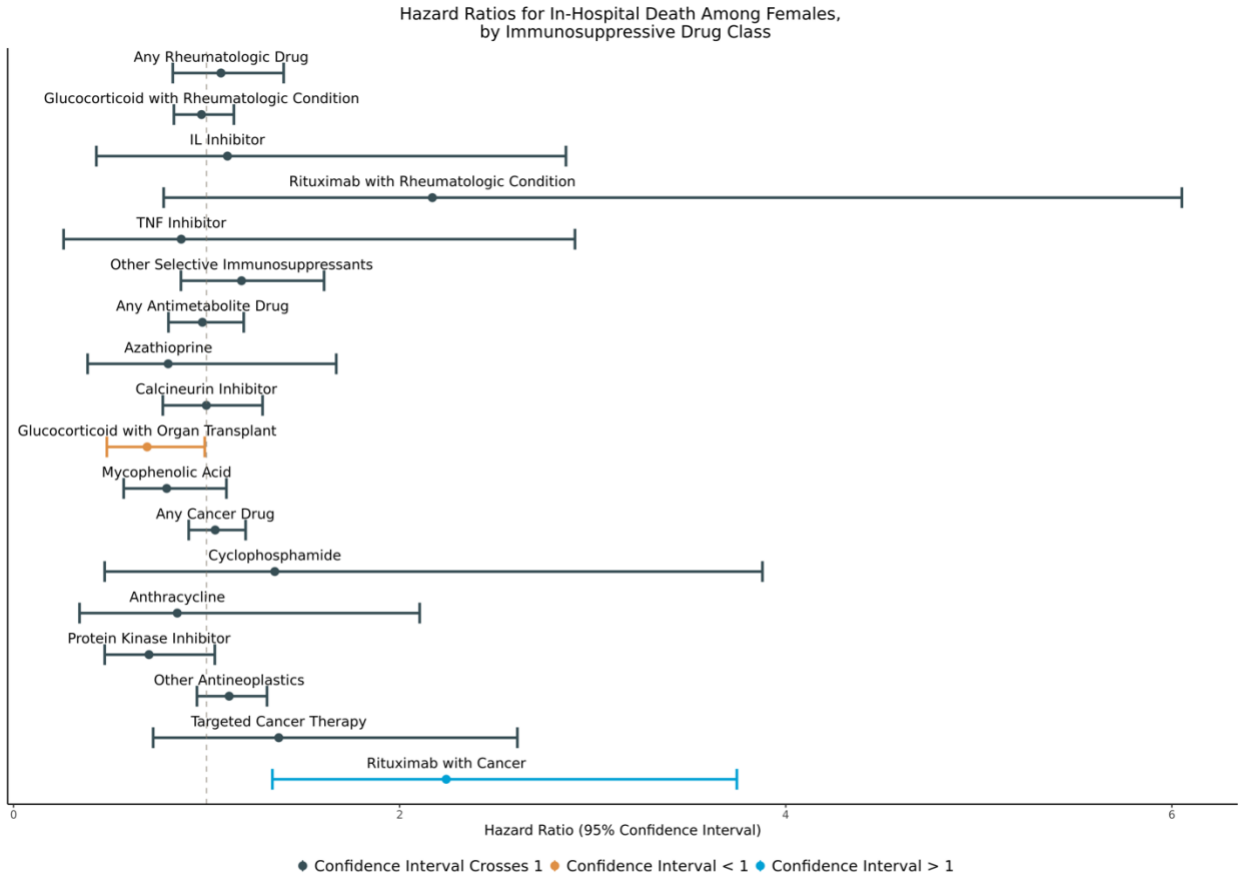


eFigure 9. Association Between Chronic Immunosuppression and In-Hospital Death Among Males, by Medication Classes.



There were no males with janus kinase (JAK) inhibitors who required invasive mechanical ventilation in the propensity score matched cohort.

eFigure 10. Association Between Chronic Immunosuppression and In-Hospital Death Among Females, by Medication Classes.



The hazard ratio calculated for checkpoint inhibitors was 2.89 (95% confidence interval 0.71-11.76), and is not represented on this plot.