

Appendix

Appendix to ‘The effect of immunosuppressants on the prognosis of SARS-CoV-2 infection: a nationwide Danish cohort study.’

Table of Contents

Investigators	3
Appendix Table A1	4
Appendix Table A2	5
Appendix Table A3	6
Appendix Table A4	9
Appendix Table A5	9
Appendix Table A6	10
Appendix Table A7	10
Appendix Table A8	11
Appendix Table A9	12
Appendix Table A10	13
Appendix Table A11	14
Appendix Table A12	14
Appendix Figure A1	15
Appendix Table A13	16
Appendix Table A14	17
Appendix Table A15	18
Appendix Table A16	19
Appendix Table A17	20
Appendix Table A18	21
Appendix Table A19	22
Appendix Table A20	23
Appendix Table A21	24
Appendix Methods	25
INTRODUCTION	25
RESULTS	25
PROOF	25
Appendix Table S1.	25
Appendix Table S2.	26
Appendix Figure A2.	27

Investigators

Daniel Ward (0000-0003-0405-7250), Sanne Gørtz, Martin Thomsen Ernst (0000-0001-9003-3823), Nynne Nyboe Andersen (0000-0003-0874-0356), Susanne K Kjær (0000-0002-8347-1398), Jesper Hallas (0000-0002-8097-8708), Steffen Christensen, Christian Fynbo Christiansen (0000-0002-0727-953X), Simone Bastrup Israelsen, Thomas Benfield (0000-0003-0698-9385), Anton Pottegård (0000-0001-9314-5679), Tine Jess (0000-0002-4391-7332).

Department of Epidemiology Research, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen, Denmark;
Center for Molecular Prediction of Inflammatory Bowel Disease (PREDICT), Department of Clinical Medicine, Aalborg University, Copenhagen, Denmark.

Daniel Ward
doctoral student

Department of Epidemiology Research, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen, Denmark

Sanne Gørtz
statistician

Department of Public Health, Clinical Pharmacology, Pharmacy and Environmental Medicine, University of Southern Denmark, J.B. Winsløvs Vej 19, 5000 Odense, Denmark

Martin Thomsen Ernst
data manager

Department of Medical Gastroenterology and Hepatology, Rigshospitalet, Inge Lehmanns Vej 5, 2100 Copenhagen, Denmark

Nynne Nyboe Andersen
Senior registrar

Unit of Virus, Lifestyle and Genes, Danish Cancer Society Research Center, Strandboulevarden 9, 2100 Copenhagen, Denmark

Susanne K Kjær
professor

Research Unit of Clinical Pharmacology, University of Southern Denmark, J.B. Winsløvs Vej 9, 5000 Odense, Denmark

Jesper Hallas
professor

Department of Intensive Care, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus, Denmark

Steffen Christensen
Associate professor

Department of Clinical Epidemiology, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus, Denmark

Christian Fynbo Christiansen
Associate professor

Center of Research & Disruption of Infectious Diseases (CREDID), Department of Infectious Diseases, Copenhagen University Hospital, Amager and Hvidovre Hospital, Kettergård Allé 30, 2650 Hvidovre, Denmark

Simone Elisabeth Bastrup Israelsen
Doctoral student

Center of Research & Disruption of Infectious Diseases (CREDID), Department of Infectious Diseases, Copenhagen University Hospital, Amager and Hvidovre Hospital, Kettergård Allé 30, 2650 Hvidovre, Denmark

Thomas Benfield
professor

Department of Clinical Pharmacology and Pharmacy, University of Southern Denmark, J.B. Winsløvs Vej 9, 5000 Odense, Denmark

Anton Pottegård
Professor

Department of Epidemiology Research, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen, Denmark;
Center for Molecular Prediction of Inflammatory Bowel Disease (PREDICT), Department of Clinical
Medicine, Aalborg University, Copenhagen, Denmark.

Tine Jess
professor

Correspondence to: Daniel Ward

email: djwa@dcm.aau.dk

Telephone: 0045 4278 4188

Address: Center for Molecular Prediction of Inflammatory Bowel Disease (PREDICT),
Department of Clinical Medicine, Aalborg University, Copenhagen, Denmark.

Appendix Table A1. Medications studied as exposures and corresponding ATC and procedure codes.

Medication	ATC code	Procedure code
Selective immunosuppressants		
Muromonab-CD3	L04AA02	
Antilymphocyte immunoglobulin (horse)	L04AA03	
Antithymocyte immunoglobulin (rabbit)	L04AA04	BOHJ12
Mycophenolic acid	L04AA06	BOHJ22
Sirolimus	L04AA10	BOHJ23
Leflunomide	L04AA13	
Everolimus	L04AA18	BOHJ24
Natalizumab	L04AA23	BOHJ26
Abatacept	L04AA24	BOHJ18C1
Eculizumab	L04AA25	BWHB84
Belimumab	L04AA26	BOHJ19H6
Fingolimod	L04AA27	BOHJ27
Belatacept	L04AA28	
Tofacitinib	L04AA29	BOHJ28D
Teriflunomide	L04AA31	BOHJ28A
Aprelimast	L04AA32	
Vedolizumab	L04AA33	BOHJ19H4
Alemtuzumab	L04AA34	BOHJ16A
Ocrelizumab	L04AA36	
Baricitinib	L04AA37	
Ozanimod	L04AA38	
Emapalumab	L04AA39	
Cladribine	L04AA40	BWHA178
Imlifidase	L04AA41	
Siponimod	L04AA42	BWHB87
Ravulizumab	L04AA43	
Upadacitinib	L04AA44	
Tumor necrosis factor inhibitors		
Etanercept	L04AB01	BOHJ18A2
Infliximab	L04AB02	BOHJ18A1
Adalimumab	L04AB04	BOHJ18A3
Certolizumab pegol	L04AB05	BOHJ18A5
Golimumab	L04AB06	BOHJ18A4
Interleukin inhibitors		
Basiliximab	L04AC02	
Anakinra	L04AC03	BOHJ18B1
Ustekinumab	L04AC05	BOHJ18B3
Tocilizumab	L04AC07	BOHJ18B2
Canakinumab	L04AC08	BOHJ18B4
Secukinumab	L04AC10	BOHJ18B5
Siltuximab	L04AC11	
Brodalumab	L04AC12	BOHJ18B6
Ixekizumab	L04AC13	
Sarilumab	L04AC14	BOHJ18B9
Guselkumab	L04AC16	
Tildrakizumab	L04AC17	BOHJ18B7
Risankizumab	L04AC18	BOHJ19N1
Calcineurin inhibitors		
Ciclosporin	L04AD01	BOHJ20
Tacrolimus	L04AD02	BOHJ21
Other immunosuppressants		
Azathioprine	L04AX01	BWHB83
Thalidomide	L04AX02	BWHB81
Methotrexate	L04AX03	BWHA115

Lenalidomide	L04AX04	BWHB82
Pirfenidone	L04AX05	BWHB85
Pomalidomide	L04AX06	BWHB86
Dimethyl fumarate	L04AX07	BOHJ28B
Darvadstrocel	L04AX08	
Systemic glucocorticoids	H02AB	
Aminoquinolines		
Chloroquine	P01BA01	
Hydroxychloroquine	P01BA02	
Rituximab	L01XC02	

Abbreviations: ATC; anatomical therapeutic chemicals.

Appendix Table A2. Minimum daily dose of glucocorticoids in exposed persons

Compound	Equivalent dose
Cortisone	38 mg
Hydrocortisone	30 mg
Prednisone	7.5 mg
Prednisolone	7.5 mg
Triamcinolone	6 mg
Methylprednisolone	6 mg
Betamethasone	1.2 mg
Dexamethasone	1.2 mg

Appendix Table A3. Covariates for propensity scores.

Variable	Categories/ ATC/ICD codes	Time window prior to prior to cohort entry
<i>Demographics</i>		
Date of birth	Restricted cubic spline with 3 knots	
Sex	Male/female	
<i>Healthcare utilisation</i>		
Hospital admissions and outpatient contacts	0, 1-2, 3-5, 6+	1 year before cohort entry date
Date of SARS-COV-2 testing	Restricted cubic spline with 3 knots	
<i>Co-medications</i>		
Antianaemic drugs	B03	Since 1994
Cardiovascular drugs	C01-10	Since 1994
Antimicrobials	J01-06	Since 1994
Anticoagulants	B01AA	Since 1994
Drugs used in diabetes	A10	Since 1994
Drugs for obstructive airway diseases	R03	Since 1994
<i>Conditions indicating immunosuppressive therapy</i>		
Neoplasms, blood and blood-forming organs Paroxysmal nocturnal haemoglobinuria Sarcoidosis Osteomyelofibrosis (Castleman's disease) Multiple myeloma	DD595 DD86 DD474 DC900	All since 1994
Neurological and musculoskeletal disease Seronegative arthritis Seropositive arthritis Psoriatic arthropathy Juvenile idiopathic arthritis Generalized connective tissue diseases Spondylopathies Diseases of the muscles Soft-tissue rheumatism Neuromuscular and muscular disease Multiple sclerosis	DM05 DM06 DM07 DM08 DM30-36 DM45-49 DM60-63 DM70-79 DG70-73 DG35	All since 1994
Solid organ transplantation Kidney transplanted Heart transplanted Lung transplanted Heart and lung transplanted Liver transplanted	DZ940 DZ941 DZ942 DZ943 DZ944	All since 1994
Pulmonary disease Chronic disease of the lower airways Other interstitial lung disease Diseases with pus and necrosis in the lower airway Interstitial lung emphysema compensatory emphysema	DJ4 DJ84 DJ85 DJ982 DJ983	All since 1994
Liver disease	DK7	All since 1994
Kidney disease Glomerular disease Tubulointerstitial kidney disease and kidney insufficiency	DN0 DN1	All since 1994
Diseases of the gastrointestinal tract Crohn's disease Ulcerative colitis Cholangitis	DK50 DK51 DK830	All since 1994
Skin disease Hidradenitis suppurativa Psoriasis Bullous skin disease Dermatitis and eczema Alopecia areata Vitiligo Granulomatous disease in the skin and subcutaneous tissue Lupus Other localised connective tissue disease Vasculitis limited to the skin	DL73.2 DL40 DL10-14 DL20-30 DL63 DL80 DL92 DL93 DL94 DL95	All since 1994
<i>Other comorbidities</i>		
Cardiovascular disease Ischaemic heart disease Diseases of the endocardium, pericardium and valves	DI2 DI3	All since 1994

Diseases of the endocardium, conductive tissue and cardiac arrest Vascular disease in the brain Heart failure Disease the arteries, arterioles and capillaries Oesophageal varices Abdominal varices Hypertensive liver disease Vascular disease in the bowel	DI4 DI5 DI6 DI7 DI85 DI864 DI12 DK550	
<i>Indicators of severity of the underlying disease</i>		
Medications for immune-mediated inflammatory diseases Intestinal corticosteroids Aminosalicylic acid and similar agents Topical corticosteroids Antipsoriatic medications Anti-rheumatic therapies, non-steroidals, and combination medications	A07EA A07EC D07 D05 M01	1 year before cohort entry
Gastrointestinal pathologies Gingivitis and periodontal disease Inflammation of the oral mucosa and related Stomach and duodenal ulcers Fissure and rifts in and around the anus Abscess in and around the anus Other diseases of the rectum and anus Other bowel disease	DK05 DK12 DK25-27 DK60 DK61 DK62 DK63	All since 1994
Procedures on the skin, GI tract, or joints Ultraviolet therapy: UV-A with psoralen/broad-spectrum UVB / narrow-spectrum UVB Operations on the skin or subcutaneous tissue Drainage of pelvic abscess to the rectum Lysis of adhesions in the abdominal cavity Operations of the small intestine and colon Operations on the rectum Operations on the anus and perianal tissue Closure of intestinovaginal fistula with graft or flap Closure of vesicointestinal fistula Endoscopy of the gastro-intestinal tract Shoulder and upper arm Primary insertion of joint prosthesis Secondary insertion of joint prosthesis Operations on the joint capsule and ligaments Operations of the synovia and joint surface Joint resections, arthroplasties, and arthrodesis Excision of bursa Elbow and lower arm Primary insertion of joint prosthesis Secondary insertion of joint prosthesis Operations on the joint capsule and ligaments Operations of the synovia and joint surface Joint resections, arthroplasties, and arthrodesis Excision of bursa Wrist and hand Primary insertion of joint prosthesis Secondary insertion of joint prosthesis Operations on the joint capsule and ligaments Operations of the synovia and joint surface Joint resections, arthroplasties, and arthrodesis Operations on the fascia, tendon sheaths, ganglia and bursae Hip and thigh Primary insertion of joint prosthesis Secondary insertion of joint prosthesis Operations on the joint capsule and ligaments Operations of the synovia and joint surface Joint resections, arthroplasties, and arthrodesis Excision of bursa Knee and lower leg Primary insertion of joint prosthesis Secondary insertion of joint prosthesis Operations on the joint capsule and ligaments Operations of the synovia and joint surface	BNGA1-3 KQ KJAJ KJAP KJF KJG KJH KLEE30 KKCH30 KUJ KNBB KNBC KNBE KNBF KNBG KBM79 KNCB KNCC KNCE KNCF KNCG KNCM79 KNDB KNDC KNDE KNDF KNDG KNDM KNFB KNFC KNFE KNFF KNFG KNFM79 KNGB KNGC KNGE KNGF	1 year before cohort entry

Joint resections, arthroplasties, and arthrodesis	KNGG	
Excision of bursae	KNGM79	
Ankle and foot		
Primary insertion of joint prosthesis	KNHB	
Secondary insertion of joint prosthesis	KNHC	
Operations on the joint capsule and ligaments	KNHE	
Operations of the synovia and joint surface	KNHF	
Joint resections, arthroplasties, and arthrodesis	KNHG	
Operations on the fascia, tendon sheaths, ganglia and bursae	KNHM	
Therapeutic steroid injection in the joints and soft tissues	BLHN0	

Abbreviations: ATC; anatomical therapeutic chemicals, ICD: international classifications of diseases. Each cell with a heading in bold represents one variable, comprising the diseases or medications listed below, with corresponding ICD/ATC codes.

Appendix Table A4. Relative risk of severe outcomes of SARS-CoV-2 infection for patients exposed to immunosuppressants compared to unexposed patients, with crude, inverse probability of treatment weighting (IPTW) and matching weights models, with further adjustment for antianaemic drugs.

Outcome	Events/ Exposed	Risk % (95% CI)	Events/ Unexposed	Risk % (95% CI)	Risk difference % (95% CI)	Relative risk (95% CI)	Relative risk adjusted for antianaemics (95% CI)
<i>Crude</i>							
Death	57/527	10.8 (8.2 to 13.5)	658/36200	1.8 (1.7 to 2.0)	9.0 (6.3-11.7)	5.95 (4.60-7.69)	2.46 (1.83-3.30)
ICU admission	25/527	4.7 (2.9 to 6.6)	400/36200	1.1 (1.0 to 1.2)	3.6 (1.8-5.5)	4.29 (2.89-6.37)	3.00 (1.91-4.72)
Admission	165/527	31.3 (27.3 to 35.3)	3373/36200	9.3 (9.0 to 9.6)	22.0 (18.0-26.0)	3.36 (2.95-3.83)	1.93 (1.67-2.23)
<i>IPTW</i>							
Death	29/273	10.7 (4.2 to 17.2)	606/22570	2.7 (2.5 to 2.9)	8.0 (1.5-14.5)	3.99 (2.17-7.35)	1.98 (1.06-3.68)
ICU admission	4/273	1.5 (0.2 to 2.8)	362/22570	1.6 (1.4 to 1.8)	-0.1 (-1.4-1.2)	0.93 (0.40-2.18)	0.73 (0.30-1.74)
Admission	60/273	22.0 (11.5 to 32.5)	2981/22570	13.2 (12.8 to 13.7)	8.8 (-1.7-19.3)	1.67 (1.03-2.69)	1.11 (0.69-1.80)
<i>Matching weights</i>							
Death	32/346	9.2 (6.2 to 12.3)	20/339	5.9 (5.2 to 6.7)	3.3 (0.2-6.5)	1.56 (1.10-2.22)	1.71 (1.11-2.65)
ICU admission	13/346	3.8 (1.8 to 5.8)	11/339	3.2 (2.7 to 3.8)	0.5 (-1.6-2.6)	1.16 (0.66-2.03)	1.40 (0.74-2.66)
Admission	100/346	28.9 (24.1 to 33.7)	87/339	25.5 (24.2 to 26.8)	3.4 (-1.6-8.3)	1.13 (0.95-1.35)	1.25 (1.01-1.55)

Abbreviations: ICU; intensive care unit. Numbers of exposed and unexposed in the propensity score weighted dataset are weighted subjects and do not refer to individual subjects.

Appendix Table A5. Relative risk of severe outcomes of SARS-CoV-2 infection for patients exposed to selective immunosuppressants, TNF inhibitors, or interleukin inhibitors compared to unexposed patients, with crude, inverse probability of treatment weighting (IPTW) and matching weights models, with further adjustment for antianaemic drugs.

Outcome	Events/ Exposed	Risk % (95%CI)	Events/ Unexposed	Risk % (95% CI)	Risk difference % (95% CI)	Relative risk (95% CI)	Relative risk adjusted for antianaemics (95% CI)
<i>Crude</i>							
Death	5/192	2.6 (0.3 to 4.9)	658/36200	1.8 (1.7 to 2.0)	0.8 (-1.5 to 3.0)	1.43 (0.60 to 3.41)	0.58 (0.24 to 1.39)
ICU admission	6/192	3.1 (0.7 to 5.6)	400/36200	1.1 (1.0 to 1.2)	2.0 (-0.4 to 4.5)	2.83 (1.28 to 6.25)	1.88 (0.83 to 4.27)
Admission	33/192	17.2 (11.8 to 22.5)	3373/36200	9.3 (9.0 to 9.6)	7.9 (2.5 to 13.2)	1.84 (1.35 to 2.52)	1.07 (0.79 to 1.47)
<i>IPTW</i>							
Death	0/46	0.7 (to 0.2 to 1.6)	280/8468	3.3 (2.9 to 3.7)	-2.6 (-3.6 to -1.6)	0.22 (0.06 to 0.76)	0.15 (0.04 to 0.50)
ICU admission	0/46	0.4 (to 0.2 to 1.1)	183/8468	2.2 (1.9 to 2.5)	-1.7 (-2.4 to -1.0)	0.20 (0.05 to 0.88)	0.17 (0.04 to 0.74)
Hospital admission	13/46	27.6 (0.9 to 54.2)	1479/8468	17.5 (16.7 to 18.3)	10.1 (-16.4 to 36.6)	1.58 (0.60 to 4.14)	1.23 (0.49 to 3.08)
<i>Matching weights</i>							
Death	-	-	-	-	-	1.17 (0.38 to 3.62)	0.83 (0.22 to 3.10)
ICU admission	-	-	-	-	-	0.92 (0.23 to 3.71)	1.32 (0.25 to 6.93)
Hospital admission	14/87	16.1 (8.3 to 23.9)	18/91	19.5 (18.0 to 21.0)	-3.4 (-11.3 to 4.5)	0.83 (0.51 to 1.34)	0.76 (0.43 to 1.34)

Abbreviations: ICU; intensive care unit. Numbers of exposed and unexposed in the propensity score weighted dataset are weighted subjects and do not refer to individual subjects.

Appendix Table A6. Relative risk of severe outcomes of SARS-CoV-2 infection for patients exposed to calcineurin inhibitors, other immunosuppressants, hydroxychloroquine or chloroquine compared to unexposed patients, with crude, inverse probability of treatment weighting (IPTW) and matching weights models, with further adjustment for antianaemic drugs.

Outcome	Events/ Exposed	Risk % (95%CI)	Events/ Unexposed	Risk % (95% CI)	Risk difference % (95% CI)	Relative risk (95% CI)	Relative risk adjusted for antianaemics (95% CI)
<i>Crude</i>							
Death	17/268	6.3 (3.4 to 9.3)	658/36200	1.8 (1.7 to 2.0)	4.5 (1.6 to 7.4)	3.49 (2.19 to 5.56)	1.15 (0.71 to 1.86)
ICU admission	16/268	6.0 (3.1 to 8.8)	400/36200	1.1 (1.0 to 1.2)	4.9 (2.0 to 7.7)	5.40 (3.33 to 8.78)	3.32 (1.91 to 5.77)
Admission	77/268	28.7 (23.3 to 34.2)	3373/36200	9.3 (9.0 to 9.6)	19.4 (14.0-24.8)	3.08 (2.55 to 3.73)	1.57 (1.29 to 1.91)
<i>IPTW</i>							
Death	8/161	4.9 (to 2.0 to 11.9)	599/23922	2.5 (2.3 to 2.7)	2.4 (-4.5 to 9.3)	1.96 (0.48 to 8.06)	0.86 (0.22 to 3.45)
ICU admission	2/161	1.2 (to 0.2 to 2.6)	368/23922	1.5 (1.4 to 1.7)	-0.3 (-1.7 to 1.0)	0.78 (0.25 to 2.44)	0.57 (0.18 to 1.82)
Admission	16/161	10.1 (2.6 to 17.7)	3044/23922	12.7 (12.3 to 13.1)	-2.6 (-10.1 to 4.9)	0.79 (0.38 to 1.67)	0.52 (0.25 to 1.07)
<i>Matching weights</i>							
Death	8/171	4.7 (1.5 to 7.9)	9/170	5.0 (4.4 to 5.7)	-0.4 (-3.6 to 2.9)	0.93 (0.47 to 1.85)	0.75 (0.28 to 1.99)
ICU admission	5/171	2.9 (0.4 to 5.5)	5/170	2.8 (2.4 to 3.3)	0.1 (-2.5 to 2.7)	1.03 (0.43 to 2.49)	1.48 (0.46 to 4.75)
Admission	33/171	19.3 (13.4 to 25.2)	40/170	23.5 (22.3 to 24.7)	-4.2 (-10.2 to 1.8)	0.82 (0.60 to 1.12)	0.75 (0.49 to 1.14)

Abbreviations: ICU; intensive care unit. Numbers of exposed and unexposed in the propensity score weighted dataset are weighted subjects and do not refer to individual subjects.

Appendix Table A7. Relative risk of severe outcomes of SARS-CoV-2 infection for patients exposed to systemic glucocorticoids compared to unexposed patients, with crude, inverse probability of treatment weighting (IPTW) and matching weights models, with further adjustment for antianaemic drugs.

Outcome	Events/ Exposed	Risk % (95%CI)	Events/ Unexposed	Risk % (95% CI)	Risk difference % (95% CI)	Relative risk (95% CI)	Relative risk adjusted for antianaemics (95% CI)
<i>Crude</i>							
Death	42/136	30.9 (23.1 to 38.7)	658/36200	1.8 (1.7 to 2.0)	29.1 (21.3 to 36.8)	16.99 (13.07 to 22.09)	8.33 (6.44 to 10.78)
ICU admission	10/136	7.4 (3.0 to 11.8)	400/36200	1.1 (1.0 to 1.2)	6.2 (1.9 to 10.6)	6.65 (3.64 to 12.18)	5.34 (2.90 to 9.86)
Hospital admission	83/136	61.0 (52.8 to 69.3)	3373/36200	9.3 (9.0 to 9.6)	51.7 (43.5 to 59.9)	6.55 (5.71 to 7.52)	3.78 (3.32 to 4.30)
<i>IPTW</i>							
Death	5/70	7.6 (2.0 to 13.1)	565/18196	3.1 (2.8 to 3.4)	4.5 (-1.0 to 10.0)	2.45 (1.18 to 5.08)	2.07 (1.06 to 4.05)
ICU admission	2/70	2.2 (to 0.2 to 4.6)	362/18196	2.0 (1.8 to 2.2)	0.2 (-2.1 to 2.6)	1.12 (0.38 to 3.28)	1.08 (0.37 to 3.09)
Hospital admission	25/70	35.4 (7.9 to 62.9)	2911/18196	16.0 (15.5 to 16.5)	19.4 (-7.9 to 46.7)	2.21 (1.02 to 4.79)	1.96 (0.97 to 3.96)
<i>Matching weights</i>							
Death	28/94	29.8 (20.5 to 39.1)	11/85	12.5 (11.2 to 13.8)	17.3 (7.9 to 26.6)	2.38 (1.72 to 3.30)	2.36 (1.69 to 3.28)
ICU admission	9/94	9.6 (3.6 to 15.6)	5/85	5.4 (4.6 to 6.3)	4.1 (-1.9 to 10.2)	1.76 (0.93 to 3.35)	1.75 (0.92 to 3.32)
Hospital admission	50/94	53.2 (43.1 to 63.3)	34/85	39.8 (38.1 to 41.5)	13.4 (3.2 to 23.6)	1.34 (1.10 to 1.62)	1.34 (1.10 to 1.64)

Abbreviations: ICU; intensive care unit. Numbers of exposed and unexposed in the propensity score weighted dataset are weighted subjects and do not refer to individual subjects.

Appendix Table A8. Relative risk of severe outcomes of SARS-CoV-2 infection in patients exposed to cumulative dose <2000mg (moderate dose) or ≥2000mg (high dose) compared to unexposed patients, with crude, inverse probability of treatment weighting (IPTW) and matching weights models, with further adjustment for antianaemic drugs.

Outcome	Events/ Exposed	Risk % (95%CI)	Events/ Unexposed	Risk % (95% CI)	Risk difference % (95% CI)	Relative risk (95% CI)	Relative risk adjusted for antianaemics (95%CI)
<i>Crude</i>							
Death							
Moderate dose	18/69	26.1 (15.7 to 36.5)	658/36200	1.8 (1.7 to 2.0)	24.3 (13.9 to 34.6)	14.35 (9.58 to 21.50)	1.70 (1.16 to 2.49)
High dose	24/67	35.8 (24.3 to 47.4)	658/36200	1.8 (1.7 to 2.0)	34.0 (22.5 to 45.5)	19.71 (14.18 to 27.39)	4.79 (. to .)
ICU admission							
Moderate dose	5/69	7.2 (1.1 to 13.4)	400/36200	1.1 (1.0 to 1.2)	6.1 (0.0 to 12.3)	6.56 (2.80 to 15.34)	5.41 (2.31 to 12.68)
High dose	5/67	7.5 (1.1 to 13.8)	400/36200	1.1 (1.0 to 1.2)	6.4 (0.1 to 12.7)	6.75 (2.89 to 15.78)	5.28 (2.26 to 12.36)
Hospital admission							
Moderate dose	38/69	55.1 (43.2 to 66.9)	3373/36200	9.3 (9.0 to 9.6)	45.8 (34.0 to 57.5)	5.91 (4.76 to 7.33)	3.77 (3.16 to 4.50)
High dose	45/67	67.2 (55.8 to 78.5)	3373/36200	9.3 (9.0 to 9.6)	57.8 (46.6 to 69.1)	7.21 (6.08 to 8.55)	3.79 (3.23 to 4.44)
<i>IPTW</i>							
Death							
Moderate dose	2/39	6.0 (to 0.5 to 12.5)	565/18196	3.1 (2.8 to 3.4)	2.9 (-3.5 to 9.3)	1.93 (0.66 to 5.64)	1.98 (0.73 to 5.39)
High dose	3/31	9.6 (to 0.5 to 19.7)	565/18196	3.1 (2.8 to 3.4)	6.5 (-3.5 to 16.4)	3.09 (1.09 to 8.76)	2.15 (0.87 to 5.28)
ICU admission							
Moderate dose	1/39	2.9 (to 1.2 to 7.1)	362/18196	2.0 (1.8 to 2.2)	1.0 (-3.1 to 5.0)	1.48 (0.37 to 5.91)	1.48 (0.38 to 5.81)
High dose	0/31	1.4 (to 0.5 to 3.2)	362/18196	2.0 (1.8 to 2.2)	-0.6 (-2.5 to 1.2)	0.68 (0.18 to 2.63)	0.62 (0.17 to 2.29)
Hospital admission							
Moderate dose	17/39	44.2 (5.7 to 82.6)	2911/18196	16.0 (15.5 to 16.5)	28.2 (-9.9 to 66.2)	2.76 (1.16 to 6.54)	1.87 (. to .)
High dose	8/31	24.5 (0.1 to 48.9)	2911/18196	16.0 (15.5 to 16.5)	8.5 (-15.6 to 32.6)	1.53 (0.57 to 4.10)	0.53 (0.21 to 1.30)
<i>Matching weights</i>							
Death							
Moderate dose	11/48	22.9 (10.9 to 34.9)	11/85	12.5 (11.2 to 13.8)	10.4 (-1.5 to 22.4)	1.83 (1.08 to 3.11)	1.84 (1.08 to 3.13)
High dose	17/46	37.0 (22.9 to 51.1)	11/85	12.5 (11.2 to 13.8)	24.5 (10.4 to 38.5)	2.96 (2.00 to 4.37)	2.91 (1.92 to 4.39)
ICU admission							
Moderate dose	5/48	10.4 (1.7 to 19.1)	5/85	5.4 (4.6 to 6.3)	5.0 (-3.7 to 13.7)	1.92 (0.83 to 4.46)	1.92 (0.82 to 4.46)
High dose	4/46	8.7 (0.5 to 16.9)	5/85	5.4 (4.6 to 6.3)	3.3 (-4.9 to 11.5)	1.60 (0.62 to 4.14)	1.58 (0.62 to 4.04)
Hospital admission							
Moderate dose	23/48	47.9 (33.6 to 62.2)	34/85	39.8 (38.1 to 41.5)	8.1 (-6.1 to 22.3)	1.20 (0.89 to 1.62)	1.21 (0.90 to 1.63)
High dose	27/46	58.7 (44.3 to 73.1)	34/85	39.8 (38.1 to 41.5)	18.9 (4.6 to 33.2)	1.47 (1.15 to 1.89)	1.50 (1.16 to 1.94)

Abbreviations: ICU; intensive care unit. Numbers of exposed and unexposed in the propensity score weighted dataset are weighted subjects and do not refer to individual subjects.

Appendix Table A9. Relative risk of severe outcomes of SARS-CoV-2 infection in current users versus former users of immunosuppressants, with crude, inverse probability of treatment weighting (IPTW) and matching weights models, with further adjustment for antianaemic drugs.

Outcome	Events/ Exposed	Risk % (95%CI)	Events/ Unexposed	Risk % (95% CI)	Risk difference % (95% CI)	Relative risk (95% CI)	Relative risk adjusted for antianaemics (95%CI)
<i>Crude</i>							
Death	57/527	10.8 (8.2 to 13.5)	14/177	7.9 (3.9 to 11.9)	2.9 (-1.9 to 7.7)	1.37 (0.78 to 2.39)	1.37 (0.79 to 2.40)
ICU admission	-	-	-	-	-	2.80 (0.85 to 9.17)	2.81 (0.86 to 9.17)
Admission	165/527	31.3 (27.3 to 35.3)	43/177	24.3 (18.0 to 30.6)	7.0 (-0.4 to 14.5)	1.29 (0.96 to 1.72)	1.30 (0.97 to 1.74)
<i>IPTW</i>							
Death	55/509	10.8 (8.1 to 13.4)	16/171	9.6 (4.6 to 14.6)	1.2 (-4.5 to 6.9)	1.12 (0.63 to 2.00)	1.12 (0.63 to 2.00)
ICU admission	23/509	4.5 (2.7 to 6.3)	4/171	2.5 (-0.4 to 5.5)	1.9 (-1.5 to 5.4)	1.76 (0.52 to 5.96)	1.76 (0.52 to 5.94)
Hospital admission	155/509	30.4 (26.4 to 34.4)	52/171	30.4 (22.5 to 38.3)	-0.0 (-8.8 to 8.8)	1.00 (0.75 to 1.34)	1.01 (0.75 to 1.35)
<i>Matching weights</i>							
Death	17/168	10.2 (7.3 to 13.1)	14/166	8.4 (4.2 to 12.7)	1.8 (-3.3 to 6.9)	1.21 (0.68 to 2.15)	1.22 (0.69 to 2.16)
ICU admission	-	-	-	-	-	2.39 (0.71 to 8.11)	2.39 (0.71 to 8.08)
Hospital admission	48/168	28.5 (24.2 to 32.8)	42/166	25.3 (18.7 to 31.9)	3.2 (-4.7 to 11.1)	1.13 (0.83 to 1.52)	1.12 (0.83 to 1.53)

Abbreviations: ICU; intensive care unit. Numbers of exposed and unexposed in the propensity score weighted dataset are weighted subjects and do not refer to individual subjects.

Appendix Table A10. Relative risk of severe outcomes of SARS-CoV-2 infection in patients admitted to hospital with COVID-19 exposed to immunosuppressants, compared to unexposed patients, with crude, inverse probability of treatment weighting (IPTW) and matching weights models, with further adjustment for antianaemic drugs.

Outcome	Events/ Exposed	Risk % (95%CI)	Events/ Unexposed	Risk % (95% CI)	Risk difference % (95% CI)	Relative risk (95% CI)	Relative risk adjusted for antianaemics (95% CI)
<i>Crude</i>							
Death	42/165	25.5 (18.8 to 32.1)	467/3373	13.8 (12.7 to 15.0)	11.6 (4.9 to 18.4)	1.84 (1.40 to 2.42)	1.48 (1.11 to 1.97)
ICU admission	19/165	11.5 (6.6 to 16.4)	387/3373	11.5 (10.4 to 12.5)	0.0 (-4.9 to 5.0)	1.00 (0.65 to 1.55)	1.05 (0.68 to 1.62)
<i>IPTW</i>							
Death	43/116	37.3 (19.4 to 55.3)	372/2180	17.1 (15.5 to 18.6)	20.3 (2.3 to 38.3)	2.19 (1.34 to 3.57)	2.13 (1.33 to 3.38)
ICU admission	10/116	8.4 (1.0 to 15.8)	259/2180	11.9 (10.5 to 13.2)	-3.5 (-11.0 to 4.0)	0.71 (0.29 to 1.72)	0.71 (0.29 to 1.72)
<i>Matching weights</i>							
Death	32/120	26.7 (18.7 to 34.6)	25/122	20.4 (17.4 to 23.5)	6.2 (-2.2 to 14.7)	1.30 (0.94 to 1.82)	1.31 (0.94 to 1.82)
ICU admission	12/120	10.0 (4.6 to 15.4)	14/122	11.3 (9.2 to 13.4)	-1.3 (-7.0 to 4.5)	0.89 (0.50 to 1.56)	0.88 (0.50 to 1.55)

Abbreviations: ICU; intensive care unit. Numbers of exposed and unexposed in the propensity score weighted dataset are weighted subjects and do not refer to individual subjects.

Appendix Table A11. Relative risk of severe outcomes of SARS-CoV-2 infection in patients exposed to immunosuppressants, 26 February–20 April, with crude, inverse probability of treatment weighting (IPTW) and matching weights models, with further adjustment for antianaemic drugs.

Outcome	Events/ Exposed	Risk % (95%CI)	Events/ Unexposed	Risk % (95% CI)	Risk difference % (95% CI)	Relative risk (95% CI)	Relative risk adjusted for antianaemics (95% CI)
<i>Crude</i>							
Death	34/199	17.1 (11.8 to 22.3)	439/7794	5.6 (5.1 to 6.1)	11.5 (6.2 to 16.7)	3.03 (2.20 to 4.17)	1.61 (1.13 to 2.29)
ICU admission	13/199	6.5 (3.1 to 10.0)	288/7794	3.7 (3.3 to 4.1)	2.8 (-0.6 to 6.3)	1.77 (1.03 to 3.03)	1.48 (0.83 to 2.62)
Admission	94/199	47.2 (40.3 to 54.2)	1951/7794	25.0 (24.1 to 26.0)	22.2 (15.2 to 29.2)	1.89 (1.62 to 2.20)	1.37 (1.17 to 1.62)
<i>IPTW</i>							
Death	29/106	27.5 (9.1 to 45.9)	420/6258	6.7 (6.1 to 7.3)	20.8 (2.5 to 39.1)	4.10 (2.09 to 8.03)	2.90 (1.47 to 5.73)
ICU admission	2/106	1.7 (0.2 to 3.3)	263/6258	4.2 (3.7 to 4.7)	-2.5 (-4.1 to -0.9)	0.41 (0.16 to 1.02)	0.39 (0.16 to 0.96)
Admission	42/106	39.8 (24.2 to 55.5)	1793/6258	28.6 (27.5 to 29.8)	11.2 (-4.5 to 26.8)	1.39 (0.94 to 2.06)	1.21 (0.84 to 1.75)
<i>Matching weights</i>							
Death	21/136	15.4 (9.3 to 21.5)	19/134	14.5 (12.2 to 16.8)	0.9 (-5.6 to 7.4)	1.06 (0.70 to 1.63)	1.08 (0.69 to 1.68)
ICU admission	6/136	4.4 (0.9 to 7.9)	9/134	6.8 (5.3 to 8.3)	-2.4 (-6.1 to 1.4)	0.65 (0.29 to 1.46)	0.67 (0.29 to 1.52)
Admission	64/136	47.1 (38.6 to 55.5)	63/134	47.4 (44.5 to 50.4)	-0.4 (-9.3 to 8.5)	0.99 (0.82 to 1.20)	1.00 (0.82 to 1.22)

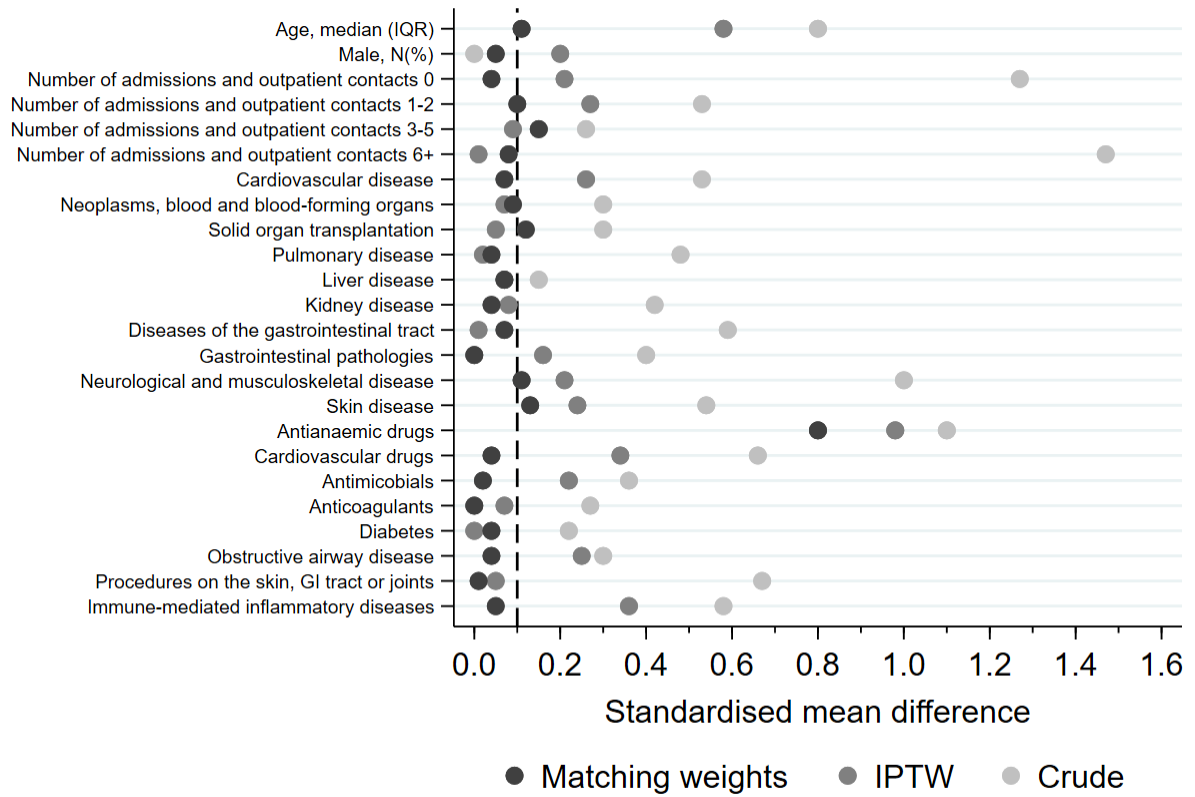
Abbreviations: ICU; intensive care unit. Numbers of exposed and unexposed in the propensity score weighted dataset are weighted subjects and do not refer to individual subjects.

Appendix Table A12. Relative risk of severe outcomes of SARS-CoV-2 infection in patients exposed to immunosuppressants, 21 April–18 October, with crude, inverse probability of treatment weighting (IPTW) and matching weights models, with further adjustment for antianaemic drugs.

Outcome	Events/ Exposed	Risk % (95%CI)	Events/ Unexposed	Risk % (95% CI)	Risk difference % (95% CI)	Relative risk (95% CI)	Relative risk adjusted for antianaemics (95% CI)
<i>Crude</i>							
Death	23/328	7.0 (4.2 to 9.8)	219/28406	0.8 (0.7 to 0.9)	6.2 (3.5 to 9.0)	9.10 (6.00 to 13.78)	3.32 (2.02 to 5.45)
ICU admission	12/328	3.7 (1.6 to 5.7)	112/28406	0.4 (0.3 to 0.5)	3.3 (1.2 to 5.3)	9.28 (5.17 to 16.66)	6.19 (2.91 to 13.17)
Hospital admission	71/328	21.6 (17.2 to 26.1)	1422/28406	5.0 (4.8 to 5.3)	16.6 (12.2 to 21.1)	4.32 (3.50 to 5.35)	2.26 (1.78 to 2.87)
<i>IPTW</i>							
Death	13/146	8.8 (1.3 to 16.3)	198/18300	1.1 (0.9 to 1.2)	7.7 (0.3 to 15.2)	8.13 (3.44 to 19.19)	6.32 (2.79 to 14.28)
ICU admission	5/146	3.1 (to 0.5 to 6.7)	98/18300	0.5 (0.4 to 0.6)	2.6 (-1.1 to 6.2)	5.76 (1.75 to 18.92)	5.43 (1.65 to 17.89)
Hospital admission	25/146	17.2 (6.9 to 27.5)	1226/18300	6.7 (6.3 to 7.1)	10.5 (0.2 to 20.8)	2.57 (1.41 to 4.68)	2.27 (1.30 to 3.96)
<i>Matching weights</i>							
Death	15/183	8.2 (4.2 to 12.2)	6/178	3.1 (2.4 to 3.9)	5.1 (1.0 to 9.1)	2.60 (1.52 to 4.46)	2.64 (1.51 to 4.64)
ICU admission	-	-	-	-	-	3.23 (1.50 to 6.98)	3.41 (1.56 to 7.43)
Hospital admission	39/183	21.3 (15.4 to 27.3)	28/178	15.9 (14.4 to 17.3)	5.5 (-0.6 to 11.6)	1.34 (1.00 to 1.80)	1.42 (1.05 to 1.92)

Abbreviations: ICU; intensive care unit. Numbers of exposed and unexposed in the propensity score weighted dataset are weighted subjects and do not refer to individual subjects.

Appendix Figure A1. Standardised mean differences of covariates with unadjusted (crude), inverse probability of treatment weighting and matching weights models, for patients exposed to immunosuppressants compared to unexposed.



Abbreviations: IPTW: inverse probability of treatment weighting.

Appendix Table A13. Characteristics of SARS-CoV-2 PCR test positive patients in Denmark 26 February–18 October 2020, by exposure to immunosuppressants, and with inverse probability of treatment weighting (IPTW) and matching weights propensity score models.

Characteristics	Unadjusted			Adjusted with IPTW			Adjusted with matching weights		
	Exposed (n=527)	Unexposed (n=36,200)	SMD	Exposed (n=273)	Unexposed (n=22,570)	SMD	Exposed (n=346)	Unexposed (n=339)	SMD
Age, median (IQR)	57 (42-73)	39 (23-55)	0.80	57 (41-77)	47 (29-60)	0.58	57 (43-74)	56 (41-71)	0.11
Male, N (%)	256 (48.6)	17,544 (48.5)	0.00	104 (38.1)	10,810 (47.9)	0.20	149 (43.1)	154 (45.4)	0.05
Number of admissions and outpatient contacts	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
0	20 (3.8)	18,787 (51.9)	1.27	92 (33.7)	5,449 (24.1)	0.21	14 (4.0)	11 (3.4)	0.04
1-2	38 (7.2)	9,574 (26.4)	0.53	80 (29.4)	9,474 (42.0)	0.27	36 (10.4)	47 (13.8)	0.10
3-5	113 (21.4)	4,264 (11.8)	0.26	61 (22.4)	4,243 (18.8)	0.09	107 (30.9)	82 (24.2)	0.15
6+	356 (67.6)	3,575 (9.9)	1.47	40 (14.6)	3,404 (15.1)	0.01	189 (54.6)	199 (58.7)	0.08
Diagnoses	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Cardiovascular disease	176 (33.4)	4,269 (11.8)	0.53	73 (26.7)	3,601 (16.0)	0.26	111 (32.1)	98 (29.0)	0.07
Neoplasms, blood and blood-forming organs	27 (5.1)	101 (0.3)	0.30	0 (0.0)	71 (0.3)	0.07	1 (0.3)	(n<5)	0.09
Solid organ transplantation	24 (4.6)	27 (0.1)	0.30	0 (0.1)	(n<5)	0.05	(n<5)	0 (0.0)	0.12
Pulmonary disease	131 (24.9)	2,742 (7.6)	0.48	31 (11.3)	2,435 (10.8)	0.02	73 (21.1)	66 (19.6)	0.04
Liver disease	15 (2.8)	302 (0.8)	0.15	5 (1.9)	253 (1.1)	0.07	11 (3.2)	7 (2.0)	0.07
Kidney disease	76 (14.4)	1,049 (2.9)	0.42	15 (5.5)	856 (3.8)	0.08	34 (9.8)	30 (8.8)	0.04
Diseases of the gastrointestinal tract	91 (17.3)	365 (1.0)	0.59	(n<5)	257 (1.1)	0.01	17 (4.9)	12 (3.4)	0.07
Gastrointestinal pathologies	94 (17.8)	1,934 (5.3)	0.40	10 (3.6)	1,616 (7.2)	0.16	43 (12.4)	43 (12.5)	0.00
Neurological and musculoskeletal disease	353 (67.0)	8,101 (22.4)	1.00	123 (45.1)	7,896 (35.0)	0.21	231 (66.8)	209 (61.7)	0.11
Skin disease	112 (21.3)	1,399 (3.9)	0.54	33 (12.3)	1,244 (5.5)	0.24	51 (14.7)	35 (10.3)	0.13
Medications	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Antianaemic drugs	276 (52.4)	2,946 (8.1)	1.10	139 (51.0)	2,341 (10.4)	0.98	185 (53.5)	61 (18.0)	0.80
Cardiovascular drugs	370 (70.2)	14,144 (39.1)	0.66	178 (65.2)	10,921 (48.4)	0.34	235 (67.9)	224 (66.2)	0.04
Antimicrobials	515 (97.7)	32,201 (89.0)	0.36	267 (98.0)	21,136 (93.6)	0.22	335 (96.8)	329 (97.1)	0.02
Anticoagulants	39 (7.4)	633 (1.7)	0.27	(n<5)	551 (2.4)	0.07	19 (5.5)	19 (5.5)	0.00
Diabetes	65 (12.3)	2,211 (6.1)	0.22	22 (8.0)	1,779 (7.9)	0.00	44 (12.7)	39 (11.4)	0.04
Obstructive airway disease	212 (40.2)	9,502 (26.2)	0.30	111 (40.7)	6,483 (28.7)	0.25	135 (39.0)	126 (37.1)	0.04
Proxies for IMID severity	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Procedures on the skin, GI tract or joints	162 (30.7)	2,239 (6.2)	0.67	22 (7.9)	2,131 (9.4)	0.05	82 (23.7)	78 (23.1)	0.01
Immune-mediated inflammatory disease drugs	252 (47.8)	7,651 (21.1)	0.58	124 (45.4)	6,384 (28.3)	0.36	156 (45.1)	144 (42.6)	0.05

Abbreviations: IMID; immune mediated inflammatory diseases.

Appendix Table A14. Characteristics of SARS-CoV-2 PCR test positive patients in Denmark 26 February–18 October 2020, by exposure to selective immunosuppressants, TNF inhibitors, interleukin inhibitors, with inverse probability of treatment weighting (IPTW) and matching weights propensity score models.

Characteristics	Unadjusted			Adjusted with IPTW			Adjusted with matching weights		
	Exposed (n=192)	Unexposed (n=36,200)	SMD	Exposed (n=46)	Unexposed (n=8468)	SMD	Exposed (n=87)	Unexposed (n=91)	SMD
Age, median (IQR)	48 (33-58)	39 (23-55)	0.34	55 (29-61)	47 (30-61)	0.20	52 (40-62)	47 (32-59)	0.23
Male, N (%)	96 (50.0)	17,544 (48.5)	0.03	17 (37.5)	3,812 (45.0)	0.15	34 (39.1)	38 (42.0)	0.06
Number of admissions and outpatient contacts	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
0	n<5	18,787 (51.9)	1.47	n<5	36 (0.4)	0.09	n<5	0 (0.1)	0.04
1-2	n<5	9,574 (26.4)	0.79	6 (12.0)	1,405 (16.6)	0.13	n<5	(n<5)	0.11
3-5	29 (15.1)	4,264 (11.8)	0.10	27 (59.1)	3,732 (44.1)	0.30	26 (29.9)	16 (17.8)	0.29
6+	161 (83.9)	3,575 (9.9)	2.21	13 (28.8)	3,295 (38.9)	0.21	60 (69.0)	72 (79.5)	0.24
Diagnoses	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Cardiovascular disease	42 (21.9)	4,269 (11.8)	0.27	20 (43.3)	1,750 (20.7)	0.50	25 (28.7)	18 (19.6)	0.21
Neoplasms, blood and blood-forming organs	5 (2.6)	101 (0.3)	0.20	1 (1.3)	50 (0.6)	0.07	n<5	n<5	0.13
Solid organ transplantation	13 (6.8)	27 (0.1)	0.37	0 (0.5)	5 (0.1)	0.09	n<5	0 (0.1)	0.20
Pulmonary disease	37 (19.3)	2,742 (7.6)	0.35	10 (22.4)	1,112 (13.1)	0.24	13 (14.9)	14 (15.8)	0.02
Liver disease	6 (3.1)	302 (0.8)	0.17	0 (0.8)	157 (1.8)	0.09	n<5	n<5	0.10
Kidney disease	23 (12.0)	1,049 (2.9)	0.35	9 (19.1)	534 (6.3)	0.39	8 (9.2)	7 (7.7)	0.06
Diseases of the gastrointestinal tract	59 (30.7)	365 (1.0)	0.89	0 (0.7)	206 (2.4)	0.14	n<5	n<5	0.01
Gastrointestinal pathologies	36 (18.8)	1,934 (5.3)	0.42	n<5	834 (9.8)	0.11	9 (10.3)	11 (12.1)	0.06
Neurological and musculoskeletal disease	135 (70.3)	8,101 (22.4)	1.10	26 (55.7)	3,931 (46.4)	0.19	65 (74.7)	55 (60.7)	0.30
Skin disease	48 (25.0)	1,399 (3.9)	0.63	n<5	619 (7.3)	0.10	16 (18.4)	10 (10.5)	0.23
Medications	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Antianaemic drugs	98 (51.0)	2,946 (8.1)	1.06	18 (39.6)	1,234 (14.6)	0.59	46 (52.9)	15 (16.5)	0.83
Cardiovascular drugs	123 (64.1)	14,144 (39.1)	0.52	30 (63.6)	4,820 (56.9)	0.14	55 (63.2)	55 (60.6)	0.05
Antimicrobials	192 (100.0)	32,201 (89.0)	0.50	46 (100.0)	8,056 (95.1)	0.32	87 (100.0)	88 (96.4)	0.28
Anticoagulants	11 (5.7)	633 (1.7)	0.21	n<5	295 (3.5)	0.05	5 (5.7)	n<5	0.12
Diabetes	16 (8.3)	2,211 (6.1)	0.09	0 (0.9)	990 (11.7)	0.46	(n<5)	12 (13.3)	0.31
Obstructive airway disease	61 (31.8)	9,502 (26.2)	0.12	19 (41.0)	2,779 (32.8)	0.17	24 (27.6)	32 (35.6)	0.17
Proxies for IMID severity	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Procedures on the skin, GI tract or joints	62 (32.3)	2,239 (6.2)	0.70	7 (14.2)	1,504 (17.8)	0.10	21 (24.1)	22 (23.7)	0.01
Immune-mediated inflammatory disease drugs	89 (46.4)	7,651 (21.1)	0.55	19 (41.8)	2,901 (34.3)	0.16	40 (46.0)	37 (40.8)	0.10

Abbreviations: IMID; immune mediated inflammatory diseases.

Appendix Table A15. Characteristics of SARS-CoV-2 PCR test positive patients in Denmark 26 February–18 October 2020, by exposure to calcineurin inhibitors, other immunosuppressants, hydroxychloroquine or chloroquine with inverse probability of treatment weighting (IPTW) and matching weights propensity score models.

Characteristics	Unadjusted			Adjusted with IPTW			Adjusted with matching weights		
	Exposed (n=268)	Unexposed (n=36,200)	SMD	Exposed (n=161)	Unexposed (n=23,922)	SMD	Exposed (n=171)	Unexposed (n=170)	SMD
Age, median (IQR)	56 (44-69)	39 (23-55)	0.78	51 (40-70)	47 (30-60)	0.35	54 (40-70)	54 (41-68)	0.01
Male, N (%)	118 (44.0)	17,544 (48.5)	0.09	69 (42.9)	11,052 (46.2)	0.07	72 (42.1)	72 (42.1)	0.00
Number of admissions and outpatient contacts	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
0	16 (6.0)	18,787 (51.9)	1.17	78 (48.2)	6,997 (29.2)	0.40	14 (8.2)	10 (5.7)	0.10
1-2	21 (7.8)	9,574 (26.4)	0.51	39 (24.1)	9,364 (39.1)	0.33	21 (12.3)	29 (17.0)	0.13
3-5	65 (24.3)	4,264 (11.8)	0.33	24 (15.1)	4,229 (17.7)	0.07	56 (32.7)	43 (25.2)	0.17
6+	166 (61.9)	3,575 (9.9)	1.29	20 (12.7)	3,333 (13.9)	0.04	80 (46.8)	89 (52.1)	0.11
Diagnoses	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Cardiovascular disease	83 (31.0)	4,269 (11.8)	0.48	32 (19.8)	3,546 (14.8)	0.13	46 (26.9)	42 (24.6)	0.05
Neoplasms, blood and blood-forming organs	20 (7.5)	101 (0.3)	0.38	-	56 (0.2)	0.07	-	(n<5)	0.14
Solid organ transplantation	21 (7.8)	27 (0.1)	0.41	-	-	-	-	-	-
Pulmonary disease	58 (21.6)	2,742 (7.6)	0.41	9 (5.4)	2,272 (9.5)	0.16	26 (15.2)	30 (17.6)	0.06
Liver disease	11 (4.1)	302 (0.8)	0.21	(n<5)	266 (1.1)	0.04	(n<5)	(n<5)	0.01
Kidney disease	45 (16.8)	1,049 (2.9)	0.48	7 (4.2)	880 (3.7)	0.02	15 (8.8)	15 (8.7)	0.00
Diseases of the gastrointestinal tract	36 (13.4)	365 (1.0)	0.49	(n<5)	275 (1.1)	0.08	12 (7.0)	6 (3.5)	0.16
Gastrointestinal pathologies	42 (15.7)	1,934 (5.3)	0.34	(n<5)	1,586 (6.6)	0.18	15 (8.8)	19 (11.2)	0.08
Neurological and musculoskeletal disease	183 (68.3)	8,101 (22.4)	1.04	59 (36.5)	7,839 (32.8)	0.08	113 (66.1)	105 (62.0)	0.09
Skin disease	66 (24.6)	1,399 (3.9)	0.62	19 (11.8)	1,207 (5.0)	0.24	30 (17.5)	18 (10.4)	0.21
Medications	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Antianaemic drugs	182 (67.9)	2,946 (8.1)	1.56	98 (60.9)	2,446 (10.2)	1.25	119 (69.6)	30 (17.6)	1.23
Cardiovascular drugs	188 (70.1)	14,144 (39.1)	0.66	111 (69.1)	11,808 (49.4)	0.41	107 (62.6)	113 (66.7)	0.09
Antimicrobials	261 (97.4)	32,201 (89.0)	0.34	147 (91.3)	22,228 (92.9)	0.06	164 (95.9)	165 (96.9)	0.05
Anticoagulants	16 (6.0)	633 (1.7)	0.22	1 (0.4)	546 (2.3)	0.17	(n<5)	8 (4.5)	0.12
Diabetes	38 (14.2)	2,211 (6.1)	0.27	6 (3.6)	1,968 (8.2)	0.20	18 (10.5)	24 (14.0)	0.11
Obstructive airway disease	100 (37.3)	9,502 (26.2)	0.24	52 (32.6)	6,703 (28.0)	0.10	58 (33.9)	63 (36.8)	0.06
Proxies for IMID severity	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Procedures on the skin, GI tract or joints	82 (30.6)	2,239 (6.2)	0.66	11 (7.1)	2,113 (8.8)	0.06	37 (21.6)	40 (23.3)	0.04
Immune-mediated inflammatory diseases	132 (49.3)	7,651 (21.1)	0.62	75 (46.9)	6,861 (28.7)	0.38	84 (49.1)	77 (45.6)	0.07

Abbreviations: IMID; immune mediated inflammatory diseases.

Appendix Table A16. Characteristics of SARS-CoV-2 PCR test positive patients in Denmark 26 February–18 October 2020, by exposure to systemic glucocorticoids with inverse probability of treatment weighting (IPTW) and matching weights propensity score models.

Characteristics	Unadjusted			Adjusted with IPTW			Adjusted with matching weights		
	Exposed (n=136)	Unexposed (n=36,200)	SMD	Exposed (n=70)	Unexposed (n=18,196)	SMD	Exposed (n=94)	Unexposed (n=85)	SMD
Age, median (IQR)	75 (65-82)	39 (23-55)	1.75	42 (29-60)	53 (42-64)	0.30	73 (60-82)	71 (58-80)	0.09
Male, N (%)	73 (53.7)	17,544 (48.5)	0.10	29 (41.1)	8,701 (47.8)	0.14	47 (50.0)	43 (50.3)	0.01
Number of admissions and outpatient contacts	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
0	5 (3.7)	18,787 (51.9)	1.28	14 (19.5)	4,579 (25.2)	0.14	n<5	n<5	0.03
1-2	16 (11.8)	9,574 (26.4)	0.38	29 (41.3)	6,433 (35.4)	0.12	15 (16.0)	14 (15.9)	0.00
3-5	25 (18.4)	4,264 (11.8)	0.19	19 (27.3)	3,912 (21.5)	0.13	25 (26.6)	23 (27.2)	0.01
6+	90 (66.2)	3,575 (9.9)	1.42	8 (11.9)	3,271 (18.0)	0.17	50 (53.2)	44 (52.0)	0.02
Diagnoses	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Cardiovascular disease	81 (59.6)	4,269 (11.8)	1.15	14 (19.7)	3,722 (20.5)	0.02	52 (55.3)	43 (50.3)	0.10
Neoplasms, blood and blood-forming organs	7 (5.1)	101 (0.3)	0.30	n<5	75 (0.4)	0.09	n<5	n<5	0.16
Solid organ transplantation	n<5	27 (0.1)	0.04	n<5	27 (0.1)	0.05	n<5	0 (0.3)	0.08
Pulmonary disease	57 (41.9)	2,742 (7.6)	0.87	6 (8.4)	1,989 (10.9)	0.09	29 (30.9)	20 (23.7)	0.16
Liver disease	n<5	302 (0.8)	0.06	n<5	237 (1.3)	0.03	n<5	n<5	0.00
Kidney disease	23 (16.9)	1,049 (2.9)	0.48	n<5	736 (4.0)	0.03	16 (17.0)	10 (11.9)	0.15
Diseases of the gastrointestinal tract	15 (11.0)	365 (1.0)	0.43	n<5	286 (1.6)	0.20	9 (9.6)	n<5	0.27
Gastrointestinal pathologies	27 (19.9)	1,934 (5.3)	0.45	n<5	1,544 (8.5)	0.11	17 (18.1)	14 (16.4)	0.04
Neurological and musculoskeletal disease	82 (60.3)	8,101 (22.4)	0.83	34 (47.9)	6,594 (36.2)	0.24	53 (56.4)	45 (53.2)	0.06
Skin disease	11 (8.1)	1,399 (3.9)	0.18	6 (8.0)	848 (4.7)	0.14	9 (9.6)	6 (6.8)	0.10
Medications	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Antianaemic drugs	38 (27.9)	2,946 (8.1)	0.53	14 (19.9)	2,191 (12.0)	0.22	25 (26.6)	20 (23.2)	0.08
Cardiovascular drugs	113 (83.1)	14,144 (39.1)	1.01	38 (54.3)	10,704 (58.8)	0.09	75 (79.8)	70 (82.7)	0.07
Antimicrobials	130 (95.6)	32,201 (89.0)	0.25	67 (96.1)	17,146 (94.2)	0.09	90 (95.7)	83 (97.7)	0.11
Anticoagulants	18 (13.2)	633 (1.7)	0.45	n<5	550 (3.0)	0.09	10 (10.6)	8 (9.4)	0.04
Diabetes	22 (16.2)	2,211 (6.1)	0.32	7 (10.0)	1,881 (10.3)	0.01	14 (14.9)	17 (20.2)	0.14
Obstructive airway disease	74 (54.4)	9,502 (26.2)	0.60	23 (32.5)	5,180 (28.5)	0.09	44 (46.8)	35 (41.3)	0.11
Proxies for IMID severity	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Procedures on the skin, GI tract or joints	42 (30.9)	2,239 (6.2)	0.67	6 (8.7)	1,937 (10.6)	0.07	22 (23.4)	22 (25.3)	0.04
Immune-mediated inflammatory diseases	60 (44.1)	7,651 (21.1)	0.51	51 (72.5)	5,640 (31.0)	0.91	41 (43.6)	35 (41.3)	0.05

Abbreviations: IMID; immune mediated inflammatory diseases.

Appendix Table A17. Characteristics of SARS-CoV-2 PCR test positive patients in Denmark 26 February–18 October 2020, by current or former use of immunosuppressants, and with inverse probability of treatment weighting (IPTW) and matching weights propensity score models.

Characteristics	Unadjusted			Adjusted with IPTW			Adjusted with matching weights		
	Current (n=527)	former (n=177)	SMD	Current (n=509)	former (n=171)	SMD	Current (n=168)	Former (n=166)	SMD
Age, median (IQR)	57 (42-73)	54 (40-71)	0.10	56 (42-73)	58 (43-74)	0.05	56 (42-72)	56 (42-72)	0.02
Male, N (%)	256 (48.6)	81 (45.8)	0.06	242 (47.6)	81 (47.3)	0.01	77 (45.7)	74 (44.6)	0.02
Number of admissions and outpatient contacts	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
0	20 (3.8)	16 (9.0)	0.22	21 (4.1)	6 (3.4)	0.04	11 (6.4)	9 (5.4)	0.04
1-2	38 (7.2)	25 (14.1)	0.23	43 (8.4)	16 (9.4)	0.04	19 (11.2)	23 (13.9)	0.08
3-5	113 (21.4)	34 (19.2)	0.06	115 (22.6)	33 (19.4)	0.08	42 (24.8)	34 (20.5)	0.10
6+	356 (67.6)	102 (57.6)	0.21	331 (65.0)	116 (67.9)	0.06	97 (57.6)	100 (60.3)	0.05
Diagnoses	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Cardiovascular disease	176 (33.4)	65 (36.7)	0.07	175 (34.5)	62 (36.0)	0.03	63 (37.8)	63 (37.9)	0.00
Neoplasms, blood and blood-forming organs	27 (5.1)	7 (4.0)	0.06	25 (4.9)	(n<5)	0.10	6 (3.6)	5 (3.0)	0.03
Solid organ transplantation	24 (4.6)	9 (5.1)	0.02	23 (4.4)	8 (4.8)	0.02	8 (4.9)	9 (5.4)	0.03
Pulmonary disease	131 (24.9)	39 (22.0)	0.07	125 (24.5)	42 (24.5)	0.00	39 (23.0)	39 (23.5)	0.01
Liver disease	15 (2.8)	8 (4.5)	0.09	15 (2.9)	7 (3.9)	0.05	7 (3.9)	7 (4.2)	0.02
Kidney disease	76 (14.4)	28 (15.8)	0.04	74 (14.6)	26 (15.3)	0.02	26 (15.5)	27 (16.3)	0.02
Diseases of the gastrointestinal tract	91 (17.3)	23 (13.0)	0.12	82 (16.1)	28 (16.2)	0.00	23 (13.5)	22 (13.3)	0.01
Gastrointestinal pathologies	94 (17.8)	21 (11.9)	0.17	80 (15.8)	29 (17.1)	0.04	20 (12.0)	21 (12.7)	0.02
Neurological and musculoskeletal disease	353 (67.0)	105 (59.3)	0.16	333 (65.4)	115 (67.3)	0.04	102 (61.0)	103 (62.0)	0.02
Skin disease	112 (21.3)	34 (19.2)	0.05	107 (21.0)	35 (20.7)	0.01	34 (20.2)	33 (19.9)	0.01
Medications	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Antianaemic drugs	276 (52.4)	92 (52.0)	0.01	266 (52.3)	89 (52.2)	0.00	87 (51.6)	86 (51.8)	0.00
Cardiovascular drugs	370 (70.2)	125 (70.6)	0.01	359 (70.5)	126 (73.4)	0.07	120 (71.7)	121 (72.9)	0.03
Antimicrobials	515 (97.7)	167 (94.4)	0.17	497 (97.7)	169 (98.6)	0.06	162 (96.7)	162 (97.6)	0.06
Anticoagulants	39 (7.4)	12 (6.8)	0.02	33 (6.5)	11 (6.4)	0.00	10 (6.0)	12 (7.2)	0.05
Diabetes	65 (12.3)	26 (14.7)	0.07	65 (12.7)	21 (12.2)	0.02	23 (14.0)	25 (15.0)	0.03
Obstructive airway disease	212 (40.2)	65 (36.7)	0.07	204 (40.1)	70 (40.8)	0.01	65 (38.9)	64 (38.5)	0.01
Proxies for IMID severity	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Procedures on the skin, GI tract or joints	162 (30.7)	52 (29.4)	0.03	156 (30.6)	50 (29.4)	0.03	50 (29.9)	50 (30.1)	0.01
Immune-mediated inflammatory disease drugs	252 (47.8)	80 (45.2)	0.05	236 (46.4)	79 (46.2)	0.00	74 (44.3)	74 (44.6)	0.01

Abbreviations: IMID; immune mediated inflammatory diseases.

Appendix Table A18. Characteristics of SARS-CoV-2 PCR test positive patients in Denmark 26 February–18 October 2020 restricted to those admitted with COVID-19, by exposure to immunosuppressants with inverse probability of treatment weighting (IPTW) and matching weights propensity score models.

Characteristics	Unadjusted			Adjusted with IPTW			Adjusted with matching weights		
	Exposed (n=165)	Unexposed (n=3,373)	SMD	Exposed (n=116)	Unexposed (n=2180)	SMD	Exposed (n=120)	Unexposed (n=122)	SMD
Age, median (IQR)	73 (61-80)	66 (50-78)	0.43	81 (69-87)	71 (57-80)	0.45	74 (61-82)	74 (63-81)	0.03
Male, N (%)	87 (52.7)	1,823 (54.0)	0.03	57 (49.6)	1,162 (53.3)	0.07	63 (52.5)	63 (51.5)	0.02
Number of admissions and outpatient contacts	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
0	(n<5)	814 (24.1)	0.70	17 (14.9)	84 (3.8)	0.39	(n<5)	1 (0.6)	0.10
1-2	5 (3.0)	935 (27.7)	0.73	21 (18.3)	508 (23.3)	0.12	5 (4.2)	8 (6.8)	0.12
3-5	30 (18.2)	646 (19.2)	0.02	31 (26.9)	605 (27.7)	0.02	29 (24.2)	20 (16.7)	0.19
6+	127 (77.0)	978 (29.0)	1.10	46 (39.9)	983 (45.1)	0.11	84 (70.0)	92 (75.9)	0.13
Diagnoses	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Cardiovascular disease	97 (58.8)	1,337 (39.6)	0.39	76 (65.4)	1,041 (47.8)	0.36	68 (56.7)	68 (56.0)	0.01
Neoplasms, blood and blood-forming organs	11 (6.7)	23 (0.7)	0.32	1 (0.6)	18 (0.8)	0.03	(n<5)	(n<5)	0.06
Solid organ transplantation	16 (9.7)	9 (0.3)	0.44	0 (0.3)	(n<5)	0.03	(n<5)	1 (0.7)	0.09
Pulmonary disease	69 (41.8)	537 (15.9)	0.60	22 (19.2)	514 (23.6)	0.11	47 (39.2)	52 (43.0)	0.08
Liver disease	9 (5.5)	83 (2.5)	0.15	(n<5)	68 (3.1)	0.06	5 (4.2)	(n<5)	0.04
Kidney disease	43 (26.1)	336 (10.0)	0.43	14 (11.8)	297 (13.6)	0.05	26 (21.7)	24 (19.9)	0.04
Diseases of the gastrointestinal tract	22 (13.3)	64 (1.9)	0.44	(n<5)	57 (2.6)	0.07	8 (6.7)	8 (6.4)	0.01
Gastrointestinal pathologies	37 (22.4)	430 (12.7)	0.26	16 (13.7)	353 (16.2)	0.07	23 (19.2)	27 (22.4)	0.08
Neurological and musculoskeletal disease	106 (64.2)	1,305 (38.7)	0.53	61 (52.5)	1,074 (49.3)	0.06	73 (60.8)	77 (63.0)	0.05
Skin disease	27 (16.4)	202 (6.0)	0.33	13 (10.9)	179 (8.2)	0.09	18 (15.0)	16 (13.4)	0.05
Medications	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Antianaemic drugs	74 (44.8)	657 (19.5)	0.56	31 (26.7)	590 (27.1)	0.01	45 (37.5)	49 (40.0)	0.05
Cardiovascular drugs	141 (85.5)	2,463 (73.0)	0.31	88 (76.2)	1,729 (79.3)	0.08	100 (83.3)	103 (84.2)	0.02
Antimicrobials	160 (97.0)	3,201 (94.9)	0.10	114 (98.3)	2,087 (95.7)	0.15	115 (95.8)	118 (96.6)	0.04
Anticoagulants	26 (15.8)	274 (8.1)	0.24	8 (6.6)	224 (10.3)	0.13	16 (13.3)	16 (13.5)	0.00
Diabetes	26 (15.8)	636 (18.9)	0.08	17 (14.9)	428 (19.6)	0.13	19 (15.8)	21 (16.9)	0.03
Obstructive airway disease	95 (57.6)	1,162 (34.5)	0.48	44 (37.7)	940 (43.1)	0.11	67 (55.8)	72 (59.1)	0.07
Proxies for IMID severity	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Procedures on the skin, GI tract or joints	64 (38.8)	508 (15.1)	0.56	19 (16.8)	478 (21.9)	0.13	38 (31.7)	40 (32.5)	0.02
Immune-mediated inflammatory disease drugs	64 (38.8)	1,057 (31.3)	0.16	38 (32.5)	788 (36.1)	0.08	47 (39.2)	50 (41.1)	0.04

Abbreviations: IMID; immune mediated inflammatory diseases.

Appendix Table A19. Characteristics of SARS-CoV-2 PCR test positive patients in Denmark 26 February–20 April 2020, by exposure to immunosuppressants with inverse probability of treatment weighting (IPTW) and matching weights propensity score models.

Characteristics	Unadjusted			Adjusted with IPTW			Adjusted with matching weights		
	Exposed (n=199)	Unexposed (n=7794)	SMD	Exposed (n=106)	Unexposed (n=6258)	SMD	Exposed (n=136)	Unexposed (n=134)	SMD
Age, median (IQR)	63 (50-79)	50 (35-63)	0.61	65 (53-84)	53 (39-66)	0.67	67 (51-79)	63 (50-77)	0.04
Male, N (%)	95 (47.7)	3,321 (42.6)	0.10	39 (36.9)	2,931 (46.8)	0.20	61 (44.9)	61 (45.8)	0.02
Number of admissions and outpatient contacts	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
0	9 (4.5)	3,122 (40.1)	0.94	17 (15.9)	1,671 (26.7)	0.27	7 (5.1)	(n<5)	0.09
1-2	11 (5.5)	2,317 (29.7)	0.67	24 (23.0)	2,257 (36.1)	0.29	10 (7.4)	17 (13.0)	0.19
3-5	37 (18.6)	1,202 (15.4)	0.08	35 (32.6)	1,198 (19.1)	0.31	33 (24.3)	31 (23.0)	0.03
6+	142 (71.4)	1,153 (14.8)	1.39	30 (28.5)	1,132 (18.1)	0.25	86 (63.2)	81 (60.7)	0.05
Diagnoses	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Cardiovascular disease	77 (38.7)	1,534 (19.7)	0.43	51 (48.5)	1,367 (21.8)	0.58	52 (38.2)	51 (38.1)	0.00
Neoplasms, blood and blood-forming organs	14 (7.0)	34 (0.4)	0.35	0 (0.3)	31 (0.5)	0.03	(n<5)	(n<5)	0.09
Solid organ transplantation	10 (5.0)	8 (0.1)	0.32	0 (0.1)	(n<5)	0.01	1 (0.7)	1 (0.6)	0.01
Pulmonary disease	61 (30.7)	723 (9.3)	0.55	28 (26.1)	702 (11.2)	0.39	36 (26.5)	36 (27.0)	0.01
Liver disease	5 (2.5)	108 (1.4)	0.08	1 (0.5)	95 (1.5)	0.10	(n<5)	(n<5)	0.04
Kidney disease	31 (15.6)	363 (4.7)	0.37	13 (12.3)	320 (5.1)	0.26	16 (11.8)	16 (12.3)	0.02
Diseases of the gastrointestinal tract	28 (14.1)	112 (1.4)	0.49	(n<5)	100 (1.6)	0.12	10 (7.4)	8 (6.3)	0.04
Gastrointestinal pathologies	42 (21.1)	566 (7.3)	0.40	10 (9.0)	523 (8.4)	0.02	23 (16.9)	22 (16.3)	0.02
Neurological and musculoskeletal disease	143 (71.9)	2,380 (30.5)	0.91	45 (42.9)	2,335 (37.3)	0.11	92 (67.6)	87 (65.3)	0.05
Skin disease	33 (16.6)	378 (4.8)	0.39	5 (4.9)	352 (5.6)	0.03	17 (12.5)	17 (12.6)	0.00
Medications	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Antianaemic drugs	109 (54.8)	871 (11.2)	1.05	30 (28.0)	843 (13.5)	0.37	62 (45.6)	56 (41.9)	0.07
Cardiovascular drugs	150 (75.4)	4,317 (55.4)	0.43	79 (74.7)	3,585 (57.3)	0.37	102 (75.0)	100 (74.8)	0.01
Antimicrobials	196 (98.5)	7,339 (94.2)	0.23	104 (98.1)	5,975 (95.5)	0.15	133 (97.8)	131 (97.8)	0.00
Anticoagulants	17 (8.5)	265 (3.4)	0.22	(n<5)	245 (3.9)	0.00	12 (8.8)	12 (8.6)	0.01
Diabetes	27 (13.6)	720 (9.2)	0.14	23 (21.5)	616 (9.8)	0.32	16 (11.8)	22 (16.2)	0.13
Obstructive airway disease	90 (45.2)	2,189 (28.1)	0.36	50 (47.2)	1,839 (29.4)	0.37	57 (41.9)	58 (43.4)	0.03
Proxies for IMID severity	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Procedures on the skin, GI tract or joints	61 (30.7)	724 (9.3)	0.55	16 (15.4)	712 (11.4)	0.12	35 (25.7)	35 (26.0)	0.01
Immune-mediated inflammatory disease drugs	84 (42.2)	2,110 (27.1)	0.32	39 (36.6)	1,875 (30.0)	0.14	55 (40.4)	58 (43.3)	0.06

Abbreviations: IMID; immune mediated inflammatory diseases.

Appendix Table A20. Characteristics of SARS-CoV-2 PCR test positive patients in Denmark 20 April-18 October 2020, by exposure to immunosuppressants, with inverse probability of treatment weighting (IPTW) and matching weights propensity score models.

Characteristics	Unadjusted			Adjusted with IPTW			Adjusted with matching weights		
	Exposed (n=328)	Unexposed (n=28,406)	SMD	Exposed (n=146)	Unexposed (n=18,300)	SMD	Exposed (n=183)	Unexposed (n=178)	SMD
Age, median (IQR)	54 (36-69)	34 (21-52)	0.78	70 (42-79)	43 (26-56)	0.92	54 (37-73)	52 (35-66)	0.14
Male, N (%)	161 (49.1)	14,223 (50.1)	0.02	54 (36.7)	9,624 (52.6)	0.32	82 (44.8)	80 (44.8)	0.00
Number of admissions and outpatient contacts	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
0	11 (3.4)	15,665 (55.1)	1.38	51 (35.0)	5,838 (31.9)	0.07	8 (4.4)	9 (5.1)	0.03
1-2	27 (8.2)	7,257 (25.5)	0.48	39 (26.6)	7,178 (39.2)	0.27	26 (14.2)	29 (16.2)	0.05
3-5	76 (23.2)	3,062 (10.8)	0.33	31 (21.0)	3,040 (16.6)	0.11	65 (35.5)	48 (26.9)	0.19
6+	214 (65.2)	2,422 (8.5)	1.45	26 (17.5)	2,245 (12.3)	0.15	84 (45.9)	93 (51.8)	0.12
Diagnoses	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Cardiovascular disease	99 (30.2)	2,735 (9.6)	0.53	37 (25.1)	2,239 (12.2)	0.33	59 (32.2)	43 (24.2)	0.18
Neoplasms, blood and blood-forming organs	13 (4.0)	67 (0.2)	0.26	0 (0.2)	55 (0.3)	0.01	(n<5)	(n<5)	0.04
Solid organ transplantation	14 (4.3)	19 (0.1)	0.29	1 (0.4)	(n<5)	0.08	(n<5)	0 (0.1)	0.20
Pulmonary disease	70 (21.3)	2,019 (7.1)	0.42	11 (7.5)	1,634 (8.9)	0.05	33 (18.0)	29 (16.4)	0.04
Liver disease	10 (3.0)	194 (0.7)	0.18	(n<5)	161 (0.9)	0.15	7 (3.8)	(n<5)	0.12
Kidney disease	45 (13.7)	686 (2.4)	0.42	9 (6.2)	553 (3.0)	0.15	22 (12.0)	14 (7.9)	0.14
Diseases of the gastrointestinal tract	63 (19.2)	253 (0.9)	0.64	(n<5)	188 (1.0)	0.02	10 (5.5)	8 (4.7)	0.04
Gastrointestinal pathologies	52 (15.9)	1,368 (4.8)	0.37	6 (4.2)	1,076 (5.9)	0.08	21 (11.5)	20 (10.9)	0.02
Neurological and musculoskeletal disease	210 (64.0)	5,721 (20.1)	0.99	50 (34.5)	5,492 (30.0)	0.10	109 (59.6)	97 (54.2)	0.11
Skin disease	79 (24.1)	1,021 (3.6)	0.62	12 (8.1)	927 (5.1)	0.12	31 (16.9)	21 (11.5)	0.16
Medications	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Antianaemic drugs	167 (50.9)	2,075 (7.3)	1.09	27 (18.1)	1,896 (10.4)	0.22	69 (37.7)	56 (31.5)	0.13
Cardiovascular drugs	220 (67.1)	9,827 (34.6)	0.69	115 (78.7)	7,567 (41.4)	0.83	121 (66.1)	111 (62.1)	0.08
Antimicrobials	319 (97.3)	24,862 (87.5)	0.37	140 (95.9)	16,353 (89.4)	0.25	175 (95.6)	171 (96.1)	0.02
Anticoagulants	22 (6.7)	368 (1.3)	0.28	(n<5)	303 (1.7)	0.05	9 (4.9)	8 (4.5)	0.02
Diabetes	38 (11.6)	1,491 (5.2)	0.23	13 (8.7)	1,183 (6.5)	0.08	21 (11.5)	19 (10.9)	0.02
Obstructive airway disease	122 (37.2)	7,313 (25.7)	0.25	69 (47.0)	4,710 (25.7)	0.45	71 (38.8)	60 (33.4)	0.11
Proxies for IMID severity	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Procedures on the skin, GI tract or joints	101 (30.8)	1,515 (5.3)	0.70	10 (6.6)	1,421 (7.8)	0.05	33 (18.0)	37 (21.0)	0.07
Immune-mediated inflammatory disease drugs	168 (51.2)	5,541 (19.5)	0.70	61 (41.4)	4,914 (26.9)	0.31	80 (43.7)	79 (44.1)	0.01

Abbreviations: IMID; immune mediated inflammatory diseases.

Appendix Table A21. Variables for subgroups' propensity scores models.

Subgroup	Propensity score variables
Selective immunosuppressants (ATC group L04AA), TNF inhibitors (L04AB), and interleukin inhibitors (L04AC), and rituximab (L01XC02).	Date of birth Sex Date of SARS-COV-2 testing Hospital admission and outpatient contacts Neoplasms, blood and blood forming organs Neurological and musculoskeletal disease Solid organ transplant Pulmonary disease Diseases of the gastrointestinal tract Skin disease Cardiovascular disease Medications for IMID
Calcineurin inhibitors (L04AD), other immunosuppressants (L04AX), hydroxychloroquine and chloroquine (P01BA01 and P01BA02).	Date of birth Sex Date of SARS-COV-2 testing Hospital admission and outpatient contacts Neoplasms, blood and blood forming organs Neurological and musculoskeletal disease Solid organ transplant Pulmonary disease Diseases of the gastrointestinal tract Skin disease Cardiovascular disease Medications for IMID Procedures on the skin, GI tract, or joints Gastrointestinal pathologies Liver disease Kidney disease
Systemic glucocorticoids (H02AB).	Date of birth Sex Date of SARS-COV-2 testing Hospital admission and outpatient contacts Neoplasms, blood and blood forming organs Neurological and musculoskeletal disease Solid organ transplant Pulmonary disease Diseases of the gastrointestinal tract Skin disease Cardiovascular disease Medications for IMID Procedures on the skin, GI tract, or joints Gastrointestinal pathologies Liver disease Kidney disease Cardiovascular drugs Antimicrobials Anticoagulants Drugs used in diabetes Drugs for obstructive airway diseases

Abbreviations: ATC; anatomical therapeutic chemicals, GI: gastrointestinal, IMID: immune-mediated inflammatory diseases.

Appendix Methods

INTRODUCTION

During the first months of the pandemic people in defined risk groups, such as patients receiving immunosuppressants, as well as elderly people and people with chronic diseases, who were expected to be more susceptible to a severe course of COVID-19 disease than the general population, were prioritised for testing. From 21 April 2020, testing was open to a wider population, however, it cannot be ruled out that persons in risk groups could be more inclined towards being tested. Therefore, we expected that patients exposed to immunosuppressants were overrepresented in our cohort. However, as virtually all individuals infected with SARS-CoV-2 who required hospital admission and a large part of those who died were tested, this overrepresentation only occurs to a small degree among individuals with the outcomes. This oversampling decreases the proportion of the exposed who have the outcome, compared to a random sample of individuals infected with SARS-CoV-2. This selection bias lowers risk estimates, but the influence will be attenuated as other persons in the risk groups, as well as health care workers, were also tested more than the general population.

RESULTS

We show below that the bias depends on known numbers from our dataset as well as the risk ratio of being tested, for the composite exposure of persons in the risk groups and health care workers compared to others, among those infected with SARS-CoV-2 and not requiring immediate hospital admission. Appendix Figure 2 shows bias corrected estimates for the main results comparing immunosuppressant exposed patients to unexposed patients, with this risk ratio ranging from 1 to 3.

PROOF

The argument uses the assumption that all persons with the outcomes among those with SARS-CoV-2 are tested. We will consider hospital admission first, and use the notation in Table S1 for the data in the sampled population (SARS-CoV-2 infected with a positive test) and the population of interest (SARS-CoV-2 infected).

Appendix Table S1. Notation for the numbers of individuals with or without the outcome hospital admission, by risk group and exposure status, for individuals tested and individuals infected with SARS-CoV-2.

		SARS-CoV-2 infected			
		Tested		All	
I	R	Y=0	Y=1	Y=0	Y=1
0	0	A	C	a.A	C
0	1	B		b.B	
1	0 or 1	D	E	b.D	E

I: immunosuppressant medications; R: risk groups and health care workers; Y: hospital admission. A-E: cell numbers; a and b: one over the probability of being tested in the respective cell.

As hospital admission is relatively rare for the total group of SARS-CoV-2 infected, we can approximate the risk ratio of Y (hospital admission) given I (exposure to immunosuppressants) with the odds ratio:

$$RR_{Y|I} \approx OR_{Y|I} = \frac{E}{C} \times \frac{aA + bB}{bD}$$

Among those that have been tested (T):

$$RR_{Y|I,T=1} = \frac{E}{C} \times \frac{A + B + C}{D + E}$$

which gives

$$\begin{aligned} RR_{Y|I} &= RR_{Y|I,T=1} \times \frac{D+E}{A+B+C} \times \frac{aA+bB}{bD} \\ &= RR_{Y|I,T=1} \frac{D+E}{A+B+C} \times \frac{\frac{a}{b}A+B}{D} \end{aligned}$$

Note that

$$\frac{a}{b} = \frac{1}{\frac{b}{a}} = RR_{T|R,Y=0}$$

which is the risk ratio of being tested for risk groups and health care workers compared to others, restricted to those without hospital admission. The risk of testing given no hospital admission possibly later in time is hard to interpret, so we will make an approximation. As around 80% of the hospital admissions happen on the same day as testing, we will make an approximation by changing the restriction from those without hospital admission to those without hospital admission on the day of the test (S):

$$RR_{T|R,Y=0} \approx RR_{T|R,S=0}$$

Thus, we have the following equation for the risk ratio (RR) of hospital admission (Y) given exposure (I) among those who have been tested (T=1):

$$RR_{Y|I} \approx RR_{Y|I,T=1} \times \frac{D+E}{A+B+C} \times \frac{A \times RR_{T,(S=0)|R} + B}{D}$$

Where A is unexposed people, not in risk groups, without the outcome; B is unexposed people, in risk groups, without the outcome; C is unexposed people with the outcome; D exposed people without the outcome; and E is exposed people with the outcome.

To apply the equation to our data we split the matching weights dataset for hospital admission, with 89 events among 208 exposed, and 77 events among 201 exposed (as per Appendix Table 15) into risk and non-risk groups based on rough definitions and to produce the values in Table S2 (corresponding to Appendix Table S1).

Appendix Table S2. The numbers of individuals with or without the outcome hospital admission, by risk group and exposure status, for individuals tested and individuals infected with SARS-CoV-2.

		SARS-CoV-2 infected			
		Tested		All	
I	R	Y=0	Y=1	Y=0	Y=1
0	0	115	87	a x 115	87
0	1	137		b x 137	
1	0 or 1	246	100	b x 246	100

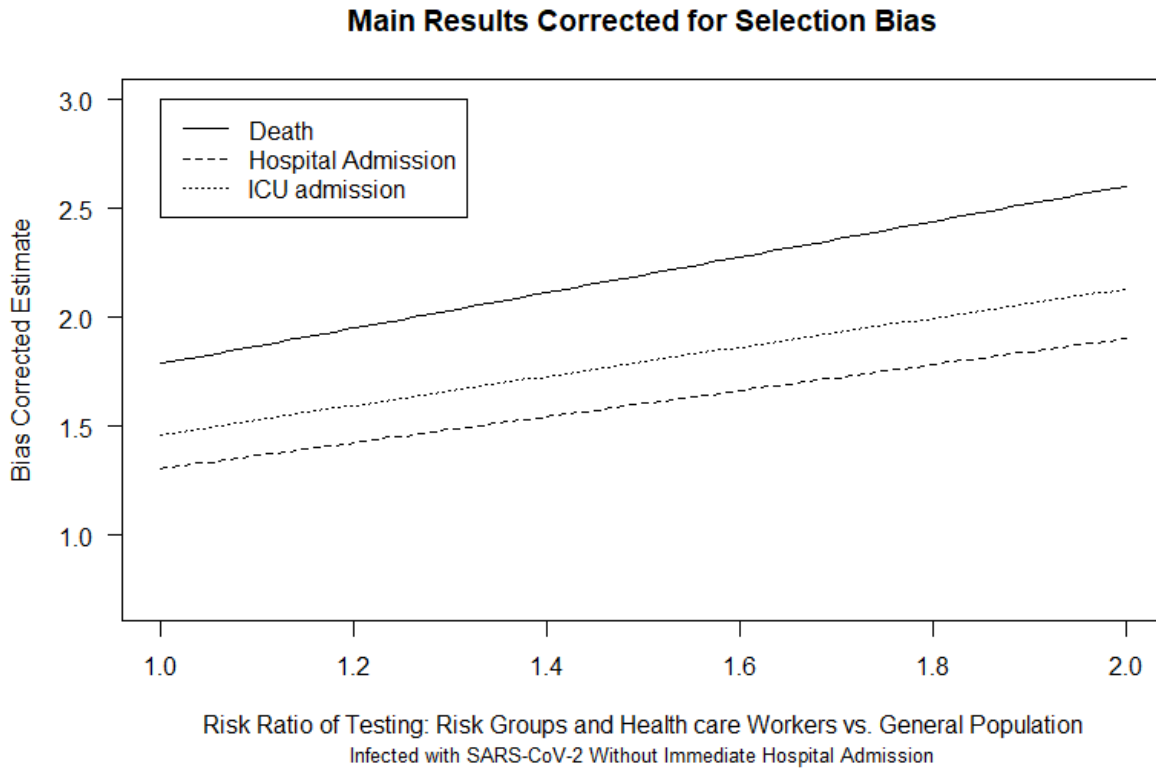
I: immunosuppressant medications; R: risk groups and health care workers; Y: hospital admission; a and b: one over the probability of being tested in the respective cell.

The values in Appendix Table S2 therefore give the following equation:

$$RR_{Y|I} \approx RR_{Y|I,T=1} \times \frac{346}{339} \times \frac{115 \times RR_{T|R,S=0} + 137}{246}$$

For intensive care unit (ICU) admission and death, we can again use the premise that hospital admission is relatively rare so $\frac{aA+bB}{aD}$ will not change much by adding any number of unexposed to the numerator, or exposed with admission to hospital to the denominator. Thus, as $\frac{D+E}{A+B+C}$ only depends on the total number of exposed and unexposed, the bias for ICU admission and death can be approximated by that for hospital admission. N.B, this bias analysis applies the main relative risk estimate with the composite exposure.

Appendix Figure A2. Relative risk of severe outcomes of SARS-CoV-2 in patients exposed to immunosuppressants compared to unexposed patients, corrected for selection bias (the risk ratio of being tested, for risk groups and health care workers compared to the general population, ranging from 1 to 3).



Abbreviations: ICU; Intensive care unit.