

The Impact of Immunosuppressive Therapy on SARS-CoV-2 mRNA Vaccine Effectiveness in Patients with Immune-mediated Inflammatory Diseases: A Danish Nationwide Cohort Study

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SUPPLEMENTARY TABLES

Supplementary Table 1. Exposures and corresponding ATC and procedure codes for immunosuppressives

| Medication | ATC code | Procedure code |
|---------------------------------------|----------|----------------|
| Selective immunosuppressants | | |
| Muromonab-CD3 | L04AA02 | |
| Antilymphocyte immunoglobulin (horse) | L04AA03 | |
| | L04AA04 | BOHJ12 |
| Antithymocyte immunoglobulin (rabbit) | L04AA06 | BOHJ22 |
| Mycophenolic acid | L04AA10 | BOHJ23 |
| Sirolimus | L04AA13 | |
| Leflunomide | L04AA18 | BOHJ24 |
| Everolimus | L04AA23 | BOHJ26 |
| Natalizumab | L04AA24 | BOHJ18C1 |
| Abatacept | L04AA25 | BWHB84 |
| Eculizumab | L04AA26 | BOHJ19H6 |
| Belimumab | L04AA27 | BOHJ27 |
| Fingolimod | L04AA28 | |
| Belatacept | L04AA29 | BOHJ28D |
| Tofacitinib | L04AA31 | BOHJ28A |
| Teriflunomide | L04AA32 | |
| Aprelimast | L04AA33 | BOHJ19H4 |
| Vedolizumab | L04AA34 | BOHJ16A |
| Alemtuzumab | L04AA36 | |
| Ocrelizumab | L04AA37 | |
| Baricitinib | L04AA38 | |
| Ozanimod | L04AA39 | |
| Emapalumab | L04AA40 | BWHA178 |
| Cladribine | L04AA41 | |
| Imlifidase | L04AA42 | BWHB87 |
| Siponimod | L04AA43 | |
| Ravulizumab | L04AA44 | |
| Upadacitinib | | |

| | | |
|--|---------|----------|
| Tumour 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 corticosteroids | H02AB | |
| Rituximab | L01XC02 | |

Supplementary Table 2. Minimum daily dose of corticosteroid in exposed persons

| Compound | Equivalent dose |
|--------------------|------------------------|
| Cortisone | 38mg |
| Hydrocortisone | 30mg |
| Prednisone | 7.5mg |
| Prednisolone | 7.5mg |
| Triamcinolone | 6mg |
| Methylprednisolone | 6mg |
| Betamethasone | 0.9mg |
| Dexamethasone | 1.2mg |

Supplementary Table 3. Covariates by disease cohort

| IBD COHORT | | |
|--|---------------------------------|--------------------------------|
| Covariate | Categories/ ATC/ICD codes | Assessment window |
| Age | - | At cohort entry |
| Sex | - | At cohort entry |
| SARS-CoV-2 tests in the previous month | - | At cohort entry |
| Ever previous SARS-CoV-2 positive test | - | From February 2020 |
| IBD specific covariates | | |
| Any IBD-related hospital admissions in the previous year | K50/K51 | 1 year before cohort entry |
| Crohn's disease | K50 | At cohort entry |
| Ulcerative colitis | K51 | At cohort entry |
| 5-ASA/sulfasalazine | MA07EC0 | 1 year before matching date |
| Budesonide | MA07EA06 | 3 months before matching date |
| IBD related procedures | | Any time before cohort entry |
| Operations of the small bowel and colon | KJF | |
| Operations of the rectum | KJG | |
| Operations of the anus and perianal tissue | KJH | |
| Operational of the abdominal wall, peritoneum, mesentery and omentum | KJA | |
| Lysis of adhesion in the abdominal cavity | KJAP | |
| Closure of intestinovaginal fistula | KLEE30 | |
| Closure of vesiculointestinal fistula | KKCH30 | |
| Endoscopy of the gastrointestinal tract | KUJ | 1 year before the cohort entry |
| Comorbidities | | |
| Cardiovascular disease | DI1-I7 | Any time before cohort entry |
| Pulmonary disease | | Any time before cohort entry |
| Chronic disease of the lower airways | DJ4 | |
| Other interstitial lung disease | DJ84 | |
| Diseases with pus and necrosis in the lower airway | DJ85 | |
| Interstitial lung emphysema | DJ982 | |
| compensatory emphysema | DJ983 | |
| Liver disease | DK70-K77 | Any time before cohort entry |
| Kidney disease | | Any time before cohort entry |
| Glomerular disease | DN0 | |
| Tubulointerstitial kidney disease and kidney insufficiency | DN1 | |
| Other gastrointestinal diseases | | Any time before cohort entry |
| Gingivitis and periodontal disease | DK05 | |
| Inflammation of the oral mucosa and related | DK12 | |
| Stomach and duodenal ulcers | DK25-27 | |
| Fissure and rifts in and around the anus | DK60 | |
| Abscess in and around the anus | DK61 | |
| Other diseases of the rectum and anus | DK62 | |
| Other bowel disease | DK63 | |

| | | |
|--|---|------------------------------|
| Skin disease 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 | DL10-14 DL20-30 DL63 DL80 DL92 DL93 DL94 DL95 | Any time before cohort entry |
| Musculoskeletal disease Generalised connective tissue diseases Diseases of the muscles Soft-tissue rheumatism | DM30- DM36 DM60-63 DM70-79 | Any time before cohort entry |
| Medications | | |
| Cardiovascular drugs | MC01-MC10 | Any time before cohort entry |
| Antibiotics | MJ01 | Any time before cohort entry |
| Oral anticoagulants | MB01AA MB01AF | Any time before cohort entry |
| Drugs used in diabetes | MA10 | Any time before cohort entry |
| Drugs for obstructive airway diseases | MR03 | Any time before cohort entry |
| INFLAMMATORY ARTHROPATHIES COHORT | | |
| Age | - | At cohort entry |
| Sex | - | At cohort entry |
| SARS-CoV-2 tests in the previous month | - | At cohort entry |
| Arthropathy-specific covariates | | |
| Arthropathy-related procedures 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 | KNBB KNBC KNBE KNBF KNBG KBM79 KNCB KNCC KNCE KNCF KNCG KNCM79 KNDB KNDC KNDE KNDF KNDG KNDM | Any time before cohort entry |

| | | |
|---|---|---|
| <p>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 in the 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 Joint resections, arthroplasties, and arthrodesis Excision of bursae Ankle and foot 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</p> | <p>KNFB KNFC KNFE KNFF KNFG KNFM79 KNGB KNGC KNGE KNGF KNGG KNGM79 KNHB KNHC KNHE KNHF KNHG KNHM</p> | |
| <p>Anti-inflammatory and anti-rheumatic drugs inc. specific anti-rheumatic therapies, non-steroidals, and combination medications Hydroxychloroquine</p> | <p>M01 P01BA02</p> | <p>3 months before before cohort entry</p> |
| Comorbidities | | |
| <p>Cardiovascular disease</p> | <p>DI1-I7</p> | <p>Any time before cohort entry</p> |
| <p>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</p> | <p>DJ4 DJ84 DJ85 DJ982 DJ983</p> | <p>Any time before cohort entry</p> |
| <p>Liver disease</p> | <p>DK70-K77</p> | <p>Any time before cohort entry</p> |
| <p>Kidney disease Glomerular disease Tubulointerstitial kidney disease and kidney insufficiency</p> | <p>DN0 DN1</p> | <p>Any time before cohort entry</p> |
| <p>Other gastrointestinal diseases 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</p> | <p>DK05 DK12 DK25-27 DK60 DK61 DK62 DK63</p> | <p>Any time before cohort entry</p> |
| <p>Skin disease Bullous skin disease Dermatitis and eczema Alopecia areata</p> | <p>DL10-14 DL20-30 DL63</p> | <p>Any time before cohort entry</p> |

| | | |
|---|---------------------------------------|------------------------------|
| Vitiligo Granulomatous disease in the skin and subcutaneous tissue Lupus Other localised connective tissue disease Vasculitis limited to the skin | DL80 DL92 DL93 DL94 DL95 | |
| Musculoskeletal disease Generalised connective tissue diseases Diseases of the muscles Soft-tissue rheumatism | DM30- DM36 DM60-63 DM70-79 | Any time before cohort entry |
| Medications | | |
| Cardiovascular drugs | MC01-MC10 | Any time before cohort entry |
| Antibiotics | MJ01 | Any time before cohort entry |
| Oral anticoagulants | MB01AA MB01AF | Any time before cohort entry |
| Drugs used in diabetes | MA10 | Any time before cohort entry |
| Drugs for obstructive airway diseases | MR03 | Any time before cohort entry |
| PSORIASIS COHORT | | |
| Age | - | At cohort entry |
| Sex | - | At cohort entry |
| SARS-CoV-2 tests in the previous month | - | At cohort entry |
| Psoriasis-specific covariates | | |
| Procedures Ultraviolet therapy: UV-A with psoralen/broad-spectrum UVB / narrow-spectrum UVB | BNGA1/ BNGA2/ BNGA3 | Any time before cohort entry |
| Therapeutic steroid injection in the joints and soft tissues | BLHN0 | Any time before cohort entry |
| 5-ASA/sulfasalazine | A07EC0 | 1 year before cohort entry |
| Topical corticosteroids | D07 | 1 year before cohort entry |
| Antipsoriatic medication | D05 | 1 year before cohort entry |
| Topical calcineurin inhibitors | D11AH01-02, | 1 year before cohort entry |
| Comorbidities | | |
| Cardiovascular disease | DI1-I7 | Any time before cohort entry |
| 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 | Any time before cohort entry |

| | | |
|---|--|------------------------------|
| Liver disease | DK70-K77 | Any time before cohort entry |
| Kidney disease Glomerular disease Tubulointerstitial kidney disease and kidney insufficiency | DN0 DN1 | Any time before cohort entry |
| Other gastrointestinal diseases 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 | Any time before cohort entry |
| Skin disease 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 | DL10-14 DL20-30 DL63 DL80 DL92 DL93 DL94 DL95 | Any time before cohort entry |
| Musculoskeletal disease Generalised connective tissue diseases Diseases of the muscles Soft-tissue rheumatism | DM30- DM36 DM60-63 DM70-79 | Any time before cohort entry |
| Medications | | |
| Cardiovascular drugs | MC01-MC10 | Any time before cohort entry |
| Antibiotics | MJ01 | Any time before cohort entry |
| Oral anticoagulants | MB01AA MB01AF | Any time before cohort entry |
| Drugs used in diabetes | MA10 | Any time before cohort entry |
| Drugs for obstructive airway diseases | MR03 | Any time before cohort entry |

Supplementary Table 4. Risk of infection, hospitalisation and death associated with immunosuppressive therapy in vaccinated patients with immune-mediated inflammatory diseases.

| | Exposed | | | | Unexposed | | | | Crude HR (95% CI) *** | Weighted HR (95% CI) *** |
|----------------------------------|---------|--------|-------------------------------|--------|-----------|--------|-------------------------------|--------|--------------------------|-----------------------------|
| | Total | Events | Incidence rate (95% CI) ** | PY | Total | Events | Incidence rate (95% CI) ** | PY | | |
| COVID-19 Infection* | | | | | | | | | | |
| IBD | 10 477 | 287 | 54.7 (48.7-61.4) | 5 246 | 46 974 | 885 | 42.5 (39.8-45.4) | 20 809 | 1.7 (1.5-1.9) | 1.6 (1.4-1.9) |
| Arthropathy | 24 255 | 476 | 40.3 (36.8-44.1) | 11 822 | 44 650 | 800 | 37.8 (35.3-40.6) | 21 140 | 1.3 (1.1-1.4) | 1.3 (1.1-1.4) |
| Psoriasis | 5 023 | 103 | 45.3 (37.4-55.00) | 2 273 | 20 995 | 392 | 41.5 (37.6-45.8) | 9 441 | 1.1 (0.9-1.4) | 1.1 (0.9-1.4) |
| Combined cohorts | 39 755 | 866 | - | 19 341 | 112 619 | 2 077 | - | 51 390 | 1.4 (1.3-1.5) | 1.4 (1.2-1.5) |
| COVID-19 Hospitalization* | | | | | | | | | | |
| IBD | 10 477 | 15 | 2.8 (1.7-4.7) | 5 280 | 46 980 | 43 | 2.1 (1.5-2.8) | 20 892 | 2.8 (1.5-5.1) | 2.1 (1.0-4.1) |
| Arthropathy | 24 256 | 37 | 3.1 (2.3-4.3) | 11 873 | 44 650 | 59 | 2.8 (2.2-3.6) | 21 215 | 1.3 (0.9-2.0) | 1.3 (0.9-2.0) |
| Psoriasis | 5 023 | <5 | - | 2 284 | 20 999 | 20 | 2.1 (1.4-3.3) | 9 479 | 0.5 (0.1-2.3) | 0.6 (0.1-2.5) |
| Combined cohorts | 39 756 | <57 | - | 19 437 | 112 629 | 122 | - | 51 594 | 1.6 | 1.4 |

| | | | | | | | | | (1.1-2.2) | (1.0-2.0) |
|---|--------|-----|-------------------|--------|---------|-----|------------------|--------|------------------|------------------|
| Death* | | | | | | | | | | |
| IBD | 10 477 | <5 | - | 5 281 | 46 980 | 6 | 0.3 (0.1-0.6) | 20 897 | 1.1 (0.1-9.7) | 0.4 (0-5.6) |
| Arthropathy | 24 256 | 6 | 0.51 (0.2-1.1) | 11 875 | 44 650 | 13 | 0.6 (0.4-1.1) | 21 222 | 1.0 (0.4-2.7) | 1.0 (0.4-2.6) |
| Psoriasis | 5 023 | 0 | - | 2 284 | 20 999 | <5 | - | 9 480 | - | - |
| Combined cohorts | 39 756 | <11 | - | 19 440 | 112 629 | <24 | - | 51 599 | 1.0 (0.4-2.5) | 0.9 (0.4-2.2) |
| Abbreviations: CI = confidence interval; HR = hazard ratio; IBD= inflammatory bowel disease; PY = person-years. | | | | | | | | | | |
| *COVID19- Infection = confirmed positive antigen or PCR test result for SARS-CoV2; COVID-19 Hospital Admission = Hospitalisation with SARS-CoV2 infection as primary diagnosis code; Death within 60 days of positive SARS-CoV2 test. | | | | | | | | | | |
| **Events/1000 PY (95% CI) | | | | | | | | | | |
| *** Sex and age adjusted crude and weighted hazard ratios | | | | | | | | | | |

Supplementary Table 5. Risk of COVID-19 infection associated with immunosuppressive therapy in vaccinated patients with immune-mediated inflammatory diseases at 0-3 months, 3-6 months, and 6-11 months post-vaccination.

| | Exposed | | | | Unexposed | | | | Crude HR (95% CI)** | Weighted HR (95% CI)** |
|---|---------|--------|-----------------------------|--------|-----------|--------|-----------------------------|--------|------------------------|---------------------------|
| | Total | Events | Incidence rate (95% CI)* | PY | Total | Events | Incidence rate (95% CI)* | PY | | |
| COVID-19 infection 0-3 months post-vaccination | | | | | | | | | | |
| IBD | 10 477 | 57 | 22.2 (17.1-28.8) | 2 570 | 46 974 | 196 | 17.0 (14.8-19.5) | 11 546 | 1.6 (1.2-2.2) | 1.5 (1.1-2.2) |
| Arthropathy | 24 255 | 96 | 16.1 (13.2-19.6) | 5 978 | 44 650 | 166 | 15.1 (13.0-17.6) | 10 990 | 1.3 (1.0-1.7) | 1.3 (1.0-1.7) |
| Psoriasis | 5 023 | 24 | 19.4 (13.0-29.0) | 1 236 | 20 995 | 83 | 16.1 (13.0-19.9) | 5 163 | 1.3 (0.3-2.1) | 1.3 (0.8-2.1) |
| Combined cohorts | 39 755 | 177 | - | 4 403 | 112 619 | 445 | - | 27 699 | 1.4 (1.2-1.7) | 1.4 (1.1-1.6) |
| COVID-19 infection 3-6 months post-vaccination | | | | | | | | | | |
| IBD | 10 010 | 123 | 45.8 (38.4-54.7) | 2 683 | 45 202 | 526 | 56.8 (52.1-61.8) | 9 266 | 0.9 (0.8-1.2) | 1.0 (0.8-1.2) |
| Arthropathy | 23 503 | 284 | 48.6 (43.2-54.5) | 5 849 | 43 186 | 482 | 47.5 (43.4-51.9) | 10 149 | 1.2 (1.1-1.4) | 1.2 (1.1-1.4) |
| Psoriasis | 4 860 | 63 | 60.7 (47.4-77.7) | 1 038 | 20 203 | 233 | 54.5 (47.9-61.9) | 4 279 | 1.1 (0.8-1.4) | 1.0 (0.8-1.4) |
| Combined cohorts | 38 373 | 470 | - | 19 437 | 108 591 | 1 241 | - | 23 694 | 1.1 (1.0-1.2) | 1.1 (1.0-1.3) |

| COVID-19 infection 6-11 months post-vaccination | | | | | | | | | | |
|---|--------|-----|------------------------|-------|--------|-----|-----------------------|-------|------------------|-------------------|
| IBD | 6 058 | 107 | 160.6 (132.9-194.1) | 666 | 15 742 | 163 | 107.1 (91.9-124.9) | 1 522 | 1.3 (0.9-1.7) | 1.4 (1.1-1.9) |
| Arthropathy | 12 223 | 96 | 82.7 (67.7-101.0) | 1 160 | 19 839 | 152 | 80.8 (68.9-94.7) | 1 881 | 1.1 (0.8-1.4) | 1.1 (0.8-1.4) |
| Psoriasis | 1 719 | 16 | 93.8 (57.5-153.1) | 170 | 7 444 | 76 | 109.8 (87.7-137.5) | 691 | 0.9 (0.5-1.5) | 0.9 (0.5-1.5) |
| Combined cohorts | 20 000 | 219 | - | 1 996 | 43 025 | 391 | - | 4 094 | 1.1 (0.9-1.3) | 1.11 (0.9-1.3) |
| Abbreviations: CI = confidence interval; HR = hazard ratio; IBD= inflammatory bowel disease; PY = person-years. | | | | | | | | | | |
| *Events/1000 PY | | | | | | | | | | |
| **Sex and age adjusted crude and weighted hazard ratios | | | | | | | | | | |

Supplementary Table 6. Risk of COVID infection associated with immunosuppressive therapy in vaccinated patients with immune-mediated inflammatory diseases by calendar period (1st January-31st November 2021)

| | Exposed | | Unexposed | | Hazard Ratio (HR) | |
|--|---------|--------|-----------|--------|-------------------|-------------------------|
| | Total | Events | Total | Events | Crude HR (95% CI) | Weighted HR (95% CI) ** |
| *COVID-19 infection from 1st January to 30th April | | | | | | |
| IBD | 5 745 | n<5 | 10 306 | 7 | 0.67 (0.17-2.61) | 0.39 (0.09-1.71) |
| Arthropathy | 9 646 | 9 | 13 044 | 17 | 0.75 (0.33-1.69) | 0.78 (0.35-1.71) |
| Psoriasis | 1 298 | n<5 | 4 512 | 6 | 2.00 (0.50-8.02) | 1.98 (0.48-8.19) |
| Combined IMID | 16 689 | <19 | 27 862 | 30 | 0.87 (0.48-1.59) | 0.83 (0.44-1.54) |
| COVID-19 infection 1st May to 31st August | | | | | | |
| IBD | 10 141 | 56 | 45 486 | 121 | 1.61 (1.17-2.22) | 1.19 (0.82-1.73) |
| Arthropathy | 23 885 | 74 | 43 457 | 116 | 1.08 (0.81-1.45) | 1.07 (0.79-1.43) |
| Psoriasis | 4 912 | 12 | 20 337 | 53 | 0.88 (0.47-1.65) | 0.84 (0.44-1.58) |
| Combined IMID | 38 938 | 142 | 109 280 | 290 | 1.24 (1.01-1.52) | 1.08 (0.87-1.34) |
| COVID-19 infection 1st September to 30st November | | | | | | |
| IBD | 1 0349 | 228 | 46 590 | 757 | 1.69 (1.45-1.97) | 1.74 (1.48-2.04) |
| Arthropathy | 23 898 | 393 | 44 079 | 667 | 1.34 (1.18-1.51) | 1.33 (1.17-1.51) |
| Psoriasis | 4 974 | 88 | 20 803 | 333 | 1.17 (0.93-1.48) | 1.13 (0.89-1.44) |
| Combined IMID | 39 221 | 709 | 111 472 | 1757 | 1.42 (1.30-1.55) | 1.42 (1.29-1.56) |
| Abbreviations: CI = confidence interval; HR = hazard ratio; IBD= inflammatory bowel disease. | | | | | | |
| *COVID19- Infection = confirmed positive antigen or PCR test result for SARS-CoV2 | | | | | | |
| ** Sex and age adjusted crude and weighted hazard ratios | | | | | | |

Supplementary Table 7. Risk of infection, hospitalisation and death associated with immunosuppressive therapy in vaccinated patients with immune-mediated inflammatory diseases by immunosuppressive drug class.

| | Exposed | | | | Unexposed | | | | Crude HR (95% CI)*** | Weighted HR (95% CI)*** |
|--|---------|--------|--------|---------------------------|-----------|--------|--------|---------------------------|----------------------|-------------------------|
| | Total | Events | PY | Incidence rate (95% CI)** | Total | Events | PY | Incidence rate (95% CI)** | | |
| COVID-19 Infection* | | | | | | | | | | |
| Selective Immunosuppressants | 3 384 | 68 | 1 846 | 39.4 (31.0-49.9) | 151 936 | 2 079 | 51 334 | 40.5 (38.8-42.3) | 1.3 (1.0-1.7) | 1.3 (1.0-1.6) |
| Tumour Necrosis Factor Inhibitors | 14 277 | 418 | 6 908 | 62.5 (56.7-68.7) | 140 797 | 2 070 | 51 355 | 40.3 (38.6-42.1) | 1.8 (1.6-2.0) | 1.8 (1.6-2.0) |
| Interleukin Inhibitors | 2 781 | 52 | 1 385 | 40.1 (30.6-52.7) | 152 584 | 2 082 | 51 352 | 40.5 (38.8-42.3) | 1.1 (0.8-1.4) | 1.0 (0.8-1.4) |
| Calcineurin Inhibitors | 154 | n<5 | 129 | - | 155 309 | 2 073 | 51 298 | 40.4 (38.7-42.2) | 1.3 (0.3-5.2) | 0.5 (0.2-1.5) |
| Systemic Corticosteroids | 5 504 | 97 | 2 991 | 34.6 (28.4-42.3) | 149 667 | 2 079 | 51 503 | 40.4 (38.7-42.1) | 1.3 (1.0-1.6) | 1.2 (1.0-1.5) |
| Rituximab and Other Immunosuppressants | 21 038 | 426 | 10 703 | 41.2 (37.5-45.3) | 112 593 | 2 075 | 51 409 | 40.4 (38.7-42.1) | 1.3 (1.2-1.4) | 1.3 (1.1-1.4) |
| COVID-19 Hospitalization* | | | | | | | | | | |
| Selective Immunosuppressants | 3 384 | 7 | 1 735 | 4.0 (1.9-8.5) | 112 479 | 122 | 51 531 | 2.4 (2.0-2.8) | 3.0 (1.4-6.5) | 2.2 (1.0-5.2) |
| Tumour Necrosis Factor Inhibitors | 14 277 | 16 | 6 740 | 2.4 (1.5-3.9) | 112 506 | 116 | 51 551 | 2.3 (1.9-2.1) | 2.0 (1.2-3.3) | 1.8 (1.0-3.3) |

| | | | | | | | | | | |
|--|--------|-----|--------|-------------------|---------|-----|-----------|------------------|------------------|------------------|
| Interleukin Inhibitors | 2 781 | 0 | 1 302 | - | 112 445 | 125 | 51 549 | 2.4 (2.0-2.9) | - | - |
| Calcineurin Inhibitors | 154 | 0 | 83 | - | 112 404 | 122 | 51 493 | 2.4 (2.0-2.8) | - | - |
| Systemic Corticosteroids | 5 504 | 18 | 2 811 | 6.4 (4.0-10.2) | 112 587 | 122 | 51 699 | 2.4 (2.0-2.8) | 2.4 (1.4-3.9) | 1.8 (1.0-3.0) |
| Rituximab and Other Immunosuppressants | 21 038 | 25 | 10 387 | 2.4 (1.6-3.6) | 112 593 | 121 | 51 604 | 2.3 (2.0-2.8) | 1.2 (0.5-1.0) | 1.1 (0.7-1.8) |
| Death* | | | | | | | | | | |
| Selective Immunosuppressants | 3 384 | 0 | 1 736 | - | 112479 | 23 | 51 545 | 0.5 (0.3-0.7) | - | - |
| Tumour Necrosis Factor Inhibitors | 14 277 | 0 | 6 741 | - | 112506 | 19 | 5 1564 | 0.4 (0.2-0.6) | - | - |
| Interleukin Inhibitors | 2 781 | 0 | 1 302 | - | 112 445 | 24 | 51 564 | 0.5 (0.3-0.7) | - | - |
| Calcineurin Inhibitors | 154 | 0 | 83 | - | 112 404 | 24 | 51 507 | 0.5 (0.3-0.7) | - | - |
| Systemic Corticosteroids | 5 504 | 6 | 2 812 | 2.1 (2.0-4.8) | 112 587 | 23 | 51 713 | 0.4 (0.3-0.7) | 4.0 (1.6-9.9) | 2.3 (0.9-6.2) |
| Rituximab and Other Immunosuppressants | 21 038 | n<5 | 10 388 | - | 112 593 | 22 | 51 619 | 0.4 (0.3-0.7) | 0.5 (0.1-2.3) | 0.5 (0.1-2.4) |

Abbreviations: CI = confidence interval; HR = hazard ratio; IBD= inflammatory bowel disease; PY = person-years.

Immunosuppressive Drug Class: Selective Immunosuppressants, Tumour Necrosis Factor Inhibitors, Interleukin Inhibitors, Calcineurin Inhibitors, Systemic Corticosteroids, and Other Immunosuppressants including Rituximab (See Supplementary for complete ATC codes)

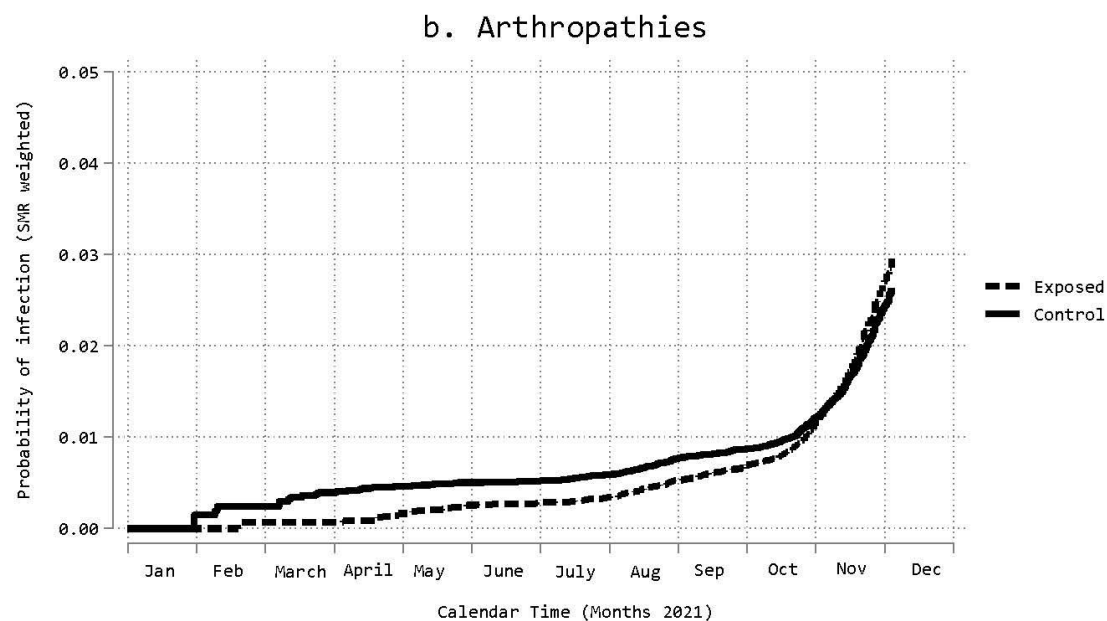
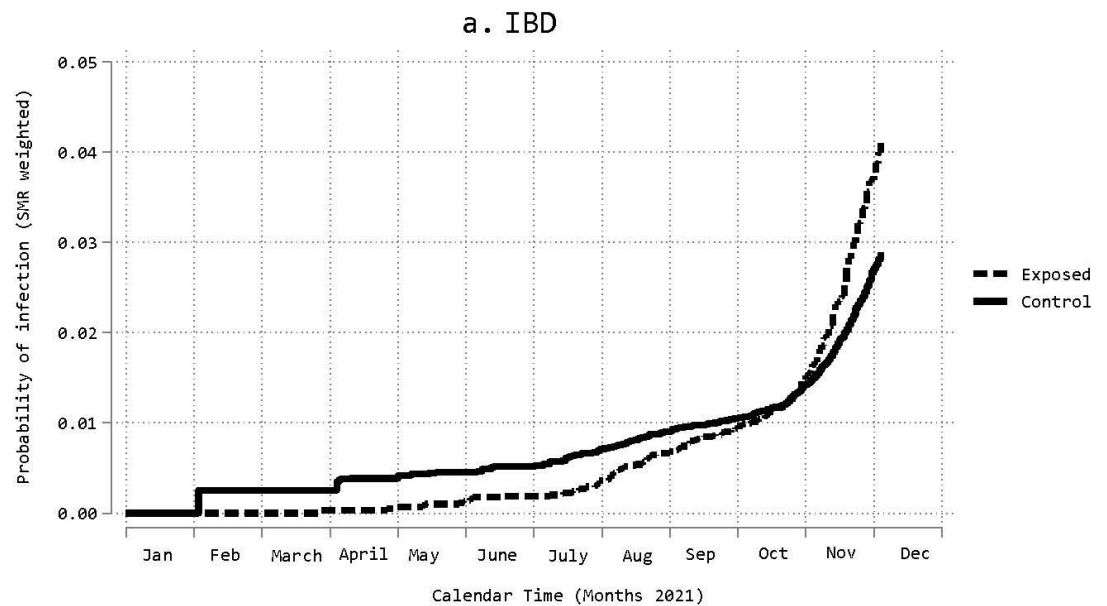
*COVID19- Infection = confirmed positive antigen or PCR test result for SARS-CoV2; COVID-19 Hospital Admission = Hospitalisation with SARS-CoV2 infection as primary diagnosis code; Death within 60 days of positive SARS-CoV2 test.

**Events/1000 PY

*** Sex and age adjusted crude and weighted hazard ratios

SUPPLEMENTARY FIGURES

Supplementary Figure 1. Kaplan-Meier plots for probability of infection with COVID-19 following second mRNA vaccination in immunosuppressive exposed compared to propensity score matched immunosuppressive unexposed a. IBD patients b. Arthropathy patients c. Psoriasis patients over the calendar year from January 1st to 31st November 2021. SMR weighted = standardized mortality ratio weighted.



c. Psoriasis

