Taylor & Francis
Taylor & Francis Group

Scandinavian Journal of Rheumatology

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/irhe20

Risk of severe COVID-19 in patients with inflammatory rheumatic diseases treated with immunosuppressive therapy in Scotland

PM McKeigue, D Porter, RJ Hollick, SH Ralston, DA McAllister & HM Colhoun

To cite this article: PM McKeigue, D Porter, RJ Hollick, SH Ralston, DA McAllister & HM Colhoun (2023) Risk of severe COVID-19 in patients with inflammatory rheumatic diseases treated with immunosuppressive therapy in Scotland, Scandinavian Journal of Rheumatology, 52:4, 412-417, DOI: 10.1080/03009742.2022.2063376

To link to this article: https://doi.org/10.1080/03009742.2022.2063376

Published online: 12 May 2022.

Risk of severe COVID-19 in patients with inflammatory rheumatic diseases treated with immunosuppressive therapy in Scotland

PM McKeigue[1,2], D Porter[3], RJ Hollick[4], SH Ralston[5], DA McAllister[2,6], HM Colhoun[2,5]

[1]Usher Institute, College of Medicine and Veterinary Medicine, University of Edinburgh, Edinburgh, UK
[2]Public Health Scotland, Glasgow, UK
[3]Department of Rheumatology, Gartnavel General Hospital, Glasgow, UK
[4]Aberdeen Centre for Arthritis and Musculoskeletal Health (Epidemiology Group), School of Medicine, Medical Sciences and Nutrition, University of Aberdeen, Aberdeen, UK
[5]Institute of Genetics and Cancer, College of Medicine and Veterinary Medicine, University of Edinburgh, Western General Hospital Campus, Edinburgh, UK
[6]Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK

Objective: To investigate the association of severe coronavirus disease 2019 (COVID-19) in patients with inflammatory rheumatic diseases (IRDs) treated with immunosuppressive drugs.

Method: A list of 4633 patients on targeted – biological or targeted synthetic – DMARDs in March 2020 was linked to a case–control study that includes all cases of COVID-19 in Scotland.

Results: By 22 November 2021, 433 of the 4633 patients treated with targeted DMARDS had been diagnosed with COVID-19, of whom 58 had been hospitalized. With all those in the population not on DMARDs as the reference category, the rate ratio for hospitalized COVID-19 associated with DMARD treatment was 2.14 [95% confidence interval (CI) 2.02–2.26] in those on conventional synthetic (cs) DMARDs, 2.01 (95% CI 1.38–2.91) in those on tumour necrosis factor (TNF) inhibitors as the only targeted agent, and 3.83 (95% CI 2.65–5.56) in those on other targeted DMARDs. Among those on csDMARDs, rate ratios for hospitalized COVID-19 were lowest at 1.66 (95% CI 1.51–1.82) in those on methotrexate and highest at 5.4 (95% CI 4.4–6.7) in those on glucocorticoids at an average dose > 10 mg/day prednisolone equivalent.

Conclusion: The risk of hospitalized COVID-19 is elevated in IRD patients treated with immunosuppressive drugs compared with the general population. Of these drugs, methotrexate, hydroxychloroquine, and TNF inhibitors carry the lowest risk. The highest risk is associated with prednisolone. A larger study is needed to estimate reliably the risks associated with each class of targeted DMARD.

Early in the coronavirus disease 2019 (COVID-19) epidemic in the UK, people on 'immunosuppression therapies sufficient to increase risk of infection' were designated by public health agencies as clinically extremely vulnerable and thus eligible for shielding (1). In Scotland, letters advising these individuals to shield themselves were issued from April 2020 onwards, and in November 2020, a further letter was issued with 'extra protection level advice for people at highest risk' based on the current classification of the protection level of the area in which they were resident. The list of those eligible for shielding has been regularly updated, and was used to identify those at highest priority for vaccination. More recently, the Joint Committee on Vaccination and Immunization has recommended a third primary dose of vaccine to achieve maximal protection for those on biological immunosuppressants, targeted synthetic immunosuppressants, or non-biological oral immune-modulating drugs, including corticosteroids, at a dose equivalent to ≥ 10 mg prednisolone per day (2). A 2021 review, however, concluded that 'a diagnosis of inflammatory arthritis, psoriasis, or inflammatory bowel diseases does not increase risk for SARS-CoV-2 infection or severe COVID-19' and that cytokine inhibitors 'might even lower the risk of severe COVID-19' (3). The objective of this study was to investigate the associations between hospitalized or fatal COVID-19 and autoimmune rheumatological disease and disease-modifying anti-rheumatic drugs (DMARDs).

Method

Because targeted – biological or synthetic – immunosuppressants are prescribed only in hospital and not captured by prescribing databases, Public Health Scotland (PHS) asked clinicians in relevant specialities to provide lists of patients on these drugs in March 2020, at the outset of the

PM McKeigue, Usher Institute, College of Medicine and Veterinary Medicine, University of Edinburgh, Teviot Place, Edinburgh EH8 9AG, UK.
Email: paul.mckeigue@ed.ac.uk

Accepted 5 April 2022

DOI: 10.1080/03009742.2022.2063376

COVID-19 epidemic (4, 5). This study focuses on lists provided by NHS Lothian, NHS Grampian, and part of NHS Greater Glasgow and Clyde, covering about one-third of the Scottish population. These lists were not updated. The merged list, hereafter the 'targeted DMARDs list', was linked to the REACT-SCOT case–control study to take advantage of data linkages. This study includes all 700 022 diagnosed cases of COVID-19 in Scotland since the start of the epidemic, and 3 238 432 individuals who have been sampled at least once as controls.

The design of the REACT-SCOT study has been described previously (6). In brief, for every incident case of COVID-19 in the population, 10 controls matched for 1 year age, sex, and primary care practice, and alive on the day of presentation of the case to which they were matched, were selected using the Community Health Index database. With this incidence density sampling design, it is possible and correct for an individual to appear more than once as a control and subsequently as a case. COVID-19 cases are those with a positive nucleic acid test, a hospital discharge diagnosis, or death with COVID-19 mentioned on death certificate. The REACT-SCOT case–control data set is linked to national data on vaccinations, hospital discharges, and outpatient consultations in the last 5 years before presentation date, dispensed prescriptions written in primary care in the last 240 days, and the list of individuals eligible for shielding. The data set used for this study was based on cases presenting up to 22 November 2021 and their matched controls. The main outcome measure was hospitalization within 14 days of a positive test for COVID-19, or fatal outcome defined as death within 28 days of a positive test, or any death certified with COVID-19 as an underlying cause. For brevity, we refer to this outcome as 'hospitalized COVID-19'. Ascertainment of this outcome is complete, as polymerase chain reaction (PCR) tests are performed for all patients admitted to hospital. As only a fraction of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infections in the population are detected by unscheduled testing, and testing rates vary widely, this design cannot be used to study the effect on infection rates; this would require follow-up of a cohort tested at least every 2 weeks.

Patients attending rheumatology clinics were identified from the outpatient speciality codes in the Scottish Morbidity Record (SMR00) data set. Outpatient diagnoses are not recorded in the SMR. International Classification of Diseases, 10th Revision (ICD-10) diagnostic codes (as main condition or other condition) for autoimmune rheumatic diseases in hospital discharge records were grouped into three broad categories: rheumatoid arthritis (M05–M09, M12.3, M13), psoriatic or other seronegative arthritis (M07, M45, M46), and connective tissue disorders (M30–M35). From drug prescribing records, patients were identified who had had received conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) – methotrexate, hydroxychloroquine, sulfasalazine, leflunomide – or prednisolone in the last 120 days. To exclude those who had been prescribed these drugs for non-rheumatic conditions, patients were classified as on csDMARDs only if they had had a rheumatology outpatient consultation (speciality code AR) in the last 5 years.

The average weekly dose of prednisolone equivalent was calculated from the total quantity dispensed during the last 120 days before the date of presentation as the sum of equivalent doses of prednisolone, cortisone acetate, deflazacort, dexamethasone, methylprednisolone, and prednisone (7).

Rate ratios for hospitalized/fatal COVID-19 were estimated by conditional logistic regression, with vaccination status (zero, one, or two doses), care home residence, and recent hospital inpatient stay (5–14 days before presentation date) as covariates. Unthresholded p-values are reported, allowing comparison of the contribution of each risk factor to prediction of the outcome (the logarithm of the p-value scales with the deviance explained). With this incidence density sampling design, the conditional odds ratio is the rate ratio, with effects of age, sex, calendar time, and general practice eliminated by matching. The reader is cautioned that rate ratios cannot be estimated from unconditional odds ratios because of the matched design (8, 9). For any variable with two or more levels, rate ratios are estimated with respect to a reference category for which the rate ratio is 1. For each drug, the exposed category is all those on the drug who were attending a rheumatology clinic irrespective of diagnosis, and the reference category is all those not on the drug. Although individuals prescribed targeted DMARDs in other centres will be misclassified as not on targeted DMARDs, this does not seriously affect the estimate of the estimate of the rate ratio because matching on general practice ensures that patients on the targeted DMARDs list are compared with other individuals from the catchment population of the clinics that provided the targeted DMARDs list. We have reported both univariate and multivariate rate ratios: for identifying those at high risk, the univariate rate ratios are more relevant, but for inference about possible drug effects the multivariate rate ratios are more relevant.

This study was conducted under approval from the Public Benefit and Privacy Panel for Health and Social Care, which includes public and patient representatives. The study was performed within PHS as part of its statutory duty to monitor and investigate public health problems. Under the UK Policy Framework for Health and Social Care Research set out by the NHS Health Research Authority, this does not fall within the definition of research and ethical review is not required. Individual consent is not required for PHS staff to process personal data to perform specific tasks in the

Table 1. Rate ratios for hospitalized or fatal COVID-19 associated with disease-modifying anti-rheumatic drug (DMARD) treatment.

			Univariate		Multivariable	
	Controls (405 597)	Cases (44 020)	Rate ratio (95% CI)	p	Rate ratio (95% CI)	p
Vaccine doses						
Unvaccinated	278 309 (69%)	32 740 (74%)		–		–
1 dose	26 631 (7%)	2528 (6%)	0.51 (0.48, 0.54)	1×10^{-116}	0.46 (0.43, 0.48)	3×10^{-142}
2 doses	96 304 (24%)	8563 (19%)	0.27 (0.26, 0.28)	5×10^{-570}	0.25 (0.23, 0.26)	3×10^{-583}
3 doses	4353 (1%)	189 (0%)	0.07 (0.06, 0.09)	2×10^{-173}	0.08 (0.06, 0.09)	6×10^{-154}
Care home	16 985 (4%)	6244 (14%)	5.3 (5.0, 5.5)	9×10^{-1383}	5.0 (4.8, 5.3)	2×10^{-1006}
Recent hospital stay	6602 (2%)	10 131 (23%)	19.3 (18.6, 20.0)	3×10^{-5429}	18.5 (17.8, 19.2)	1×10^{-4951}
Any csDMARD	7017 (2%)	1565 (4%)	2.14 (2.02, 2.26)	4×10^{-153}	2.26 (2.13, 2.41)	1×10^{-140}
Targeted DMARDs category						
No targeted DMARD	405 333 (100%)	43 946 (100%)		–		–
TNFi only	164 (0%)	34 (0%)	2.01 (1.38, 2.91)	2×10^{-4}	1.34 (0.88, 2.04)	0.2
Other biologic or JAKi	100 (0%)	40 (0%)	3.83 (2.65, 5.56)	1×10^{-12}	2.87 (1.89, 4.35)	7×10^{-7}

Presentation dates up to 22 November 2021
csDMARD exposure is defined as: (i) any prescription for a conventional synthetic disease-modifying anti-rheumatic drug in the last 240 days; and (ii) a rheumatology outpatient consultation in the last 5 years.
Rate ratios are estimated by conditional logistic regression.
The multivariable model includes all covariates shown in the table.
TNFi, tumour necrosis factor inhibitor; JAKi, janus kinase inhibitor; CI, confidence interval.

public interest that fall within its statutory role. The statutory basis for this is set out in PHS's privacy notice. A Data Protection Impact Assessment allows PHS staff to link existing data sets.

Results

The targeted DMARDs list comprised 4633 individuals: the diagnostic category was rheumatoid arthritis in 2702, psoriatic arthritis or other seronegative arthropathy in 1765, connective tissue disorder in 141, and other conditions in 25. Of the 4633 individuals on the list, 433 had been diagnosed with COVID-19 by 22 November 2021. Of these 433 cases, 58 were hospitalized within 14 days, seven entered critical care within 21 days, and 14 were fatal within 28 days. Of the 4633, 2527 (55%) had been added by PHS to the shielding list based on criteria suggested by the British Society for Rheumatology (BSR) (10). Of those added to the shielding list, 43 (1.7%) were hospitalized with COVID-19, compared with 15 (0.7%) of those not added. The algorithm used by PHS to identify those eligible for shielding thus discriminated between low-risk and high-risk patients.

Of the 4633 on the targeted DMARDs list, 2586 were sampled in the REACT-SCOT case–control study. Of these 2586, 2583 had had a rheumatology outpatient consultation within the last 5 years but only 1229 had a dispensed prescription for a csDMARD within the last 240 days. Of the 2586 who were sampled in the case–control study, 1581 had a hospital discharge diagnosis with a rheumatology code.

In comparison with those with no rheumatological diagnosis, the rate ratio for hospitalized or fatal COVID-19 in those with a hospital discharge diagnosis with a rheumatology code was 2.68 [95% confidence interval (CI) 2.47–2.91] in those with rheumatoid arthritis, 3.27 (95% CI 2.77–3.86) in those with psoriatic or other seronegative arthritis, and 2.28 (95% CI 2.03–2.57) in those with connective tissue disorders.

Table 1 shows that the rate ratio for hospitalized COVID-19 associated with DMARD treatment (with those not on DMARDs as the reference category) was 2.14 (95% CI 2.02–2.26) in those on csDMARDs, 2.01 (95% CI 1.38–2.91) in those on tumour necrosis factor (TNF) inhibitors as the only targeted agent, and 3.83 (95% CI 2.65–5.56) in those on other targeted agents.

Table 2 shows the rate ratios for hospitalized or fatal COVID-19 associated with each specific csDMARD or targeted class. The univariate rate ratios associated with csDMARDs ranged from 1.66 (95% CI 1.51–1.82) for methotrexate to 5.4 (95% CI 4.4–6.7) for prednisolone dose equivalent to > 10 mg/day. The rate ratio associated with targeted DMARDs was highest in those on B-cell depletion (5.9, 95% CI 3.1–11.4), but for other classes of targeted DMARD the confidence intervals were too wide to allow any conclusion on whether the rate ratios differed. In a multivariable analysis, the effect sizes associated with most drug classes were reduced, but the association with glucocorticoids as prednisolone dose equivalent remained strong, with a rate ratio of 5.2 (95% CI 4.1–6.6).

Discussion

The principal findings of this study are as follows. First, individuals treated with csDMARDs for inflammatory rheumatic diseases have more than two-fold increased risk of hospitalized COVID-19 in comparison with the general population. This increased risk may be at least

Table 2. Rate ratios for hospitalized or fatal COVID-19 associated with treatment with specific disease-modifying anti-rheumatic drugs (DMARDs).

			Univariate		Multivariable	
	Controls (405 597)	Cases (44 020)	Rate ratio (95% CI)	p	Rate ratio (95% CI)	p
Conventional synthetic DMARDs						
Methotrexate	3010 (1%)	531 (1%)	1.66 (1.51, 1.82)	2×10^{-26}	1.29 (1.15, 1.45)	1×10^{-5}
Hydroxychloroquine	1898 (0%)	361 (1%)	1.80 (1.61, 2.02)	4×10^{-24}	1.17 (1.02, 1.35)	0.02
Sulfasalazine	1661 (0%)	420 (1%)	2.41 (2.16, 2.68)	5×10^{-57}	2.09 (1.83, 2.38)	1×10^{-27}
Leflunomide	265 (0%)	52 (0%)	1.86 (1.38, 2.50)	5×10^{-5}	1.21 (0.86, 1.71)	0.3
Glucocorticoids (prednisolone equivalent mg daily)						
0	403 211 (99%)	43 214 (98%)		–		–
> 0 to 5	1574 (0%)	467 (1%)	2.78 (2.50, 3.08)	2×10^{-81}	2.53 (2.24, 2.86)	3×10^{-51}
> 5 to 10	566 (0%)	201 (0%)	3.33 (2.83, 3.92)	7×10^{-48}	2.73 (2.26, 3.30)	3×10^{-25}
> 10	246 (0%)	138 (0%)	5.4 (4.4, 6.7)	9×10^{-56}	5.2 (4.1, 6.6)	1×10^{-40}
Targeted DMARDs						
TNF inhibitors	164 (0%)	34 (0%)	2.00 (1.38, 2.90)	2×10^{-4}	1.44 (0.94, 2.20)	0.09
B-cell depletion	25 (0%)	15 (0%)	5.9 (3.1, 11.4)	7×10^{-8}	3.61 (1.68, 7.77)	0.001
IL-6 inhibitors	21 (0%)	9 (0%)	4.07 (1.86, 8.90)	4×10^{-4}	3.04 (1.23, 7.51)	0.02
IL-17 inhibitors	24 (0%)	5 (0%)	1.79 (0.66, 4.83)	0.2	0.99 (0.30, 3.22)	1
JAK inhibitors	27 (0%)	12 (0%)	4.37 (2.20, 8.68)	2×10^{-5}	2.30 (1.04, 5.07)	0.04

Presentation dates up to 22 November 2021.
For each conventional synthetic DMARD, exposure is defined as: (i) any prescription for that drug in the last 240 days; and (ii) a rheumatology outpatient consultation in the last 5 years.
Rate ratios are estimated by conditional logistic regression.
The multivariable model includes all covariates shown in the table, together with vaccination status, care home residence, and recent hospital stay, as in Table 1.
TNF, tumour necrosis factor; IL, interleukin; JAK, janus kinase; CI, confidence interval.

partly attributable to disease rather than to immunosuppressive therapy. Secondly, the rate ratio for hospitalized COVID-19 in those treated with TNF inhibitors was similar to that in those treated with methotrexate, but the rate ratio in those treated with B-cell-depleting agents was higher than in those treated with methotrexate. Thirdly, in individuals treated with glucocorticoids at doses equivalent to > 10 mg/day prednisolone, the risk of hospitalization with COVID-19 was higher than that associated with most targeted DMARDs.

Strengths of this study are the complete ascertainment of cases, the comprehensive linkage to electronic health records, and the incidence density sampling design, which controls for calendar time, age, sex, and general practice.

A limitation is that the data set on prescribing of targeted DMARDs is only a snapshot of those on targeted DMARDs in March 2020, and covers only about one-third of the Scottish population. Hospital outpatient prescribing is not recorded in electronic form within the NHS, and the prescription records held by the medication homecare services companies were not available for this study. Although the clinics that provided the targeted DMARDs list are not representative of the Scottish population, the matching of cases and controls on general practice ensures that the controls are drawn from the catchment population of these clinics. However, because the coverage of the list is limited, the sample size is not large enough to estimate reliably the effects of specific classes of targeted DMARDs such as B-cell depleters, or the efficacy of vaccines in those on targeted DMARDs.

The rate ratio of 2.1 for hospitalized COVID-19 in rheumatology patients treated with csDMARDs is higher than the rate ratio of 1.3 for mortality associated with any diagnosis of rheumatoid arthritis, lupus, or psoriasis (not restricted to those with arthritis) in the OpenSAFELY study (11), but similar to the rate ratios reported for a cohort of rheumatology patients in Sweden compared with the general population (12). The rate ratios associated with immunosuppressive therapy in rheumatology patients are modest in comparison with the rate ratio of 13 that we have reported for severe COVID-19 in solid organ transplant recipients (1).

Others have reported that hospitalized COVID-19 is associated with use of glucocorticoids and B-cell-depleting agents but not with TNF inhibitors. In a registry of 600 rheumatology patients diagnosed with COVID-19, the odds ratio for hospitalization (with methotrexate use as the reference category) was 2.1 for glucocorticoid use equivalent to > 10 mg/day prednisone, and 0.4 for TNF inhibitors (13). In a later analysis based on 2869 patients with rheumatoid arthritis, the odds ratios (with TNF inhibitors as the reference category) were 4.5 for rituximab and 2.1 for janus kinase (JAK) inhibitors (14). In a French series of 694 patients, the odds ratio for fatal disease was 2.8 for any glucocorticoid, 0.2 for TNF inhibitors, and 3.1 for rituximab (15). These registries, however, were based on cases notified by clinicians, and the reference category for

hospitalized cases was patients diagnosed with COVID-19 but not hospitalized, rather than the general population. This may give rise to various forms of selection bias. In an Israeli cohort of 6112 psoriasis patients, the rate ratio for hospitalization associated with TNF inhibitors, with methotrexate as the reference category, was 0.08, but the number of events was small (16). In the Swedish cohort (with users of csDMARDs as the reference category), neither TNF inhibitors nor rituximab were associated with higher rates of hospitalized COVID-19 (12).

In this study, the rate ratio for hospitalized COVID-19 was similar in users of TNF inhibitors to that in methotrexate users, with no support for a protective effect of TNF inhibitors against severe COVID-19. Other targeted DMARDs, including JAK inhibitors and B-cell depleters, were associated with higher risk of severe COVID-19, although the numbers are too small for reliable estimates of the risk associated with each drug class. Rituximab therapy is associated with failure to seroconvert in response to COVID-19 vaccines (17), but the extent to which this affects vaccine efficacy against severe disease is not known. BSR guidance in early 2020 had suggested that hydroxychloroquine and sulfasalazine were unlikely to influence susceptibility to COVID-19 (10), yet the rate ratio for hospitalized COVID-19 was at least as high in those treated with hydroxychloroquine and sulfasalazine as in those treated with methotrexate; a possible explanation for this is that the elevated risk associated with csDMARDs is related to the disease rather than to any immunosuppressive effects of these drugs. Although more than half of those on targeted DMARDs had been classified as clinically extremely vulnerable and advised to shield, we have shown elsewhere that the effectiveness of this advice was limited by failure to control nosocomial transmission in hospital or to provide support for other adults in the household to co-isolate (1).

Conclusion

This study suggests that all patients on DMARDs are at significantly increased risk of hospitalized COVID-19 compared with the general population. Within the group of treatments that are currently available, methotrexate, hydroxychloroquine, and TNF inhibitors appear to be more favourable than JAK inhibitors and B-cell-depleting agents. Prednisolone is associated with high risk even at modest doses, and the risk increases steeply with average dose. A larger study is required to estimate the association of severe COVID-19 with other targeted DMARDs such as interleukin-6 and interleukin-17 inhibitors. Our study brings the risk–benefit of all immunosuppressive therapies for inflammatory rheumatic disease into sharp focus. Most rheumatology patients on immunosuppressant therapy have now received third primary doses of COVID-19 vaccines as recommended; for the effectiveness of this intervention to be monitored it will be necessary to capture and link data on prescribing of csDMARDs, biological DMARDs, and targeted synthetic DMARDs.

Acknowledgements

We thank Jen Bishop, Ciara Gribben, and David Caldwell for undertaking the linkage analysis in Public Health Scotland, and staff from the rheumatology service in the contributing centres for preparing the list of patients receiving these treatments.

Funding

No specific funding was received for this study.

Disclosure statement

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. No potential conflict of interest was reported by the authors.

Authors' contributions and transparency declaration

All authors provided substantial contributions to the conception of the study and the drafting of the manuscript. PM undertook the statistical analysis. All authors contributed to revising the manuscript critically for important intellectual content and approved the final manuscript. PM, as the manuscript's guarantor, affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned and registered have been explained. This manuscript has been generated directly from the source data by a reproducible research pipeline.

Data availability statement

The component data sets used here are available via the Public Benefits and Privacy Panel for Health and Social Care at https://www.informationgovernance.scot.nhs.uk/pbpphsc/ for researchers who meet the criteria for access to confidential data. All source code used for derivation of variables, statistical analysis, and generation of this manuscript is available at https://github.com/pmckeigue/covid-scotland_public.

ORCID

PM McKeigue http://orcid.org/0000-0002-5217-1034
D Porter http://orcid.org/0000-0001-8481-5204
RJ Hollick http://orcid.org/0000-0001-6558-7189
SH Ralston http://orcid.org/0000-0002-2804-7586
DA McAllister http://orcid.org/0000-0003-3550-1764
HM Colhoun http://orcid.org/0000-0002-8345-3288

References

1. McKeigue PM, McAllister DA, Caldwell D, Gribben C, Bishop J, McGurnaghan S, et al. Relation of severe COVID-19 in Scotland to transmission-related factors and risk conditions eligible for shielding support: REACT-scot case-control study. BMC Med 2021;19:149.

2. Joint Committee on Vaccination and Immunisation. Joint Committee on Vaccination and Immunisation (JCVI) advice on third primary dose vaccination [Internet]. 2021 [cited 2021 Sep 15]. Available from: https://www.gov.uk/government/publications/third-primary-covid-19-vaccine-dose-for-people-who-are-immunosuppressed-jcvi-advice/joint-committee-on-vaccination-and-immunisation-jcvi-advice-on-third-primary-dose-vaccination
3. Fagni F, Simon D, Tascilar K, Schoenau V, Sticherling M, Neurath MF, et al. COVID-19 and immune-mediated inflammatory diseases: effect of disease and treatment on COVID-19 outcomes and vaccine responses. Lancet Rheumatol 2021;3:e724–36.
4. Public Health Scotland. Search criteria for highest risk patients for shielding [Internet]. Public Health Scotland; 2021 [cited 2021 Dec 11]. Report No.: Version 6.0. Available from: https://hpspubsrepo.blob.core.windows.net/hps-website/nss/3008/documents/1_covid-19-search-criteria-highest-risk-patients.pdf
5. Kanani N. Waller E. Caring for people at highest risk during COVID-19 incident [Internet]. Redditch, UK: NHS England; 2020. Available from: https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/200321_GP-letter_Annex-2_FINAL_2.pdf
6. McKeigue PM, Weir A, Bishop J, McGurnaghan SJ, Kennedy S, McAllister D, et al. Rapid Epidemiological Analysis of Comorbidities and Treatments as risk factors for COVID-19 in Scotland (REACT-Scot): a population-based case-control study. PLoS Med 2020;17:e1003374.
7. National Institute for Health and Care Excellence. Equivalent anti-inflammatory doses: corticosteroids - oral [Internet]. NICE. 2020 [cited 2021 Sep 1]. Available from: https://cks.nice.org.uk/topics/corticosteroids-oral/background-information/equivalent-anti-inflammatory-doses/
8. Breslow NE, Day NE, Halvorsen KT, Prentice RL, Sabai C. Estimation of multiple relative risk functions in matched case-control studies. Am J Epidemiol 1978;108:299–307.
9. Greenland S, Thomas DC. On the need for the rare disease assumption in case-control studies. Am J Epidemiol 1982;116:547–53.
10. British Society for Rheumatology. COVID-19 - Identifying patients for shielding in England, Internet]. London, UK: British Society for Rheumatology; 2020. Report No.: V3. Available from: https://www.rheumatology.org.uk/Portals/0/Documents/COVID-19/Rheumatology_advice_coronavirus_immunosuppressed_patients_220320.pdf?ver=2020-03-24-171132-407
11. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. OpenSAFELY: factors associated with COVID-19 death in 17 million patients. Nature 2020;584:430–6.
12. Bower H, Frisell T, Di Giuseppe D, Delcoigne B, Ahlenius G-M, Baecklund E, et al. Impact of the COVID-19 pandemic on morbidity and mortality in patients with inflammatory joint diseases and in the general population: a nationwide Swedish cohort study. Ann Rheum Dis 2021;80:1086–93.
13. Gianfrancesco M, Hyrich KL, Al-Adely S, Carmona L, Danila MI, Gossec L, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis 2020;79:859–66.
14. Sparks JA, Wallace ZS, Seet AM, Gianfrancesco MA, Izadi Z, Hyrich KL, et al. Associations of baseline use of biologic or targeted synthetic DMARDs with COVID-19 severity in rheumatoid arthritis: results from the COVID-19 Global Rheumatology Alliance physician registry. Ann Rheum Dis 2021;80:1137–46.
15. FAI2R /SFR/SNFMI/SOFREMIP/CRI/IMIDIATE consortium and contributors. Severity of COVID-19 and survival in patients with rheumatic and inflammatory diseases: data from the French RMD COVID-19 cohort of 694 patients. Ann Rheum Dis 2020;80:527–38.
16. Kridin K, Schonmann Y, Damiani G, Peretz A, Onn E, Bitan DT, et al. Tumor necrosis factor inhibitors are associated with a decreased risk of COVID-19-associated hospitalization in patients with psoriasis – a population-based cohort study. Dermatol Ther 2021;34:e15003.
17. Kearns P, Siebert S, Willicombe M, Gaskell C, Kirkham A, Pirrie S, et al. Examining the immunological effects of COVID-19 vaccination in patients with conditions potentially leading to diminished immune response capacity [Internet]. Rochester, NY: Social Science Research Network; 2021 [cited 2021 Sep 1]. Report No.: ID 3910058. Available from: https://papers.ssrn.com/abstract=3910058