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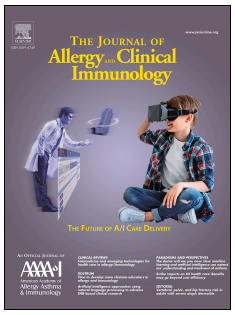

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Factors associated with adverse COVID-19 outcomes in patients with psoriasis – insights from a global registry-based study

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PCP is a consultant for AbbVie, Almirall, Leo, Galderma, Sanofi, Pierre Fabre.

HM is employed by the Psoriasis Association who have received grants from Almirral, Abbvie, Amgen, Celgene, Dermal Laboratories, Eli Lilly, Janssen, LEO Pharma, T and R Derma and UCB. The Psoriasis Association has a policy that no more than 15% of income can come from the pharmaceutical industry.

HB has had paid consulting activities for AbbVie, Almirall, Biocad, Boehringer-Ingelheim, Janssen, Kyowa Kirin, Novartis and UCB, and received grant support from Janssen, Leo Pharma and Pfizer.

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CDLC has been a speaker or principal investigator for AbbVie, Pfizer, Lilly, Janssen, Novartis, Amgen, Boehringer Ingelheim and Sanofi.

PS has done consultancies in the past for Sanofi 111017 and AbbVie 041217 (unpaid), received a departmental independent research grant for TREAT NL registry LeoPharma December 2019, is involved in performing clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of e.g. psoriasis and atopic dermatitis for which they get financial compensation paid to the department/hospital and is Chief Investigator (CI) of the systemic and phototherapy atopic eczema registry (TREAT NL) for adults and children and one of the main investigator of the SECURE-AD registry.

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Abstract

Background: The multi-morbid burden and use of systemic immunosuppressants in people with psoriasis may confer greater risk of adverse COVID-19 outcomes but data are limited.

Objective: Characterize the course of COVID-19 in psoriasis and identify factors associated with hospitalization.

Methods: Clinicians reported psoriasis patients with confirmed/suspected COVID-19 via an international registry, PsoProtect. Multiple logistic regression assessed the association between clinical/demographic characteristics and hospitalization. A separate patient-facing registry characterized risk-mitigating behaviours.

Results: Of 374 clinician-reported patients from 25 countries, 71% were receiving a biologic, 18% a non-biologic and 10% no systemic treatment for psoriasis. 348 (93%) fully recovered from COVID-19, 77 (21%) were hospitalized and nine (2%) died. Increased hospitalization risk was associated with older age (multivariable-adjusted OR 1.59 per 10 years, 95% CI 1.19-2.13), male sex (OR 2.51, 95% CI 1.23-5.12), non-white ethnicity (OR 3.15, 95% CI 1.24-8.03) and comorbid chronic lung disease (OR 3.87, 95% CI 1.52-9.83). Hospitalization was more frequent in patients using non-biologic systemic therapy than biologics (OR 2.84, 95% CI 1.31-6.18). No significant differences were found between biologic classes. Independent patient-reported data (n=1,626 across 48 countries) suggested lower levels of social isolation in individuals receiving non-biologic systemic therapy compared to biologics (OR 0.68, 95% CI 0.50-0.94).

Conclusion: In this international moderate-severe psoriasis case series, biologics use was associated with lower risk of COVID-19-related hospitalization than non-biologic systemic therapies, however further investigation is warranted due to potential selection bias and unmeasured confounding. Established risk factors (being older, male, non-white ethnicity, comorbidities) were associated with higher hospitalization rates.

Clinical Implications.

We identify risk factors for COVID-19-related hospitalization in psoriasis patients, including older age, male sex, non-white ethnicity and comorbidities. Use of biologics was associated with lower hospitalization risk than non-biologic systemic therapies.

Capsule summary

In this global registry-based study, risk factors for COVID-19-related hospitalization in psoriasis patients were older age, male sex, non-white ethnicity and comorbidities. Use of biologics was associated with lower hospitalization risk than non-biologic systemic treatment.

Key words

COVID-19; hospitalization; psoriasis; risk factors; biologics; immunosuppressants

Abbreviations

COVID-19 (Coronavirus disease 2019), SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), IMID (immune-mediated inflammatory disease), IFN (interferon), IL (interleukin), TNF (tumor necrosis factor), JAK (Janus kinase), OR (odds ratio), 95% CI (95% confidence interval), IQR (interquartile range), PsoProtect (Psoriasis Patient Registry for Outcomes, Therapy and Epidemiology of COVID-19 infecTion), ACEi (angiotensin-converting enzyme inhibitor), ARB (angiotensin II receptor blocker), NSAID (non-steroidal anti-inflammatory drug), BMI (body mass index).

Introduction

The COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to unprecedented challenges for the international clinical and scientific community (1). Although most patients with COVID-19 experience mild symptoms, an estimated 15% develop pneumonia and 5% progress to systemic hyperinflammation and acute respiratory distress syndrome requiring critical care management, with risk of septic shock, multi-organ failure and death (2). Reported mortality rates range from 2.3% to 7.2% (2,3). Increased age, male sex and non-white ethnicity have emerged as risk factors of poor COVID-19 outcome in the general population, in addition to comorbidities including cardiovascular disease, diabetes and obesity (4–6). Since multimorbidity is prevalent in psoriasis (7), there is an urgent need to understand the impact of COVID-19 in individuals with this common lifelong immune-mediated skin disease. Psoriasis affects more than 60 million people worldwide (8) and pre-COVID-19 observational data suggest greater risk of respiratory infection-related hospitalization compared to the general population(9). Furthermore, there is uncertainty about whether additional serious infection risk is conferred by immunosuppressant drugs, which are the mainstay of treatment in moderate-severe psoriasis (10,11).

The immune pathways implicated in the pathogenesis of psoriasis, as well as the drugs used to treat it, may differentially influence the clinical course of COVID-19. Psoriasis is characterized by dysregulated innate and adaptive immune responses, with type I interferon (IFN)-secreting dendritic cells propagating pathogenic interleukin (IL)-23/T17 circuits (12). In the initial phase of COVID-19, viral pathogenicity is dominant, and viral clearance by early host type I IFN-mediated responses prevents further viral replication, T cell exhaustion and hyperinflammation (13). A reduced or delayed type I IFN response has been associated with poor COVID-19 outcomes (14); thus it is possible that the immune dysregulation in psoriasis may be advantageous, whilst its therapeutic suppression may be detrimental. The second phase of COVID-19 comprises hyperinflammation and cytokine storm, with elevation of pro-inflammatory cytokines also implicated in psoriasis including tumor necrosis factor (TNF), IL-1β, IL-6, IL-8, IFNγ and IL-17. It is unclear whether individuals with psoriasis are at greater risk of progression to this phase and conversely, whether immunosuppressants are effective therapies for severe COVID-19. Treatments targeting the over-exuberant host immune response in COVID-19, including inhibitors of IL-1, IL-6, Janus kinase (JAK) and TNF, are currently undergoing clinical trial (15,16).

Psoriasis, rheumatoid arthritis and systemic lupus erythematosus were collectively highlighted as potential risk factors for COVID-19-related death using primary care data linked to hospital records from 17 million adults in the UK (6). However, the risk attributed to psoriasis alone or its therapies remains uncertain. Preliminary reports in individuals with psoriasis have not demonstrated higher levels of COVID-19-related hospitalization among those receiving biologic therapies (17–20). However, these data have limited external validity since the case series were all from Northern Italy and included few patients with adverse outcomes. There is thus an urgent need to collate reports of COVID-19 in psoriasis

to understand the determinants of severe infection and help inform clinical decision-making. Here, we describe the first international series of psoriasis patients with COVID-19 and identify demographic and clinical factors associated with hospitalization.

Methods

Study Design, Setting, Participants

This registry-based study comprised two data sources. The primary data source was an online clinician-reported registry, Psoriasis Patient Registry for Outcomes, Therapy and Epidemiology of COVID-19 infecTion (PsoProtect), which launched globally on 27 March 2020 (21). Data were collected and managed using REDCap electronic data capture tools licensed to King's College London Division of Health and Social Care Research (22,23). REDCap is a secure, web-based software platform designed to support data capture.

The eligibility criterion was any patient with psoriasis and confirmed/suspected COVID-19 identified by their supervising clinician. Case submission was requested at least 14 days following symptom onset, and once sufficient time had passed to observe the outcome of infection. Clinicians were invited to participate via the communication channels of multiple international professional organizations (Table E1). We also invited case reports from two United States COVID-19 registries (SECURE-Psoriasis, AAD COVID-19) (24,25). Thirty-eight of the cases are published elsewhere (n=29 (17) and n=9 (18)).

The second data source was a separate online self-report patient-facing registry, PsoProtect*Me*, which launched globally on 4 May 2020. The eligibility criterion was a clinician-confirmed diagnosis of psoriasis, irrespective of COVID-19 status. Participants were invited via the communication channels of multiple international psoriasis patient organizations (Table E1).

Variables

Minimum sufficient core sets of variables within the PsoProtect and PsoProtect*Me* case report forms (26,27) were defined by our study group of clinicians, epidemiologists, health data researchers and patient representatives, aligned with those of other immune-mediated inflammatory disease (IMID) COVID-19 registries (28,29). Key variables in both registries included demographics (age, sex, ethnicity, country), smoking status, comorbidities, details of psoriasis (phenotype, treatment) and COVID-19 (symptoms, treatment, outcome). Medication adherence and social isolation behaviour during the pandemic were collected in PsoProtect*Me*.

Statistical methods

PsoProtect and PsoProtect*Me* data were extracted on 1 and 3 July 2020, respectively. Incomplete, duplicate and erroneous entries were manually reviewed by the study team and removed. All analysis was performed using the R statistical programming language (30).

Demographic and clinical characteristics and COVID-19 outcomes of the study population were summarized using descriptive statistics. Continuous variables were reported using median and interquartile range (IQR), and categorical/dichotomous variables as number and percentage.

We used clinician-reported registry data to investigate the demographic and disease-specific factors associated with the primary outcome of hospitalization for COVID-19. The key exposure measure was treatment type for psoriasis at or up to four weeks prior to COVID-19 onset, comprising: biologics (TNF inhibitors: adalimumab, certolizumab pegol, etanercept, infliximab, golimumab; IL-17 inhibitors: brodalumab, ixekizumab, secukinumab; IL12/IL-23p40 or IL-23p19 [collectively IL-23] inhibitors: guselkumab, risankizumab, tildrakizumab, ustekinumab), non-biologic systemic agents (acitretin, apremilast, ciclosporin, methotrexate, fumaric acid esters/dimethylfumarate, prednisolone), and no systemic treatment.

The association between treatment type (biologic, non-biologic systemic or no systemic treatment) and hospitalization for COVID-19 was assessed using: (a) a minimally adjusted logistic regression model including age and sex covariates; and (b) a fully adjusted model including a consensus list of covariates selected *a priori* as potentially influential on adverse COVID-19 outcome on the basis of expert clinical opinion and existing evidence (2,3,6,31), namely, age, sex, ethnicity, country, smoking, BMI and comorbidities. Other relevant variables (use of angiotensin-converting enzyme inhibitor, use of angiotensin II receptor blocker, obesity comorbidity) that correlated ($|r|>0.5$) with included covariates were excluded. Levels of categorical variables exhibiting small counts (<10 observations of either outcome) were merged. Comorbid obesity was assumed where BMI$\geq$30, even where not directly reported. Selection bias in missing data was explored by comparing patients with missing data for variables included in the fully adjusted model (BMI, smoking, or BMI and smoking) to patients with complete data (Table E2). Small differences were observed in proportions of men, white ethnicity, confirmed COVID-19 diagnosis and hospitalization. Therefore, to maximise included data, the final regression models were based on 20 multiply imputed datasets generated with the Multivariate Imputation by Chained Equations (MICE) R package (32).

Quadratic terms for age and sex covariates were considered but rejected due to lack of improvement in model fit (likelihood ratio test). Minimally and fully adjusted odds ratios (OR) and 95% confidence intervals (CI) were reported for each variable. Sensitivity analyses were performed on the fully adjusted multivariable regression models. To assess the association between biologic class and the primary outcome, a fully adjusted model was fitted in which treatment type was further categorized by biologic class (TNF, IL-17 or IL-23 inhibitor). Improvement in fit relative to the original treatment type model was assessed using a likelihood ratio test. The STROBE statement for cross-sectional studies was used as a basis for reporting (33).

Ethical approval

Ethical approval was granted by the Leeds Research Ethics Committee (20/YH/0135) and the study was registered in the European Union electronic Register of Post-Authorisation Studies (34). Only de-identified data were collected, hence written informed patient consent was not required. Data collection, transfer and storage were compliant with statutory requirements, ICH Good Clinical Practice and EU General Data Protection Regulation.

Results

Demographic and clinical characteristics of a global series of individuals with COVID-19 and psoriasis

In total, 374 psoriasis patients with confirmed (172, 46%) or suspected (202, 54%) COVID-19 were reported by clinicians from 25 countries (including UK [135, 36%], Italy [80, 21%], Spain [56, 15%]; Table E3). Demographic and clinical characteristics are summarized in Table I. The median age was 50 years (IQR 41-58). There was a predominance of males (227, 61%) and individuals of white ethnicity (316, 85%). Among 304 patients with known smoking status, 165 (54%) had never smoked and 44 (15%) were current smokers. The majority of patients had plaque psoriasis (365, 98%) and clear/nearly clear/mild psoriasis at COVID-19 onset (298, 80%). The most commonly reported comorbidities were obesity (123, 33%), hypertension (97, 26%), psoriatic arthritis (96, 26%) and diabetes (61, 16%).

Most patients were receiving a biologic treatment (267, 71%) for their psoriasis rather than a non-biologic systemic agent (67, 18%) or no systemic therapy (36, 10%). Of those receiving a biologic, similar numbers of patients were receiving either a TNF, IL-17 or IL-23 inhibitor (99, 78 and 90, respectively). Demographic and clinical characteristics by biologic class are summarized in Table E4, and split by confirmed and suspected COVID-19 in Table E5.

Most reported patients fully recovered from COVID-19

Three hundred and forty-eight (93%) of the reported patients fully recovered from COVID-19 (Table II). The most common COVID-19 symptoms were fever (244, 68%), fatigue (174, 48%) and dry continuous cough (167, 46%), and the median duration of symptoms was 14 days (IQR 7-21).

Seventy-seven patients (21%) were hospitalized for COVID-19, seven (2%) required high flow oxygen supplementation and 12 (3%) mechanical ventilation. The median length of hospital stay was 11 days (IQR 6-20). Nine patients died (2%); their median age was 65 years (range 43 to 89 years), and all had at least one comorbidity, with hypertension (6, 67%) and diabetes (5, 56%) being the most prevalent. COVID-19 outcomes by biologic class are summarized in Table E6, and split by confirmed and suspected COVID-19 in Table E7.

Rates of hospitalization differed by psoriasis treatment type, in addition to established risk factors for COVID-19

After excluding nine individuals due to unknown drug type (clinical trial participants), unknown hospitalization status or unknown COVID-19 outcome, 365 patients with psoriasis were available to assess factors associated with hospitalization. Rates of hospitalization for COVID-19 were higher among males (26%, versus 12% among females), older patients (60% among over-70s, versus 26% among 50-70 year-olds and 10% below age 50) and non-white

ethnicity (32%, versus 19% among white ethnicity). Comorbidities were also highly prevalent: 76% of hospitalized patients were reported to have hypertension, cardiovascular disease, diabetes, chronic liver disease or chronic lung disease (including asthma), compared to 34% of non-hospitalized patients.

Hospitalization for COVID-19 was less common among patients receiving biologic therapy for their psoriasis (at or up to four weeks prior to COVID-19 onset; 44 of 265, 17%) than among those receiving non-biologic systemic therapy (22 of 65, 34%) or no systemic therapy (10 of 35, 29%). Patients receiving biologic therapy also had lower rates of mechanical ventilation (3%, versus 5% among those receiving non-biologics) and death (2%, versus 5%).

Compared to the reference group of biologic users, an age- and sex-adjusted model for hospitalization rate estimated an odds ratio of 2.72 for non-biologic systemic users and a 95% CI that did not cross unity (1.37-5.40) (Table III).

To account for potential confounding from a range of established COVID-19 risk factors, a fully adjusted multivariable logistic regression model was fitted (Table III). Significant associations with increased hospitalization rate were observed for age (OR 1.59 per 10 years, 95% CI 1.19-2.13), male sex (OR 2.51, 95% CI 1.23-5.12), non-white ethnicity (OR 3.15, 95% CI 1.24-8.03) and comorbid chronic lung disease (OR 3.87, 95% CI 1.52-9.83). Despite imprecise 95% CIs, elevated risk of hospitalization was suggested for several comorbidities with odds ratios above 2: hypertension (2.03, 95% CI 0.99-4.16), cardiovascular disease (2.01, 95% CI 0.74-5.46) and chronic liver disease (2.12, 95% CI 0.81, 5.55). No association was found with having ever smoked (OR 1.16, 95% CI 0.54-2.49).

In the fully adjusted model, non-biologic systemic therapy for psoriasis remained associated with increased risk of hospitalization compared with the group of biologic users (OR 2.84, 95% CI 1.31-6.18). Patients receiving no systemic therapy were estimated to have a similarly increased risk of hospitalization (OR 2.35, 95% CI 0.82-6.72). This suggests that use of biologics is associated with a reduced risk of hospitalization compared with either non-biologic systemic therapy or no therapy, although interpretation of these estimates should take into account possible sources of bias (as detailed in the discussion).

Patients reported in Spain were more likely to have been hospitalized for COVID-19 (43%, versus 17% elsewhere) and more likely to receive a non-biologic systemic agent (30%, versus 16% elsewhere), which could potentially confound the estimated association between treatment type and hospitalization. Although country of assessment was included in the fully adjusted model (Spain OR 4.79, 95% CI 1.88-12.19), a sensitivity test using only non-Spanish patients identified broadly similar effect size estimates for treatment type (Table E8). A multiple regression model fitted in confirmed cases only (Table E9) indicated a stronger association with hospitalization risk for use of non-biologic systemic agents compared with biologics (OR 3.98, 95% CI 1.38-11.46). However, this estimate is likely inflated since most hospitalized patients had confirmed COVID-19 (69 of 76, 91%).

To assess potential differences in COVID-19 hospitalization risk between classes of biologics, a multiple logistic regression model was fitted in which biologics were split into TNF, IL-23 and IL-17 inhibitor groups (n = 98, 89 and 78, respectively) (Table E10). Hospitalization was observed more frequently in patients receiving IL-23 inhibitors (23%) than those on TNF (14%) or IL-17 inhibitors (13%); a fully adjusted odds ratio of 1.65 for the IL-23 inhibitor group was estimated relative to the TNF inhibitor group. However, the 95% confidence interval was wide (0.64-4.25) and the split by biologic type did not significantly improve model fit (P = 0.48).

The limited numbers of patients using combination therapy or any individual agent precluded analysing their association with hospitalization.

Risk-mitigating behaviours may vary between psoriasis patients receiving biologics and those receiving non-biologic systemic therapies

To help inform our interpretation of hospitalization rates among psoriasis patients receiving different types of therapy, we investigated potential differences in COVID-19 risk mitigating behaviours. Self-reported data from 1,626 individuals with psoriasis (with and without COVID-19) from 48 countries were available (Table E3). Baseline characteristics including demographics, psoriasis phenotype and comorbidities are summarized in Table IV. These were similar to the clinician-reported registry, except for sex (female predominance in the self-report registry, 64%). Of 96 patients (6%) who self-reported suspected or confirmed COVID-19, 25 (26%) were receiving a biologic, 13 (14%) a non-biologic systemic agent and 58 (60%) no treatment.

To assess baseline risk-mitigating behaviours, we interrogated self-reported data from individuals without COVID-19 infection (n=1,476). Four hundred and seventy-eight (32%) individuals reported receiving a biologic and 249 (17%) a non-biologic systemic agent for psoriasis during the pandemic. Individuals in both treatment groups had similar baseline characteristics such as age, ethnicity and comorbidity rates (including obesity, hypertension, cardiovascular disease, psoriatic arthritis). Reported rates of social isolation (shielding: quarantine, distancing within the home; or self-isolation: staying home, avoiding others) were higher in those receiving biologics for psoriasis (346 of 478, 72%) compared with those receiving non-biologic systemic therapies (161 of 249, 65%; age- and sex-adjusted OR 0.68, 95% CI 0.50-0.94) and those receiving no systemic therapy (470 of 747, 63%; OR 0.63, 95% CI 0.50-0.80). However, treatment non-adherence rates were slightly lower with 17% (79) of those receiving biologics and 20% (48) of those receiving non-biologic systemic therapies reporting stopping treatment during the pandemic. These independent patient-reported data suggest there may be potential variation in COVID-19 risk-mitigating behaviour between treatment groups.

Discussion

Summary of main findings

We present the largest and first global case series of COVID-19 in people with psoriasis. Of 374 patients from 25 countries reported by clinicians, 93% fully recovered from COVID-19. Older age, male sex and non-white ethnicity were associated with greater risk of hospitalization for COVID-19, in addition to chronic lung disease. Comorbidities such as hypertension, cardiovascular disease and chronic liver disease were more prevalent in hospitalized patients compared to those not hospitalized. Our data also indicate an association between use of biologics for psoriasis and reduced risk of hospitalization, in comparison to non-biologic systemic therapies. We cannot exclude the possibility that unmeasured confounders may be driving this association: for example, our patient-reported data (1,626 participants across 48 countries) suggest that COVID-19 risk-mitigating behaviours (social isolation) may differ between psoriasis treatment groups. Finally, no significant difference was found in risk of hospitalization between different classes of biologics. Further investigation of the higher rate of hospitalization observed among patients using IL-23 inhibitors (compared with TNF or IL-17 inhibitors) in larger datasets is warranted.

Comparison with the literature

The baseline characteristics of our international case series suggest our findings are likely to be applicable to people with moderate to severe psoriasis since 90% of those reported were taking systemic therapies and there was a high prevalence of comorbidities (7,35). Our study underscores older age, male sex, non-white ethnicity and comorbidities as important risk factors for adverse COVID-19 outcomes in people with psoriasis, which is consistent with those risk factors already established for the general population (2,6). A cohort study of 17 million adults in the UK found that death from COVID-19 was associated with comorbidities including cardiovascular disease, diabetes, obesity, reduced kidney function and chronic liver disease (6). Similarly, a case series of 44,672 COVID-19 patients in China showed that cardiovascular disease, hypertension and diabetes were risk factors for death (4). There are very limited data in psoriasis, with four regional psoriasis case series in Northern Italy suggesting no increased rate of hospitalization or death from COVID-19 in those receiving biologics compared to the local population (17–20). Only six patients were hospitalized across the four reports, with few non-severe COVID-19 patients captured (n=5 (17), n=8 (18), not reported (19,20)), hence risk factors for adverse COVID-19 outcome could not be characterized. We addressed this through a larger collection of cases, which was more diverse with respect to geography, psoriasis therapies and COVID-19 severity and outcomes. The comprehensive capture of clinician-reported demographic and clinical variables enabled adjustment for important covariates in our logistic regression analysis.

Our finding of differential hospitalization risk associated with different treatment groups builds on the emerging literature across IMIDs. A recent single-centre COVID-19 case series from New York of 86 patients with IMIDs (14 of whom had psoriasis) observed that use of biologics was lower among those hospitalized for COVID-19 (6 of 14, 43%) than those not hospitalized (50 of 72, 69%) (36). Use of non-biologic systemic agents, including the common psoriasis therapy methotrexate, was higher among hospitalized patients than those not hospitalized.

Our data also aligns with findings from global clinician-reporting COVID-19 registries in inflammatory bowel disease (IBD; 525 patients across 33 countries) and rheumatic disease (600 patients across 40 countries) (28,29). The hospitalization and case fatality rates were 31% and 3% respectively in IBD, and 46% and 9% respectively in rheumatic disease (versus 21% and 2% in our psoriasis dataset). Severe COVID-19 was associated with older age and comorbidities in both studies. TNF inhibitor use was associated with decreased risk of COVID-19-related hospitalization among patients with rheumatic disease (OR 0.4, 95% CI 0.19-0.81) and decreased risk of hospitalization or death in IBD (OR 0.6, 95% CI 0.38-0.96). These findings, together with our data, contrast with pre-COVID-19 observational data, in which use of biologics including TNF inhibitors was associated with an increased risk of serious infections (for example, a higher incidence of lower respiratory tract infections/pneumonia has been observed for infliximab compared with methotrexate) (10,11). A meta-estimate of phase III randomized controlled trials of IL-17 inhibitors in psoriasis also indicated an increased risk of respiratory tract infections compared to placebo (OR 1.31, 95% CI 1.05-1.62) (37), however a similar analysis (albeit it with smaller sample sizes) found no statistically significant signal associated with IL-23 inhibitor use (OR 1.15, 95% CI 0.88-1.49) (38). Phase III trial data also suggest that use of psoriasis biologics (TNF, IL-17 and IL-23 inhibitors) is not associated with increases in viral infections such as influenza compared with placebo (39), which is consistent with data from long-term registries (10) and studies of other IMIDs (40).

Given the cytokine upregulation from aberrant immune activation observed in severe COVID-19, there is biological plausibility for a protective effect of cytokine-targeted biologics on adverse outcomes, compared with broader immunosuppressants that may detrimentally suppress host anti-viral immunity (41). This notion is currently under evaluation in trials of re-purposed IMID biologics in patients with COVID-19 (42). Existing reports of elevated plasma levels of TNF and IL-17 in patients manifesting severe COVID-19 (31) also align with our observation of a lower hospitalization rate in individuals receiving TNF inhibitors or IL-17 inhibitors compared to those receiving IL-23 inhibitors. Given the close interplay between IL-17 and IL-23 cytokines (IL-23 promotes the terminal differentiation, proliferation and activation of IL-17 secreting Th17 cells (43)) and the more established role of the IL-23/IL-17 axis in bacterial and fungal immunity (as opposed to viral defence), these observations require further study. We were unable to draw firm conclusions since our sample numbers limited the power to detect all but large differences in hospitalization risk between biologic

classes. Inhibitors of TNF, IL-17 and IL-23 are widely used for the treatment of moderate-severe psoriasis, so further accrual of cases over time will enable more robust interrogation of the differential risks associated with different biologic classes, which has important implications for clinical practice.

Alternatively, the association between use of biologics and reduced hospitalization may not be causal, but rather due to unmeasured confounders. Our patient-reported data suggest increased risk-mitigating behaviour (social isolation) in individuals receiving biologics compared with those receiving non-biologic systemic agents, which may reflect public perceptions of differential risk associated with different treatments. Social isolation may influence the initial exposure dose of SARS-CoV-2, which may affect the viral load and clinical course of COVID-19. Behavioural variation between treatment groups, and the consequent impact on COVID-19 risk/severity, warrants urgent further investigation since it is potentially relevant for public health policy.

Strengths and limitations

Major strengths are the global reach and size of the case series. The speed with which data has been accrued has enabled the timely release of results in response to the current global public health emergency. As the largest international study of COVID-19 outcomes in patients with psoriasis, our findings are more generalisable than the regional reports published to date. The key demographic associations with hospitalization for COVID-19 (sex, age, ethnicity) in our psoriasis dataset are in keeping with prior findings in the general population, which suggests robust data capture. We also present independent global patient-reported data on risk-mitigating behaviours during the pandemic, thus addressing for the first time a potential unmeasured confounder in clinician-reported datasets.

Information on the registries was disseminated worldwide, but the larger numbers of patients from Spain, Italy and UK (albeit areas of high COVID-19 prevalence) indicate potential ascertainment bias, which limits the generalizability of the results. Although our hospitalization rate of 22% is comparable to other global IMID registries, more severe COVID-19 cases may be over-represented since these may have been preferentially brought to the attention of clinicians. In contrast, patients who have died or those remaining in hospital may not yet have been reported. The higher hospitalization rate in Spain may represent a selective capture of severe cases or different international thresholds for hospital admission; the latter is a limitation of using hospitalization as a proxy for severe COVID-19. Reassuringly, a sensitivity analysis excluding Spanish cases did not change our conclusions, and differences in rates of death and mechanical ventilation among psoriasis patients receiving biologics versus non-biologic systemic therapies were consistent with our primary findings for hospitalization. Diverse COVID-19 testing practices may also have affected reporting (e.g. preferential testing of severe/hospitalized patients), although we

encouraged submission of suspected cases and our sensitivity analysis restricted to patients with only confirmed COVID-19 yielded similar results to the main analysis.

Our case series is dominated by patients with moderate-severe psoriasis, therefore our findings may not be generalisable to those with milder psoriasis. The majority of clinician-reported cases were receiving biologics, which contrasts with our patient-reported data. If this represents a different propensity for clinicians to report patients on different treatment types, then together with a higher likelihood of hospitalized cases being reported, this could lead to inflated effect size estimates due to selection bias. In contrast to clinician-reported data, a potential limitation of the self-report dataset is exposure misclassification, but it is reassuring that the overall baseline characteristics of both registries are comparable.

Although not an objective of this study, the clinical course of COVID-19 in individuals with and without psoriasis cannot be compared due to the lack of a matched control group from the general population. COVID-19 outcomes in those receiving biologics in our study also cannot be directly compared to studies of the general population due to fundamental differences in the ascertainment of cases. However, the observed median length of hospital stay and COVID-19 symptom characteristics in our biologic-treated clinician-reported case series are similar to those published on general populations. For example, the median length of hospital stay for psoriasis patients with COVID-19 who were receiving biologics in our study (14 days [IQR 6-23 days]) is similar to that of 1099 hospitalized patients with COVID-19 across 552 hospitals in China (12 days [IQR 10-14 days])(44). The most common three symptoms of COVID-19 in both the Chinese cohort and our patients receiving psoriasis biologics were fever, cough and fatigue.

The incidence of COVID-19 in psoriasis cannot be determined due to the lack of denominator (source population) data and uncertainty regarding those psoriasis patients with COVID-19 who were not reported. The incidence of COVID-19 in individuals receiving particular therapies also cannot be deduced, however future linkage to pharmacovigilance registry data should facilitate this.

Conclusions

In this large international series of patients with psoriasis and COVID-19, use of biologics was associated with a reduced risk of adverse COVID-19 outcome when compared to non-biologic systemic agents. This effect appeared to be primarily associated with use of TNF and IL-17 inhibitors, however further investigation of the observed differential rate of hospitalization between different classes of biologics is warranted. The accumulation of further data is required to clarify these observations before any recommendations for changes in clinical practice can be considered. Possible selection bias should be addressed through robust global clinician and patient participation in COVID-19 registries and alternative study designs such as cohort studies. This will open avenues for characterising

615 the determinants of additional COVID-19 outcomes and the impacts of specific treatments
616 at higher resolution.

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Table I – **Demographic and clinical characteristics of clinician-reported patients with psoriasis and COVID-19**

	All patients n (%) or median (IQR)	**Biologics** n (%) or median (IQR)	**Non-biologic systemic therapy** n (%) or median (IQR)	**No systemic agent** n (%) or median (IQR)	**Missing** n
N	374	267	67	36	
Sex					0
Female	147 (39.3)	107 (40.1)	29 (43.3)	9 (25.0)	
Male	227 (60.7)	160 (59.9)	38 (56.7)	27 (75.0)	
Age (years)	50 (41-58)	50 (42-57)	49 (40-60)	53 (35-63)	0
Ethnicity					3
White	316 (85.2)	230 (86.5)	57 (86.4)	27 (77.1)	
South Asian	21 (5.7)	16 (6.0)	3 (4.5)	2 (5.7)	
Hispanic or Latino	19 (5.1)	13 (4.9)	3 (4.5)	1 (2.9)	
Other	15 (4.0)	7 (2.6)	3 (4.5)	5 (14.3)	
Country of assessment					0
United Kingdom	135 (36.1)	103 (38.6)	21 (31.3)	11 (30.6)	
Italy	80 (21.4)	69 (25.8)	11 (16.4)	0 (0.0)	
Spain	56 (15.0)	35 (13.1)	16 (23.9)	3 (8.3)	
United States	25 (6.7)	15 (5.6)	2 (3.0)	8 (22.2)	
France	24 (6.4)	14 (5.2)	6 (9.0)	4 (11.1)	
Netherlands	11 (2.9)	7 (2.6)	4 (6.0)	0 (0.0)	
Rest of Europe	22 (5.9)	16 (6.0)	3 (4.5)	3 (8.3)	
Rest of the world	21 (5.6)	8 (3.0)	4 (6.0)	7 (19.4)	
Psoriasis phenotype					1
Plaque	365 (97.9)	263 (98.5)	63 (94.0)	35 (100.0)	
Pustular	8 (2.1)	4 (1.5)	4 (6.0)	0 (0.0)	
Psoriatic arthritis					0
No	238 (63.6)	162 (60.7)	48 (71.6)	26 (72.2)	
Yes	96 (25.7)	78 (29.2)	15 (22.4)	1 (2.8)	
Unknown	40 (10.7)	27 (10.1)	4 (6.0)	9 (25.0)	
Baseline psoriasis severity (PGA)					1
Clear	87 (23.3)	72 (27.0)	9 (13.4)	5 (14.3)	
Nearly clear	113 (30.3)	99 (37.1)	6 (9.0)	7 (20.0)	
Mild	98 (26.3)	59 (22.1)	27 (40.3)	11 (31.4)	
Moderate	51 (13.7)	22 (8.2)	21 (31.3)	7 (20.0)	
Moderate-severe	18 (4.8)	11 (4.1)	4 (6.0)	3 (8.6)	
Severe	6 (1.6)	4 (1.5)	0 (0.0)	2 (5.7)	
Months on treatment	24.0 (9.2-49.7)	23.2 (9.3-48.2)	25.8 (9.2-65.6)	-	21
Treatment stopped during COVID-19					0
Yes	185 (55.4)	143 (53.6)	42 (62.7)	-	
No	139 (41.6)	117 (43.8)	22 (32.8)	-	
Unknown	10 (3.0)	7 (2.6)	3 (4.5)	-	
Biologic type					0
TNF inhibitor	99 (37.1)	99 (37.1)	-	-	
IL-23 inhibitor	90 (33.7)	90 (33.7)	-	-	
IL-17 inhibitor	78 (29.2)	78 (29.2)	-	-	
Measures of obesity					
BMI	27.4 (24.8-33.1)	28.4 (25.1-34.2)	27.5 (23.8-32.0)	25.6 (23.9-26.9)	73
Obesity	123 (32.9)	96 (36.0)	22 (32.8)	5 (13.9)	0
Comorbidities					
Hypertension	97 (25.9)	71 (26.6)	18 (26.9)	7 (19.4)	0

Diabetes	61 (16.3)	44 (16.5)	11 (16.4)	6 (16.7)	0
Anxiety or depression	40 (10.7)	27 (10.1)	9 (13.4)	3 (8.3)	0
Cardiovascular disease	36 (9.6)	21 (7.9)	9 (13.4)	6 (16.7)	0
Chronic liver disease	31 (8.3)	24 (9.0)	3 (4.5)	3 (8.3)	0
Asthma	25 (6.7)	18 (6.7)	6 (9.0)	1 (2.8)	0
Cancer (incl. remission)	15 (4.0)	8 (3.0)	4 (6.0)	3 (8.3)	0
COPD or other chronic lung disease	14 (3.7)	11 (4.1)	1 (1.5)	2 (5.6)	0
Chronic kidney disease	9 (2.4)	5 (1.9)	3 (4.5)	1 (2.8)	0
Alcohol excess	8 (2.1)	4 (1.5)	3 (4.5)	1 (2.8)	0
ACEi at onset	41 (12.8)	31 (13.4)	6 (10.0)	3 (12.5)	54
ARB at onset	41 (12.7)	27 (11.5)	11 (18.0)	2 (8.3)	50
NSAID at onset	26 (8.3)	19 (8.4)	3 (5.1)	2 (8.3)	60
Smoking					70
Current smoker	44 (14.5)	34 (15.5)	7 (13.5)	3 (10.0)	
Former smoker	95 (31.2)	66 (30.1)	19 (36.5)	9 (30.0)	
Never smoked	165 (54.3)	119 (54.3)	26 (50.0)	18 (60.0)	

Table footnotes

4 participants excluded from treatment groups due to unknown drug (clinical trial)

'Biologics' category includes participants reporting co-therapy with conventional systemic or steroids (15), small molecule inhibitor (0) or both (0)

'Non-biologic systemic therapy' category includes participants reporting conventional systemic or steroids (39), small molecule inhibitor (26) or both (2)

Plaque psoriasis phenotype includes 1 patient with erythroderma and 3 with plaque and erythroderma. Pustular psoriasis phenotype includes 3 with plaque and/or erythroderma also present.

13 records imported directly from the AAD COVID-19 registry were assumed to have plaque psoriasis.

For patients on multiple systemic therapies, time on treatment was measured from the latest date (i.e. start of co-therapy)

For patients on multiple systemic therapies, treatment stoppage was taken as stopping any of the treatments.

'Obesity' combines patients for whom obesity is selected as a comorbidity with those having BMI $\geq$30. It may therefore miss some of the 73 patients for whom BMI is not available.

Table II – **COVID-19 outcomes in clinician-reported psoriasis patients**

	All patients n (%) or median (IQR)	**Biologics** n (%) or median (IQR)	**Non-biologic systemic therapy** n (%) or median (IQR)	**No systemic agent** n (%) or median (IQR)	**Missing** n
N	374	267	67	36	
COVID-19 diagnosis					0
Suspected	202 (54.0)	154 (57.7)	33 (49.3)	15 (41.7)	
Confirmed	172 (46.0)	113 (42.3)	34 (50.7)	21 (58.3)	
COVID-19 outcome					0
Unresolved	4 (1.1)	2 (0.7)	2 (3.0)	0 (0.0)	
Recovery	348 (93.0)	254 (95.1)	60 (89.6)	30 (83.3)	
Chronic complication	13 (3.5)	7 (2.6)	2 (3.0)	4 (11.1)	
Death	9 (2.4)	4 (1.5)	3 (4.5)	2 (5.6)	
Hospitalization					4
Hospitalized	77 (20.8)	44 (16.6)	22 (33.8)	10 (27.8)	
Not hospitalized	292 (78.9)	221 (83.4)	43 (66.2)	25 (69.4)	
Unknown	1 (0.3)	0 (0.0)	0 (0.0)	1 (2.8)	
Level of hospital care (% among all cases)					
No supplementary oxygen	8 (2.2)	4 (1.5)	1 (1.5)	3 (8.6)	5
Oxygen via mask	42 (11.4)	20 (7.5)	16 (24.6)	6 (17.1)	5
Non-invasive vent./hi flow	7 (1.9)	5 (1.9)	2 (3.1)	0 (0.0)	5
Mechanical ventilation	12 (3.3)	9 (3.4)	3 (4.6)	0 (0.0)	5
Ventilation (unknown type)	3 (0.8)	3 (1.1)	0 (0.0)	0 (0.0)	5
Unknown interventions	8 (2.2)	5 (1.9)	1 (1.5)	1 (2.9)	5
Composite outcome: mechanical ventilation or death	20 (5.4)	12 (4.5)	6 (9.2)	2 (5.6)	4
Days in hospital	11 (6-20)	14 (6-23)	10 (5-19)	10 (8-18)	13
Asymptomatic	12 (3.2)	9 (3.4)	1 (1.5)	2 (5.6)	4
Common COVID-19 symptoms (% among symptomatic cases)					
Fever	244 (69.7)	168 (67.5)	51 (81.0)	22 (64.7)	12
Fatigue (Malaise)	174 (49.7)	123 (49.4)	35 (55.6)	15 (44.1)	12
Dry continuous cough	167 (47.7)	119 (47.8)	31 (49.2)	15 (44.1)	12
Muscle aches (Myalgia)	130 (37.1)	92 (36.9)	21 (33.3)	15 (44.1)	12
Shortness of breath (Dyspnea)	116 (33.1)	87 (34.9)	18 (28.6)	10 (29.4)	12
Anosmia and/or dysgeusia	83 (23.7)	62 (24.9)	13 (20.6)	8 (23.5)	12
Joint pain (Arthralgia)	64 (18.3)	49 (19.7)	11 (17.5)	2 (5.9)	12
Sore throat	62 (17.7)	45 (18.1)	14 (22.2)	3 (8.8)	12
Headache	49 (14.0)	39 (15.7)	7 (11.1)	3 (8.8)	12
Diarrhoea	42 (12.0)	23 (9.2)	16 (25.4)	3 (8.8)	12
Chest pain	31 (8.9)	25 (10.0)	4 (6.3)	1 (2.9)	12
Cough with sputum production	26 (7.4)	20 (8.0)	5 (7.9)	0 (0.0)	12
Runny nose (Rhinorrhea)	26 (7.4)	20 (8.0)	1 (1.6)	5 (14.7)	12
Wheezing	25 (7.1)	20 (8.0)	3 (4.8)	2 (5.9)	12
Nausea and/or vomiting	20 (5.7)	9 (3.6)	6 (9.5)	5 (14.7)	12
Abdominal pain	13 (3.7)	9 (3.6)	1 (1.6)	3 (8.8)	12
Conjunctivitis	10 (2.9)	8 (3.2)	1 (1.6)	1 (2.9)	12
Days of COVID-19 symptoms	14 (7-21)	14 (7-21)	14 (10-22)	10 (7-18)	18

Table footnotes

4 participants excluded from treatment groups due to unknown drug (clinical trial)

'Biologics' category includes participants reporting co-therapy with conventional systemic or steroids (15), small molecule inhibitor (0) or both (0)

'Non-biologic systemic therapy' category includes participants reporting conventional systemic or steroids (39), small molecule inhibitor (26) or both (2)

4 patients with unresolved COVID-19 are excluded from COVID-19 outcome summaries (treated as missing)

Symptom of ‘unspecified cough’ allocated to 'dry continuous cough' (2 patients)

Table III –**Multivariate logistic regression models for hospitalization due to COVID-19**

	Counts n hospitalized/ total n (%)	**Minimally adjusted model** OR (95% CI)	**Fully adjusted model** OR (95% CI)
Treatment type			
Biologic	44/265 (16.6)	Ref	Ref
Non-biologic systemic	22/65 (33.8)	2.72 (1.37, 5.40)	2.84 (1.31, 6.18)
No systemic agent	10/35 (28.6)	1.88 (0.75, 4.68)	2.35 (0.82, 6.72)
Male	58/220 (26.4)	2.29 (1.22, 4.32)	2.51 (1.23, 5.12)
Age (effect per 10 years)	-	2.01 (1.59, 2.52)	1.59 (1.19, 2.13)
Non-white ethnicity	17/53 (32.1)	-	3.15 (1.24, 8.03)
Assessment country			
United Kingdom	19/133 (14.3)	-	Ref
Spain	23/53 (43.4)	-	4.79 (1.88, 12.19)
Rest of Europe	23/136 (16.9)	-	1.61 (0.70, 3.72)
Rest of the world	11/43 (25.6)	-	1.27 (0.43, 3.79)
BMI (effect per 5 kg/m2)	-	-	1.09 (0.87, 1.37)
Hypertension	38/93 (40.9)	-	2.03 (0.99, 4.16)
Cardiovascular disease	20/34 (58.8)	-	2.01 (0.74, 5.46)
Chronic liver disease	14/30 (46.7)	-	2.12 (0.81, 5.55)
Diabetes	22/60 (36.7)	-	1.05 (0.46, 2.38)
Chronic lung disease (incl. asthma, COPD)	16/38 (42.1)	-	3.87 (1.52, 9.83)
Other comorbidities	30/77 (39.0)	-	1.69 (0.83, 3.43)
Ever smoked	34/136 (25.0)	-	1.16 (0.54, 2.49)

Table footnotes

'Ref' is the reference group in the multivariable logistic regression models.

Table IV – **Characteristics self-reported to the PsoProtect*Me* registry by individuals with psoriasis during the COVID-19 pandemic**

	All patients n (%) or median (IQR)	**Biologics** n (%) or median (IQR)	**Non-biologic systemic therapy** n (%) or median (IQR)	**No systemic agent** n (%) or median (IQR)	**Missing** n
N	1,626	512	273	839	
COVID infection					0
Yes, with test	15 (0.9)	1 (0.2)	2 (0.7)	12 (1.4)	
Yes, no test	81 (5.0)	24 (4.7)	11 (4.0)	46 (5.5)	
Unsure	54 (3.3)	9 (1.8)	11 (4.0)	34 (4.1)	
No	1,476 (90.8)	478 (93.4)	249 (91.2)	747 (89.0)	
Age (years)	48 (36-59)	49 (39-58)	50 (38-60)	46 (33-60)	0
Sex					0
Female	1,041 (64.0)	287 (56.1)	184 (67.4)	570 (67.9)	
Male	583 (35.9)	223 (43.6)	89 (32.6)	269 (32.1)	
Unknown	2 (0.1)	2 (0.4)	0 (0.0)	0 (0.0)	
Ethnicity					19
White	1,399 (87.1)	436 (85.8)	231 (85.2)	730 (88.4)	
Non-white	208 (12.9)	72 (14.2)	40 (14.8)	96 (11.6)	
Country of assessment					2
United Kingdom	1,191 (73.3)	370 (72.3)	206 (75.5)	614 (73.4)	
United States	98 (6.0)	48 (9.4)	11 (4.0)	39 (4.7)	
Denmark	49 (3.0)	25 (4.9)	4 (1.5)	20 (2.4)	
Sweden	33 (2.0)	10 (2.0)	7 (2.6)	16 (1.9)	
Philippines	31 (1.9)	1 (0.2)	6 (2.2)	24 (2.9)	
Canada	27 (1.7)	10 (2.0)	6 (2.2)	10 (1.2)	
Ireland	26 (1.6)	8 (1.6)	1 (0.4)	17 (2.0)	
Hong Kong	16 (1.0)	5 (1.0)	2 (0.7)	9 (1.1)	
Norway	14 (0.9)	6 (1.2)	4 (1.5)	4 (0.5)	
Australia	14 (0.9)	7 (1.4)	0 (0.0)	7 (0.8)	
Singapore	11 (0.7)	0 (0.0)	4 (1.5)	7 (0.8)	
Japan	10 (0.6)	7 (1.4)	2 (0.7)	1 (0.1)	
Rest of Europe	53 (3.3)	9 (1.8)	4 (1.5)	40 (4.8)	
Rest of the world	51 (3.1)	6 (1.2)	16 (5.9)	29 (3.5)	
Psoriasis phenotype					20
Plaque	1,446 (90.0)	457 (91.0)	232 (85.9)	755 (90.7)	
Pustular	104 (6.5)	35 (7.0)	28 (10.4)	41 (4.9)	
Unsure	56 (3.5)	10 (2.0)	10 (3.7)	36 (4.3)	
Psoriatic arthritis					0
Yes	548 (33.7)	246 (48.0)	128 (46.9)	173 (20.6)	
No	993 (61.1)	243 (47.5)	128 (46.9)	621 (74.0)	
Unsure	85 (5.2)	23 (4.5)	17 (6.2)	45 (5.4)	
Baseline psoriasis severity (self-reported using PGA scale)					0
Clear	218 (13.4)	158 (30.9)	23 (8.4)	36 (4.3)	
Nearly clear	364 (22.4)	184 (35.9)	60 (22.0)	119 (14.2)	
Mild	423 (26.0)	88 (17.2)	68 (24.9)	267 (31.8)	
Moderate	359 (22.1)	40 (7.8)	73 (26.7)	246 (29.3)	
Moderate-severe	188 (11.6)	30 (5.9)	32 (11.7)	126 (15.0)	
Severe	63 (3.9)	9 (1.8)	16 (5.9)	38 (4.5)	
Not sure	11 (0.7)	3 (0.6)	1 (0.4)	7 (0.8)	
Months on treatment (COVID-19 group, at onset)	25.3 (6.0-51.0)	23.4 (9.2-49.8)	27.7 (2.9-51.9)	-	11
Months on treatment (uninfected	25.2 (9.1-60.2)	24.8 (9.5-52.5)	26.1 (7.9-74.4)	-	48

group, at survey date)					
Treatment stopped during COVID-19	22 (40.7)	11 (35.5)	11 (47.8)	-	4
Treatment stopped during pandemic (uninfected group)	127 (17.9)	79 (17.0)	48 (19.8)	-	21
Biologic type					0
TNF inhibitor	225 (43.9)	225 (43.9)	-	-	
IL-23 inhibitor	171 (33.4)	171 (33.4)	-	-	
IL-17 inhibitor	115 (22.5)	115 (22.5)	-	-	
IL-1R inhibitor	1 (0.2)	1 (0.2)	-	-	
Measures of obesity					
BMI	26.8 (23.4-31.2)	27.9 (24.3-32.5)	26.6 (23.3-31.2)	26.0 (22.8-29.8)	114
Obesity	478 (29.4)	176 (34.4)	91 (33.3)	210 (25.0)	0
Comorbidities					
Hypertension	344 (21.2)	135 (26.4)	69 (25.3)	139 (16.6)	0
Diabetes	105 (6.5)	43 (8.4)	14 (5.1)	48 (5.7)	0
Anxiety or depression	384 (23.6)	120 (23.4)	58 (21.2)	206 (24.6)	0
Cardiovascular disease	95 (5.8)	26 (5.1)	17 (6.2)	52 (6.2)	0
Chronic liver disease	81 (5.0)	42 (8.2)	10 (3.7)	29 (3.5)	0
Asthma	181 (11.1)	66 (12.9)	25 (9.2)	90 (10.7)	0
Cancer (incl. remission)	43 (2.6)	10 (2.0)	6 (2.2)	27 (3.2)	0
COPD or other chronic lung disease	44 (2.7)	17 (3.3)	8 (2.9)	19 (2.3)	0
Chronic kidney disease	16 (1.0)	8 (1.6)	3 (1.1)	5 (0.6)	0
ACEi user	204 (13.9)	76 (16.8)	41 (16.9)	87 (11.3)	162
ARB user	140 (10.0)	62 (14.4)	22 (9.7)	55 (7.4)	219
NSAID user	288 (20.2)	112 (25.2)	39 (17.3)	137 (18.2)	202
Smoking					28
Never smoked	837 (52.4)	254 (50.3)	150 (55.8)	433 (52.7)	
Former smoker	571 (35.7)	184 (36.4)	88 (32.7)	299 (36.4)	
Current smoker	190 (11.9)	67 (13.3)	31 (11.5)	90 (10.9)	
Risk-mitigating behaviours (uninfected group)					
Shielding	319 (21.6)	134 (28.0)	54 (21.7)	131 (17.5)	0
Self-isolating	831 (56.3)	273 (57.1)	130 (52.2)	426 (57.0)	0
Shielding or self-isolating	979 (66.3)	346 (72.4)	161 (64.7)	470 (62.9)	0
Social distancing	989 (67.0)	275 (57.5)	161 (64.7)	552 (73.9)	0
Wearing gloves or masks	555 (37.6)	190 (39.7)	87 (34.9)	278 (37.2)	0
Other risk-mitigating behaviour	42 (2.8)	14 (2.9)	3 (1.2)	25 (3.3)	0
No risk-mitigating behaviour	11 (0.7)	2 (0.4)	2 (0.8)	7 (0.9)	0

Table footnotes

2 participants excluded from treatment groups due to unknown drug (clinical trial)

'Biologics' category includes participants reporting co-therapy with conventional systemic or steroids (61), small molecule inhibitor (2) or both (3)

'Non-biologic systemic therapy' category includes participants reporting conventional systemic or steroids (229), small molecule inhibitor (39) or both (6)

Time on treatment and adherence data were excluded for participants reporting multiple biologics (5), multiple conventional systemics or steroids (10) or multiple small molecule inhibitors (0)

For participants reporting systemic treatments in more than one category, time on treatment was measured from the latest date (i.e. start of co-therapy)

Obesity combines participants selecting obesity as a comorbidity with those having BMI $\geq$30. It may therefore miss some of the 114 participants for whom BMI is not available.