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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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**Background:** The multimorbid burden and use of systemic immunosuppressants in people with psoriasis may confer greater risk of adverse outcomes of coronavirus disease 2019 (COVID-19), but the data are limited.

**Objective:** Our aim was to characterize the course of COVID-19 in patients with psoriasis and identify factors associated with hospitalization.

**Methods:** Clinicians reported patients with psoriasis with confirmed/suspected COVID-19 via an international registry, Psoriasis Patient Registry for Outcomes, Therapy and

**Epidemiology of COVID-19 Infection.** Multiple logistic regression was used to assess the association between clinical and/or demographic characteristics and hospitalization.

**A separate patient-facing registry characterized risk-mitigating behaviors.**

**Results:** Of 374 clinician-reported patients from 25 countries, 71% were receiving a biologic, 18% were receiving a nonbiologic, and 10% were not receiving any systemic treatment for psoriasis. In all, 348 patients (93%) were fully recovered from COVID-19, 77 (21%) were hospitalized, and 9

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We acknowledge financial support from the Department of Health via the National Institute for Health Research (NIHR) Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust and King's College London, the NIHR Manchester Biomedical Research Centre and the Psoriasis Association. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, or the Department of Health and Social Care. S.K.M. is funded by a Medical Research Council Clinical Academic Research Partnership award (MR/T02383X/1). N.D. is funded by Health Data Research UK (MR/S003126/1), which is funded by the UK Medical Research Council, Engineering and Physical Sciences Research Council; Economic and Social Research Council; Department of Health & Social Care (England); Chief Scientist Office of the Scottish Government Health and Social Care Directorates; Health and Social Care Research and Development Division (Welsh Government); Public Health Agency (Northern Ireland); British Heart Foundation; and Wellcome. Z.Z.N.Y. is funded by a NIHR Academic Clinical Lectureship through the University of Manchester. C.E.M.G. is an NIHR Emeritus Senior Investigator and is funded in part by the Medical Research Council (MR/101 1808/1). C.E.M.G. and R.B.W. are in part supported by the NIHR Manchester Biomedical Research Centre. S.M.L. is supported by a Wellcome Senior Research Fellowship in clinical science (205039/Z/16/Z). S.M.L. is also supported by Health Data Research UK (grant LOND1), which is funded by the UK Medical Research Council, Engineering and Physical Sciences Research Council, Economic and Social Research Council, Department of Health and Social Care (England), Chief Scientist Office of the Scottish Government Health and Social Care Directorates, Health and Social Care Research and Development Division (Welsh government), Public Health Agency (Northern Ireland), British Heart Foundation, and Wellcome Trust.

Disclosure of potential conflict of interest: T. Mackenzie has received honoraria from AbbVie, Sanofi, and Leo. C. H. Smith has received departmental research funding from AbbVie, Novartis, Pfizer, and Sanofi and has served as an investigator on Medical Research Council- and Horizon 2020-funded consortia with industry partners (see

(2%) died. Increased hospitalization risk was associated with older age (multivariable-adjusted odds ratio [OR] = 1.59 per 10 years; 95% CI = 1.19-2.13), male sex (OR = 2.51; 95% CI = 1.23-5.12), nonwhite 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 nonbiologic systemic therapy than in those using biologics (OR = 2.84; 95% CI = 1.31-6.18). No significant differences were found between classes of biologics. Independent patient-reported data (n = 1626 across 48 countries) suggested lower levels of social isolation in individuals receiving nonbiologic systemic therapy than in those receiving biologics (OR = 0.68; 95% CI = 0.50-0.94).

**Conclusion:** In this international case series of patients with moderate-to-severe psoriasis, biologic use was associated with lower risk of COVID-19–related hospitalization than with use of nonbiologic systemic therapies; however, further investigation is warranted on account of potential selection bias and unmeasured confounding. Established risk factors (being older, being male, being of nonwhite ethnicity, and having comorbidities) were associated with higher hospitalization rates. (J Allergy Clin Immunol 2021;147:60-71.)

**Key words:** COVID-19, hospitalization, psoriasis, risk factors, biologics, immunosuppressants

The coronavirus disease 2019 (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.<sup>1</sup> 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

*Abbreviations used*

|             |   |
|-------------|---|
| BMI:        | Body mass index   |
| IBD:        | Inflammatory bowel disease  |
| IMID:       | Immune-mediated inflammatory disease  |
| IQR:        | Interquartile range   |
| OR:         | Odds ratio  |
| PsoProtect: | Psoriasis Patient Registry for Outcomes, Therapy and Epidemiology of COVID-19 Infection |

care management, with risk of septic shock, multiorgan failure, and death.<sup>2</sup> Reported mortality rates range from 2.3% to 7.2%.<sup>2,3</sup> Increased age, male sex, and nonwhite 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.<sup>4-6</sup> Because multimorbidity is prevalent in psoriasis,<sup>7</sup> 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<sup>8</sup> and pre-COVID-19 observational data suggest greater risk of respiratory infection–related hospitalization than in the general population.<sup>9</sup> Furthermore, there is uncertainty about whether additional serious infection risk is conferred by drugs that affect the immune system, which are the mainstay of treatment in moderate-to-severe psoriasis.<sup>10,11</sup>

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–secreting dendritic cells propagating pathogenic IL-23/T17 circuits.<sup>12</sup> In the initial phase of COVID-19, viral pathogenicity is dominant and viral clearance by early host type I IFN–mediated


psort.org.uk and biomap—imi.eu); SOBI provided the drug for a National Institute for Health Research–funded trial in pustular psoriasis. S. K. Mahil has received departmental funding from AbbVie, Celgene, Eli Lilly, Janssen-Cilag, Novartis, Sanofi, and UCB. K. J. Masib has received honoraria from Janssen, LEO Pharma, Lilly, and Novartis. P. Di Meglio has received research grants from UCB and consultancy/speaker honoraria from Novartis, UCB, and Janssen. F. Capon has received funding and consulting fees from Boehringer Ingelheim and AnaptysBio. E. Mahe has received honoraria from AbbVie, Celgene, Amgen, Janssen Cilag, Novartis, Lilly, and Leo Pharma. L. Moorhead has received honoraria from AbbVie, Celgene, Janssen, Leo, Novartis, and UCB. R. Rivera has been a consultant and adviser and/or received speaking fees and/or grants and/or served as an investigator in clinical trials for AbbVie, Almirall, Amgen, Boehringer, Celgene, Janssen, LEO Pharma, Lilly, MSD, Novartis, Pfizer, and UCB. L. Puig has perceived consultancy/speaker honoraria from and/or participated in clinical trials sponsored by AbbVie, Almirall, Amgen, Baxalta, Biogen, Boehringer Ingelheim, Celgene, Gebro, Janssen, JS BIOCAD, Leo-Pharma, Lilly, Merck-Serono, MSD, Mylan, Novartis, Pfizer, Regeneron, Roche, Sandoz, Samsung-Bioepis, Sanofi, and UCB. J. N. Barker has received honoraria and/or research grants from AbbVie, Almirall, Amgen, Boehringer-Ingelheim, Bristol-Myers Squibb, Celgene, Janssen, Leo, Lilly, Novartis, Samsung, and Sun Pharma. C. E. M. Griffiths has received honoraria and/or research grants from AbbVie, BMS, Almirall, Amgen, Celgene, Eli Lilly Galderma, LEO Pharma, Stiefel GSK, Janssen, MSD, Novartis, Pfizer, Sandoz, Sun Pharmaceuticals, and UCB Pharma. R. B. Warren has received grants and/or honoraria from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Janssen, Lilly, Leo Pharma, Novartis, Pfizer, Sanofi, UCB Pharma, and Xenoport. S. R. Feldman has received research, speaking and/or consulting support from Galderma, GSK/Stiefel, Almirall, Leo Pharma, Boehringer Ingelheim, Mylan, Celgene, Pfizer, Valeant, AbbVie, Samsung, Janssen, Lilly, Menlo, Merck, Novartis, Regeneron, Sanofi, Novan, Quriert, National Biological Corporation, Caremark, Advance Medical, Sun Pharma, Suncare Research, Informa, UpToDate, and the National Psoriasis Foundation; he is founder and majority owner of [www.DrScore.com](http://www.DrScore.com) and founder and part owner of Causa Research, a company dedicated to enhancing patients' adherence to treatment. H. McAteer is employed by the

Psoriasis Association, which has received grants from Almirall, 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. H. Bachelez 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. D. Jullien has acted as, participated in, or received consultancy for the following: speaker bureau, clinical research, honoraria, scientific officer, steering committees, advisory boards for AbbVie, Almirall, Amgen, Biogen, Celgene, Fresenius-Kabi, Janssen-Cilag, Leo, Lilly, MEDAC, Novartis, Pfizer, Sanofi, and UCB. C. De La Cruz has been a speaker or principal investigator for AbbVie, Pfizer, Lilly, Janssen, Novartis, Amgen, Boehringer Ingelheim, and Sanofi. P. Spuls 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; he is involved in performing clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of diseases such as psoriasis and atopic dermatitis, for which financial compensation is paid to the department/hospital; and he is chief investigator of the systemic and phototherapy atopic eczema registry (TREAT NL) for adults and children, as well as one of the main investigators of the SECURE-AD registry. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication July 10, 2020; revised October 1, 2020; accepted for publication October 8, 2020.

Available online October 16, 2020.

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0091-6749/\$36.00

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<https://doi.org/10.1016/j.jaci.2020.10.007>

responses prevents further viral replication, T-cell exhaustion, and hyperinflammation.<sup>13</sup> A reduced or delayed type I IFN response has been associated with poor COVID-19 outcomes<sup>14</sup>; thus, it is possible that the immune dysregulation in psoriasis may be advantageous, although its therapeutic suppression may be detrimental. The second phase of COVID-19 comprises hyperinflammation and cytokine storm, with elevation of proinflammatory cytokines also implicated in psoriasis, including TNF, IL-1 $\beta$ , IL-6, IL-8, IFN- $\gamma$ , and IL-17. It is unclear whether individuals with psoriasis are at greater risk of progression to this phase, and conversely, whether drugs that affect the immune system (biologics and standard systemic agents) are effective therapies for severe COVID-19. Treatments targeting the overexuberant host immune response in COVID-19, including inhibitors of IL-1, IL-6, Janus kinase, and TNF, are currently undergoing clinical trial.<sup>15,16</sup>

Psoriasis, rheumatoid arthritis, and SLE were collectively highlighted as potential risk factors for COVID-19–related death through use of primary care data linked to hospital records from 17 million adults in the United Kingdom.<sup>6</sup> 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.<sup>17–20</sup> However, these data have limited external validity because 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 patients with psoriasis to understand the determinants of severe infection and help inform clinical decision making. Here, we have described the first international series of patients with psoriasis and COVID-19 and identified demographic and clinical factors associated with hospitalization.

## METHODS

### Study design, setting, and participants

This registry-based study used 2 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 March 27, 2020.<sup>21</sup> Data were collected and managed by using Research Electronic Data Capture (REDCap) electronic data capture tools licensed to the King's College London Division of Health and Social Care Research.<sup>22,23</sup> REDCap is a secure, web-based software platform designed to support data capture.

The eligibility criterion was any patient with psoriasis and confirmed or suspected COVID-19 identified by his or her supervising clinician. Case submission was requested at least 14 days following onset of symptoms 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 (see Table E1 in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)). We also invited case reports from 2 US COVID-19 registries (SECURE-Psoriasis and American Academy of Dermatology COVID-19 [AAD COVID-19]).<sup>24,25</sup> In all, 38 of the cases have been published elsewhere ( $n = 29$ <sup>17</sup> and  $n = 9$ <sup>18</sup>).

The second data source was a separate online self-report patient-facing registry, PsoProtectMe, which launched globally on May 4, 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 organizations focused on individuals with psoriasis (see Table E1).

### Variables

Minimum sufficient core sets of variables within the PsoProtect and PsoProtectMe case report forms<sup>26,27</sup> 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.<sup>28,29</sup> Key variables in both registries included demographics (age, sex, ethnicity, and country), smoking status, comorbidities, details of psoriasis (phenotype and treatment) and COVID-19 (symptoms, treatment, and outcome). Medication adherence and social isolation behavior during the pandemic were collected in PsoProtectMe.

### Statistical methods

PsoProtect and PsoProtectMe data were extracted on July 1 and 3, 2020, respectively. Incomplete, duplicate, and erroneous entries were manually reviewed by the study team and removed. All analysis was performed by using the R statistical programming language.<sup>30</sup>

Demographic and clinical characteristics and COVID-19 outcomes of the study population were summarized by using descriptive statistics. Continuous variables were reported by using median and interquartile range (IQR), and categorical/dichotomous variables were reported 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 4 weeks before COVID-19 onset, comprising biologics (the TNF inhibitors adalimumab, certolizumab pegol, etanercept, infliximab, and golimumab; the IL-17 inhibitors brodalumab, ixekizumab, secukinumab; the IL12/IL-23p40 or IL-23p19 [collectively IL-23] inhibitors guselkumab, risankizumab, tildrakizumab, and ustekinumab), nonbiologic systemic agents (acitretin, apremilast, ciclosporin, methotrexate, fumaric acid esters/dimethylfumarate, and prednisolone), and no systemic treatment.

The association between treatment type (biologic, nonbiologic systemic, or no systemic treatment) and hospitalization for COVID-19 was assessed by using (1) a minimally adjusted logistic regression model that included age and sex covariates and (2) a fully adjusted model that included 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,<sup>2,3,6,31</sup> namely, age, sex, ethnicity, country, smoking, body mass index (BMI), and comorbidities. Other relevant variables (use of an angiotensin-converting enzyme inhibitor, use of an angiotensin II receptor blocker, and obesity as a 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 in cases in which BMI was 30 or higher, even when 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) with patients with complete data (see Table E2 in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)). Small differences were observed in the proportions of men, white ethnicity, confirmed COVID-19 diagnosis, and hospitalization. Therefore, to maximize the included data, the final regression models were based on 20 multiply imputed data sets generated with the R software package Multivariate Imputation by Chained Equations (MICE).<sup>32</sup>

Quadratic terms for age and sex covariates were considered but rejected owing to lack of improvement in model fit (likelihood ratio test). Minimally and fully adjusted odds ratios (ORs) and 95% CIs 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, we fitted a fully adjusted model 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 by using a likelihood ratio test. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cross-sectional studies was used as a basis for reporting.<sup>33</sup>

### 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.<sup>34</sup> Only de-identified data were collected; hence, written informed patient consent was not required. Data

collection, transfer, and storage were compliant with statutory requirements, International Council for Harmonization Good Clinical Practice, and the European Union General Data Protection Regulation.

## RESULTS

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

In total, 374 patients with psoriasis and confirmed ( $n = 172$  [46%]) or suspected ( $n = 202$  [54%]) COVID-19 were reported by clinicians from 25 countries (including the United Kingdom [ $n = 135$  (36%)], Italy [ $n = 80$  (21%)], and Spain [ $n = 56$  (15%)] [see [Table E3](#) in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)]). Demographic and clinical characteristics are summarized in [Table I](#). The median age was 50 years (IQR = 41-58). There was a predominance of males ( $n = 227$  [61%]) and individuals of white ethnicity ( $n = 316$  [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 ( $n = 365$  [98%]) and clear, nearly clear, or mild psoriasis at COVID-19 onset ( $n = 298$  [80%]). The most commonly reported comorbidities were obesity ( $n = 123$  [33%]), hypertension ( $n = 97$  [26%]), psoriatic arthritis ( $n = 96$  [26%]), and diabetes ( $n = 61$  [16%]).

Most patients were receiving a biologic treatment ( $n = 267$  [71%]) for their psoriasis rather than a nonbiologic systemic agent ( $n = 67$  [18%]) or no systemic therapy ( $n = 36$  [10%]). Of those receiving a biologic, similar numbers of patients were receiving either a TNF, IL-17, or IL-23 inhibitor ( $n = 99$ , 78, and 90, respectively). Demographic and clinical characteristics by biologic class are summarized in [Table E4](#) (in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)) and split by confirmed and suspected COVID-19 in [Table E5](#) (in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)).

### Most reported patients fully recovered from COVID-19

Of the reported patients, 348 (93%) fully recovered from COVID-19 ([Table II](#)). The most common COVID-19 symptoms were fever ( $n = 244$  [68%]), fatigue ( $n = 174$  [48%]), and dry continuous cough ( $n = 167$  [46%]); the median duration of symptoms was 14 days (IQR = 7-21).

In all, 77 patients (21%) were hospitalized for COVID-19, 7 (2%) required high-flow oxygen supplementation and 12 (3%) required mechanical ventilation. The median length of hospital stay was 11 days (IQR = 6-20). A total of 9 patients died (2%); their median age was 65 years (range 43-89 years), and all had at least 1 comorbidity, with hypertension ( $n = 6$  [67%]) and diabetes ( $n = 5$  [56%]) being the most prevalent. COVID-19 outcomes by biologic class. The data for these patients are summarized in [Table E6](#) (in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)) and split by confirmed and suspected COVID-19 in [Table E7](#) (in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)).

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

After exclusion of 9 individuals because of 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% vs 12% among females), older patients (60% among those older than 70 years vs 26% among those aged 50-70 years and 10% of those younger than 50 years), and nonwhite ethnicity (32% versus 19% among individuals of 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 with 34% of nonhospitalized patients.

Hospitalization for COVID-19 was less common among patients receiving biologic therapy for their psoriasis ( $\leq 4$  weeks before COVID-19 onset; 44 of 265 [17%]) than among those receiving nonbiologic 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% vs 5% among those receiving nonbiologics) and death (2% vs 5%).

Compared with the reference group of biologic users, an age- and sex-adjusted model for hospitalization rate estimated an OR of 2.72 for nonbiologic 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), nonwhite 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 ORs greater than 2: hypertension (OR = 2.03; 95% CI = 0.99-4.16), cardiovascular disease (OR = 2.01; 95% CI = 0.74-5.46), and chronic liver disease (OR = 2.12; 95% CI = 0.81-5.55). No association was found with ever having smoked (OR = 1.16; 95% CI = 0.54-2.49).

In the fully adjusted model, use of a nonbiologic systemic therapy for psoriasis remained associated with increased risk of hospitalization compared with use of a biologic (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 nonbiologic systemic therapy or no therapy, although interpretation of these estimates should take into account possible sources of bias (as detailed in the Discussion section).

Patients reported in Spain were more likely to have been hospitalized for COVID-19 (43% vs 17% elsewhere) and more likely to have received a nonbiologic systemic agent (30% vs 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 (see [Table E8](#) in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)). A multiple regression model fitted in confirmed cases only (see [Table E9](#) in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)) indicated a stronger association with hospitalization risk for use of nonbiologic systemic agents than with hospitalization risk for use of biologics

**TABLE I.** Demographic and clinical characteristics of clinician-reported patients with psoriasis and COVID-19

| Characteristic                                 | All patients     | Patients receiving biologics | Patients receiving nonbiologic systemic therapy | Patients receiving no systemic agent | Missing (no.) |
|--|------------------|------------------------------|---|--------------------------------------|---------------|
|  | (n = 374)        | (n = 267)                    | (n = 67)  | (n = 36)                             |               |
| Sex, no. (%)                                   |                  |                              |   |                                      | 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 (y), median (IQR)                          | 50 (41-58)       | 50 (42-57)                   | 49 (40-60)                                      | 53 (35-63)                           | 0             |
| Ethnicity, no. (%)                             |                  |                              |   |                                      | 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, no. (%)                 |                  |                              |   |                                      | 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)                             |               |
| The 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, no. (%)                   |                  |                              |   |                                      | 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, no. (%)                   |                  |                              |   |                                      | 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 (per PGA), no. (%) |                  |                              |   |                                      | 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-to-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)                              |               |
| Time receiving treatment (mo), median (IQR)    | 24.0 (9.2-49.7)  | 23.2 (9.3-48.2)              | 25.8 (9.2-65.6)                                 | —                                    | 21            |
| Treatment stopped during COVID-19, no. (%)     |                  |                              |   |                                      | 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, no. (%)                         |                  |                              |   |                                      | 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, median (IQR)                              | 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, no. (%)                               | 123 (32.9)       | 96 (36.0)                    | 22 (32.8)                                       | 5 (13.9)                             | 0             |
| Comorbidities, no. (%)                         |                  |                              |   |                                      |               |
| 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 (including 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, no. (%)                         | 41 (12.8)        | 31 (13.4)                    | 6 (10.0)  | 3 (12.5)                             | 54            |
| ARB at onset, no. (%)                          | 41 (12.7)        | 27 (11.5)                    | 11 (18.0)                                       | 2 (8.3)                              | 50            |
| NSAID at onset, no. (%)                        | 26 (8.3)         | 19 (8.4)                     | 3 (5.1)   | 2 (8.3)                              | 60            |

(Continued)

TABLE I. (Continued)

| Characteristic   | All patients<br>(n = 374) | Patients receiving biologics<br>(n = 267) | Patients receiving nonbiologic systemic therapy<br>(n = 67) | Patients receiving no systemic agent<br>(n = 36) | Missing<br>(no.) |
|------------------|---------------------------|---|---|--|------------------|
| Smoking, no. (%) |                           |   |   |  | 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)  |                  |

ACEI, Angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; COPD, chronic obstructive pulmonary disease; NSAID, nonsteroidal anti-inflammatory drug; PGA, Physician's Global Assessment.

Four participants have been excluded from the treatment groups because of unknown drug (clinical trial). The category biologics includes participants reporting cotherapy with conventional systemic agents or steroids (n = 15), small-molecule inhibitor (n = 0), or both (n = 0).

The category nonbiologic systemic therapy includes participants reporting use of conventional systemic agents or steroids (n = 39), small-molecule inhibitor (n = 26), or both (n = 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. A total of 13 records imported directly from the American Academy of Dermatology COVID-19 (AAD COVID-19) registry were assumed to be records of patients with plaque psoriasis. For patients receiving multiple systemic therapies, time receiving treatment was measured from the latest date (ie, start of cotherapy). For patients receiving multiple systemic therapies, treatment stoppage was taken as stopping any of the treatments. The category obesity combines patients for whom obesity is selected as a comorbidity with patients having a BMI of 30 or higher; it may therefore miss some of the 73 patients for whom BMI is not available.

(OR = 3.98; 95% CI = 1.38-11.46). However, this estimate is likely inflated because most hospitalized patients had confirmed COVID-19 (69 of 76 [91%]).

To assess potential differences in COVID-19 hospitalization risk between classes of biologics, we fitted a multiple logistic regression model in which biologics were split into TNF, IL-23, and IL-17 inhibitor groups (n = 98, 89, and 78, respectively) (see Table E10 in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)). Hospitalization was observed more frequently in patients receiving IL-23 inhibitors (23%) than in those receiving 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 group receiving a TNF inhibitor. However, the 95% CI was wide (0.64-4.25), and the split by biologic type did not significantly improve model fit ( $P = .48$ ).

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

### Risk-mitigating behaviors may vary between patients with psoriasis receiving biologics and those receiving nonbiologic systemic therapies

To help inform our interpretation of hospitalization rates among patients with psoriasis who were receiving different types of therapy, we investigated potential differences in COVID-19 risk-mitigating behaviors. Self-reported data from 1626 individuals with psoriasis (with and without COVID-19) from 48 countries were available (see Table E3). Baseline characteristics, including demographics, psoriasis phenotype, and comorbidities, are summarized in Table IV. These were similar to characteristics in the clinician-reported registry, except for sex (a female predominance of 64% in the self-report registry). Of 96 patients (6%) who self-reported suspected or confirmed COVID-19, 25 (26%) were receiving a biologic, 13 (14%) were receiving a nonbiologic systemic agent, and 58 (60%) were receiving no treatment.

To assess baseline risk-mitigating behaviors, we interrogated self-reported data from individuals without COVID-19 infection (n = 1476). In all, 478 individuals (32%) reported receiving a biologic and 249 (17%) reported receiving a nonbiologic 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, and psoriatic arthritis). Reported rates of social isolation (shielding [ie, quarantine and distancing within the home] or self-isolation [ie, staying home and avoiding others]) were higher in those receiving biologics for psoriasis (346 of 478 [72%]) than in those receiving nonbiologic 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, rates of treatment nonadherence were slightly lower, with 17% of those receiving biologics (n = 79) and 20% of those receiving nonbiologic systemic therapies (n = 48) reporting stopping treatment during the pandemic. These independent patient-reported data suggest that there may be potential variation in COVID-19 risk-mitigating behavior between treatment groups.

## DISCUSSION

### Summary of main findings

We have presented 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 nonwhite 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 than in those not hospitalized. Our data also indicate an association between use of biologics for psoriasis and reduced risk of hospitalization compared with the risk associated with nonbiologic systemic therapies. We cannot exclude the possibility that unmeasured confounders may be driving this association: for example, our patient-reported data (1626 participants across 48 countries) suggest that COVID-19 risk-mitigating behaviors (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 data sets is warranted.

**TABLE II.** COVID-19 outcomes in clinician-reported patients with psoriasis

| Outcome   | All patients<br>(n = 374) | Patients receiving<br>biologics (n = 267) | Patients receiving<br>nonbiologic<br>systemic therapy<br>(n = 67) | Patients receiving<br>no systemic<br>agent<br>(n = 36) | Missing<br>(no.)<br>n |
|---|---------------------------|---|---|--|-----------------------|
| COVID-19 diagnosis, no. (%)                                   |                           |   |   |  | 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, no. (%)                                     |                           |   |   |  | 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, no. (%)                                      |                           |   |   |  | 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, no. (%)                               |                           |   |   |  |                       |
| 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                     |
| Noninvasive ventilation/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, no. (%)   | 20 (5.4)                  | 12 (4.5)                                  | 6 (9.2)   | 2 (5.6)  | 4                     |
| Duration of hospitalization (d), median (IQR)                 | 11 (6-20)                 | 14 (6-23)                                 | 10 (5-19)   | 10 (8-18)  | 13                    |
| Asymptomatic, no. (%)   | 12 (3.2)                  | 9 (3.4)                                   | 1 (1.5)   | 2 (5.6)  | 4                     |
| Common COVID-19 symptoms (% among symptomatic cases), no. (%) |                           |   |   |  |                       |
| 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                    |
| Diarrhea  | 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                    |
| Duration of COVID-19 symptoms, (d), median (IQR)              | 14 (7-21)                 | 14 (7-21)                                 | 14 (10-22)  | 10 (7-18)  | 18                    |

Four participants have been excluded from the treatment groups because of unknown drug (clinical trial). The category biologics includes participants reporting cotherapy with conventional systemic agents or steroids (n = 15), small-molecule inhibitor (n = 0), or both (n = 0). The category nonbiologic systemic therapy includes participants reporting use of conventional systemic agents or steroids (n = 39), small-molecule inhibitor (n = 26), or both (n = 2). Four patients with unresolved COVID-19 have been excluded from the COVID-19 outcome summaries (treated as missing). The symptom unspecified cough has been allocated to the category dry continuous cough (n = 2 patients).

### Comparison with the literature

The baseline characteristics of our international case series suggest that our findings are likely to be applicable to people with moderate-to-severe psoriasis because 90% of those reported were taking systemic therapies and there was a high prevalence of comorbidities.<sup>7,35</sup> Our study underscores older age, male sex, nonwhite 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.<sup>2,6</sup> A cohort study of 17 million adults in the United Kingdom found that death from COVID-19 was associated with comorbidities, including cardiovascular disease,

diabetes, obesity, reduced kidney function, and chronic liver disease.<sup>6</sup> Similarly, a case series of 44,672 patients with COVID-19 in China showed that cardiovascular disease, hypertension, and diabetes were risk factors for death.<sup>4</sup> There are very limited data on psoriasis, with 4 regional psoriasis case series in Northern Italy, suggesting no increased rate of hospitalization or death from COVID-19 in those receiving biologics compared with the rates among the local population.<sup>17-20</sup> Only 6 patients were hospitalized across the 4 reports, with few patients with nonsevere COVID-19 captured (n = 5<sup>17</sup>; n = 8<sup>18</sup>; n not reported<sup>19,20</sup>); hence, risk factors for adverse COVID-19 outcome could not be characterized. We addressed this through a larger collection of cases that



**TABLE III.** Multivariate logistic regression models for hospitalization due to COVID-19

| Characteristic                                   | Counts, no. hospitalized/total no. (%) | Minimally adjusted model OR (95% CI) | Fully adjusted model OR (95% CI) |
|--|--|--------------------------------------|----------------------------------|
| Treatment type                                   |  |                                      |                                  |
| Biologic   | 44/265 (16.6)                          | Ref                                  | Ref                              |
| Nonbiologic 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 y)                            | —                                      | 2.01 (1.59-2.52)                     | 1.59 (1.19-2.13)                 |
| Nonwhite 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/m <sup>2</sup> )            | —                                      | —                                    | 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 (including asthma and 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)                 |

COPD, Chronic obstructive pulmonary disease; Ref, reference (refers to the reference group in the multivariable logistic regression models).

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-center COVID-19 case series of 86 patients with IMIDs from New York (14 of whom had psoriasis) observed that use of biologics was lower among those hospitalized for COVID-19 (6 of 14 [43%]) than among those not hospitalized (50 of 72 [69%]).<sup>36</sup> Use of nonbiologic systemic agents, including the common psoriasis therapy methotrexate, was higher among hospitalized patients than among those not hospitalized.

Our data also align 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).<sup>28,29</sup> The hospitalization and case fatality rates were 31% and 3%, respectively, in IBD, and 46% and 9%, respectively, in rheumatic disease (vs 21% and 2% in our psoriasis data set). 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 among those with 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 (eg, a higher incidence of lower respiratory tract infections and/or pneumonia has been observed for infliximab compared with methotrexate).<sup>10,11</sup> 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 with placebo (OR = 1.31; 95% CI = 1.05-

1.62)<sup>37</sup>; 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).<sup>38</sup> Phase III trial data also suggest that use of psoriasis biologics (TNF, IL-17, and IL-23 inhibitors) is not associated with increases in rates of viral infections such as influenza compared with placebo,<sup>39</sup> which is consistent with the data from long-term registries<sup>10</sup> and studies of other IMIDs.<sup>40</sup>

Given the cytokine upregulation from aberrant immune activation observed in severe COVID-19, there is biologic plausibility for a protective effect of cytokine-targeted biologics on adverse outcomes, compared with the effect of broader immunosuppressants that may detrimentally suppress host antiviral immunity.<sup>41</sup> This notion is currently under evaluation in trials of repurposed IMID biologics in patients with COVID-19.<sup>42</sup> Existing reports of elevated plasma levels of TNF and IL-17 in patients manifesting severe COVID-19<sup>31</sup> also align with our observation of a lower hospitalization rate in individuals receiving TNF inhibitors or IL-17 inhibitors compared with the rate in 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 T<sub>H</sub>17 cells<sup>43</sup>) and the more established role of the IL-23/IL-17 axis in bacterial and fungal immunity (as opposed to viral defense), these observations require further study. We were unable to draw firm conclusions because 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-to-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 may instead be due to unmeasured confounders. Our patient-reported data suggest increased risk-mitigating behavior (social isolation) in

**TABLE IV.** Characteristics self-reported to the PsoProtectMe registry by individuals with psoriasis during the COVID-19 pandemic

| Characteristic   | All patients     | Patients receiving biologics | Patients receiving nonbiologic systemic therapy | Patients receiving no systemic agent | Missing (no.) |
|--|------------------|------------------------------|---|--------------------------------------|---------------|
|  | (n = 1626)       | (n = 512)                    | (n = 273)                                       | (n = 839)                            | n             |
| COVID-19 infection, no. (%)  |                  |                              |   |                                      | 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   | 1476 (90.8)      | 478 (93.4)                   | 249 (91.2)                                      | 747 (89.0)                           |               |
| Age (y), median (range)  | 48 (36-59)       | 49 (39-58)                   | 50 (38-60)                                      | 46 (33-60)                           | 0             |
| Sex, no. (%)   |                  |                              |   |                                      | 0             |
| Female   | 1041 (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, no. (%)   |                  |                              |   |                                      | 19            |
| White  | 1399 (87.1)      | 436 (85.8)                   | 231 (85.2)                                      | 730 (88.4)                           |               |
| Nonwhite   | 208 (12.9)       | 72 (14.2)                    | 40 (14.8)                                       | 96 (11.6)                            |               |
| Country of assessment, no. (%)   |                  |                              |   |                                      | 2             |
| United Kingdom   | 1191 (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, no. (%)   |                  |                              |   |                                      | 20            |
| Plaque   | 1446 (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, no. (%)   |                  |                              |   |                                      | 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 the PGA scale), no. (%)       |                  |                              |   |                                      | 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-to-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)                              |               |
| Duration of treatment of group with COVID-19, at onset (mo), median (range)    | 25.3 (6.0-51.0)  | 23.4 (9.2-49.8)              | 27.7 (2.9-51.9)                                 | —                                    | 11            |
| Duration of treatment of uninfected group, at survey date (mo), median (range) | 25.2 (9.1-60.2)  | 24.8 (9.5-52.5)              | 26.1 (7.9-74.4)                                 | —                                    | 48            |
| Treatment stopped during COVID-19, no. (%)                                     | 22 (40.7)        | 11 (35.5)                    | 11 (47.8)                                       | —                                    | 4             |
| Treatment stopped during pandemic (uninfected group), no. (%)                  | 127 (17.9)       | 79 (17.0)                    | 48 (19.8)                                       | —                                    | 21            |
| Biologic type, no. (%)   |                  |                              |   |                                      | 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 (kg/m <sup>2</sup> ), median (range)                                       | 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, no. (%)   | 478 (29.4)       | 176 (34.4)                   | 91 (33.3)                                       | 210 (25.0)                           | 0             |

(Continued)

TABLE IV. (Continued)

| Characteristic  | All patients<br>(n = 1626) | Patients receiving biologics<br>(n = 512) | Patients receiving nonbiologic systemic therapy<br>(n = 273) | Patients receiving no systemic agent<br>(n = 839) | Missing (no.)<br>n |
|---|----------------------------|---|--|---|--------------------|
| Comorbidities no. (%)                                 |                            |   |  |   |                    |
| 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, no. (%)                                    | 204 (13.9)                 | 76 (16.8)                                 | 41 (16.9)  | 87 (11.3)   | 162                |
| ARB user, no. (%)                                     | 140 (10.0)                 | 62 (14.4)                                 | 22 (9.7)   | 55 (7.4)  | 219                |
| NSAID user, no. (%)                                   | 288 (20.2)                 | 112 (25.2)                                | 39 (17.3)  | 137 (18.2)  | 202                |
| Smoking, no. (%)                                      |                            |   |  |   | 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 behaviors (uninfected group), no. (%) |                            |   |  |   |                    |
| 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 behavior                        | 42 (2.8)                   | 14 (2.9)                                  | 3 (1.2)  | 25 (3.3)  | 0                  |
| No risk-mitigating behavior                           | 11 (0.7)                   | 2 (0.4)                                   | 2 (0.8)  | 7 (0.9)   | 0                  |

ACEI, Angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; COPD, chronic obstructive pulmonary disease; NSAID, nonsteroidal anti-inflammatory drug; PGA, Physician's Global Assessment.

Two participants have been excluded from the treatment groups because of unknown drug (clinical trial). The category biologics includes participants reporting cotherapy with conventional systemic or steroids (n = 61), small-molecule inhibitor (n = 2), or both (n = 3). The category nonbiologic systemic therapy includes participants reporting use of conventional systemic or steroids (n = 229), small-molecule inhibitor (n = 39), or both (n = 6). Time receiving treatment and adherence data have been excluded for participants reporting use of multiple biologics (n = 5), multiple conventional systemics or steroids (n = 10), or multiple small-molecule inhibitors (n = 0). For participants reporting systemic treatments in more than 1 category, time receiving treatment was measured from the latest date (ie, start of cotherapy). The category obesity combines participants selecting obesity as a comorbidity with those having a BMI of 30 or higher; it may therefore miss some of the 114 participants for whom BMI is not available.

individuals receiving biologics compared with the risk in those receiving nonbiologic 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. Behavioral variation between treatment groups and the consequent impact on COVID-19 risk and/or severity warrant urgent further investigation because it is potentially relevant for public health policy.

### Strengths and limitations

Major strengths of this case series are its global reach and size. The speed with which data have 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 generalizable than those of the regional reports published to date. The key demographic associations with hospitalization for COVID-19 (sex, age, and ethnicity) in our psoriasis data set 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 behaviors during the pandemic, thus addressing for the first time a potential unmeasured confounder in clinician-reported data sets.

Information on the registries was disseminated worldwide, but the larger numbers of patients from Spain, Italy, and the United Kingdom (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 that in other global IMID registries, more severe COVID-19 cases may be overrepresented because these may have been preferentially brought to the attention of clinicians. In contrast, patients who have died or those remaining in the 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 patients with psoriasis receiving biologics versus among those receiving nonbiologic systemic therapies were consistent with our primary findings for hospitalization. Diverse COVID-19 testing practices may also have affected reporting (eg, preferential testing of severely ill and/or hospitalized patients), although we encouraged submission of suspected cases and our sensitivity analysis restricted to patients with only confirmed COVID-19 yielded results to similar those of the main analysis.

Our case series is dominated by patients with moderate-to-severe psoriasis; therefore, our findings may not be generalizable to those with milder psoriasis. The majority of clinician-reported patients were receiving biologics, which contrasts with our patient-reported data. If this represents a different propensity for clinicians to report patients receiving different types of treatment, then together with a higher likelihood of hospitalized cases being reported, this could lead to inflated effect size estimates on account of selection bias. In contrast to the limitations of clinician-reported data, a potential limitation of the self-report data set 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 owing 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 with the outcomes studies of the general population because of 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 is similar to the median lengths published for general populations. For example, the median length of hospital stay for patients with psoriasis and 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]).<sup>44</sup> The 3 most common symptoms of COVID-19 in both the Chinese cohort and our patients who were receiving psoriasis biologics were fever, cough, and fatigue.

The incidence of COVID-19 in psoriasis cannot be determined on account of the lack of denominator (source population) data and uncertainty regarding those patients with psoriasis and 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 with the risk associated with use of nonbiologic 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 characterizing the determinants of additional COVID-19 outcomes and the impact of specific treatments at higher resolution.

We are very grateful to the health care professionals who have reported cases to the PsoProtect registry and to the patients who have contributed to PsoProtectMe. We would like to acknowledge the professional and patient

organizations who supported or promoted the PsoProtect and PsoProtectMe registries (see Table E1). We are grateful for the input of John Weinman, PhD, Lars Iversen, MD, PhD, Professor Nick Reynolds, MD, FRCP, Joel Gelfand, MD MSCE, Hoseah Waweru, MD, Christine Janus, and Michael Kappelman, MD, MPH. We are grateful to Dominic Urmston, Amber Vesty, and Jade Kelly for their support with social media. We are also incredibly thankful to Engine Group UK for their generous creative input and website expertise. The following individuals are health care professionals who have reported cases to the PsoProtect registry (banner author list of PsoProtect study group collaborators): Aadarsh Shah, MRCP, Alberto Barea, MSc, Alberto Romero-Maté, MD, Alekya Singapore, MD, Alexandra Paolino, MRCP, Alice Mwale, BSc, Ana Maria Morales Callaghan, MD, Ana María Martínez de Salinas, MD, Andrew DeCrescenzo, MD, Andrew E. Pink, MRCP, PhD, Ann Jones, BSc, Ann Sergeant, MD, Annette Essex, RGN, Anthony Bewley, FRCP, Areti Makrygeorgou, MBBS, Astrid van Huizen, MD, Beatriz Pérez-Suárez, MD, PhD, Benhadou Farida, MD, PhD, Birgitta Wilson Claréus, MD, Carla Tubau Prims, MD, Carrie Davis, MD, Catherine Quinlan, MRCPI, Catriona Maybury, MRCP, PhD, Gonzalez A. Cesar, MD, Charlotte Barclay, BSc, Claudio Greco, MD, Danielle Brassard, MD, Deanna Cummings, BSc, Deepti Kolli, MD, Vincent Descamps, MD, PhD, Diana Ruiz Genao, MD, Efrossini Carras, BSc, MRCP, Elena Hawryluk, MD, PhD, Eliseo Martínez-García, MD, PhD, Elzbieta Klujso, MD, Emily Dwyer, BSc, Emmanuel Toni, BSc, Enikő Sonkoly, MD, PhD, Enrique Loayza, MD, Esteban Daudén, MD, PhD, Fernando Valenzuela, MD, Georgi Popov, MD, PhD, Georgie King, MSc, Girard Celine, MD, Gloria Aparicio, MD, Graham A. Johnston, FRCP, Gustavo Anibal Cardozo, MD, Ian Pearson, MRCP, Ignacio Yanguas, MD, Jamie Weisman, MD, Jennifer E. Carolan, MSc, Jenny Hughes, FRCP, Jose-Maria Ortiz-Salvador, MD, PhD, Jose-Manuel Carrascosa, MD, PhD, Joseph J Schwartz, MD, Karina Jackson, MSc, Kathryn G Kerisit, MD, MPH, Keith Wu, MD, Leila Asfour, MRCP, Leontien de Graaf, MD, Cécile Lesort, MD, Lieve Meuleman, MD, Liv Eidsmo, MD, PhD, Lone Skov, MD, PhD, Lorraine Gribben, BSc, Malcolm Rustin, MD, Manel Velasco, MD, Manisha Panchal, MD, Manpreet Lakhani, MRCP, Manuel D. Franco, MD, Marie-Louise Svensson, BSc, Mark Vandaele, MD, Maruska Marovt, MD, PhD, Omid Zargari, MD, Pablo De Caso, MD, Paulo Varela, MD, Peter Jenkin, MD, FAAD, Céline Phan, MD, Philip Hampton, FRCP, PhD, Portia Goldsmith, MD, FRCP, Rachel Bak, MD, Reinhart Speeckaert, MD, PhD, Ricardo Romiti, MD, PhD, Richard Woolf, MRCP, PhD, Rogelio Mercado-Seda, MD, Rohima Khatun, BSc, Romana Ceovic, MD, Rosa Taberner, MD, Russell W. Cohen, MD, FAAD, Simina Stefanescu, MD, Sarah Kirk, BSc, Saskia Reeken, BSc, Shanti Ayob, MRCP, Silvia Pérez-Barrio, MD, Stefano Piaserico, MD, PhD, Susannah Hoey, MD, Tiago Torres, MD, PhD, Toomas Talme, MD, PhD, Trupti V. Desai, MD, Adrienne J. van Geest, MD, Victoria King, BSc, Vito Di Lernia, MD, Zahira Koreja, BSc, and Vito Zeeshaan Hasab, MBBS.

**Clinical implications: We identify risk factors for COVID-19-related hospitalization in patients with psoriasis, including older age, male sex, nonwhite ethnicity, and comorbidities. Use of biologics was associated with lower hospitalization risk than were nonbiologic systemic therapies, however further study is required on account of potential selection bias and unmeasured confounding.**

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