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# Nonadherence to systemic immune-modifying therapy in people with psoriasis during the COVID-19 pandemic: findings from a global cross-sectional survey

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### **Abstract**

**Background** Nonadherence to immune-modifying therapy is a complex behaviour which, before the COVID-19 pandemic, was shown to be associated with mental health disorders in people with immune-mediated diseases. The COVID-19 pandemic has led to a rise in the global prevalence of anxiety and depression, and limited data exist on the association between mental health and nonadherence to immune-modifying therapy during the pandemic.

**Objectives** To assess the extent of and reasons underlying nonadherence to systemic immune-modifying therapy during the COVID-19 pandemic in individuals with psoriasis, and the association between mental health and nonadherence.

**Methods** Online self-report surveys (PsoProtect*Me*), including validated screens for anxiety and depression, were completed globally during the first year of the pandemic. We assessed the association between anxiety or depression and nonadherence to systemic immune-modifying therapy using binomial logistic regression, adjusting for potential cofounders (age, sex, ethnicity, comorbidity) and country of residence.

Results Of 3980 participants from 77 countries, 1611 (40.5%) were prescribed a systemic immune-modifying therapy. Of these, 408 (25.3%) reported nonadherence during the pandemic, most commonly due to concerns about their immunity. In the unadjusted model, a positive anxiety screen was associated with nonadherence to systemic immune-modifying therapy [odds ratio (OR) 1.37, 95% confidence interval (Cl) 1.07–1.76]. Specifically, anxiety was associated with nonadherence to targeted therapy (OR 1.41, 95% CI 1.01–1.96) but not standard systemic therapy (OR 1.16, 95% CI 0.81–1.67). In the adjusted model, although the directions of the effects remained, anxiety was not significantly associated with nonadherence to overall systemic (OR 1.20, 95% CI 0.92–1.56) or targeted (OR 1.33, 95% CI 0.94–1.89) immune-modifying therapy. A positive depression screen was not strongly associated with nonadherence to systemic immune-modifying therapy in the unadjusted (OR 1.22, 95% CI 0.94–1.57) or adjusted models (OR 1.14, 95% CI 0.87–1.49).

**Conclusions** These data indicate substantial nonadherence to immune-modifying therapy in people with psoriasis during the pandemic, with attenuation of the association with mental health after adjusting for confounders. Future research in larger populations should further explore pandemic-specific drivers of treatment nonadherence. Clear communication of the reassuring findings from population-based research regarding immune-modifying therapy-associated adverse COVID-19 risks to people with psoriasis is essential, to optimize adherence and disease outcomes.

### What is already known about this topic?

- Before the COVID-19 pandemic, mental health disorders including anxiety and depression were shown to be associated with nonadherence to immune-modifying therapy in individuals with immune-mediated diseases.
- The COVID-19 pandemic has led to a rise in the global prevalence of mental health disorders in the general population.
- The extent of nonadherence to immune-modifying therapy in individuals with psoriasis and its association with mental health during the COVID-19 pandemic remains poorly understood.

### What does this study add?

- One-quarter of individuals with psoriasis who completed PsoProtectMe reported nonadherence to systemic immune-modifying therapy during the pandemic, primarily due to concerns around their immunity.
- After adjusting for confounders (age, sex, ethnicity, comorbidity) and country of residence, the association between a positive screen for anxiety and nonadherence to immune-modifying therapy in individuals with psoriasis was attenuated and no longer significant.
- Future research in larger populations should further explore pandemic-specific drivers of treatment nonadherence.
- Clear communication of the reassuring findings from population-based research regarding immune-modifying therapy-associated adverse COVID-19 risks to individuals with psoriasis is essential, to optimize adherence and disease outcomes.

Treatment adherence refers to the extent to which a person's behaviour in taking medication corresponds with agreed recommendations from a healthcare provider. This is in terms of dosage, timing and frequency of drug administration, and is based on available clinical evidence demonstrating optimal outcomes with minimal side-effects.1 Nonadherence can be described as either unintentional or intentional. Unintentional nonadherence occurs when an individual wants to follow their prescribed treatment regimen but is unable to do so due to lack of capacity or specific resources (e.g. forgetfulness or cost of medications).<sup>2</sup> In contrast, intentional nonadherence occurs when an individual decides not to follow recommendations.<sup>2</sup> Intentional nonadherence is a complex behaviour influenced by several factors, including perceptual factors that influence their motivation to start and continue treatment (e.g. beliefs and preferences) and mental health.3-5 Before the COVID-19 pandemic, an association between mental health conditions such as anxiety or depression and nonadherence was found in a range of long-term conditions, 3,5 including immune-mediated inflammatory diseases such as psoriasis;6 however, it is unclear whether these associations have changed during the pandemic.

The mainstay of treatment for moderate-to-severe psoriasis is systemic immune-modifying therapy, either standard systemic or targeted biologic therapies. These agents have been the subject of considerable attention during the COVID-19 pandemic due to their mechanism of action (i.e. immune modulation) and established association with infections. 8,9 At the beginning of the COVID-19 pandemic, risk mitigation strategies for individuals receiving immune-modifying therapies focused on behaviours to limit exposure to the virus (e.g. shielding) rather than discontinuing treatment, given the importance of ensuring ongoing control of psoriasis, 10 including avoiding demand on healthcare services due to disease flares. Data from registry- and population-based COVID-19 studies<sup>9,11–16</sup> have supported this approach, with evidence suggesting that risks of adverse outcomes in this group are mainly driven by the same factors as in the general population (e.g. age, sex, ethnicity and comorbid burden).

Emerging research indicates that the COVID-19 pandemic may have negatively impacted adherence to systemic immune-modifying therapies in people with psoriasis, <sup>17–24</sup> with nonadherence ranging between 1.6%<sup>20</sup> and 68.5%<sup>21</sup> and considerable variation reported across systemic immune-modifying therapy types.<sup>21</sup> Global mental health

has also been adversely affected in the COVID-19 pandemic.<sup>25-28</sup> Understanding the extent of nonadherence to different systemic immune-modifying therapies, and the potential factors contributing to it, is the first necessary step in helping patients to gain more benefit from their medication(s). Furthermore, the COVID-19 pandemic provides an important opportunity to better understand the potential complex relationship between mental health and treatment nonadherence.

To address this, we analysed self-report data from the PsoProtect*Me* international survey, which explores the global impact of the COVID-19 pandemic on individuals with psoriasis and includes validated screens for anxiety (Generalized Anxiety Disorder-2<sup>29</sup>) and depression (Patient Health Questionnaire-2<sup>30</sup>). Our specific objectives were:

1To characterize the extent of, and reasons underlying, self-reported nonadherence to systemic immune-modifying therapy in people with psoriasis during the COVID-19 pandemic.

2To assess whether an association exists between a positive screen for anxiety or depression and self-reported non-adherence to systemic immune-modifying therapy in people with psoriasis during the COVID-19 pandemic.

### Materials and methods

## Design, study participants and recruitment strategy

A cross-sectional survey design was employed. The inclusion criterion was any individual reporting a clinician-confirmed diagnosis of psoriasis. There was no age limit (questions could be completed by the individual or on behalf of someone else). Following its launch on 4 May 2020, PsoProtect*Me* (https://psoprotectme.org/; available in nine different languages) was promoted globally via social media, patient organizations and clinical networks (REC reference 20/YH/0135). Data were collected and managed using REDCap (Research Electronic Data Capture) tools licensed to King's College London Division of Health and Social Care Research.<sup>31</sup>

#### Materials

We defined a minimum sufficient core set of variables within PsoProtect Me with our study group of clinicians, researchers and patient representatives. 10,32 Treatment adherence was determined by a question which asked whether the participant had stopped or delayed their systemic immune-modifying medication during the COVID-19 pandemic, and the underlying reason(s) for doing so (see https://psoprotectme. org/ for full questionnaire). All immune-modifying treatments are listed in Table S1; see Supporting Information. If a respondent was on co-therapy (i.e. prescribed more than one standard systemic and/or targeted therapy), their adherence was assessed for each medication separately. If a respondent who was receiving co-therapy was nonadherent to one or more of their medications, they were classified as nonadherent overall. We used the Generalized Anxiety Disorder 2-item (GAD-2)<sup>29</sup> and the Patient Health Questionnaire-2 (PHQ-2)<sup>30</sup> to screen for anxiety and depression, respectively; scores of > 3 were considered positive.

### Statistical analysis

Data were analysed using SPSS (version 27.0 for Windows). Due to the continuously evolving nature of the COVID-19 pandemic, we specifically assessed the extent, reasons for, and potential determinants of systemic immune-modifying therapy nonadherence during the first year of the pandemic (to 16 March 2021), when most global populations were being affected by some form of containment measure.

We used descriptive statistics to summarize the findings; we reported continuous variables using medians and interquartile ranges (IQRs), and categorical/dichotomous variables as numbers and percentages. We used binomial logistic regression to assess associations between positive screens for anxiety or depression and nonadherence to systemic immune-modifying therapy. These models were then adjusted for potential confounders (age, sex, ethnicity and medical comorbidity), as well as country of residence. All underlying assumptions for all statistical tests were met, unless otherwise stated. A P-value of  $\leq$  0.05 was used to demonstrate statistical significance.

### Results

# Clinical and sociodemographic characteristics of the study population

A total of 3980 individuals with psoriasis completed PsoProtectMe between 4 May 2020 and 16 March 2021, 1611 (40.5%) of whom were receiving systemic immune-modifying therapy. Of those receiving a systemic immune-modifying therapy, 619 (38.4%) were receiving a standard systemic therapy (n=121 as co-therapy) and 1113 (69.1%) were receiving a targeted therapy. The median age of respondents who were receiving systemic immunemodifying therapy was 49.0 years (IQR 20.0), with the majority being female (n=962, 59.7%), of white ethnicity (n=1268, 78.7%) and residing in the UK (n=960, 59.6%). Clinical and sociodemographic characteristics of those receiving systemic immune-modifying therapy are summarized in Table 1. Table S1 provides a breakdown of the standard systemic and targeted immune-modifying therapies used by respondents.

Of 1611 individuals who reported receiving systemic immune-modifying therapy for psoriasis, 1573 (97.6%) completed the anxiety (GAD-2) and depression (PHQ-2) screens. Of these, 405 (25.7%) and 379 (24.1%) respondents had a positive screen for anxiety and depression, respectively.

# Extent of, and reasons underlying, nonadherence to systemic immune-modifying therapy during the COVID-19 pandemic

A total of 408 (25.3%) respondents reported nonadherence to their systemic immune-modifying therapy. Specifically, 191 (30.9%) and 235 (21.1%) respondents reported nonadherence to their standard systemic and targeted immune-modifying therapy, respectively (Table 1).

Reasons for nonadherence to systemic immune-modifying therapy are presented in Table 2. Concerns about their own immunity ('I didn't want it to affect my immunity') was the

**Table 1** Clinical and sociodemographic characteristics of PsoProtectMe respondents who were receiving systemic immune-modifying therapy (total N=1611), including those receiving standard systemic (n=619) and targeted therapy (n=1113)

Clinical and sociodemographic characteristics	Total systemic immune- modifying therapy	Standard systemic therapy	Targeted therapy
Median age, years (IQR)	49.0 (20.0)	48.0 (19.0)	49.0 (19.0)
Sex, N(%)			
Male	645 (40.0%)	219 (35.4%)	465 (41.8%)
Female	962 (59.7%)	399 (64.4%)	644 (57.9%)
Prefer not to say	4 (0.2%)	1 (0.1%)	4 (0.3%)
Ethnicity, N (%)	. (0.2.0)	(01110)	. (,
White (e.g. European)	1268 (78.7%)	464 (74.9%)	889 (79.9%)
Hispanic or Latino	106 (6.6%)	59 (9.5%)	54 (4.8%)
South Asian (e.g. Indian)	66 (4.1%)	32 (5.2%)	42 (3.7%)
Japanese	60 (3.7%)	17 (2.7%)	51 (4.6%)
Prefer not to say	14 (0.9%)	8 (1.3%)	7 (0.6%)
Unknown	5 (0.3%)	4 (0.6%)	2 (0.2%)
Other <sup>a</sup>	92 (5.7%)	35 (5.7%)	68 (6.1%)
Country of residence, N(%)	32 (3.7 70)	33 (3.7 70)	00 (0.1 70)
UK	960 (59.6%)	370 (59.8%)	651 (58.5%)
Denmark	28 (1.8%)	9 (1.5%)	24 (2.2%)
Spain	27 (1.7%)	11 (1.8%)	18 (1.6%)
Portugal	73 (4.5%)	27 (4.4%)	48 (4.3%)
Japan	62 (3.8%)	16 (2.6%)	54 (4.9%)
Philippines	20 (1.2%)	18 (2.9%)	3 (0.3%)
Australia	23 (1.4%)	5 (0.8%)	19 (1.7%)
Canada	24 (1.5%)	10 (1.6%)	16 (1.4%)
USA	155 (9.6%)	24 (3.9%)	150 (13.5%)
Chile	50 (3.1%)	40 (6.5%)	11 (1.0%)
Argentina	27 (1.7%)	16 (2.6%)	16 (1.4%)
Other <sup>a</sup>	162 (10.1%)	73 (11.8%)	103 (9.3%)
BMI, kg m <sup>-2</sup> , median (IQR)	27.3 (8.39)	27.2 (8.5)	27.4 (8.4)
Age of psoriasis onset, years, median (IQR) <sup>b</sup> Psoriasis type <sup>c</sup> , N(%)	20.0 (17.0)	20.0 (19.0)	20.0 (17.0)
Plague	1371 (85.1%)	497 (80.3%)	971 (87.2%)
Guttate	310 (19.2%)	138 (22.3%)	195 (17.5%)
Pustular	123 (7.6%)	62 (10.0%)	73 (6.6%)
Erythroderma	47 (2.9%)	16 (2.6%)	35 (3.1%)
Not sure	66 (4.1%)	34 (5.5%)	36 (3.2%)
Other	58 (3.6%)	27 (4.4%)	36 (3.2%)
Comorbidity <sup>d</sup> , N (%)	00 (0.070)	27 (4.470)	00 (0.2 70)
Yes	914 (56.7%)	445 (71.9%)	801 (72.0%)
No	876 (54.4%)	194 (31.3%)	350 (31.4%)
Prior COVID-19 diagnosis (as confirmed on a test), N (%)	148 (9.2%)	26 (4.2%)	36 (3.2%)
Nonadherence <sup>e</sup> , N (%)	408 (25.3%)	191 (30.9%)	235 (21.1%)
Positive GAD-2 screen, N (%)	406 (25.7%)	191 (30.9%)	252 (22.6%)
Positive PHQ-2 screen, N (%)	379 (24.1%)	178 (28.8%)	231 (20.8%)
FUSITIVE FITQ-Z SCIEBII, IV (70)	3/3 (24.170)	1/0 (20.070)	231 (20.6%)

 $^{a}$ See Table S2 in Supporting Information for 'other' responses.  $^{b}$ Missing responses for age of psoriasis onset: total immune-modifying therapy n=20; standard systemic therapy n=13; targeted therapy n=7.  $^{c}$ Respondents could select more than one psoriasis type.  $^{d}$ Respondents could select more than one comorbidity.  $^{e}$ Stopped or delayed their standard systemic and/or targeted therapy during the COVID-19 pandemic.BMI, body mass index; GAD-2, Generalized Anxiety Disorder 2-item; IQR, interquartile range; PHQ-2, Patient Health Questionnaire-2.

Table 2 Reasons for nonadherence to systemic immune-modifying therapy (n=388), including standard systemic (n=186) and targeted (n=220) therapy

Reason for nonadherence <sup>a</sup>	Total systemic immune- modifying therapy, N (%) <sup>b</sup>	Standard systemic therapy, <i>N</i> (%)°	Targeted therapy, N (%) <sup>d</sup>
I didn't want it to affect my immunity	187 (48.2%)	87 (46.8%)	100 (45.5%)
My doctor told me to stop it	119 (30.7%)	57 (30.6%)	62 (28.2%)
I did not have a supply	59 (15.2%)	27 (14.5%)	32 (14.5%)
I was worried about complications	74 (19.1%)	29 (15.6%)	45 (20.5%)
I wanted to focus on COVID	20 (5.2%)	7 (3.8%)	13 (5.9%)
I forgot to take it because I was worried	11 (2.8%)	7 (3.8%)	4 (1.8%)
I forgot to take it because my routine has changed in the pandemic	19 (4.9%)	10 (5.4%)	9 (4.1%)
It was not effective for my psoriasis	37 (9.5%)	20 (10.7%)	17 (7.7%)
Othere	87 (22.4%)	34 (18.3%)	53 (24.1%)

<sup>&</sup>lt;sup>a</sup>Respondents could select more than one reason for nonadherence. <sup>b</sup>Missing responses n=20. <sup>c</sup>Missing responses n=5. <sup>d</sup>Missing responses n=15. <sup>e</sup>See Table S3 in Supporting Information for 'other' reasons for nonadherence.

most common reason for discontinuation (48.2%), followed by advice from their doctor ['My doctor told me to stop it' (30.7%)], concern about complications (19.1%) and having no medicine supply (15.2%).

# Relationship between nonadherence to systemic immune-modifying therapy and anxiety or depression

### Anxiety

A total of 405 (25.7%) respondents had a positive GAD-2 anxiety screen; 30.1% of those with a positive anxiety screen were nonadherent to systemic immune-modifying therapy, compared with 23.1% of those with a negative screen (data not shown). A positive screen for anxiety was associated with nonadherence to systemic immune-modifying therapy in the unadjusted model [odds ratio (OR) 1.37, 95% confidence interval (CI) 1.07–1.76]. In particular, there was a significant association between anxiety and nonadherence to targeted therapy (OR 1.41, 95% CI 1.01–1.96). Conversely, anxiety was not associated with nonadherence to standard systemic therapy (OR 1.16, 95% CI 0.81–1.67).

After adjustment for potential confounders (age, sex, ethnicity, medical comorbidity) and country of residence, although the direction of the effect remained, the associations were attenuated and anxiety was no longer significantly associated with nonadherence to overall systemic (OR 1.20, 95% CI 0.92–1.56) or targeted (OR 1.33, 95% CI 0.94–1.89) immune-modifying therapy. After removing respondents whose reason for nonadherence was solely their doctor's advice or having no supply, a positive screen for anxiety was also associated with nonadherence to systemic immune-modifying therapy in the unadjusted model (OR 1.34, 95% CI 1.02–1.76), and this association was similarly attenuated and no longer significant after adjustment for confounders (OR 1.20, 95% CI 0.89–1.60).

#### Depression

A total of 379 (24.1%) respondents had a positive PHQ-2 depression screen; 28.5% of those with a positive depression screen were nonadherent to systemic immune-modifying therapy, compared with 23.5% of those with a negative screen (data not shown). A positive screen for depression was not strongly associated with nonadherence to systemic immune-modifying therapy in unadjusted (OR 1.22, 95% CI 0.94-1.57) or adjusted (OR 1.14, 95% CI 0.87-1.49) logistic regression models. There was also no association between depression and either standard systemic (unadjusted OR 1.07, 95% CI 0.73-1.56; adjusted OR 0.92, 95% CI 0.61-137) or targeted (unadjusted OR 1.18, 95% CI 0.83-1.67; adjusted OR 1.20, 95% CI 0.84-1.73) therapy. After removing respondents whose reason for nonadherence was solely their doctor's advice or having no supply, there was similarly no association between depression and nonadherence to systemic immune-modifying therapy (unadjusted OR 1.12, 95% CI 0.84-1.50; adjusted OR 1.03, 95% CI 0.76-1.40).

### **Discussion**

The extent of nonadherence to systemic immune-modifying therapy within our global sample of individuals with psoriasis

during the first year of the COVID-19 pandemic is substantial (25.3%). Furthermore, these data indicate that although a positive screen for anxiety was associated with nonadherence in crude analyses, the association was attenuated after adjustment for confounders.

The proportion of individuals with psoriasis reporting nonadherence to systemic immune-modifying therapy is higher than indicated by some studies conducted before the pandemic.<sup>33,34</sup> For example, in studies by Chan et al.<sup>33</sup> and Thorneloe et al., 34 14.2% and 16.4% of study participants were nonadherent, respectively. Immediately following the worldwide spread of COVID-19, concern emerged regarding the safety of immune-modifying medications, specifically in relation to potential increased susceptibility to and/or severity of COVID-19. Biologic drugs targeting tumour necrosis factors interleukin (IL)-12/23, IL-23 and IL-17 can increase individuals' risk of contracting common and opportunistic infections.8,9 However, importantly, there is now a growing reassuring evidence base supporting the continuation of systemic immune-modifying therapies during the pandemic. Registry data suggest that biologics do not increase susceptibility to and/or severity of COVID-19.8,12,20,23,24,35-38 For example, our registry-based studies<sup>12,13</sup> and others<sup>11,14,15</sup> indicated that biologic use was associated with lower risk of COVID-19-related hospitalization compared with nonbiologic systemic therapies, albeit with potentially confounding shielding behaviour differences across treatment groups. 10 Larger-scale population-based research suggests no differences in COVID-19-related death in adults prescribed targeted immune-modifying therapy compared with those on standard systemic therapy. 16 These data have helped to inform international clinical guidance supporting treatment adherence during the pandemic.11

Our findings (both unadjusted and adjusted logistic regression models) indicate that depression was not significantly associated with nonadherence to systemic immune-modifying therapy during the pandemic. In contrast, prior research conducted before the pandemic suggested an association between depression and treatment nonadherence across a range of chronic conditions, 3,5 including immune-mediated inflammatory diseases.<sup>6</sup> Pre-pandemic research in psoriasis also indicated that medication nonadherence was linked to feeling anxious about potential drug adverse effects.<sup>39</sup> Indeed, in our unadjusted logistic regression model, we identified an association between anxiety and nonadherence to systemic immune-modifying therapy, more specifically targeted therapy. As targeted therapies are a newer treatment compared with standard systemic therapies, 40 patients may be more concerned about the potential adverse effects of this therapy both during and beyond the COVID-19 pandemic. Because good clinician communication is positively correlated with patient treatment adherence,41 it is important for clinicians to clearly communicate the findings from population-based research regarding immune-modifying therapy-associated risks to patients, both during and beyond the COVID-19 pandemic.

However, after adjustment for potential confounders, while the direction of the effect remained, the association between anxiety and nonadherence to targeted immune-modifying therapy was attenuated and no longer significant, although wide confidence intervals reflect a lack of precision of the estimate, and replication in larger

populations would be of value. The COVID-19 pandemic is a unique period, with major impacts on global mental health in the general population. There may be different drivers of treatment nonadherence during this period compared with pre-pandemic, such as concerns surrounding own immunity, as suggested in our study and others. Necessary As the COVID-19 pandemic evolves, it is important to understand and address pandemic-specific drivers of treatment nonadherence in psoriasis, to improve medication behaviours and subsequent patient outcomes.

A strength of our study is that we have expanded a limited evidence base on the association between immune-modifying treatment nonadherence and mental health during the COVID-19 pandemic in individuals with psoriasis using our global dataset. However, this study has several limitations; for example, the cross-sectional design precludes any inferences about causality or directionality of associations. The statistical tests employed may have been underpowered, increasing the probability of type II errors, as reflected by the width of the confidence intervals reducing the certainty of the estimates, and do not take into account the duration of nonadherence. Self-report assessments have been shown to underestimate true levels of medication nonadherence<sup>42</sup> due to reasons such as social desirability bias. Individuals nonadherent to immune-modifying treatment or with low computer literacy may have been disinclined to participate in this online study, potentially introducing ascertainment bias and under-estimating some of our findings. Our study population included self-selecting responders to PsoProtectMe and was dominated by females of white ethnicity residing in the UK, therefore limiting the generalizability of our results. To validate self-reported sociodemographic and clinical characteristics, future research should consider linkage to registry and healthcare records.

In conclusion, we have identified a substantial prevalence of nonadherence to immune-modifying treatment (roughly 25%) during the COVID-19 pandemic in our international sample of individuals with psoriasis, primarily due to concerns surrounding respondents' immunity. As global mental health has been adversely affected in the pandemic, <sup>25–28</sup> our finding that depression and anxiety were not strongly related to treatment nonadherence is reassuring. Future research should further explore pandemic-specific drivers of treatment nonadherence in larger populations. Communication of the reassuring findings from population-based research regarding immune-modifying therapy-associated adverse COVID-19 risks to individuals with psoriasis is essential, to optimize adherence and disease outcomes.

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### Conflict of interests

J.W. has presented talks for Abbott, AbbVie, Bayer, Boehringer Ingelheim, Chiesi, Merck and Roche. K.J.M. reports personal fees from LEO Pharma and Novartis, outside the submitted work. H.M. reports grants from AbbVie, Almirall, Celgene, Dermal Laboratories, Eli Lilly, Janssen, LEO Pharma, T & R Derma and UCB, outside the submitted work. D.U. reports grants from AbbVie, Almirall, Amgen, Celgene, Dermal Laboratories, Eli Lilly, Janssen, LEO Pharma, T & R Derma and UCB, outside the submitted work. L.M. reports personal fees from AbbVie, Celgene, Janssen, LEO Pharma, Novartis and UCB, outside the submitted work. Additional disclosures from L.M. include Almirall, BMS and Lilly. H.B. reports personal fees from AbbVie, Almirall, Biocad, Boehringer-Ingelheim, Janssen, Kyowa Kirin, LEO Pharma, Novartis, Pfizer and UCB, outside the submitted work. F.C. reports consultancy fees from AnaptysBio, grants from Boehringer Ingelheim, outside the submitted work. C.D.I.C. reports personal fees from Boehringer Ingelheim and UCB Pharma; grants from Janssen, Pfizer, Sandoz, Sanofi; grants and personal fees from AbbVie, Novartis, outside the submitted work. P.D.M. reports grants and personal fees from UCB; personal fees from Janssen and Novartis, outside the submitted work. P.G. reports personal fees from AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pierre Fabre, Sandoz and UCB, outside the submitted work. D.J. reports personal fees and nonfinancial support from AbbVie, Celgene, Janssen-Cilag, Lilly, LEO Pharma, MEDAC and Novartis; and personal fees from Amgen, outside the submitted work. L.P. reports grants and personal fees from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Janssen, Lilly, Novartis and UCB; and personal fees from Bristol Myers Squibb, Fresenius-Kabi, Mylan, Pfizer, Samsung-Bioepis, Sandoz, Sanofi, outside the submitted work. P.S. has done consultancies in the past for Sanofi 111017 and AbbVie 041217 (unpaid); has received departmental independent research grants for TREAT NL registry from pharma companies since December 2019; 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 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. T.T. reports grants and personal fees from AbbVie, Almirall, Amgen, Arena Pharmaceuticals, Biocad, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, LEO Pharma, MSD, Novartis, Pfizer, Samsung-Bioepis and Sandoz, during the conduct of the study. R.B.W. reports grants from AbbVie, Almirall, Amgen, Celgene, Janssen, LEO, Lilly, Medac, Novartis, Pfizer and UCB. R.B.W. also reports consultancy fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, DiCE, GSK, Janssen, LEO, Lilly, Medac, Novartis, Pfizer, Sanofi, Sun Pharma, UCB and UNION. H.W. is on the Board of the International Federation of Psoriasis Associations who have received grants from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Sun Pharma and UCB, outside the submitted work. J.B.G. reports personal fees from AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi and UCB, outside the submitted work, C.E.M.G. reports grants and personal fees from AbbVie, Janssen, Lilly and Novartis and UCB Pharma; and grants from Almirall, Amgen, BMS, LEO and Pfizer, outside the submitted work. J.N.B. reports grants and personal fees from AbbVie, J&J, Lilly and Novartis during the conduct of the study. J.N.B. has attended advisory boards, and/or received consultancy fees, and/or spoken at sponsored symposia, and/or received grant funding from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Meyers Squibb, Celgene, Janssen, LEO Pharma, Lilly, Novartis, Pfizer, Samsung, Sun Pharma and UCB. C.H.S. reports grants from AbbVie, Novartis, Pfizer and Sanofi; and through consortia with multiple academic partners (psort.org.uk, BIOMAP-IMI.eu), outside the submitted work. S.K.M. reports departmental income from AbbVie, Almirall, Eli Lilly, Janssen-Cilag, Novartis, Sanofi and UCB, outside the submitted work.

### Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

### **Ethics statement**

REC reference 20/YH/0135.

### **Supporting Information**

Additional Supporting Information may be found in the online version of this article at the publisher's website.

### References

- 1 World Health Organization. Adherence to long-term therapies: evidence for action/[edited by Eduardo Sabaté] [Internet]. 2003. [cited May 4 May 2022]. Available from: https://apps.who.int/iris/handle/10665/42682.
- 2 Horne R, Weinman J, Barber N et al. Concordance, Adherence and Compliance in Medicine Taking. London: National Co-ordinating Centre for NHS Service Delivery and Organisation, 2005.
- 3 DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med* 2000: **160**:2101–7.
- 4 Thunander Sundbom L, Bingefors K. The influence of symptoms of anxiety and depression on medication nonadherence and its causes: a population based survey of prescription drug users in Sweden. *Patient Prefer Adherence* 2013; **7**:805.
- 5 Grenard JL, Munjas BA, Adams JL et al. Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis. J Gen Intern Med 2011; 26:1175–82.
- 6 Vangeli E, Bakhshi S, Baker A et al. A systematic review of factors associated with non-adherence to treatment for immune-mediated inflammatory diseases. Adv Ther 2015; 32:983–1028.
- 7 Raharja A, Mahil SK, Barker JN. Psoriasis: a brief overview. Clin Med 2021; 21:170.
- 8 Kamiya K, Komine M, Ohtsuki M. Biologics for psoriasis during the COVID-19 pandemic. *J Clin Med* 2021; **10**:1390.
- 9 Dávila-Seijo P, Dauden E, Descalzo MA et al. Infections in moderate to severe psoriasis patients treated with biological drugs compared to classic systemic drugs: findings from the BIOBADADERM Registry. J Invest Dermatol 2017; 137:313–21.
- 10 Mahil SK, Yates M, Langan SM et al.; for PsoProtect, CORE-UK study groups. Risk-mitigating behaviours in people with inflammatory skin and joint disease during the COVID-19 pandemic differ by treatment type: a cross-sectional patient survey. Br J Dermatol 2021; 185:80–90. https://doi.org/10.1111/bjd.19755.
- 11 Gelfand JM, Armstrong AW, Bell S et al. National Psoriasis Foundation COVID-19 Task Force guidance for management of psoriatic disease during the pandemic: Version 2 – Advances in psoriatic disease management, COVID-19 vaccines, and COVID-19 treatments. J Am Acad Dermatol 2021; 84:1254–68.
- 12 Mahil SK, Dand N, Mason KJ *et al.* Factors associated with adverse COVID-19 outcomes in patients with psoriasis insights from a global registry-based study. *J Allergy Clin Immunol* 2021; **147**:60–71.
- 13 Izadi Z, Brenner EJ, Mahil SK et al. Association between tumor necrosis factor inhibitors and the risk of hospitalization or death among patients with immune-mediated inflammatory disease and COVID-19. JAMA Netw Open 2021; 4:e2129639.
- 14 Strangfeld A, Schäfer M, Gianfrancesco MA et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis 2021; 80:930–42.
- 15 Sperger J, Shah KS, Lu M et al. Development and validation of multivariable prediction models for adverse COVID-19 outcomes in patients with IBD. BMJ Open 2021; 11:e049740.
- 16 MacKenna B, Kennedy NA, Mehrkar A et al. Risk of severe COVID-19 outcomes associated with immune-mediated inflammatory diseases and immune-modifying therapies: a nationwide cohort study in the OpenSAFELY platform. Lancet Rheumatol 2022; 4:e490–506.

- 17 Kara Polat A, Oguz Topal I, Karadag AS et al. The impact of COVID-19 in patients with psoriasis: a multicenter study in Istanbul. *Dermatol Ther* 2021; 34:e14691.
- 18 Rob F, Hugo J, Tivadar S et al. Compliance, safety concerns and anxiety in patients treated with biologics for psoriasis during the COVID-19 pandemic national lockdown: a multicenter study in the Czech Republic. J Eur Acad Dermatol Venereol 2020; 34:e682–4.
- 19 Vakirlis E, Bakirtzi K, Papadimitriou I et al. Treatment adherence in psoriatic patients during COVID-19 pandemic: real-world data from a tertiary hospital in Greece. J Eur Acad Dermatol Venereol 2020; 34:e673–5.
- 20 Camela E, Fabbrocini G, Cinelli E et al. Biologic therapies, psoriasis, and COVID-19: our experience at the Psoriasis Unit of the University of Naples Federico II. Dermatology 2021; 237:13–14.
- 21 Wang Q, Luo Y, Lv C et al. Nonadherence to treatment and patient-reported outcomes of psoriasis during the COVID-19 epidemic: a web-based survey. Patient Prefer Adherence 2020; 14:1403.
- 22 Oguz Topal I, Kara Polat A, Zindancı İ et al. Adherence to systemic therapy in patients with psoriasis during the COVID-19 pandemic: a multicenter study. J Cosmet Dermatol 2022; 21:39–47.
- 23 Kartal SP, Çelik G, Yılmaz O et al. The impact of COVID-19 pandemic on psoriasis patients, and their immunosuppressive treatment: a cross-sectional multicenter study from Turkey. J Dermatolog Treat 2022; 33:2137–44. https://doi.org/10.1080/09546634.2021.1927947.
- 24 Yalici-Armagan B, Tabak GH, Dogan-Gunaydin S et al. Treatment of psoriasis with biologics in the early COVID-19 pandemic: a study examining patient attitudes toward the treatment and disease course. J Cosmet Dermatol 2021; 20:3098–102.
- 25 Xiong J, Lipsitz O, Nasri F et al. Impact of COVID-19 pandemic on mental health in the general population: a systematic review. J Affect Disord 2020; 277:55–64.
- 26 Salari N, Hosseinian-Far A, Jalali R *et al.* Prevalence of stress, anxiety, depression among the general population during the COVID-19 pandemic: a systematic review and meta-analysis. *Global Health* 2020; **16**:57. https://doi.org/10.1186/s12992-020-00589-w.
- 27 Pashazadeh Kan F, Raoofi S, Rafiei S et al. A systematic review of the prevalence of anxiety among the general population during the COVID-19 pandemic. J Affect Disord 2021; 293:391–8.
- 28 Santomauro DF, Mantilla Herrera AM, Shadid J *et al.* Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. *Lancet* 2021; **398**:1700–12.
- 29 Kroenke K, Spitzer RL, Williams JBW et al. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Ann Intern Med 2007; 146:317–25.

- 30 Kroenke K, Spitzer RL, Williams JBW. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care* 2003: 41:1284–92.
- 31 Harris PA, Taylor R, Thielke R *et al.* Research electronic data capture (REDCap) a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009; **42**:377–81.
- 32 Mahil SK, Yates M, Yiu ZZN *et al.* Describing the burden of the COVID-19 pandemic in people with psoriasis: findings from a global cross-sectional study. *J Eur Acad Dermatol Venereol* 2021; **35**:e636–40.
- 33 Chan SA, Hussain F, Lawson LG, Ormerod AD. Factors affecting adherence to treatment of psoriasis: comparing biologic therapy to other modalities. *J Dermatolog Treat* 2013; **24**:64–9. https://doi.org/10.3109/09546634.2011.607425.
- 34 Thorneloe RJ, Griffiths CEM, Emsley R *et al.* Intentional and unintentional medication non-adherence in psoriasis: the role of patients' medication beliefs and habit strength. *J Invest Dermatol* 2018; **138**:785–94.
- 35 Amerio P, Prignano F, Giuliani F, Gualdi G. COVID-19 and psoriasis: should we fear for patients treated with biologics? *Dermatol Ther* 2020; **33**:e13434.
- 36 Akiyama S, Hamdeh S, Micic D, Sakuraba A. Prevalence and clinical outcomes of COVID-19 in patients with autoimmune diseases: a systematic review and meta-analysis. *Ann Rheum Dis* 2021; **80**:384–91.
- 37 Burlando M, Carmisciano L, Cozzani E, Parodi A. A survey of psoriasis patients on biologics during COVID-19: a single centre experience. *J Dermatolog Treat* 2022; 33:596. https://doi.org/ 10.1080/09546634.2020.1770165.
- 38 Pahalyants V, Murphy WS, Klebanov N et al. Immunosuppressive biologics did not increase the risk of COVID-19 or subsequent mortality: a retrospective matched cohort study from Massachusetts. J Am Acad Dermatol 2022; 86:252–5.
- 39 Thorneloe RJ, Bundy C, Griffiths CEM *et al.* Nonadherence to psoriasis medication as an outcome of limited coping resources and conflicting goals: findings from a qualitative interview study with people with psoriasis. *Br J Dermatol* 2017; **176**:667–76.
- 40 Honma M, Hayashi K. Psoriasis: recent progress in molecular-targeted therapies. *J Dermatol* 2021; **48**:761–77.
- 41 Haskard Zolnierek KB, Dimatteo MR. Physician communication and patient adherence to treatment: a meta-analysis. *Med Care* 2009; **47**:826.
- 42 Stirratt MJ, Dunbar-Jacob J, Crane HM *et al.* Self-report measures of medication adherence behavior: recommendations on optimal use. *Transl Behav Med* 2015; **5**:470–82.