Describing the burden of the COVID-19 pandemic in people with psoriasis: findings from a global cross-sectional study

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3

Indirect excess morbidity in the COVID-19 pandemic may arise from public health risk-mitigation efforts such as stay-at-home orders and re-purposing of healthcare services¹. Increased mental health disorders and shortfalls in the care of long-term conditions are described^{2,3}. We used global self-reported cross-sectional data to characterise the factors associated with worsening psoriasis in the pandemic, focusing on the impact of anxiety and depression.

Data from a cross-sectional survey (PsoProtect Me^4) were extracted on 15th January 2021. After excluding participants self-reporting COVID-19, the association between mental health and worsening psoriasis was assessed using a fully adjusted logistic regression model including covariates selected *a priori* as potentially influential on psoriasis severity and anxiety/depression. Participants scoring ≥ 3 in GAD-2 or PHQ-2 defined a positive mental health screen⁵.

4,043 people with psoriasis from 86 countries were included (Table 1). 1,728 (42.7%) reported worsening psoriasis in the pandemic. A greater proportion of those reporting worsening psoriasis had a positive mental health screen (814, 47.1%) compared to those without worsening psoriasis (562/1954, 28.8%). A greater proportion of females reported worsening psoriasis (1322/2684, 49.3%) compared with males (406/1354, 30.0%).

A fully adjusted regression model for worsening psoriasis estimated an odds ratio (OR) 2.01 (95%CI 1.72-2.34) for those with a positive screen for anxiety or depression, compared to those without a positive screen (Figure 1). Associations were also observed for female gender (OR 1.82, 95%CI 1.56-2.13); obesity (OR 1.22, 95% CI 1.09-1.36) and shielding (OR 1.18, 95%CI 1.03-1.35).

There were inverse associations with systemic therapy use (standard systemic OR 0.69 [95%CI 0.56-0.86] and targeted therapy OR 0.49 [95%CI 0.38-0.64]). Of 1,541 (38.1%) participants receiving systemic therapies for psoriasis, 284 (18.5%) reported non-adherence during the pandemic (Table 1). The commonest reason was concern regarding complications related to COVID-19 (n=217). Non-adherence was associated with worsening psoriasis (OR 2.90, 95%CI 2.31-3.63). A positive mental health screen was more common in those reporting non-adherence compared to those who were adherent (42.8% vs 32.4%).

These data indicate a burden due to the COVID-19 pandemic in people with psoriasis; worsening psoriasis is common and is associated with poor mental health. We find that in the subset on systemic therapy, non-adherence is associated with worsening disease and is driven by concerns about immunosuppressant-related risks of COVID-19. This is an important observation since current guidelines (informed by reassuring data on drug-related risks of severe COVID-19⁶) recommend continuing immunosuppression in people without COVID-19 to maintain disease control⁷.

Our findings parallel data from the general population indicating an increased mental health burden during the pandemic, particularly in women⁸. People with psoriasis - especially those with severe psoriasis, and women – have a high prevalence of anxiety and depression, and may thus be particularly vulnerable to the adverse impact of the pandemic on mental health⁹. Whilst men are known to be at greater risk of severe outcomes from COVID-19, our data suggest that women may be more susceptible to indirect excess morbidity – poor mental health and worsening skin disease – than men.

The generalizability of results is limited given the self-selecting bias of our study population towards UK white women. Individuals non-adherent to treatment, with low

computer literacy or less anxiety may be disinclined to participate, which may introduce ascertainment bias.

Our data underscore the importance of holistic models of care and indicate a need to provide access to psychological support. In those with worsening psoriasis, possible non-adherence should be explored. Evidence-based communication around medication-related COVID-19 risks and behavioural approaches for supporting adherence may help address fears, anxieties and confusion¹⁰. Attention given now to address this may mitigate a long-lasting detrimental impact of the pandemic on health outcomes in people with psoriasis.

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Data availability statement

The pre-print for this manuscript has been archived in the MedRxiv server: https://www.medrxiv.org/content/10.1101/2021.05.04.21256507v1

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References

- 1. Zylke, J. W. & Bauchner, H. Mortality and Morbidity: The Measure of a Pandemic. *JAMA* **324**, 458–459 (2020).
- 2. Pfefferbaum, B. & North, C. S. Mental Health and the Covid-19 Pandemic. N. Engl. J. Med. 383, 510–512 (2020).
- Wright, A., Salazar, A., Mirica, M., Volk, L. A. & Schiff, G. D. The Invisible Epidemic: Neglected Chronic Disease Management During COVID-19. *J. Gen. Intern. Med.* 35, 2816–2817 (2020).
- 4. Mahil, S. K. *et al.* 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.* (2020) doi:10.1111/bjd.19755.
- Kroenke, K., Spitzer, R. L., Williams, J. B. W. & Löwe, B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. *Psychosomatics* 50, 613–621 (2009).
- Mahil, S. K. et al. Factors associated with adverse COVID-19 outcomes in patients with psoriasis-insights from a global registry-based study. J. Allergy Clin. Immunol. 147, 60–71 (2021).
- Gelfand, J. M. et al. National Psoriasis Foundation COVID-19 Task Force
 Guidance for Management of Psoriatic Disease During the Pandemic: Version 1.
 J. Am. Acad. Dermatol. 83, 1704–1716 (2020).
- Pierce, M. et al. Mental health before and during the COVID-19 pandemic: a longitudinal probability sample survey of the UK population. Lancet Psychiatry 7, 883–892 (2020).

- 9. Lamb, R. C. *et al.* Screening for anxiety and depression in people with psoriasis: a cross-sectional study in a tertiary referral setting. *Br. J. Dermatol.* **176**, 1028–1034 (2017).
- Read, S. et al. Chronic Conditions and Behavioural Change Approaches to Medication Adherence: Rethinking Clinical Guidance and Recommendations.
 Patient Prefer. Adherence 14, 581–586 (2020).

Fig. 1 title: Fully adjusted model for associations with worsening psoriasis.

Fig. 1 legend: Odds ratios for associations with worsening psoriasis. Anxiety/depression is defined as those who screened positive for either anxiety or depression. Obesity is defined as a BMI greater than 30.

Table 1. Participant demographics and clinical characteristics stratified by disease state.

	Total	Non- worsening disease	Worsening Disease	p-value
	N=4,043	N=2,315	N=1,728	
Shielded	2,224 (55.1%)	1,240 (53.8%)	984 (56.9%)	0.045
Advised to shield	742 (33.6%)	465 (37.5%)	277 (28.6%)	<0.001
Female gender	2,684 (66.4%)	1,362 (59.0%)	1,322 (76.5%)	<0.001
Age, mean (SD)	47.2 (15.1)	49.5 (15.3)	44.2 (14.3)	<0.001
White European ethnicity	3,016 (74.6%)	1,707 (73.7%)	1,309 (75.8%)	0.15
BMI, mean (SD)	27.6 (6.0)	27.4 (5.8)	28.0 (6.3)	0.003
Alcohol >14 units a week	495 (13.8%)	295 (15.0%)	200 (12.3%)	0.018
Current smoker	559 (15.8%)	291 (15.0%)	268 (16.7%)	0.18
Full time employed	1,929 (47.7%)	1,072 (46.3%)	857 (49.6%)	0.038
Household number, mean (SD)	2.8 (1.8)	2.8 (1.7)	2.9 (1.9)	0.003
Key worker	1,131 (28.1%)	595 (25.9%)	536 (31.1%)	<0.001
Psoriasis severity prior to COVID-19 pandemic				<0.001
Clear	451 (12.0%)	299 (14.6%)	152 (8.9%)	
Nearly clear	767 (20.4%)	463 (22.7%)	304 (17.7%)	
Mild	989 (26.3%)	477 (23.3%)	512 (29.9%)	
Moderate	892 (23.7%)	442 (21.6%)	450 (26.2%)	
Moderate-severe	480 (12.8%)	273 (13.4%)	207 (12.1%)	
Severe	180 (4.8%)	90 (4.4%)	90 (5.2%)	
Systemic therapy				<0.001
No Systemic Therapy	1,980 (56.2%)	938 (49.4%)	1,042 (64.2%)	
Standard Systemic Therapy	560 (15.9%)	309 (16.3%)	251 (15.5%)	
Targeted Therapy	981 (27.9%)	652 (34.3%)	329 (20.3%)	
Non adherent to systemic therapy	284 (18.5%)	114 (11.9%)	170 (29.6%)	<0.001
1 or more comorbidity	1,606 (39.7%)	908 (39.2%)	698 (40.4%)	0.45
Anxiety	1,069 (30.1%)	408 (21.0%)	661 (41.0%)	<0.001
Depression	977 (27.5%)	392 (20.1%)	585 (36.5%)	<0.001
Anxiety or Depression	1,376 (38.5%)	562 (28.8%)	814 (50.2%)	<0.001
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Table 1. SD = standard deviation, BMI = body mass index. Targeted therapy was defined as anyone taking TNF inhibitors (adalimumab, certolizumab, etanercept, infliximab), IL-17 inhibitors (ixekizumab, secukinumab, brodalumab), IL-23 inhibitors (guselkumab, risankizumab, ustekinumab) or apremilast. Standard systemic therapy was defined as anyone taking acitretin, ciclosporin, or methotrexate and not taking a targeted therapy.