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DOI:
[10.1111/bjd.14833](https://doi.org/10.1111/bjd.14833)

Document Version
Peer reviewed version

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Citation for published version (APA):

Lamb, R. C., Matcham, F., Turner, M., Rayner, L., Simpson, A., Hotopf, M., Barker, J. N. W. N., Jackson, K., & Smith, C. H. (2016). Screening for Anxiety and Depression in people with psoriasis: a cross sectional study in a tertiary referral setting: A cross-sectional study in a tertiary referral setting. *British Journal of Dermatology*.
<https://doi.org/10.1111/bjd.14833>

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Received Date : 06-Feb-2016
Revised Date : 26-May-2016
Accepted Date : 27-Jun-2016
Article type : Original Article

Corresponding author mail id : rlamb@nhs.net

Title: Screening for Anxiety and Depression in people with psoriasis: a cross sectional study in a tertiary referral setting

Running Head: Anxiety and depression screening in psoriasis

Authors: R.C. Lamb*, F. Matcham[†], M. Turner*, L. Rayner[†], A. Simpson[†], M. Hotopf[†], J.N.W.N. Barker*, K. Jackson*, C.H. Smith*

*St John's Institute of Dermatology, Guy's and St Thomas' NHS Foundation Trust, Great Maze Pond, London, SE1 9RT.

[†]Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, Denmark Hill, London, SE5 9RJ.

Corresponding author: Dr R C Lamb
St John's Institute of Dermatology
Guy's and St Thomas' NHS Foundation Trust
Great Maze Pond
London
SE1 9RT

Funding Source: IMPARTS is part funded by King's Health Partners and part by the National Institute for Health Research (NIHR) Biomedical Research Centre and Dementia Unit at South London and Maudsley NHS Foundation Trust and King's College London.

The research was also funded/supported by 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 views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/bjd.14833

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Conflict of Interest:

RL has received honoraria for an advisory board from Abbvie.

MT salary was part funded by Abbvie.

FM: Nil.

LR: Nil.

AS: Nil.

MH: Nil.

JNWNB has received honoraria for advisory boards and lectures at sponsored symposia together with grants for research in the past 5 years from Abbvie, Amgen, Celgene, Janssen, Lilly, Novartis, and Pfizer.

CHS has received grant funding for research in the past 5 years from MRC, NIHR, BSF, Abbvie, Celgene, Janssen, Novartis, Pfizer, Regeneron, Roche.

KJ has received honoraria for advisory boards and lectures at sponsored symposia from Janssen Pfizer; Lilly, Novartis and received an unrestricted grant from Abbvie.

What is already known on this topic?

- Depression and anxiety have been shown to affect patients with psoriasis

What does this study add?

- Routine use of screening questionnaires will identify new, clinically significant depression and anxiety in people with psoriasis.
- Risk factors for major depressive disorder and / or generalised anxiety disorder in people with psoriasis include female sex, psoriatic arthritis, psoriasis severity and prior psychiatric morbidity.
- The quality of life screening tool in routine use misses important psychiatric morbidity.

ABSTRACT

Background: National Institute for Health and Care Excellence (NICE) guidance recommends assessment of psychological and social well-being in people with psoriasis.

Objectives: To systematically screen for depression and anxiety in patients with psoriasis in routine clinical practice and identify at-risk groups for psychiatric morbidity.

Methods: Consecutive patients attending a single, tertiary centre over a 10-month period were invited to complete Patient Health Questionnaire Depression Scale (PHQ-9), Generalized Anxiety Disorder Scale (GAD-7) and Dermatology Life Quality Index (DLQI) as part of the IMPARTS: Integrating Mental and Physical healthcare; Research, Training and

Services. Information on demographics, treatment and clinical disease severity were collated from EPR. Regression models were used to identify at-risk groups for psychiatric morbidity.

Results: Of 607 patients (56.2% on biologics) included, 9.9% (95%CI: 7.5-12.3%) screened positive for major depressive disorder and 13.1% (95%CI: 10.4-15.8%) for generalised anxiety disorder ([GAD] GAD-7 >9). Suicidal ideation was reported in 35% of MDD; DLQI was <10 in 38.3% and 45.6% cases of MDD and GAD respectively. After adjusting for covariates, risk of MDD or GAD was significantly increased in women, those with severe clinical disease, psoriatic arthritis and previous depression/anxiety; risk of GAD was significantly increased with Asian ethnicity and use of topical treatments only.

Conclusions: Systematic screening for anxiety and depression identifies clinically important levels of depression and anxiety that may be missed using DLQI alone. Women, those with severe disease, psoriatic arthritis and/or a prior history of psychiatric morbidity may be at particular risk.

1. INTRODUCTION

Psoriasis is a chronic inflammatory skin condition affecting 1-3% of the population. Even when not clinically severe, psoriasis can adversely impact on psychological and social wellbeing, demonstrating a complex relationship between psychological and dermatological health.¹ People with psoriasis may have difficulty coping with their appearance and feel stigmatised, which in turn can lead to overt clinical depression and/or anxiety.² Whilst important in their own right, anxiety and depression may also prevent effective treatment.³ Guidelines on management of long-term conditions, and specifically psoriasis,⁴ recommend direct enquiry about the impact of psoriasis on well-being yet few clinicians work in this way as the acceptability and time taken for such holistic assessment may be problematic.⁵

The IMPARTS (Integrating Mental and Physical Healthcare: Research Training and Services) programme aims to address this by providing a multifaceted platform of clinical and research services to integrate mental healthcare into routine care. Patients' health needs are identified via patient-completed questionnaires on an e-tablet and results automatically populate the electronic patient record (EPR). In parallel the programme trains staff in basic mental health skills, identifies care pathways for individuals with mental health needs, and develops disease specific self-help materials. The programme has been implemented in 25 clinical services across two NHS Foundation Trusts in South London and has been shown to be acceptable to patients and staff.⁶

IMPARTS programme was introduced in our tertiary psoriasis service to systematically assess for psychiatric morbidity as part of a planned, specialty wide roll out. Using data made available via the programme we aimed to (i) estimate the prevalence of psychiatric disorders (depression and anxiety) in our patient cohort and (ii) to identify any baseline demographic and /or clinical characteristics (including disease severity, psoriatic arthritis, prior psychiatric morbidity) that are associated with depression and/or anxiety. Identification of at risk groups may be of value to clinicians in settings with limited resources and/or prompt earlier referral.

2. METHODS

This is a cross-sectional, single centre study in a tertiary psoriasis service. As the IMPARTS programme is a clinical innovation used in routine care, patients were not formally consented to participate, but were informed that data might be used for research purposes and could opt out. This complies with the basis of the IMPARTS programme ethical approval (IMPARTS Research Database REC reference: 12/SC/0422). All applications to use data collected routinely under the IMPARTS programme are scrutinised by a patient-led oversight committee to ensure that the use of data is appropriate and in line with ethics committee approval.

2.1 Patients: All patients (new and return) with a clinical diagnosis of psoriasis were invited to complete self-report questionnaires using a touch-screen tablet device with Wi-Fi connectivity to the hospital EPR. A health-care assistant or registered nurse (trained in use of the tablet device) explained the process, and issued an information leaflet detailing the reasons for collecting data. An opt-out consent process was followed; those who chose not to participate were invited to participate on subsequent attendances.

2.2 Procedure: Self-report questionnaires Patient Health Questionnaire (PHQ),⁷ Generalised Anxiety Disorder (GAD)⁸ and Dermatology Life Quality Index (DLQI)⁹ were completed on the electronic tablet. The PHQ-9 has been shown to be a reliable and valid measure of depression severity in primary care⁷ and physically ill populations in secondary care.¹⁰⁻¹² The GAD-7 is a reliable and valid measure of anxiety in primary care,⁸ the general population¹³ and secondary care.¹⁴ The DLQI is widely used in dermatology for research purposes and has adequate validity and reliability.⁹ Each patient completed PHQ-2¹⁵ and GAD-2¹⁶ consisting of the first two items of the PHQ-9 and GAD-7, respectively. Patients answering positively (“more than half the days” or “nearly every day”) to at least one item went on to complete remaining items of the corresponding measure. Completed data from PHQ-9, GAD-7 and DLQI questionnaires automatically populated the EPR and was

assigned depression and anxiety severity categories (see Table 1) alongside corresponding referral advice. Using a stepped care approach, pathways of referral were developed with the IMPARTS programme and included: alert general practitioner (GP) and advise referral to local primary care psychology team (Improving Access to Psychological Therapies; IAPT); review by dedicated psoriasis clinic psychologist; and liaison psychiatry review.^{17, 18} Referral to the psoriasis service clinical psychologist (present during clinic) was recommended where a complex interaction between dermatological condition and emotional health was identified. Identification of suicidal ideation or MDD with severe symptoms generated referral advice for non-urgent liaison psychiatry review. An urgent referral was advised for those screening positive for both. The expectation was that the reviewing clinician would discuss positive findings with the patient and the requirement for onward referral.

Data from patients who attended clinic more than once during the study period were included only once (first recording) although participation occurs serially at each subsequent attendance. Incomplete questionnaires (1 or more questions) were excluded.

2.3 Demographic and clinical information were extracted from EPR and included baseline demographics (age, sex, and ethnicity), history of psoriatic arthritis (diagnosed by a rheumatologist); past or on-going depression (defined as at least one of the following: diagnosis of depression in a clinic letter during the preceding year, treatment with antidepressant medication, e.g. selective serotonin reuptake inhibitors or tricyclic antidepressant, listed in the clinic letter during the preceding year and/or a GP letter from the last 5 years with a diagnostic coding for depression); past or on-going anxiety (defined as a diagnosis of anxiety or obsessive compulsive disorder listed in a clinic letter in the last year and/or a GP letter from the last 5 years with a diagnostic coding for anxiety); psoriasis phenotype; current treatment for psoriasis (none, topical only, phototherapy [UVB and bath PUVA], standard systemic [any of ciclosporin, methotrexate, fumaric acid esters, acitretin, systemic PUVA]) or therapy with a biologic agent (any of etanercept, adalimumab, ustekinumab or infliximab). If a patient was receiving biologic and standard systemic therapy they were placed in the biologic therapy category. Similarly, if a patient was taking systemic therapy and undergoing phototherapy they were placed in the systemic category. Disease severity was recorded from a PASI score taken within one month before/after PHQ-9, GAD-7 and DLQI questionnaire completion.

2.4 Statistical analysis

Statistical analysis was performed using STATA v.10. The prevalence of MDD and GAD is expressed as the percentage of cases determined by PHQ-9 and GAD-7 variables, respectively. Multiple logistic regression models were then created to examine the

relationships between disease severity, age, gender, ethnicity, treatment type, presence of Psoriatic Arthritis (PsA) and a historic psychiatric diagnosis and the presence of psychiatric disorder (GAD and MDD), providing odds ratios (OR), 95% confidence intervals (95%CI) and p-values.

3. RESULTS

3.1 Patients

636 patients completed screening for the first time during the study period 13/6/13-24/4/14. Out of 636, 607 had a diagnosis of psoriasis thus were eligible for inclusion (5.1% [31/607] newly referred patients, 95.0% [576/607] return patients). We evaluated take up of screening in the first 165 patients and found 1.8% (3/165) were not screened for the following reasons: patient declined, insufficient time, and IT problems.⁶

3.2 Descriptive data

Patient demographics are shown in Table 2. The majority of patients were male (65.4%), White British (69.5%), with chronic plaque psoriasis (95.7%). In total, 56.2% of patients were receiving biologics. A previous history of depression and anxiety was noted in 8.1% and 2.3% of patients respectively. The mean PASI and DLQI scores were 5.5 (SD= 5.7, range 0-50) and 3.6 (SD= 7.1, range 0-30) respectively.

3.3 Prevalence and severity of psychiatric disorder identified by screening

Sixty patients (9.9%, 95%CI: 7.5-12.3%) screened positive for probable major depressive disorder (MDD), see Figure 1a. Of these, 41.7% (95%CI: 28.9-54.5%) reported severe symptoms of MDD, see Figure 1b. A total of 3.5% (95%CI: 2.0-4.9%) indicated the presence of suicidal ideation 4.8% of whom were new patients. 68.3% of those identified cases of MDD had no recorded history of depression (see Table 3) and 23 (38.3%) patients with MDD had DLQI scores <10. Seventy-nine (13.1%, 95%CI: 10.4-15.8%) patients had probable generalised anxiety disorder (GAD) (see Table 3). 69.6% of those identified cases of GAD had no recorded history of anxiety (see Table 3). Additionally, 36 (45.6%) patients with GAD had DLQI scores <10.

In total, 8.1% (95%CI: 5.9%-10.2%) of patients had both MDD and GAD, and 14.8% (95%CI: 12.0%-17.7%) had MDD or GAD (see Figure 1a). Of note 35% of this group with both psychiatric disorders had a DLQI of less than 10 including 2 patients with DLQI of 0 despite screening positive for both GAD and MDD.

19.4% (6/31) of new patients screened positive for MDD (66.6% of whom had severe MDD) compared with 9.1% (55/607) of return patients. Eight new patients (8/31, 25.8%) screened positive for GAD compared with 71 (71/576, 12.3%) of return patients (patient/treatment variables not controlled for between new/return groups).

3.4 Referral pathway advice

For anxiety, the threshold for clinical psychologist review was reached in 78.3% (47/60) of patients and 34.0% (16/47) of these patients took up the offer to see the clinical psychologist. In the remainder, signposting advice to alert the GP and advise referral to IAPT was given, although uptake of this advice was not recorded.

For depression, the threshold for urgent referral to liaison psychiatry was reached in 25% (15/60) of patients and clinical psychologist review was suggested in 35% (21/60), 23.8% (5/21) of whom wished to see the psychologist when offered. In the remainder, non-urgent referral to liaison psychiatry or alert GP and advise referral to IAPT was suggested (uptake not recorded).

3.5 Risk factors identified for Psychiatric Disorder

(i) Anxiety

Risk of GAD was significantly increased in females (OR 1.88, $p=0.04$), Asian patients (OR 3.42, $p=0.001$), those with co-existent PsA (OR 1.92, $p=0.003$), severe psoriasis (OR 1.07, $p=0.007$) and those with a history of anxiety (OR 8.70, $p<0.001$). In comparison to patients receiving biologic therapy, patients using topical treatments only had three times the odds of having GAD (OR 3.66, $p=0.001$). There were no significant relationships between age or psoriasis phenotype and presence of GAD (see Table 3).

(ii) Depression

Female patients (OR 2.07, $p=0.03$), patients with PsA (OR 2.11, $p=0.003$) and those with previous depression (OR 6.86, $p<0.001$) were at increased risk of screening positive for MDD. Patients with more severe psoriasis had increased odds of MDD (OR 1.10, $p<0.001$) than those with less severe disease. There were no significant relationships between age, ethnicity, psoriasis phenotype or treatment modality and presence of MDD (see Table 3).

It is known that a proportion of Dermatology patients are at increased risk of suicide and screening has been suggested since early detection can minimise risk of suicide.¹⁹ In the group with MDD, 35.0% (3.5% of total cohort) had suicidal ideation and 20.0% of this group were known to have a previous diagnosis of depression. The proportion of patients receiving the various different treatment modalities was similar to the total cohort.

4. DISCUSSION

We demonstrate that women, those with severe clinical disease, psoriatic arthritis and/or a prior history of psychiatric morbidity may be at particular risk of anxiety and/or depression. Additionally, DLQI as a means to assess impact of disease misses clinically important psychiatric disorders. Strengths of our study include high uptake and the use of validated tools to detect depression and anxiety.

4.1 Prevalence

Rates of depression in psoriasis are known to be high.^{20,21} We were surprised that the prevalence of probable depression in our cohort (9.9%), from a tertiary centre and thus a likely “high-need” cohort, was lower than other tertiary centres.²² We also found the prevalence of anxiety (13.1%) to be lower than previous authors in a tertiary psoriasis clinic (43%).² In line with others, we found anxiety to be more prevalent than depression in our cohort.² In keeping with the lower prevalence of depression in our cohort, active suicidal ideation (3.5%), was approximately half that in similar patient groups (5.5%).²³

Reasons for lower prevalence of psychiatric disorders in this study compared with others may be due to the likely high uptake in our group (1.8% only not screened in the first 165 patients) thus reducing volunteer bias with a near complete cohort of patients. Additionally, use of more stringent screening tools may have contributed. PHQ-9 more closely follows the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) classification of psychiatric disorders compared with, for example, the Hospital Anxiety and Depression Scale,²⁴ used by other authors,² making direct comparison difficult. The GAD-7 questionnaire was also developed based on DSM-IV criteria for generalised anxiety disorder.⁸

It is notable that previous studies looking at psoriasis and psychiatric disorders used data from 1987-2002 and included no patients treated with biologic agents.²⁵ Since 2002, biologic agents are more widely used with the majority of patients in our cohort receiving biologic therapy (56.2%).

Another interesting finding in our cohort was the detection of both high numbers of probable “new” or previously “undetected” diagnoses of MDD/GAD in patients not already known to have psychiatric co-morbidity (71.3% and 8.6% respectively). Furthermore, in patients with DLQI less than 10 (suggestive of no to moderate effect of skin disease on quality of life), 38.3% and 45.6% cases had MDD and GAD respectively, suggesting that 1 in 3 cases of

MDD and GAD would be missed without additional screening tools. Thus our data demonstrate the use of DLQI alone to assess impact of disease is insufficient.

4.2 Risk Factors for Depression / Anxiety in Psoriasis

We found the risk of GAD and MDD was increased in females, those with co-existent PsA, severe psoriasis and those with a previous history of anxiety or depression respectively.

GAD was also increased in patients using topical treatments only compared to biologic therapy. Similarly, Asian ethnicity was associated with increased risk for GAD in this cohort compared to White British patients after controlling for disease severity.

With respect to ethnicity, we are not aware of quantitative data in psoriasis patients looking at this as a risk factor for psychiatric morbidity. However, PHQ-9 and GAD-7 questionnaires have not been extensively evaluated in different racial/ethnic populations.²⁶ Sex as a risk factor for psychiatric morbidity in psoriasis has been explored before with mixed results.^{2,21}

In both depression and anxiety we noted those with psoriatic arthritis to be at high risk.

Perhaps, in part, these findings can be explained by the association of depression with increasing co-morbidities.²⁷ Additionally symptom overlap may exist between depressive symptoms and those related to living with psoriatic arthritis, for example pain affecting loss of desire to go out rather than mood per se.²⁸ Nevertheless, our data highlight that psoriasis patients with arthritis are a population particularly vulnerable to adjustment difficulties.

The finding that previous psychiatric morbidity further increased risk of GAD/MDD may reflect continued difficulties in coping with psoriasis in the absence of psychological intervention or reflect the same depressive episode and notwithstanding, a depressive episode increases risk of depressive relapse.²⁹ Unsurprisingly, MDD/GAD appeared to be higher in patients attending for the first time than return patients to this tertiary clinic.

4.3 Limitations

These data are collected from a single, high need, tertiary centre and thus may not be generalisable. Additionally as these data are extrapolated from screening tools, all discussions are based on probable diagnoses of anxiety or depression rather than equating to actual diagnosis of these psychiatric disorders. However PHQ-9 has been shown to have a sensitivity of 78% and specificity of 91% for major depression³⁰ in secondary care. The GAD-7 questionnaire (at a cut off score of 5) has been shown to have a sensitivity of 78.1% and specificity of 74.6% in secondary care.¹⁴ Our inability to control for co-morbidities e.g. history of cancer, ischaemic heart disease, and obesity may also have affected our results.³¹

It should also be noted that these screening tools are unable to determine causation: depression and anxiety could be a direct consequence of skin disease or in fact coincident

findings. It is likely an understanding of this would affect onward pathway for treatment of these co-morbidities and thus should perhaps be a focus of future research.

Although uptake data of suggested strategies to deal with identified psychiatric morbidity was missing in this study, it would be interesting to address this and examine effects on health outcomes.

An additional consideration is the statistical power of these analyses. Although our overall sample size of 607 makes this one of the largest studies of its kind in dermatology, the small table cell sizes for patients with MDD and GAD make power low for some variables. A retrospective power calculation indicates that for depression we had a prevalence of 9.9% and a sample size of 607. This would allow us to detect a difference in proportions of 20% versus 40% with 83% power and 95% confidence. For anxiety, a prevalence of 13.1% and a sample size of 607 enables us to detect a difference in proportions of 20% versus 40% with 81% power and 95% confidence.

CONCLUSIONS

These data suggest that the burden of depression and anxiety in tertiary psoriasis populations is significant. Psychological support and a multidisciplinary approach in psoriasis patients may be indicated for adjustment difficulties of mood and anxiety in line with current NICE guidance in promoting an holistic approach to care and improving quality of life.^{4, 18} Some patient groups may be at greater risk of MDD and/or GAD due to other medical or social factors, and quality of life screening tools in routine use do not reflect psychiatric morbidity. Additionally, through improved detection, this evidence may support a business case for increased access to psychological services in specialist departments.

FUNDING

IMPARTS is funded by King's Health Partners. This paper represents independent research part funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

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Table 1: Depression and anxiety categories and severity using PHQ and GAD questionnaires.

Depression	Categories	Criteria
PHQ-9 questionnaire*	Probable Major Depressive Disorder (MDD)	Patients answering positively to at least 1 PHQ-2 item AND to 4 or more of the remaining 7 PHQ-9 items. (Severity of MDD: Severe MDD: PHQ-9 20-27 Moderate MDD: PHQ-9 15-19 Mild MDD: PHQ-9 9-14)
	Some Symptoms of Depression	Patients answering positively to at least 1 PHQ-2 item
	No symptoms of Depression	Patients answering positively to neither PHQ-2 item
Anxiety		
GAD-7 questionnaire	Probable Generalised Anxiety Disorder	GAD-7: 10-21 (Severity of GAD: Severe GAD: GAD-7 \geq 15 [†])
	Some symptoms of anxiety	GAD-7: 5-9
	Anxiety screen negative	GAD-7: <5

* Suicidal ideation was defined as a score of “2” or “3” on item 9 of the PHQ-9.

[†]In probable GAD, only 1 category of symptom severity exists (severe) as shown.

Table 2. Descriptive statistics of demographics and disease-related variables.

		N	%	M	SD
Total Number		607			
Female Gender		211	34.8		
Age (years)				47.0	13.9
Ethnicity	White British	422	69.5		
	White Other	47	7.7		
	Asian	90	14.8		
	Black	12	2.0		
	Mixed	6	1.0		
	Other	9	1.5		
	Unknown	21	3.5		

Psoriasis Phenotype	Chronic Plaque	581	95.7		
	Generalised Pustular	8	1.3		
	Localised Pustular	11	1.8		
	Non-pustular Acral	7	1.2		
Treatment	Biologics	341	56.2		
	Systemic	154	25.4		
	Phototherapy	4	0.7		
	Topical	74	12.2		
	None	34	5.6		
Psoriatic Arthritis	No	146	24.1		
	Yes	109	18.0		
	Unknown	352	58.0		
Previous Depression	No	553	91.1		
	Yes	49	8.1		
	Unknown	5	0.8		
Previous Anxiety	No	588	96.9		
	Yes	14	2.3		
	Unknown	5	0.8		
PASI				5.5	5.7
DLQI				3.6	7.1

N= number of patients; %= percentage of patient group; M= mean; SD= standard deviation; PASI= psoriasis area severity index; DLQI= dermatology life quality index.

Table 3. Demographic and disease variables associated with presence of anxiety and depression in psoriasis patients

		Anxiety				Depression			
		N(%)	OR	95%CI	p	N(%)	OR	95%CI	p
Total		79 (13.1)				60 (9.9)			
PASI (0-50)		-	1.07	1.02-0.12	0.007	-	1.10	1.05-1.15	<0.001
Age (8-86)		-	1.00	0.97-1.02	0.69	-	0.99	0.97-1.01	0.46
Gender	Male	44 (55.7)	-	-	-	33 (55.0)	-	-	-
	Female	35 (44.3)	1.88	1.03-3.42	0.04	27 (45.0)	2.07	1.08-3.97	0.03
Ethnicity	White British	45 (57.0)	-	-	-	36 (60.0)	-	-	-
	White Other	9 (11.4)	1.82	0.69-4.81	0.23	6 (10.0)	1.06	0.35-3.26	0.92
	Asian	19 (24.1)	3.42	1.63-7.20	0.001	12 (20.0)	1.96	0.85-4.53	0.12
	Black	1 (1.3)	1.49	0.17-12.97	0.72	1 (1.7)	1.48	0.17-12.88	0.72
	Mixed	1 (1.3)	1.19	0.11-12.88	0.89	1 (1.7)	1.78	0.17-19.15	0.63
	Other	2 (2.5)	1.66	0.23-12.04	0.62	2 (3.3)	1.38	0.19-9.10	0.75
Psoriasis Phenotype	Unknown	2 (2.5)	0.48	0.09-2.49	0.38	2 (3.3)	0.56	0.11-3.00	0.50
	Chronic Plaque	74 (93.7)	-	-	-	57 (95.0)	-	-	-
	Generalised							0.23-	
	Pustular	1 (1.3)	1.72	0.19-15.91	0.63	1 (1.7)	2.10	18.98	0.51
	Localised Pustular	3 (3.8)	3.20	0.30-33.80	0.13	1 (1.7)	0.24	0.00-28.58	0.56
	Non-pustular Acral	1 (1.3)	1.13	0.31-4.15	0.86	1 (1.7)	4.98	0.39-63.60	0.22
Treatment	Biologics	35 (44.3)	-	-	-	31 (51.7)	-	-	-
	Systemic	13 (16.5)	0.86	0.38-1.90	0.70	9 (15.0)	0.59	0.24-1.42	0.24
	Phototherapy	1 (1.3)	7.03	0.58-85.2	0.13	0 (0.0)	-	-	-
	Topical	26 (32.9)	3.66	1.65-8.10	0.001	16 (26.7)	1.51	0.64-3.58	0.34
	None	4 (5.1)	1.13	0.31-4.15	0.86	4 (6.7)	0.90	0.24-3.33	0.87
Psoriatic Arthritis [§]	No	7 (8.9)	-	-	-	4 (6.7)	-	-	-
	Yes	14 (17.7)	1.92	1.24-2.98	0.003	12 (20.0)	2.11	1.29-3.45	0.003
Previous Depression or	No	55 (69.6)	-	-	-	41 (68.3)	-	-	-

Anxiety

Yes

24 (30.4)

8.70

4.14-18.27

<0.001

19 (31.7)

6.86

3.24-

14.56

<0.001

§ This information was unknown for 44/60 patients (73.3%). Significant results are shown in bold.

N; number of patients, OR; odds ratio, 95%CI; 95% confidence interval, p; significance level, PASI; psoriasis area severity index, DLQI; dermatology life quality index.

