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ISKANDAR, Ireny YK, LUNT, Mark, THORNELOE, Rachael, CORDINGLEY, Lis, GRIFFITHS, Christopher EM and ASHCROFT, Darren M

BJD
British Journal of Dermatology

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I.Y.K. Iskandar[1] M. Lunt,[2] R.J. Thorneloe[3] L. Cordingley,[4] C.E.M. Griffiths[5,6] D.M. Ashcroft[1,5,7] on behalf the British Association of Dermatologists Biologics and Immunomodulators Register and Psoriasis Stratification to Optimise Relevant Therapy Study Groups

[1]Centre for Pharmacoepidemiology and Drug Safety, Division of Pharmacy and Optometry, School of Health Sciences, University of Manchester, Manchester, UK
[2]Arthritis Research UK Epidemiology Unit, Centre for Musculoskeletal Research, Manchester Academic Health Science Centre, University of Manchester, Manchester
[3]Centre for Behavioural Science & Applied Psychology, Department of Psychology, Sociology & Politics, Sheffield Hallam University, Sheffield, UK
[4]Division of Musculoskeletal and Dermatological Sciences, Manchester Academic Health Science Centre, University of Manchester, Manchester
[5]NIHR Manchester Biomedical Research Centre, Manchester Academic Health Science Centre, University of Manchester, Manchester
[6]Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester Academic Health Science Centre, University of Manchester, Manchester, UK
[7]NIHR Greater Manchester Patient Safety Translational Research Centre, Manchester Academic Health Science Centre, University of Manchester, Manchester, UK

Correspondence
Ireny Y.K. Iskandar.
Email: ireny.iskandar@manchester.ac.uk

Accepted for publication
13 June 2021

Funding sources
The Investigating Medication Adherence in Psoriasis (iMAP) study was initially funded by a Medical Research Council (MRC) doctoral fellowship and studentship award by the Psoriasis Association of Great Britain and Ireland awarded to R.J.T. Subsequent funding came from an MRC (MR/1011808/1) award to the Psoriasis Stratification to Optimise Relevant Therapy (PSORT) consortium. The British Association of Dermatologists Biologics and Immunomodulators Register (BADBIR) is coordinated by the University of Manchester. The BADBIR is funded by the British Association of Dermatologists. The British Association of Dermatologists has received income from AbbVie, Eli Lilly, Janssen Cilag, Novartis, Pfizer, and Samsung Bioepis for providing pharmacovigilance services. This income finances a separate contract between the British Association of Dermatologists and the University of Manchester, which coordinates the BADBIR. C.E.M.G. and D.M.A. are funded in part by the MRC (MR/L011808/1) and the NIHR Manchester Biomedical Research Centre. The funders/sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review or approval of the manuscript; and decision to submit the manuscript for publication.

Summary

Background Factors that might influence response to systemic treatment for moderate-to-severe psoriasis are varied, and generally, are poorly understood, aside from high bodyweight, suggesting that other unidentified factors may be relevant in determining response to treatment. The impact of alcohol misuse on treatment response has not been previously investigated.
Objectives To investigate whether alcohol misuse is associated with poor response to treatment for psoriasis.
Methods This was a prospective cohort study in which response to systemic therapies was assessed using the Psoriasis Area and Severity Index (PASI). The CAGE (Cut down, Annoyed, Guilty, Eye opener) questionnaire was used to screen for alcohol misuse. A multivariable factional polynomial linear regression model was used to examine factors associated with change in PASI between baseline and follow-up.
Results The cohort comprised 266 patients (biologic cohort, n = 134; conventional systemic cohort, n = 132). For the entire cohort, the median (interquartile range) PASI improved from 13 (10·0–18·3) at baseline to 3 (1·0–7·5) during follow-up. A higher CAGE score [regression coefficient: 1·40, 95% confidence interval (CI) 0·04–2·77]; obesity (1·84, 95% CI 0·48–3·20); and receiving a conventional systemic rather than a biologic therapy (4·39, 95% CI 2·84–5·95) were significantly associated with poor response to treatment; whereas a higher baseline PASI (–0·83, 95% CI –0·92 to –0·74) was associated with a better response to treatment.
Conclusions The poor response to therapy associated with alcohol misuse and obesity found in people with psoriasis calls for lifestyle behaviour change interventions and support as part of routine clinical care. Targeting interventions to prevent, detect and manage alcohol misuse among people with psoriasis is needed to minimize adverse health consequences and improve treatment response.

What is already known about this topic?

- Factors that might influence response to systemic treatment for moderate-to-severe psoriasis are generally poorly understood, aside from high bodyweight, suggesting

Conflicts of interest

C.E.M.G. 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. D.M.A. has received grant funding from AbbVie, Almirall, Celgene, Eli Lilly, Novartis, UCB and the Leo Foundation. L.C has received honoraria from Janssen, AbbVie, Novartis and Sanofi for educational events and an unrestricted research award as a co-applicant from Pfizer. R.J.T. has received an honorarium from Novartis. None of these awards are associated with the submitted manuscript. The remaining authors declare they have no conflicts of interest.

Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

DOI 10.1111/bjd.20577

that other unidentified factors may be relevant in determining response to treatment.
- The potential influence of alcohol misuse on response to treatment for psoriasis has not been previously investigated.

What does this study add?

- After adjusting for important factors that could influence response to treatment such as psychological distress and medication nonadherence, alcohol misuse was found to be significantly associated with poor response to treatment.
- Identification of potentially modifiable factors associated with poor treatment response emphasizes the need for lifestyle behaviour change support as part of routine clinical care.
- Effective interventions to detect and address high alcohol consumption should form part of routine care for people with psoriasis.

Psoriasis is a chronic, immune-mediated inflammatory skin condition. It is recognized by the World Health Organization as a serious noncommunicable disease that requires effective management.[1] Psychological and social difficulties in combination with the physical discomfort associated with psoriasis may contribute to psychological distress (anxiety and depression) and alcohol misuse.[2–4]

The treatment effectiveness of conventional systemic and biologic therapies used in the management of moderate-to-severe psoriasis is much lower in real-world clinical practice than in clinical trials.[5,6] Factors that might influence response to treatment are varied, and generally, are poorly understood, aside from high bodyweight, which has consistently been associated with worse outcomes for most therapies.[7–12] This suggests that other unidentified factors may be relevant in determining response.[13] To date, previous research has focused on demographic and clinical factors as predictors of response to treatment in psoriasis.[12] However, there are no studies examining the role of alcohol misuse in predicting response to treatment, taking into account other important factors that could also influence treatment response such as psychological distress and medication nonadherence.

The iMAP (Investigating Medication Adherence in Psoriasis) is a multicentre study collecting biomedical and psychological data from patients with psoriasis prescribed biologic or conventional systemic therapies.[14] All patients in iMAP are also enrolled in the British Association of Dermatologists Biologics and Immunomodulators Register (BADBIR), a longitudinal pharmacovigilance register representing a 'real-world' cohort of patients with psoriasis receiving biologic or conventional systemic therapies.[15,16] This presents an ideal resource to assess the impact of alcohol misuse, alongside patient behavioural and psychological factors on response to conventional systemic and biologic therapies in routine clinical practice.

The objectives of this study were to: (i) assess real-world levels of alcohol misuse, psychological distress and medication nonadherence among patients with moderate-to-severe psoriasis, and (ii) investigate whether alcohol misuse is associated with poor response to systemic therapies after controlling for other factors.

Patients and methods

Data source

Patients attending 35 dermatology centres across England were recruited into iMAP between March 2013 and September 2016. Patients aged ≥ 18 years with a diagnosis of psoriasis under the care of a dermatologist, prescribed a conventional systemic and/or a biologic treatment and enrolled in BADBIR were eligible for inclusion into iMAP.[14]

Data collection

The CAGE (Cut down, Annoyed, Guilty, Eye opener) questionnaire assessed self-perception of alcohol misuse. It consists of four questions beginning with the stem 'Have you ever': felt the need to *cut* down drinking; felt *annoyed* by criticism of drinking; had *guilty* feelings about drinking; and taken a morning *eye* opener. The items are rated on a scale of 0–1, with a

total score ranging from 0 to 4, with a score of ≥ 2 indicating alcohol misuse.[17,18]

The Medication Adherence Report Scale (MARS) assessed the frequency of nonadherent behaviours on a 5-point Likert scale ranging from very often (1 point) to never (5 points), with scores ranging from 8 to 40, with higher scores indicating higher levels of adherent behaviour.[19] Patients were classified into an overall nonadherent category if they scored ≤ 38/40.[14]

The Hospital Anxiety and Depression Scale (HADS) is a 14-items scale that provides an assessment of symptoms of anxiety (7 items) and depression (7 items). Items are rated on a scale of 0–3, indicating the strength of agreement with that item and are summed to create a HADS anxiety and depression score, both ranging from 0 to 21, with a score of ≥ 8 indicating a possible 'caseness' of anxiety or depression.[20,21] A score ranging between 8–10, 11–14 and 15–21 indicate mild, moderate and severe symptoms, respectively.[22]

Patients were instructed to independently and anonymously complete an iMAP questionnaire that contained the MARS and the HADS at baseline (upon recruitment) and every 6 months thereafter for up to 18 months. Patients' demographic characteristics (age, sex, height and weight); lifestyle information [smoking status and alcohol misuse (CAGE)]; details of type and severity of psoriasis [Psoriasis Area and Severity Index (PASI)] and year of onset; standardized measures of health status using self-reported outcome measures [Dermatology Life Quality Index (DLQI)]; detailed information about the patients' current and previous treatments for psoriasis (any change in therapy, concomitant use of systemic therapies, gaps in treatment, start and stop dates, and reasons for discontinuation); and the patients' comorbidities were extracted from BADBIR (with written informed patient consent) at times corresponding to the dates when the patients completed the iMAP questionnaires. Data were extracted from the October 2018 database build.

Study population

Patients were eligible for inclusion in this analysis if they had at least one PASI measurement recorded before and after completing at least one iMAP questionnaire. The PASI recorded closest to the date of completing the iMAP questionnaire were identified and referred to as either 'baseline' (recorded prior to completing the questionnaire) or 'follow-up' PASI (recorded after completing the questionnaire). The majority of the patients had only one iMAP questionnaire, although a few had multiple questionnaires completed between the time the baseline and follow-up PASIs were recorded (File S1 and Figure S1; see Supporting Information). Patients were excluded from the analysis if the baseline PASI was measured > 12 months prior to or > 1 month after the start of therapy; and/or if their follow-up PASI was measured > 24 months after the start of their treatment. Patients were assigned to either the biologic or conventional systemic cohort based on the therapy they were receiving at the time of completing their first iMAP questionnaire, and patients were recorded as either biologic naive or non-naive.

Statistical analysis

Multivariable linear regression model, where fractional polynomials were used to model nonlinear relationships between the covariates and the outcome, was conducted to investigate factors associated with the change in PASI between baseline and follow-up. An a priori list of covariates was determined to address potential predictors of response. Alcohol misuse (CAGE), medication nonadherence and psychological distress recorded at times corresponding to the dates when the patients completed the iMAP questionnaires were included in the model. In the few patients with more than one valid measurement of the CAGE (19 patients, 7%), patients' medication nonadherence status (28 patients, 11%) and psychological distress (28 patients, 11%) during the study period, an average was taken. An interaction between overall medication nonadherence status and the cohort the patients were assigned to was also included in the model.

Other potential confounders included in the model were body mass index (dated around the start date of the therapy) which was categorized into a binary obese/nonobese variable. The patients' age and disease duration were calculated from the patients' date of birth and year of disease onset recorded at the time of registration into BADBIR and the start date of their therapy, respectively. Participants' baseline DLQI were identified if they were dated within 12 months prior to and 1 month after the start of treatment to be consistent with how baseline PASI were identified. The median [interquartile range (IQR)] time period between the baseline DLQI measurement and start of therapy was −4 days (−37 to 0 days).

Inflammatory arthritis and other comorbidities as well as the patients' smoking status were collected at the time of registration into BADBIR. Concomitant use of methotrexate, ciclosporin and/or other conventional systemic therapies was analysed as a binary variable (ever exposed/never exposed) throughout the study. A sensitivity analysis was conducted in which an interaction between alcohol misuse and obesity was also included in the model.

To account for missing data (Table S1, see Supporting Information), we generated 50 imputed datasets. In each dataset, missing values were replaced by values randomly selected from the expected distribution of that variable conditional on the measured or imputed values of all other variables for that individual. This approach enables all participants to be included in the analysis, avoiding the selection bias that would be likely if only participants with complete data were included for analysis.[23] The multivariable linear regression assumptions were assessed by scatterplots and statistical testing. Analyses were performed using Stata version 15·0 (Stata Corp, College Station, TX).

Ethical approval

Ethical approval for BADBIR and iMAP were obtained from the NHS research Ethics Committee North West England (references 07/MRE08/9 and 12/NW/0619, respectively) in

March 2007 and December 2012, respectively, and from research ethics committees local to each recruiting site. All participants gave written informed patient consent for their participation in the registry prior to data collection.

Results

In total, 266 patients with psoriasis (biologic cohort, n = 134; conventional systemic cohort, n = 132) were included in our analyses (Figure 1); they were followed-up for a median (IQR) of 7 (6–10) months. The mean (SD) age of patients and disease duration were 48·2 (13·1) and 22·1 (14·5) years, respectively, and 45·1% of participants were women.

At baseline, the median PASI was 13 (IQR 10–18·3) and the mean DLQI was 16·2 (SD 8·5). Overall, 19·5% of participants reported having inflammatory arthritis, and 67·3% reported having ≥1 comorbidities other than inflammatory arthritis. Patients' demographic and disease characteristics are summarized in Table 1.

The mean CAGE score was 0·3 (SD 0·8), with 5·6% of patients scoring ≥ 2 indicating alcohol misuse (Table 1). The mean (SD) HADS anxiety and depression scores were 6·9 (4·5)

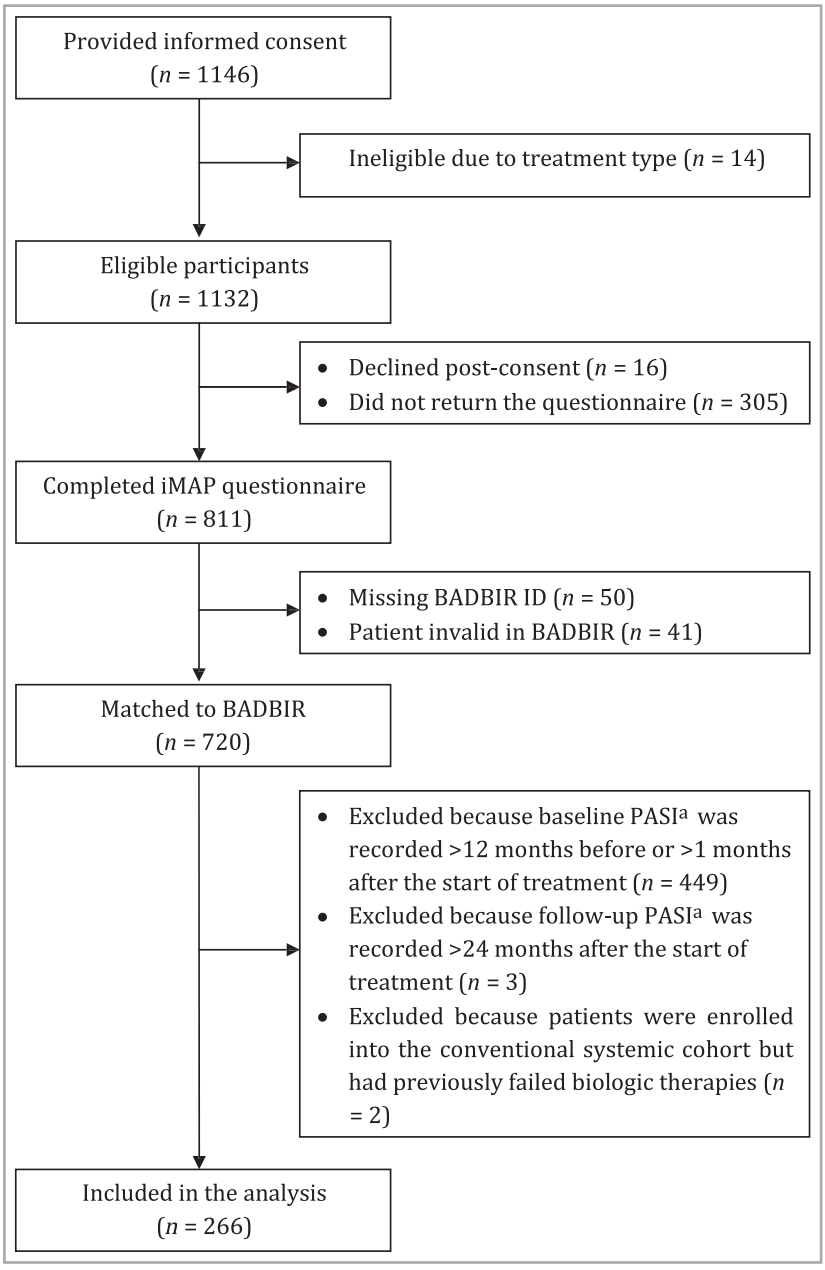

Figure 1 Flow chart showing selection of study participants. [a]The Psoriasis Area and Severity Index (PASI) recorded closest to the date of completing the iMAP (Investigating Medication Adherence in Psoriasis) questionnaire were identified and referred to as either baseline PASI (recorded prior to completing the questionnaire) or follow-up PASI (recorded after completing the questionnaire).

Table 1 Patient demographic and disease characteristics

	All patients (n = 266)	Biologic cohort[a] (50·4%, n = 134)	Conventional cohort[b] (49·6%, n = 132)
Age (years), mean (SD)	48·2 (13·1)	48·1 (13·5)	48·4 (12·8)
Female	120 (45·1)	52 (38·8)	68 (51·5)
BMI category, kg/m^2			
Nonobese (BMI < 30)	145 (54·5)	63 (47·0)	82 (62·1)
Obese (BMI ≥ 30)	121 (45·5)	71 (53·0)	50 (37·9)
Smoking status			
Never smoked	86 (32·3)	47 (35·1)	39 (29·5)
Ex-smoker	98 (36·8)	52 (38·8)	46 (34·8)
Current smoker	82 (30·8)	35 (26·1)	47 (35·6)
Alcohol use			
CAGE,[c] mean (SD)	0·3 (0·8)	0·3 (0·7)	0·3 (0·8)
Alcohol misuse	15 (5·6)	7 (5·2)	8 (6·1)
Inflammatory arthritis/other comorbidities			
Inflammatory arthritis	52 (19·5)	30 (22·4)	22 (16·7)
No comorbidities[d]	87 (32·7)	39 (29·1)	48 (36·4)
1–2 comorbidities[d]	122 (45·9)	63 (47·0)	59 (44·7)
3–4 comorbidities[d]	50 (18·8)	28 (20·9)	22 (16·7)
≥ 5 comorbidities[d]	7 (2·6)	4 (3·0)	3 (2·3)
Disease			
Disease duration (years), mean (SD)	22·1 (14·5)	23·6 (14·0)	20·5 (14·9)
Age of onset (years), mean (SD)	26·2 (15·9)	24·4 (15·2)	27·9 (16·5)
PASI at baseline, median (IQR)	13·1 (10–18·3)	13·4 (9·2–19·4)	12·8 (10·2–17·1)
DLQI at baseline, mean (SD)	16·2 (8·5)	15·8 (9·4)	16·5 (7·6)
Unstable psoriasis	37 (13·9)	17 (12·7)	20 (15·2)
Psychological distress (HADS)			
Anxiety score,[e] mean (SD)	6·9 (4·5)	6·7 (4·3)	7·0 (4·6)
Anxiety severity[f]			
No anxiety	158 (59·4)	80 (59·7)	78 (59·3)
Mild anxiety	53 (19·9)	29 (21·6)	24 (18·5)
Moderate anxiety	39 (14·7)	19 (14·2)	20 (14·6)
Severe anxiety	16 (6·0)	6 (4·5)	10 (7·6)
Depression score,[e] mean (SD)	5·3 (4·1)	5·3 (4·1)	5·3 (4·2)
Depression severity[f]			
No depression	193 (72·6)	99 (73·9)	94 (70·9)
Mild depression	41 (15·4)	20 (14·9)	21 (16·1)
Moderate depression	27 (10·2)	13 (9·7)	14 (10·7)
Severe depression	5 (1·9)	2 (1·5)	3 (2·3)
Medication nonadherence			
Overall nonadherent	44 (16·5)	8 (6·0)	36 (27·6)
Medication history			
Biologic naive	238 (89·5)	106 (79·1)	132 (100·0)
Concomitant systemic therapy[g]	28 (10·5)	17 (12·7)	11 (8·2)
Stopped therapy[h]	42 (15·8)	16 (11·9)	26 (19·4)

Results are n (%) unless otherwise indicated. BMI, body mass index; CAGE, Cut down, Annoyed, Guilty and Eye opener; DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale; IQR, Interquartile range; PASI, Psoriasis Area and Severity Index. [a]Includes adalimumab (69, 51·5%); etanercept (17, 12·7%); ustekinumab (45, 33·6%); and other biologic therapies (infliximab, golimumab, secukinumab) (3, 2·3%). [b]Includes acitretin (33, 25·0%); ciclosporin (32, 24·2%); Fumaric acid esters (7, 5·3%); methotrexate (60, 45·5%). [c]The possible score range for CAGE is 0–4. [d]Includes any of (excluding inflammatory arthritis) hypertension, angina, ischaemic heart disease, stroke, epilepsy, asthma, chronic obstructive pulmonary disease, peptic ulcer, renal disease, hepatic disease, tuberculosis, demyelinating disease, diabetes, impaired glucose tolerance, depression, nonskin cancer, immunodeficiency syndrome, thyroid disease, other. [e]The possible score range for HADS anxiety and HADS depression is 0–21. [f]The possible score range for HADS anxiety and HADS depression severity is mild, 8–10; moderate, 11–14; severe, 15–21. [g]Includes any of acitretin, fumaric acid esters, ciclosporin, methotrexate and mycophenolate mofetil. [h]Patients stopped therapy received at the time of completing the iMAP (iMAP, Investigating Medication Adherence in Psoriasis) questionnaire during the study period.

Table 2 Multivariable linear regression of potential factors associated with changes in Psoriasis Area Severity Index (PASI) between baseline and follow-up

Variable	β coefficient (95% CIs)	P-value
Demographics		
Age[a]	−0·63 (−1·22 to −0·05)	**0·035**
Female	−0·05 (−1·37 to 1·27)	0·940
Obesity status[b]		
Obese (BMI 30 kg/m^2)	1·84 (0·48 to 3·20)	**0·008**
Smoking status[c]		
Ex-smoker	−1·21 (−2·75 to 0·33)	0·123
Current smoker	−1·20 (−2·83 to 0·44)	0·151
Comorbidities[d]		
Inflammatory arthritis	−0·28 (−1·96 to 1·40)	0·745
1–2 comorbidities	−0·40 (−1·88 to 1·08)	0·595
3–4 comorbidities	0·30 (−1·75 to 2·35)	0·774
≥ 5 comorbidities	−1·31 (−5·62 to 2·99)	0·549
Disease		
Disease duration[a]	0·28 (−0·21 to 0·77)	0·258
Baseline PASI	−0·83 (−0·92 to −0·74)	**<0·001**
Baseline DLQI	−0·06 (−0·17 to 0·06)	0·339
CAGE	1·40 (0·04 to 2·77)	**0·044**
Psychological distress (HADS)		
Anxiety	−0·03 (−0·24 to 0·17)	0·74
Depression	0·18 (−0·04 to 0·39)	0·110
Overall nonadherent	2·65 (−5·49 to 10·79)	0·522
Treatment		
Conventional systemic cohort[e]	4·39 (2·84 to 5·95)	**<0·001**
Biologic naive[f]	−1·76 (−4·19 to 0·68)	0·156
Concomitantly using conventional systemic therapy[g]	1·78 (−0·36 to 3·91)	0·102
Stopped therapy[h]	4·18 (2·38 to 5·97)	**<0·001**
Time gap between start of therapy and time the baseline PASI was measured	0·21 (−0·22 to 0·65)	0·334
Time gap between start of therapy and time the follow-up PASI was measured	−0·12 (−0·28 to 0·04)	0·138
Nonadherence: conventional systemic cohort[i]	−2·20 (−6·68 to 2·29)	0·336

BMI, body mass index; CAGE, Cut down, Annoyed, Guilty and Eye opener; CI, confidence interval; DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale. Results in bold indicates P ≤ 0·05. Fractional polynomials were used to determine if any non-linear association between the covariates and the outcome provided a better fit than a simple linear association, but none did. [a]To evaluate regression coefficients for every 10-year increase in age and disease duration at enrolment into the British Association of Dermatologists Biologics and Immunomodulators Register, baseline continuous variables of age and disease duration were transformed to age and disease duration divided by 10. At follow-up, older age at enrolment (by 10 years) was associated with greater improvement in PASI values. [b]Reference category: nonobese (BMI < 30 kg/m^2). [c]Reference category: never smoked. [d]Reference category: no comorbidities (excluding inflammatory arthritis); includes any of hypertension, angina, ischaemic heart disease, stroke, epilepsy, asthma, chronic obstructive pulmonary disease, peptic ulcer, renal disease, hepatic disease, tuberculosis, demyelinating disease, diabetes, impaired glucose tolerance, depression, nonskin cancer, immunodeficiency syndrome, thyroid disease, other. [e]Reference category: biologic cohort. [f]Reference category: biologic non-naive. [g]Includes any of acitretin, fumaric acid esters, ciclosporin, methotrexate and mycophenolate mofetil. Included as a binary variable (ever exposed/never exposed). Reference category: never exposed. [h]Patients stopped therapy received at the time of completing the iMAP (Investigating Medication Adherence in Psoriasis) questionnaire during the study period. Reference category: continuously used therapy throughout the study period. [i]An interaction term between cohort and overall nonadherence status.

and 5·3 (4·1), with 40·6% and 27·4% of patients scoring ≥ 8 indicating a possible caseness of anxiety and depression, respectively (Table 1). A notable proportion of the study cohort were classified as nonadherent to medication (16·5%; Table 1), with a significantly higher proportion of patients using conventional systemic therapies classified as nonadherent (27·6%) compared with those using biologic therapies (6·0%).

Table 2 presents results from the multivariable linear regression analysis examining factors that affect the change in PASI between baseline and follow-up. Having a higher CAGE score was significantly associated with poor response to treatment as measured by change in PASI [for every 1-point increase in the CAGE score; regression coefficient 1·40, 95% confidence interval (CI) 0·04– 2·77. Thus, a maximum change in CAGE score from 0 to 4 would be associated with a change in PASI of 5·60, 95% CI 0·16–11·08].

Of the demographic factors, with each 10-year increase in a patient's age there was significantly better response to treatment (−0·63, 95% CI −1·22 to −0·05). Having a higher baseline PASI (for every 1-point increase in the baseline PASI, −

0·83, 95% CI −0·92 to −0·74) was also significantly associated with a better response to treatment. In contrast, being obese (1·84, 95% CI 0·48–3·20), receiving a conventional systemic therapy rather than a biologic therapy (4·39, 95% CI 2·84–5·95), and stopping the therapy during the follow-up (4·18, 95% CI 2·38–5·97) were significantly associated with poor response to treatment. No significant interaction was found between medication nonadherence and treatment cohort (P = 0·336, Table 2) and also between alcohol misuse (CAGE) and obesity (P = 0·930, Table S2, see Supporting Information).

Discussion

In this real-world cohort of patients with psoriasis, alcohol misuse, obesity and receiving a conventional systemic therapy were significantly associated with poor response to treatment as measured by change in PASI between baseline and follow-up. To our knowledge this is the first study to investigate alcohol misuse in a real-world cohort of patients with psoriasis, and explore how it affects response to treatment.

Consistent with other studies, we found that obesity was also associated with poor response to systemic therapies.[7–9] Obesity has also been found to be associated with poor response to therapies in rheumatoid arthritis[24,25] and ankylosing spondylitis.[26] Our findings are also in line with those reported by Gelfand *et al.*,[5] who found biologic therapies to be more effective than conventional systemic therapies. However, by comparison, our study has an important strength: we accounted for important clinical and social factors including smoking status, alcohol misuse, the presence of comorbidities and medication nonadherence. Although overall nonadherence did not significantly predict response to therapy (P = 0·522), the results suggest that it was associated with poor response for those exposed to conventional systemic therapies (2·65, 95% CI −5·49 to 10·79). Clinicians should therefore explore patients' adherence, especially in those who are poor responders to therapy, and provide additional support to improve adherence to treatment regimens.[27] Future studies investigating predictors of response to therapy should ideally include a measure of adherence to reduce potential confounding.

To our knowledge, no previous study has assessed the association of alcohol misuse with poor response to therapies.[7] Our results demonstrate that alcohol misuse is associated with poor response to treatment. We would be interested to see whether our findings can be replicated independently. The implications of our findings are important. The economic, social and health consequences of alcohol misuse are considerable. Excessive alcohol may worsen the disease, has implications for treatment and increases the risk of dying in people with psoriasis – this is on average 3 years younger compared with peers of the same age and sex in the general population.[28,29]

One of the key strengths of this study is the real-world prospective cohort study design thereby ensuring that patients are representative of those receiving treatment in routine clinical practice. Furthermore, the participation of multiple dermatology centres (n = 35) across England ensures the external validity of the results. We also performed multiple imputation to account for missing data thus minimizing the bias that could have been introduced by only considering a complete case analysis.

Limitations include the use of self-reported tools for alcohol misuse, medication nonadherence and psychological distress, which can be criticized for being influenced by poor patient recall or reporting bias and so may underestimate alcohol misuse or overestimate adherence and psychological distress. The CAGE questionnaire can also be criticized for identifying mostly severe forms of harmful alcohol misuse and dependence, and so can fail to adequately identify those with hazardous use of alcohol. Nevertheless, it is reported that the CAGE has a sensitivity of 93% and a specificity of 76% for the identification of excessive drinking and the use of appropriate theoretical frameworks and validated data-collection tools are major strengths.[30,31]

An inherent limitation in any observational study is lack of randomization, which may introduce confounding bias, and although this is partially negated by adjustment for clinically relevant covariates, the presence of other unmeasured confounders, such as the intention behind concomitant medication, cannot be determined. One particular challenge we faced is that some of the patients' demographic characteristics were recorded only at the time of registration with BADBIR. This included data on smoking status and comorbidities. It is possible that some patients may have developed new comorbidities or changed smoking status during the study period. Furthermore, the influence of treatment dose escalation on the PASI response was not assessed. However, we have shown previously that patients in BADBIR routinely receive the recommended dosing regimen but that concomitant treatment with other systemic therapies occurs commonly.[32]

Clinicians should be aware of the considerable psychological distress and psychosocial challenges that are faced by patients with psoriasis, which can lead to chronic alcohol misuse and dependence as coping mechanisms.[29] Our findings highlight that at least 40% of our study cohort reported having psychological distress and that alcohol misuse has a negative effect on response to treatment. Psychological and educational interventions for newly diagnosed patients with psoriasis have been developed to minimize distress and to alert patients to the negative impact of alcohol on psoriasis outcomes (for example Chisholm *et al.*[33] and Nelson *et al.*[34]). For those with established disease, the recognition by clinicians of the risks associated with the dual stigma of psoriasis and alcohol misuse on response to treatment is important. Discussions about alcohol use, especially high use, are challenging for both clinicians and patients through fear of stigmatization, and as a result, are frequently avoided in consultations.[35] Patients may also be unaware of the extent to which they are using alcohol as a coping mechanism. Nevertheless, provision of skilled

screening and brief interventions by healthcare teams can enable patients to achieve reduction or abstinence, reduce health harms and improve prognosis without increasing stigma.[36–38]

Our findings also indicate that clinicians need to be aware of, and address, the possibility of medication nonadherence. The behaviour of more than 15% of patients in this study were classified as being nonadherent. Patients' beliefs about their medication, including concerns about the potential for adverse events, are key drivers of nonadherence. Concerns about unwanted treatment effects are common in patients with psoriasis, including those who adhere to treatments,[39] and so provision of accessible patient-centred materials (using traditional written or e-health delivery formats) that address these issues may allay some worry in a time efficient way. This can be further supported by all those involved in provision of treatment, including medical, nursing and pharmacy staff, all of whom have a role in shaping patients' treatment beliefs. People are more likely to forget to use their medication if they have weak medication-taking habits or routines.[14] Again, very brief messages either delivered directly from relevant clinical staff, or via traditional or electronic media, may enable patients to recognize that habit formation requires an initial period of active engagement in change and could optimize treatment outcomes.[27]

In conclusion, this study provides evidence that alcohol misuse and obesity are associated with poor response to treatment in patients receiving systemic therapies. These are modifiable factors and confirm the important role that clinical teams can play in supporting lifestyle behaviour change in people with psoriasis. Interventions to prevent or address alcohol misuse and weight gain are important parts of psoriasis health management. Patients may need additional support to recognize the relevance of these lifestyle factors to their skin health;[34,40] and this study highlights how these factors detrimentally affect psoriasis treatment effectiveness. Routine screening and identification, using simple screening tools, can be used to detect early signs of hazardous, harmful and dependent alcohol consumption, and can be implemented in healthcare settings to detect alcohol misuse among people with psoriasis.[38]

Acknowledgments

The authors acknowledge the contribution of the Psoriasis Stratification to Optimise Relevant Therapy (PSORT) partners, and the PSORT Executive Committee (in alphabetical order): Jonathan Barker, Michael Barnes, David Burden, Paola DiMeglio, Richard Emsley, Christopher Griffiths (Chair), Katherine Payne, Nick Reynolds, Catherine Smith, Deborah Stocken and Richard Warren.

The British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR) acknowledges the support of the National Institute for Health Research (NIHR) through the clinical research networks and its contribution in facilitating recruitment into the registry. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the BADBIR, NIHR, the National Health Service or the Department of Health.

The authors are also grateful to the members of the Data Monitoring Committee: Robert Chalmers, Carsten Flohr (Chair), Richard Weller, and David Prieto-Merino and the BADBIR Steering Committee (in alphabetical order): Jonathan Barker, Marilyn Benham (CEO of BAD), David Burden (Chair), Ian Evans, Christopher Griffiths, Sagair Hussain, Brian Kirby, Linda Lawson, Kayleigh Mason, Kathleen McElhone, Ruth Murphy, Anthony Ormerod, Caroline Owen, Nick Reynolds, Catherine Smith and Richard Warren.

Christopher Griffiths is an NIHR Emeritus Senior Investigator. We acknowledge the enthusiastic collaboration of all of the dermatologists and specialist nurses in the UK and the Republic of Ireland who provided the data. The principal investigators at the BADBIR participating sites are listed on the following website: http://www.badbir.org.

Finally, we are very grateful to all individuals with psoriasis who took part in this study.

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Supporting Information

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

File S1. Methods.

Table S1. Missing data.

Table S2. Multivariable fractional polynomial linear regression of potential factors associated with changes in Psoriasis Area Severity Index (PASI) between baseline and follow-up.

Figure S1. iMAP (Investigating Medication Adherence in Psoriasis) questionnaire completion in relation to time of Psoriasis Area Severity Index (PASI) measurement.

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