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Reversibility of alexithymia with effective treatment of moderate-to-severe psoriasis: longitudinal data from EPIDEPSO*

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Summary

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Conflicts of interest

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Background Alexithymia refers to difficulty in identifying and expressing emotions. Alexithymia is associated with high burden of disease in patients with psoriasis. **Objectives** To investigate whether alexithymia was reversible in patients with psoriasis following real-life therapeutic intervention.

Methods The Epidemiological Study in Patients with Recently Diagnosed Psoriasis (EPIDEPSO; NCT01964443) was a 1-year multicentre observational study investigating the prevalence of alexithymia and other psychosocial comorbidities in patients with psoriasis with ≤ 10 years' disease duration and eligible for systemic treatment. Alexithymia was assessed using the Toronto Alexithymia Scale (TAS-20) at baseline, 6 months and 1 year.

Results There was a statistically significant decrease in the prevalence of alexithymia in the follow-up cohort, from 26.7% at baseline to 21.2% at 6 months and 18.8% at 1 year. More than half of the patients ($n = 77$, 53.8%) who were alexithymic at baseline experienced reversion of their alexithymia. Reversion of alexithymia was higher in patients who reached a high level of disease control, defined as $\geq 75\%$ or $\geq 90\%$ improvement in Psoriasis Area and Severity Index. Reversion of alexithymia was associated with dramatic improvement in quality of life, anxiety and depression. Moreover, hazardous alcohol use, highly prevalent in patients with alexithymia, was reduced almost threefold at 1 year.

Conclusions Alexithymia and associated high disease burden may be reversible in patients with effective treatment of psoriasis. Proactive recognition of patients who are unable to identify and express their feelings is important.

What's already known about this topic?

- Alexithymia, the inability to identify and express emotions, is highly prevalent in patients with psoriasis.
- Patients with alexithymia have a high disease burden, with impaired quality of life, anxiety and depression.

What does this study add?

- Alexithymia may be reversible in patients with psoriasis.
- Higher psoriasis clearance is associated with a lower prevalence of alexithymia at 1 year.
- Anxiety, depression and harmful alcohol use are reduced in patients who have a reversion in alexithymia.

Alexithymia refers to a difficulty in identifying and expressing emotions.¹ People with alexithymia have a reduced ability to connect with their feelings and to recognize those of others. Difficulty in identifying and expressing emotions has been associated with reduced social skills and isolation. A high prevalence of alexithymia has been reported in patients with chronic inflammatory diseases, such as ulcerative colitis, asthma and rheumatoid arthritis.²

We and others have investigated the prevalence of alexithymia in adult patients with psoriasis. The observed prevalence of alexithymia in patients with psoriasis ranges between 15.6%³ and around 33%.^{4–6} Our study⁷ showed that patients with psoriasis with difficulty in identifying and expressing emotions were characterized by high psoriasis burden, including markedly reduced quality of life, high prevalence of anxiety and depression, and high risk of alcohol dependency. In addition, patients with alexithymia had low work productivity and a high risk of unemployment.

An important question concerning alexithymia is whether it is reversible or whether it is a stable personality trait that cannot be modified by intervention. Some studies have shown that alexithymia is stable over time in the general population,^{8,9} while studies in patients with substance-abuse disorders have shown that alexithymia may disappear.¹⁰ In psoriasis, published studies are cross-sectional and have not addressed the issue of alexithymia reversibility.

The aim of the Epidemiological Study in Patients with Recently Diagnosed Psoriasis (EPIDEPSO) longitudinal study was to investigate whether reduction of alexithymia may be associated with psoriasis therapeutic intervention. The rationale for reduction of alexithymia with clearance of psoriasis is based on the concept that patients with psoriasis may reduce their perception of emotion as a defence mechanism against stigmatization induced by skin lesions. By clearing psoriasis lesions, it may be hypothesized that this defence mechanism disappears. Patients described in the cross-sectional publication of the EPIDEPSO study⁷ were followed up for 1 year to evaluate the changes in alexithymia and psoriasis burden following real-life therapeutic intervention.

Patients and methods

Study design and population

EPIDEPSO is an observational, multicentre study with 1-year follow-up. The study population included consecutive patients

with a diagnosis of plaque psoriasis from outpatient dermatological clinics in 61 centres in 13 countries: Austria, Belgium, France, Greece, Ireland, Israel, Italy, the Netherlands, Norway, Russia, South Africa, Spain and the U.K. Included patients were adults with psoriasis with a duration of < 10 years, eligible for phototherapy or systemic therapy. The study design and the cross-sectional baseline analysis have been reported previously.⁷ Patients were included and followed up at 6 months and 1 year. The severity of psoriasis was assessed using the static Physician's Global Assessment (PGA),¹¹ scored from 0 (cleared) to 5 (severe), and the Psoriasis Area and Severity Index (PASI).¹²

Evaluation of alexithymia

Alexithymia was defined by a score ≥ 61 in the 20-item Toronto Alexithymia Scale (TAS-20),^{13,14} a self-administered questionnaire evaluating the three components of alexithymia: difficulty in identifying feelings (seven questions), difficulty in describing feelings (five questions) and externally oriented thinking (eight questions).

Patient-reported outcomes

Health-related quality of life was measured using the Dermatology Life Quality Index (DLQI).¹⁵ Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS),^{16,17} a 14-item scale with seven of the items relating to anxiety (HADS-A) and seven relating to depression (HADS-D). Patients were categorized as noncases (score 0–7), doubtful cases (8–10) or cases (11–21).

The self-reported Alcohol Use Disorders Identification Test (AUDIT) questionnaire¹⁸ was used to screen for excessive drinking. It consists of 10 questions, and a score ≥ 8 is associated with hazardous drinking and risk of alcohol dependency.

To assess impairment in work and activities, the Work Productivity and Activity Impairment Questionnaire: Psoriasis (WPAI:PSO)^{19,20} was used. It gives four scores: absenteeism (work time missed), presenteeism (impairment at work and reduced on-the-job effectiveness), work productivity loss (overall work impairment; absenteeism plus presenteeism) and activity impairment. The WPAI:PSO outcomes were expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity (i.e. worse outcomes).

Statistical analyses

The sample size was based on a clinically acceptable 95% confidence interval (CI) of the prevalence of alexithymia in a subgroup of 160 patients who had psoriasis for < 5 years (estimated to be around 20% of the total sample of 800 patients).⁷

The prevalence rates of alexithymia were calculated at the 6-month and 1-year follow-ups. Last observation carried forward (LOCF) analysis was performed in addition to observed case analysis. The prevalence of alexithymia was compared in subgroups of patients, depending on demographic characteristics, clinical variables and patient-reported outcomes, using Fisher's exact test for independent categorical variables, McNemar's test for dependent categorical variables and Wilcoxon's two-sample test (or t-test) for continuous variables. A P-value < 0.05 was considered statistically significant. TAS-20 data at baseline and the LOCF end point were used to calculate reliable-change indices.²¹ For the measurement scales, such as the TAS-20, DLQI, HADS, AUDIT and WPAI:PSO, the scores were calculated and missing items were handled according to the recommendations of the developers of the scales.

Results

Study population

Out of 670 patients included at baseline, LOCF data for 543 patients (81.0%) were available (follow-up analysis set). Six-month follow-up data were available for 522 individuals (77.9%) and 1-year data for 467 (69.7%). The TAS-20 questionnaire was completed by 536 patients at one or more of the follow-up visits, representing the follow-up analysis population.

The demographic and clinical characteristics of the 543 patients with follow-up data were comparable with those of the 127 patients who were not analysed, except for a slightly higher mean age in the follow-up analysis set: 44.5 ± 16.1 vs. 40.5 ± 16.3 years.

Psoriasis treatment in the cohort

In total, 49.6% of patients were treated with phototherapy and 50.4% received a systemic psoriasis treatment. The most frequently used systemic treatment in the cohort was methotrexate (48%), followed by ciclosporin (26%). Biological agents were prescribed in 14% of patients, with approximately half of the patients receiving ustekinumab and half receiving a tumour necrosis factor- α antagonist. Acitretin and fumaric acid were used by 7.9% and 3.5% of patients, respectively.

Change in alexithymia prevalence during the 1-year follow-up and relationship with demographic and psoriasis clinical characteristics

The overall prevalence of alexithymia in the follow-up set at baseline was 26.7% (95% CI 23.0–30.6). The prevalence was

21.2% (95% CI 17.8–25.0, $n = 515$) at 6 months and 18.8% (95% CI 15.3–22.7, $n = 458$) at 1 year. The decrease in alexithymia prevalence was significant at each time point compared with baseline (month 6, $P = 0.0032$; month 12, $P < 0.001$; LOCF end point $P = 0.001$; McNemar's test). At the end of the study (LOCF end point) more than half of the patients ($n = 77$, 53.8%) who were alexithymic at baseline became nonalexithymic. The mean percentage reduction in the TAS-20 in patients who shifted from alexithymic to nonalexithymic at 12 months was 27% (95% CI –30.6 to –24). Calculation of reliable-change indices for this group revealed that the change in TAS-20 score was reliable in 60% of the cases.

Of the three factors of the TAS-20, factor 1, difficulty in identifying feelings, displayed the highest mean percentage reduction at 12 months (–42.5%, 95% CI –47.6 to –37.3). Factor 2, difficulty in describing feelings, showed a mean 28.6% reduction at 12 months (95% CI –33.5 to –23.6). Factor 3, the externally oriented thinking subscale, showed the lowest mean percentage reduction (–7.6%, 95% CI –11.6 to –3.6). When looking at individual items of the TAS-20, the largest changes in patients who shifted to nonalexithymic were seen in questions relating to identifying and describing feelings (Table S1; see Supporting Information). Among the patients who had no or possible alexithymia at baseline, 36 (9.2%) had shifted towards alexithymia.

The prevalence of alexithymia at baseline and at the end of the study, according to demographic and clinical variables, is shown in Table S2 (see Supporting Information). The prevalence of alexithymia decreased in almost all patient categories. The decrease in alexithymia was higher in patients aged ≤ 40 years than in those aged > 40 years, in patients with a disease duration > 1 year from the first symptom or the first diagnosis compared with duration ≤ 1 year, and in patients with psoriasis of the face/neck or hands compared with patients who did not have psoriasis in those sites. For patients with PASI > 10 at baseline, the prevalence of alexithymia decreased from 33.6% at baseline to 16.8% at the end point, while for patients with baseline PASI ≤ 10 the prevalence remained approximately the same.

Relationship between change in alexithymia prevalence and change in psoriasis severity

The mean $\pm$ SD PASI improved from 10.2 $\pm$ 6.9 at baseline to 3.7 $\pm$ 5.3 at the LOCF end point. At the LOCF end point, 30.5% of patients reached $\geq 90\%$ improvement in PASI (PASI 90) and 46.3% reached PASI 75. The improvement in PASI was significantly higher in patients with alexithymia at baseline than in the other group (42.3% vs. 26.3% reached PASI 90, $P < 0.001$). Among patients who reached an outcome of PASI 75 or PASI 90, the prevalence of alexithymia significantly decreased (Table S2; see Supporting Information). For example, among patients who reached PASI 90, only 12.5% had alexithymia at follow-up. Similar results were obtained for the PGA: only 15.6% of patients with PGA ≤ 1 at follow-up had

alexithymia, while the prevalence of alexithymia in patients with PASI > 10 at follow-up was 41.5%.

Change in alexithymia prevalence during the 1-year follow-up and relationship with anxiety, depression and alcohol dependency

Table 1 describes the prevalence of alexithymia at baseline and at the end of the study in patients categorized by the presence or absence of anxiety, depression and hazardous alcohol use. As shown in our previous report,⁷ the prevalence of alexithymia at baseline was significantly higher in patients with anxiety, depression and hazardous alcohol use than in the others. During the 12-month follow-up, a striking decrease in alexithymia prevalence was observed in patients with depression and/or anxiety at baseline. Also, patients with an AUDIT score ≥ 8 at baseline had almost threefold reduction in alexithymia prevalence at the end of the study.

Evolution of work productivity

WPAI:PSO showed a decrease in the mean overall work productivity loss from 21.8 ± 29.9 at baseline to 11.3 ± 20.7 at the end point. Activity impairment at baseline had a mean score of 26.0 ± 28.9 ; at follow-up it decreased to 12.7 ± 22.0 . The WPAI absenteeism mean score was 7.9 ± 22.5 at baseline and 2.7 ± 11.5 at the end point.

Changes in patient-reported outcomes were more dramatic in patients with alexithymia

The changes from baseline to the end of the study in depression, anxiety, quality of life and hazardous drinking, according to alexithymic status at baseline, are graphically represented in Figure 1. The mean $\pm$ SD DLQI score reduced from 9.0 ± 6.7 at baseline to 4.5 ± 5.5 at follow-up. At baseline, patients with alexithymia reported worse quality of life, with a mean DLQI score of 12.5 ± 7.0 compared with 7.8 ± 6.1 in patients with no or possible alexithymia. The number of patients with a DLQI score > 10 decreased from 56.0% at baseline to 22.0% for the alexithymia group, and

from 27.8% to 10.3% for the no or possible alexithymia group.

The mean HADS-A and HADS-D scores improved in the follow-up cohort from 7.7 ± 4.3 and 5.4 ± 4.2 , respectively, at baseline to 6.1 ± 4.4 and 4.3 ± 4.1 at follow-up. HADS-A and HADS-D improvement was significantly higher in patients with baseline alexithymia than in patients with no or possible alexithymia at baseline: HADS-A: -3.5 ± 5.2 vs. -0.99 ± 3.3 , respectively; and HADS-D: -3.0 ± 5.0 vs. -0.39 ± 3.2 , respectively (both $P < 0.001$, Wilcoxon two-sample test).

Considering the presence of depression and anxiety, 29.5% of patients reported depression at baseline and 19.0% reported depression at the LOCF end point. In the group of patients who were alexithymic at baseline, the prevalence of depression decreased from 61.9% to 32.4%, while in the group with no or possible alexithymia that prevalence decreased from 17.6% to 14.1%. The rate of anxiety was 48.3% at baseline and 30.9% at the LOCF end point (change from 78.6% to 41.4% in the alexithymia group and from 37.0% to 27.0% in patients with no alexithymia at baseline).

Hazardous drinking, as defined by an AUDIT score ≥ 8 , was more frequent at baseline in patients who were alexithymic (30%) than in patients with no or possible alexithymia (13%). At the end of the study, the percentage of patients with an AUDIT score ≥ 8 was reduced more than twofold in patients who were alexithymic at baseline (from 30.3% to 12.7%).

Characteristics of patients with alexithymia who became nonalexithymic at follow-up

Based on the alexithymia status at baseline and the end point, four groups of patients can be identified: patients who did not change their alexithymic or nonalexithymic status, and those who did change their status. Figure 2 shows the difference between the follow-up and baseline mean scores for PASI, DLQI, HADS-A, HADS-D and AUDIT in these four groups. The most striking improvement (i.e. a decrease in the scores) was observed in the group of patients with alexithymia who became nonalexithymic at follow-up.

Table 1 Prevalence of alexithymia at baseline and at the end of the study according to patient-reported outcomes (n = 536)

	Total, n (%)	Alexithymia at baseline ^a	Alexithymia at end of study ^a
Baseline anxiety (HADS-A)			
Yes	250 (48.3)	110, 44.0 (37.8–50.4)	73, 29.2 (23.6–35.3)
No	268 (51.7)	30, 11.2 (7.7–15.6)	28, 10.4 (7.1–14.7)
Baseline depression (HADS-D)			
Yes	152 (29.5)	86, 56.6 (48.3–64.6)	52, 34.2 (26.7–42.3)
No	363 (70.5)	53, 14.6 (11.1–18.7)	45, 12.4 (9.2–16.2)
Baseline AUDIT score ≥ 8			
Yes	94 (17.6)	43, 46 (35.4–56.3)	15, 16 (9.2–25.0)
No	439 (82.4)	99, 22.6 (18.7–26.8)	86, 19.6 (16.0–23.6)

HADS, Hospital Anxiety and Depression Scale (A, anxiety; D, depression); AUDIT, Alcohol Use Disorders Identification Test. ^aData are given as n, % (95% confidence interval).

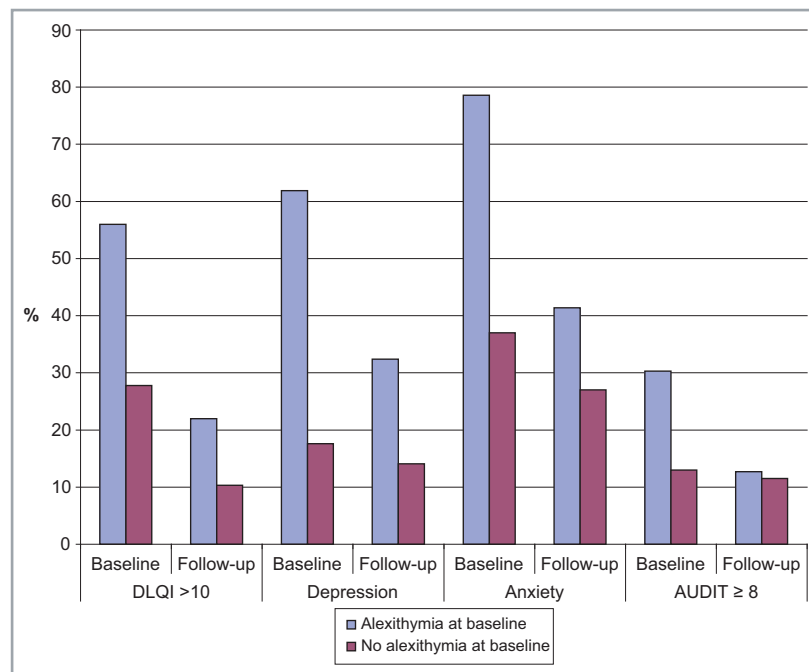


Fig 1. Percentage of patients with depression, anxiety, Dermatology Life Quality Index (DLQI) > 10 and Alcohol Use Disorders Identification Test (AUDIT) ≥ 8 at baseline and at follow-up (last observation carried forward), according to alexithymia status at baseline.

Table 2 compares the level of psoriasis severity improvement, quality-of-life improvement and psychological burden in patients with alexithymia who had a reversion in alexithymia compared with patients who remained alexithymic. Patients who became nonalexithymic had a much better control of their psoriasis at the end of the study, with a higher chance of reaching PASI 90 than patients who stayed alexithymic. Similarly, the prevalences of anxiety, depression and hazardous alcohol use at 1 year were much lower in patients who had a reversion in alexithymia.

Discussion

The 1-year follow-up of the EPIDEPSO study shows that the prevalence of alexithymia in patients with psoriasis treated with systemic agents in real-life conditions decreased significantly. This reduction was especially evident in patients younger than 40 years, in patients with a disease duration of > 1 year, in patients with psoriasis that was localized to the face/neck or hands, and in patients who reached a high level of disease control, defined by PASI 75 or PASI 90. The reversibility of alexithymia was associated with a dramatic improvement in quality of life, anxiety and depression. Moreover, hazardous alcohol use, which was highly prevalent in patients with alexithymia, was reduced almost threefold at 1 year, the reduction being more dramatic in patients who reversed their alexithymia.

The reversibility of alexithymia shown in psoriasis is in line with the notion that alexithymia may be partly modifiable with psychological interventions.²² In the present study, the therapeutic intervention consisted of real-life systemic

treatment for psoriasis. We observed a strong association between reversibility of alexithymia and tight control of psoriasis. Patients who reached PASI 90 after 1 year of treatment, and patients who were cleared or almost clear of psoriasis at follow-up, showed the highest reduction in alexithymia prevalence compared with patients who had lower clinical improvement.

The reversibility of alexithymia in psoriasis supports the concept that two forms of alexithymia exist – a ‘trait’ and a ‘state’²³ – the first being a personality characteristic and the latter being an acquired state that may be modified by a therapeutic intervention or a change in psychological status. Psoriasis is a chronic visible disease associated with a high level of stigmatization and has a profound effect on affective and social well-being. Kleyn *et al.*²⁴ have shown that patients with psoriasis shut down their neural and cognitive responses to certain emotions probably as a protective measure to cope with the permanent social stigmatization. This may explain the low emotional awareness identified in patients with psoriasis and the high prevalence of alexithymia, which may be considered a defence mechanism against stigmatization.^{7,25}

We and others have shown that alexithymia identifies a group of patients with psoriasis with severely impaired quality of life, high risk of depression and anxiety, high alcohol dependency and reduced work productivity. Here we show that reversibility of alexithymia is associated with a dramatic improvement in quality of life, reduction of depression and anxiety, and improvement in work productivity. Interestingly, hazardous alcohol use and alcohol dependency, as measured by AUDIT, were very prevalent in the EPIDEPSO cohort.⁷ High alcohol use has been associated with psoriasis,²⁶ and

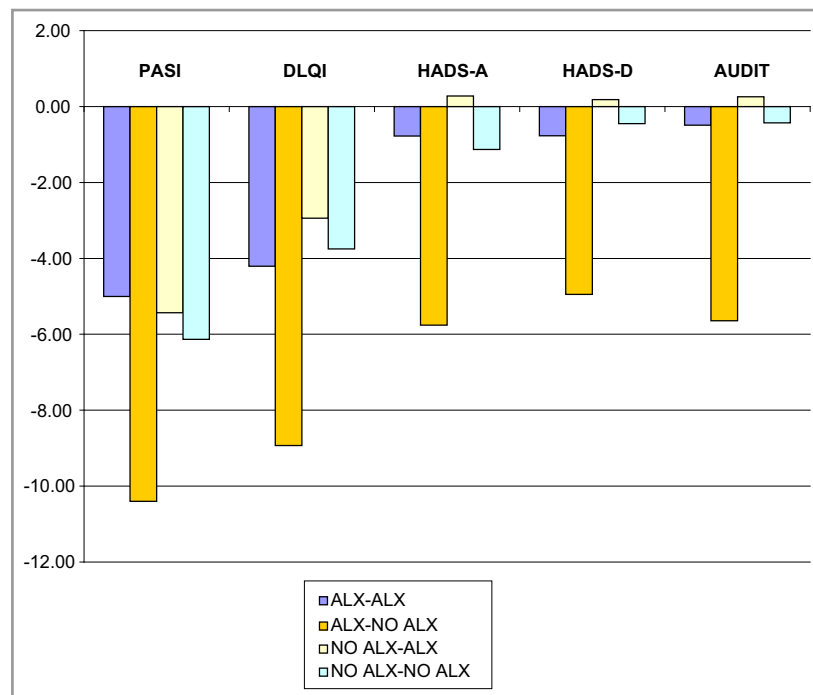


Fig 2. Difference between the follow-up and baseline scores according to change in alexithymia status. ALX-ALX, alexithymia at baseline and alexithymia at end point; ALX-NO ALX, alexithymia at baseline and no alexithymia at end point; NO ALX-ALX, no alexithymia at baseline and alexithymia at end point; NO ALX-NO ALX, no alexithymia at baseline and no alexithymia at end point. PASI, Psoriasis Area and Severity Index; DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale (A, anxiety; D, depression); AUDIT, Alcohol Use Disorders Identification Test. Negative changes represent improvement for all scales.

Table 2 Differences in outcomes for patients with alexithymia who became nonalexithymic at the end of the study vs. the patients who remained alexithymic

End point	Remained alexithymic (n = 66), % (95% CI)	Became nonalexithymic (n = 77), % (95% CI)
PASI < 3	50 (37–63)	75 (64–84)
PASI 75	36 (24–49)	70 (58–80)
PASI 90	21 (12–34)	59 (47–70)
DLQI 0/1	20 (11–31)	53 (41–65)
Anxiety (HADS-A > 8)	59 (46–71)	27 (17–38)
Depression (HADS-D > 8)	52 (39–64)	16 (9–26)
AUDIT > 8	20 (11–31)	7 (2–15)

CI, confidence interval; PASI, Psoriasis Area and Severity Index; PASI 75, $\geq 75\%$ improvement in PASI; DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale (A, anxiety; D, depression); AUDIT, Alcohol Use Disorders Identification Test.

recently, increased alcohol-related mortality has been shown in patients with psoriasis.²⁷ Thus the reduction of hazardous alcohol use observed in the cohort, especially in patients who had a reversion of alexithymia, is of particular importance for prevention.

To our knowledge, this is the first longitudinal study evaluating the change in the ability of patients with psoriasis to identify and describe emotions during treatment. In fact, the existing studies were cross-sectional.^{3–6} Only a longitudinal design may allow evaluation of changes over time and evaluation of the complex association between alexithymia, disease severity and disease burden. According to the results of the present study, there is at least a part of alexithymia that is reversible upon clinical improvement of psoriasis according to the TAS-20 questionnaire, a validated instrument to measure alexithymia. It has been shown that improvement in clinical severity and symptoms of psoriasis is associated with a decreased frequency of psychiatric disturbance, such as depression and anxiety.²⁸

There are some limitations in our study. Firstly, as the study concerns patients with a short disease duration, it is not possible to know whether the results apply to patients with longer disease duration. Secondly, even though we show a close association between the degree of psoriasis clearance and reversion of alexithymia, causality cannot be established due to the observational nature of the study. Thirdly, the relationship between alexithymia and depression should be interpreted with caution as the HADS, used in this study, has shown limitations in the ability to diagnose depression, and its diagnostic accuracy is currently under scrutiny.²⁹ Finally, the changes observed in the TAS-20 were variable across patients, and in a

minority of them the changes might not be clinically significant.

In conclusion, this study shows that the inability of patients to identify and describe emotions may be reversible in patients with psoriasis. Reversion of alexithymia is associated with improvement in several important domains, including quality of life, depression, anxiety, work productivity and addictive behaviour. Proactive recognition of patients with alexithymia, who have high psoriasis burden but are unable to express their feelings, may help to propose a therapeutic plan that includes tight control of psoriasis and psychological counselling.

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Supporting Information

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

Table S1 Magnitude of changes in 20-item Toronto Alexithymia Scale question responses in patients who experienced a reversion in alexithymia.

Table S2 Prevalence of alexithymia at baseline and at the end of the study, according to demographic and clinical variables.