three different underlying diseases. Buckley et al. reported that the incidence rate of TNFi-associated psoriasis for children with IBD was 10.9 per 1000 patient-years, 33.5 per 1000 patient-years for children with CNO and 14.7 per 1000 patient-years for children with JIA, which suggested a higher risk among children with underlying CNO. A prospective study with intention to collect specific data surrounding initiation of TNFi is required and longitudinal monitoring for paradoxical psoriasis within these populations needs to be further investigated. Particular attention to specific TNFi (including dosage, frequency, route of administration) and concomitant medications, severity of skin lesions, and response to treatment would provide additional information that may influence long-term treatment planning.

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References

1 Buckley LH, Xiao R, Perman MJ, Grossman AB, Weiss PF. Psoriasis associated with tumor necrosis factor inhibitors in children with inflammatory diseases. Arthritis Care Res (Hoboken) 2019; 73:215–20.

2 Mazloom SE, Yan D, Hu JZ et al. TNF-α inhibitor-induced psoriasis: a decade of experience at the Cleveland Clinic. J Am Acad Dermatol 2020; 83:1590–8.

3 Sherlock ME, Walters T, Tabbers MM et al. Infliximab-induced psoriasis and psoriasiform skin lesions in pediatric Crohn disease and a potential association with IL-23 receptor polymorphisms. J Pediatr Gastroenterol Nutr 2013; 56:512–18.

4 Shale M, Ghosh S. Learning the lessons of antitumour necrosis factor therapy-associated psoriasis. Can J Gastroenterol 2009; 23:674–6.

5 Groth D, Perez M, Treat JR et al. Tumor necrosis factor-α inhibitor-induced psoriasis in juvenile idiopathic arthritis patients. Pediatr Dermatol 2019; 36:613–17.

6 Perman MJ, Lovell DJ, Denson LA et al. Five cases of anti-tumor necrosis factor alpha-induced psoriasis presenting with severe scalp involvement in children. Pediatr Dermatol 2012; 29:454–9.

7 Campbell JA, Kodama SS, Gupta D, Zhao Y. Case series of psoriasis associated with tumor necrosis factor-α inhibitors in children with chronic recurrent multifocal osteomyelitis. JAAD Case Rep 2018; 4:767–71.

8 Zhao Y, Foster SK, Murdock Tj, Schlesinger M, Wallace CA. A rare case of chronic recurrent multifocal osteomyelitis with undifferentiated juvenile idiopathic arthritis, uveitis, and psoriasis. Case Reports Clin Med 2016; 5:225–32.

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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.

Validation of an Oral Disease Severity Score for use in oral lichen planus

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Dear Editor, Oral lichen planus (OLP) is a chronic inflammatory condition with a long clinical course and potentially negative impact on quality of life.1,2 The heterogeneous clinical presentation, lack of treatment consensus yet a need to ensure therapeutic efficacy, is compounded by the absence of a standardized and comprehensively validated disease scoring methodology. The Oral Disease Severity Score (ODSS) is a detailed oral scoring system that has been validated for use in oral pemphigus vulgaris (PV) and mucous membrane pemphigoid (MMP).3 We have previously demonstrated its usefulness for oral lichen planus.4,6 The aim of this study was to formally validate the ODSS in OLP.

Research ethics approval was obtained (REC15/ES/0038). Sixteen patients (aged 48–78 years) with active OLP (histologically confirmed) were recruited from oral medicine and dermatology clinics at Guy’s Hospital, London. Nine were on systemic treatment [mycophenolate mofetil (five), hydroxychloroquine (nine), low-dose prednisolone (three)] and seven on topical corticosteroid treatment alone [betamethasone soluble tablets (four) and flu tacson propionate nasules (three)].

Ten clinicians from four UK oral medicine centres participated. All were oral medicine specialists; one additionally a dermatologist. Patients were scored using the ODSS and the Physician Global Assessment (PGA).

The ODSS scores 17 oral mucosal sites. Each unit of site is given an activity score. Further details are given in the Table 1 legend.

Five clinicians were familiar with the scoring systems. Prior to the study, those unfamiliar were sent training slides demonstrating the ODSS and PGA. On the study day, all clinicians met for a detailed discussion of methodologies and a calibration exercise.
using clinical images. Each patient was scored by all 10 clinicians, with two clinicians rescoring all patients after a 2-h interval providing 12 sets of scores.

Fifteen subjects were required to achieve intraclass correlations (ICC) of 0.77 for the interobserver reliability. Interobserver reliability was tested by two raters performing two replications. This provided 80% power to detect an ICC difference of 0.50 (null value of 0.20). ICC level of agreement for ordinal or continuous measures followed Fleiss and Altman’s benchmark values for overall benchmark scales and Landis and Koch’s benchmark values for categorical outcomes.7–9

Sixteen patients (15 F : 1 M) with OLP and a mean (SD) age of 65 (8.4) (range 48–78) years were included (Table 1). The mean (SD) total ODSS score of 24.5 (10.6) (range 7–56) and median (interquartile range) 23 (16–30) reflected mild to moderately severe disease. The mean and median ODSS site, activity and pain score are listed in Table 1. The mean PGA score was 3.4 (1.8) (range 0–9) and median 3 (2–4).

The interobserver ICC (95% confidence interval) for the ODSS total was 0.98 (0.96–0.99). For the PGA, the ICC was 0.96 (0.91–0.98). Intra-observer agreement between initial scoring and rescoring of the same patients demonstrated an ICC for ODSS total of 0.85 (0.63–0.95) and 0.92 (0.71–0.98). The data pertaining to the inter- and intra-observer for site, activity and pain are presented in Table 1. All were rated as excellent. The PGA ICCs were 0.75 (0.42–0.91) and 0.88 (0.69–0.96).

There was good correlation between the ODSS total score and PGA (0.753, P < 0.0001). The mean (SD) time taken to complete the ODSS (total) was 124 (40) s. The PGA time was not recorded as it took less than 5 s.

This study has demonstrated ODSS to be a valid tool for assessing OLP with excellent intra- and interobserver reliability.

Sixteen participants were more than adequate to assess reliability. Using two clinicians to rescore patients resulted in 30 datasets compared with 20 if each clinician had rescored one patient. A minimum 2-h interval reduced recall bias.

No gold standard scoring system exists for OLP. Many disease severity scoring systems have been proposed, including two, the Modified White–Erosive–Atrophic (WEA-MOD) and Reticular–Erythematous/Ulcation (REU), that have been partially validated.10 No other system records as many clinical sites as the ODSS and the clinical descriptors are limited in comparison, which may mask subtle clinical changes.

The ODSS was designed by a consensus of experts and was already validated for use in PV and MMP offers wide clinical application and is quick to use. For use in OLP white asymptomatic lesions are given a site score proportional to the size of the area affected but an activity score of zero. The composite score encompassing 17 oral sites, activity and pain ensures a granular assessment and facilitates accurate monitoring of treatment response. The ODSS is primarily a disease severity scoring system; the subjective element of ODSS does not replace validated patient-reported outcome measures, such as the Chronic Oral Mucosal Disease Questionnaire.11 Construct validity was not examined, and this may be an area for further investigation. There was no difference in the reliability of scores between the clinicians familiar with and new to the ODSS. Clinician feedback was positive (‘quick to learn’, ‘easy to use’, ‘accurate’).

We propose that the ODSS be considered for routine recording of sequential disease activity in the clinic as well as in future multicentre studies.

Table 1 Scores, inter- and intra-observer reliability for each of the disease severity scoring systems and their individual components

| Scoring system | Range | Mean (SD) | Median (IQR) | Intraclass correlation coefficient (95% CI) |
|----------------|-------|-----------|--------------|-------------------------------------------|
| ODSS Site      | 3–19  | 10.6 (3.5) | 10 (8–13)    | 0.97 (0.93–0.99) Intrarater 1 Observer 1 |
| ODSS Activity  | 0–34  | 11.2 (7.2) | 10 (5–15)    | 0.97 (0.95–0.99) Intrarater 1 Observer 1 |
| ODSS Pain      | 0–8   | 3.0 (2.3)  | 3 (1–5)      | 0.99 (0.99–1.00) Intrarater 1 Observer 1 |
| ODSS Total (0–106) | 7–56 | 24.5 (10.8) | 23 (16–30)  | 0.98 (0.96–0.99) Intrarater 1 Observer 1 |
| PGA (0–10)     | 0–9   | 3.4 (1.8)  | 3 (2–4)      | 0.96 (0.91–0.98) Intrarater 1 Observer 1 |

*The sites are the outer lip, inner lips, buccal mucosa right/left, soft palate right/left, hard palate right/left, dorsum of tongue right/left, ventrolateral tongue right/left, floor of mouth right/left, oropharynx right/left and the gingivae (divided into 6 segments). Site score 0 (no lesion) or 1 (lesion), buccal mucosa: 1 (∋ 50%) or 2 (∋ 50%); dorsum of tongue, floor of mouth, hard or soft palate or oropharynx: 1 (unilateral) or 2 (bilateral). Where a site has a score of 2, each site unit is allocated an activity score, which are then added together. Activity score: 1, mild erythema; 2, marked erythema without ulceration; 3, erosion or ulceration. White asymptomatic lesions are given a site score proportional to the size of the area affected but an activity score of zero. Pain score: Analogue scale from 0 (no discomfort) to 10 (the most severe pain they have encountered with this condition so far); the patient is asked to provide a score reflecting their pain/discomfort as an average of the preceding week. Total Score = Site Score + Activity Score + Pain Score (0–10) (maximum 106). Overall benchmark values = excellent in all instances. Assessment for the level of agreement in terms of the intraclass correlation coefficients followed Fleiss and Altman’s benchmark scales.7,8 *P-values < 0.0001 in all instances. ODSS, Oral Disease Severity Score; PGA, Physician Global Assessment; IQR, interquartile range; CI, confidence interval.*
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References
1 Alrashdan MS, Cirillo N, McCullough M. Oral lichen planus: a literature review and update. Arch Dermatol Res 2016; 308: 539–51.
2 Winyakijja P, Porter S, Fedele S et al. Health-related quality of life and its associated predictors in patients with oral lichen planus: a cross-sectional study. Int Dmt J 2020; https://doi.org/10.1111/idj.12607.
3 Ormond M, McParland H, Donaldson ANA et al. An Oral Disease Severity Score validated for use in oral pemphigus vulgaris. Br J Dermatol 2017; 177: 872–81.
4 Ormond M, McParland H, Thakrar P et al. Validation of an Oral Disease Severity Score (ODSS) for use in oral mucous membrane pemphigoid. Br J DERMATOL 2020; 183: 78–85.
5 Escudier M, Ahmed N, Shirlaw P et al. A scoring system for mucosal disease severity with special reference to oral lichen planus. Br J Dermatol 2007; 157: 765–70.
6 Wee J, Shirlaw PJ, Challacombe SJ, Setterfield JF. Efficacy of mycopHENolate mofetil in severe mucocutaneous lichen planus: a retrospective review of 10 patients. Br J Dermatol 2012; 167: 36–43.
7 Shroud PE, Fleiss JL. Intraclass correlations uses in assessing rater reliability. Psychol Bull 1979; 86: 420–8.
8 Altman DG. Practical Statistics for Medical Research. London: Chapman and Hall, 1991.
9 Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977; 33: 159–74.
10 Wang J, van der Waal I. Disease scoring systems for oral lichen planus: a critical appraisal. Med Oral Patol Oral Cir Bucal 2015; 20: e199–e204.
11 Ni Riordain R, McCreary C. Validity and reliability of a newly developed quality of life questionnaire for patients with chronic oral mucosal diseases. J Oral Pathol Med 2011; 40: 604–9.

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The contribution of itch and skin severity improvements to the Dermatology Life Quality Index in patients with atopic dermatitis in baricitinib phase III trials

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Dear editor, Baricitinib, an oral, selective Janus kinase (JAK)1/2 inhibitor, is approved in several countries for the treatment of moderate-to-severe atopic dermatitis (AD) in adults who are candidates for systemic therapy. With data from three monotherapy baricitinib phase III randomized clinical trials (RCTs),1,2 we conducted a post hoc mediator analysis to assess whether changes in itch or skin severity mediated the treatment effect over placebo in health-related quality of life (HRQoL).

This analysis included data from BREEZE-AD1 (NCT03334396), BREEZE-AD2 (NCT03334422) and BREEZE-AD5 (NCT03435081). Detailed methods of the RCTs have been published.1,2 The RCTs were double-blind, parallel-group, placebo-controlled trials of adults with moderate-to-severe AD with inadequate or intolerable responses to topical therapy. Patients were randomly allocated to once-daily placebo, baricitinib 2 mg or baricitinib 4 mg in BREEZE-AD1 and BREEZE-AD2; and to placebo, baricitinib 1 mg or baricitinib 2 mg in BREEZE-AD5. Here, we focus on data from the arms receiving placebo, baricitinib 2 mg and baricitinib 4 mg. Because BREEZE-AD1 and BREEZE-AD2 were twin studies conducted at the same time in Europe, Asia, Latin America and Australia, data from these studies were pooled together for the mediator analysis. The BREEZE-AD5 study was conducted in North America, and its data are presented separately.

Patients were aged ≥18 years and had a ≥1-year history of AD. At screening and baseline, patients were required to have an Eczema Area and Severity Index (EASI) score ≥16, a validated Investigator’s Global Assessment for AD (vIGA-AD) score ≥3, and body surface area of involvement ≥10%, as derived from the EASI assessment.1,2

Itch was measured by change from baseline in a numerical rating scale (NRS) with ranges from 0 (no itch) to 10 (worst itch imaginable). We assessed the weekly average in itch NRS, skin severity with EASI, and the Dermatology Life Quality Index (DLQI).

This post hoc analysis was based on data from the first 16 weeks of treatment. We assessed the least-squares mean change from baseline to week 4 or week 16. The multiple mediation model used change in DLQI from week 4 or 16 as the dependent variable, and treatment (baricitinib 2 mg, baricitinib 4 mg or placebo) as the independent variable.1,2 Itch and EASI at weeks 4 or 16 were the mediators. The total treatment effect over placebo for changes in