Item-Level Psychometric Properties for a New Patient-Reported Psoriasis Symptom Diary

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ABSTRACT

Objectives: This research evaluated the psychometric properties of a new Psoriasis Symptom Diary, identified diary responder definitions for use in determining whether a patient has experienced clinically meaningful change, and refined diary item content for use in future clinical trials. Methods: The Psoriasis Symptom Diary was administered in a phase 2 clinical trial of AIN457 to US adult outpatients (N = 172) with physician-diagnosed moderate to severe chronic plaque-type psoriasis. Participant compliance with daily diary administration and item score variability, reliability, construct and discriminant validity, sensitivity to change, and interpretation were all evaluated. Results: Participants completed 94% of scheduled diary assessments across 12 study weeks. Diary items were generally normally distributed, and no floor or ceiling effects were observed. Item reliability (reproducibility) was acceptable (intraclass correlation coefficients > 0.80), with an exception for one item (skin color). At week 12, items significantly related to criterion measures as predicted (Psoriasis Area and Severity Index r = 0.27–0.57; Investigator’s Global Assessment r = 0.25–0.59), with the exception of items that measured skin color and difficulty using hands. Most items generated change scores that were synchronous to changes as measured by the Psoriasis Area and Severity Index, Investigator’s Global Assessment, Dermatology Life Quality Index (r > 0.37), as well as the Patient Global Impression of Change. Responders experienced a 2- to 3-point and 3- to 5-point change in item scores for minimal and large improvements, respectively. Four items that did not perform well were dropped from the diary. Conclusions: The 16-item Psoriasis Symptom Diary demonstrated favorable psychometric properties and is a brief, useful tool for measuring patient-based symptoms and the impact of chronic plaque psoriasis.

Keywords: diary, patient-reported outcome, psoriasis, symptom.

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Introduction

Psoriasis is a chronic inflammatory disease of the skin with prevalence rates estimated between 2.2% and 4.6% in the United States [1]. Patients with the most common form, plaque psoriasis, demonstrate red and white scaly patches and plaques (most frequently on the knees, elbows, palms of hands, soles of feet, scalp, and genitals). Many patients experience localized plaques, though some, psoriasis covers the entire body. Common symptoms reported by patients with plaque psoriasis include plaque-related pain, changes in skin appearance, and pruritus [2]. The impact of psoriasis on health-related quality of life is substantial [3]; in fact, reductions in physical and emotional functioning are comparable to those reported for major medical conditions such as cancer, arthritis, hypertension, heart disease, diabetes, and depression [4]. Psoriasis’ impact on daily activities, social relationships, work productivity, sleep, body image, and sexual and other functional areas has been reported in several studies [5–11]. Because patients’ experience of psoriasis varies greatly from person to person and because some treatment effects are known only to patients, the assessment of disease severity and outcomes from the patient perspective is especially important for comprehensive health assessment and clinical decision making.

Clinician measures of psoriasis have traditionally been used in trials and practice. And, while existing clinician-reported instruments capture valuable aspects of disease severity and outcomes, there are notable limitations [12]. For instance, the Psoriasis Area and Severity Index (PASI) is used by clinicians to assess the severity of psoriatic lesions on the basis of area coverage and plaque appearance. Although it is one of the most widely used measures in psoriasis research, the PASI has been criticized as limited by insufficient interrater reliability and construct validity, and lack of sensitivity and consensus on interpretability [12–15]. Also, clinician measures such as the PASI may not reflect the most important aspects of psoriasis to the patient. For instance, the PASI is only modestly correlated with patient-reported outcome (PRO) measures of psoriasis, and many patients who are categorized as a “treatment success” on the PASI report dissatisfaction with their condition [16,17]. PRO measures of psoriasis are only modestly correlated with patient-reported outcome (PRO) measures of psoriasis, and many patients who are categorized as a “treatment success” on the PASI report dissatisfaction with their condition [16,17].
Various PRO measures have been used to assess patients with psoriasis, including generic PRO measures (e.g., short-form 36 health survey and EuroQol five-dimensional [EQ-5D] questionnaire), which do not address psoriasis-specific symptoms and impacts, and dermatology-specific instruments including the Dermatology Life Quality Index (DLQI), Skindex-29, Skindex-16, Psoriasis Symptom Assessment, Koo-Menter Psoriasis Instrument, the Psoriasis Disability Index, and the QualiPso Questionnaire [17,19–24]. While these measures assess varied aspects of a patient’s daily life, it is not clear whether any of them adequately measures the signs and symptoms of psoriasis. Because signs and symptoms are more directly related to underlying disease pathology than other indicators [25], sign/symptom measures may be more sensitive to treatment effects and may be more likely to support label claims in a regulatory context than more generic concepts, such as quality of life [26]. Existing dermatology-specific PRO measures may not include symptoms and impacts that are most relevant to patients with psoriasis. Other potential limitations include numerous items, relatively long recall periods, no measure of symptom severity, or assessment of multiple symptoms in a single item.

The Psoriasis Symptom Diary (referred to here as “Psoriasis Diary”) was developed to address the limitations of existing instruments. Psoriasis Diary items were constructed on the basis of results from qualitative interviews with patients and psoriasis experts and a review of the published literature [2]. Items address key symptoms (severity and bother) and functional impacts that are most relevant to patients with chronic plaque psoriasis, including psoriasis-related pruritus, stinging, burning, pain, pain from cracking, scaling, affected skin color, embarrassment due to plaques, avoidance of activities with other people due to plaques, and difficulties with mobility due to plaques, including bending joints, walking, and using hands and fingers. Because of potential variability in signs and symptoms during and across days, particularly in the context of a clinical trial in which treatment is administered, the Psoriasis Diary was developed as a daily diary.

Previous work on the Psoriasis Diary established the content validity of the measure and demonstrated patient understanding of instructions, items, and response scales [2]. The present study focuses on the Psoriasis Diary item-level scores and their performance and is not intended to address the potential for scaling and broader applications of the measure, which may be the subject of future research. The specific objectives of the current research were to 1) examine the quantitative psychometric characteristics of 20 items comprising the Psoriasis Diary, 2) identify responder definitions that can be used to determine whether a patient has experienced clinically meaningful change on the diary items, and 3) refine the item content for a version of the measure that can be used in future clinical trials.

Methods

Study Design

This multicenter, parallel-group, randomized, double-blind, placebo controlled trial assessing the efficacy and safety of a new treatment for chronic plaque psoriasis consisted of four periods: screening, induction treatment, maintenance treatment, and follow-up. The screening period lasted up to 4 weeks and was used to assess eligibility and to taper patients off disallowed medications. Eligible patients were randomized to one of the induction treatment arms, 1) induction with single injection —“Single”: AIN457 150 mg subcutaneously administered at randomization (or baseline); 2) induction with monthly injections —“Monthly”: AIN457 150 mg subcutaneously administered at randomization, week 4, and week 8; 3) early loading induction —“Early”: AIN457 150 mg subcutaneously administered at randomization, week 1, week 2, and week 4; or 4) “Placebo” administered at randomization, week 1, week 2, week 4, and week 8, and received study medication according to the treatment schedule of their assigned treatment arm up to week 12.

Sample

Adult (ages ≥18 years) outpatients with physician-diagnosed moderate to severe chronic plaque-type psoriasis for at least 6 months at the time of randomization were eligible to participate in the study. Patients were required to have a PASI score of 12 or more, 10% or more body surface area affected by plaque psoriasis, and Investigator’s Global Assessment (IGA) score of 3 or more to ensure that the enrolled sample included patients with moderate to severe psoriasis. Eligible patients’ psoriasis was inadequately controlled by topical treatment, phototherapy, and/or previous systemic therapy at the time of screening and randomization. Participants were excluded from the study if they had forms of psoriasis other than the chronic plaque-type, drug-induced psoriasis, or known immunosuppression (e.g., AIDS) at screening or randomization; active tuberculosis at screening; or active systemic infections, ongoing use of prohibited psoriasis or other treatments/medications, use of other biological agents, systemic psoriasis treatments or photochemotherapy (i.e., psoralen plus ultraviolet light therapy), phototherapy (i.e., ultraviolet A light, ultraviolet B light) or topical psoriasis treatments, or any investigational psoriasis or nonpsoriasis drug use prior to randomization.

Measures

Psoriasis Symptom Diary

The Psoriasis Symptom Diary (or “Psoriasis Diary”) is a 20-item electronic daily (24-hour recall) assessment that measures psoriasis symptoms and impact on functional health [2]. Symptom items assess the severity and bother of psoriasis-related itching, stinging, burning, pain, scaling, and skin color. Impact items assess the embarrassment, avoidance of activities with other people, and movement restriction that psoriasis is known to impose on individuals with the condition. Symptom severity, bother, and impact items use a 0 to 10 numerical rating scale, with higher scores indicating more severe symptoms, bother, or impact. Color of psoriasis-affected skin is assessed by using a categorical rating scale (pink; light red or brown; bright red or purple; deep dark red, purple, or brown; gray, white, or silver). Symptom bother items are administered only if a patient selects a numerical rating scale rating greater than 0 on the corresponding symptom severity item (i.e., he or she reported experiencing the psoriasis-related symptom on a given day) (see Table 1).

Criterion measures used to evaluate the Psoriasis Diary included the following:

PASI [27]

The PASI was used in evaluating construct validity at baseline and week 12, sensitivity to change (baseline to week 12), and the interpretation of change scores (responder analysis, day 85 administration) produced by the Psoriasis Diary. At week 12, the PASI score classified participants as treatment responders (patients achieving ≥75% improvement [reduction] from baseline PASI score [also referred as PASI 75]), partial responders (patients achieving a ≥50% improvement from baseline PASI score [PASI
<table>
<thead>
<tr>
<th>Psoriasis Symptom Diary item</th>
<th>Response options (0–10 NRS)*</th>
<th>n</th>
<th>Mean</th>
<th>Median</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
<th>Reliability analysis (ICC; 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Overall, how severe was your psoriasis-related itching over the past 24 hours?</td>
<td>0 = No itching 10 = Itching as bad as you can imagine</td>
<td>169</td>
<td>6.43</td>
<td>7.00</td>
<td>2.46</td>
<td>0</td>
<td>10</td>
<td>.91 (0.88–0.94)</td>
</tr>
<tr>
<td>2. Overall, how bothered were you by your psoriasis-related itching over the past 24 hours?</td>
<td>0 = Not bothered at all 10 = Bothered as bad as you can imagine</td>
<td>168</td>
<td>6.61</td>
<td>7.17</td>
<td>2.46</td>
<td>1</td>
<td>10</td>
<td>.91 (0.88–0.94)</td>
</tr>
<tr>
<td>3. Overall, how severe was your psoriasis-related stinging over the past 24 hours?</td>
<td>0 = No stinging 10 = Stinging as bad as you can imagine</td>
<td>169</td>
<td>4.92</td>
<td>5.29</td>
<td>2.90</td>
<td>0</td>
<td>10</td>
<td>.92 (0.89–0.95)</td>
</tr>
<tr>
<td>4. Overall, how bothered were you by your psoriasis-related stinging over the past 24 hours?</td>
<td>0 = Not bothered at all 10 = Bothered as bad as you can imagine</td>
<td>159</td>
<td>5.48</td>
<td>5.50</td>
<td>2.67</td>
<td>0</td>
<td>10</td>
<td>.91 (0.88–0.94)</td>
</tr>
<tr>
<td>5. Overall, how severe was your psoriasis-related burning over the past 24 hours?</td>
<td>0 = No burning 10 = Burning as bad as you can imagine</td>
<td>169</td>
<td>4.67</td>
<td>4.71</td>
<td>3.00</td>
<td>0</td>
<td>10</td>
<td>.94 (0.92–0.96)</td>
</tr>
<tr>
<td>6. Overall, how bothered were you by your psoriasis-related burning over the past 24 hours?</td>
<td>0 = Not bothered at all 10 = Bothered as bad as you can imagine</td>
<td>151</td>
<td>5.54</td>
<td>5.43</td>
<td>2.53</td>
<td>0</td>
<td>10</td>
<td>.90 (0.85–0.93)</td>
</tr>
<tr>
<td>7. Overall, how severe was the pain from your psoriasis-affected skin cracking over the past 24 hours?</td>
<td>0 = No pain 10 = Pain as bad as you can imagine</td>
<td>169</td>
<td>4.88</td>
<td>5.00</td>
<td>2.96</td>
<td>0</td>
<td>10</td>
<td>.93 (0.90–0.95)</td>
</tr>
<tr>
<td>8. Overall, how bothered were you by the pain from your psoriasis-affected skin cracking over the past 24 hours?</td>
<td>0 = Not bothered at all 10 = Bothered as bad as you can imagine</td>
<td>159</td>
<td>5.46</td>
<td>5.57</td>
<td>2.71</td>
<td>0</td>
<td>10</td>
<td>.89 (0.84–0.92)</td>
</tr>
<tr>
<td>9. Overall, how severe was your psoriasis-related pain over the past 24 hours?</td>
<td>0 = No pain 10 = Pain as bad as you can imagine</td>
<td>169</td>
<td>4.75</td>
<td>4.75</td>
<td>2.98</td>
<td>0</td>
<td>10</td>
<td>.93 (0.90–0.95)</td>
</tr>
<tr>
<td>10. Overall, how bothered were you by your psoriasis-related pain over the past 24 hours?</td>
<td>0 = Not bothered at all 10 = Bothered as bad as you can imagine</td>
<td>155</td>
<td>5.49</td>
<td>5.43</td>
<td>2.64</td>
<td>0</td>
<td>10</td>
<td>.90 (0.86–0.93)</td>
</tr>
<tr>
<td>11. Overall, how severe was your psoriasis scaling over the past 24 hours?</td>
<td>0 = No scaling 10 = Scaling as bad as you can imagine</td>
<td>169</td>
<td>6.61</td>
<td>7.00</td>
<td>2.34</td>
<td>0</td>
<td>10</td>
<td>.90 (0.87–0.93)</td>
</tr>
<tr>
<td>12. Overall, how bothered were you by your psoriasis scaling over the past 24 hours?</td>
<td>0 = Not bothered at all 10 = Bothered as bad as you can imagine</td>
<td>168</td>
<td>6.72</td>
<td>7.14</td>
<td>2.43</td>
<td>0.4</td>
<td>10</td>
<td>.91 (0.88–0.94)</td>
</tr>
<tr>
<td>13. Overall, what was the color of most of your psoriasis-affected skin over the past 24 hours?</td>
<td>A. Pink  B. Light red or brown  C. Bright red or purple  D. Deep dark red, purple, or brown  E. Gray, white, or silver</td>
<td>169</td>
<td>3.12</td>
<td>3.00</td>
<td>1.42</td>
<td>1</td>
<td>5</td>
<td>.75 (0.67–0.82)</td>
</tr>
<tr>
<td>14. Overall, how noticeable did you think the color of your psoriasis-affected skin was over the past 24 hours?</td>
<td>0 = Not at all noticeable 10 = Noticeable as bad as you can imagine</td>
<td>169</td>
<td>7.28</td>
<td>7.83</td>
<td>2.42</td>
<td>0</td>
<td>10</td>
<td>.93 (0.90–0.95)</td>
</tr>
<tr>
<td>15. Overall, how much did you try to hide your psoriasis-affected skin over the past 24 hours?</td>
<td>0 = Did not try to hide at all 10 = Totally avoided being seen by others</td>
<td>169</td>
<td>6.65</td>
<td>7.60</td>
<td>3.04</td>
<td>0</td>
<td>10</td>
<td>.92 (0.88–0.94)</td>
</tr>
<tr>
<td>16. Overall, how much did your psoriasis cause you to avoid activities with other people over the past 24 hours?</td>
<td>0 = You did not avoid other people 10 = Avoided other people as much as you ever have</td>
<td>169</td>
<td>4.66</td>
<td>5.43</td>
<td>3.58</td>
<td>0</td>
<td>10</td>
<td>.96 (0.95–0.98)</td>
</tr>
<tr>
<td>17. Overall, how embarrassed were you because of your psoriasis over the past 24 hours?</td>
<td>0 = No embarrassment 10 = Embarrassment as bad as you can imagine</td>
<td>169</td>
<td>6.50</td>
<td>7.43</td>
<td>3.16</td>
<td>0</td>
<td>10</td>
<td>.94 (0.91–0.95)</td>
</tr>
<tr>
<td>18. In the past 24 hours, how hard was it to bend your joints because of the psoriasis on your skin?</td>
<td>0 = Not hard 10 = As hard as you can imagine</td>
<td>169</td>
<td>2.64</td>
<td>1.71</td>
<td>2.80</td>
<td>0</td>
<td>10</td>
<td>.92 (0.89–0.95)</td>
</tr>
</tbody>
</table>
PGIC as part of a broader study assessing the efficacy and safety of a new treatment for chronic plaque psoriasis. Physicians reported PASI results through an interactive voice response system, and IGA scores were used to evaluate the efficacy and safety of the treatment. The IGA score is expected to complete across a specified time period (e.g., 12 weeks) of the study.

Analyses

Psychometric performance of the Psoriasis Diary was evaluated by using standard analytic procedures and measurement review criteria developed by the Scientific Advisory Committee of the Medical Outcomes Trust and further elaborated by the Food and Drug Administration.

Data from a subsample of study participants completing the measures through week 12 were used in the analysis of measurement properties. Data collected during both the screening and induction periods of the study were used to evaluate item reliability, validity, responsiveness, and interpretability. Analyses focused on baseline, week 1, and week 12 data.

Handling of Data

Daily Psoriasis Diary scores were averaged into a weekly (i.e., 7 day) score for each item (no subscales were derived through aggregation across items). Four completed days (consecutive or nonconsecutive) were necessary to derive a weekly score for each Psoriasis Diary item; otherwise, data were considered missing for that week. The last observation carried forward principle was applied to the PASI, IGA, DLQI, EQ-5D questionnaire, and Pruritus VAS measurements that were missing at week 12 if at least one postbaseline assessment was available.

Compliance

Compliance rates were calculated to evaluate participants’ ability and willingness to self-administer the Psoriasis Diary. Compliance rates reflect the number of completed assessments relative to the total number of evening assessments the participants were expected to complete across a specified time period (e.g., 12 weeks) of the study.

Item Distributions

The Psoriasis Diary item scores at baseline were assessed through an examination of descriptive and frequency statistics. Item floor or ceiling effects were concluded if more than 50% of the participants reported no experience or the highest level of severity of the symptom, respectively. Item-to-item correlations were used to evaluate possible redundancy (r > 0.80) between Psoriasis Diary items.

Reliability

Intraclass correlation coefficients were calculated to assess whether the Psoriasis Diary yields reproducible scores during a stable period (when minimal or no change in the condition is expected). Analyses were conducted on a subsample (n = 128) of participants indicating no change (“About the same”) on the PGIC at a 2-week interval (between week 2 and week 1 of the screening period/before the first study medication administration).
Cronbach’s alpha, an internal consistency estimate of the reliability of test scores, was not estimated in this study because scaling has not yet been evaluated for the Psoriasis Diary.

Construct Validity
Construct validity was evaluated through an examination of correlations between Psoriasis Diary items and criterion measures. Pearson and Spearman correlation coefficients were computed between each Psoriasis Diary item and the PASI and the IGA (baseline, week 12), and the DLQI, the EQ-5D questionnaire, and the Pruritus VAS (week 1) with the following hypotheses: 1) Psoriasis Diary symptom severity items would be more strongly associated with the PASI and the IGA than with the EQ-5D questionnaire, 2) Psoriasis Diary symptom bother items would be more strongly correlated with the DLQI than with the EQ-5D questionnaire, and 3) Psoriasis Diary items on itching (severity and bother) would be strongly correlated with the Pruritus VAS.

Discriminant Validity
Analysis of variance was used to evaluate whether the Psoriasis Diary items were able to distinguish between groups expected to differ clinically. Clinically distinct groups were defined in two ways: on the basis of the IGA (mild 0–2, moderate 3, and severe 4–5) and PASI (tertiles) score levels at week 12.

Sensitivity to Change
Sensitivity of the Psoriasis Diary items to actual changes in the clinical condition over time was assessed by examining correlations between change scores for the Psoriasis Diary and criterion measures. Change scores were calculated for the Psoriasis Diary, the PASI, and the IGA (week 12 – baseline) and for the DLQI (week 12 – week 1), and Pearson correlation coefficients were generated to assess the relationship between change scores. Analysis of variance was used to examine differences in Psoriasis Diary symptom severity mean change scores by PGIC level. In addition, mean change in Psoriasis Diary items at each week up to week 12 was evaluated with Cohen’s effect size statistics [36].

Responder Definition
Clinically meaningful change reflects the point at which a change in a score can be interpreted as clinically important, and is used to understand test scores beyond what is provided for by “statistically significant” results. An anchor-based approach was used to assess clinically meaningful change in Psoriasis Diary item scores. Psoriasis Diary symptom severity item scores (means and SDs) were computed for each level of change reported by the PGIC items. Minimally important differences were defined as differences between the scores reported for the “About the same” group and the group reporting “A little better.”

Another way to evaluate a patient’s response to treatment as measured by the Psoriasis Diary is to attend to within-person changes in each study group to determine the proportion of patients who respond adequately to treatment. At week 12, the PASI score classified patients as responders (PASI 75%, patients achieving ≥75% improvement [reduction] from baseline PASI score), partial responders (PASI 50%, patients achieving a ≥50% improvement from baseline PASI score but <75%), or nonresponders (patients not achieving a PASI reduction of at least 50% from baseline PASI score). The PASI responder definitions were used to classify patients, the mean Psoriasis Diary symptom severity scores were computed for each PASI classification, and differences were evaluated for each responder group.

Results
A subset of participants (N = 172) from the larger US trial was used in the current study to evaluate the psychometric properties of the Psoriasis Diary and included patients who completed the Psoriasis Diary up to week 12. The number of patients providing data for each week varied because of some missing data. The sample ranged in age from 18 to 75 years (mean age = 43.78 ± 12.57), and was predominantly male (69%) and Caucasian (96%).

Compliance
Of the 1,183 assessment opportunities that were available to the n = 169 patients during the baseline week, only 57 were missed, resulting in a compliance rate of 95.2%. When examining the total number of assessments over the entire database (17,524 assessment opportunities), there were 6.1% (1,072) missed evening reports, resulting in an overall compliance rate of 93.9% across the 12 weeks of the study.

Item Distributions
Table 1 presents descriptive statistics for each of the Psoriasis Diary items during the baseline week. Participants reported experiencing a variety of psoriasis symptoms and impacts, and each symptom was reported (score > 0 on the numerical rating scale on at least 1 day) by 90% to 99% of the patients during the baseline week. Psoriasis Diary items were generally normally distributed, with the exception of three items asking about difficulty moving, which were positively skewed, indicating that few patients endorsed these effects. No floor or ceiling effects were observed from this analysis. Strong correlations were found for some items (i.e., burning, stinging, and pain), though the items were retained at this point given that they were uniquely identified by patients as important and relevant to them and not fully represented in existing measures. The question of whether to ultimately retain them in future versions of the questionnaire can be addressed on further psychometric evaluation. Severity and bother items on the same symptom (e.g., itching severity and itching bother) were highly correlated (r = 0.83–0.97).

Reliability
Intraclass correlation coefficients were acceptable (>0.80) [37] for all items except for color of psoriasis-affected skin (see Table 1).

Construct Validity
Table 2 presents correlations for Psoriasis Diary item scores and scores produced by the PASI and the IGA at baseline and week 12 and the Pruritus VAS, the DLQI, and the EQ-5D questionnaire VAS at week 1. Correlations at baseline between Psoriasis Diary items and the clinician-based PASI and IGA assessments were weak and nonstatistically significant; however, with the exception of the item assessing difficulty using hands, correlations were much stronger and statistically significant at week 12. Psoriasis symptom severity and bother items were significantly related to the DLQI and itching VAS (with the exception of color of skin) but were not strongly correlated with the EQ-5D questionnaire, as expected (correlations < 0.25). As predicted, the Psoriasis Diary symptom severity items were more strongly associated with the PASI and the IGA than with the EQ-5D questionnaire, and the Psoriasis Diary symptom bother items were more strongly correlated with the DLQI than with the EQ-5D questionnaire. The Psoriasis Diary items on itching (severity and bother) strongly correlated with the Pruritus VAS Scale, as well as with the PASI, IGA, and DLQI.
Discriminant Validity
Psoriasis Diary item scores significantly distinguished between PASI tertile and IGA severity groups, with the exception of the item to assess difficulty using fingers. Figure 1 demonstrates discrimination results for the itching severity item.

Sensitivity to Change
Changes in Psoriasis Diary item scores from baseline to week 12 were significantly and moderately (r > 0.37) correlated with changes in the PASI, IGA, and DLQI, except for items assessing color of skin, ability to move joints, walk, and use hands (see Table 3). Statistically significant differences were found in Psoriasis Diary item mean change scores by PGIC level at 12 weeks (see Fig. 2; e.g., itching severity). Participants reporting an improvement on the PGIC had significantly higher Psoriasis Diary mean scores (for all items) than did those who reported that their psoriasis stayed about the same or worsened. Effect size coefficients were moderate to large (>0.40) for most items, with the exception of items concerning color of skin and difficulty bending joints, walking, and use of hand/fingers.

Responder Definition
Average changes in the Psoriasis Diary items associated with clinically meaningful changes in the PGIC, IGA, and PGIC are shown in Table 4. A “Psoriasis Diary responder” (or a patient whose Psoriasis Diary scores reflect clinically meaningful improvements) would likely show point changes on items ranging from 2.0 to 3.0 for minimal change and 3.0 to 5.0 for larger changes. A patient whose Psoriasis Diary scores reflect clinically meaningful improvements (a Psoriasis Diary “responder”) would likely show point changes on items ranging from 2.0 to 3.0 for minimal change and 3.0 to 5.0 for larger changes.

Diary Revisions
Consistently poor performance was observed for items assessing color of affected skin, difficulty bending joints, difficulty walking, and difficulty using hands or fingers; thus, these four items were dropped from the measure (see Table 1).

Conclusions
Psoriasis is a common condition that significantly impacts patients’ daily life. This study examined the psychometric characteristics of a new PRO measure of psoriasis symptoms and functional impacts, developed to address the most relevant psoriasis patient experiences and the limitations of existing instruments. Results from this study provide compelling support for the psychometric characteristics of the items comprising the Psoriasis Diary.

Unlike other measures, the Psoriasis Diary is completed daily by the patient. Daily assessments may be particularly useful for symptom assessment because for many conditions, symptoms vary from day to day. Daily assessments, however, could affect patient compliance. In this study, patients completed greater than 90% of all scheduled assessments over a 16-week interval.
Although no universally accepted “gold standard” for compliance exists, rates at or above 85% to 90% can be interpreted as strong for clinical trials [38]. In this context, compliance with the Psoriasis Diary is observed to be excellent and supports the daily diary approach to measuring psoriasis symptoms and functional impacts.

Several clinician and PRO instruments exist for measuring psoriasis disease severity. We expected that the Psoriasis Diary would be associated, but not redundant, with other clinician and PRO psoriasis measures. Psoriasis Diary items were unrelated to the PASI and the IGA at baseline. This finding is consistent with prior research that found weak correlations among clinician and PRO measures at baseline among patients with psoriasis [16,17] and may be attributed to both restricted range in PASI scores at baseline (due to inclusion/exclusion criteria) and that each measure (i.e., patient- vs. clinician-reported) may be assessing uniquely different concepts associated with the condition. For instance, a number of concepts assessed by the Psoriasis Diary (e.g., itch, sting, burn, and pain) are not individually measured (e.g., the DQLI) or not measured at all (e.g., the PASI) in existing clinician assessments.

Most Psoriasis Diary items were correlated with the PASI and the IGA at week 12, and results generally supported our hypotheses: Psoriasis Diary symptom severity items were more strongly correlated with the PASI and the IGA than with the EQ-5D questionnaire, and symptom bother items were more strongly correlated with the DLQI than with the EQ-5D questionnaire. The Psoriasis Diary itching items (severity and bother), however, were strongly correlated with the PASI, the IGA, and the DLQI.

**Table 3 – Correlations between changes in scores on Psoriasis Symptom Diary and the PASI, the IGA, and the DLQI**

<table>
<thead>
<tr>
<th>Psoriasis diary item change: Baseline to week 12</th>
<th>PASI score change: baseline to week 12 (n = 147)</th>
<th>IGA change: baseline to week 12 (n = 141)</th>
<th>DLQI change: week 1 to week 12 (n = 138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Severe-itching</td>
<td>.606*</td>
<td>.578*</td>
<td>.566*</td>
</tr>
<tr>
<td>2: Bother-itching</td>
<td>.593*</td>
<td>.546*</td>
<td>.530*</td>
</tr>
<tr>
<td>3: Severe-stinging</td>
<td>.413*</td>
<td>.432*</td>
<td>.594*</td>
</tr>
<tr>
<td>4: Bother-stinging</td>
<td>.437*</td>
<td>.496*</td>
<td>.603*</td>
</tr>
<tr>
<td>5: Severe-burning</td>
<td>.378*</td>
<td>.428*</td>
<td>.576*</td>
</tr>
<tr>
<td>6: Bother-burning</td>
<td>.492*</td>
<td>.510*</td>
<td>.615*</td>
</tr>
<tr>
<td>7: Severe-pain-cracking</td>
<td>.378*</td>
<td>.427*</td>
<td>.496*</td>
</tr>
<tr>
<td>8: Bother-pain-cracking</td>
<td>.406*</td>
<td>.497*</td>
<td>.543*</td>
</tr>
<tr>
<td>9: Severe-pain</td>
<td>.368*</td>
<td>.407*</td>
<td>.535*</td>
</tr>
<tr>
<td>10: Bother-pain</td>
<td>.486*</td>
<td>.460*</td>
<td>.561*</td>
</tr>
<tr>
<td>11: Severe-scaling</td>
<td>.593*</td>
<td>.604*</td>
<td>.572*</td>
</tr>
<tr>
<td>12: Bother-scaling</td>
<td>.551*</td>
<td>.523*</td>
<td>.571*</td>
</tr>
<tr>
<td>13: Color of skin</td>
<td>.287*</td>
<td>.248*</td>
<td>.235*</td>
</tr>
<tr>
<td>14: Notice-color</td>
<td>.540*</td>
<td>.595*</td>
<td>.597*</td>
</tr>
<tr>
<td>15: Hide skin</td>
<td>.477*</td>
<td>.506*</td>
<td>.526*</td>
</tr>
<tr>
<td>16: Avoid activities</td>
<td>.372*</td>
<td>.451*</td>
<td>.623*</td>
</tr>
<tr>
<td>17: Embarrassed</td>
<td>.506*</td>
<td>.565*</td>
<td>.599*</td>
</tr>
<tr>
<td>18: Hard-bend joints</td>
<td>.185†</td>
<td>.165†</td>
<td>.334†</td>
</tr>
<tr>
<td>19: Hard-walk</td>
<td>.151</td>
<td>.157</td>
<td>.280†</td>
</tr>
<tr>
<td>20: Hard-use hands</td>
<td>.177†</td>
<td>.187†</td>
<td>.234†</td>
</tr>
</tbody>
</table>

DLQI, Dermatology Life Quality Index; IGA, Investigator’s Global Assessment; PASI, Psoriasis Area and Severity Index.
* Correlation is significant at the 0.01 level (two-tailed).
† Correlation is significant at the 0.05 level (two-tailed).
correlated as well with the PASI, the IGA, and the DLQI as they did with the Pruritus VAS. Results suggest that the Psoriasis Diary is capturing unique information that may be an important complement to standard clinician-reported end points in understanding the efficacy of psoriasis treatments.

The Food and Drug Administration Guidance for Industry [26] recommends a priori responder definitions for outcome measures used in clinical trials. Results from this study identified Psoriasis Diary responder definitions for use in determining whether a patient has experienced clinically meaningful change (2–3-point and 3–5-point change in item scores for minimal and large improvements, respectively).

Although the majority of items performed well in psychometric testing, four items (assessing color of affected skin, difficulty bending joints, difficulty walking, and difficulty using hands or fingers) did not perform as well as others. These items were dropped, resulting in a 16-item Psoriasis Diary. The item assessing color of affected skin showed poor score reproducibility and construct validity, and was not sensitive. The three items assessing difficulty moving (bending joints, walking, and using hands or fingers) had skewed item distributions and were not sensitive, and showed poor construct (using hands) and discriminant validity (using hands or fingers). It should be noted that these three items were originally included in the Psoriasis Diary after the completion of concept evaluation (literature review, expert clinician interviews, and patient interviews) and item generation, with a secondary goal in mind: that these items may be used in future applications to help discriminate between patients with and without psoriatic arthritis. Thus, their deletion is not expected to limit the Psoriasis Diary’s content validity.

Although this study had notable strengths, it also had some limitations. Our sample included adults with moderate to severe chronic plaque psoriasis and the sample was primarily white (96%); thus, results may not be generalizable beyond this type of sample (e.g., the measure may perform differently in a sample with different skin types and tones). Additional psychometric research is needed if the Psoriasis Diary is to be used in clinical trials with other patient populations. In particular, future studies should investigate the applicability of the color of psoriasis-affected skin item to subgroups of all skin tones and evaluate the quantitative uniqueness of potentially overlapping concepts including burning, stinging, and pain. This measure was tested in the context of a carefully controlled clinical trial; future research should evaluate whether compliance with the assessment is similar in less controlled situations. Also, while results from this study demonstrate sound psychometric performance of the Psoriasis Diary items, consideration and adjustment for multiplicity should be made if using individual items as unique study end points. Future research will investigate the potential for scaling of the Psoriasis Diary items, which may yield an overall score or

Table 4 – Meanings changes of key Psoriasis Symptom Diary items by the PASI response, the PGIC, and the IGA.

<table>
<thead>
<tr>
<th>Psoriasis Symptom Diary item</th>
<th>PASI response† (n = 147)</th>
<th>Mean ± SD</th>
<th>PGIC improvement (n = 138)</th>
<th>IGA improvement (n = 141)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Partial (≥50% but &lt;75% improvement)</td>
<td>Complete (≥75% improvement)</td>
<td>Little</td>
<td>Large</td>
</tr>
<tr>
<td>1: Severe-itching</td>
<td>–3.2 ± 2.46</td>
<td>–5.1 ± 2.67</td>
<td>–2.2 ± 1.91</td>
<td>–4.6 ± 2.52</td>
</tr>
<tr>
<td>3: Severe-stinging</td>
<td>–2.3 ± 2.07</td>
<td>–3.7 ± 2.65</td>
<td>–2.1 ± 1.34</td>
<td>–3.6 ± 2.64</td>
</tr>
<tr>
<td>5: Severe-burning</td>
<td>–2.2 ± 2.08</td>
<td>–3.5 ± 2.7</td>
<td>–2.1 ± 1.30</td>
<td>–3.4 ± 2.68</td>
</tr>
<tr>
<td>7: Severe-pain-cracking</td>
<td>–2.5 ± 2.45</td>
<td>–3.8 ± 2.72</td>
<td>–2.2 ± 1.88</td>
<td>–3.6 ± 2.72</td>
</tr>
<tr>
<td>9: Severe-pain</td>
<td>–2.6 ± 2.52</td>
<td>–3.4 ± 2.64</td>
<td>–2.2 ± 1.83</td>
<td>–3.3 ± 2.61</td>
</tr>
<tr>
<td>11: Severe-scaling</td>
<td>–3.5 ± 2.64</td>
<td>–5.5 ± 2.63</td>
<td>–2.3 ± 2.19</td>
<td>–4.9 ± 2.75</td>
</tr>
<tr>
<td>14: Notice-color</td>
<td>–3.1 ± 2.93</td>
<td>–5.2 ± 2.84</td>
<td>–1.6 ± 1.98</td>
<td>–4.8 ± 2.80</td>
</tr>
</tbody>
</table>

* *Partial* responders were patients achieving a 50% or more (but <75%) improvement in PASI score from baseline to week 12. *Complete* responders were patients achieving 75% or more improvement (reduction) in PASI score from baseline to week 12."
subscale scores from the measure, and associated interpretation guidelines (responder definitions, clinically meaningful change).

Understanding the patient’s perspective on their psoriasis can allow for a more informed assessment of treatment efficacy. The Psoriasis Symptom Diary indexes the patient's perspective on psoriasis symptoms (itch, sting, burn, pain, scaling) and impacts that are related to the underlying pathophysiology of the disease and are important to patients. Items from this PRO measure may be useful for efficacy endpoints alongside other measures of disease severity in future clinical trials testing new treatments for chronic plaque psoriasis.

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We thank all the US investigators who participated in the Psoriasis Symptom Diary evaluations. We also acknowledge Jennifer Cline, MBA, invivodata (now part of ERT), for her managerial contribution to this research project.

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REFERENCES