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## Preference-Based Assessments

# Development of a Disease-Specific Version of the EQ-5D-5L for Use in Patients Suffering from Psoriasis: Lessons Learned from a Feasibility Study in the UK

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### ABSTRACT

**Objectives:** The EuroQol five-dimensional (EQ-5D) questionnaire is a generic measure widely used for the assessment of health status. Research has suggested that it may be insensitive to the burdens associated with particular conditions. This study was designed to explore the feasibility of developing and valuing a disease-specific “bolt-on” version of the EQ-5D questionnaire for use in psoriasis.

**Methods:** A series of steps were undertaken to develop, test, and evaluate dimensions for a psoriasis-specific version of the EQ-5D questionnaire (hereafter referred to as the EQ-PSO questionnaire). Candidate dimensions were explored through a review of published literature, in-depth qualitative interviews with patients, and consultation with a clinical expert. A psychometric validation exercise was then undertaken to establish how well dimensions functioned. Two dimensions were selected for inclusion in a draft measure alongside the existing EQ-5D questionnaire dimensions: “skin irritation” and “self-confidence.” Last, a time trade-off valuation exercise was

conducted with 300 members of the UK general public to derive utilities for health states described by the measure. **Results:** The psychometric analyses indicated that the two new candidate dimensions captured additional variance over and above the existing five dimensions. Data from the valuation exercise were analyzed by using different models. A collapsed random effects model was put forward as a parsimonious and accurate approach. Based on this model, estimated utilities ranged from  $0.98 \pm 0.02$  for state “111111” to  $0.03 \pm 0.29$  for state “555555.” **Conclusions:** This study has developed the EQ-PSO questionnaire to support future psoriasis research and has informed the development of future bolt-on versions of the EQ-5D questionnaire.

**Keywords:** disease-specific, economic evaluation, EQ-5D, health-related quality of life, instrument development, psoriasis, utilities.

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## Introduction

The EuroQol five-dimensional (EQ-5D) questionnaire is a standardized generic instrument used for describing and valuing health status, which is scored as a single index ranging from 1 (full health) to 0 (dead) and below 0 for states worse than dead [1]. The single index is used to estimate quality-adjusted life-years for cost-effectiveness analysis [2]. The original EQ-5D questionnaire was designed as a generic instrument with dimensions relevant to all patient groups and the general population. Five dimensions describe health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). For some conditions, however, important aspects of a disease or symptom may not be captured by these core dimensions of health and as such the EQ-5D questionnaire may be insensitive in these conditions.

Research has been undertaken in different therapy areas to explore the validity or sensitivity of the EQ-5D questionnaire

[3–6]. In summary, this research has demonstrated limitations with regard to vision, hearing, and some psychological disorders. This has been recognized in the latest version of the National Institute for Health and Care Excellence guidance for methods of technology appraisal, which states, “In some circumstances, evidence suggests that using the EQ-5D may not be valid (for example in certain mental health conditions related to psychosis, mania or cognition, or in conditions affecting sensory functions like vision or hearing)” [7].

One solution that has been proposed to improve the validity of the EQ-5D questionnaire is the inclusion of additional dimensions that are designed to capture important elements of the condition [8]. These so-called bolt-on measures would include the standard EQ-5D questionnaire five dimensions with the addition of one or more condition-specific dimension to address the particular disease. Such an approach has the potential advantage of retaining the core dimensions of the EQ-5D

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Published by Elsevier Inc.

<http://dx.doi.org/10.1016/j.jval.2013.10.003>

questionnaire while also achieving greater sensitivity within specific health conditions. It should also help to retain the strengths of the current version of the EQ-5D questionnaire.

There has been relatively limited research so far on the development of the EQ-5D questionnaire bolt-on measures. Some work has been undertaken in cognitive problems, sensory impairments, and difficulties related to sleep [9–11]. The present study team also considered that there is inconclusive evidence for the effectiveness of the EQ-5D questionnaire for use in dermatological conditions [12,13]. Research into the impact of psoriasis has shown that it can have a very significant impact on patients' health-related quality of life. One study reported that patients were willing to accept a 40% shorter life expectancy to avoid uncontrolled disease [14]. The nature of the specific burden traditionally associated with psoriasis (skin lesions, itch, embarrassment, etc.) may not be reflected in the EQ-5D questionnaire descriptive system and as such it may be an appropriate candidate for the development of an EQ-5D questionnaire bolt-on module.

The EuroQol Group has an interest in the potential for the development of bolt-on versions of the EQ-5D questionnaire. The project reported here was designed to develop a psoriasis-specific version of the EQ-5D questionnaire (the EQ-PSO questionnaire). In addition, the project was designed to explore the feasibility of methods for the development of bolt-on measures.

## Methods

The study comprised two main phases: the development and psychometric testing of the bolt-on instrument and a subsequent valuation exercise.

### Phase 1: Development of the EQ-PSO Questionnaire Bolt-On Instrument

The EQ-PSO questionnaire was specifically designed to retain all the current five-level EQ-5D questionnaire (EQ-5D-5L) dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), which would be supplemented with additional disease-specific dimensions. The five-level version of the EQ-5D questionnaire was chosen as the basis because it was hypothesized that this would permit easier interpretation of the study findings in the context of future research. To develop a condition-specific version of the EQ-5D questionnaire, we sought to initially identify important issues and concerns for patients with psoriasis through review of the available literature, and interviews with clinicians and patients.

#### Literature review and clinician interview

Rather than undertaking a full systematic review, a more focused literature review was conducted to understand the symptom and treatment burden associated with psoriasis. The literature search incorporated Medline, Embase, and other specialist databases and was conducted by using OVID in March 2010. Articles were restricted to those published in English between 1990 and 2010, with particular attention paid to the identification of articles that used qualitative research methods to further examine patient perspectives on the experience of psoriasis.

The literature review provided evidence regarding how psoriasis affects physical, psychological, and social well-being. Psoriatic lesions are frequently itchy, but patients also experience burning, stinging, pain, and bleeding [15]. Skin lesions may further lead to disrupted sleep and can restrict the use of the hands [16]. The skin lesions associated with psoriasis can also be large in area, raised from the normal surface of the skin, and visually obvious. Studies have reported rates of depression in patients with psoriasis ranging from 10% to 58% [17], with the severity of

depression linked to the degree of skin area affected by psoriasis [18]. People with more severe psoriasis are more likely to report feeling anxious, hopeless, or ashamed [19]. Social contacts with family, friends, and neighbors; physical activities; group activities; going out socially; and going to public places can also be limited by psoriasis [20]. Skin disease is additionally noted as leading people to feel physically unattractive and/or sexually undesirable [21]. Previous research has noted a genetic component to the susceptibility of individuals to developing psoriasis [22].

An interview was conducted with a US-based dermatologist who has experience of working with patients with psoriasis. An interview discussion guide was developed on the basis of findings from the literature. The dermatologist was asked to characterize the nature of difficulties experienced by patients with respect to their symptoms and in managing their disease.

The dermatologist described the impact of psoriasis in terms of physical, social, and psychological difficulties, and how these varied in terms of the extent and visibility of the disease. The clinician described very common problems of skin irritation including itching, which can lead to further irritation. The psychosocial consequences of the condition could be severe, with patients often reporting anxiety and/or depression due to their skin complaints. The dermatologist also described how patients often worried about the prospect of further disease outbreaks or flare-ups.

#### Patient interviews

To identify candidate dimensions for the psoriasis module, a series of in-depth semi-structured qualitative interviews were conducted in the United Kingdom ( $n = 8$ ) with individuals with self-reported psoriasis at varying degrees of severity. The interviews were recorded and transcribed for qualitative analysis by using the Atlas.ti (Scientific Soft., Berlin, Germany) software package. A summary of the themes and typical quotes are presented (Table 1); see also Lloyd et al. [23].

Psoriasis was reported as having a widespread effect on the lives of patients with psoriasis. Most individuals experienced a significant degree of pain or discomfort directly attributable to their condition. Frequent and often nonconscious scratching could serve to aggravate lesions, resulting in soreness and bleeding. This could result in sleep disturbance and daytime fatigue from inadequate rest. The prescribed skin care routine of some individuals was described as bothersome.

Some individuals reported an unwillingness to engage in social activities in which their psoriasis would be more visible (e.g., swimming, sunbathing, or visiting hairdressers). Psoriasis often resulted in embarrassment for patients, which affected self-confidence and self-esteem. Most participants also reported anxiety and/or depression because of their psoriasis as well as feelings of frustration due to their inability to successfully control the disease.

Two of the participants were diagnosed with psoriatic arthritis. These patients experienced arthritic problems of pain and loss of mobility. They did however report experiencing similar concerns related to their skin (although these were of secondary importance when compared with the very severe consequences related to arthritis).

#### Identification of candidate dimensions

The findings from the literature review and interviews were used to draft four new dimensions: skin irritation (including itching), skin appearance (e.g., redness, dry skin, and flakiness), self-confidence, and social/relationship difficulties (e.g., embarrassment, relationship problems). These dimensions reflected the findings from the qualitative research. New dimensions were chosen to minimize any overlap with existing EQ-5D questionnaire dimensions. The language of new dimensions and their

**Table 1 – Qualitative evidence supporting the proposed candidate dimensions.**

Themes	Sample quotes	Candidate dimensions
Physical impact of psoriasis symptoms	“... the itching can drive you mad. You just can’t scratch it.” “It’s not like a normal itch. [...] It’s like it is right inside your skin.”	Skin irritation
Desire to cover up psoriasis lesions	“It just makes me look gross.” “It is not nice to have bad skin [...] I do feel less physically attractive because of it.”	Skin appearance
Intrapersonal psychological impact	“I feel like there is something really wrong with me.” “... it’s just embarrassing. You’re too busy being conscious of yourself ...”	Self-confidence
Interpersonal psychological impact; avoidance of social situations	“If it gets very bad then I just won’t get close to people.” “I’d rather just be at home. I’d rather just stay out of people’s way.”	Social/relationship difficulties

labels was consistent with the existing EQ-5D-5L questionnaire and was chosen to avoid translation problems.

#### *Cognitive debriefing of candidate dimensions*

The candidate dimensions were examined in cognitive debriefing interviews (n = 10) with patients with questionnaire. A cognitive debriefing guide was used to assess the suitability of the proposed dimensions for inclusion in the new measure. The interviews assessed whether the concepts were important to patients, whether patients thought the language used was appropriate, and whether people thought the response options were suitable. Findings from the cognitive debriefing interviews suggested that all candidate dimensions were identified as reflecting legitimate concerns for patients with psoriasis. Individuals reported good understanding of the descriptions of different dimensions and response options. All participants expressed the opinion that candidate dimensions were appropriate for inclusion in the intended measure and were not intrusive or likely to cause discomfort for respondents.

#### *Psychometric validation*

An initial assessment of the psychometric performance of the candidate dimensions was undertaken. One hundred individuals in the United Kingdom with varying severity of psoriasis were recruited and completed the EQ-5D-5L questionnaire instrument plus the four psoriasis dimensions. Participants also completed two additional dermatology-specific measures to permit assessment of item functioning: the Dermatology Life Quality Index (DLQI) [24] and the Self-Administered Psoriasis Area and Severity Index (SAPASI) [25].

#### **Phase 2: Valuation of the EQ-PSO Questionnaire Bolt-On Instrument**

To generate the EQ-5D-PSO questionnaire value set, a series of valuation interviews were undertaken with a sample of the UK general public. A convenience sample was recruited to match the demographic profile of the United Kingdom. Participants were aged at least 18 years, currently resident in the United Kingdom, able to understand the interview as judged by the interviewer, and able to give informed consent. People were to be excluded if at the screening phase they reported that they had an acute illness or cognitive impairment that in the opinion of the investigator would interfere with the study requirements. Face-to-face interviews were undertaken by trained experienced interviewers.

Interview participants completed a sociodemographic form, the EQ-5D-5L questionnaire, and the time trade-off (TTO) interview [26]. Participants were randomly allocated to assess one of five blocks of health states. Each participant was asked to rate 11

health states that varied in terms of the seven EQ-PSO questionnaire dimensions. The selection of health states was based on an orthogonal array that included 49 states plus four additional states (comprising of a level 1 problem on all dimensions, level 5 problem on all dimensions, and either a level 1 problem or a level 5 problem on the newly added dimensions).

Participants rated each state by using a 100-point visual analogue scale (VAS) anchored at best imaginable health (100) and worst imaginable health (0). Participants also rated a state described as “dead.” This task provided participants with an introduction to the concept of rating health states and also provided an indication of which states participants assessed as worse than dead.

In the TTO exercise, participants were first asked to rate all states that were assessed as better than dead (i.e., scored above dead on the VAS). The TTO procedure used 10 years as the time horizon and the time in full health iterated between 10 years, then 1 year, then 9 years, and so on. An indifference point was inferred if participants’ preference switched or if they indicated that the two prospects were the same. The procedure did not iterate below a time period of 6 months. A modified approach was undertaken to assess states that had been rated as worse than dead. This required participants to rate a given state as being equal to or lower than dead on the VAS. In this instance, the trade-off occurs between being dead and spending time in a particular state followed by a period of full health. Interviewers used a crib sheet to determine the rating for each state.

Written informed consent was obtained from all participants before study initiation, and the study protocol underwent independent ethical review. Participants in the study received £25 compensation. Participants’ data were excluded on the grounds of rationality if they scored the same value for all health states, if respondents valued two or more health states higher than 1111111, or if respondents valued two or more health states lower than 5555555.

## **Results**

### *Psychometric Validation*

Analyses were undertaken to assess the psychometric properties of the new instrument. Exploratory factor analysis was used to examine the underlying factor structure of the measure and to explore the potential for item reduction (using direct oblimin rotation). This analysis indicated that two of the dimensions—skin irritation and self-confidence (Fig. 1)—emerged as separate factors and were more important predictors of the measure variance than the other two candidate dimensions, which were subsequently dropped.

<b>Skin irritation (e.g. itching)</b>	
I have no itching	<input type="checkbox"/>
I have slight itching	<input type="checkbox"/>
I have moderate itching	<input type="checkbox"/>
I have severe itching	<input type="checkbox"/>
I have extreme itching	<input type="checkbox"/>
<b>Self-confidence</b>	
I have no problems with self confidence	<input type="checkbox"/>
I have slight problems with self confidence	<input type="checkbox"/>
I have moderate problems with self confidence	<input type="checkbox"/>
I have severe problems with self confidence	<input type="checkbox"/>
I have extreme problems with self confidence	<input type="checkbox"/>

**Fig. 1 – Psoriasis-specific dimension descriptions.**

Hierarchical linear regression models were fitted to examine the ability of the EQ-5D questionnaire (with or without the additional candidate dimensions) to predict scores on the DLQI and SAPASI (Table 2). For the DLQI, the explanatory power of the model (measured by R<sup>2</sup>) increased from 0.422 to 0.646 when the psoriasis-specific dimensions were added as independent variables. For SAPASI, the explanatory power increased from 0.182 to 0.445 when the psoriasis-specific dimensions were added.

**Valuation Data Analysis**

A number of different post hoc modeling approaches to the valuation data were attempted. The initial models used ordinary least squares (OLS) and random effects (RE) approaches in explaining the TTO-derived utility. The performance of these models was compared by using different fit statistics including

root mean squared error and adjusted R<sup>2</sup>. Analyses were also conducted to examine the presence of logical inconsistencies.

In addition to the initial approaches, a series of other models were also explored including Tobit, loglinear, and two-stage modeling. Numerous different interaction models were also attempted, using full factorial first-order interactions between dimensions as a whole, and using level 4 and level 5 interactions between dimensions. Also, models with N2, N3, N4, N5 (any impairment at level 2, level 3, etc.) terms were contrasted with models with at least two level 4s, at least three level 4s, at least two level 5s, at least three level 5s, at least two level 4s OR 5s, at least three level 4s OR 5s, and so on. Analyses were exploratory in nature, and only a summary of the final models is presented.

EQ-PSO questionnaire utilities were estimated from an available data set to explore how they varied in line with established SAPASI and DLQI severity gradings [27] for patients with psoriasis (Table 3). The mean utilities were also compared with EQ-5D-5L questionnaire values [28].

**Valuation Results**

Three hundred valuation interviews were completed. The data set had no missing data, and very few states rated as worse than dead (1.2% of all responses). There were also no nontraders for TTO (i.e., no respondents scored 1 for all health states). Seven respondents were excluded for failing rationality tests.

**TTO Modeling Results**

The main-effects OLS and RE models (models 1 and 2; Table 4) generally show good results; almost all parameter values are significant, and most coefficients are in the right order. For usual activities, levels 2 and 3 are almost identical, and for self-confidence, levels 2 and 3 are reversed but both are not significant. The RE model shows a much better fit, with a root mean squared error of 0.197 versus 0.255 for the OLS model. Both new dimensions have a significant impact on participants' strength of

**Table 2 – Regression coefficients for the two EQ-5D questionnaire models predicting DLQI and SAPASI scores.**

Model	Dimension	P	
		DLQI score	SAPASI score
1	(Constant)	0.417	0.836
	Mobility	0.126	0.917
	Self-care	0.107	0.405
	Usual activities	0.239	0.088
	Pain/discomfort	0.214	0.021
	Anxiety/depression	<0.001	0.009
2	(Constant)	<0.001	<0.001
	Mobility	0.071	0.895
	Self-care	0.188	0.685
	Usual activities	0.273	0.097
	Pain/discomfort	0.656	0.091
	Anxiety/depression	0.484	0.394
	Skin irritation	0.013	0.029
	Skin appearance	0.002	0.001
	Self-confidence	0.015	0.071
	Social/relationship difficulties	0.111	0.461
		Model 1 R <sup>2</sup> = 0.422	Model 1 R <sup>2</sup> = 0.182
	P < 0.001	P = 0.002	
	Model 2 R <sup>2</sup> = 0.646	Model 2 R <sup>2</sup> = 0.445	
	P < 0.001	P < 0.001	

DLQI, Dermatology Life Quality Index; EQ-5D, EuroQol five-dimensional; SAPASI, Self-Administered Psoriasis Area and Severity Index.

**Table 3 – The EQ-5D-PSO questionnaire utility values stratified by DLQI and SAPASI scores (n = 100).**

	N	Mean SD	
		EQ-5D-PSO	EQ-5D-5L*
All patients	100	0.75 ± 0.17	0.71 ± 0.26
DLQI			
0–1	10	0.83 ± 0.14	0.82 ± 0.23
2–5	35	0.82 ± 0.12	0.80 ± 0.23
6–10	23	0.76 ± 0.13	0.75 ± 0.21
11–20	26	0.71 ± 0.11	0.65 ± 0.20
21–30	6	0.38 ± 0.28	0.20 ± 0.33
SAPASI			
<3	33	0.84 ± 0.10	0.83 ± 0.19
3–15	50	0.75 ± 0.12	0.71 ± 0.23
>15	17	0.59 ± 0.26	0.50 ± 0.36

DLQI, Dermatology Life Quality Index; EQ-5D-5L, five-level Euro-Qol five-dimensional; EQ-5D-PSO, EuroQol five-dimensional psoriasis; SAPASI, Self-Administered Psoriasis Area and Severity Index.  
 \* EQ-5D-5L crosswalk values for the United Kingdom [28].

preference for health states. Self-confidence has the smallest impact of the seven dimensions but is still significant.

*Level 4 and 5 “reversals”*

It should be noted that for five dimensions for the OLS model and four dimensions for the RE model, level 4 has a higher disutility than level 5, but level 4 and 5 parameter values are not statistically significantly different. There is very little evidence, however, of differentiation between levels 4 and 5 in the expected direction.

*Collapsed RE model*

The presence of inconsistencies in the utility weights from the present study is a significant issue. Analyses were run with levels collapsed to address this problem (levels 4 and 5 dimension scores, and levels 2 and 3 for skin irritation and self-confidence). This resulted in a model with 22 parameters and a constant with similar model-adjusted R<sup>2</sup> and root mean squared error values compared with other models that were tested (models 3 and 4; Table 4).

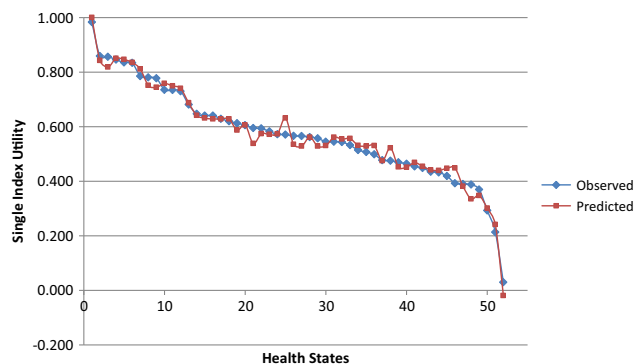
*Other models*

Many other models including Tobit, loglinear, and two-stage modeling were explored, but findings are not reported here. Fit

**Table 4 – Coefficients derived from TTO models 1 and 2 (dummy model) by using OLS and RE and models 3 and 4 based on collapsed levels.**

Dimension	Model 1 OLS	Model 2 RE		Model 3 OLS		Model 4 RE
MO2	0.027	0.024	MO2	0.028	MO2	0.025
MO3	0.047	0.045	MO3	0.047	MO3	0.046
MO4	0.122	0.133	MO4	0.123	MO4	0.135
MO5	0.169	0.160	MO5	0.166	MO5	0.159
SC2	0.026	0.024	SC2	0.026	SC2	0.023
SC3	0.047	0.049	SC3	0.047	SC3	0.050
SC4	0.115	0.110	SC45	0.107	SC45	0.108
SC5	0.101	0.106				
UA2	0.035	0.035	UA23	0.035	UA2	0.034
UA3	0.034	0.036	UA45	0.119	UA3	0.036
UA4	0.124	0.129			UA45	0.122
UA5	0.116	0.116				
PD2	0.029	0.029	PD2	0.029	PD2	0.031
PD3	0.037	0.036	PD3	0.038	PD3	0.036
PD4	0.210	0.204	PD45	0.205	PD4	0.201
PD5	0.201	0.210			PD5	0.207
AD2	0.016*	0.015*	AD2	0.017*	AD2	0.015*
AD3	0.034	0.039	AD3	0.035	AD3	0.040
AD4	0.158	0.160	AD45	0.148	AD45	0.151
AD5	0.140	0.141				
SI2	0.054	0.053	SI23	0.052	SI23	0.052
SI3	0.045	0.044	SI4	0.099	SI4	0.103
SI4	0.097	0.101	SI5	0.131	SI5	0.123
SI5	0.133	0.124				
SE2	0.018*	0.020*	SE23	0.013*	SE23	0.016*
SE3	0.004*	0.011*	SE45	0.074	SE45	0.084
SE4	0.088	0.091				
SE5	0.066	0.078				
Constant	0.069	0.067		0.069		0.066
Adjusted R <sup>2</sup>	0.319	0.324		0.319		0.323
RMSE	0.255	0.197		0.255		0.197

AD, anxiety/depression; MO, mobility; OLS, ordinary least squares; PD, pain/discomfort; RE, random effects; RMSE, root mean square error; SC, self-care; SE, self-confidence; SI, skin irritation; TTO, time trade-off; UA, usual activities.  
 \* Nonsignificant (P > 0.05).



**Fig. 2 – Mean observed versus predicted utility values.**

statistics did not improve and because these only lead to increasingly complex models, these were abandoned. Many models including interaction variables were explored, but most interaction variables were nonsignificant. Backward and forward regression was used to explore patterns of interaction, but although some level 4 and level 5 variables were significant, no clear patterns were found.

The collapsed RE model is proposed as the best model for estimating preference weights for the EQ-5D-Psoriasis questionnaire. Figure 2 shows the predictive ability of the model against observed data.

## Discussion

This report describes the findings from a study designed to develop a psoriasis-specific bolt-on version of the EQ-5D questionnaire. The EQ-PSO questionnaire was partly conceived as a study to explore the feasibility and methods for developing bolt-ons that would permit more effective economic evaluations in specific disease areas (rather than as a replacement for disease-specific measures in clinical practice). We believe that there are some useful findings from this work that can inform the debate regarding the development of bolt-ons.

The development of bolt-ons or disease-specific versions of the EQ-5D questionnaire must be driven by evidence that the existing EQ-5D questionnaire has some limitations in a specific context. Different methods have been suggested for exploring this issue. Longworth et al. [13] previously used systematic reviews of the EQ-5D questionnaire data to identify disease areas in which it is insensitive. Other methods based on exploring discrepancies between single-index and VAS scores may also be possible. In the present study, however, the need for a psoriasis-specific version of the EQ-5D questionnaire was primarily explored by using qualitative research with patients with psoriasis. The findings outlined above highlighted how important elements of their health status were not currently captured by the EQ-5D questionnaire. The qualitative research also informed the development of the additional dimensions. We recommend that future development of bolt-on measures should be informed by in-depth qualitative research with patients to ensure that the most appropriate issues are captured and that the new dimensions are described in an optimal way.

The second stage of the development process of the new instrument was a psychometric validation study. People with psoriasis completed the EQ-PSO questionnaire and other measures. The validation study found evidence that the additional dimensions were capturing important additional information. The regression analysis showed that the new measure was much better at predicting psoriasis outcomes (DLQI and SAPASI) when compared with the unmodified EQ-5D questionnaire. The

exploratory factor analysis identified that skin irritation and skin appearance grouped together, while self-confidence and social/relationship difficulties loaded on a separate factor. The factor loadings and other psychometric analyses were also used to identify two dimensions that could be dropped. We believe that this is also a useful step for identifying the most salient or important additional dimensions to include in a bolt-on. There is only limited scope for adding dimensions to the EQ-5D questionnaire (because of econometric constraints) and so selecting the most appropriate dimension is very important.

The final stage in this instrument development was the collection of preference weights so that a single index score can be estimated from the measure. We used a slightly modified version of the TTO exercise that was used in the original EQ-5D questionnaire valuation work. The selection of states was based on an orthogonal design, which was one important difference. Three hundred face-to-face interviews were completed by using skilled interviewers. This resulted in very high data quality, with very little missing data and only 2% of people excluded for failing tests of rationality. A substantial amount of analysis work was undertaken on the data set, of which only a small proportion is presented here. The initial analyses failed to reliably differentiate between some of the levels of each dimension—in particular, levels 4 and 5. Therefore, it was decided that these response options should be collapsed in the modeling. A lot of work was undertaken including interaction terms and constants, but it was concluded that this did not improve the explanatory power of the models. The final model that was agreed by the study team was a collapsed version of the RE model. Subsequent analyses based on this model show how well it can predict observed data (Fig. 2) and differences in psoriasis severity (Table 3).

This study highlights an important issue in the development of bolt-ons related to the role of the existing five dimensions. The data analyses have estimated coefficient weights for the existing five dimensions of the EQ-5D questionnaire as well as the two new dimensions. The analyses show that in this study the five original dimensions have different weights compared with other studies (e.g., van Hout et al. [28]). In future analyses, we will explore the effect of maintaining the existing five dimension weights constant (based on the ongoing EQ-5D-5L questionnaire valuation work) and using the analysis to estimate weights only for the two additional dimensions.

There are a number of important limitations in this study that should be considered. First, the study was primarily designed to explore methodological feasibility for the development of bolt-ons. There are opportunities for understanding more about the performance of the measure, including the use of the EQ-PSO questionnaire as compared with the use of disease-specific measures such as the DLQI, as well as the responsiveness of the EQ-PSO questionnaire to change in health status. Second, the initial literature review undertaken was not systematic in nature but rather focused on the identification of key issues for patients with psoriasis. Third, various aspects of the study may also be limited in part by sample size. The initial qualitative work, the psychometric validation study, and valuation work may all have been limited by their sample size to an extent. While only eight qualitative interviews were completed, however, we found that no substantial new information was emerging from the interviews. On the basis of additional analysis, we also believe that the findings from the psychometric validation work would not have changed substantially with a larger sample size. The lack of differentiation between levels of the EQ-PSO questionnaire may have emerged as a result of insufficient data. Fourth, there may have been value in collecting additional data around patients' prescription drug use as the potential exists for some bias to have been introduced by side effects associated with

immunomodulatory drugs impacting reported health status. Last, we note that the comparison of EQ-5D-5L questionnaire and EQ-PSO questionnaire-derived utilities in Table 3 is not straightforward because the 5L utilities are based on a mapping to the EQ-5D-3L questionnaire while EQ-PSO questionnaire values are based on a de novo valuation study. Therefore, it is not possible to conclude from this comparison whether the EQ-PSO questionnaire is more sensitive than the EQ-5D questionnaire.

This work has tested methods for the development and valuation of a disease-specific version of the EQ-5D questionnaire. Furthermore, the work has provided a direction and insight into potential future EQ-5D questionnaire bolt-on research. Last, the EQ-PSO questionnaire instrument may prove valuable for the future of research demonstrating the burden associated with psoriasis.

Source of financial support: The work was funded by Eli Lilly and conducted by Oxford Outcomes, part of ICON plc.

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