Balancing the Benefits and Risks of Drug Treatment

A Stated-Preference, Discrete Choice Experiment With Patients With Psoriasis

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Objective: To examine the extent to which the attributes of a treatment affect patients’ choice of treatment for psoriasis and the magnitude and nature of trade-offs between risks and benefits of treatment.

Design: A questionnaire, including a stated-preference, discrete choice experiment, was used to elicit patients’ preferences for the treatment of psoriasis.

Setting: Dermatology clinics in England.

Patients: A total of 126 patients with psoriasis.

Main Outcome Measures: Preferences of patients for, and trade-offs between, the 6 attributes of time to moderate (50%) improvement, relapse, and risks of experiencing skin irritation, high blood pressure, liver damage, and skin cancer.

Results: The mean age of respondents was 47.6 years, and the mean duration of psoriasis was 23 years. All 6 attributes were important factors affecting choice of treatment. The results indicated that patients with psoriasis prioritized low risk of skin cancer ($\beta = -0.054; P < .01$) and liver damage ($\beta = -0.054; P < .01$) and preferred treatment that resulted in a shorter time to achieve a moderate improvement ($\beta = -0.034; P < .01$) over a longer time to relapse ($\beta = 0.028; P < .01$). Patients were most willing to wait longer for a treatment to work if the likelihood of skin cancer or liver damage was reduced.

Conclusions: This study shows that treatment attributes influence patients with psoriasis in their choice of treatment. The results of the discrete choice experiment presented herein indicate that most respondents would be willing to trade between different aspects of treatment to achieve improvements in their psoriasis and minimize the risks of adverse events.

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SorIASIS IS A CHRONIC IN-flammatory, hyperprolifera-tive skin disease that affects approximately 1% to 2% of the general population in the United Kingdom. The morbidity associated with psoriasis is well documented in terms of its impact on patients’ quality of life. Many patients experience problems with body image, self-esteem and self-concept, poor psychological adaptation, and feelings of stigmatization, shame, and embarrassment concerning their appearance. The disease also places an economic burden on patients, particularly those with severe psoriasis, because they incur out-of-pocket expenses.

There is currently no cure for psoriasis, although a wide range of therapies are available, varying considerably in terms of efficacy and toxic effects. Levels of adherence to treatment among patients with psoriasis are low, with nonadherence rates reported in 40% of patients. Factors such as efficacy and duration of treatment can influence the decision whether to continue with treatment. Previous studies have shown that many patients with psoriasis often feel frustrated with the ineffectiveness of current therapies and want treatment to be more aggressive. It has also been suggested that dermatologists (and other physicians) may not appreciate fully the impact that skin diseases have on individual patients.

Little is known about how patients with psoriasis evaluate the risks and benefits of the treatments they are offered. Given the low levels of adherence among these patients, information about the decision-making process could be useful for physicians considering which treatment to offer. This study used a stated-preference, discrete choice experiment (DCE) to explore the attitudes of patients toward the risks and benefits of drug treatment for psoriasis. The objectives were to (1) identify the extent to which the attributes of a treatment (eg, degree of improvement, duration of remission, and adverse effects) affect patients’ choice of treatment for their psoriasis, (2) determine the hierarchical im-

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Tradable levels are assigned to these attributes, and scenarios of key attributes of a good or service are identified. Realistic and meaningful treatment scenarios, which patients make trade-offs between risks and benefits of treatment options would always be expected to be chosen as a test for consistency. Each patient, therefore, completed 8 pair-wise choices and 1 test of consistency. Table 2 shows an example of a choice set presented to respondents.

Demographic data were also collected from each patient relating to age, sex, duration of psoriasis, and age at onset. The Self-Assessment Psoriasis Area and Severity Index, which has a 0 to 72-point scale, was used to determine clinical severity of a patient's psoriasis, with a higher score indicating greater severity.

The treatment attributes used in the DCE were derived from a review of the published literature, and their relevance was confirmed through discussions with 3 consultant dermatologists (one of whom was C.E.M.G.).17-21 In all, 6 attributes were included, namely: (1) time to achieve a moderate (50%) improvement in psoriasis, (2) time to relapse, (3) risk of skin irritation, (4) 20-year risk of liver damage, (5) 20-year risk of skin cancer, and (6) 20-year risk of high blood pressure. Our survey was administered to patients currently being treated for psoriasis in routine practice and not in a trial setting. We therefore chose a 50% improvement as one of the attributes because this has previously been acknowledged to be a clinically important end point in the assessment of psoriasis.22,23 The levels used for each of these attributes are shown in Table 1.

The levels were organized into treatment scenarios using a fractional factorial design. This type of design was used because a full factorial design would have produced 512 (4 x 4 x 4 x 2 x 2 x 2) treatment scenarios, which was felt to be too burdensome for respondents. Using experimental design theory, we were able to identify 16 pair-wise treatment choices in which the levels were varied independently, thus avoiding multicollinearity (a situation in which 2 variables within the model are highly correlated).

These 16 choice sets were split randomly into 2 separate versions of the questionnaire, each containing 8 choice sets, which were distributed to patients. For each choice set, the respondents were asked to select which treatment scenario they would prefer for the management of their psoriasis. Each version of the questionnaire also included a single choice set in which 1 of the treatment options would always be expected to be chosen as a test for consistency. Each patient, therefore, completed 8 pair-wise choices and 1 test of consistency. Table 2 shows an example of a choice set presented to respondents.

Demographic data were also collected from each patient relating to age, sex, duration of psoriasis, and age at onset. The Self-Assessment Psoriasis Area and Severity Index, which has a 0 to 72-point scale, was used to determine clinical severity of a patient’s psoriasis, with a higher score indicating greater severity.
In addition, respondents were asked to rank the 6 treatment attributes in order of importance ranging from 1 (most important) to 6 (least important). The study was approved by the local National Health Service research ethics committees in the 3 areas where the study was conducted and also by the University of Manchester Ethics Committee.

**STUDY SAMPLE AND DATA ANALYSIS**

Patients were recruited from the dermatology departments of 3 Acute National Health Service Hospital Trusts located in northwest England. Questionnaires were distributed to patients who were attending a dermatology outpatient clinic, and postage-paid envelopes were provided for the returns.

Because each respondent provided up to 8 responses (having completed 8 choice sets), a random effects probit model was considered appropriate, as this accounts for correlations between responses given by the same individual. A probit model is a popular specification of a generalized linear model, using the probit link function. Because the response is a series of binomial results, the likelihood is often assumed to follow the binomial distribution. Let \( Y \) be a binary outcome variable, and let \( X \) be a vector of regressors. The probit model assumes that

\[
Pr(Y = 1|X = x) = \Phi(x'\beta),
\]

where \( \Phi \) is the cumulative distribution function of the standard normal distribution. Parameters for \( \beta \) are typically estimated by maximum likelihood.

All calculations were conducted using Intercooled Stata statistical software (version 8.0; StataCorp LP, College Station, Texas). In the model, the choice of treatment option was the binary-dependent variable, and the differences in levels for each of the 6 attributes were the independent variables. Differences were calculated by subtracting the levels. A main-effects linear additive model was estimated in which \( \Delta \beta \) is the dependent variable; \( \beta \) is the constant, representing unobserved influences on choices; \( \beta \) is the coefficient of the attributes included in the design, \( e \) represents the error term due to differences among observations, and \( u \) represents the error terms due to differences among respondents:

\[
\Delta \beta = \beta_0 + \beta_{\text{IMPROVE}} + \beta_{\text{RELAPSE}} + \beta_{\text{SKIN}} + \beta_{\text{BLOOD}} + \beta_{\text{LIVER}} + \beta_{\text{CANCER}} + e + u.
\]

The theoretical validity of the model was tested by examining the signs and significance of coefficient estimates in relation to a priori hypotheses. The longer the time to improvement and increased risks of adverse effects of treatment were all expected to have negative coefficients, whereas the longer the time to relapse was expected to have a positive coefficient. The trade-offs that patients were willing to make were determined by calculating the marginal rate of substitution, that is, the ratio of any 2 attributes.

27 Trade-offs were calculated by dividing the coefficients of the attributes by the coefficient for time to improvement (\( \beta_t \)), giving the estimated trade-offs in time to improvement for a 1-unit change in each of the other attributes. Confidence intervals for coefficients and the marginal rate of substitution were derived using nonparametric bootstrapping with Stata software (StataCorp LP).28 Bootstrapping allows the confidence intervals to be determined through repeated sampling with replacement, using parameter point estimates and their estimated variance-covariance matrix.

The respondents' treatment choices were explored to see if they showed evidence of nontrading behavior among the different treatment attributes. Respondents were classified as having a dominant preference if they always chose the “best” level of a particular attribute and if they also ranked that attribute as the most important in the ranking exercise.29 To determine whether including respondents with dominant preferences affected the results of the random effects probit model, the data were analyzed in 2 separate models by including and excluding these respondents.

### RESULTS

#### INFLUENCE OF ATTRIBUTES ON TREATMENT CHOICES

In all, 126 patients with psoriasis completed the questionnaire. A total of 64 respondents (51%) were female, and 62 (49%) were male. Their mean age was 47.6 years (range, 21-82 years), the mean duration of their psoriasis was 22.8 years (range, 1-63 years), their mean age at onset of psoriasis was 24.9 years (range, birth to 67 years), and the mean Self-Assessment Psoriasis Area and Severity Index score was 11.1 (range, 0.4-55.2). All 126 respondents passed the consistency test, suggesting that they had understood the DCE.

Twenty-nine respondents (23%) showed evidence of dominant preferences for specific treatment attributes. Most of these (19/29) always chose the option for which there was no risk of experiencing skin cancer. A few respondents also showed evidence of dominant preferences for time to relapse (5 subjects), no risk of liver damage (3 subjects), and no risk of high blood pressure (2 subjects).
Two random effects probit models were estimated; 1 with all respondents and 1 with “dominant” respondents excluded. A comparison of the models indicated no significant differences in coefficient estimates, relative size of the coefficients, or the significance of the fit of the models. Therefore, only the model that included all respondents is presented in Table 3. The coefficients for all 6 treatment attributes were statistically significantly different from zero (P<.01), indicating that all the attributes were important factors affecting patients’ choice of treatment. The constant term was also significant (P<.05), indicating that other unobserved attributes were also likely to influence treatment preferences.

The size and direction of the coefficients were in accordance with our a priori hypotheses. The negative signs on the coefficient for the adverse effects indicated that the higher the risk of experiencing these events, the less likely patients were to choose this scenario. Similarly, the negative sign for the time to improvement attribute indicated that the longer the time to achieve a moderate improvement, the less likely the patients were to choose that scenario. Positive values for the time to relapse indicated that the greater the duration of time to relapse, the more likely the patients were to choose that scenario.

### RELATIVE IMPORTANCE OF THE TREATMENT ATTRIBUTES

Comparison of the magnitude of the coefficients indicated that respondents considered both the long-term risks of experiencing skin cancer and liver damage to be the most important adverse events influencing their choice of treatment, followed by the risk of experiencing high blood pressure. The risk of skin irritation was considered to be least important. The patients also prioritized time to moderate improvement over time to relapse. This corresponds with the results of the ranking exercise in which 30 of 103 respondents ranked the time to achieving a moderate improvement in psoriasis as the most important attribute (29.1%), whereas 17 of 103 (16.5%) ranked time to relapse as the most important, as shown in Table 4. (It should be noted that 23 respondents [18.3%] did not complete the ranking exercise.)

### TRADE-OFFS BETWEEN THE BENEFITS AND RISKS OF TREATMENT

Table 3 also shows the marginal rates of substitution between time to achieve a moderate improvement in the severity of psoriasis and the other attributes; that is, how much more time to improvement the respondents were willing to trade off to achieve an improvement in 1 level of the other treatment attributes. For example, the results show that respondents were willing to wait 0.8 weeks longer to achieve a moderate improvement if the treatment prolonged the time to relapse following such improvement by 1 week. The least important marginal rates of substitution were for the risk of skin irritation during treatment, and the most important were for the 20-year risks of liver damage and skin cancer.

### COMMENT

This study has shown that treatment attributes, such as adverse effects, time to improvement, and time to relapse, influence the treatment preferences of patients with psoriasis. Most respondents would be willing to trade among different aspects of treatment to achieve an improvement in their psoriasis with minimal adverse effects. In other words, patients indicated that they would wait longer for a treatment to work if the chance of a severe adverse effect, such as skin cancer or liver damage, was considerably reduced. Respondents considered the long-term risks of skin cancer and liver damage to be the most important adverse effects and were prioritized above short-term risks of drug-induced hypertension or skin irritation.

Almost a quarter of the sample were unwilling to trade among the attributes and always chose the treatment option with a particular level of their chosen attribute, most often no risk of skin cancer. The level of nontrading in this study was low compared with other DCE studies in which nontrading respondents have accounted for 30% to 71% of all respondents. It is important to take these into account because they reveal strong preferences on the part of some respondents. These studies suggest that some patients may not accept a treatment offered to them, no matter how efficacious, if they have serious concerns about adverse effects. These findings may provide some insight into why patients demonstrate intentional nonadherence to treatments for psoriasis and provide a useful starting point for meaningful dialogue between patients and physicians about choice of treatment.

Previous studies have explored attitudes to risks and benefits of treatments in patients with rheumatoid arthritis and other musculoskeletal conditions. Fraenkel et al found that as many as 60% of respondents would not accept an arthritis treatment if there was a risk, however small, of developing cancer. Another study showed that patients would be willing to accept the risk of treatment if the benefits were seen to be high. More recently, it was reported that patients with arthritis prioritized eliminating the risk of adverse effects, whether short- or long-term, much more highly than the chance of the treatment providing benefit.

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*Table 4. Ranking of Attributes by 103 Respondents*

<table>
<thead>
<tr>
<th>Treatment Attribute</th>
<th>Respondents Ranking It as “Most Important,” No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to achieve moderate (50%) improvement</td>
<td>30 (29.1)</td>
</tr>
<tr>
<td>Time to relapse</td>
<td>17 (16.5)</td>
</tr>
<tr>
<td>Risk of experiencing skin irritation during treatment</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Risk of high blood pressure during treatment</td>
<td>9 (8.7)</td>
</tr>
<tr>
<td>20-y risk of experiencing liver damage</td>
<td>17 (16.6)</td>
</tr>
<tr>
<td>20-y risk of experiencing skin cancer</td>
<td>28 (27.2)</td>
</tr>
</tbody>
</table>

*aThere are some missing values.*
To our knowledge, this is the first study to examine the nature and extent of some of the specific trade-offs that patients routinely face when choosing among the risks and benefits of drug treatments for psoriasis. However, there are several limitations that should be taken into account in interpreting the findings. First, the patients were presented with scenarios in which we systematically manipulated specific treatment attributes. Respondents were making decisions based on the state of their psoriasis at the time of the study; however, their attitudes may have varied according to the severity of their psoriasis. In the words of one patient, who provided written comments to support her answers, “If my psoriasis was severe, which indeed it has been at various times of my life, if I look back...I would probably, in desperation, have agreed to any treatment that would improve my skin condition.” The results were averaged across the sample, and as a result there is inevitable variation between patients.

It is likely that our sample does not represent fully the general population of patients with psoriasis; rather, it is more representative of those being treated in dermatology clinics in the hospital setting. Future work should explore whether these findings are mirrored by those derived from patients who are being cared for in ambulatory care alone. Likewise, it would also be of interest to explore patients’ preferences toward other treatment attributes, such as the route or mode of administration and the associated treatment costs.

Nonetheless, this study has provided novel insight into the attitudes of patients with psoriasis toward the risks and benefits of the treatments they receive. Given the heavy psychological burden associated with psoriasis, the high levels of dissatisfaction with the effectiveness of current treatment, and poor levels of adherence, a greater understanding of how these patients perceive their treatment may enhance the dialogue between them and their physicians.

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Author Contributions: Dr Ashcroft had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Seston, Ashcroft, and Griffiths. Acquisition of data: Seston and Ashcroft. Analysis and interpretation of data: Seston, Ashcroft, and Griffiths. Drafting of the manuscript: Seston and Ashcroft. Critical revision of the manuscript for important intellectual content: Seston, Ashcroft, and Griffiths. Statistical analysis: Seston and Ashcroft. Obtained funding: Ashcroft and Griffiths. Administrative, technical, and material support: Ashcroft. Study supervision: Ashcroft and Griffiths.

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REFERENCES