Patient preferences for stratified medicine in psoriasis: a discrete choice experiment

Short title: Patient preferences for stratified medicine in psoriasis

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Abstract

Background: New technologies have enabled the potential for stratified medicine in psoriasis. It is important to understand patients’ preferences to enable the informed introduction of stratified medicine which is likely to involve a number of individual tests that could be collated into a prescribing-algorithm for biologic selection to be used in clinical practice.

Objective: To quantify patient preferences for an algorithm-based approach to prescribing biologics (‘biologic-calculator’) in psoriasis.

Methods: An online survey comprising a discrete choice experiment (DCE) was conducted to elicit the preferences of two purposive samples of adults living with psoriasis in the UK, identified from a psoriasis patient organisation (Psoriasis Association) and an online-panel provider (Dynata). Respondents chose between two biologic-calculators and conventional prescribing described using five attributes: treatment delay; positive and negative predictive values; risk of infection; cost-saving to the NHS. Each participant selected their preferred alternative from six hypothetical choice-sets. Additional data including socio-demographic characteristics were collected. Choice data were analysed using conditional logit and fully correlated random-parameters logit models.

Results: Data from 212 respondents (Psoriasis Association = 67; Dynata = 145) were analysed. The signs of all estimated coefficients were consistent with a priori expectations. Respondents had a strong preference for high predictive accuracy and avoiding serious infection but there was evidence of systematic differences in preferences between the samples.

Conclusion: This study indicates that individuals with psoriasis would value a biologic-calculator and suggested that such a biologic-calculator should have sufficient accuracy to predict future response and risk of serious infection from the biologic.
What is already known about the topic?

- Factors such as patient characteristics, location of psoriasis and genetics, have been found to affect response to targeted biologic therapy in people with psoriasis.
- The knowledge of such factors paves the way for algorithm-based prescribing (stratified medicine).

What does this study add?

- We investigated patient preferences for a hypothetical example of algorithm-based prescribing of biologics for psoriasis compared with the conventional approach to prescribing. The strongest predictors of patient preferences for stratified medicine were the ability to predict non-response to a biologic, ability to predict a positive response and the risk of avoiding a serious infection from the biologic.
Introduction

Targeted biological therapies (‘biologics’) are a highly effective addition to systemic treatments available for moderate-to-severe psoriasis.\textsuperscript{1} The use of biologics, however, may be linked to adverse events (AEs) such as injection site reactions and infections (tuberculosis, lower respiratory tract, skin and soft tissue).\textsuperscript{2-4} Not all patients will respond to the selected biologic, and secondary failure complicates treatment in an important subset. Given that biologics are expensive and delays in achieving effective treatment are undesirable, there is a sizeable interest in the development of tools to help inform clinicians about targeted treatment selection (stratified medicine).

Ongoing programmes of work seek to develop ‘stratified medicine’ approaches to the prescribing of biologics with the objective of enabling cost- and time-savings through improved response rates and decreased probability of AEs.\textsuperscript{5,6} There have been significant advances in recent years, suggesting that targeted biologic selection may be feasible in psoriasis through therapeutic drug monitoring (TDM) and potentially by genomic testing.\textsuperscript{7,8} The information from the results of these individual assessments and patient characteristics could be collated into a prescribing-algorithm (hereafter termed ‘biologic-calculator’) to aid clinicians’ and patients’ decision-making when choosing an appropriate biologic. Using such a biologic-calculator would, in theory, result in a more efficient use of healthcare resources and enhanced quality-of-life for people with psoriasis.

Prescribing algorithms, in general, and a biologic-calculator specifically, may be characterised by their ability to accurately predict who will [positive predictive value (PPV)], or who will not [negative predictive value (NPV)] safely respond. It is possible to improve the predictive value of a prescribing-algorithm by including specific variables (such as body mass index, smoking status, gender, location of psoriasis\textsuperscript{7} as well as relevant biomarkers (e.g. HLA-C*06:02 genotype status)).\textsuperscript{5} The introduction of such variables may delay treatment initiation and increase financial burden due to additional tests, such as those to determine genotype status. Researchers developing a biologic-calculator must weigh the incremental benefit gained from additional information against the incremental cost of collecting it when determining the required predictive values of a prescribing algorithm.

Discrete choice experiments (DCEs) are a potentially useful method to use to understand the benefits, harms and risks associated with new interventions such as a prescribing algorithm.\textsuperscript{9} Published studies have used DCEs to quantify patient preferences for biologics in psoriasis but to
our knowledge, preferences for an algorithm-based approach to the prescribing of these biologics have not been quantified.\textsuperscript{10,11} Including predictive (positive and negative) values as an attribute in a DCE can provide information on the required level of predictive (NPV and/or PPV) accuracy for a biologic-calculator to be deemed sufficiently acceptable to inform prescribing. Such evidence could help those involved in the development of stratified medicine approaches to guide the informed introduction into clinical practice. This study aimed to quantify the preferences of people with psoriasis for a ‘biologic-calculator’ to aid selection of a first-line biologic.

**Materials and methods**

A DCE to elicit the preferences of a sample of people with psoriasis for a biologic-calculator compared with the conventional prescribing approach to select a biologic was embedded in an online survey. Survey respondents were asked to choose between two algorithm-based approaches (biologic-calculators A and B) and an opt-out alternative of ‘conventional prescribing.’ The opt-out was phrased to represent current prescribing without an algorithm. The algorithm-based approach was framed as representing predictive information in addition to current clinician-informed prescribing. Ethical approval was obtained from The University of Manchester’s Research Ethics Committee (reference: 2016-0172-470).

**Survey Design**

The DCE was designed and analysed in line with published recommendations.\textsuperscript{12,13} The survey was programmed for online administration using SSI Web 8.3.8 Sawtooth software.\textsuperscript{14} This survey was developed parallel to, and shared many design features with, a version for people with rheumatoid arthritis (RA).\textsuperscript{15} The final survey version for people with psoriasis (Supplementary Material S1; see Supporting Information) comprised three sections: training materials to help the respondents understand the rationale behind the survey; the choice questions; and questions asking the respondents about themselves.

**Designing the DCE**

Five attributes and relevant levels (see Table 1) were selected to address the choice question: ‘If these were the only approaches to prescribing biologics, which, if any, would you choose?’ An iterative process, conducted alongside developing a similar survey for people with RA, identified the relevant attributes.\textsuperscript{15} The results from interviews conducted as part of a qualitative study in
RA and five focus groups (attended by a total of 51 individuals with RA) were supplemented with a psoriasis support group meeting (n = 7 individuals), literature review of psoriasis and DCEs, and two clinical expert interviews to inform the selection of attributes and to ensure that participants understood the survey. The psoriasis support group meeting involved collating views of the online survey by presenting and discussing the training materials and the framing of the attributes and levels. The findings from the psoriasis group meeting were consistent with those from the RA group meetings.

Four levels were assigned to each of these five attributes (Table 1) and identified through a review of the literature, and consultation with two clinical experts, to establish plausible and clinically relevant ranges. Supplementary Material S2 (see Supporting Information) describes the levels attached to each attribute and the rationale for their selection.17-21

**Experimental design**

It was not possible to present all potential scenarios for a DCE using five attributes, each with four levels (4^5 × (4^5 – 1) / 2 = 523,776) and a main-effects fractional factorial design was used. This approach selected a subset of scenarios which were identified by generating an experimental design to minimise the D-error using Ngene software.22 Pilot work informed the optimal number of choice sets. The final experimental design consisted of four blocks of five choice-sets. An additional choice-set was included as a ‘dominance check’ question, in which the levels were set to suggest an ‘obvious’ best option, to check that respondents were answering in line with economic theory. Each respondent was, therefore, asked to complete six choice-sets but data from five of them were used in the analysis.

**Piloting**

The DCE survey went through an extensive piloting process (pilot survey with 82 patients; consultation with two academic dermatologists) that was run in parallel with a similar survey designed for people with RA.15 Changes were made to the levels and their associated images for ‘cost saving to the NHS’ based on the results from the quantitative pilot.

**Training materials**
Training materials\textsuperscript{15} were used at the start of the survey to provide respondents with sufficient information required to make choices in the DCE. Bespoke training materials (see https://mindbytes.be/our-work/patient-preference-survey-psoriasis/) were created using a narrative storyline in collaboration with MindBytes\textsuperscript{23} because this study required respondents to become familiar with complex attributes for a biologic-calculator described in terms of predictive values (NPV and PPV), infection risk as well as potential cost saving to the NHS. Respondents were asked to indicate if anything was unclear after being shown the narrative storyline by answering a specific question about whether they understood the information provided.

**Background questions**

To be able to describe the sample, respondents were asked to complete key socio-demographic questions including age, gender, employment status, psoriasis history (time since diagnosis, experience of biologics), a self-reported generic measure of health status (EQ-5D-5L\textsuperscript{24} and a disease-specific measure (Dermatology Life Quality Index (DLQI)).\textsuperscript{25} Their responses to the EQ-5D questionnaire were valued using a published UK-specific set of preference weights where the resulting score is anchored on zero (representing being dead) and 1 (representing full health) with the possibility of scores below zero (equivalent to worse than being dead) for serious health conditions.\textsuperscript{26}

**Study population and sample**

Individuals with psoriasis, aged 18 years or older, were recruited from two sampling frames: a UK patient organisation for people with psoriasis (the Psoriasis Association)\textsuperscript{27} and an online-panel provider (Dynata previously known as ResearchNow).\textsuperscript{28} Respondents were sent a link to the online survey (no reminders were used). The first question was a screening question used to exclude those who did not have a diagnosis of psoriasis. No restrictions were placed on the date of diagnosis, disease severity or treatment experiences for current patients to be eligible.

**Data analysis**

A pre-specified analysis plan was created at the design stage of the DCE which stated that respondents who did not complete the survey, failed the dominance check question or always chose either biologic calculator A or B in all choice sets would be excluded. The dominance check question is a ‘test’ question that is used to verify whether the respondents are engaging with the
questions and/or understand the questions. The ‘correct’ answer to the dominance check question should be obvious to the respondent. The decision to exclude those who failed the dominance check question was taken because this question had quantitative attributes with levels that showed a logical direction of impact. Therefore, if a respondent failed the dominance check question with an obvious direction of preferences then they were clearly not engaging with the survey. Descriptive statistics were produced for respondents that were included in the final sample.

In the base-case analysis all attributes were specified as linear, continuous variables and the choice data were analysed using conditional logit models for each sample. Tests for non-linear preferences for each attribute were conducted by effects coding the attribute levels and comparing the model fit using Bayesian Information Criterion (BIC) across the model containing the effects coded variables and the base-case model. A Swait and Louviere plot was created (Supplementary Material S3; see Supporting Information) for identifying potential differences in scale between samples (scale heterogeneity) and true differences in preferences (preference heterogeneity). The analysis plan specified that, if there was evidence of heterogeneity (scale or preference), a fully correlated random parameters logit (RPL) model would be used for each sample to account for it and allow for variation in preference parameters across individual respondents (Supplementary Material S3; see Supporting Information). All analyses were performed using Stata 14.0 (StataCorp, College Station, TX).

Balancing benefits and harms

The observed balance between the specified benefits (improved predictive value) and harms (delay to treatment and risk of serious infection) was quantified by generating estimates of marginal rates of substitution (MRS) and their associated 95% confidence intervals (CIs) using the delta method. The MRS corresponds to the amount of an attribute respondents were willing to accept in exchange for higher levels of another attribute (see Supplementary Material S4 for additional information).

Results

In total, a purposive sample (comprising a mix of gender and age groups) of 250 people with psoriasis completed the survey. The final sample size of 212 respondents was available for analysis after excluding those who failed the dominance check question (n = 33; three of whom originated from the patient organisation sample) and those who always chose either biologic
calculator A or biologic calculator B in every choice set (n = 7). Out of those who failed the dominance check question, only one respondent did not have any formal qualifications which implied that failure of dominance check was not related to lower educational attainment in this sample. The study results were based on a final sample size of 145 respondents from the online-panel provider and 67 respondents from the patient organisation.

Descriptive statistics for sample characteristics are reported in Table 2 for all respondents and the two subsamples. On average, people from the patient organisation were more likely to be male, over the age of 45 years, in full-time employment or retired and a greater proportion possessed a Master’s degree or PhD. There were also observed differences in self-reported health status (Supplementary Material S5; see Supporting Information) between respondents recruited through the patient organisation, who tended to have a higher level of health status according to the EQ-5D (mean utility score = 0.844), and those identified from the online-panel provider (mean utility score = 0.792). These values were lower than the reported mean health status score of 0.856 for the UK general population.\textsuperscript{36} The mean DLQI for both samples suggested that psoriasis had a moderate effect on respondents’ lives. The DLQI potential scores range from one (small effect on patient’s life) to 30 (large effect on patient’s life). The online-panel provider sample reported a slightly greater impact of living with psoriasis (mean DLQI = 7.12) compared with the patient organisation sample (mean DLQI = 7.03). When asked if anything was unclear in the narrative storyline, the majority of respondents (94\% of the online-panel provider sample and 96\% of the patient organisation sample) indicated that they understood the information provided.

\begin{table}
<insert table 2 here>
\end{table}

Sample-reported experience of psoriasis and biologics (see Table 3) indicated that those in the online-panel provider group were more likely to have received their diagnosis in the past 5 years and reported more recent flare-ups compared with those from the patient organisation. The vast majority of respondents in either group had never been prescribed biologics.

\begin{table}
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\textit{Patients’ preferences}

The results from the conditional logit models for each sample and the ‘Swait and Louviere’ plot\textsuperscript{31} confirmed the presence of potential scale and preference heterogeneity (Supplementary Material
Therefore, a fully correlated RPL model was used to estimate parameters of the distribution of individual preferences for each sample while adjusting for differences in scale and preferences within the sample. The signs of all estimated coefficients were consistent with *a priori* expectations about the direction of the effect of an attribute on preferences. A higher amount of NPV, PPV and cost saving were preferred as denoted by the positive signs on these coefficients whereas a lower amount of delay and risk were preferred as implied by their negative coefficients.

All estimated attribute coefficients, except NPV and cost saving, were statistically significant (p <0.01) predictors of choice in the overall sample, indicating that respondents considered most attributes while making their choices. In the sample collected from the patient organisation, all coefficients except cost saving (p = 0.056) and NPV (p = 0.102) were statistically significant at the <0.05 level, meaning that for participants in this group cost saving to the NHS and negative predictive ability (ability to predict who will not respond) were not statistically significant predictors of the observed choices. In the sample collected from the online-panel provider, all estimated coefficients were statistically significant at the <0.05 level suggesting that respondents in this group considered all attributes when making a choice. PPV and risk were statistically highly significant (p <0.001) in this sample. The negative and statistically significant term for alternative-specific constant (ASC) in the online-panel provider sample indicated that respondents in this sample preferred the biologic-calculator to conventional prescribing when attribute levels were set to be the same for all alternatives. The negative ASC term for the patient organisation sample failed to reach statistical significance meaning that these respondents did not have a strong preference for either of the alternatives when attribute levels were set to be the same.

<insert table 4 here>

**Balancing benefits and harms**

The MRS were calculated using ‘delay to treatment’ (see Table 5) as the denominator because this attribute appeared to be the closest to a linear functional form (see Supplementary Material S4 for further details). Respondents collated from the patient organisation were willing to delay the start of treatment by 3.25 days (statistically significant) and those from the online-panel provider by 3.89 days (statistically significant) for a £100 cost saving. The most valued attribute in both samples was the ability of the biologic-calculator to determine who will not respond to treatment.
(NPV), as both groups were willing to wait 23-29 days for a 10% increase. Respondents collated from the online-panel provider were willing to delay treatment by 22.95 days compared to 28.84 days in the patient organisation sample for an increase of 10% in NPV but this was not statistically significant in either group. Another important attribute in both samples was the ability of the biologic-calculator to determine who will respond to treatment (PPV) as respondents from the patient organisation were willing to delay treatment by 19.22 days and those from the online-panel provider by 14.09 days (statistically significant in both groups). The patient organisation group of respondents displayed stronger preferences for predictive accuracy of the algorithm. The MRS values for the ability to predict response (PPV) and non-response (NPV) were not statistically different from one another in either of the samples.

Discussion

This study was designed to quantify the preferences of individuals with psoriasis for an algorithm-based approach to prescribing biologics. All five attributes (NPV, PPV, risk of serious infection, delay to treatment and cost saving to the NHS) were consistent with a priori expectations in terms of the direction and magnitude of the estimated coefficients.

The ability of the algorithm to determine response (PPV) and non-response (NPV) were the two most important attributes driving preferences in both samples relative to the other attributes in the DCE. However, NPV was not statistically significant in the patient organisation sample. The next most influential attribute was the risk of infection. These data on the trade-offs that patients were willing to make are informative to researchers involved in the development of prescribing-algorithms to introduce stratified medicine into practice. Importantly, this study suggests that NPV was as important as PPV to patients although it was not statistically significant in the patient organisation sample. This suggests that patients showed a clear preference to avoid being prescribed a biologic treatment that will not work for them. This finding is important since most research aims to identify markers of response (rather than non-response).\textsuperscript{37,38}

The observation that probability of non-response was a key factor driving preferences has been shown in other DCEs. For example, in a DCE comparing algorithm-based prescribing to conventional prescribing in RA, the authors reported that NPV was a predictor of preferences.\textsuperscript{15} Another DCE that elicited preferences of neurologists for pharmacogenetic testing in epilepsy also
suggested NPV to be a strong predictor of preferences. This suggests that NPV is important not only for people with psoriasis, but also for physicians and for people with RA and other autoimmune conditions.

The presence of scale and preference heterogeneity indicated that there were variations in the preferences of the samples. In such cases, it would be incorrect to form conclusions from merging the data from both samples and using a pooled conditional logit model. This meant that the estimated coefficients across the two samples should not be directly compared. To overcome this, values for MRS were estimated using delay to the start of treatment as a value attribute to provide a way of comparing the observed choices from both samples. Using this approach provides a solution to overcome the issue of heterogeneity due to the simple division of attribute coefficients to obtain ratios.

The findings of this DCE survey come with limitations. The use of an online-panel provider for patient recruitment could limit the generalisability of the results to the population of people with psoriasis likely to be prescribed a biologic. The main motivation behind this source of recruitment was to increase the sample size and acquire responses in a quick and low-cost manner when compared with telephone interviews or postal surveys.

The choice data collected in this study suggested there was a considerable variation in preferences within and across the two samples. This finding suggests that there is not a common MRS for all respondents and the reported MRS should be viewed with caution.

Further research should aim to recruit a more representative sample of respondents capturing the preferences of people likely to be prescribed a biologic that would allow us to determine the generalisability of the results observed in this study. Preferences of clinicians involved in the prescribing of biologic therapies could also be investigated and compared with those of the patients. Further methodological research is required to assess the impact of non-linear attributes on estimates of MRS.

The potential contribution of eliciting patient preferences is to use these results to inform the subsequent design of a biologic-calculator that takes account of the need to achieve adequate levels of, for example, PPV and NPV. Currently, the types and number of tests to include in a prescribing-algorithm are unknown. Future development would involve developing a prediction algorithm and embedding the biologic-calculator (using the results of tests as an input into a
prediction algorithm), informed by known patient and/or genetic characteristics, into the prescribing pathway of biologics for people with psoriasis. Therefore a model of service delivery will be required to enable clinicians to collect information to feed into the biologic-calculator and inform the patient of the subsequent treatment choice. Further research, using methods from implementation science,\textsuperscript{44,45} should be undertaken to understand how the biologic-calculator could be used in clinical practice.

This study aimed to quantify the preferences of patients for algorithm-based prescribing (biologic-calculator) compared with conventional prescribing of biologics for people with psoriasis. The results suggested that patients assigned the greatest value to the ability of the biologic-calculator to predict response (PPV) and non-response (NPV), followed by the risk of serious infection from the biologic. These findings have important implications for the implementation of stratified medicine in psoriasis and suggest that tools should be designed with the goal of reaching a sufficient level of predictive accuracy given the cost of implementing these into clinical practice.
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Table 1: Attributes labels, definitions and the assigned levels

| Attribute                        | Definition                                                                                                                                                                                                 | Four assigned levels              |
|----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
| Delay until the start of treatment (delay) | Time spent without biologics whilst waiting for results.                                                                                                                                                 | 0 days, 7 days, 14 days, 30 days |
| Positive predictive value (PPV)  | Ability to correctly predict who will respond to a certain dose of a biologic                                                                                                                              | 0%, 40%, 80%, 100%               |
| Negative predictive value (NPV)  | Ability to correctly predict who will not respond to a certain dose of a biologic                                                                                                                           | 80%, 90%, 95%, 100%              |
| Risk of a serious infection (risk) | Probability of developing a serious infection requiring antibiotics and/or hospitalisation as a result of taking the biologic.                                                                          | 1%, 3%, 7%, 10%                  |
| Annual cost saving to the NHS (cost) | Net saving to the NHS of using the approach.                                                                                                                                                             | £0, £300, £750, £1,500            |

*Defined as ‘No predictive ability’ in the opt-out*
## Table 2: Sample characteristics

|                          | Patient organisation (n=67) | Online-panel provider (n=145) | Overall (n=212) |
|--------------------------|-----------------------------|-------------------------------|-----------------|
| **Sex**                  |                             |                               |                 |
| Male                     | 44 (65.67)                  | 68 (46.90)                    | 112 (52.83)     |
| Age group (years)        |                             |                               |                 |
| Under 18                 | 0 (0.00)                    | 0 (0.00)                      | 0 (0.00)        |
| 18-24                    | 1 (1.49)                    | 7 (4.83)                      | 8 (3.77)        |
| 25-34                    | 3 (4.48)                    | 17 (11.72)                    | 20 (9.43)       |
| 35-44                    | 9 (13.43)                   | 24 (16.55)                    | 33 (15.57)      |
| 45-54                    | 15 (22.39)                  | 26 (17.93)                    | 41 (19.34)      |
| 55-64                    | 18 (26.87)                  | 41 (28.28)                    | 59 (27.83)      |
| 65 years and over        | 21 (31.34)                  | 30 (20.69)                    | 51 (24.06)      |
| **Occupational status**  |                             |                               |                 |
| Employed full-time       | 28 (41.79)                  | 51 (35.17)                    | 79 (37.26)      |
| Employed part-time       | 4 (5.97)                    | 12 (8.28)                     | 16 (7.55)       |
| Self-employed            | 2 (2.99)                    | 16 (11.03)                    | 18 (8.49)       |
| Unemployed               | 2 (2.99)                    | 7 (4.83)                      | 9 (4.25)        |
| Retired                  | 26 (38.81)                  | 39 (26.90)                    | 65 (30.66)      |
| Looking after home/family| 0 (0.00)                    | 7 (4.83)                      | 7 (3.30)        |
| Student                  | 0 (0.00)                    | 4 (2.76)                      | 4 (1.89)        |
| Freelance/temping        | 1 (1.49)                    | 0 (0.00)                      | 1 (0.47)        |
| Long-term sickness       | 4 (5.97)                    | 9 (6.21)                      | 13 (6.13)       |
| Temporarily laid off     | 0 (0.00)                    | 0 (0.00)                      | 0 (0.00)        |
| **Religion**             |                             |                               |                 |
| No religion              | 35 (52.24)                  | 68 (46.90)                    | 103 (48.58)     |
| Christian                | 30 (44.78)                  | 65 (44.83)                    | 95 (44.81)      |
| Buddhist                 | 1 (1.49)                    | 3 (2.07)                      | 4 (1.89)        |
| Jewish                   | 1 (1.49)                    | 4 (2.76)                      | 5 (2.36)        |
| Hindu                    | 0 (0.00)                    | 0 (0.00)                      | 0 (0.00)        |
| Muslim                   | 0 (0.00)                    | 2 (1.38)                      | 2 (0.94)        |
| Sikh                     | 0 (0.00)                    | 1 (0.69)                      | 1 (0.47)        |
| Other                    | 0 (0.00)                    | 2 (1.38)                      | 2 (0.94)        |
| **Highest level of education obtained** |                     |                               |                 |
| No formal qualifications | 0 (0.00)                    | 10 (6.90)                     | 10 (4.72)       |
| 1-4 O-levels/GCSEs       | 6 (8.96)                    | 16 (11.03)                    | 22 (10.38)      |
| 5+ O-levels/GCSEs        | 5 (7.46)                    | 11 (7.59)                     | 16 (7.55)       |
| NVQs                     | 1 (1.49)                    | 8 (5.52)                      | 9 (4.25)        |
Table 3 Sample reported experience of psoriasis and taking biologics

|                        | Patient organisation (n=67) | Online-panel provider (n=145) |
|------------------------|-----------------------------|-----------------------------|
| **Time since diagnosis of psoriasis** |                            |                             |
| Less than one month    | 1 (1.49)                    | 0 (0.00)                    |
| More than 1 month but less than 3 months | 0 (0.00)              | 6 (4.14)                    |
| More than 3 months but less than 6 months | 0 (0.00)              | 0 (0.00)                    |
| More than 6 months but less than a year | 0 (0.00)              | 7 (4.83)                    |
| More than a year but less than 2 years | 0 (0.00)              | 7 (4.83)                    |
| More than 2 years but less than 5 years | 4 (5.97)               | 14 (9.66)                   |
| More than 5 years but less than 10 years | 6 (8.96)              | 24 (16.55)                  |
| More than 10 years     | 56 (83.58)                  | 87 (60.00)                  |
| **Time taken from formal diagnosis to initiating an effective treatment** |                            |                             |
| It happened immediately | 3 (4.48)                    | 20 (13.79)                  |
| Less than one 1 month  | 9 (13.43)                   | 29 (20.00)                  |
| More than 1 month but less than 3 months | 7 (10.45)              | 14 (9.66)                   |
| More than 3 months but less than 6 months | 6 (8.96)               | 17 (11.72)                  |
| More than 6 months but less than a year | 4 (5.97)               | 10 (6.90)                   |
| More than 1 year but less than 2 years | 7 (10.45)              | 5 (3.45)                    |
| More than 2 year but less than 5 years | 5 (7.46)               | 8 (5.52)                    |
| More than 5 years      | 13 (19.4)                   | 16 (11.03)                  |
Table 4: Results of the random parameters logit model

|                        | Patient Organisation Coefficient (SE) | Online-panel provider Coefficient (SE) | All respondents Coefficient (SE) |
|------------------------|---------------------------------------|----------------------------------------|----------------------------------|
| ASC(none)              | -2.409 (10.34)                        | -18.777** (6.85)                       | -6.253* (2.48)                   |
| Delay                  | -0.094* (0.04)                        | -0.031** (0.01)                       | -0.028** (0.01)                  |

Data are presented as n (%)
| Variable | Estimate | SE | p-value | Estimate | SE | p-value | Estimate | SE | p-value |
|----------|----------|----|---------|----------|----|---------|----------|----|---------|
| PPV+     | 1.807**  | 0.59 | 0.0001  | 0.432*** | 0.07 | 0.0000  | 0.425*** | 0.06 |         |
| NPV+     | 2.712    | 1.66 | 0.0092  | 0.704*   | 0.31 | 0.0031  | 0.155     | 0.34 |         |
| Risk     | -0.679*  | 0.29 | 0.0011  | -0.323***| 0.07 | 0.0000  | -0.217*** | 0.06 |         |
| Cost     | 0.306    | 0.16 | 0.0022  | 0.119**  | 0.04 | 0.0000  | 0.067     | 0.04 |         |

Number of observations: 1005, 2175, 3180

SE = Standard error; * p<0.05; ** p<0.01; *** p<0.001; "attribute rescaled so 1% = 10%; "attribute rescaled so £1 = £100.

ASC, alternative specific constant; PPV, positive predictive value (ability to predict response); NPV, negative predictive value (ability to predict non-response); BIC, Bayesian Information Criterion.

1 The Bayesian Information Criterion (BIC) for the patient organisation sample suggested that the random parameters logit (RPL) model does not provide sufficient explanatory power given the number of additional parameters it includes. However, the RPL model is presented here to ensure the results are comparable across models.
Table 5: Estimated marginal rates of substitution for willingness to delay treatment

| Willingness to delay treatment | Patient organisation (n = 67) | Online-panel provider (n = 145) |
|-------------------------------|-------------------------------|--------------------------------|
| For a biologic calculator with attributes and levels set to be the same as current prescribing (constant) | 25.62 (-189.28 to 240.52) | 611.68 (44.32 to 1179.03) |
| For a £100 saving | 3.25 days (0.00 to 6.50) | 3.89 days (0.50 to 7.27) |
| For a 10% increase in PPV | 19.22 days (6.41 to 32.03) | 14.09 days (5.34 to 22.84) |
| For a 10% increase in NPV | 28.84 days (-7.28 to 64.96) | 22.95 days (-3.50 to 49.39) |
| For a 1% decrease in risk of serious infection | 7.23 days (0.73 to 13.72) | 10.51 days (3.37 to 17.65) |

PPV, positive predictive value (ability to predict response); NPV, negative predictive value (ability to predict non-response).
Figure 1: Example choice question

If these were the only approaches to prescribing biologics, which, if any, would you choose? Choose by clicking one of the buttons at the bottom of the page:

| Delay to start treatment | Biologic Calculator A | Biologic Calculator B | Conventional Approach (no Biologic Calculator) |
|--------------------------|-----------------------|-----------------------|-----------------------------------------------|
| 30 days                  |                       | 7 days                | No delay                                      |
| Ability to predict who will respond | 80% Of 100 people predicted to respond, 80 respond | 40% Of 100 people predicted to respond, 40 respond | No predictive ability |
| Ability to predict who will not respond | 95% Of 100 people predicted not to respond, 5 would have 5 people miss effective treatment | 90% Of 100 people predicted not to respond, 10 would have 10 people miss effective treatment | No predictive ability |
| Risk of infection        | 7%                    | 3%                    | 10%                                           |
| Annual cost saving to the NHS | £300 a patient          | £750 a patient         | No cost saving |

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