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

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Summary

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 biological drug selection to be used in clinical practice.

Objectives 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 organization (Psoriasis Association) and an online panel provider (Dynata). Respondents chose between two biologic calculators and conventional prescribing described using five attributes: treatment delay; positive predictive value; negative predictive value; risk of infection; and cost saving to the National Health Service. Each participant selected their preferred alternative from six hypothetical choice sets. Additional data, including sociodemographic characteristics, were collected. Choice data were analysed using conditional logit and fully correlated random parameters logit models.

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

Conclusions 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 biological therapy in people with psoriasis.
- The knowledge of such factors paves the way for algorithm-based prescribing (stratified medicine).

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Conflicts of interest
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Data availability statement
The survey (.pdf version of the online survey) used to collate the data for this study is available in

the Supporting Information. The data generated by the survey remain the intellectual property of The University of Manchester.

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What does this study add?

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

What are the clinical implications of this work?

- This study suggests that clinical tools to enable the implementation of stratified medicine in psoriasis should be designed with the goal of reaching a sufficient level of predictive accuracy and predicting the risk of serious infection given the cost of implementing these into clinical practice.

Targeted biological therapies ('biologics') are a highly effective addition to systemic treatments available for moderate-to-severe psoriasis.[1] However, the use of biologics may be linked to adverse events (AEs) such as injection site reactions and infections (tuberculosis, lower respiratory tract, and skin and soft tissue).[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 a decreased probability of AEs.[5,6] There have been significant advances in recent years, suggesting that targeted biologic selection may be feasible in psoriasis through therapeutic drug monitoring and, potentially, by genomic testing.[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 characterized by their ability to predict accurately who will [positive predictive value (PPV)] or 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, sex and location of psoriasis,[7] as well as relevant biomarkers (e.g. HLA-C*06:02 genotype status)].[5] The introduction of such variables may delay treatment initiation and increase financial burden owing to additional tests, such as those to determine genotype status. When determining the required predictive values of a prescribing algorithm, researchers developing a biologic calculator must weigh the incremental benefit gained from additional information against the incremental cost of collecting it.

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.[9] Published studies have used DCEs to quantify patient preferences for biologics in psoriasis; however, to our knowledge, preferences for an algorithm-based approach to the prescribing of these biologics have not been quantified.[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' (Figure 1). 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).

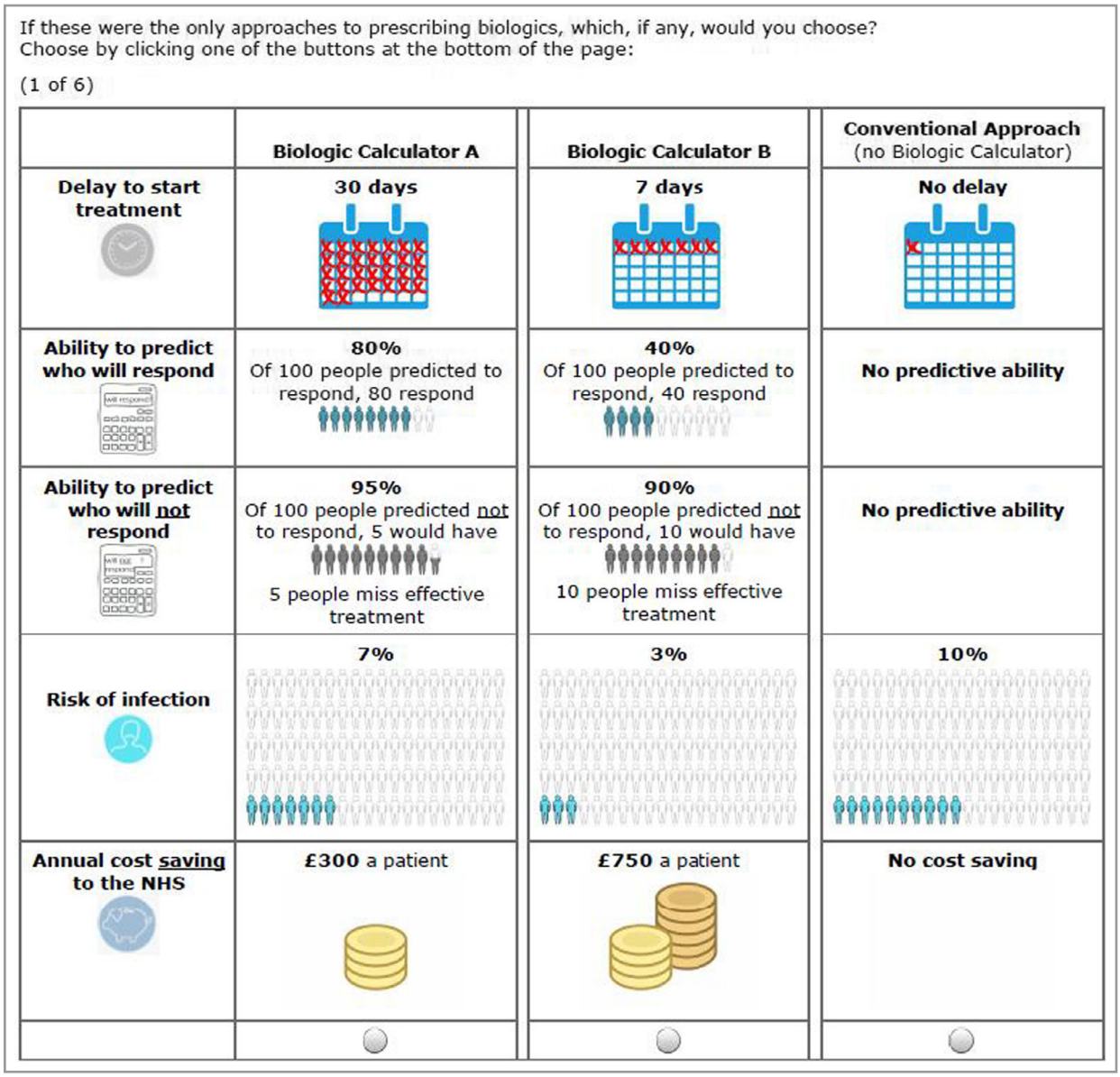

Figure 1 Example choice question. NHS, National Health Service

Survey design

The DCE was designed and analysed in line with published recommendations.[12,13] The survey was programmed for online administration using SSI Web 8·3.8 Sawtooth software.[14] This survey was developed parallel to, and shared many design features with, a version for people with rheumatoid arthritis (RA).[15] The final survey version for people with psoriasis (Appendix 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 discrete choice experiment

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.[15] The results from interviews conducted as part of a qualitative study in RA[16] and five focus groups (attended by a total of 51 individuals with RA) were supplemented with a psoriasis support group meeting (seven 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.

Table 1 Attribute labels, definitions and the assigned levels

Attribute	Definition	Four assigned levels
Delay until the start of treatment (delay)	Time spent without biologics while awaiting results	0 days, 7 days, 14 days, 30 days
Positive predictive value (PPV)	Ability to predict correctly who will respond to a certain dose of a biologic[a]	0%, 40%, 80%, 100%
Negative predictive value (NPV)	Ability to predict correctly who will *not* respond to a certain dose of a biologic[a]	80%, 90%, 95%, 100%
Risk of a serious infection (risk)	Probability of developing a serious infection requiring antibiotics and/or hospitalization 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, £1500

NHS, National Health Service. [a]Defined as 'No predictive ability' in the opt-out.

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. Appendix 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 ($4^5 \times (4^5 - 1) / 2 = 523\ 776$) and a main-effects fractional factorial design was used. This approach selected a subset of scenarios that were identified by generating an experimental design to minimize 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 only 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 National Health Service (NHS)' based on the results from the quantitative pilot.

Training materials

Training materials were used at the start of the survey to provide respondents with sufficient information required to make choices in the DCE.[15] Bespoke training materials (see https://mindbytes.be/our-work/patient-preference-survey-psoriasis/) were created using a narrative storyline in collaboration with MindBytes©,[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 and 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 sociodemographic questions, including age, sex, employment status, psoriasis history (time since diagnosis and experience of biologics), a self-reported generic measure of health status (EQ-5D-5L)[24] and a disease-specific measure [Dermatology Life Quality Index (DLQI)].[25] Their responses to the EQ-5D-5L 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.[26]

Study population and sample

Individuals with psoriasis, aged 18 years or older, were recruited from two sampling frames: a UK patient organization for people with psoriasis (the Psoriasis Association)[27] and an online panel provider [Dynata (previously known as ResearchNow)].[28] Respondents were sent a link to the online survey (no reminders were issued). 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 patients to be eligible.

Data analysis

A prespecified 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.[29] 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 who 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.[30] Tests for nonlinear preferences for each attribute were conducted by effects coding the attribute levels and comparing the model fit using Bayesian Information Criterion across the model containing the effects-coded variables and the base case model. A Swait and Louviere plot was created (Appendix S3; see Supporting Information) to identify potential differences in scale between samples (scale heterogeneity) and true differences in preferences (preference heterogeneity).[31] The analysis plan specified that, if there were 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 (Appendix S3).[32,33] All analyses were performed using Stata 14·0 (StataCorp, College Station, TX, USA).[34]

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.[35] 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

A purposive sample (comprising both sexes and a mix of age groups) of 250 people with psoriasis completed the survey. A final sample size of 212 respondents was available for analysis after those who failed the dominance check question were excluded (n = 33; three of whom originated from the patient organization sample) and those who always chose either biologic calculator A or biologic calculator B in every choice set (n = 7). Of those who failed the dominance check question, only one respondent did not have any formal qualifications, which implied that failure of the dominance check was not

Table 2 Sample characteristics

	Patient organization (n = 67)	Online panel provider (n = 145)	Overall (n = 212)
Male	44 (66)	68 (46·9)	112 (52·8)
Age group (years)			
< 18	0 (0)	0 (0·0)	0 (0·0)
18–24	1 (1)	7 (4·8)	8 (3·8)
25–34	3 (5)	17 (11·7)	20 (9·4)
35–44	9 (13)	24 (16·6)	33 (15·6)
45–54	15 (22)	26 (17·9)	41 (19·3)
55–64	18 (27)	41 (28·3)	59 (27·8)
≥ 65	21 (31)	30 (20·7)	51 (24·1)
Occupational status			
Employed full-time	28 (42)	51 (35·2)	79 (37·3)
Employed part-time	4 (6)	12 (8·3)	16 (7·6)
Self-employed	2 (3)	16 (11·0)	18 (8·5)
Unemployed	2 (3)	7 (4·8)	9 (4·3)
Retired	26 (39)	39 (26·9)	65 (30·7)
Looking after home/family	0 (0)	7 (4·8)	7 (3·3)
Student	0 (0)	4 (2·8)	4 (1·9)
Freelance/temping	1 (1)	0 (0·0)	1 (0·5)
Long-term sickness	4 (6)	9 (6·2)	13 (6·1)
Temporarily laid off	0 (0)	0 (0·0)	0 (0·0)
Religion			
No religion	35 (52)	68 (46·9)	103 (48·6)
Christian	30 (45)	65 (44·8)	95 (44·8)
Buddhist	1 (1)	3 (2·1)	4 (1·9)
Jewish	1 (1)	4 (2·8)	5 (2·4)
Hindu	0 (0)	0 (0·0)	0 (0·0)
Muslim	0 (0)	2 (1·4)	2 (0·9)
Sikh	0 (0)	1 (0·7)	1 (0·5)
Other	0 (0)	2 (1·4)	2 (0·9)
Highest level of education obtained			
No formal qualifications	0 (0)	10 (6·9)	10 (4·7)
1–4 O-levels/GCSEs	6 (9)	16 (11·0)	22 (10·4)
≥ 5 O-levels/GCSEs	5 (7)	11 (7·6)	16 (7·6)
NVQs	1 (1)	8 (5·5)	9 (4·3)
A-levels/AS-levels	10 (15)	24 (16·6)	34 (16·0)
Undergraduate degree	21 (31)	49 (33·8)	70 (33·0)
Master's degree	17 (25)	15 (10·3)	32 (15·1)
PhD	3 (4)	4 (2·8)	7 (3·3)
Other formal qualification	4 (6)	8 (5·5)	12 (5·7)
Ethnicity			
White British/Irish	63 (94)	126 (86·9)	189 (89·1)
White other	3 (4)	7 (4·8)	10 (4·7)
Mixed	0 (0)	3 (2·1)	3 (1·4)
Black/Black British	0 (0)	3 (2·1)	3 (1·4)
Asian/Asian British	1 (1)	4 (2·8)	5 (2·4)
Other	0 (0)	1 (0·7)	1 (0·5)
Missing	0 (0)	1 (0·7)	1 (0·5)

Data are presented as n (%). GCSE, General Certificate of Secondary Education; NVQ, National Vocational Qualification.

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 organization.

Descriptive statistics for sample characteristics for all respondents and the two subsamples are reported in Table 2. On average, people from the patient organization were more likely to be male, > 45 years of age, 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 (Appendix S5; see Supporting Information) between respondents recruited via the patient organization, 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.[36] The mean DLQI for both samples suggested that psoriasis had a moderate effect on respondents' lives. The DLQI potential scores range from 1 (small effect on the patient's life) to 30 (a large effect on the patient's life). The online panel provider sample reported a slightly greater impact of living with psoriasis (mean DLQI 7·12) vs. the patient organization 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 organization sample) indicated that they understood the information provided.

Sample-reported experience of psoriasis and biologics 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 than those from the patient organization (see Table 3). The vast majority of respondents in either group had never been prescribed biologics.

Table 3 Patient-reported experience of psoriasis and taking biologics

	Patient organization (n = 67)	Online panel provider (n = 145)
Time since diagnosis of psoriasis		
< 1 month	1 (1)	0 (0·0)
> 1 month but < 3 months	0 (0)	6 (4·1)
> 3 months but < 6 months	0 (0)	0 (0·0)
> 6 months but < 1 year	0 (0)	7 (4·8)
> 1 year but < 2 years	0 (0)	7 (4·8)
> 2 years but < 5 years	4 (6)	14 (9·7)
> 5 years but < 10 years	6 (9)	24 (16·6)
> 10 years	56 (84)	87 (60·0)
Time taken from formal diagnosis to initiating an effective treatment		
It happened immediately	3 (4)	20 (13·8)
< 1 month	9 (13)	29 (20·0)
> 1 month but < 3 months	7 (10)	14 (9·7)
> 3 months but < 6 months	6 (9)	17 (11·7)
> 6 months but < 1 year	4 (6)	10 (6·9)
> 1 year but < 2 years	7 (10)	5 (3·5)
> 2 years but < 5 years	5 (7)	8 (5·5)
> 5 years	13 (19)	16 (11·0)
Still not on effective treatment	13 (19)	26 (17·9)
Last flare-up since the diagnosis of psoriasis		
I am having a flare-up now	12 (18)	30 (20·7)
In the last month	8 (12)	27 (18·6)
In the last 3 months	4 (6)	16 (11·0)
In the last 6 months	6 (9)	17 (11·7)
In the last year	10 (15)	18 (12·4)
> 1 year ago	21 (31)	24 (16·6)
I have not had a flare-up	6 (9)	13 (9·0)
Currently on original treatment		
Yes	9 (13)	49 (33·8)
Yes but on a different dosage	1 (1)	12 (8·3)
No	57 (85)	84 (57·9)
Previous experience with biologics		
Adalimumab (Humira®)	6 (9)	7 (4·8)
Etanercept (Enbrel®)	6 (9)	4 (2·8)
Infliximab (Remicade®)	0 (0)	10 (6·9)
Ustekinumab (Stelara®)	4 (6)	5 (3·5)
Secukinumab (Cosentyx®)	2 (3)	4 (2·8)
Other biologic	1 (1)	4 (2·8)
I have not been prescribed biologics	56 (84)	112 (77·2)
Not sure	0 (0)	11 (7·6)
Side-effects from psoriasis treatment		
Yes	36 (54)	21 (14·5)
No	29 (43)	117 (80·7)
Don't know	2 (3)	7 (4·8)

Data are presented as n (%).

Patient preferences

The results from the conditional logit models for each sample and the Swait and Louviere plot confirmed the presence of potential scale and preference heterogeneity (Appendix S3).[31] 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 organization, 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 (the 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

Table 4 Results of the random parameters logit model

	Patient organization coefficient (SE)[a]	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)**
PPV[b]	1·807 (0·59)**	0·432 (0·07)***	0·425 (0·06)***
NPV[b]	2·712 (1·66)	0·704 (0·31)*	0·155 (0·34)
Risk	−0·679 (0·29)*	−0·323 (0·07)***	−0·217 (0·06)***
Cost[c]	0·306 (0·16)	0·119 (0·04)**	0·067 (0·04)
Number of observations	1005	2175	3180

ASC, alternative-specific constant; BIC, Bayesian Information Criterion; NPV, negative predictive value (ability to predict nonresponse); PPV, positive predictive value (ability to predict response); SE, standard error. [a]The BIC for the patient organization sample suggested that the random parameters logit [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. [b]Attribute rescaled so 1% = 10%. [c]Attribute rescaled so £1 = £100. *P < 0·05; **P < 0·01; ***P < 0·001.

Table 5 Estimated marginal rates of substitution for willingness to delay treatment

	Willingness to delay treatment	
	Patient organization (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 days (−189·28 to 240·52)	611·68 days (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)

NPV, negative predictive value (ability to predict nonresponse); PPV, positive predictive value (ability to predict response).

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 organization 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 (Table 4).

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 (Appendix S4; see Supporting Information). Respondents collated from the patient organization 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 vs. 28·84 days in the patient organization 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 organization 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 organization group of respondents displayed stronger preferences for predictive accuracy of the algorithm. The MRS values for the ability to predict response (PPV) and nonresponse (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 nonresponse (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 organization 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 suggested that NPV was as important as PPV to patients, although it was not statistically significant in the patient organization sample. This suggests that patients showed a clear preference to avoid being prescribed a biological treatment that will not work for them. This finding is important as most research aims to identify markers of response (rather than nonresponse).[37,38]

The observation that probability of nonresponse 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.[15] Another DCE that elicited preferences of neurologists for pharmacogenetic testing in epilepsy also suggested NPV to be a strong predictor of preferences.[39] 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.[40] 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 owing to the simple division of attribute coefficients to obtain ratios.[40,41]

The findings of this DCE survey come with limitations. The use of an online panel provider for patient recruitment could limit the generalizability 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.[42]

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 to capture the preferences of people likely to be prescribed a biologic, which would allow us to determine the generalizability of the results of this study. The preferences of clinicians involved in the prescribing of biological therapies could also be investigated and compared with those of the patients. Further methodological research is required to assess the impact of nonlinear attributes on estimates of MRS.[43]

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,[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) vs. 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 nonresponse (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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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Appendix S1 The survey.
Appendix S2 Defining the levels for each attribute.
Appendix S3 Understanding the impact of heterogeneity.
Appendix S4 Quantifying the balance between benefits and harms.
Appendix S5 Illustration of reported health status in survey respondents.