BMJ Open Personal preferences for Personalised Trials among patients with chronic diseases: an empirical Bayesian analysis of a conjoint survey

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ABSTRACT

Objective To describe individual patient preferences for Personalised Trials and to identify factors and conditions associated with patient preferences.

Design Each participant was presented with 18 conjoint questions via an online survey. Each question provided two choices of Personalised Trials that were defined by up to eight attributes, including treatment types, clinician involvement, study logistics and trial burden on a patient.

Setting Online survey of adults with at least two common chronic conditions in the USA.

Participants A nationally representative sample of 501 individuals were recruited from the Chronic Illness Panel by Harris Poll Online. Participants were recruited from several sources, including emails, social media and telephone recruitment of the target population.

Main outcome measures The choice of Personalised Trial design that the participant preferred with each conjoint question.

Results There was large variability in participants' preferences for the design of Personalised Trials. On average, they preferred certain attributes, such as a short time commitment and no cost. Notably, a population-level analysis correctly predicted 62% of the conjoint responses. An empirical Bayesian analysis of the conjoint data, which supported the estimation of individual-level preferences, improved the accuracy to 86%. Based on estimates of individual-level preferences, patients with chronic pain preferred a long study duration ($p \leq 0.001$). Asthma patients were less averse to participation burden in terms of data-collection frequency than patients with other conditions ($p = 0.002$). Patients with hypertension were more cost-sensitive ($p < 0.001$).

Conclusion These analyses provide a framework for elucidating individual-level preferences when implementing novel patient-centred interventions. The data showed that patient preference in Personalised Trials is highly variable, suggesting that individual differences must be accounted for when marketing Personalised Trials. These results have implications for advancing precise interventions in Personalised Trials by indicating when rigorous scientific principles, such as frequent monitoring, is feasible in a substantial subset of patients.

Strengths and limitations of this study

- This large online conjoint survey leveraged a rigorously assembled panel by Harris Poll Online.
- We surveyed a nationally representative sample for age, gender, race/ethnicity, socioeconomic status and geography in the USA.
- The individual-level analyses took advantage of an empirical Bayesian procedure that borrowed information from across individuals.
- Utilities in conjoint analysis are interpreted relatively among the attributes included in the survey, and cannot be interpreted in any absolute sense.
- Generalisability of our findings might be limited to patients with two or more chronic conditions pre-defined in the study.

INTRODUCTION

When managing chronic diseases and conditions, patients commonly try different treatments over time before finding the 'right' treatments for them. Personalised Trials, also known as N-of-1 trials, aim to facilitate this type of patient-centred experimentation. Contrast to the conventional randomised clinical trials where each participant is randomised once to a single treatment, Personalised Trials randomise treatments to the patient in multiple crossover periods using clinical trial principles, such as blinding and ascertaining ecological outcomes.^{1 2} These methods are particularly suitable for identifying long-term treatments for chronic conditions for which treatment effects are heterogeneous across patients and thus require individualised treatments.³ In a series of demonstration trials, Personalised Trials led to valuable changes in treatment, cessation of treatment or confirmation of the original treatment.^{4–8} Due to its pragmatic nature, the practice of Personalised Trials may provide individual patients

with the best evidence about their treatment choices. As a result, some have placed Personalised Trials at the top of the methodological hierarchy of evidence-based medicine for informing treatment decisions.⁴ Recently, there has been renewed interest in using Personalised Trials for a variety of conditions,^{9–12} however, their clinical practice remains scattered due, in part, to insufficient patient acceptability and demand.^{13–15}

With a goal of increasing the adoption of Personalised Trials into clinical practice, we developed a ‘collaboratory’ comprising a diverse pool of stakeholders—including patients—relevant to the design and implementation of Personalised Trials.¹⁶ Under the guidance of the collaboratory, we conducted an online conjoint survey in a representative sample of adults with chronic conditions who reside in the USA. In a primary analysis, which ascertained patient preferences for the design of Personalised Trials, we identified significantly positive utilities for Personalised Trials that would impose no out-of-pocket costs on patients and for those that would require a short time commitment for daily self-tracking.¹⁷ These findings generally reflect that the average patient prefers Personalised Trials that are less burdensome in terms of cost and time commitment. They also provide useful information on design acceptability on a population level. However, the degree to which *individual-level* preferences are driving acceptability of Personalised Trials remains unknown.

Conjoint surveys are a well-established method for assessing product acceptability in market research and economics, and more recently, for assessing patient preferences in healthcare at the population level.^{18–22} Recent interest in precision medicine has increased the focus on elucidating patient preferences at both the population and individual levels. While heterogeneity of treatment effects in the population motivates Personalised Trials, heterogeneity in individual preferences of attributes for Personalised Trials may be critical to explaining acceptability and improving dissemination of this approach. In this article, we used the full conjoint data to assess variations in *individual-level* preferences for the design of Personalised Trials and to identify subpopulations of patients according to their preferences.

METHODS

Survey development

We designed an online survey study by engaging stakeholders through a Personalised Trial collaboratory. This collaboratory consisted of 30 members, including patients with multiple comorbidities, clinicians with and without experience conducting N-of-1 trials, healthcare administrators, scientists, methodologists/statisticians, ethicists and experts in dissemination. Between July 2014 to September 2017, the collaboratory met quarterly to review the study design, conduct, analysis and dissemination/interpretability. Collaboratory meetings were conducted by phone and in person, and they were scheduled to maximise the availability of all participants. This

Table 1 Design attributes of Personalised Trials

Domain	Design attributes	Levels
Clinician involvement	Treatment selection	<ul style="list-style-type: none"> ▶ Patient chooses treatments to compare in the study ▶ Clinician chooses treatments to compare in the study
	Trial conduct	<ul style="list-style-type: none"> ▶ Study is conducted without clinician involvement ▶ Study is conducted with clinician involvement
Treatment	Type of treatment	<ul style="list-style-type: none"> ▶ Prescription medication ▶ Lifestyle change ▶ Complementary alternative medicine
Burden of participation	Time commitment	<ul style="list-style-type: none"> ▶ 5 min per day ▶ 30 min per day
	Data collection frequency	<ul style="list-style-type: none"> ▶ Once per day ▶ Three times per day
	Study duration	<ul style="list-style-type: none"> ▶ 2 weeks ▶ 12 weeks
Patient burden	Out-of-pocket cost	<ul style="list-style-type: none"> ▶ No cost (all costs, including travel, are covered) ▶ US\$100
Logistics	Blinding	<ul style="list-style-type: none"> ▶ The study is not blinded ▶ The study is blinded

approach fostered a transparent process and helped to improve the relevance of the study question. To inform survey development, we first conducted focus groups with providers (n=24) and patients (n=54) to understand attitudes toward Personalised Trials and design features.^{23 24} We then conducted an initial survey and literature review to identify the key design attributes that could be informed by patient preferences (eg, blinding, intensity of self-tracking, extent of clinician involvement).

As part of a second survey, each participant answered 18 choice-based conjoint questions that simulated the selection of a Personalised Trial. Each question prompted participants to select which prototype they preferred in two hypothetical trial prototypes with up to eight design attributes (table 1). Of the 18 conjoint questions, 15 used a short format in which participants chose between two hypothetical trials that differed by only two attributes (eg, no-cost and long-duration trial vs some-cost and low-duration trial) (figure 1). The remaining three conjoint questions used a long format in which participants chose between two hypothetical trials that differed across all eight attributes at once (figure 2). We tested for interactions between attributes in our previous work, considering only data from the three long-format questions, and

Figure 1 Example of a short-format question shown to a participant in the online survey. This screenshot presents two attributes (study duration and cost) in each of the two hypothetical trials (option A and option B).

we did not find any evidence.¹⁷ In the present analysis, in which we were interested in identifying *individual-level* preferences, we used data from all 18 questions per individual. We developed a statistically efficient design using Sawtooth Choice-Based Conjoint software (Sawtooth, 2010) to generate a pool of 60 conjoint questions (45 short and 15 long). For the short questions, each attribute appeared with other attributes in the same question at least once to allow for direct contrast. The method for generating the long-format questions was similar to that previously reported.¹⁷ In all, each participant was randomly assigned 18 conjoint questions, 15 of which were drawn from the 45 short questions and 3 from the 15 long questions. In addition to conjoint questions, we collected data on the survey participants' demographics and diagnosis of chronic disease. The survey used in the study is provided in online supplementary file 1.

Patient public involvement

Fifty-four patients were involved in the development of the initial survey through the collaboratory and focus groups. This process helped informed how we defined the parameters in the conjoint survey.

Study participants

We conducted the survey among 501 participants who were at least 18 years old, resided in the USA and reported

having two or more chronic diseases from a list of six diseases (asthma, osteoporosis, depression, diabetes, hypertension and hyperlipidaemia). This eligibility list of diseases reflected a mix of symptomatic, asymptomatic and mental health conditions that are among the most highly prevalent and burdensome in the USA.^{25 26}

Recruitment of the participants was achieved through a general population panel maintained by Harris Poll Online (HPOL), which includes several million online members. The HPOL panel was recruited from several sources, including targeted emails sent by online partners, social media, news and telephone recruitment of targeted populations. Each recruitment source was carefully vetted through a rigorous interviewing and testing process and then continually monitored for response quality. For the present study, the HPOL database of respondent information was actively screened and updated along with numerous demographic and psychographic variables to allow for precision in the online sample provided. These sampling procedures have been widely used and support a rigorous, scientifically acceptable practice without spending considerable time and energy assembling large, comprehensive samples.²⁷ To reach the target sample size and achieve a representative sample with at least two chronic diseases,²⁸ we screened and invited 15883 potentially eligible individuals from the HPOL to participate in the study via email. Details about sample size determination and participant inclusion were reported previously.¹⁷ All participants provided informed consent via e-signature. Only those participants at least minimally interested in participating in a Personalised Trial for hypertension, hyperlipidaemia, diabetes, depression, arthritis/joint pain, breathing problems/bronchitis/asthma, back pain or sleeping problems/insomnia completed the survey. These patient conditions were the highest-ranked, patient-preferred conditions and deemed appropriate for Personalised Trials in our prior research. The cohort selection and participant characteristics are described in a previous report.¹⁷

Statistical analysis

Estimating individual-level utilities and preferences

Individual patient preferences for different attributes of Personalised Trials were estimated using empirical Bayesian latent utility modelling on all conjoint responses of the participants. Details of the model are given in online supplementary file 2. Briefly, under this model, the latent utility of trial prototype j to a participant i (denoted as u_{ij}) was postulated to follow a logistic distribution in which the mean depended on a linear combination of trial attributes. Specifically, having $u_{ij} = \beta_i^T x_{ij} + \varepsilon_{ij}$, where ε_{ij} is a standard logistic error and the design x_{ij} indicated the presence/absence of attributes in prototype j presented to the participant. The coefficient β_i captured the *individual-level utility* of participant i and was estimated by the posterior mode assuming a mean zero normal prior on β_i . We circumvented the subjectivity of postulating the prior variance-covariance matrix by estimating

Figure 2 Example of a long-format question shown to a participant in the online survey. This screenshot presents eight attributes in each of the two hypothetical trials (option A and option B).

the matrix empirically using the marginal likelihood.²⁹ For each attribute, a participant was indicated to have a positive or negative preference if the estimated individual utility was positive or negative, respectively. The reliability of the estimate for individual-level utilities depended on the number of questions answered per participant. Thus, we excluded from the analysis those who answered 16 or fewer of the 18 questions.

In addition, we fitted a latent utility model at a population level to all conjoint responses. This model assumed no individual deviations from the population average and set $\beta_i = \beta$ for all participants. Under this population model, every individual would be estimated to have the same preference for a given attribute.

The benefits of accounting for individual preferences were assessed by comparing the classification rates of correct responses in the personalised and population-level models. Correlations among the design attributes were explored graphically and using Pearson correlation coefficients based on the individual-level utilities estimated by the personalised model.

Sample segmentation

We recorded the following baseline characteristics for each participant and summarised them as categorical variables: age (younger than 65 years vs 65 years or older), sex (male vs female), race/ethnicity (non-Hispanic white vs others), income (less than US\$35 000 vs US\$35 000 or more), education (some college or more vs less than college), work status (employed full-time/part-time vs not employed), insurance status (with vs without insurance) and region of residence (Northeast vs South vs Midwest vs West). Associations between these characteristics and individual preferences were summarised using contingency tables and tested using χ^2 tests; two-sided p values were reported. As exploratory analyses, we also compared the variability of individual-level utilities by these characteristics using Bartlett's test, and we displayed the utility distributions in graphs.

We also considered the following chronic conditions in the analysis: joint pain, asthma, back pain, depression, diabetes, hypertension, hyperlipidaemia and insomnia. We asked whether a participant had a given condition; those who had the condition were asked to indicate their interest in participating in Personalised Trials. Association between chronic conditions and individual preferences were analysed in the same manner as above.

RESULTS

Population-level utilities

Among the 501 survey participants, most (n=497) answered all 18 conjoint questions and three answered 17 questions (14 short-format, 3 long-format). One participant who answered all 15 short questions but not the long questions was excluded from the analysis. Thus, we estimated the utilities in 500 participants with a total of 8997 conjoint responses (1500 long-format and 7497

Table 2 Participant characteristics and conditions

Characteristics	N (%)	Conditions	N (%)
Age		Joint pain	
65 or above	182 (36%)	Yes	215 (43%)
Below 65	318 (64%)	No	285 (57%)
Sex		Asthma	
Male	222 (44%)	Yes	149 (30%)
Female	278 (56%)	No	351 (70%)
Race/ethnicity		Back pain	
Non-Hispanic whites	341 (68%)	Yes	177 (35%)
Others	159 (32%)	No	323 (65%)
Education		Depression	
College or more	400 (80%)	Yes	210 (42%)
Less than college	100 (20%)	No	290 (58%)
Work status		Diabetes	
Employed (full-time/part-time)	230 (46%)	Yes	180 (36%)
Not employed	270 (54%)	No	320 (64%)
Income		Hypertension	
US\$35 000 or above	309 (62%)	Yes	371 (74%)
Below US\$35 000	191 (38%)	No	129 (26%)
Insurance		Hyperlipidaemia	
Have insurance	452 (90%)	Yes	270 (54%)
No insurance	48 (10%)	No	230 (46%)
Region		Insomnia	
Northeast	86 (17%)	Yes	121 (24%)
South	194 (39%)	No	379 (76%)
Midwest	116 (23%)		
West	104 (21%)		

short-format) from the participants recruited through HPOL. Table 2 describes the participant characteristics and gives the distribution of the chronic conditions.

Table 3 presents the estimated utilities of trial design attributes according to the population-level model, along with the 95% CIs. The analysis that used only the long-format questions identified two statistically significant attributes preferred by the participants on a population level: requiring short (5 min) time commitment (utility difference=0.16; p=0.015) and having no cost (utility difference=1.52; p<0.001). The analysis using all conjoint questions confirmed the findings for these two attributes with greater precision. It also revealed that participants preferred complementary alternative medicine (CAM) over prescription medication (utility difference=0.15;

Table 3 Population-level utilities for design attributes of Personalised Trials

Attribute description	Utility (95% CI)	
	Long-format questions only (n=1500)	All questions (n=8997)
Patient lets <u>clinician choose treatments</u> instead of choosing own	0.03 (-0.10 to 0.17)	-0.01 (-0.10 to 0.07)
Study is conducted <u>with clinician involvement</u> instead of without	0.11 (-0.02 to 0.25)	0.17 (0.09 to 0.25)*
Treatment is <u>lifestyle change</u> instead of prescription medication	0.02 (-0.17 to 0.21)	-0.14 (-0.24 to -0.05)*
Treatment is <u>CAM</u> instead of prescription medication	0.15 (-0.04 to 0.34)	0.15 (0.06 to 0.24)*
Study requires <u>5 min</u> commitment daily instead of 30 min	0.16 (0.03 to 0.30)*	0.42 (0.34 to 0.50)*
Study <u>collects data one time per day</u> instead of three times per day	0.08 (-0.06 to 0.21)	0.34 (0.25 to 0.42)*
Study lasts <u>2 weeks</u> instead of 12 weeks	0.05 (-0.09 to 0.18)	0.00 (-0.09 to 0.09)
Study has <u>no cost</u> instead of costing US\$100	1.52 (1.39 to 1.66)*	1.40 (1.30 to 1.50)*
Study is <u>blinded</u> instead of not being blinded	-0.08 (-0.22 to 0.05)	-0.34 (-0.42 to -0.25)*

*P<0.05, indicated by 95% CIs excluding zero.

CAM, complementary alternative medicine.

p=0.001), which was preferred over lifestyle changes (utility difference=0.14; p=0.002), and to have clinician involvement (vs no involvement) during the study (utility difference=0.17; p<0.001). We also found that a low frequency of data collection had a positive utility (utility difference=0.34; p<0.001) and blinding had a negative utility (utility difference=-0.34; p<0.001).

In summary, the population-level analysis depicted that participants favoured Personalised Trials with an experiment of CAM and clinician supervision in an unblinded fashion. They also preferred a low level of burden in terms of time commitment and data-collection frequency, as well as no out-of-pocket cost. Using this typified protocol would yield a 62% correct prediction in all 8997 conjoint responses, while randomly guessing a response would yield 50%.

Individual-level utilities

Several participants had preferences that deviated from the population results shown above. Twelve per cent (n=59) of the participants preferred bearing out-of-pocket costs, 18% (n=91) preferred a long daily time commitment and 16% (n=78) preferred a frequent data-collection schedule (table 4). The cohort's average preference was skewed towards not being blinded during a trial, although to a lesser extent (30% preferred blinding). The preferences for the other design attributes (eg, study duration) were relatively evenly distributed, suggesting heterogeneity in preferences among the participants.

Figure 3 demonstrates the variations in the numerical individual-level utilities for design attributes according to the personalised model. For example, while most participants had a strong positive preference for no cost (ie, having a positive utility vs US\$100 cost), some individuals had large negative utility for bearing no cost. Similarly, while the whole population had a negative utility on blinding, some individuals had positive utilities for blinding.

Using these estimated individual-level utilities based on the personalised model to predict responses in the conjoint survey would yield an 86% correct prediction in all 8997 responses. This result is a marked increase of 24 percentage points above the population-level analysis.

There was a strong correlation between utilities for clinician involvement during a study and a clinician choosing the treatments when planning the study (correlation=0.96; p<0.001; figure 4A). Attributes related to burden of participation were correlated: participants who had high utilities for short daily time commitment tended to have high utilities for fewer data collections per day (correlation=0.87; p<0.001; figure 4B), for short study duration (correlation=0.20; p<0.001; figure 4C) and for not paying out-of-pocket costs (correlation=0.69; p<0.001; figure 4D). Preferences for medication and CAM compared with lifestyle change were statistically associated with preference for blinding: the correlation with utilities for blinding was 0.28 (p<0.001) for utilities for medication over lifestyle change, and 0.36 (p<0.001) for utilities for CAM over lifestyle change.

Association between individual-level preferences and demographics

Of the male participants, about 60% preferred a clinician choosing the treatment (online supplementary table S1 in online supplementary file 3) and being involved in conducting the trial (online supplementary table S2), while 53% were estimated to prefer prescription medication (online supplementary table S3). The preferences among female participants on these attributes were relatively evenly distributed.

Race/ethnicity groups other than non-Hispanic whites were less averse to participation burden (ie, time commitment, data-collection frequency, study duration and out-of-pocket cost) compared with non-Hispanic whites (online supplementary tables S4–S7), although the whole cohort would prefer less burden.

Table 4 Individual preferences for attributes of Personalised Trials

Attribute description	Number of participants (%)
Treatment selection	
Prefer patient choosing treatments	235 (47%)
Prefer clinician choosing treatments	265 (53%)
Trial conduct	
Prefer no clinician involvement during study	226 (45%)
Prefer clinician involvement during study	274 (55%)
Treatment types	
Prefer prescription medications	209 (42%)
Prefer lifestyle change	123 (25%)
Prefer CAM	168 (34%)
Patient burden/commitment	
5 min daily	409 (82%)
30 min daily	91 (18%)
Data-collection frequency	
One time per day	422 (84%)
Three times per day	78 (16%)
Study duration	
2 weeks	243 (49%)
12 weeks	257 (51%)
Out-of-pocket costs	
None	441 (88%)
US\$100	59 (12%)
Blinding	
Prefer not blinding	352 (70%)
Prefer blinding	148 (30%)

CAM, complementary alternative medicine.

Participants younger than 65 years were overall less averse to participation burden than the older group (except for study duration). In addition, the younger participants demonstrated greater variability in their utilities for data collection frequency (variance ratio=1.32; $p=0.040$; figure 5A) and cost (variance ratio=1.48; $p=0.004$) than the older participants, resulting in some outlying values favouring high burden (figure 5B).

Participants who were employed were less averse to costs (online supplementary table S7) and high frequency of data collection (online supplementary table S5) than those who were unemployed. They also demonstrated greater heterogeneity in their preferences for these attributes with variance ratios 2.07 ($p<0.001$; figure 5C) and 1.66 ($p<0.001$; figure 5D), respectively. Participants with high income were less averse to bearing some out-of-pocket costs than those with low income (online supplementary table S7), with greater heterogeneity in their

Figure 3 Distribution of individual-level utilities for different attributes. The vertical red lines indicate the average utility in the cohort. CAM, complementary alternative medicine.

preference for high data-collection frequency (variance ratio=1.45; $p=0.005$; figure 5E) and out-of-pocket costs (variance ratio=1.72; $p<0.001$; figure 5F).

Education was associated with treatment types: participants with a college education or more preferred prescription medication, whereas the others preferred CAM (online supplementary table S3).

Insurance status and region of residence did not correlate with any preferences in design attributes. No

Figure 4 Correlations of individual-level utilities for some attributes.

Figure 5 Distribution of individual-level utilities for data-collection frequency (top) and out-of-pocket cost (bottom) by age, employment status and income.

association was found between preference for blinding and any demographics, suggesting blinding was consistently undesirable across the demographic spectrum (online supplementary table S8).

Association between individual-level preferences and chronic conditions

Patients with diabetes (and to a lesser extent those with hyperlipidaemia) preferred clinician involvement (online supplementary tables S9 and S10). In addition, diabetic patients with interest in Personalised Trials preferred medications compared with the other groups (online supplementary table S11).

Patients with asthma preferred no clinician involvement (online supplementary table S10). They were less averse to participation burden in terms of daily time commitment (online supplementary table S12) and data-collection frequency (online supplementary table S13), although no difference was noted for study duration (online supplementary table S14). A larger percentage of asthma patients preferred out-of-pocket cost compared with other patients (online supplementary table S15). In particular, participants with hypertension were more cost-sensitive than those with other conditions (online supplementary table S15).

Participants with joint pain or back pain who were interested in participating in a Personalised Trial preferred a long study duration (online supplementary table S14), but were also much less willing to bear costs compared with those without the diagnosis (online supplementary table S15).

None of the patient conditions were correlated with blinding (online supplementary table S16).

DISCUSSION

In this article, we analysed a conjoint survey conducted in a representative sample of patients with multiple chronic conditions living in the USA and aimed to understand

the variability in preferences for design attributes in Personalised Trials. Using empirical Bayesian estimation, we assessed the individual-level utilities of the design attributes in the cohort. We found that the personalised model would improve on prediction of response to participation in Personalised Trials in a population-level model.

Comparison of findings

Our analysis offers important insights into the heterogeneity in preferences among individuals and suggests the need to personalise design features of Personalised Trials, including attributes that were deemed or thought to be undesirable. For example, while focussing on minimal time commitment and cost may be the best marketing approach based on the population-level analysis, we identified small segments in the cohort that were less averse to out-of-pocket costs (eg, high income, asthma) and long daily time commitment (eg, younger). The implication on practice is even greater for attributes with marked heterogeneity, such as study duration. Because one-half of the cohort preferred a short study duration and the other half preferred long duration, it may be beneficial to market the study duration based on patient preference. Our results also provide trialists of pain studies based on insights that long study trials are generally acceptable and even preferred among patients with chronic joint pain or back pain. Overall, our findings suggest that for those attributes with marked heterogeneity, the best approach may be to allow patients to design their own trials (eg, around treatment options, level of clinician involvement) to maximally improve acceptability and uptake of Personalised Trials.

We also confirmed our previous descriptive analysis and showed that out-of-pocket costs and long daily time commitment were two major deterrents of participation in Personalised Trials when averaged across patients. By using the full conjoint data (short and long questions, not only long questions), we also found additional undesirable attributes. For example, blinding negatively affected interest in participating in Personalised Trials at the population level (table 3). Our results are consistent with studies showing that blinding is a strong negative driver of patient decision-making regarding participation in clinical trials.^{30 31} On the other hand, our analyses of the individual preferences indicated that almost 30% of the participants actually preferred blinding as a design feature (table 4). This trend was quite robust across demographics and chronic conditions (online supplementary tables S8 and S16). Thus, our results suggest that providers and researchers may want to design trials in which blinding is optional in order to reach the maximum number of patients. This is particularly true for trials involving lifestyle change where blinding may not be feasible in the first place. Scientific validity in these settings should be further scrutinised by measuring and studying the underlying mechanisms of action (eg, self-efficacy). On the other hand, it is interesting to note that participants who preferred medication or CAM were less

averse to blinding. Therefore, blinding might still be a feasible choice to explore among patients who chose to test medication and CAM.

Clinical implications

Personalised Trials are designed to help a patient and his or her clinician make healthcare decisions that are informed by high-integrity, evidence-based information that is uniquely relevant to that patient's preferred outcomes and values. However, in the past, patients have not been willing to engage in these trials. Consequently, this powerful approach is almost never used. Only 108 series of Personalised Trials have been published,¹⁵ a marked dearth compared with other research methods. Major barriers to implementing Personalised Trials include a lack of knowledge about the conditions, treatments and outcomes for which patients would view such trials as beneficial; lack of design features that have been widely agreed on and would be acceptable to patients considering involvement in a Personalised Trial and poor understanding of patient tolerance for outcome assessment and burden.^{23 32}

Our findings support the implementation of Personalised Trials by providing information about the conditions and characteristics associated with greater acceptance of these trials, especially when combined with the use of technology. They also suggest useful strategies for improving uptake in select populations. For example, we found that asthma patients were more open to a greater frequency in data collection during a day, which might be best facilitated by smartphone and mobile technologies that automate daily collection and alleviate the burden on outcome assessments.^{33–35}

Strengths, limitations and future research

Our survey leveraged the panel assembled and maintained by the rigorous Harris Poll Online and was performed in a cohort representative for age, gender, race/ethnicity, socioeconomic status and region of residence in the USA. The 18 questions in the conjoint survey were completely answered in all but four participants, giving reliability in the assessment of individual-level preference for the eight design attributes, and resulting in new insights beyond our previous report that focussed on design acceptability at a population level. In addition, the empirical Bayesian procedure facilitated borrowing information from across individuals, and yielded stable computational results when estimating the individual utilities. The correlation among utilities for certain attributes and demographic variables demonstrated high level internal consistency.

Despite the strengths in the survey design and conduct, this study has a few limitations. First, the generalisability of our findings might have been limited by the eligibility criteria that included only participants with two or more predefined chronic conditions. In addition, due to the online survey methodology, our sample consisted of those with Internet access and those

who could self-report the symptoms of their conditions. However, as we created the list of chronic conditions using a careful process involving focus groups and national survey, these conditions captured the most common and burdensome symptomatic and asymptomatic conditions in the USA. Furthermore, the cohort was sampled to achieve the demographic, geographic and socioeconomic diversity representative of the USA.

Second, the individual-level analysis was performed as an exploratory analysis to describe the heterogeneity in the population. As a result, the number of conjoint questions as well as the survey sample size were not determined a priori to ensure adequate precision in this analysis. Specifically, the sample size would not be adequate to assess the interaction of chronic conditions on preference differences. For example, only 28 participants with asthma and hypertension indicated they were very interested in participation in an asthma Personalised Trial and a hypertension Personalised Trial. Our study data might however suggest the more prevalent comorbidity combinations for further investigation. Third, the attributes and the levels of attributes considered in the survey was not disease specific. As a result, some of the levels might not be ideally defined; for example, 12 weeks might not be considered a long study in the asthma population. Fourth, our analyses were not designed to assess the relationship between attributes and actual behaviour around or acceptance for a Personalised Trial protocol in the survey, as the conjoint choice-based questions aimed to elicit implicit *relative* utilities for different levels of attributes in the protocol and to identify important attributes for personalisation. While disseminating the results to the online study participants is not applicable, future research should focus on testing whether including these individual preferences in a Personalised Trial design will increase acceptability by the patients and facilitate dissemination and integration into clinical practice.

CONCLUSIONS

In the true spirit of Personalised Trials, we sought to ascertain individual variability in preferences for the design of Personalised Trials. Incorporating individual preferences may improve willingness to participate in Personalised Trials. Our study also provides a framework for elucidating the degree to which individual-level (vs population-level) factors drive willingness and behaviour, with widespread implications for improving the uptake of other patient-centred evidence-based innovations and programmes. Just as Personalised Trials are intended to best match patients with effective treatments, understanding individual preferences for Personalised Trials is an equally important consideration for matching the design of a Personalised Trial with a patient's preference.

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