



# Preferences for Treatments for Major Depressive Disorder: Formative Qualitative Research Using the Patient Experience

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## Abstract

**Objectives** The goals of this formative research are to elicit attributes of treatment and desired outcomes that are important to individuals with major depressive disorder (MDD), to develop a stated preference instrument, and to pre-test the instrument.

**Methods** A three-phase survey study design elicited the patient's journey with MDD to design and pre-test the discrete choice experiment (DCE) instrument. Participants were 20 adults aged  $\geq 18$  with MDD who did not also have bipolar disorder or post-partum depression. We engaged patient advocates and a multi-disciplinary stakeholder advisory group to select and refine attributes for inclusion in a DCE instrument. The DCE was incorporated into a survey that also collected depression treatment and management and sociodemographic characteristics. The DCE was pre-tested with ten adults with MDD.

**Results** Six attributes were included in the DCE: mode of treatment (medicine only, psychotherapy only, all modalities including brain stimulation), time to treatment effect (6, 9, 12 weeks), days of hopefulness (2, 4, 6 days/week), effect on productivity (40%, 60%, 90% increase), relations with others (strained, improved, no impact), and out-of-pocket costs (\$30, \$60, \$90/month). The DCE test led to the refinement of mode of treatment (medicine, medicine and psychotherapy, and all modalities); time to treatment effect (4, 6, 9 weeks); monthly out-of-pocket costs (\$30, \$90, \$270).

**Conclusions** MDD treatment preferences revealed trade-offs among mode of treatment, time to treatment effect, functional outcomes, and cost. The findings demonstrate the potential for meaningfully incorporating the patient experience in preference measures.

## 1 Introduction

Major depressive disorder (MDD) affects 7–10% of US adults and is the largest contributor of disability-adjusted life years among all mental disorders [1]. Nearly two-thirds of adults living with MDD have severe impairment that affects their daily activities [2]. The prevalence increased 13% from 2010 to 2018 [2, 3], and the coronavirus disease 2019 (COVID-19) pandemic contributed to a threefold

increase in depression symptoms [4]. Therapeutic options for managing depression include antidepressant medications and psychotherapy, alone or in combination. Approximately 70% of adults with MDD use an antidepressant [3]. However, electroconvulsive therapy (ECT), vagus nerve stimulation, transcranial magnetic stimulation, and deep brain stimulation are other alternatives [5]. Available therapeutic options vary in their benefits and risks, and some may be more or less preferred by individuals living with MDD.

An understanding of individuals' journeys with MDD would shed light on patient experiences that influence preferences for treatment options and desired outcomes. The patient experience could meaningfully inform measures to evaluate treatment decisions, adherence, and outcomes. With as many as 50% of individuals non-adherent to depression treatment [6], it is plausible that preferences for specific attributes of treatment or tolerance of benefits and risks may underpin adherence. A qualitative study found that, while taking antidepressants, over 85% of adults with depression reported symptom reduction and improved quality of life, but 30% continued to experience

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### Key Points for Decision Makers

Engaging patients, patient advocates, and a multidisciplinary stakeholder advisory group, we identified six key factors that matter most to individuals with major depressive disorder when considering treatment options.

Important outcomes were feeling hopeful about their life, improving their productivity, and maintaining relations with people important to them.

Persons with major depressive disorder weighed the benefits of hopeful days and productivity against mode of treatment and cost.

moderate-to-severe depression [7]. Using a choice-based conjoint analysis to evaluate the relative importance of eight depression treatment outcomes, investigators found that four outcomes related to daily functioning (fatigue, loss of enjoyment, guilt, and depressed mood) explained 52% of the variance in treatment preferences [8]. Increasingly, studies are using health preference methods to quantify the utility of attributes of a healthcare intervention [9, 10] and to generate a quantifiable measure of the relative importance of intervention attributes. [11]

The present study's approach starts with identifying what matters most to individuals with MDD regarding their depression management and tailored a core set of patient-informed value elements [12, 13] to the patient experience. The objectives of the present research are to (1) apply the patient-informed value element framework to elicit the elements that are important to individuals' treatment decisions; (2) select and refine candidate attributes and levels for inclusion in a stated preference tool; and (3) develop and pre-test a stated preference instrument to quantify the attributes of depression treatment that adults with MDD most prefer. The underlying premise for the research hypotheses is that individuals' experiences living with MDD influence what they value the most from different treatment options.

## 2 Methods

### 2.1 Study Design

The study was implemented sequentially through iterative steps to elicit the individual's journey with MDD. Interviews incorporated guided activities to identify the most important elements from the PAVE patient-informed value element

framework [12]. Triangulating data from the literature, individual interviews, and a secondary data analysis, we designed and pre-tested a discrete choice experiment (DCE) instrument. The study procedures follow the methodologic approach used previously by our group [13, 14] and comprise formative work for a future stated preference instrument [15]. The University of Maryland Baltimore Institutional Review Board approved the study protocol.

### 2.2 Study Sample

We enrolled a convenience sample of 20 adults who were aged 18 and older, could speak and read English, and had been diagnosed with MDD by a healthcare professional. Exclusion criteria were a diagnosis of bipolar disorder, psychosis, cognitive disability, or post-partum depression, or residence in an institutional setting (i.e., residential treatment facility or group home).

### 2.3 Study Procedures

#### 2.3.1 Literature Review

A comprehensive literature review identified relevant attributes of depression treatment and outcomes that are important to individuals living with depression. We used PubMed and Embase search engines with the following terms: treatment decision-making, patient preferences, and patient values. The inclusion criteria were articles where the study sample was age 18 or older, the focus was on preferences for depression treatment, the data were collected from patients, and empirical data were reported. We excluded editorials, viewpoints, and conference abstracts, unless the full paper was published. Following title/abstract screening, a full-text review identified eight relevant papers. Data abstraction for the key themes are provided in Table S1 (see the electronic supplementary material).

#### 2.3.2 Stakeholder Advisors

Stakeholders representing the patient voice served as key consultants to the research team and were engaged in key decisions in all phases of this research. A co-author and patient stakeholder from the PAVE Center, who raised a child with a mental health condition, assisted with the interpretation and contextualization of the patient-informed value elements influencing treatment decisions for MDD. A 20-member MDD-specific multi-stakeholder advisory group (SAG) [16] with representation from patient communities, payers, manufacturers, clinical experts, researchers, and employers assisted with the selection and definition of the key value elements and with participant recruitment.

### 2.3.3 Value Element Elicitation from Adults Living with MDD

Adults with MDD were recruited through a national patient advocacy organization and community clinics. A study flyer was distributed via email to members of the patient advocacy organization and to the community clinic director assisting with recruitment. Interested individuals contacted the Principal Investigator by email or phone. We (SDR, LMB, JFS) scheduled a date and time to conduct the screening and interview for those deemed eligible based on the criteria listed above. Study instruments were administered using a web-based platform that enabled phone and video capabilities. If videoconferencing technology was not available, the research team emailed the study instruments in advance so that participants could follow along. We obtained informed consent prior to the administration of the study instruments.

To elicit the individual's journey with MDD, the research team member asked participants the following question: 'Can you describe what it has been like for you from the beginning to where you currently are today?' During the discussion, the research team member asked questions about current and past treatments, access to treatment modalities, and the impact of MDD and treatment on their daily activities and social relationships. The discussion was recorded, and notes were taken to capture key details of the individual's journey.

Next, we used five guided activities (Table S2; see the electronic supplementary material), one for each domain of the patient-informed value element conceptual framework, i.e., treatment effects, treatment access, treatment cost, life impact, and social impact [12]. A total of 42 elements were shown, with the number of elements per domain as follows: 11 for treatment effects; ten for treatment access; eight for treatment cost; seven for life impact; six for social impact. Within each domain, participants first selected all elements that were important when considering their selection of the best MDD treatment. Of the elements selected, they chose up to five elements that were the most important in each domain. The guided activities generated a list of value elements that reflected the most important considerations for participants' MDD treatment choices. The interview guide is included with the electronic supplementary material.

### 2.3.4 Attribute Selection and Refinement

Next, we developed the descriptive framework that will underpin the DCE. To do this, we triangulated data from the open-ended question that captured the patient experience with the guided activities and the attributes identified from the published literature on patient preferences for MDD treatment. We identified the top two to three

patient-informed value elements selected within each of the five domains and distributed this information as pre-read material in advance of a 90-min meeting with the SAG. The SAG reviewed this list and provided feedback on the relevance of the patient-informed value elements to adults living with MDD. The goal was to identify the most important elements to serve as candidate attributes for inclusion in a DCE. Next, we extracted the patient voice from the transcribed interviews with adults with MDD to contextualize the statements for each candidate attribute. A candidate attribute could be expressed in more than one way, depending upon an individual's experience with MDD. The published literature was used to identify the language used in relevant patient preference studies involving individuals with MDD [17–20]. Separately, a secondary, retrospective claims data analysis examined pharmacologic and non-pharmacologic treatment patterns, health resource utilization, and cost among commercially-insured individuals diagnosed with MDD in the 2-year follow-up period. The goal was to corroborate the treatment modalities identified as attributes. Feedback elicited from the SAG members of two national mental health patient advocacy organizations guided our selection and phrasing of the most relevant statement for each candidate attribute. Some statements were re-worded, or the candidate attribute was removed based on their recommendation. They also commented on the appropriateness of the attribute-level wording and the range of options across levels.

### 2.3.5 Discrete Choice Experiment Development

The SAG provided feedback on the format for the choice task selections. The decision was based on balancing the amount of information presented in each choice task with the number of choice tasks needed for efficiency. The goal of this work was to identify individual preferences that are relevant for value assessment of MDD treatment regimens, and so an opt-out option was not considered. Rather, we included a follow-up question to identify selections that individuals would or would not use.

The DCE design was developed in SAS using the macros MKTRUNS to identify the orthogonal array, MKTEX to evaluate the D-efficiency, and CHOICEFF to establish the experimental design for the choice tasks [21]. A full factorial, orthogonal array with 100% D-efficiency generated a balanced the design where all attribute levels were displayed the same number of times. The design assigned sets of discrete objects in a random manner to better infer causality. The DCE had six choice task questions with three profiles shown in each choice task, and an overarching question: 'If you could only choose 1 option for treating depression, which do you most prefer?' The DCE was incorporated into a pre-test survey (available upon request) that also collected sociodemographic characteristics.

The DCE was administered in a web-based platform as a pre-test survey with ten adults with MDD who participated in the value element elicitation. A member of the research team guided participants through the survey. For the section on the DCE, the research team member asked participants how they considered each of the attributes and what influenced their selection. The research team member took notes during the discussion, listened for the trade-offs made among the attributes, asked participants if the range in the attribute levels was appropriate, and sought feedback for modifications to the attributes and attribute levels.

## 2.4 Data Analysis

Descriptive statistics summarized the participants' demographic characteristics using means and frequencies. The guided activities to select the key value elements were summarized as frequency counts and ranked. All data were analyzed using SAS 9.4 (Carey, NC). Data are available in the electronic supplemental material.

## 3 Results

### 3.1 Sample Characteristics

Sociodemographic characteristics of the adult participants are displayed in Table 1. Most participants had been living with MDD for over 20 years. More than half were not employed, and half had private insurance, with the other half reporting public or no insurance. The primary modes of treatment were medication and psychotherapy. One-quarter had used ECT. Approximately one-quarter reported lifestyle modifications as part of their treatment for MDD.

### 3.2 Value Element Elicitation

Figure 1 illustrates the value element elicitation process. With the goal of identifying six to eight attributes for inclusion in a stated preference instrument, we first identified the top two to three selected patient-informed value elements within each of the five domains. This resulted in 14 candidate attributes (Table S3; see the electronic supplementary material) as follows: three for treatment effects (*symptoms of importance, side effects, life expectancy*), three for treatment access (*provider relationship and trust, available treatment, consistency of care*), three for treatment cost (*affordability, autonomy, long-term effects on the family*), three for life impact (*emotional status, fatigue, ability to work*), and two for social impact (*relations with family members, social activities*).

Feedback from the SAG narrowed the candidate attribute list from 14 to seven (Table S4). The seven elements

**Table 1** Sociodemographic characteristics of the 20 individuals with MDD who participated in phase 1 interviews

Demographic characteristic	N	%
Age		
25–44 years old	5	25%
45–64 years old	10	50%
65+ years old	5	25%
Age at diagnosis		
≤ 17 years old	4	20%
18–34 years old	9	45%
35–64 years old	7	35%
Sex		
Female	14	70%
Male	6	30%
Race		
Caucasian	14	70%
African-American	4	20%
Hispanic	2	10%
Marital status		
Married	8	40%
Divorced/separated	7	35%
Never married	5	25%
Education		
High school/GED	2	10%
≤ 2 years of college	5	25%
Bachelor's degree	7	35%
Graduate degree	6	30%
Annual household income		
≤ \$24,999	6	30%
\$25,000–\$74,999	6	30%
≥ \$75,000	8	40%
Employment status		
Full/part-time	8	40%
Disabled	6	30%
Retired	4	20%
Unemployed	2	10%
Insurance type		
Private insurance	10	50%
Public insurance (Medicaid/VA)	4	20%
Public insurance and private insurance	4	20%
Other	2	10%
US region		
South	7	35%
Northeast	6	30%
Midwest	4	20%
West	2	10%
Mid-Atlantic	1	5%
Residential community		
Suburb	12	60%
Urban	7	35%
Rural	1	5%
Current depression treatments		

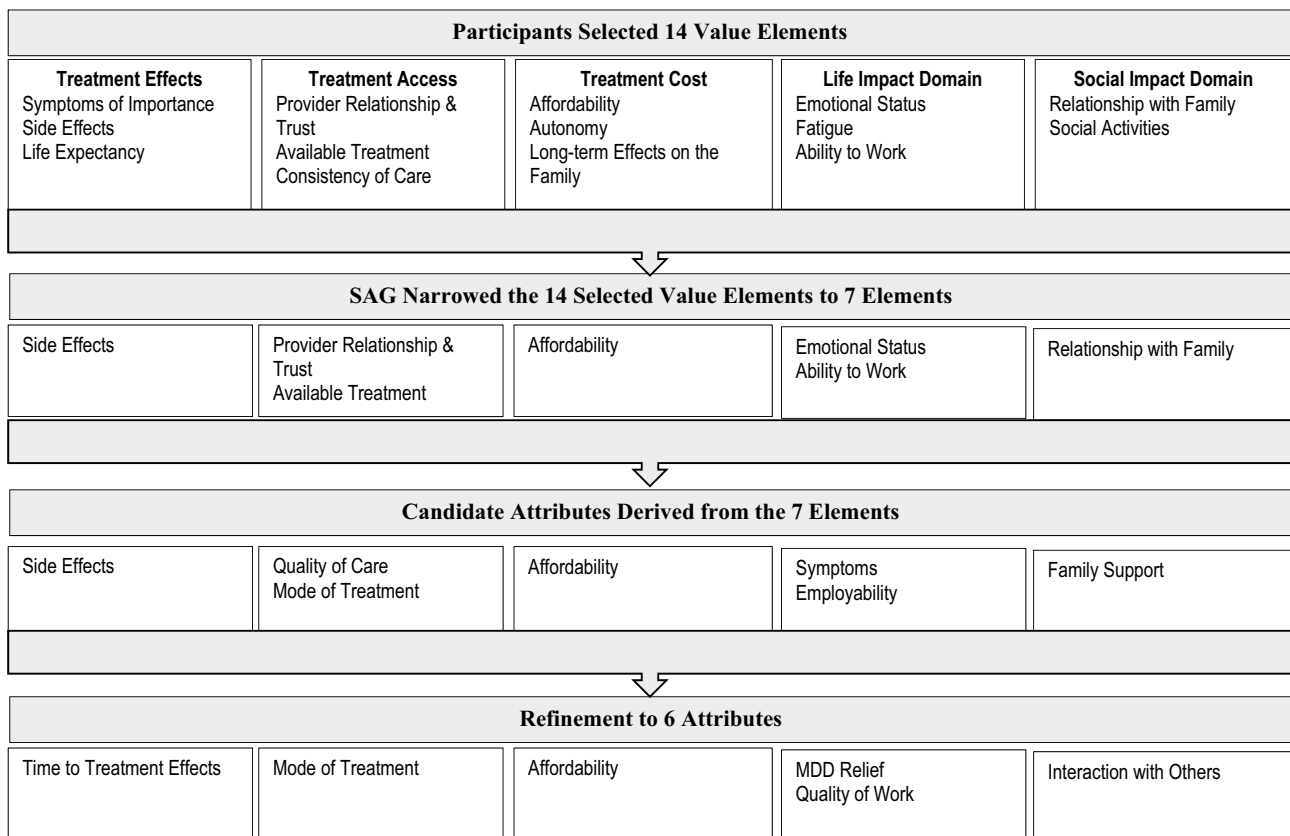
**Table 1** (continued)

Demographic characteristic	N	%
Medication	17	85%
Therapy	13	65%
ECT	5	25%
TMS/deep brain stimulation	4	20%
CBT	4	20%
Group therapy	2	10%
MBCT	1	5%
EMDR therapy	1	5%
Lifestyle modifications		
Exercise	3	15%
Meditation/prayer	2	10%
Light therapy box	1	5%
Diet	1	5%
Ever hospitalized for depression	1	5%

CBT cognitive behavioral therapy, ECT electroconvulsive therapy, EMDR eye movement desensitization and reprocessing, GED general educational development, MBCT mindfulness-based cognitive therapy, MDD major depressive disorder, TMS transcranial magnetic stimulation, VA veterans administration

selected in five domains were as follows: *available treatment* and *provider relationship and trust* (treatment access), *emotional status* and *ability to work* (life impact), *side effects* (treatment effect), *affordability* (treatment cost), and *relationship with family* (social impact). These elements were translated into candidate attributes based on discussions with SAG representatives from the patient community. Table S4 shows how each candidate attribute was defined. Available treatment was defined as mode of treatment, i.e., medication, psychotherapy, and other services. Treatment cost was defined as affordability, treatment effects as side effects, emotional status as symptoms. For provider relationship and trust, the SAG members of a national mental health patient advocacy organization relayed that this element reflected the quality of care. The ability to work was defined as employability, and relationship with family was defined as family support.

The descriptive system emerging from this work comprises six value element dimensions: available treatment, treatment effects, emotional status, ability to work, family and peer relations, and affordability (Table 2). Each dimension has three levels corresponding to the context of the patient experience. The scenario balances available treatment with two dimensions of treatment benefit (i.e.,



**Fig. 1** Value element elicitation and candidate attribute selection. MDD major depressive disorder, SAG stakeholder advisory group



treatment effects and emotional status), two dimensions of treatment outcomes (i.e., ability to work and family and peer relations), and one dimension of treatment cost (i.e., affordability). The setting is a trade-off among treatment type with benefits, outcomes, and cost.

### 3.3 Candidate Attribute Refinement

We used the transcribed interviews with participants to contextualize the initial draft of attribute statements and levels (Table 2). The initial attribute statements underwent two rounds of review with SAG members who represented the MDD patient community. Important feedback was to ensure

**Table 2** Selection and refinement of candidate attributes after patient stakeholder input

Value element	Candidate attributes	Initial attribute statement and levels	Round 1 attribute statement and levels	Round 2 attribute statement and levels
Available treatment	Mode of treatment	Your depression treatment is: 1. Medicine 2. Psychotherapy 3. Medicine, psychotherapy, and non-medicine options	Treatment available to you is: 1. Medicine 2. Psychotherapy 3. Medicine, psychotherapy, and other services (e.g.: peer support, ECT)	Treatment Available to you is: 1. Medicine 2. Psychotherapy 3. Medicine, psychotherapy, and other services (e.g. peer support, ECT)
Treatment effects	Time to treatment helpfulness	You feel the effects of treatment in: 1. 6 weeks 2. 9 weeks 3. 12 weeks	You feel the effects of treatment in: 1. 6 weeks 2. 9 weeks 3. 12 weeks	Time to when you start to feel some effect is: 1. 6 weeks 2. 9 weeks 3. 12 weeks
Emotional status	MDD relief	The number of days in the week that you feel sad lessens by: 1. 2 days 2. 4 days 3. 6 days	You will feel hopeful: 1. 2 days/week 2. 4 days/week 3. 6 days/week	You will feel hopeful: 1. 2 days/week 2. 4 days/week 3. 6 days/week
Ability to work	Ability to work	You work/go to school: 1. Full-time (40 h/week) 2. Part-time (20 h/week) 3. Unable to work or go to school	You will be able to work at: 1. 40% of your potential 2. 60% of your potential 3. 90% of your potential	
	Quality of work	The number of days in the week that you feel productive at work is: 1. 2 days 2. 3 days 3. 4 days		Your productivity increases: Increase 1. 40% 2. 60% 3. 90%
Family and peer relations	Interaction with others	Your social activities are disrupted: 1. Mildly 2. Moderately 3. Markedly	Relations with those important to you are disrupted: 1. < 50% of the time 2. 50% of the time 3. ≥ 50% of the time	Relations with people important to you: 1. Are strained 2. Stay the same 3. Get better
Affordability	Affordability	You pay out-of-pocket: 1. \$30/month 2. \$60/month 3. \$90/month	Out-of-pocket costs for this treatment are: 1. \$30/month 2. \$60/month 3. \$90/month	You are willing to pay out-of-pocket for this treatment: 1. \$30/month 2. \$60/month 3. \$90/month

*ECT* electroconvulsive therapy, *MDD* major depressive disorder

the phrasing was in a positive voice, e.g., change ‘*number of days in the week that you feel sad lessens by...*’ to ‘*you will feel hopeful...*’ Through these discussions, we learned that time to treatment effects was more relevant than side effects. We also learned that ability to work was not optimally represented as hours per week that one was able to work; rather, meeting one’s potential was more relevant and would be widely applicable to those in the workforce as well as those who were not for a variety of reasons, e.g., student, retired, disabled. Further discussions with our patient community representatives revealed that productivity was the best way to represent ability to work because it would be broadly applicable and best reflected the quality of work, which was more important. We were guided by their advice to anchor this on productivity, such as ‘Overall performance/productivity increased by’ and levels should be a percentage (i.e., 40%, 50%, 70%). Advice from a mental health patient advocacy organization was that percentage disruption in social activities would be difficult to quantify in this context. It was better to state relations with others as ‘Improved relationships with those who are important to me.’ Feedback from the initial and round 1 review was that the attribute levels for interactions

with others would be difficult for people to relate to, but describing relations as improved/strained was more relevant.

### 3.4 Discrete Choice Experiment Pre-test

The pre-test with the ten adults with MDD revealed that the DCE was easy to understand and the profiles were reasonable options. A sample choice task is illustrated in Fig. 2. Probing about the attributes influencing their choice revealed that individuals made trade-offs between time to some effects of treatment, days feeling hopeful, and productivity. The research team member asked for specific feedback on the attribute and attribute levels. Individuals who made choices simply to avoid medication signaled that they were not considering other options within the profile when making their selection. Therefore, the attribute levels for mode of treatment were changed so that medication was present in all three levels, either as sole treatment or in combination with other non-medication treatment for MDD. Including an attribute level that did not have medicine would jeopardize the interpretation of the findings. For one, most individuals have used medicine at some point in their journey with

Fig. 2 Choice task example

**If you could only choose 1 option for treating depression, which do you most prefer?**

<p><b>OPTION A</b></p> <p>Treatment is Medicine &amp; Psychotherapy                      Feel some effects in 9 weeks                      Hopeful 6 days/week                      Productivity increases 40%                      Better relations with people important to you                      \$270 monthly out-of-pocket costs</p>	<input type="radio"/>
<p><b>OPTION B</b></p> <p>Treatment is Medicine, Psychotherapy, &amp; Other Services                      Feel some effects in 4 weeks                      Hopeful 2 days/week                      Productivity increases 90%                      Strained relations with people important to you                      \$30 monthly out-of-pocket costs</p>	<input type="radio"/>
<p><b>OPTION C</b></p> <p>Treatment is Medicine                      Feel some effects in 6 weeks                      Hopeful 4 days/week                      Productivity increases 60%                      Relations with people important to you stay the same                      \$90 monthly out-of-pocket costs</p>	<input type="radio"/>

depression, even if they express dislike for using medicine. Second, we would potentially diminish compensatory decision-making because individuals would not be weighing the positive and negative attributes across all alternatives. Finally, a second level question allowing individuals to indicate whether they would use the choice selected provides information to assess the attributes that would not outweigh the negative aspects of medicine. Some noted that 12 weeks to feel some effects of treatment was too long, while others reflected that the timing seemed appropriate. It would not be logical or practical to wait 12 weeks to feel some effects because individuals would not continue with the treatment regimen if this was the case. Also, many individuals noted that they continue to have ups/downs regardless of treatment as opposed to full recovery. To accommodate this feedback, we shortened the time to feel some effects by 2–3 weeks in each level. The only other change was the range of monthly out-of-pocket costs. Most respondents reported that the upper threshold was too low. Participants could see providers multiple times within a month, and the insurance copays for each visit could be much more than \$90 per month. To address this feedback, we adapted the second and third levels to be \$90 and \$270 monthly out-of-pocket costs, respectively.

We evaluated several metrics after completing the DCE pre-test. Compensatory choices, meaning certain profiles were always selected, was evaluated. Selections where a particular attribute level was always (or never) selected (i.e., avoiding psychotherapy; avoiding medicine) signaled attribute non-attendance, and led to a change in the mode of treatment. The pre-test response time was 15–20 min for the DCE, and 40 min to complete all components (e.g., eligibility, informed consent, DCE, and other survey questions). Iterative and incremental changes were implemented through this process, as shown by the bolded text in Table 3.

## 4 Discussion

This formative qualitative research integrated information from the patient's experience with MDD with a patient-informed value framework to develop a tool to quantitatively measure treatment preferences. We translated a core set of patient-informed value elements selected by adults living with MDD into attributes of treatment, and triangulated this with the published literature, stakeholder feedback, and empirical data. Using the patient experience to contextualize the attributes, we identified six treatment attributes across four domains, i.e., treatment type, benefits, outcomes, and cost. The DCE pre-test revealed that, when selecting a treatment profile for MDD, individuals consider trade-offs between time to treatment effect, days feeling hopeful, productivity, and cost.

We used an iterative process in refining the attribute phrasing to best reflected the concepts conveyed by participants. This information was the basis for the prototype of the DCE. The prototype underwent alpha-testing with our stakeholders prior to launching the pre-test (i.e., beta-test). Our next step will be to field the DCE in a survey instrument that will also collect information about MDD symptoms and functional impact. The experimental design minimizes cognitive burden by inclusion of fewer choice tasks in a D-efficient design. Fielding the instrument in a larger sample, we will use a main-effects conditional logit to estimate the preference weights and relative attribute importance.

The patient experience demonstrated that functional and social indices were important considerations for managing MDD. This is consistent with other research showing that solely accounting for core symptoms is not sufficient, but rather consideration of quality of life and other functional outcomes should be documented [22]. In the present study, social relationships and family support emerged as an attribute about relations with people important to the individual with MDD. Others have noted that individuals who perceive insufficient social support did not have a well-functioning network, which affected their emotional well-being [23]. The preference instrument developed in the present study will enable evaluation of the importance of relationships relative to other MDD treatment attributes.

Estimating the relative importance of functional outcomes, treatment effects, and costs has the potential to make health services more patient centered. For example, monitoring the functional outcomes that patients most value, such as hopefulness and productivity as found in this study, will help healthcare providers assess whether treatment is addressing what is most important to individuals in their care. Just as endpoint selection in phase III clinical trials can be optimized to those most relevant to patients [24], the same can be true for clinical practice. Moreover, preference data can be analyzed to identify latent sub-groups [25, 26] and to assess trade-offs among treatment attributes [27]. Our pre-test revealed potential latent subgroups given variability in how days feeling hopeful were weighed against productivity, others focused more on their relationships, and others were more treatment focused, i.e., the importance of the range of treatments and how soon they would feel the effects. A more nuanced understanding of the heterogeneity across individuals can translate into enhanced patient-centered care and drive future research to better evaluate what treatment works best and for whom.

This study has some limitations. The sample may not adequately represent the diversity of individuals with MDD. We attempted to mitigate this with the engagement of a diverse SAG that included advisors representing or working closely with under-represented subgroups. Geographic differences in access to MDD treatment may not have been



**Table 3** DCE development and refinement following the pre-test

Value element	Attribute domain	Initial attribute statements and levels	Revised attribute statements and levels after the DCE test
Available treatment	Mode of treatment	You will have access to this treatment: 1. Medicine 2. Psychotherapy 3. Medicine, psychotherapy, and other services	<b>Your treatment will include:</b> <b>1. Medicine</b> <b>2. Medicine and psychotherapy</b> <b>3. Medicine, psychotherapy, and other services</b>
Treatment effects	Time to treatment helpfulness	Feel some effects in: 1. 6 weeks 2. 9 weeks 3. 12 weeks	Feel some effects in: <b>1. 4 weeks</b> <b>2. 6 weeks</b> <b>3. 9 weeks</b>
Emotional status	MDD relief	Hopeful: 1. 2 days/week 2. 4 days/week 3. 6 days/week	Hopeful: 1. 2 days/week 2. 4 days/week 3. 6 days/week
Ability to work	Quality of work	Productivity increases: 1. 40% 2. 60% 3. 90%	Productivity increases: 1. 40% 2. 60% 3. 90%
Family and peer relations	Interaction with others	Relations with people important to you: 1. Are strained 2. Stay the same 3. Are better	Relations with people important to you: 1. Are strained 2. Stay the same 3. Are better
Affordability	Affordability	Monthly out-of-pocket costs: 1. \$30/month 2. \$60/month 3. \$90/month	Monthly out-of-pocket costs: <b>1. \$30/month</b> <b>2. \$90/month</b> <b>3. \$270/month</b>

Bolded text reflects changes made

*DCE* discrete choice experiment, *MDD* major depressive disorder

fully captured despite the national reach for this formative research. It is possible that we may have omitted important attributes of MDD treatment; however, the triangulation of information from the qualitative interviews, SAG patient organizations, and the DCE pre-test was intended to minimize the potential for missing key attributes.

## 5 Conclusion

In summary, this formative qualitative research was based on the patient experience with MDD to develop a quantitative treatment preference instrument. These insights are important for quantifying the preference utility of treatment attributes and for demonstrating the potential for the patient journey to be meaningfully applied in patient-centered research. This work demonstrates a systematic and feasible approach for quantifying the patient experience to inform clinical decision-making and value assessment. By including an SAG, we ensure critical stakeholder input and buy-in to increase the likelihood that data on value elements can be applied in value assessments. Next steps for this research

will be to evaluate the relative importance and trade-offs among treatment attributes and to assess preference heterogeneity among a large diverse sample of adults living with MDD.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s40271-022-00596-6>.

## Declarations

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**Conflict of interest** Drs. Xie and Chapman, Ms. Bright, and Ms. Malik are employees of IVI. The authors do not have any other financial or non-financial interests that are directly or indirectly related to the work submitted for publication.

**Data Availability** All data are provided in the supplemental material or in the tables; we have made all data available.

**Author contributions** SDR conceptualized the study design and implementation, conducted interviews, supervised the data analysis, and drafted and edited the manuscript. LB assisted with the data collection, data analysis, and study management. She also reviewed and edited

the manuscript and prepared the results tables. BB contributed to the instrument development, reviewed the data collected, and reviewed and edited the manuscript. RX assisted with participant recruitment, review of the data, and reviewing and editing the manuscript. RC assisted with the review of the data and reviewing and editing the manuscript. JB conceptualized the study idea, assisted with participant recruitment, led the advisory group meetings, and reviewed and edited the manuscript. EM assisted with participant recruitment, organized meetings with patient advocates, reviewed the data, and reviewed and edited the manuscript. JS assisted with data collection, review of the data, and reviewing and editing of the manuscript.

## References

- Pan American Health Organization. The Burden of Mental Disorders in the Region of the Americas, 2018. 2018.
- Greenberg PE, Fournier AA, Sisitsky T, et al. The economic burden of adults with major depressive disorder in the United States (2010 and 2018). *Pharmacoeconomics*. 2021;39(6):653–65. <https://doi.org/10.1007/s40273-021-01019-4>.
- Luo Y, Kataoaka Y, Ostinelli EG, Cipriani A, Furukawa TA. National prescription patterns of antidepressants in the treatment of adults with major depression in the US between 1996 and 2015: a population representative survey based analysis. *Front Psychiatry*. 2020;11:1–11. <https://doi.org/10.3389/fpsy.2020.00035>.
- Ettman CK, Abdalla SM, Cohen GH, Sampson L, Vivier PM, Galea S. Prevalence of depression symptoms in US adults before and during the COVID-19 pandemic. *JAMA Netw Open*. 2020;3(9):e2019686. <https://doi.org/10.1001/jamanetworkopen.2020.19686>.
- Holtzheimer PE 3rd, Nemeroff CB. Advances in the treatment of depression. *NeuroRx*. 2006;3(1):42–56. <https://doi.org/10.1016/j.nurx.2005.12.007>.
- Stein-Shvachman I, Karpas DS, Werner P. Depression treatment non-adherence and its psychosocial predictors: differences between young and older adults? *Aging Dis*. 2013;4(6):329–36. <https://doi.org/10.14336/AD.2013.0400329>.
- Cartwright C, Gibson K, Read J, Cowan O, Dehar T. Long-term antidepressant use: patient perspectives of benefits and adverse effects. *Patient Prefer Adherence*. 2016;10:1401–7. <https://doi.org/10.2147/PPA.S110632>.
- Zimmermann TM, Clouth J, Elosge M, et al. Patient preferences for outcomes of depression treatment in Germany: a choice-based conjoint analysis study. *J Affect Disord*. 2013;148(2–3):210–9. <https://doi.org/10.1016/j.jad.2012.11.062>.
- Louviere JJ, Flynn TN. Using best-worst scaling choice experiments to measure public perceptions and preferences for health-care reform in Australia. *Patient*. 2010;3(4):275–83. <https://doi.org/10.2165/11539660-000000000-00000>.
- Ryan M, Farrar S. Using conjoint analysis to elicit preferences for health care. *BMJ*. 2000;320(7248):1530–3. <https://doi.org/10.1136/bmj.320.7248.1530>.
- Lancsar E, Louviere J. Conducting discrete choice experiments to inform healthcare decision making: a user's guide. *Pharmacoeconomics*. 2008;26(8):661–77.
- dosReis S, Butler B, Caicedo J, et al. Stakeholder-engaged derivation of patient-informed value elements. *Patient*. 2020;13(5):611–21. <https://doi.org/10.1007/s40271-020-00433-8>.
- Slejko JF, Hong YD, Sullivan JL, Reed RM, dosReis S. Prioritization and refinement of patient-informed value elements as attributes for chronic obstructive pulmonary disease treatment preferences. *Patient*. 2021;14(5):569–79. <https://doi.org/10.1007/s40271-021-00495-2>.
- dosReis S, Castillo WC, Ross M, Fitz-Randolph M, Vaughn-Lee A, Butler B. Attribute development using continuous stakeholder engagement to prioritize treatment decisions: a framework for patient-centered research. *Value Health*. 2016;19(6):758–66. <https://doi.org/10.1016/j.jval.2016.02.013>.
- Hollin IL, Craig BM, Coast J, et al. Reporting formative qualitative research to support the development of quantitative preference study protocols and corresponding survey instruments: guidelines for authors and reviewers. *Patient*. 2020;13(1):121–36. <https://doi.org/10.1007/s40271-019-00401-x>.
- Xie RZ, Malik ED, Linthicum MT, Bright JL. Putting stakeholder engagement at the center of health economic modeling for health technology assessment in the United States. *Pharmacoeconomics*. 2021;39(6):631–8. <https://doi.org/10.1007/s40273-021-01036-3>.
- Gebara MA, DiNapoli E, Hamm ME, et al. Illness narratives and preferences for treatment among older veterans living with treatment-resistant depression and insomnia. *Ann Clin Psychiatry*. 2020;32(2):81–9.
- Johnston O, Kumar S, Kendall K, Peveler R, Gabbay J, Kendrick T. Qualitative study of depression management in primary care: GP and patient goals, and the value of listening. *Br J Gen Pract*. 2007;57(544):872–9. <https://doi.org/10.3399/096016407782318026>.
- Lenze EJ, Ramsey A, Brown PJ, et al. Older adults' perspectives on clinical research: a focus group and survey study. *Am J Geriatr Psychiatry*. 2016;24(10):893–902. <https://doi.org/10.1016/j.jagp.2016.07.022>.
- Wiles N, Taylor A, Turner N, et al. Management of treatment-resistant depression in primary care: a mixed-methods study. *Br J Gen Pract*. 2018;68(675):e673–81. <https://doi.org/10.3399/bjgp18X699053>.
- Kuhfeld WF. Marketing research methods in SAS. 2010:1309.
- Ravindran AV, Matheson K, Griffiths J, Merali Z, Anisman H. Stress, coping, uplifts, and quality of life in subtypes of depression: a conceptual frame and emerging data. *J Affect Disord*. 2002;71(1–3):121–30. [https://doi.org/10.1016/s0165-0327\(01\)00389-5](https://doi.org/10.1016/s0165-0327(01)00389-5).
- Skarsater I, Dencker K, Agren H. The experience of social support in patients suffering from treatment-refractory depression—a pilot study. *Arch Psychiatr Nurs*. 1999;13(2):89–96. [https://doi.org/10.1016/s0883-9417\(99\)80025-9](https://doi.org/10.1016/s0883-9417(99)80025-9).
- Lewis S, Romano C, De Bruecker G, et al. Analysis of clinical trial exit interview data in patients with treatment-resistant depression. *Patient*. 2019;12(5):527–37. <https://doi.org/10.1007/s40271-019-00369-8>.
- dosReis S, Park A, Ng X, et al. Caregiver treatment preferences for children with a new versus existing attention-deficit/hyperactivity disorder diagnosis. *J Child Adolesc Psychopharmacol*. 2017;27(3):234–42. <https://doi.org/10.1089/cap.2016.0157>.
- Ng X, Bridges JF, Ross MM, et al. A latent class analysis to identify variation in caregivers' preferences for their child's attention-deficit/hyperactivity disorder treatment: do stated preferences match current treatment? *Patient*. 2017;10(2):251–62. <https://doi.org/10.1007/s40271-016-0202-z>.
- Hauber AB, Gonzalez JM, Groothuis-Oudshoorn CG, et al. Statistical methods for the analysis of discrete choice experiments: a report of the ISPOR conjoint analysis good research practices task force. *Value Health*. 2016;19(4):300–15. <https://doi.org/10.1016/j.jval.2016.04.004>.

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