STUDY REPORT

Study title:	Cognitive Debriefing Interviews to Support Development of the Migraine Clinical Outcome Assessment System (MiCOAS)
Short title:	MiCOAS CD Study
Study purpose:	To gather data from people with migraine on items, instructions, response options, and timeframes for MiCOAS

Study phase:	N/A	**Protocol:**	MiCOAS UH3 2022-02
Version Date:	November 21, 2023	**Version #:**	1.0

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VERSION HISTORY

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TABLE OF CONTENTS

List of Tables 5
List of Figures 6
Abbreviations 7
Executive Summary 8
  Results 8
Introduction 10
Methods 11
Cognitive Debriefing Interview Study 12
    Interview Participant Recruitment and Interview Procedures 12
    Wave 1 – Item Reduction, 10 interviews 13
    Wave 2 – Item Reduction, 10 interviews 14
    Waves 3 and 4 – Testing of Draft Instruments, 18 interviews 14
    Cognitive Debriefing Data Analysis 15
Recall and Response Interview Study 16
    Interview Participant Recruitment and Interview Procedures 16
Results 20
Cognitive Debriefing Study Results 21
  Sample and Participant Characteristics 21
  Results of Cognitive Debriefing Data Collection and Instrument Refinement 22
    Wave 1 Results 24
    Wave 2 Results 25
    Wave 3 and Wave 4 Results 26
    Title, Instructions, and Recall Period 28
    Response Options 29
    Missing Concepts 31
Recall and Response Study Results 32
  Sample and Participant Characteristics 32
  Results of the Recall/Response Interviews 33
    Ability to recall and preferences for reference periods 33
    Challenges with using a specific reference period 37
    Preferred response options 38
    Challenges with using non-preferred response options 39

    - Perspectives on importance of assessing typical experiences, worst experiences, or variation in experience 41
    - Level of endorsement and variations in experience among participants 42
  - Cross Cutting Response Strategy Findings 44
- Discussion and Implications 46
  - Understanding, interpretation, relevance, and comprehensiveness of the final draft instruments 46
  - Tradeoffs among recall reference periods 46
  - Conceptual content of frequency and difficulty as responses for 7/14 day measurement 47
  - Recommendations for MiCOAS Core Measures for Clinical Trials 48
- Final Draft Instruments 51
  - 24-Hour Daily Measure of Symptoms and Functioning 51
  - 7/14-Day Measure of Functioning and Quality of Life 53
- References 57
- Appendix A. Cognitive Debriefing Interview Guide 58
- Appendix B. Recall and Response Interview Guide 65
- Appendix C. Item Tracking Matrix 72

LIST OF TABLES

Table 1. Clinical Sites For Recruitment 12
Table 2. Overview of Recall Response Interview Materials 17
Table 3. Cognitive Debriefing Participant Characteristics (n= 38) 21
Table 4. Recall and Response Participant Characteristics (n= 17) 32
Table 5. Perspectives on Ability to Recall 36
Table 6. Preferred Response Options by Topic Area 38
Table 7. Perceived Challenges of Responding with Non-Preferred Response Scale 40
Table 8. Endorsement and Perceived Variation in Experiences 42

LIST OF FIGURES

Figure 1. Summary of Cognitive Debriefing Data Collection and Instrument Refinement Waves................23

ABBREVIATIONS

CHAMP	Coalition for Headache and Migraine Patients
CM	chronic migraine
COA	clinical outcome assessment
Einstein	Albert Einstein College of Medicine
EM	episodic migraine
HRQoL	health-related quality of life
MiCOAS	Migraine Clinical Outcome Assessment System
PRO	patient reported outcome
PROM	patient-reported outcome measure
VPG	Vector Psychometric Group, LLC

EXECUTIVE SUMMARY

On the basis of literature reviews, including a review of existing patient-reported outcome measures for headache and migraine, iterative consultation with experts, and the results of two concept elicitation studies, the Migraine Clinical Outcome Assessment System (MiCOAS) research team developed a large set of candidate items designed to capture core outcomes for migraine that are important to patients and relevant to assessment of treatment. To evaluate these items and develop draft instruments suitable for psychometric assessment, the MiCOAS team conducted 38 cognitive debriefing interviews to gather data about the comprehension, interpretation, relevance, and comprehensiveness of the items from people living with migraine. In addition, the team conducted a parallel debriefing study with 17 interviews that examined the perspectives and preferences of people with migraine regarding recall reference periods and response options proposed for the MiCOAS instruments.

RESULTS

Interview participants recruited via clinical sites and a patient advocacy group were purposefully selected to represent diverse demographic characteristics and a range of average number of migraine headache days per month.

Two initial waves of cognitive debriefing interview data were used to eliminate items seen as irrelevant, poorly worded, and overly redundant and to delineate between items that study participants thought important to assess on a daily basis and items thought appropriate for a periodic assessment (7- or 14-days). Two subsequent waves of interview data were used to confirm consistent comprehension and interpretation of all components of the two draft instruments, and to further assess the relevance and comprehensiveness of measure items.

Data from the recall and response study were used to further evaluate the suitability of proposed recall time frames and response options, to understand any challenges with recall and rating respondents might encounter, and to understand how different strategies for responding to questionnaire items might contribute to variability in measurement.

The study resulted in two draft instruments, each including multiple proposed scales:

A 24-hour instrument intended for daily use that includes 21 items assessing migraine symptoms, including most bothersome symptom, basic functioning (e.g., walking, thinking), and ability to complete daily activities (e.g., getting dressed, keeping to one’s plans for the day)

An instrument designed to be used with either a 7- or 14-day recall reference period that includes 36 items assessing functioning and quality of life across physical, cognitive, and psychosocial domains

Cumulative study results indicate that all items, responses, and instructions in the final draft instruments were understood and interpreted as intended by the vast majority of participants and were regarded as relevant for understanding treatment. Most participants regarded the draft instrument as comprehensive, with few suggestions of missing content. Results also indicated that study participants were able to recall their experiences for all items for the relevant time period, although some participants indicated that longer time periods could require more effort to recall and rate. Perceptions of level of effort were linked to both the ability to recall quickly and to the underlying variability and frequency of migraine attacks.

INTRODUCTION

To assess and address limitations in patient-reported outcome (PRO) metrics for evaluation of therapies in migraine, Vector Psychometric Group, LLC (VPG), in collaboration with Albert Einstein College of Medicine (Einstein), was awarded an FDA grant to support the development of a patient-informed and publicly available standard core set of clinical outcome assessments (COAs) for migraine. This project to develop the Migraine Clinical Outcome Assessment System (MiCOAS) focuses on incorporating data about the experience of people living with migraine into the questions included in the core COAs.

The MiCOAS research team developed a set of PRO measure (PROM) items designed to capture the symptoms and impacts of migraine that had been identified as important and potentially suitable for a COA used in clinical trials of treatment. Item development was based on two systematic literature reviews (Houts et al., 2021; McGinley et al., 2021), a review of existing headache and migraine measures, and concept elicitation studies with people who live with migraine (Gerstein et al., 2023; Mangrum et al., 2023). Detailed information about the measure development methods is provided in a separate report, which also describes modifications and alterations to the final draft instruments that resulted from the findings described in this report and/or input from stakeholders.

To assess respondent understanding and interpretation of the proposed items, response options, and recall periods, the MiCOAS team conducted two studies during 2022-2023. The first study focused on assessing respondent comprehension and interpretation of proposed measure instructions, items, responses, and reference time periods. This study also gathered data about respondent perspectives on the relevance of each item for assessment of symptoms and impacts in the context of a clinical trial of migraine treatment; comprehensiveness of the questions in capturing all relevant experiences; unnecessary redundancy among items; and any content that was unclear or ambiguous. The second study focused on understanding respondents' perspectives on their ability to recall and rate their experiences using the proposed reference periods and response options, as well as their preferences for different recall periods or response options.

METHODS

The first study, described in section 3.1, was a cognitive debriefing study to review all items and response options, and gather data on comprehension, interpretation, relevance, and comprehensiveness of all proposed elements of MiCOAS. Interview data were used iteratively to reduce and refine the proposed items and to organize them into draft instruments for continued assessment. The second study, described in section 3.2, focused on gathering data regarding patient views on the possible response options and time frames for MiCOAS. Results of this study were used to further assess the suitability of different recall reference periods or response options, as well as to identify possible sources of variability in measure results that might arise from respondents' strategies for answering questions under different combinations of reference periods and response options. Study protocols and protocol amendments for both studies were reviewed by WCG IRB, an independent central institutional review board.

COGNITIVE DEBRIEFING INTERVIEW STUDY

Interview Participant Recruitment and Interview Procedures

Interview participants with a confirmed diagnosis of migraine were recruited by five clinical sites in geographically diverse regions of the United States (Table 1). Site coordinators identified and screened participants for eligibility criteria and conducted informed consent. Enrolled participants were then directed to complete the MiCOAS health and demographic questionnaire to gather additional background information. Participants who completed the questionnaire were then scheduled for an interview at their convenience. Interviews were 60 minutes in duration and conducted virtually using the Microsoft Teams platform. All interviews were recorded and professionally transcribed verbatim. VPG analysts reviewed transcripts and removed personally identifying details. Deidentified transcripts were then analyzed item by item. Analytic judgments regarding participant understanding and interpretation were recorded in a customized Item Tracker programmed in Excel, along with supporting quotations. Data about length of time to complete instruments and participant comments about item relevance, missing content, and the suitability of response options were also recorded.

Interviews were conducted in waves and the accumulated background characteristics of participants were used to adjust subsequent recruitment to ensure adequate balance between episodic migraine (EM) and chronic migraine (CM) and diverse representation of people of different demographic backgrounds. Efforts included identifying sites with the capacity to recruit populations typically underrepresented in migraine research (e.g., males). Finally, to further improve inclusion of male and Hispanic participants, 4 individuals were recruited via study outreach messages shared by the Coalition for Headache and Migraine Patients (CHAMP) during wave 4. These individuals were not asked to provide proof of diagnosis but instead were vetted by the study coordinator using the same procedures used to enroll participants for the recall and response study described in section 3.2.

Table 1. Clinical Sites For Recruitment

Site ID	Location	Type of Practice	# Recruited	# Interviewed
100	California	Headache specific clinic	16	6
200	Illinois	Headache specific clinic	8	6
300	Connecticut	Neurology Practice	11	6
400	Alabama	Hospital affiliated clinic	27	7
500	Ohio	Headache specific clinic	10	9

A semi-structured interview guide (see Appendix A) was developed to include questions to elicit data that would indicate whether each participant

- Understood the instructions, recall time frame, items, and response options as intended

- Endorsed each item as relevant to their experience with migraine
- Perceived each item as important for assessing migraine status or benefits of treatment
- Was able to recall and rate their experience as applicable using the time frames and response options provided

Interviewers also asked participants whether the instrument they reviewed seemed comprehensive or needed improvement. In waves 1-2, interviewers also asked participants for their views on the number of items that, in the context of participation in a clinical trial, would be acceptable to ask on a daily or 7/14-day basis.

Wave 1 – Item Reduction, 10 interviews

In wave 1, two initial instruments were designed to provide a logical and balanced way of gathering evidence that could be used to reduce the number of PROM items under consideration by identifying:

- Questions that were unclear, confusing, misread, or not understood as intended
- Questions that seemed redundant or overlapping to participants
- The preferred version of competing questions that aimed to capture a specific concept (e.g., which was clearest and best captured the construct)

The two instruments were designed to be roughly equivalent in length and to gather data for items using different reference time frames and response options. A total of 93 unique items were reviewed, but many items were asked with both frequency and difficulty response scales, and nine items were asked under both 24-hour and 14-day reference periods. As a result, a total of 144 items were debriefed across the two instruments:

- Instrument 1 included 70 items related to symptoms and physical function concepts and included all the questions thought to be appropriate for a 24-hour daily questionnaire
- Instrument 2 included 74 items related to cognitive and psychosocial concepts

The small number of 'general function' questions were divided between the two instruments including some items with a positive valence (e.g., how often did you feel good, how often were you able to enjoy all or part of a day).

VPG conducted 10 debriefing interviews in wave 1, comprising five interviews for each instrument. To accommodate the length of the draft instruments in the context of a 60-minute cognitive debriefing interview, interview participants were provided with a personal link to VPG's electronic clinical outcome assessment (eCOA) platform to complete their designated questionnaire 1-3 days prior to their interview. During each interview, participants then reviewed the items and their responses with a focus on identifying redundancies and items that were unclear or difficult to understand, as well as items that did not work well with the offered time frame and response options. When participants identified redundancies, data regarding preference for alternative items was collected. Data related to the suitability of response options and time frames was also collected. For example, participants were asked how they would feel about answering for a 7-day period but having to complete the instrument more frequently or whether there were questions with a 14-day timeframe that seemed more appropriate for a daily questionnaire or vice versa.

Even with the instrument completed ahead of time, interviewers were rarely able to discuss every item in detail with participants. This resulted in limited data collection for some items during wave 1. Items with limited data were not considered for removal prior to wave 2.

Wave 2 – Item Reduction, 10 interviews

Following wave 1, 62 unique items were retained along with a substantial number of duplicate items offered with different response options or timeframes. In all, 100 items were debriefed in wave 2, with the instruments structured as follows:

- Instrument 1 contained 61 items focused on symptoms and physical functioning, and included items with both a 24-hour and 14-day recall period
- Instrument 2 contained 39 items focused on cognitive and psychosocial functioning, and all items used a 14-day recall period

VPG conducted 10 additional debriefing interviews, five for each instrument. Interview procedures were the same as wave 1, with the exception that participants were not asked to complete the instruments ahead of time. Instead, participants completed the instruments during a think aloud debriefing procedure during the interview (Beatty & Willis, 2007).

Waves 3 and 4 – Testing of Draft Instruments, 18 interviews

Following wave 2, 56 unique items were retained and only one item was duplicated between the 24-hour and 14-day instruments. The duplicate item, “Was it difficult for you to concentrate?,” addresses a concept that may play an important role in understanding changes in subjective mental acuity (‘brain fog”) as a migraine attack symptom or as a proximal impact of other symptoms like pain that may interfere with concentration. The question was also deemed important for understanding overall health-related quality of life (HRQoL) and interictal impacts of migraine. For example, lingering fatigue after an attack may contribute to difficulties with concentration.

The final draft instruments were structured as follows and were not altered between waves 3 and 4:

- Instrument 1 was a 24-hour recall measure with 21 items related to symptoms and basic physical and daily functioning; all items were tested with yes\no responses (e.g., for “did you have any migraine symptoms), severity responses (e.g., for symptoms like pain or tiredness), or difficulty responses (e.g., for functions like walking or concentrating))

- Instrument 2 was a 14-day recall measure with 36 questions: 35 questions about functioning and one question asking, “On how many days did you have migraine symptoms?” with a response scale of 0-14 days. Of the 35 questions on functioning, 29 items were tested with frequency responses and six items were tested with difficulty responses (5 questions on cognition and 1 question on ability to enjoy social activity)

The draft instruments were evaluated through a total of 18 additional interviews (n=9 interviews per instrument) using a ‘think aloud’ debriefing procedure during the interview (Beatty & Willis, 2007). Data collection concluded when iterative analysis indicated that further interviews were unlikely to alter findings or result in modifications to the instrument based on qualitative data alone.

Cognitive Debriefing Data Analysis

Data analysis was conducted iteratively as each interview was completed and analysis activities were carried out on the deidentified transcript in a stepwise fashion in an item tracking spreadsheet, as follows:

Two analysts independently reviewed each transcript and recorded, for each item and response option, an assessment of whether the participant interpreted the content as intended and was able to recall and rate their experience appropriately for each item. Supporting quotes were extracted from transcripts for each assessment, as appropriate. Analysts also recorded instances when participants did not interpret content as intended or expressed any difficulty in responding, or indicated that an item seemed otherwise inappropriate or unacceptable.

One analyst recorded participant perspectives on the comprehensiveness of the instrument reviewed, the acceptable number of questions for daily or 7/14-day assessments, and any protocol deviations that may have occurred. The length of time required for initial ‘think aloud’ reviews was also recorded to provide an indication of the measurement burden for each instrument.

One analyst audited data for each wave, by verifying analytic judgments against the original transcript. After the audit was completed, counts were generated for each item to reflect the number of interviews in which no problems were identified; the number of interviews in which there was a problem identified; and the number of interviews in which the item was not reviewed (i.e., missing data).

One analyst reviewed completed analysis for each wave and developed recommendations for item reduction and modification. After MiCOAS team and FDA review of proposed removal or modification of items, per-item decisions were also recorded and an explanation of each proposed modification noted.

Finally, ad hoc analysis was conducted to address questions and concerns as they arose during analysis and measure development. For example, when the addition of a new item to address dizziness/vertigo was proposed after the conclusion of wave 4 interviews, an ad hoc analysis of transcripts was conducted to assess the content of any participant comments on these concepts.

RECALL AND RESPONSE INTERVIEW STUDY

Because existing PROMs for migraine and headache varied considerably in terms of recall time frames and response options, the MiCOAS research team recognized the value of gathering consistent data on patient perspectives about these elements of outcome measurement. However, because the initial draft instruments were so long, this proved difficult to accomplish during the cognitive debriefing interviews. Accordingly, a supplementary study was designed to focus exclusively on issues related to recall and response.

Interview Participant Recruitment and Interview Procedures

Participants with self-reported, medically diagnosed migraine were recruited via study announcements distributed by CHAMP, following the same eligibility and screening procedures that were used in the MiCOAS concept elicitation studies. To improve participation by populations often underrepresented in migraine research, outreach by CHAMP included messages specifically targeting males and people of color. Participants completed an informed consent form online then completed the health and demographic questionnaire used throughout all MiCOAS studies. A total of 17 participants were selected to complete interviews from a pool of 430 individuals who completed all enrollment steps. Participants were purposefully selected to achieve balanced representation of EM and CM and variation in background characteristics.

An interview guide (see Appendix B) was developed to guide participants through a discussion of their perspectives and preferences for reference time periods and response options. Interviews were 60 minutes in duration and were conducted virtually through Microsoft Teams. During each interview, the interviewer presented the participant with a subset of items that exemplified the different approaches to time frames and response options that were being considered for the MiCOAS instruments. Selected items also covered all domains and categories of concepts included in the draft instruments. During the interviews, participants were shown slides with sets of questions organized by topic, followed by the response option possibilities (see Table 2). Interviewers then asked each participant to share their views on the feasibility and differing value of answering with the various time frames and response options. Interview probes sought to elicit information about which time frames or response options were easiest to recall or use and thought to be most accurate in capturing actual experience (including variations in experience). Interviewers also asked about participants' internal thought processes and strategies for selecting responses under the various options and time frames. Interviews were recorded and professionally transcribed verbatim. VPG analysts reviewed transcripts and removed any personally identifying details. Deidentified transcripts were then analyzed, with data recorded in a customized analysis template programmed in Excel.

Table 2. Overview of Recall Response Interview Materials

Slide Topic	Questions	Response Options	24-hour or 7/14-day instrument
Symptoms	Did you have: headache, head pain, or throbbing in your head nausea sensitivity to light sensitivity to sound mental slowness or fogginess aura (e.g., visual spots or flashes of light, skin tingling or numbness) vomiting neck pain fatigue	Severity: Did not have this symptom Mild Moderate Severe I never experience this symptom Frequency: Never Rarely Sometimes Often Always	24-hour
Physical Function	Was it difficult for you to: get ready for the day (e.g., get showered and dressed) walk	Difficulty: Not difficult at all A little difficult Somewhat difficult Very difficult Unable to do Frequency: Never Rarely Sometimes Often Always	24-hour
Physical Function	Was it difficult for you to: do activities because you were sensitive to light, sound, or smells do strenuous physical activities	Difficulty: Not difficult at all A little difficult Somewhat difficult Very difficult Unable to do Frequency: Never Rarely Sometimes Often Always	Sensitivities, 7/14-day Strenuous physical activities, 24-hours

Slide Topic	Questions	Response Options	24-hour or 7/14-day instrument
Cognitive Function	Was it difficult for you to: Concentrate Carry out tasks that require many steps	Difficulty: Not difficult at all A little difficult Somewhat difficult Very difficult Unable to do Frequency: Never Rarely Sometimes Often Always	7/14 day
Cognitive Function	Was it difficult for you to: Speak clearly Remember the right word for something	Difficulty: Not difficult at all A little difficult Somewhat difficult Very difficult Unable to do Frequency: Never Rarely Sometimes Often Always	7/14 day
Physical Function	Was it difficult for you to: Do your usual day-to-day activities Do errands	Difficulty: Not difficult at all A little difficult Somewhat difficult Very difficult Unable to do Frequency: Never Rarely Sometimes Often Always	7/14 day

Slide Topic	Questions	Response Options	24-hour or 7/14-day instrument
Psychosocial	Was it difficult for you to manage your usual tasks and responsibilities at school or at work? Was it difficult for you to take care of people or pets that you usually take care of? How often did you want to spend time alone in a comfortable environment? (*frequency only*)	Difficulty: Not difficult at all A little difficult Somewhat difficult Very difficult Unable to do Frequency: Never Rarely Sometimes Often Always	7/14 day
Psychosocial	Was it difficult for you to enjoy social activity with other people? How often did you have to cancel or change your plans for social or recreation activities?	Frequency: Never Rarely Sometimes Often Always	7/14 day
Psychosocial	How often did you feel irritable because of migraine? How often did you feel sad or depressed because of migraine?	Frequency: Never Rarely Sometimes Often Always	7/14 day
Psychosocial	How often did you feel you did not have control over your life? How often did you feel worried about having a migraine attack? How often did you feel good?	Frequency: Never Rarely Sometimes Often Always	7/14 day

RESULTS

The study results include findings for the cognitive debriefing study, described in section 4.1, and the recall and response study, described in section 4.2. The final draft instruments, as reviewed by participants in the final waves of data collection, are provided in section 6. Deidentified transcripts for both studies have been provided in a separate ZIP file (MiCOAS Cognitive Debriefing and Recall-Response Study Deidentified Transcripts.ZIP) due to the number and length of these documents.

COGNITIVE DEBRIEFING STUDY RESULTS

SAMPLE AND PARTICIPANT CHARACTERISTICS

As shown in Table 3, the study sample achieved balanced representation of EM and CM and diverse representation across a variety of demographic characteristics, including age, sex, race, and level of education or income.

Table 3. Cognitive Debriefing Participant Characteristics (n= 38)

Characteristic	N	%
Migraine Type		
Episodic	20	53%
Chronic	18	47%
Age group		
18-40 years old	20	53%
41-60 years old	15	40%
61-75 years old	2	5%
Did not answer	1	3%
Male	9	24%
Hispanic	6	16%
Race (multiple selections permitted)		
Asian	1	3%
Black or African American	14	37%
American Indian or Alaskan Native	0	0%
Native Hawaiian or Pacific Islander	0	0%
White	21	55%
Other	2	5%
Self-reported years since diagnosis is 5 years or less	9	24%
Reported using treatments to address migraine attacks when they occur**	36	95%
Reported using treatments to prevent or reduce the severity of migraine**	28	74%
Reported current use of opioids or barbiturates to treat migraine	1	3%
Reported using a medication with known cognitive toxicity (for any reason)	11	29%
PHQ-8* score >10	13	34%
MSSS* > 24	21	55%
Employment status (multiple selections permitted)		
Paid employment	26	68%
Student	5	13%
Homemaker	2	5%

Characteristic	N	%
Retired	1	3%
Not working	4	11%
Disabled (or on disability or leave of absence)	2	5%
Education		
High school or less	6	16%
Attended or completed college, technical school, or apprenticeship	21	55%
Attended or completed graduate school	10	26%
Income		
Under $30K	7	18%
$30-59K	7	18%
$60-90K	5	13%
Over $90K	16	42%
Did not answer	3	8%
Married	16	42%
Have children	16	42%

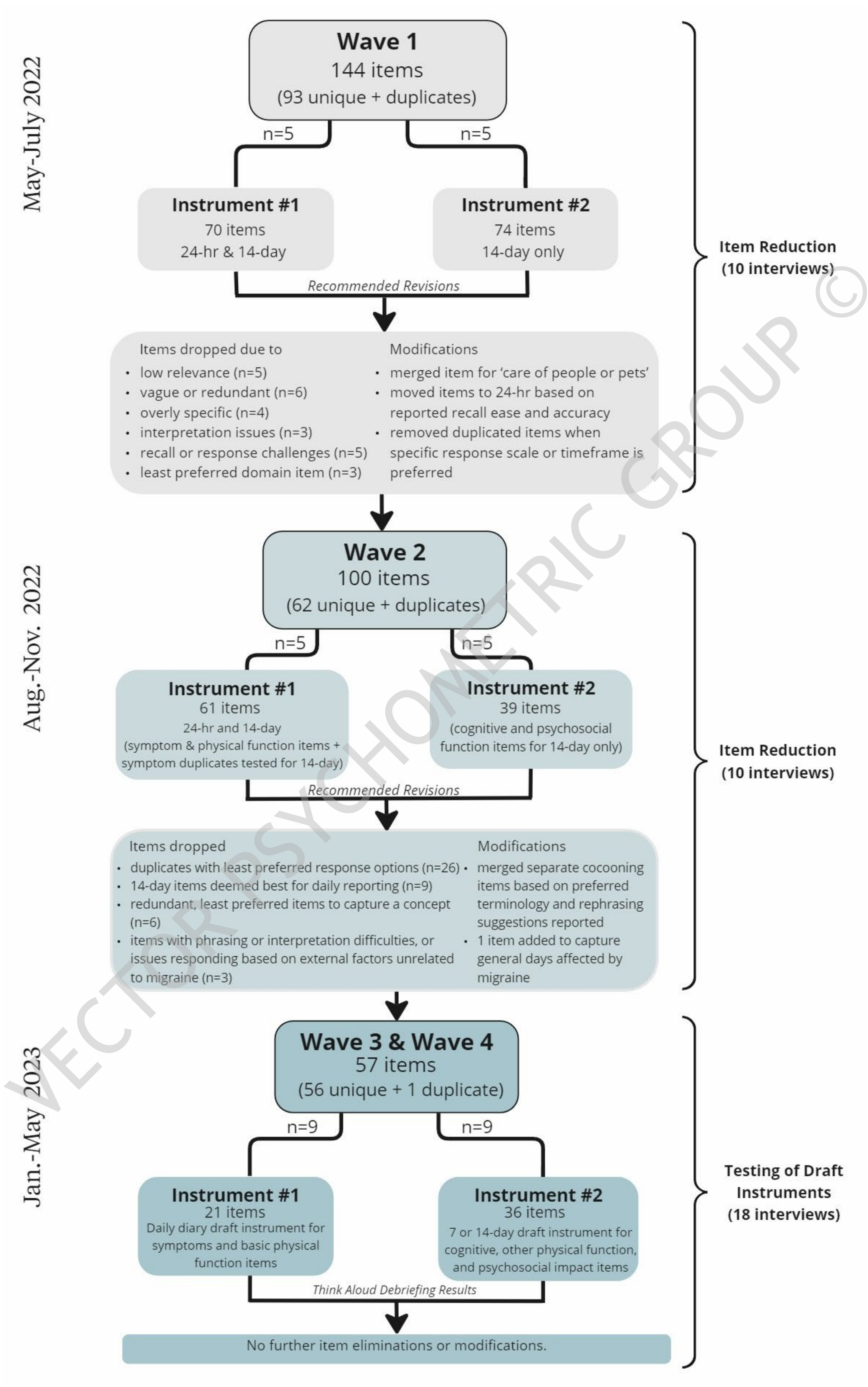
**PHQ-8: Personal Health Questionnaire; MSSS: Migraine symptom severity score.*

***Treatments included therapies other than pharmaceuticals, such as devices or vitamin or dietary supplements*

RESULTS OF COGNITIVE DEBRIEFING DATA COLLECTION AND INSTRUMENT REFINEMENT

Figure 1 depicts the waves of cognitive debriefing interviews that provided data used to reduce the initial set of items and to inform decisions regarding how to delineate draft instruments by major features such as recall period (i.e., daily assessment vs a longer time frame) and conceptual content area. In this section, reasons for eliminating or refining items are described. Detailed summary results per item per wave from debriefing are provided in Appendix C.

Figure 1. Summary of Cognitive Debriefing Data Collection and Instrument Refinement Waves



Wave 1 Results

Following wave 1, 26 items were dropped from the draft item bank due to problems or challenges identified by participants. These included:

- Three items that were not understood or were not interpreted as intended. For example, the item that used the phrase "less sharp" (meaning, impairment of clear thinking) was dropped because most participants were unsure what it meant. The item that used the phrase "express thoughts" was dropped because participants had conflicting, incompatible interpretations. The phrase was meant to capture a person's ability to put thoughts into words as an aspect of speech impairment due to brain fog or pain. However, several participants interpreted this item to mean self-expression of one's personality or ability to express one's feelings, rather than organizing speech for communication. Other items that aimed to capture these concepts worked well and were retained.

- Five items that were too difficult to recall or rate. For example, participants thought that the item "How often did you have enough energy to do everything you planned to do?" was too difficult to recall and rate because level of energy might fluctuate for reasons other than migraine, the varying levels of energy needed for different activities would need to be considered, and the question indicated that respondents should differentiate between planned and routine or unplanned activities.

- Five items deemed as not relevant or important by most participants, or that were described in strongly negative terms. For example, one item ("Was it difficult for you to do simple math without a calculator?") was described as "*silly*" and another ("Was it difficult to do your usual tasks without making errors?") was described as "*a miserable question*." A question about handling financial transactions was also eliminated because it was not considered important by most participants. When alternative items for the same construct were not retained, decisions to drop items were further justified by checking the frequency of patient report in concept elicitation studies. For these specific concepts, endorsement during concept elicitation was low, which increased confidence that eliminating the items was appropriate.

- Four items seen as too specific, meaning that the expression of the construct was too granular, required too many levels of judgment to answer, or that the level of explanation to respondents was excessive or overly directive. For example, the question "Was it difficult to do your usual tasks without making errors?" was perceived to be too granular, requiring respondents to first decide what usual tasks to consider and then decide about the degree to which their difficulty was due to error-making or potential for errors. Similarly, the question "Was it difficult for you to speak clearly (i.e., without slurring or stumbling over words)?" was seen as too directive about what clear speech comprises.

- Six items seen as vague or highly redundant. For example, the question "How often did your migraine symptoms get worse when you moved around?" was seen as too open to interpretation. Participants asked, "*worse than what?*" or wondered how to answer if only one symptom worsened. Similarly, the question “Was it difficult for you to multi-task?” was seen as highly redundant of items asking about concentration, mental acuity, physical function, and other concepts.

- Five items that were least preferred amongst alternative questions for the same construct. For example, the question “Was it difficult for you to find the right words?” was not as well liked as other items designed to capture difficulty remembering words.

Item revision and other changes to instruments

To further reduce the list of draft items for wave 2, VPG made several other changes:

- Combined separate items asking about care of other people and care of pets into a single item asking about ‘care of people or pets.’
- Items that participants noted would be best asked on a daily basis were included on the 24-hour questionnaire only. This included most symptom-related questions. Although most participants thought they could report symptoms weekly or bi-weekly, all believed daily reporting would be more accurate as well as easy to do.
- Restricted duplication of items where possible. For example, if an item was included on the 24-hour questionnaire with a difficulty response set, then the version of that item for the 7/14 day instrument only included frequency response options.

Wave 2 Results

Data from wave 2 was combined with data collected during wave 1 to make further reductions and modifications to the draft items, resulting in the elimination of 44 items from consideration as follows:

- Elimination of 26 items that were duplicates (i.e., the same item being tested with multiple response options) so that continued evaluation occurred with a single response option set based on participant feedback on which response option set was best
- Elimination of nine items assessed with a 14-day recall when most participants deemed them best for daily reporting; these items remained on the 24-hour draft instrument
- Elimination of six items that were redundant and the least preferred option to capture a concept
- Elimination of three items for which there were difficulties with item phrasing or interpretation, or many participants found it difficult to specifically attribute experiences to migraine. For example, the item “Was it difficult for you to remember what you were doing (e.g., remember why you entered a room)?” prompted most participants to assume that the item was intended to inquire about impacts from migraine. They then further noted that, even in the course of a migraine attack, it was difficult to determine whether this was due to migraine itself or some other reason (e.g., getting distracted)

Based on participant feedback, the two questions about cocooning were combined into a single item. "How often did you spend time alone in a comfortable environment because of migraine" and "How often did you want to be alone in a comfortable, soothing place because of your symptoms" were combined to generate the item "How often did you want to spend time alone in a comfortable environment." This item retained the preferred terminology "comfortable environment" with the preface "want to" since this is something participants noted they are not always able to do.

One item was added as the 24-hour instrument was finalized: the question "Did you have any migraine symptoms" was added with a yes/no response. This item was added for two reasons: it permits a significant reduction in the burden imposed by the 24-hour instrument if respondents who answer 'no' can then skip questions about specific symptoms. It also permits the instrument to capture patient report of days affected by migraine symptoms even when those symptoms are not specifically assessed by the instrument. This could be useful in understanding the differences between patient-reported and clinically-defined migraine days as well as determining if there is a gap in symptoms assessment.

Wave 3 and Wave 4 Results

No additional items were dropped or modified in wave 3. Wave 4 confirmed wave 3 findings and no additional items were dropped or modified. Overall, the cumulative debriefing data for all retained items suggests that they are well-understood, relevant, and that people with migraine can readily recall and rate their experiences within the requested time period using the provided response options. However, the qualitative data does also suggest the following potential issues that could be considered when the psychometric assessment of the draft instruments has been completed.

Item asking about vomiting (24-hour instrument). The cognitive debriefing interviews suggest that vomiting may not be very common, with many participants saying that they very rarely or never vomit due to migraine. However, for those who do vomit, the item is very important because vomiting is both unpleasant and disruptive. The quantitative study results may indicate the general prevalence of vomiting and may also indicate how often, if at all, vomiting is reported in the absence of nausea. Such results could inform a decision about whether to retain the item and whether to make it contingent upon reporting nausea.

Item asking about feeling tired (24-hour instrument). In waves 1-2, this item included the modifier "because of migraine" and participants responded accordingly. In wave 3, the modifier was removed. In waves 3-4, four of the 9 participants included fatigue unrelated to migraine when responding and several specifically noted that this item would benefit from specifying "because of migraine."

Item "Was it difficult for you to move your body?" (24-hour instrument). Three participants found this item confusing because it was too vague, and they were unsure what type of movement it referred to. A fourth participant noted that the phrasing of this item did not capture their experience because although some movements could exacerbate a migraine attack, moving your body was not something they considered difficult.

Item "Was it difficult to for you to speak clearly?" (7/14-day instrument). Four participants (21%) interpreted the item broadly to include word recall or general conversation rather than thinking specifically about slurred, halting, or jumbled speech. It is possible that posing this question *after* the item "Was it difficult for you to remember the right word for something?" could improve interpretation. However, since word recall and ability to converse are constituent components of the cognitive impacts of migraine and included in the instrument, this variation in interpretive scope may not affect the measure's performance.

Item "How often did you feel you did not have control over your life?" (7/14 day instrument). This item was reviewed by 13 of the 19 participants. Three participants (23%) answered based on considerations other than migraine, such as work or financial pressures, and one participant (8%) misinterpreted the item. As a result, the qualitative evidence supporting this item appears weaker than for other items. However, four participants (31%) also explicitly identified this question as an important one, including one who stated it was the question that best captured their experience with migraine.

Item "How often did you want to spend time alone in a comfortable environment?" (7/14 day instrument). The cocooning item was revised during the debriefing study and the version tested in waves 3-4 worked well, however several participants thought the item should specify 'because of migraine' or 'because of your migraine symptoms.' A few participants answered this question based on factors outside of migraine, such as personality in general and how often they like to be alone, but it was unclear how much this general self-perception might be attributable to being a person who lives with migraine. Overall, there was a noticeable inconsistency in the ways in which participants did or did not restrict responses to migraine. For example, the daily diary item "Did you feel tired?" elicited numerous responses that reflected tiredness from other causes (staying up late, for example, or traveling). However, the 'mentally slow or foggy' item did not, even though participants did talk about having these experiences for other reasons.

Item "Was it difficult to remember things that were important to you?" (7/14 day instrument). The cognitive debriefing interviews suggest that this experience may not be commonplace enough to capture differences in migraine experience. Only 3 out of the 9 participants who reviewed this item in waves 3 and 4 found it relevant, and of those three, one experienced it only rarely. The quantitative study results will help to understand the general prevalence and the degree to which this hangs together with other items and could inform a decision about whether to retain the item.

Response option "I never experience this symptom" (24-hour instrument). During the study, this response option was listed last. Some participants did not notice it and selected "Did not have this symptom." Additionally, some participants elected not to use this response even when they had experienced the symptom only once over many years. Consequently, this option—intended to permit understanding of whether individuals do not routinely experience a specific symptom—may not operate as intended. Depending on the specific implementation of the measure in a given context, it may be important to place this response option first to increase its noticeability. Alternatively, if the measure is implemented so that participants first check off the symptoms they had on a given day (and then are asked to rate the severity only of symptoms they did have), then this option should be removed altogether along with the companion option "Did not have this symptom." The option may also benefit from being rephrased to better capture its intended meaning, possibly as "I do not usually experience this symptom."

Assessment of Instrument Burden

The length of time required to read and respond to the draft instruments during the initial 'think aloud' review provides an indication of level of respondent burden associated with the questionnaire. Participants assigned to instrument 1 completed 21 items in an average of 7:58 minutes and those assigned to instrument 2 completed 36 items in an average of 16:14 minutes. Across waves 3 and 4, this reflects an average expenditure of roughly 23 seconds per item for the 24-hour questionnaire and 27 seconds per item for the 7/14-day questionnaire. Because the 'think aloud' is controlled by the interviewer and includes time for comments, the average time for respondents to complete the instrument on their own is likely to be considerably shorter.

Title, Instructions, and Recall Period

The title listed for participants was "Migraine Clinical Outcome Assessment System (MiCOAS)" throughout all four waves of interviews. Initial instructions for the draft instruments were minimal, as follows:

- For the 24-hour questions: The following questions are about your experiences with migraine over the <u>past 24 hours</u>. Before responding, please take a moment to think about your experiences over the past 24 hours that are <u>related to migraine</u>.

- For the 14-day questions: The following questions are about your experiences with migraine over the <u>last 14 days</u>. When answering the following questions, please think about your experiences that are <u>related to migraine</u> over the past 14 days, including times when migraine affected you even when you did <u>not</u> have migraine symptoms. In the past 14 days… [followed by individual items and responses]

Following wave 2, these instructions were modified to remove all the references to migraine at the same time that such references were removed from many items, as follows:

- For the 24-hour questions: The following questions are about your experiences during the <u>past 24 hours</u>. In the past 24 hours… [followed by individual items and responses]

- For the 14-day questions: The following questions are about your experiences over the <u>past 14 days</u>. In the last 14 days… [followed by individual items and responses]

Across waves, participants had no comments about the title and found the instructions clear and easy to follow.

During cognitive debriefing interviews, there were no instances of participants who expressed difficulty recalling their experiences over the past 24 hours, and a few instances of participants indicating they had any challenge with recall over 14 days. For example, regarding the question "On how many days did you have migraine symptoms?," one participant commented, "*I had to stop and think to calculate, "Okay, two weeks* *ago," or to include this week, last week, 14 days past, how many times did I have a migraine? How many times did I have to take my medication? And so, that's what I was trying to figure out because one thing I don't do, when I get a migraine, is to mark it on the calendar, which would be easier for me because I could have a more accurate [answer]. I just know, when I'm like, "My head." Like, "I can't. My eyes. I have to just lay down, take my medicine." So, that's what I was thinking of – how many times, and so I'm guessing four times in the past two weeks."* At some point during each interview, a number of other participants described out loud how they were anchoring their memory for the prior two weeks, for example by noting any migraine attacks they had or any memorable events or activities that occurred.

Response Options

The MiCOAS instruments use several response scales, as discussed below. Other items with unique responses were also included to capture general presence of migraine symptoms such as two items with yes/no options for the past 24 hours and one item with drop down options ranging from 0-7 or 0-14 days. All participants understood these response options and were able to apply them with no difficulty.

Severity

Participants thought about the severity options (Did not have this symptom, Mild, Moderate, Severe, I never experience this symptom) in terms of levels of impairment on normal daily functioning. Several participants also referenced a numeric rating scale when distinguishing responses. Descriptions of the meaning of severity options exhibited some overlap in bothersomeness. Participants defined the severity response options as follows:

- ‘Did not have this symptom’ was regarded as self-explanatory
- ‘Mild’ was described as “*Can I still work or at least function on this minimal level to like, meet basic needs for myself and my kids?*” or “*a 3 out of 10*” or “*it bothers me, but I can keep going*”
- ‘Moderate’ was described as *“very uncomfortable… it interrupts my functioning in some way but isn't as bad as needing to go to urgent care”* or *“when my headache is about like a 4 to 7”*
- ‘Severe’ was described as *“that's like calling off work and staying home”* or *“an eight and, at that point, I have to stop. I cannot continue with my activities for that day”*
- ‘I never experience this symptom’ was interpreted to mean never experiencing the migraine symptom in their lifetime; some participants selected this option even when they had only experienced symptoms once many years ago. One participant did not initially notice this option but, upon realizing it was available, understood and used it correctly: *“Actually, no. I should have put, "I have never experienced this symptom." I've never actually thrown up.”* A few participants hesitated to use this option due to uncertainty of past experiences: *“I don't remember every migraine, obviously. It's not out of the question that could have happened and maybe I don't realize it…so I don't want to say "Never." It's just maybe something that I didn't recognize.”*

Most Bothersome Symptom

Participants understood the most bothersome symptom options (Nausea, Sensitivity to light, Sensitivity to sound, Feeling mentally slow or foggy, Another symptom was most bothersome) and were able to apply them. Rationales for responses were based on which symptom interfered with functioning the most. A few participants also determined bothersomeness based on the inability to control or cope with a certain symptom. One participant could not decide on a single response due to the presence of all symptoms listed in which they considered to be equally bothersome.

'Another symptom was most bothersome' was indicated as a potential response by several participants (n=4) who experienced sensitivity to movement, vomiting, fatigue, or eye pain. Two participants stated that they would never select this response to the ease of selecting from listed options rather than *"having to make up a symptom in my head."*

Difficulty

Participants understood the difficulty options (Not difficult at all, A little difficult, Somewhat difficult, Very difficult, Unable to do) and were able to apply them. Descriptions of the meaning of difficulty options exhibited some overlap with frequency and severity concepts. Participants defined the difficulty response options as follows:

- 'Not difficult at all' was regarded as the ability to function normally with no restrictions in the absence or presence of migraine symptoms
- 'A little difficult' was described as minimal or limited impact on functioning due to migraine; two participants associated this with severity, describing this as "*mild symptoms*," or "*a light/moderate migraine, but you could push through*" and two other participants related this to frequency, with one individual stating: *"there were only two days out of 14 where anything like that happened, so it gets 'a little difficult'"*
- 'Somewhat difficult' was described as moderate impairment with one participant stating: *"50% harder to do just a general thing."* Other participants related this to frequency, such as *"some days, I can just go full speed, and some days, I just can't,"* or difficulty with functioning that occurs *"a little less than half the time"* over a 14-day period. Two participants did not think there was much difference between 'a little difficult' and 'somewhat difficult'
- 'Very difficult' was described as substantial difficulty or impairment in functioning with several participants expressing the ability to do very limited, light activity or only absolutely necessary things: *"it's like if I literally have to, like if I have nothing to eat in the house"*
- 'Unable to do' was regarded as being unable to function at all. Two participants stated that they would never select this response because they always push through to function regardless of difficulty

Frequency

Participants understood the frequency options (Does not apply to me [offered for 2 items only], Never, Rarely, Sometimes, Often, Always) and were able to apply them. Participants used various strategies for conceptualizing frequency with most participants thinking in terms of number of days in the past 14-day timeframe while others referenced number of occurrences across multiple attacks or during certain relevant activities rather than all activities. Participants defined the frequency response options as follows:

- 'Does not apply to me' was regarded as self-explanatory
- 'Never' was described as "*never experienced with migraine*" or "*did not experience in past 14 days.*" Two participants expressed reluctance to select this response, with one saying "*I don't believe in absolutes, like, you know? So, very few times would I ever say "never" for anything*"
- 'Rarely' was described as *"one out of 14 days"* or *"1 to 3 times"* or *"maybe once out of the migraine days"*
- 'Sometimes' was typically described as *"half the time"* or *"50% of the days."* Some participants described this as "*less than half, maybe like a third of the time*" or *"more than once, like maybe two or three times"*
- 'Often' was described as *"most days, but one or two days without"* or *"a little bit more than that middle area."* One participant described this in terms of consistency of experiences: "*it'd be more repetitive, like almost consistent…Consistency would be 'often'"*
- 'Always' was described as every day in the past 14 days or *"100% of the time"* or *"every day – 13 out of the 14 days would be 'always,' probably"*

Missing Concepts

Participants were asked if anything was missing from the instrument they completed (24 hour or 7/14 day). Most participants did not think anything was missing or responded with concepts that were addressed in the other instrument. The missing topics raised by participants that were not included in either instrument were:

- Dizziness
- Driving an automobile
- Migraine triggers (e.g., hunger)

RECALL AND RESPONSE STUDY RESULTS

SAMPLE AND PARTICIPANT CHARACTERISTICS

Characteristics of the participants in this study are shown in Table 4. The sample included balanced representation of average headache days per month and diverse representation of people with different background characteristics, such as age, sex, race, and ethnicity.

Table 4. Recall and Response Participant Characteristics (n= 17)

Characteristic	N	%
Number of self-reported headache days per month		
4-8 days	4	24%
9-14 days	4	24%
15-20 days	5	29%
21-26 days	4	24%
Age group		
18-40 years old	5	29%
41-60 years old	8	47%
61-75 years old	4	24%
Male	5	29%
Hispanic	5	29%
Race (multiple selections permitted)		
Asian	2	12%
Black or African American	4	24%
American Indian or Alaskan Native	0	0%
Native Hawaiian or Pacific Islander	0	0%
White	10	59%
Other	2	12%
Self-reported years since diagnosis is 5 years or less	3	18%
Reported using treatments to address migraine attacks when they occur**	11	65%
Reported using treatments to prevent or reduce the severity of migraine**	16	94%
Reported current use of opioids or barbiturates to treat migraine	2	12%
Reported using a medication with known cognitive toxicity (for any reason)	3	18%
PHQ-8* score >10	6	35%
MSSS* > 24	9	53%
Employment status (multiple selections permitted)		
Paid employment	9	53%
Student	1	6%

Characteristic	N	%
Homemaker	1	6%
Retired	2	12%
Not working	1	6%
Disabled (or on disability or leave of absence)	3	18%
Education		
High school or less	2	12%
Attended or completed college, technical school, or apprenticeship	10	59%
Attended or completed graduate school	5	29%
Income		
Under $30K	6	35%
$30-59K	0	0%
$60-90K	4	24%
Over $90K	5	29%
Did not answer	2	12%
Married	9	53%
Have children	6	35%

**PHQ-8: Personal Health Questionnaire, a widely-used depression scale. MSSS: Migraine symptom severity score.*

***Treatments included therapies other than pharmaceuticals, such as vitamin or dietary supplements*

RESULTS OF THE RECALL/RESPONSE INTERVIEWS

Analysis of interview data focused on two primary elements: First, identification of significant patterns in participant perspectives that could inform the selection of a final recall time frame and response scale for the MiCOAS measures and, second, identification of the aspects of recall and response strategies used by various participants that might constitute a source of variability in measurement. To guide analysis, VPG made the following assumptions about desirable features for both the reference time period and the response scale:

- They should minimize commonplace, surmountable sources of variability, such as inability to recall relevant experiences or rate those experiences in specific ways (e.g., in terms of severity or frequency)
- They should provide the majority of people who have migraine with the tools they need to characterize their symptoms and lived experiences
- They should demonstrate capacity to capture both variation in migraine disease itself (inter-respondent differences) and change in experience (intra-respondent differences)

Ability to recall and preferences for reference periods

Overall, participants had little or no difficulty recalling their experiences over any of the three timeframes, but many noted that shorter time frames are easier to recall while longer ones may require some effort (see Table 5). A few participants thought they might consult a calendar or diary to refresh their recollection when answering for a 14-day period. However, participants expressed preferences for different time frames based on factors other than ease of recall. Participants often discussed their perceptions of what time period gives the best "view" or "picture" of life with migraine and this was not invariably defined in terms of capacity to remember specifics and details.

Participants varied in their general preferences for a recall period and there was some interaction between preference for time frame and response options. All participants indicated that 24 hours is easiest to recall and provides a very detailed accounting of experiences, which was regarded as important for symptoms and the immediate impacts of migraine attacks. However, many items referenced concepts that are not meaningful for a daily questionnaire (e.g., social impacts, mood impacts, usual responsibilities). Participants also thought it was easier to recall a 7-day period than a 14-day one, but the number of people who thought they might experience challenges with recall varied considerably across items. Some participants indicated that it was not uncommon for them to go a week without any impacts from migraine and consequently thought 7-days was too little time. Participants generally thought that a 14-day timeframe would encompass enough time to factor in the variety of experiences they might have, but held different opinions on whether recalling 14 days was easy or required effort. In other words, participants did not consistently perceive potential recall challenges across the board, which would suggest a true memory issue. Instead, the number of people perceiving a potential recall issue at 14 days varied by item from none to eight (47%, see Table 5).

Exemplar quotes that illustrate the varied and conflicting perspectives include:

- *"24 hours, to me, doesn't mean anything, you know?"*
- *"I think 24 hours* [is best]*, but I think you could still be pretty accurate with seven days."*)
- *"Yeah, I might do the 24 hours. I think, yeah, that changes my mind, because I never know what the day is going to bring. I, very well, could get a headache so, yeah, it would be good to capture that every day."*
- *"Easiest would probably be 24. I think the seven days is a little bit more impactful, same with the 14, but the 14 can be a little bit harder to think back for two weeks. But overall, the easiest, I would say, is because I only have to think about yesterday, the 24-hour…You can get a better view of their experiences if you know about longer periods of time. So, the 14, again you have, like, more data to think about and look at."*
- *"I would say the best would be the seven days only because it gets a better feel for what it is."*
- *"I like seven. I just think, I mean, if I'm having headaches all the time – if I'm in what I call my migraine season, then 14 days is relevant, but if you're just looking at – even when I'm not in my migraine*

season, I still deal with a few headaches a week, so I think seven is just a good picture of that…Yes, just because it's easier to remember, and then it does show, like, you know, I can have one or two good days, but five bad days, and it still shows the trends of what's happening."

- *"I think the seven days is just spot-on for me."*
- *"I think 14 days is where you could maybe not answer as accurately."*
- *"Probably the 14, just because it's more data collected, more opportunity to actually be able to draw from different details – that's what I think – versus maybe a singular attack. Again, it all just depends on the severity of the migraines that I'm experiencing."*
- *"I'm going to say 14 days is too long. 24 hours? Mm…Yeah, 24 hours would be – you know, because it's like a day."*
- *"What I'm saying is I would prefer the shorter time frame [7 days], but I can reach back 14 days and do it."*
- *"Because I always look at, you know – a week runs so quick, you know what I mean? So it's not uncommon that you can get through a week without any of these issues, but I think being able to go back over 14 days, that kind of gives you more of a glimpse into what the month was really like."*
- *"It's easier to track and remember with the 7-day…I mean, the 24-hour would be easier to track and remember too, but 7-day would like have a better idea, like to give an overview."*
- *"I think 14 days is always a fairer time shot…Oh, because I don't think you can have an accurate time shot on something in just 24 hours or just seven days. I think 14 days is fair, and I think 30 days is too long."*
- *"Again, 14 is getting a little long-term to remember each day exactly. Seven days would be easier…I'm pretty good with remembering where I was on what day, but a couple of weeks, it's getting more out of sight, out of mind…I'd have to go back to my calendar and look to see what I did that day."*

Table 5. Perspectives on Ability to Recall

Topic Area	24 hours	7 days	14 days
Symptoms	Easy to recall	Easy to recall	8 people indicated effort needed to recall
Basic physical functions like walking or getting ready for the day	Easy to recall	1 person indicated effort needed to recall	8 people indicated effort needed to recall
Doing activities with photo/phonophobia, strenuous activity	Easy to recall	Easy to recall	3 people indicated effort needed to recall
Concentrate, carry out complex tasks	Easy to recall	1 person indicated effort needed to recall	5 people indicated effort needed to recall
Speak, remember words	Easy to recall	Easy to recall	5 people indicated effort needed to recall
Usual daily activities, errands	Easy to recall	Easy to recall	7 people indicated effort needed to recall
Usual responsibilities at work or school, cocooning	Easy to recall	1 person indicated effort needed to recall	6 people indicated effort needed to recall
Social activities	Easy to recall	Easy to recall	Easy to recall
Irritable, depressed	Easy to recall	1 person indicated effort needed to recall	2 people indicated effort needed to recall
Sense of control, worry, feel good	Easy to recall	1 person indicated effort needed to recall	1 person indicated effort needed to recall

A number of factors impacted whether responding to specific questions for 14 days would require more or less effort to recall. These factors varied across participants and some were contingent (i.e., they were linked to other factors that would first have to be present). Common factors that participants thought might affect the ease of recall included:

- **The overall prevalence, frequency, or duration of given experiences within an individual's own life.** Participants noted that some questions asked about things that were not commonplace in their daily lives, such as running errands or socializing, which made them easier to recall. For concepts that are pervasive in life, such as walking or the broad 'usual daily activities,' effort may be required to recall and rate one's experience, even over a 24-hour period. Ease of recall of specific symptoms or impacts was also contingent on each individual's general experiences with migraine: people with frequent attacks, attacks that lasted multiple days, or attacks that varied a great deal tended to note that this would contribute to the level of effort needed to recall and rate. Those with less frequent, shorter, or less variable attacks were readily able to recall and rate over 7-14 days, and some preferred longer timeframes for this reason.

- **The specific concept reflected in the item.** The number of people who thought 7 or 14 day recall would take more effort varied across the items reviewed during interviews. Notably, more participants (n=8) thought recall over 14 days would require greater effort for items that asked about symptoms and basic daily functions like walking. Comparatively few participants (n=1 to 3) thought the same about items that asked about concepts like irritability, depression, worry, or strenuous activity.
- **The ease of anchoring one's memory over a given time period.** Early in each interview, some participants engaged in a brief anchoring strategy to establish in their mind what had happened over the prior 1-2 weeks, such as notable events or activities, places they may have been, etc. This was easiest for 24 hours and required more effort for 7 or 14 days.

Challenges with using a specific reference period

Participants were asked to describe any challenges they might experience in responding for each reference period. Results indicate that the primary challenges participants identified were not principally related to recall but to the interplay of reference period and response options, or the content of specific items.

24 hours. Participants expressed that the 24-hour period seemed inappropriate for activities that large numbers of people do not do on a daily basis (e.g., socializing, errands) irrespective of response options. A 24-hour recall period together with frequency responses did not work well with items asking about activities that typically occur once per day, such as getting dressed, and did not make as much sense to participants as difficulty or severity for activities that do occur many times per day, such as moving or concentrating.

7 or 14 days. Participants noted the possibility of having multiple attacks of varying severity during the time frame and perceived that this could create challenges for selecting an accurate rating of severity/difficulty for items addressing symptoms and proximal impacts of attacks such as impairment of mobility or disruption of the day's plans. In addition, some participants who had frequent attacks or attacks that lasted multiple days expressed concern about the accuracy of their recall of the exact severity of specific symptoms or proximal impacts. As one participant noted, the challenge when reporting symptoms over 7/14 days was "*mainly to keep track of it because, if I'm experiencing, I might lose track of time, or I might, you know, not feel well enough to remember or something.*" Most participants thought these questions should be asked on a daily basis to achieve an accurate assessment of attack characteristics and immediate impacts. For other categories of items, such as running errands or speaking clearly, some participants with variable experiences with migraine attacks noted that the 7/14-day recall period generally did not work as well with difficulty responses because it is easier to recall the frequency with which *any* level of difficulty is encountered than to select an overall rating of difficulty that aggregates or averages varied experiences.

Preferred response options

For items where alternative response options (i.e., frequency, severity, or difficulty) were being considered, participants were asked to describe which response option they preferred and why. This question was further contextualized by asking respondents about their preferences for response options for each possible time frame. As shown in Table 6, results of this exercise were mixed and the margin between those who preferred one scale over the other was often very small. For the 24-hour time period, the majority of participants preferred severity/difficulty across all topics. Similarly, for migraine symptoms, the majority of participants preferred severity across all time frames. For the other six topic areas, as the time frame moved from 24 hours to 14 days, participant preferences shifted from difficulty to frequency for three topics, stayed on difficulty for two topics, and varied for one topic. Participants who preferred frequency noted that any level of difficulty with basic functioning is significant if it happens often; *"I think frequency, because this happens to everybody sometimes. But sometimes it's no big deal. If it's often, it's a big deal."* Participants who preferred difficulty noted that this better expresses the degree of disability; *"disabling symptomatology is probably more significant than the frequency, because you can have – like I do, I suffer 15 days a month, maybe more, but it's not disabling me."*

Table 6. Preferred Response Options by Topic Area

Topic Area*	**24 hours**	**7 days**	**14 days**
Symptoms	**12 preferred severity**, 2 preferred frequency, 3 were indifferent	**9 preferred severity**, 4 preferred frequency, 4 were indifferent	**10 preferred severity**, 4 preferred frequency, 3 were indifferent
Basic Physical Functions	**10 preferred difficulty**, 2 preferred frequency, 2 did not experience these outcomes, 3 did not answer	**7 preferred difficulty**, 5 preferred frequency, 2 did not experience these outcomes, 3 did not answer	**8 preferred frequency**, 6 preferred difficulty, 2 did not experience these outcomes, 1 did not answer
Doing Activities	**10 preferred difficulty**, 2 preferred frequency, 3 were indifferent, 2 did not answer	**8 preferred frequency**, 7 preferred difficulty, 1 was indifferent, 1 did not answer	**9 preferred difficulty**, 8 preferred frequency
Concentrate	**13 preferred difficulty**, 2 preferred frequency, 1 did not experience	**11 preferred difficulty**, 3 preferred frequency, 2 were indifferent, 1	**9 preferred difficulty**, 4 preferred frequency, 3 were indifferent, 1

Topic Area*	24 hours	7 days	14 days
	these outcomes, 1 did not answer	did not experience these outcomes	did not experience these outcomes
Speak	**8 preferred difficulty,** 2 preferred frequency, 1 preferred frequency for speaking but difficulty for finding the right word, 6 did not experience these outcomes	**7 preferred frequency,** 3 preferred difficulty, 1 preferred frequency for speaking but difficulty for finding the right word, 6 did not experience these outcomes	**7 preferred frequency,** 3 preferred difficulty, 1 preferred frequency for speaking but difficulty for finding the right word, 6 did not experience these outcomes
Usual Activities	**11 preferred difficulty,** 4 did not answer, 2 were indifferent	**8 preferred frequency,** 5 preferred difficulty, 3 were indifferent, 1 did not answer	**8 preferred frequency,** 6 preferred difficulty, 3 were indifferent
Usual Responsibilities (work/school and people/pets)	**10 preferred difficulty,** 4 did not answer, 2 were indifferent, 1 preferred frequency	**7 preferred difficulty,** 3 were indifferent, 2 preferred frequency, 4 did not answer, 1 preferred difficulty for work/school and frequency for people/pets	**7 preferred difficulty,** 5 preferred frequency, 2 were indifferent, 2 did not answer, 1 preferred difficulty for work/school and frequency for people/pets

**Note: difficulty response options were not provided for items about social activities, cocooning, mood impacts, sense of control, worry and good day*

Challenges with using non-preferred response options

Participants were asked to describe any challenges they thought they might encounter in answering questions with their non-preferred set of response options. While most participants were able to respond with both sets of responses even if they preferred one over the other, a few (n=2 to 4 depending on the item topic) found it difficult to select a rating with the non-preferred response set (see Table 7). While preferences for difficulty or frequency and the challenges reported with using the non-preferred response scale were not consistent across participants or across items, participants tended to prefer frequency and express challenges with difficulty for items that could be answered on a yes/no basis in their experience. It was easier to think about how often they struggled with a given task than to recall the specific level of difficulty. For example, one participant reflected, "*I think there are certain things that I can concentrate on that I feel like don't require anything. I can concentrate on watching maybe a TV show versus if I had to do a report for work or do data* *entry. So I think it really depends upon the situation. But I would be able to better answer how frequently I struggle with concentrating and/or completing tasks that have many steps easier than not, and it could be either daily or weekly or 14 day.”* Participants tended to express a preference for difficulty and have challenges with frequency when rating symptoms and impacts that are a consistent part of their experience but vary in terms of severity. For example, a participant with high frequency migraine and consistent concentration issues noted; *“I think, in this case, difficulty because the concentration is a standard thing, so I think, in this case, we'd talk about the difficulty in being able to concentrate as opposed to the frequency.”*

Table 7. Perceived Challenges of Responding with Non-Preferred Response Scale

Topic Area*	**# of Participants**	**Perceived Challenges**
Symptoms	4	Ability to accurately recall symptom severity or frequency over 7 to 14 days *“I would have to probably, like, ballpark. There are times I have more mild headaches, sometimes I have worse headaches, and I would just have to kind of, like, I guess, decide which would be the easiest way to answer it for that category of time."*
Basic Physical Functions	4	Degree of difficulty regarded as more challenging to assess compared with frequency of having *any* level of difficulty *"Difficulty is subjective, I guess, more so than frequency. Frequency is more counted and you're dealing with actual more concrete numbers, versus difficult for me could be not so difficult for someone else. It's subjective, I guess, and you're depending on my opinion of difficult."* Ability to recall frequency of having difficulty with these specific activities *"Just remembering. But, yeah, just remembering the details."*
Doing Activities	2	Degree of difficulty regarded as more challenging to assess compared with frequency of having *any* level of difficulty *“"I think the challenges I would have using the Option 1 has to do with to mention how this attack comes. At times, in a day, I may have the attack maybe more or even less."*
Concentrate	3	In between options on the difficulty scale *"It's because it says "a little" or "somewhat." It's hard to choose between those two."* Frequency is more challenging to recall because this is a constant *"I don't know. It kind of surprised me [chuckles] because I've answered the other way for all of the other questions. Because in this case, I feel like that's more descriptive, I think, of my situation, that it's getting more and more difficult to concentrate and it's kind of constant."*
Speak	2	Degree of difficulty regarded as more challenging to assess compared with frequency of having *any* level of difficulty

Topic Area*	# of Participants	Perceived Challenges
		"If it didn't always happen, I would probably try to figure out which answer. Like, maybe I would put "a little difficult" if it only happened sometimes." Frequency doesn't capture the variations in how bad it is when this happens *"I think the challenges I have there, because it won't be able - it doesn't give me more opportunity to give the best experience I had, the full experience I had…At times, I may have difficulties in speaking very clearly, but I may still speak at the hand, but it might be very sluggish. So, I will be able to give full experience I had. Just like jump for the experience."*
Usual Activities	1	Challenge responding with difficulty for errands because it depends on whether the attack strikes when doing errands *"I think no, I won't be able to use that. I won't be able to use that because any times I'm at home and this attack comes, definitely that will affect my activities, or the daily things I do, so the chores or the things I do at home. So, I think Option 1 won't give me more opportunity to give or to capture my experience relating to this question."*
Usual Responsibilities	2	Degree of difficulty regarded as more challenging to assess compared with frequency of having *any* level of difficulty *"Yeah, the specifics would be difficult to remember."*

*Note: difficulty response options were not applicable to items about social activities, cocooning, mood impacts, sense of control, worry and good day, as these questions were phrased as "How often…" Participants did not report any challenges answering these items using frequency response options.

Perspectives on importance of assessing typical experiences, worst experiences, or variation in experience

Participants were asked their perspective on which types of experiences were most important to assess to understand if a treatment is working well: typical experiences, worst experiences, or variation in experience. The results of this line of questioning were mixed. Of the 17 participants, 5 thought typical experiences were most important to assess, 4 thought worst experiences were most important, 4 selected both worst and typical experiences, and 2 participants thought it was most important to capture variations in their experiences in a single assessment. Notably, however, over the course of each interview participants tended to discuss their typical experiences with symptoms much more consistently than their worst ones. For at least one participant, "typical experience" included variation in experience. For this participant, high variability in their symptoms from attack to attack made a 14-day reference period desirable for assessing typical experience because it "*can give a person a little bit more time to look at the migraine, and then also just kind of see how often they've had it, because I feel like that kind of gives a better idea of like there's a pattern or something of that sort.*"

Level of endorsement and variations in experience among participants

As shown in Table 8, the overwhelming majority of participants endorsed each of the items as relevant. However, participants reflected a wide range of migraine experiences (i.e., inter-participant variation) and some participants also reported migraine that varied considerably from attack to attack (i.e., intra-participant variation). These differences appeared to influence preferences for recall time frames and response options, as well as strategies for responding regardless of these options. For example, participants who had very frequent, relatively predictable attacks tended to prefer the longer recall period and difficulty responses because it was easy for them to provide an aggregate overall rating of 'how bad' migraine had been in the last 14 days. However, frequency tended to be easier to recall over longer time periods for those with highly variable attacks and/or lower frequency of attacks.

Regardless of response options, some participants selected a response that reflected pragmatic practice rather than the actual impact of migraine. For example, some participants who did not socialize often indicated that they would select 'no difficulty' or 'never' responses even though their primary reason for not socializing was not migraine. These participants often also indicated that they never made plans and thus also answered these questions in a similar manner. Likewise, participants who had adapted to migraine in varying ways sometimes gave responses that under-represented the difficulty or frequency of their migraine. For example, some participants with chronic migraine considered a constant level of symptoms as their baseline and focused on how often they experienced migraine symptoms or impacts that were worse than usual. For example, a participant who experienced migraine symptoms on most days responded rarely for difficulty getting ready for the day; although he took medication and had to adjust his environment and routine to accommodate migraine, he was accustomed to this and did not consider it difficult. However, it is unclear how many MiCOAS items could be consistently influenced by this practice among what proportion of respondents. It is also unclear whether clinical trial participants would continue to answer questions in this manner given the context of trying a new treatment.

Table 8. Endorsement and Perceived Variation in Experiences

Topic Area	No. Endorsing (*n*= 17)	Perceived Variations
Symptoms	All participants thought these questions were relevant	Presence of symptoms varies from attack to attack and over the course of a single attack; symptoms come and go during an attack and over lifetime with migraine; presence of cardinal diagnostic symptoms is common to severe attacks but milder attacks may not exhibit these core symptoms Symptoms vary in intensity from attack to attack and over the course of a single attack Head pain quality and location changes from attack to attack and over the course of a single attack Level and type of activity affects symptom experience Vomiting and aura appear to be most variable within and between participants, with many participants never or rarely experiencing these symptoms while others experience them routinely

Topic Area	No. Endorsing (*n*= 17)	Perceived Variations
Basic Physical Functions	16 participants thought these questions were relevant	Basic mobility impacts like “getting ready for the day” will vary depending on when an attack occurs during a given day Impact varies with severity of attack Impact varies with specific symptoms experienced (pain, dizziness/vertigo, and aura were reported as most disruptive of basic physical functioning)
Doing Activities	All participants thought these questions were relevant	Actual impact can vary with severity of symptoms, but impacts reported as less variable across attacks due to avoidance of these activities or triggers such as bright light and noisy places
Concentrate	16 participants thought these questions were relevant	Presence varies from attack to attack and within a single attack Multiple participants spontaneously noted that cognitive impacts occur interictally Severity of cognitive impact related to specific symptoms and their intensity
Speak	15 participants thought these questions were relevant	“Remembering the right words” was a consistent issue during attacks for most participants Difficulty speaking was associated with severe attacks and more variable between participants
Usual Activities	All participants thought these questions were relevant	Highly variable in relation to specific symptoms experienced, severity and duration of symptoms, relevant types of activities/errands (demand for function), and ability to push through
Usual Responsibilities, Cocooning	All participants thought these questions were relevant	Highly variable impact on usual responsibilities, desire to cocoon is more consistent across participants Variability linked to severity and to specific symptoms, as well as the types of responsibilities (demand for function)
Social Activities	16 participants thought these questions were relevant	Most participants linked variability to frequency of severe attacks Variability across participants also linked to perceptions of what social activities comprise, personal level of sociability, and avoidance
Irritable/ Depressed	All participants thought these questions were relevant	16/17 participants reported irritability, 13/17 participants reported feeling sad/depressed Irritability occurred consistently across attacks but varied over the course of a single attack Depression linked to ‘missing out’ was less variable than general depression, and both are linked to symptom frequency and severity Depression spontaneously identified as an interictal impact
Sense of Control / Worry / Feel Good	15 participants thought these questions were relevant	Worry varied greatly across participants, with some indicating it was a constant and others linking worry to the specifics of each attack Sense of control varied greatly across participants and was linked to level of adaptation Feel good varied in accordance with number and severity of attacks

CROSS CUTTING RESPONSE STRATEGY FINDINGS

Most participants considered frequency and difficulty to be highly related. When assessing difficulty, many participants in both studies considered the frequency with which an experience occurred as an integral feature of the level of difficulty experienced. For example, one CD participant defined the response category "very difficult" in terms of frequency; *"almost every time I would do something with somebody that I would have a hard time doing it."* Similarly, a Recall Response study participant commented that difficulty is implied in frequency, although they found frequency more useful; *"so the difficulty is, for me, it's more implied, and it's more useful to know the frequency because that's like, if you're having trouble doing your usual basic things, regardless of the difficulty, the frequency is more important."* Another participant provided an example of how both scales capture frequency even when people explicitly recognize that the response options are asking for different assessments. In this case, the participant notes the different meanings, but uses the frequency to determine the selection of difficulty responses: *"I mean, you could really answer it, like, two ways, but it's like, you know, "How much of a problem was it for you?" is what option one* [difficulty] *is asking, and then option two* [frequency] *is like, "How often does it happen?" You can answer. You can say like, "Okay ..." Say, half of the times, I had problems, then I would say "somewhat difficult." And then, I might, maybe if it was frequency, I would say "sometimes" or "often," so you could still kind of like answer it both ways."*

While most participants gave responses that aligned across difficulty and frequency scales, a few participants approached the difficulty and frequency scales with different response strategies. For example, one CD participant thought about their experiences over the entire 14 days for frequency questions, yet only counted the 'bad' experiences—the times when symptoms and impacts were pronounced or hard to manage—when using the difficulty response options. This participant consistently selected 'rarely' on frequency items because they had experienced migraine symptoms on 3 out of the past 14 days. However, when asked about the difficulty of socializing with others, they selected 'very difficult' based on how difficult this was while experiencing an aura: *"So, whenever I have an aura, which can happen pretty frequently, and then my aura sort of happens before the actual pressure from the migraine occurs. And I tend to treat it with my medication regimen, but the aura makes it very difficult for me to socialize with other people, especially when it's people that I'm not maybe immediately comfortable with, like my family or my close friends. And so, that's probably the most annoying part about my migraines, is this sort of weirdness in my aura, because it causes a spatial sort of weird almost dizziness that makes it hard to talk to people."* Both responses are accurate from the participant's point of view but could result in different interpretations of a measure score: this participant might be regarded as 'minimally affected' by migraine if the frequency scale were used and 'profoundly affected' if the difficulty scale were used.

There were also some participants in both studies who answered based on worst experiences for difficulty and interpreted frequency as "how often when I had a migraine attack." These participants would answer "Always" for impacts that happened every time they got a migraine, even if they had been affected on only one day in the recall period. For example, a CD participant who had experienced migraine symptoms twice in the last 14 days responded "always" for difficulty concentrating because this is an issue with every migraine: *"It's always* *difficult for me to concentrate when I have a migraine. It's almost impossible. I just kind of shut down and just want to take my medicine and pray that I can get over it quickly."* Importantly, participants who framed frequency as "how often when I had a migraine attack" used this response strategy consistently across items.

DISCUSSION AND IMPLICATIONS

UNDERSTANDING, INTERPRETATION, RELEVANCE, AND COMPREHENSIVENESS OF THE FINAL DRAFT INSTRUMENTS

The results of the cognitive debriefing interviews indicate that all components of the final draft MiCOAS instruments were understood as intended by the vast majority of study participants. The results also indicate that two items may be unnecessary because of low endorsement (vomiting and remembering things that are important to you) and some items may benefit from minor revisions to clarify their meaning (e.g., specifying 'because of migraine' for items asking about fatigue or cocooning). However, these findings were not sufficiently robust to make changes to the draft instruments based on the qualitative study alone, thus the items have been retained 'as is' for the quantitative study.

Variations in interpretation primarily arose in the context of applying response options for specific items for longer recall periods. These variations were linked to differences in strategies for rating experiences over time as well as underlying differences in participants' experience with migraine. For example, the number of migraine attacks during a 7- or 14-day period, as well as the variability of symptoms experienced in each attack, influenced the way that participants selected responses, as discussed below.

All retained items were also regarded as relevant and important for assessing treatment outcomes by the majority of participants. For items with limited endorsement, participants who did endorse the question often described it as very important to assess and participants who did not endorse it often recognized that it could be very important to other people with migraine. Finally, the results indicate that participants found the instruments to be comprehensive, with only a few suggestions for concepts that were missing (e.g., dizziness).

TRADEOFFS AMONG RECALL REFERENCE PERIODS

All participants in both studies were able to recall their experiences over all proposed timeframes, but as the period increased in length a larger proportion of participants in the recall and response study perceived that it would require a bit more effort to recall and rate for each item. This latter finding aligned with findings from the cognitive debriefing study, in which participants were observed to spend a few seconds now and then anchoring their recall of the prior two weeks by referring to memorable events or activities or thinking back over the symptoms and impacts of any attack they had had. Most participants in both studies thought that a 24-hour timeframe was preferable for questions about symptoms and the proximal impacts of a migraine attack, largely because they considered it essential that these aspects of their experience be assessed with maximum accuracy for both frequency and severity. For questions about functioning and HRQoL, many participants preferred the 7-day period because it was easy to recall and respond, but some participants preferred the longer 14-day timeframe because they perceived that it allowed them to assess their overall function and well-being more holistically. These participants described the longer-term assessment of their experiences as giving a better picture of their day-to-day life.

Participants expressed some distinct tradeoffs between the scope and accuracy of 7-day vs. 14-day reference periods for assessing broader HRQoL concepts, such as impairment of routine activities or impacts on mood. A 14-day period does provide a greater opportunity to capture typical experiences with migraine as all participants in the study indicated that a 14-day period was likely to include at least one attack. When participants thought in this way, the 14-day recall timeframe was regarded as more accurate because they were thinking of 'accuracy in capturing my experiences.' However, the 14-day span also prompted participants in the recall and response study to indicate that effort would be required for recall and some expressed concern that their recall might be negatively affected. When participants thought this way, the 14-day timeframe was regarded as less accurate because they were thinking of 'accuracy of recall.'

The two studies strongly support the use of a daily 24-hour recall instrument to capture migraine symptoms and proximal impacts and the use of a 7- or 14-day recall instrument for broader impacts on HRQoL. However, 7- or 14-day recall may have different value for specific clinical trials based on study aims, and the planned timing of assessments is also important to consider. For example, in a preventive trial enrolling participants with higher-frequency migraine, a 7-day reference period may be valuable for capturing granular variations in the impact of migraine attacks, particularly in terms of functioning. In trials enrolling significant proportions of people with lower-frequency migraine, a 14-day reference period for measures of functioning may provide more reliable information about experience than a 7-day measure that prevents reporting of a migraine attack that occurred 10 days earlier. Accordingly, assessment timing also matters. If measures are administered intermittently during a trial (e.g., once a month), then an assessment that covers a greater span of time may be valuable if the trial population includes people with lower-frequency migraine. If measurement is frequently administered, such as administering the 7-day measure every week or 2-3 times a month, more detailed data can be collected, but the cost is increased participant burden of measurement. In addition, when participants observe that the 14-day measure provides them with a better means to provide an overall, holistic assessment of their HRQoL (i.e., "a better picture"), they are claiming for themselves the responsibility of judging their own experiences in relation to migraine. If measurement is implemented in a way that precludes or hampers that holistic assessment, there is the risk that the inferences drawn from measurements might not align with the ways that people actually think about their own experiences. Consequently, a quantitative assessment of the alignment between 7-day and 14-day responses in a population of people with migraine is needed to determine whether these metrics provide similar or different 'pictures' of their experiences.

CONCEPTUAL CONTENT OF FREQUENCY AND DIFFICULTY AS RESPONSES FOR 7/14 DAY MEASUREMENT

When assessing difficulty over a 7- or 14-day time period, many participants in both studies also considered the frequency with which an experience occurred. Some participants also noted that difficulty is implied when asking about frequency. However, when assessing frequency, many participants preferred not to factor in the specific level of difficulty because it was easier to think in yes/no terms about whether they struggled with a given task or not. Generally, participants were able to answer with both scales and approached both scales with similar response strategies, thus their responses on both were aligned. However, a small minority of participants considered the entire time frame for frequency items but focused on their worst experiences when responding to difficulty items. While both types of responses are accurate from the participant's point of view, this inconsistency is important to note given implications for measure interpretation. There were also some participants who responded to items thinking only about when they had a migraine during the response period. In this case, respondents tended to employ this strategy consistently across items, answering both frequency and difficulty items thinking only about how they felt when they had a migraine.

One possible implication of these findings is that both difficulty and frequency assessments may be expected to under- or overestimate objective experience for some portion of respondents. However, practices leading to over/underestimates were consistent even when participants had both options in front of them during the recall/response study, meaning that asking for assessments of both might not improve precision in measurement over 7- or 14-days. These practices were consistent within each individual (i.e., done with all items in the same manner), suggesting that the measure is capable of capturing intra-individual *change* in experience due to treatment in a consistent way. When comparing groups of participants, inter-individual differences in recall and rating strategies could confound interpretation of results if these practices are linked to some other characteristic not apparent in this small study (e.g., migraine attack frequency or number of years lived with migraine).

RECOMMENDATIONS FOR MICOAS CORE MEASURES FOR CLINICAL TRIALS

Include a measure with a 24-hour reference period to assess symptoms and a limited set of impacts on basic daily functioning, such as mobility. This recommendation is based on the following observations from the qualitative studies:

- Participants regard 24-hour recall as the most accurate and least challenging to remember and report
- Participants thought that a 24-hour assessment was best able to capture their direct experiences of migraine symptoms and immediate effects of symptoms on functioning, which they regarded as essential for understanding the efficacy of a treatment

Questions may be added to achieve specific migraine or headache day definitions or to meet specific trial needs; however, the number of added items should be strictly limited to keep the maximum daily assessment as close to 20 questions as possible.

Electronic implementation can be designed to streamline questions and reduce daily burden. However, specific methods of implementation may prevent assessment of interictal burdens associated with migraine. For example, if the daily assessment were implemented in a way that restricts participants to reporting symptoms and impacts that occur only on days that meet a specific clinical definition of migraine (e.g., headache lasting 4 hours, with unilateral throbbing pain), understanding of interictal burden could be limited. Consequently, the recommendation for MiCOAS implementation is that all symptoms and impacts be assessed on any day that respondents identify as a migraine day, regardless of whether their responses match a desired clinical definition.

Include a measure that could be used with either a 7- or 14-day reference period to assess impacts on other aspects of functioning. Daily assessment for these outcomes would be burdensome and inappropriate for many questions because they address activities that participants indicated are not daily in nature (e.g., errands) and/or thought would be better assessed cumulatively (e.g., ability to care for family/pets, moods, desire to self-isolate or 'cocoon').

Based on the qualitative study findings, there are benefits and drawbacks to both the 7- and 14-day reference periods that may need to be considered in alignment with the context of use. The primary benefit of the 14-day reference period is that it is likely to include assessment of impacts from at least one migraine attack for most patients that would be eligible for clinical trials. The primary drawback is that it may underestimate status or change for periods in which people have multiple attacks because some portion of respondents are likely to engage in different 'ballparking' to average or aggregate their experiences, or may only report worst experiences. The primary benefits of the 7-day reference period are that participants thought it would be easier to recall than 14-days and that it reduces the likelihood of some practices that may lead to variability in scores. The primary drawbacks are that the 7-day period may impose additional measurement burden if the instrument is administered frequently and may result in underestimation if periodic administration of the instrument results in failure to capture migraine experiences that occur outside the assessed week.

These tradeoffs have implications for measure implementation. For example, in trials of acute treatments or with populations who have episodic migraine, a 14-day period reduces measurement burden on respondents while increasing the likelihood that they would normally experience an attack within that timeframe. In trials of preventive treatments or with populations who have chronic migraine, a 7-day period may increase the sensitivity of the measure for capturing incremental changes in a variable disease. This could, however, increase the burden of measurement if the measure is then given more frequently.

Similarly, the specific assumption or endpoint to be addressed by the measure may also influence the suitability of 7- or 14-days. If the aim is to assess overall change in HRQoL from baseline to end of treatment and to correlate those with changes in symptom frequency or severity, then a comprehensive 14-day measure given periodically may suffice. The vast majority of participants in both studies indicated that the 14-day time frame seems preferable in that context, precisely because it provides a broader, integrative picture of 'how I am currently doing with migraine." By contrast, if the aim is to understand the specific impacts of a treatment—on cognitive functioning or social/emotional well-being, for example—then the underlying variability of these specific impacts combined with the underlying variability of migraine itself may make a 7-day measure valuable simply because it collects more data capable of portraying these fluctuations. Likewise, if the aim is to understand details about the relationship between specific symptom experiences and impacts on functioning in a population with frequent migraine, a 7-day measure provides a better avenue for achieving this goal. A 7-day timeframe increases the likelihood that the symptoms and proximal impacts of each attack can be linked to measures of functioning administered in the same week. However, here again a limitation applies: people with frequent migraine may also engage in avoidance or adaptation practices that could introduce variability in measurement that manifests in unexpected ways. For example, a person with frequent migraine could report minimal impairment of various functions at baseline simply because they avoid those functions entirely and thus do not experience difficulty doing them. Following successful treatment to reduce the frequency and severity of attacks, this person then might paradoxically begin to report impairment of functions they had resumed once they started feeling better. The MiCOAS studies conducted thus far do indicate that these variable approaches to responding exist, but do not shed light on how common they are or for which groups of patients.

In the longer term, consider the use of vignettes or other integrative methods for implementing measurement. From a measure development or clinical point of view, one of the obstacles to achieving optimal assessment of patient-reported outcomes in migraine is the multi-layered variation in the disease itself and the ways individual people respond to life with migraine. These co-occurring and sometimes competing variations create challenges for developing a measure that applies equally well across all people with migraine in all contexts of treatment. A longer-term solution is to develop an integrative method for assessing PROs, such as vignettes. These methods allow respondents themselves to match their own perceptions to standardized ‘pictures’ of typical patients across a spectrum, rather than querying respondents extensively and then attempting to infer the correct picture based on the data. In migraine, this approach could facilitate better understanding of where each person sits within a conceptual structure that, for example, accounts for the fact that some people will describe an activity as difficult while others will not because they have stopped trying to engage in the activity altogether. Before a method of this type could be used, however, it will be necessary to develop a more detailed understanding of what those standardized pictures should include, an endeavor that first requires further quantitative study with traditional, questionnaire-based methods.

FINAL DRAFT INSTRUMENTS

Following the cognitive debriefing study and recall/response study, the draft MiCOAS 24-hour and 7-day instruments were structured as follows.

24-HOUR DAILY MEASURE OF SYMPTOMS AND FUNCTIONING

For clinical trials or other research studies, additional questions may be added to this core measure set to capture data relevant to specific definitions of migraine/headache day, use of acute medication, or other variables.

During the past 24 hours…

Did you have any migraine symptoms?

☐ Yes ☐ No

Did you have a good day?

☐ Yes ☐ No

Did you have headache, head pain, or throbbing in your head?

☐ Did not have this symptom ☐ Mild ☐ Moderate ☐ Severe ☐ I never experience this symptom

Did you have nausea?

☐ Did not have this symptom ☐ Mild ☐ Moderate ☐ Severe ☐ I never experience this symptom

Did you vomit?

☐ Did not have this symptom ☐ Mild ☐ Moderate ☐ Severe ☐ I never experience this symptom

Did you have sensitivity to light?

☐ Did not have this symptom ☐ Mild ☐ Moderate ☐ Severe ☐ I never experience this symptom

Did you have sensitivity to sound?

☐ Did not have this symptom ☐ Mild ☐ Moderate ☐ Severe ☐ I never experience this symptom

Did you have neck pain?

☐ Did not have this symptom ☐ Mild ☐ Moderate ☐ Severe ☐ I never experience this symptom

Did you experience aura (e.g., visual spots or flashes of light, skin tingling or numbness)?

☐ Did not have this symptom ☐ Mild ☐ Moderate ☐ Severe ☐ I never experience this symptom

Did you feel mentally slow or foggy?

☐ Did not have this symptom ☐ Mild ☐ Moderate ☐ Severe ☐ I never experience this symptom

Did you feel tired?

☐ Did not have this symptom ☐ Mild ☐ Moderate ☐ Severe ☐ I never experience this symptom

Which one of the following symptoms other than pain was most bothersome to you? (Select one)

☐ Nausea ☐ Sensitivity to light ☐ Sensitivity to sound ☐ Feeling mentally slow or foggy ☐ Another symptom was most bothersome

Was it difficult for you to move your body?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to walk?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to move your head?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to bend forward?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to do strenuous physical activities?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to think clearly?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to concentrate?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to get ready for the day (e.g., get showered and dressed)?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to keep to your plans for the day?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

7/14-DAY MEASURE OF FUNCTIONING AND QUALITY OF LIFE

The following questions are about your experiences over the past 7/14 days.

In the past [7 days | 14 days] …

On how many days did you have migraine symptoms?

Drop down/check box choice of 0-7 or 0-14

How often did you feel good?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

How often were you able to enjoy all or part of a day?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

How often did you want to spend time alone in a comfortable environment?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to do your usual day-to-day activities?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to take care of people or pets that you usually take care of?

☐ Does not apply to me ☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to manage your usual tasks and responsibilities at school or at work?

☐ Does not apply to me ☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

How often were you too tired to do your regular daily activities?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

How often did you have to miss your regular daily activities? Include times that you stopped early or started late.

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to do usual activities that require physical exertion, like going up stairs?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to do your regular household chores?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to do activities because you were sensitive to light?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to do activities because you were sensitive to smells?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to do activities because you were sensitive to sound?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to do errands?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to keep plans you made?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

How often were you reluctant to make plans with other people?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

How often did you have to cancel or change your plans for social or recreation activities?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to enjoy social activity with other people?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to take part in activities you do for fun?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

How often did you feel you did not have control over your life?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

How often did you feel worried about having a migraine attack?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

How often were you concerned that your migraine attacks would affect other people's lives?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

How often did you feel sad or depressed?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

How often did you feel frustrated?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

How often did you feel irritable?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to concentrate?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to speak clearly?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to remember the right word for something?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to have a conversation?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to understand what was said to you?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to understand what you were reading?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to make day-to-day decisions?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to carry out tasks that required many steps?

☐ Not difficult at all ☐ A little difficult ☐ Somewhat difficult ☐ Very difficult ☐ Unable to do

Was it difficult for you to remember things that were important to you?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

Was it difficult for you to do tasks that required you to concentrate?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

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APPENDIX A. COGNITIVE DEBRIEFING INTERVIEW GUIDE

Instructions for the Interviewer

The primary aim of the cognitive debriefing interview is to gather evidence about how respondents understand and complete the measure instrument. A secondary aim is to learn about how interview participants perceive the relevance of the instrument to their own experiences and to gather suggestions for additions, deletions, or improvements.

Cognitive debriefing interview transcripts are analyzed to assess whether respondents understand all elements of the instrument as intended and whether they are able to complete it as required. During analysis, alignment between respondent behavior and the intended construct are evaluated and any areas of misalignment are classified according to their origin or manifestation (e.g., misreading or misunderstanding, unfamiliar language, having an alternate interpretation of item content, or expressing desired response that is not included among the response options). Analysis also synthesizes findings regarding what participants might add, delete, or change about the instrument. Data analysis results are then to modify or refine the instrument, which may then undergo further cognitive review.

As a result, the cognitive review interview is highly structured, though there is room for adaptation in some areas of inquiry.

Key considerations for interviewing:

Cognitive review interviews provide an opportunity to see how questionnaire respondents interpret and fill out the instrument. Because the questionnaire is being tested, it is not necessary for interview participants to “get it right.” Thus, it is important to resist explaining or correcting during the interview. If participants are misinterpreting or are struggling, it is important to capture that data from beginning to end.

If a participant misinterprets something, do not correct them – in one study, for example, several participants interpreted the word “weakness” to mean that a person lacked fortitude to bear up to their circumstances or was emotional and weepy. This was an important finding and led to a modification of the content.

If a participant asks for explanation, respond neutrally and ask them for their best guess. For example, if a participant asks, “what does your usual activities mean?” your response should be something like “I’m not sure. What do you think it could mean?”

Cognitive review interviews can be quite tedious for participants, particularly when there are lots of items. Be mindful of how the participant is doing and offer breaks. Acknowledge in a neutral manner that it can be tiring to answer the same questions over and over about each item on a long list. Streamline or vary the process where possible: for example, if a participant has repeated the same comments about responses several times, try asking if they have anything different to say for the next few items. Offer the participant opportunities to do some storytelling to break up the tedium by asking them a broad question such as “thinking about the questions you’ve looked at so far, how do these questions line up with your experience of migraine?”

Although interviewers should not explain or correct, it is important to pay attention to the logical consistency of a participant’s answers and to probe for clarification or elaboration when you perceive a contradiction. For example, if a person answers a question about nausea by saying they have none, but a later answer indicates that they do experience nausea, ask for clarification. Exploring these apparent contradictions can illuminate aspects of interpretation or human tendencies to misread things that could affect the instrument’s performance.

Introduction

Thank you very much for taking time to have this interview with me today and agreeing to be part of this study.

Is this still a good time for you?

My name is ___(name)___. I work for Vector Psychometric Group, LLC also called VPG.

VPG is a research organization that conducts studies to examine questionnaires that are used to measure people's health and wellbeing.

Review the interview process

In this interview, I will be asking for your thoughts on a questionnaire about migraine.

Wave 1 interviews: You completed the questionnaire online and I will have a copy of the questions with your responses onscreen for us to look at.

Subsequent waves of interviews: I'll ask you to look through the questionnaire on screen and answer the questions based on your experience. After that, I'll ask for your overall thoughts. And then we will go back through and talk about all the different parts of the questionnaire in detail.

The information from your interview will help us understand whether the questionnaire is working the way it is meant to.

Wave 1 interviews: and understand which version of similar questions may be the best one to use.

The interview will take about 60 minutes.

If you need a break or a chance to stand up and stretch at any point in the interview, please let me know.

I hope that you will feel comfortable speaking your mind. Anything that occurs to you as you look at this questionnaire could be very important for us to hear, so please don't hold anything back.

Of course, if I ask a question at any time that you would rather not answer, just let me know. We'll move on to the next question. And, if for any reason you want to stop the interview, let me know and we will stop.

Review confidentiality

Your privacy is very important to us at VPG. We will not share your name or contact information with anyone who is not directly involved with this study. We really only use your name and contact details for setting up this interview and providing your compensation.

Any information that you provide will be reported in a way that protects your privacy and without any information that could identify you individually.

Review and confirm permission to record and transcribe

I want to remind you that this interview will be video-recorded and we will prepare a transcript from the recording. This helps us to be accurate in capturing what you say for our analysis.

When we transcribe your interview, we will delete anything you happen to say that might help someone identify you later. For example, you might mention someone by name when giving an example of your experiences.

Once we have an accurate transcript, we will securely erase the recording.

If you would like, you can use a background image to block out your surroundings to increase your privacy or the privacy of others who may be nearby while we talk. Would you like to use this feature?

[As needed, help the participant active the background image feature]

Do you have any questions or concerns before we start?

Would you please confirm for me that it is okay to record your interview?

I will now start the recording.

START RECORDING

Section 1. Walk Through Think Aloud Method

[NOT USED IN WAVE 1 INTERVIEWS] The first thing I would like to ask you to do is to read and fill out the questionnaire. I'd like you to answer the questions based on your real experience as a person living with migraine. But, as you do this, I'd like you to try to tell me what is going through your mind as you are reading and answering. This is a bit of an unusual thing to ask, so let me give you an example of what I mean.

Let's say I am answering a questionnaire about food and one of the questions was "How many times have you eaten cheese in the past 3 days?" I might think to myself: So… I had cheese on my hamburger yesterday and then there was the mac and cheese the day before, but I actually ate the leftovers the next day, so I'll count that. And I had that artichoke dip and that's got cream cheese in it. Is cream cheese really cheese, though? I guess I won't count that. So that makes my answer 3."

So that's an example of what I'd like you to try to do--Just say out loud what's going through your mind as best as you can. Some people find it helpful to read all the questions out loud, too, just to kind of get into that thinking-out-loud mode. So feel free to do that if you like.

As you answer, [I will mark your answers on screen | please go ahead and mark your answers on the questionnaire].

[Interviewer will put the interview version of the instrument on screen. For interviews with a think aloud, the interviewer will prompt for think aloud as needed if the participant falls silent, but refrain from asking specific questions except when requesting elaboration. For example, if the participant says "Hmmm… that's weird" but doesn't say why, or makes a face (e.g., rolls eyes, looks puzzled) but doesn't say anything, prompt by asking "What's weird?" or "I noticed you made a bit of a face there, could you tell me what made you react that way?"]

What did you think of this questionnaire overall?

Depending on walk through and comments, follow-ups should include

Did the questions to capture your experiences with migraine?

IF APPROPRIATE: What would you [add to | take out of] the questionnaire?

What parts made it [unclear | hard | easy | good]?

[FOR LATER ROUNDS OF TESTING ONLY]: What did you think of the format – the ways things are laid out on the screen/page?

[FOR LATER ROUNDS OF TESTING ONLY]: What did you think of the sequence of questions?

[FOR LATER ROUNDS OF TESTING ONLY]: What suggestions do you have for making the questionnaire easier to fill out?

[FOR LATER ROUNDS OF TESTING ONLY]: What do you think about the amount of time it took you to complete the questionnaire?

Section 2. Probing Method: Instructions

Now, I'd like us to go back through this questionnaire section by section and I'll ask for your thoughts in more detail. Let's start with the [IN LATER ROUNDS ONLY: name of the questionnaire and the] instructions.

[Interviewer will put the instrument name and instructions on screen.]

IN LATER ROUNDS ONLY: What are your thoughts on the name of this questionnaire?

<u>If strong negative opinion</u>: What name might you suggest?

Would you tell me in your own words what the instructions are asking you to do?

Could you describe any challenges you had in understanding these instructions?

<u>If applicable:</u> What parts of these instructions would you change to make them clearer?

This part of the instructions says [timeframe]. What does [timeframe] mean to you?

What period of time did you think about when you were answering the questions?

<u>If applicable</u>: Could you help me understand why you used [participant's timeframe]?

What challenges, if any, did you have in remembering your experience over [timeframe]?

In thinking about [this timeframe]

How does [timeframe] fit with the way <u>you</u> think about [whether migraine is affecting you more or less over time | whether your symptoms are better/worse | how much migraine is affecting your day to day life]?

How does [timeframe] fit with how you think about whether [an acute treatment | a preventive treatment] is working for you?

[IF NEEDED, clarify that migraine treatments could be anything people use to address their migraine, from drugs to devices to ice packs to dietary changes].

How would you feel about answering these questions for a [ALTERNATIVE TIME FRAME: 7 days, 24 hours] time period?

Section 3. Probing Method: Items

[Interviewer will display sections of questionnaire on screen.]

Now I'd like to go through these questions one by one and get your thoughts.

For each item in the questionnaire:

How would you explain what this question is asking about in your own words?

How would you describe [item content probe] in terms of your experience?

Alternatives:

What does [item content probe] mean to you?

Where it says [item content probe], what were you thinking about when you read that part of the question?

Specific probes could include:

Terms in the item, such as "headache days" or "usual activities"

Linkages or modifiers in an item, such as "people who are close to you" or "getting as much done" or "because of migraine"

IF APPLICABLE: Could you describe the challenge you had in understanding the question? [e.g., in terms of clarity, applicability to experience]

What parts of this question would you change to make it clearer?

How might you reword the question?

[FOR MARKED 24-HOUR QUESTIONS ONLY]: How would you feel about answering this question if the time period was the past 14-days instead?

What challenges might you have in selecting an answer for a 14-day period?

[FOR MARKED QUESTIONS in 14 day version ONLY]: How would you feel about answering this question on a daily basis if you were participating in a trial of a new treatment for migraine?

If you were answering questions on a daily basis, how many questions would seem reasonable to you?

What should they focus on?

What aspects of migraine are the most important to include in a daily diary?

ONLY FOR THE FIRST ITEM WITH A SPECIFIC SET OF RESPONSE OPTIONS:

Let's take a moment to go through all these choices for answering. Please look at each choice and tell me what it means to you.

[FOR LATER ROUNDS ONLY]: When you think about how to choose among these options, how are [response option] and [response option] different | what is the difference between [response option] and [response option]?

Interviewer reminder: The aim is to elicit an understanding of how individual participants view the scaling of response options. For example, on a 5 point scale, what is the difference between 2 and 3 and is it the same as the difference between 4 and 5? Or, what is the difference between "often" and "very often"?

Are there response choices missing here?

Can you tell me a bit about why you would add that choice?

FOR EACH ITEM

For this question, you chose [response], what made that the best choice for you?

Alternative: In thinking about your experience, which response best describes your experience?

Interviewer instruction: Participants may note that, upon thinking about the question some more, they would choose a different answer than they selected during think-aloud. When that occurs, please ask for elaboration on what makes them think differently. Note that some people may find it challenging to explain exactly why and that is fine.

Are there times when you might choose a different answer? Why or why not?

Alternative: Can you think of an experience you had where you might choose [response option]?

As applicable: Is there a response option you would add to better capture your experience with [item content]?

As applicable: In your mind, how are [response option] and [response option] different?

This question asks about [topic]. How relevant is [topic] to you when you think about [your migraine experiences in general | whether a treatment for migraine is helping you]?

Alternative phrasing: How useful is this question in helping someone understand your experience with migraine or migraine treatment?

Alternative (broader): What do you think about this question being included on the questionnaire?

Alternative (narrower): Is this question asking about something that is important to you?

[WAVE 1 INTERVIEWS ONLY]

Does this question seem to be asking about something already covered in other questions?

How do you feel about answering this question twice, once to say how difficult it was and once to say how often it happened?

Does one of those things make more sense to you?

Which of those is more important to you: how difficult it was or how often it happened?

These questions all ask about [SPECIFIC TOPIC OR FUNCTION].

Which of these questions do you think is best? Most clear? Better suited to the responses?

Which question would you drop from the questionnaire to make it shorter | less repetitive?

[GO TO NEXT ITEM until all items are reviewed]

Section 4. Overall Content

Thank you for that great feedback on all these questions. Now I'd like you to take a quiet moment to just look back over the whole questionnaire. And as you are looking it over, I'd like you to tell me about…

Any experiences you have with migraine that are important to you but aren't covered on this questionnaire.

Finally, I'd like to ask: How well does this questionnaire capture the sorts of things you pay attention to when you are deciding if a migraine treatment is working for you?

If needed, to clarify: For example, if you take a medication for your migraine, what do you focus on when you are deciding how well that treatment is working for you?

What might you change? Add? Remove?

Section 5. Closing

Thank you so much for all you've shared. I really appreciate your taking the time to go through all these questions with me

Before we say goodbye, is there anything else you'd like to say about this questionnaire?

Alternative: Can you think of anything else I should have asked about?

STOP RECORDING

Do you have any questions for me?

If you think of any questions later, you can find the study contact information in your informed consent document.

Vector Psychometric Group will provide you with the payment for your participation in this study in the form of an electronic Mastercard or Visa gift card, which we will send to your email address. Let me just confirm the email address that I should use to send that card. [**Interviewer instruction**: Confirm the email address.]

Thank you again for your time. We greatly appreciate your participation in this research today.

APPENDIX B. RECALL AND RESPONSE INTERVIEW GUIDE

Instructions for the interviewer and notetaker

In the interview, sets of items that have been classified as pertaining to each component of the MiCOAS draft measurement framework will be presented on screen to participants.

Participants will then be asked the interview questions, in order.

The phrase in square brackets denotes the specific type of information sought by the question.

Introduction

Thank you very much for taking time to have this interview with me today and agreeing to be part of this study.

Is this still a good time for you?

My name is ___(name)___. I work for Vector Psychometric Group, LLC also called VPG.

VPG is a research organization that conducts studies to examine questionnaires that are used to measure people's health and wellbeing.

Review the interview process

In this interview, I will be asking for your thoughts on a questionnaire about migraine.

Most of the questions will focus on the time frame that might be used for the questionnaire as well as the options available to answer each question.

The information from your interview will be combined with information from interviews with other people who have migraine. We will use this information to help us decide which time frame and response options are best for different types of questions.

The interview will take about 60 minutes.

If you need a break or a chance to stand up and stretch at any point in the interview, please let me know.

Your participation is always voluntary. If I ask a question at any time that you would rather not answer, just let me know. We'll move on to the next question. And, if for any reason you want to stop the interview, let me know and we will stop.

Review confidentiality

Your privacy is very important to us at VPG. We will not share your name or contact information with anyone who is not directly involved with this study. We only use your name and contact details for setting up this interview and providing your compensation.

Any information that you provide will be reported in a way that protects your privacy and without any information that could identify you individually.

Review and confirm permission to record and transcribe

I want to remind you that this interview will be video-recorded and we will prepare a transcript from the recording. This helps us to be accurate in capturing what you say for our analysis.

When we transcribe your interview, we will delete anything you happen to say that might help someone identify you later. For example, you might mention someone by name when giving an example of your experiences.

You do not have to be on camera, but may have your camera on if you would like. The recording will only be seen by people directly involved in making the transcript and conducting the analysis.

I have my camera on, but if it is bothering you for any reason, please let me know and I can turn it off.

Do you have any questions or concerns before we start?

Would you please confirm for me that it is okay to record your interview?

I will now start the recording.

START RECORDING

Before we get started with questions about the questionnaire, it would be helpful to me to know a little about what you experience with migraine.

Background question options; interviewer may select a question based on any initial interactions with participant during the preamble to the interview.

Could you tell me a bit about your experiences with migraine?

When did you start experiencing migraine? How has migraine affected you?

Over the past 3 to 6 months, how would you describe what migraine has been like for you? How has it affected your life?

Thank you for sharing that with me!

As I mentioned before, the purpose of this interview is to discuss questions for a migraine questionnaire that is being developed. There are many questions being considered so I will be showing you questions by topic. Sometimes there will be several questions on the same topic and sometimes there may be only one.

The first set of questions are about common symptoms of migraine.

Are there any symptoms listed here that you <u>do not currently</u> experience?

FOR SYMPTOMS THAT PARTICIPANT DOES <u>NOT</u> EXPERIENCE: Have you *ever* experienced <symptom> in the time that you have had migraine? [VARIABILITY]

FOR THE SET OF SYMPTOMS THAT PARTICIPANT <u>DOES</u> EXPERIENCE:

How much does your experience with your symptoms change over the course of a single attack? [VARIABILITY]

How much does your experience with your symptoms vary from attack to attack? [VARIABILITY]

How much has your experience with your symptoms changed since you were first diagnosed with migraine? [VARIABILITY]

When answering questions about your symptoms, what would be the most important to you to reflect in your answer? [NARRATIVE CONSTRUCT / PATIENT'S AGENDA]

For example…

Your typical experiences?

Your best or worst experiences?

Variations in what you experience?

Something else?

GO TO QUESTIONS 8-12 AND COMPLETE FOR SYMPTOMS

After completing a review of the symptom questions, the interviewer will display the next set of questions. From this point on, the interviewer will cycle through questions 5-15 as applicable for each group of items.

These questions are about <topic area/concept>. Are these questions asking about something that you currently experience because of migraine? [RELEVANCE]

IF YES:

How much does your experience with <concept> vary from attack to attack? [VARIABILITY]

AS APPLICABLE: How much does your experience with <concept> change over the course of a single attack? [VARIABILITY]

Note: the previous question will not make sense with items that focus on aggregate experience (e.g., "How often were you concerned that your migraine attacks would affect other people's lives?"). Interviewer will skip this question as needed.

IF NO:

Use Alternate Questions for Items That Are Not Relevant to the Participant. These questions are designed to understand how people with migraine will answer questions that do not apply to them

FIRST TIME INTRO: There are several options for the time frame that could be used for this questionnaire. The questionnaire could ask people about their experiences with migraine over the past 24 hours, the past 7 days, or the past 14 days. Or, it could use a combination of these time frames, with some questions asked for 24 hours and others asked for 7 or 14 days.

How would you go about answering a question about your experience with <concept> over the past… [INFORMATION RETRIEVAL STRATEGY]

14 days?

7 days?

24 hours? (if applicable – will not apply to items with frequency responses only)

IF NEEDED:

For example, what aspects of your experience would you think about?

If you had multiple attacks in that time period, how would that affect the way you answered questions about <concept>?

What challenges do you have in recalling what you experienced in the past… [PERCEIVED RECALL CHALLENGE]

14 days?

7 days?

24 hours (if applicable)

Imagine you will fill out a questionnaire regularly for 3 months to understand your attacks and how migraine affects you.

Thinking about <concept>, which timeframe do you think…

Would be easiest for you to answer? [FEASIBILITY]

Would give the most accurate picture of what you experience? [ACCURACY]

Would best capture the variation in what you experience with migraine? [VARIABILITY]

Would best capture what you typically experience? (AGGREGATE EXPERIENCE]

Would most help you think about whether treatment is helping you? (PARTICIPANT'S OWN FRAMEWORK)

The interviewer will show applicable response options on screen.

FIRST TIME INTRO: For these questions, there are also some options for how we might ask you to respond. Please take a moment to look at these.

Thinking about these questions for the past 14 days, which set of response options makes the most sense to you? [PREFERRED RESPONSE FOR 14 DAYS]

Please explain

What difficulties might you have in choosing an answer from <the other response set>

Thinking about these questions for the past 7 days, which set of response options makes the most sense to you? [PREFERRED RESPONSE FOR 7 DAYS]

Please explain

What difficulties might you have in choosing an answer from <the other response set>

Thinking about answering these questions for the past 24 hours, which set of response options makes the most sense to you? [PREFERRED RESPONSE FOR 24 HOURS]

Please explain

What difficulties might you have in choosing an answer from <the other response set> [DIFFICULTIES WITH RESPONSE SET]

AS APPLICABLE – if participant has given varied answers, probe to understand what combination of timeframe and responses would be best for the context of use

If you were asked to answer these questions on a regular basis over a 3 month time period in order to understand whether a new treatment was helping you, what time frame do you think would be best? [PREFERRED TIMEFRAME]

Participants can choose more than one; ask for elaboration

Which response options would best? [PREFERRED RESPONSES]

Participants can choose more than one; ask for elaboration

Alternate Questions for Items That Are Not Relevant to the Participant

Have you ever experienced this as part of migraine?

If NO: Go to next question.

If YES: Please tell me a little bit about what you experienced and when.

If the participant has experienced <concept> once in a while or more than 6 months ago, continue to the next question.

If the participant has experienced <concept> on a regular basis within the past 6 months, return to the main interview guide questions and ask the participant to answer based on what they recall of those experiences.

FOR QUESTIONS WITHOUT A “NOT APPLICABLE” OPTION:

Given that you never experience this, how would you respond to these questions?

IF participant indicates they would skip the question: If it was an electronic questionnaire and you had to pick an answer to get to the next question, what would you do?

How important would it be to you to have a response option like “I never experience this”?

End of Interview Questions // If continue, go back to Q5

Finally, I'd like to ask a few follow-up questions about your migraine attacks. [ASK AS NEEDED DEPENDING ON INFORMATION SHARED DURING INTERVIEW]

In the last 4 weeks, how many migraine attacks have you had?

IF NONE: In a typical month, how many migraine attacks do you have?

About how many hours or days did your migraine attack(s) last?

And was that with or without the use of an acute treatment?

Over the last 3 months, has the severity of your migraine varied from attack to attack?

IF YES: In what ways did they vary?

Closing

Thank you so much for all that you have shared with me today. I really appreciate you taking the time to go through all these questions with me.

Before we say goodbye, is there anything else you'd like to say about this questionnaire?

STOP RECORDING

Do you have any questions for me?

If you think of any questions later, you can find the study contact information in your informed consent document.

Vector Psychometric Group will provide you with the payment for your participation in this study in the form of an electronic Mastercard or Visa gift card, which we will send to your email address. Let me just confirm the email address that I should use to send that card. [**Interviewer instruction**: Confirm the email address.]

Thank you again for your time. We greatly appreciate your participation in this research today.

APPENDIX C. ITEM TRACKING MATRIX

Item ID	**Item Text**	**Wave 1-2 Understood / preferred**	Wave 1-2 Not understood / preferred	Wave 3-4 Understood / preferred	Wave 3-4 Not understood / preferred	Total Understood / preferred	Total Not understood / preferred	Missing	# Interviews for retained items
S01y/n	Did you have a good day?	8	0	9	0	17	0	2	17
S03s	Did you have headache, head pain, or throbbing in your head?	8	0	9	0	17	0	2	17
S04s	Did you have nausea?	8	0	9	0	17	0	2	17
S05s	Did you have sensitivity to light?	8	0	9	0	17	0	2	17
S06s	Did you have sensitivity to sound?	8	1	9	0	17	1	1	18
S21s	Did you feel mentally slow or foggy?	9	1	9	0	18	1	0	19
S07pick	Which of the following symptoms was most bothersome to you?	Not retained	Not retained	-	-	-	-	-	
S09s	Did you experience aura (e.g., visual spots or flashes of light, skin tingling or numbness)?	6	1	9	0	15	1	3	16
S10s	Did you vomit?	7	1	9	0	16	1	2	17
S11s	Did you have neck pain?	7	0	9	0	16	0	3	16
PF12s	Did you feel tired because of migraine?	Not retained	Not retained	-	-	-	-	-	
S13s	Did weather conditions make your attack worse?	Not retained	Not retained	-	-	-	-	-	
GF05d	Was it difficult for you to keep to your plans for the day?	8	1	9	0	17	1	1	18
PF06d	Was it difficult for you to do usual activities that require physical exertion, like going up stairs?	Not retained	Not retained	-	-	-	-	-	
PF06f	Was it difficult for you to do usual activities that require physical exertion, like going up stairs?	7	3	9	0	16	3	0	19
PF07d	Was it difficult for you to get ready for the day (e.g., get showered and dressed)?	9	1	9	0	18	1	0	19
PF07f	Was it difficult for you to get ready for the day (e.g., get showered and dressed)?	Not retained	Not retained	-	-	-	-	-	

Item ID	Item Text	**Wave 1-2 Understood / preferred**	Wave 1-2 Not understood / preferred	Wave 3-4 Understood / preferred	Wave 3-4 Not understood / preferred	Total Understood / preferred	Total Not understood / preferred	Missing	# Interviews for retained items
PF08d	Was it difficult for you to do your regular household chores?	Not retained	Not retained	-	-	-	-	-	
PF08f	Was it difficult for you to do your regular household chores?	10	0	9	0	19	0	0	19
PF09d	Was it difficult for you to do errands (e.g., grocery shopping)?	Not retained	Not retained	-	-	-	-	-	
PF09f	Was it difficult for you to do errands (e.g., grocery shopping)?	Not retained	Not retained	-	-	-	-	-	
PF10d	Was it difficult for you to do your usual activities outside your home?	Not retained	Not retained	-	-	-	-	-	
PF10f	Was it difficult for you to do your usual activities outside your home?	Not retained	Not retained	-	-	-	-	-	
PF11f	How often were you too tired to do your regular daily activities?	7	3	9	0	16	3	0	19
S20f	How often did you feel less sharp than when you were not having a migraine attack?	Not retained	Not retained	-	-	-	-	-	
S22days	On how many days did you have head pain because of migraine?	Not retained	Not retained	-	-	-	-	-	
S21f	Did you feel mentally slow or foggy?	Not retained	Not retained	-	-	-	-	-	
PF01d	Was it difficult for you to bend forward?	8	2	8	1	16	3	0	19
PF01f	Was it difficult for you to bend forward?	Not retained	Not retained	-	-	-	-	-	
PF02d	Was it difficult for you to move your head?	8	0	9	0	17	0	2	17
PF02f	Was it difficult for you to move your head?	Not retained	Not retained	-	-	-	-	-	
PF03d	Was it difficult for you to walk?	9	0	8	1	17	1	1	18
PF03f	Was it difficult for you to walk?	Not retained	Not retained	-	-	-	-	-	
PF04d	Was it difficult for you to move your body?	8	2	7	2	15	4	0	19
PF04f	Was it difficult for you to move your body?	Not retained	Not retained	-	-	-	-	-	
PF05d	Was it difficult for you to do strenuous physical activities?	10	0	9	0	19	0	0	19
PF05f	Was it difficult for you to do strenuous physical activities?	Not retained	Not retained	-	-	-	-	-	

Item ID	**Item Text**	**Wave 1-2 Understood / preferred**	Wave 1-2 Not understood / preferred	Wave 3-4 Understood / preferred	Wave 3-4 Not understood / preferred	Total Understood / preferred	Total Not understood / preferred	Missing	# Interviews for retained items
S03f	Did you have headache, head pain, or throbbing in your head?	Not retained	Not retained	-	-	-	-	-	
S04f	Did you have nausea?	Not retained	Not retained	-	-	-	-	-	
S06f	Did you have sensitivity to sound?	Not retained	Not retained	-	-	-	-	-	
S09f	Did you experience aura (e.g., visual spots or flashes of light, skin tingling or numbness)?	Not retained	Not retained	-	-	-	-	-	
S10f	Did you vomit?	Not retained	Not retained	-	-	-	-	-	
S11f	Did you have neck pain?	Not retained	Not retained	-	-	-	-	-	
S12f	How often did your migraine symptoms get worse when you moved around?	Not retained	Not retained	-	-	-	-	-	
S13f	Did weather conditions make your migraine attack worse?	Not retained	Not retained	-	-	-	-	-	
S19d	Was it difficult for you to think clearly?	7	3	9	0	16	3	0	19
S19f	Was it difficult for you to think clearly?	Not retained	Not retained	-	-	-	-	-	
PF12f	Did you feel tired because of migraine?	Not retained	Not retained	-	-	-	-	-	
PF16d	Was it difficult for you to do your usual day-to-day activities?	Not retained	Not retained	-	-	-	-	-	
PF16f	Was it difficult for you to do your usual day-to-day activities?	8	0	9	0	17	0	2	17
PSY17f	How often did you feel worried about having a migraine attack?	6	3	9	0	15	3	1	18
S14d	Was it difficult for you to do activities because you were sensitive to light?	Not retained	Not retained	-	-	-	-	-	
S14f	Was it difficult for you to do activities because you were sensitive to light?	8	1	9	0	17	1	1	18
PSY18f	How often did you worry about how migraine would affect your daily life?	Not retained	Not retained	-	-	-	-	-	
PF13f	How often has migraine negatively affected your energy level?	Not retained	Not retained	-	-	-	-	-	
PF14f	How often did you have to miss your regular daily activities because of migraine?	Not retained	Not retained	-	-	-	-	-	

Item ID	Item Text	**Wave 1-2 Understood / preferred**	Wave 1-2 Not understood / preferred	Wave 3-4 Understood / preferred	Wave 3-4 Not understood / preferred	Total Understood / preferred	Total Not understood / preferred	Missing	# Interviews for retained items
	Include times that you stopped early or started late.								
S15d	Was it difficult for you to do activities because you were sensitive to sound?	Not retained	Not retained	-	-	-	-	-	
S15f	Was it difficult for you to do activities because you were sensitive to sound?	8	0	9	0	17	0	2	17
PF15f	How often did you get help from someone else with daily activities or tasks?	Not retained	Not retained	-	-	-	-	-	
S16d	Was it difficult for you to do activities because you were sensitive to smells?	Not retained	Not retained	-	-	-	-	-	
S16f	Was it difficult for you to do activities because you were sensitive to smells?	6	1	9	0	15	1	3	16
S17d	Was it difficult for you to do activities because you were sensitive to movement?	Not retained	Not retained	-	-	-	-	-	
S17f	Was it difficult for you to do activities because you were sensitive to movement?	Not retained	Not retained	-	-	-	-	-	
S18d	Was it difficult for you to do activities because you were sensitive to the weather?	Not retained	Not retained	-	-	-	-	-	
S18f	Was it difficult for you to do activities because you were sensitive to the weather?	Not retained	Not retained	-	-	-	-	-	
GF01f	How often did you spend time alone in a comfortable environment because of migraine?	Not retained	Not retained	-	-	-	-	-	
GF02f	How often did you need to lie down because of your migraines?	Not retained	Not retained	-	-	-	-	-	
GF03f	How often did you want to be alone in a comfortable, soothing place because of your symptoms?	Not retained	Not retained	-	-	-	-	-	
GF04d	Was it difficult for you to use a device with a lighted screen, such as a phone or computer?	Not retained	Not retained	-	-	-	-	-	
GF04f	Was it difficult for you to use a device with a lighted screen, such as a phone or computer?	Not retained	Not retained	-	-	-	-	-	
CF02d	Was it difficult for you to concentrate?	8	2	9	0	17	2	0	19
CF02f	Was it difficult for you to concentrate?	7	3	9	0	16	3	0	19

Item ID	Item Text	**Wave 1-2 Understood / preferred**	Wave 1-2 Not understood / preferred	Wave 3-4 Understood / preferred	Wave 3-4 Not understood / preferred	Total Understood / preferred	Total Not understood / preferred	Missing	# Interviews for retained items
CF03d	Was it difficult for you to do tasks that required you to concentrate?	Not retained	Not retained	-	-	-	-	-	
CF03f	Was it difficult for you to do tasks that required you to concentrate?	8	2	9	0	17	2	0	19
CF04d	Was it difficult for you to concentrate on something for longer than 15 minutes?	Not retained	Not retained	-	-	-	-	-	
CF04f	Was it difficult for you to concentrate on something for longer than 15 minutes?	Not retained	Not retained	-	-	-	-	-	
CF01f	How often did you avoid doing things that required concentration?	Not retained	Not retained	-	-	-	-	-	
CF12d	Was it difficult for you to speak clearly?	Not retained	Not retained	-	-	-	-	-	
CF12f	Was it difficult for you to speak clearly?	9	1	6	3	15	4	0	19
CF14d	Was it difficult for you to understand what was said to you?	9	1	8	1	17	2	0	19
CF14f	Was it difficult for you to understand what was said to you?	Not retained	Not retained	-	-	-	-	-	
CF16d	Was it difficult for you to express your thoughts?	Not retained	Not retained	-	-	-	-	-	
CF16f	Was it difficult for you to express your thoughts?	Not retained	Not retained	-	-	-	-	-	
CF15d	Was it difficult for you to have a conversation?	9	1	9	0	18	1	0	19
CF15f	Was it difficult for you to have a conversation?	Not retained	Not retained	-	-	-	-	-	
CF05d	Was it difficult for you to make choices that are usually easy for you?	Not retained	Not retained	-	-	-	-	-	
CF05f	Was it difficult for you to make choices that are usually easy for you?	Not retained	Not retained	-	-	-	-	-	
CF07f	Did you avoid tasks that required multiple steps?	Not retained	Not retained	-	-	-	-	-	
CF08d	Was it difficult for you to carry out tasks that required many steps?	10	0	8	1	18	1	0	19
CF08f	Was it difficult for you to carry out tasks that required many steps?	Not retained	Not retained	-	-	-	-	-	
CF06d	Was it difficult for you to make day-to-day decisions?	8	1	9	0	17	1	1	18

Item ID	**Item Text**	**Wave 1-2 Understood / preferred**	Wave 1-2 Not understood / preferred	Wave 3-4 Understood / preferred	Wave 3-4 Not understood / preferred	Total Understood / preferred	Total Not understood / preferred	Missing	# Interviews for retained items
CF06f	Was it difficult for you to make day-to-day decisions?	Not retained	Not retained	-	-	-	-	-	
CF09d	Was it difficult for you to do more than one thing at a time?	Not retained	Not retained	-	-	-	-	-	
CF09f	Was it difficult for you to do more than one thing at a time?	Not retained	Not retained	-	-	-	-	-	
CF11d	Was it difficult to do your usual tasks without making errors?	Not retained	Not retained	-	-	-	-	-	
CF11f	Was it difficult to do your usual tasks without making errors?	Not retained	Not retained	-	-	-	-	-	
CF10d	Was it difficult for you to multi-task?	Not retained	Not retained	-	-	-	-	-	
CF10f	Was it difficult for you to multi-task?	Not retained	Not retained	-	-	-	-	-	
CF13d	Was it difficult for you to speak clearly (i.e., without slurring or stumbling over words)?	Not retained	Not retained	-	-	-	-	-	
CF13f	Was it difficult for you to speak clearly (i.e., without slurring or stumbling over words)?	Not retained	Not retained	-	-	-	-	-	
CF17f	Did you avoid reading because of migraine?	Not retained	Not retained	-	-	-	-	-	
CF18d	Was it difficult for you to understand what you were reading?	8	1	7	2	15	3	1	18
CF18f	Was it difficult for you to understand what you were reading?	Not retained	Not retained	-	-	-	-	-	
CF19d	Was it difficult for you to handle routine money transactions?	Not retained	Not retained	-	-	-	-	-	
CF19f	Was it difficult for you to handle routine money transactions?	Not retained	Not retained	-	-	-	-	-	
CF20d	Was it difficult for you to do simple math without a calculator?	Not retained	Not retained	-	-	-	-	-	
CF20f	Was it difficult for you to do simple math without a calculator?	Not retained	Not retained	-	-	-	-	-	
CF21d	Was it difficult for you to remember what you were doing (e.g., remember why you entered a room)?	Not retained	Not retained	-	-	-	-	-	
CF21f	Was it difficult for you to remember what you were doing (e.g., remember why you entered a room)?	Not retained	Not retained	-	-	-	-	-	

Item ID	**Item Text**	**Wave 1-2 Understood / preferred**	Wave 1-2 Not understood / preferred	Wave 3-4 Understood / preferred	Wave 3-4 Not understood / preferred	Total Understood / preferred	Total Not understood / preferred	Missing	# Interviews for retained items
CF22d	Was it difficult for you to remember what you were talking about when speaking with someone?	Not retained	Not retained	-	-	-	-	-	
CF22f	Was it difficult for you to remember what you were talking about when speaking with someone?	Not retained	Not retained	-	-	-	-	-	
CF24d	Was it difficult for you to remember the right word for something?	Not retained	Not retained	-	-	-	-	-	
CF24f	Was it difficult for you to remember the right word for something?	8	0	8	1	16	1	2	17
CF25d	Was it difficult for you to find the right words?	Not retained	Not retained	-	-	-	-	-	
CF25f	Was it difficult for you to find the right words?	Not retained	Not retained	-	-	-	-	-	
CF23d	Was it difficult for you to remember things that were important to you?	Not retained	Not retained	-	-	-	-	-	
CF23f	Was it difficult for you to remember things that were important to you?	7	0	7	2	14	2	3	16
GF06d	Was it difficult for you to keep plans you made?	Not retained	Not retained	-	-	-	-	-	
GF06f	Was it difficult for you to keep plans you made?	9	1	9	0	18	1	0	19
GF07f	How often were you reluctant to make plans with other people because of migraine?	Not retained	Not retained	-	-	-	-	-	
PSY04f	How often did you feel good?	9	1	7	2	16	3	0	19
PSY05f	How often did you have enough energy to do everything you planned to do?	Not retained	Not retained	-	-	-	-	-	
PSY06f	How often were you able to enjoy all or part of a day?	7	2	9	0	16	2	1	18
PSY16d	Was it difficult for you to manage your usual tasks and responsibilities at school or at work?	Not retained	Not retained	-	-	-	-	-	
PSY16f	Was it difficult for you to manage your usual tasks and responsibilities at school or at work?	10	0	9	0	19	0	0	19
PSY09d	Was it difficult for you to take care of other people that you usually take care of?	Not retained	Not retained	-	-	-	-	-	

Item ID	Item Text	**Wave 1-2 Understood / preferred**	Wave 1-2 Not understood / preferred	Wave 3-4 Understood / preferred	Wave 3-4 Not understood / preferred	Total Understood / preferred	Total Not understood / preferred	Missing	# Interviews for retained items
PSY09f	Was it difficult for you to take care of other people that you usually take care of?	Not retained	Not retained	-	-	-	-	-	
PSY08d	Was it difficult for you to take care of any pets you have?	Not retained	Not retained	-	-	-	-	-	
PSY08f	Was it difficult for you to take care of any pets you have?	Not retained	Not retained	-	-	-	-	-	
PSY12d	Was it difficult for you to take part in activities you do for fun?	Not retained	Not retained	-	-	-	-	-	
PSY12f	Was it difficult for you to take part in activities you do for fun?	8	1	9	0	17	1	1	18
PSY10d	Was it difficult for you to enjoy social activity with other people?	8	1	8	1	16	2	1	18
PSY10f	Was it difficult for you to enjoy social activity with other people?	Not retained	Not retained	-	-	-	-	-	
PSY11f	Did you avoid interacting with other people?	Not retained	Not retained	-	-	-	-	-	
PSY13d	Was it difficult for you to spend time with family or friends?	Not retained	Not retained	-	-	-	-	-	
PSY13f	Was it difficult for you to spend time with family or friends?	Not retained	Not retained	-	-	-	-	-	
PSY14f	How often did you have to cancel or change your plans for social or recreation activities?	8	0	9	0	17	0	2	17
PSY15f	How often did you miss or have to leave a social or leisure event?	Not retained	Not retained	-	-	-	-	-	
PSY07f	How often did you feel sad or depressed because of migraine?	Not retained	Not retained	-	-	-	-	-	
PSY03f	How often did you feel irritable because of migraine?	Not retained	Not retained	-	-	-	-	-	
PSY02f	How often did you feel frustrated because of migraine?	Not retained	Not retained	-	-	-	-	-	
PSY01f	How often were you concerned that your migraine attacks would affect other people's lives?	7	0	9	0	16	0	3	16
GF08f	How often did you feel you did not have control over your life?	7	0	6	3	13	3	3	16
GF05f	Was it difficult for you to keep to your plans for the day?	Not retained	Not retained	-	-	-	-	-	

Item ID	**Item Text**	**Wave 1-2 Understood / preferred**	Wave 1-2 Not understood / preferred	Wave 3-4 Understood / preferred	Wave 3-4 Not understood / preferred	Total Understood / preferred	Total Not understood / preferred	Missing	# Interviews for retained items
PSY09dRev	Was it difficult for you to take care of people or pets that you usually take care of?	Revised item	Duplicate not retained	-	-	-	-	-	
PSY09fRev	Was it difficult for you to take care of people or pets that you usually take care of?	Revised item	Revised item	9	0	9	0	0	
S00yn	Did you have any migraine symptoms?	New item in wave 3	New item in wave 3	9	0	9	0	0	
PF12sRev	Did you feel tired?	Revised item	Revised item	5	4	5	4	0	
GF01fRev	How often did you want to spend time alone in a comfortable environment ?	Revised item	Revised item	9	0	9	0	0	
PF14fRev	How often did you have to miss your regular daily activities? Include times that you stopped early or started late.	Revised item	Revised item	8	1	8	1	0	
PF09fRev	Was it difficult for you to do errands?	Revised item	Revised item	9	0	9	0	0	
GF07fRev	How often were you reluctant to make plans with other people?	Revised item	Revised item	9	0	9	0	0	
PSY07fRev	How often did you feel sad or depressed?	Revised item	Revised item	9	0	9	0	0	
PSY03fRev	How often did you feel irritable?	Revised item	Revised item	9	0	9	0	0	
PSY02fRev	How often did you feel frustrated?	Revised item	Revised item	9	0	9	0	0	
S22daysRev	On how many days did you have head pain?	Revised item	Revised item	9	0	9	0	0	
S07pickREV	Which of the following symptoms other than pain was most bothersome to you?	Revised item	Revised item	8	1	8	1	0	