STUDY PROTOCOL

MICOAS UH3 2022-03

Study title: Patient Interviews on Recall and Response Options to Support Development of the Migraine Clinical Outcome Assessment System (MiCOAS)

Short title: Recall Response Study

Study purpose: To gather data regarding people's' ability to recall and evaluate experiences with migraine over different periods of time and the strategies they use to retrieve information and select responses to questionnaires

Study phase:	UH3	**Protocol:**	MiCOAS UH3 2022-03
Version Date:	11/1/2022	**Version #:**	1.0

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VECTOR PSYCHOMETRIC GROUP, LLC
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PROTOCOL ACCEPTANCE

Protocol Title	Patient Interviews on Recall and Response Options to Support Development of the Migraine Clinical Outcome Assessment System (MiCOAS)
Date	11/1/2022
Version	1.0
VPG Primary Contact	RJ Wirth
VPG Qualitative Study Director	Rikki Mangrum
Sponsor	
Sponsor Primary Contact	

I have read and agree to the study mentioned above, Patient Interviews on Recall and Response Options to Support Development of the Migraine Clinical Outcome Assessment System (MiCOAS). I am aware of my responsibilities under the Good Practices guidelines of the International Society for Pharmacoeconomics and Outcomes, U.S. federal and local regulations (as applicable), and the study protocol. I agree to conduct the study according to these guidelines and to appropriately direct and assist the staff under my control, who will be involved in the study.

SIGNATURES:

_____ _____

VPG REP, Vector Psychometric Group, LLC Date

_____ _____

Date

VERSION HISTORY

Version	Date	By	Description of Changes
1.0	11/01/2022	Rikki Mangrum, Karolina Schantz	Final

ABBREVIATIONS

Abbreviation	Definition
Einstein	Albert Einstein College of Medicine
FDA	U.S. Food and Drug Administration
HIPAA	Health Insurance Portability and Accountability Act of 1996
IRB	Institutional review board
MiCOAS	Migraine Clinical Outcome Assessment System
PROM	Patient reported outcome measure
VPG	Vector Psychometric Group, LLC

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1. PROTOCOL SYNOPSIS

STUDY TITLE: Patient Interviews on Recall and Response Options to Support Development of the Migraine Clinical Outcome Assessment System (MiCOAS)

STUDY DESIGN: Observational, non-interventional, cross-sectional, qualitative study of people with episodic or chronic migraine. The study involves recruitment of study participants through The Coalition for Headache and Migraine Patients (CHAMP) for participation in a one-time, individual, semi-structured interview conducted via video-conferencing.

STUDY OBJECTIVES: In this study, people living with migraine will be interviewed to gather data regarding their ability to recall symptoms or impacts over different time periods (24 hours, 7 days, 14 days) and the information retrieval and rating strategies they use to select responses for proposed migraine measure questionnaire items. Participants will be shown draft questionnaire items and asked to share their views on potential recall time periods (i.e., 24 hours, 7 days, 14 days) and response options (i.e., options for severity, frequency, difficulty). Participants will also be asked to comment on which time periods or response options seem easiest for them; most accurate in reflecting their migraine experiences; or capable of capturing variation in what they experience. This data will be used to inform the selection of reference time periods and response options for MiCOAS scales.

STUDY POPULATION SAMPLE: This study will include approximately 10 participants who are representative of the population of people with migraine generally included in clinical trials of acute or preventive migraine treatments. A limited sample is appropriate because the instrument does not include branching skip patterns and participants will see all items in the draft instrument. However, as is typical with qualitative research of this kind, the final sample size for this study will remain flexible as the interview data collection progresses and questionnaire validity evidence is accrued.

The study will include adults who meet the following inclusion and exclusion criteria:

Inclusion criteria:

- Be a resident of the U.S.
- Be between 18 and 75 years of age
- Have been diagnosed by a healthcare professional
- Report being able to distinguish between a day with migraine and other types of headache days
- Report experiencing 4-26 headache days per month
- Report experiencing limitations on physical or cognitive activities on at least 1 day over the last 3 months because of migraine
- Be comfortable reading and speaking in English

- Provide informed consent to participate in the study, which includes being to have their interview video recorded and transcribed

Exclusion criteria:

- Diagnosis of any other clinically significant health condition that might interfere with the person's ability to provide non-confounded descriptions of their experience, such as multiple sclerosis or dementia.
- Reported alcohol or drug abuse over the past 3 months (not inclusive of medication overuse to treat migraine).

DATA COLLECTION: Data for study analyses will be collected using the following instruments:

- Appendix B: Eligibility Screening Questionnaire
- Appendix D: Health and Demographic Information Survey (delivered via a web-based questionnaire platform)
- Appendix F: Interview Guide
- Appendix G: Draft questionnaire slides for interview

ANALYTIC APPROACH: Interviews will be transcribed verbatim and deidentified by removing any information that identifies, or could be used to identify, participants.

Analysts will examine the transcripts for relevant data for each group of items and summarize the strengths and weaknesses of each time frame and set of response options in the table and record results in the disposition table.

TIMELINE: The estimated length of this qualitative study from the time of Institutional Review Board (IRB) review to completion of the draft study report is expected to be approximately 3 months. However, study length is highly dependent upon recruitment rate and participant availability, as well as the number of rounds of testing required.

2. STUDY PROTOCOL

2.1. PURPOSE

As part of establishing the content validity of a patient-reported outcome measure (PROM), a justification is required for the specified reference time period(s) and response options offered for each item. In developing this justification, data gathered directly from people living with migraine will be used to characterize their ability to recall and evaluate their experience over different periods of time and the strategies they use to retrieve information and select responses, which could result in different forms of responder bias.

2.2. INTERVIEW PROM INSTRUMENT

The study will examine draft PROM questions. For these interviews, the draft questions and options for responses are presented on slides for discussion.

2.3. POPULATION AND SAMPLE

An initial sample of 10 people with migraine will be selected that is representative of the population of migraine patients who participate in clinical trials of novel treatments. Research has shown that substantial data saturation is often achieved in the first 8-12 interviews (Guest et al., 2006; Guest et al., 2020). As is typical with qualitative research of this kind, the final sample size for this study will remain flexible as the interview data collection progresses and questionnaire validity evidence is accrued.

To achieve review by an overall diverse population sample, the following participant attributes will be considered when selecting individuals for interviews:

- Migraine frequency type (episodic <15 days/month, chronic ≥15 days per month)
- Sex and gender identity
- Race
- Ethnicity
- Age
- Level of education
- Income
- Geographic location

2.4. METHOD

To reflect the aim of validating the draft PROM as a clinical outcome assessment for clinical trials, these interviews seek data to support the selection of appropriate recall time periods and response options for MiCOAS measure instruments. These data will be crucial to establishing a justification for the use of specific time periods and response options for each item or for the PROM instrument as a whole.

PRO development guidance emphasizes that a rationale should be provided for the appopriateness of the recall time frame and responses selected for a measure and that the selected components should be tested through cognitive debriefing (Patrick et al., 2011; United States Food and Drug Administration, 2009 Dec, 2022). However, the guidance provides little specific direction about what evidence is necessary to support assumptions made in the rationale or how that evidence should be gathered. Because the guidance is limited, methods used in this study are derived from best practices for qualitative interviewing and informed by recommendations and frameworks proposed by authors of several systematic reviews and research articles.

2.4.1. BACKGROUND SUMMARY OF LITERATURE

Research on recall time frames has suggested that patient-reported outcome measures may be affected by several forms of bias and by other factors that arise when people respond to survey questions (Stull et al., 2009). One potential source of bias arises from limitations of human memory. Because there is a predictable, inverse relationship between length of the recall period and accuracy of recollection (Clarke et al., 2008), one might infer that shorter recall periods are preferable. However, other aspects of memory functioning and forms of bias that pertain to questionnaire response are not strictly predictable or consistent, and the assumption that shorter is better does not stand up to scrutiny (Clarke et al., 2008; Kjellsson et al., 2014). For example, the rate of memory decay is not the same for all recollection: major events are easier to recall accurately over a longer time period than minor ones, and information accessibility (i.e., the complexity of what is to be recalled) also affects recall (Stull et al., 2009). Research has also shown that issues related to recall time periods may be different for health conditions like migraine that are characterized by variability (Sanghera et al., 2022; Stull et al., 2009). Finally, research has shown that recall of symptoms like pain and fatigue exhibit features that affect self-report. For example, studies have found that people report higher pain upon recall than they reported at the time, but report less fatigue on recall than in momentary assessments (Stull et al., 2009). Recall of pain is also influenced by recency and peak events, and people with chronic pain often incorporate factors other than pain itself in selecting ratings. As a result, prior researchers have emphasized the desirability of selecting recall periods that serve specific goals and achieve a balance among tradeoffs, while accepting the accompanying limitations and potential for error. In addition, prior researchers have stressed that using measures with different recall periods may be of value in capturing an accurate assessment of patients' experiences. These publications stress the importance of considering all these criteria and the tradeoffs they require when establishing a justification for recall time periods for measures.

Research on selection of response options is even more limited. A recent literature review highlighted that reporting on justification of PROM response options is inconsistent and there was limited similarity among the justifications that were reported (Gries et al., 2017). Indeed, the authors noted that publications were inconsistent even in the way that response scales were described. Studies that compared different response scales, however, generally found high levels of concurrence and studies that compared different scales for the same concept also found large correlations. The review authors concluded that response scales should offer sufficient numbers of choices for the measure's intended use, that patients themselves should be queried to understand what options make sense to them given item content, and that quantitative assessment of responses should be conducted (e.g., if options have to be collapsed to obtain stable scoring parameters, then use fewer options). As with recall periods, the review authors concluded that measure developers and

evaluators must establish a reasonable rationale, both qualitatively and quantitatively, for the selected responses.

2.4.2. THEORETICAL BASIS FOR INTERVIEW AND ANALYTIC DESIGN

The proposed interview structure is aligned with limited realism inquiry (King et al., 2019). Limited realism acknowledges that there are knowable certainties and plausible explanations that may include causal relationships, but also acknowledges that these are influenced by individual perspectives or external factors, and seeks to develop theories that explain these influences. Interviews designed from this theoretical basis are more highly structured and seek to understand the ways in which participants interact with concrete notions and the strategies they use to navigate concrete problems. Analysis of interview content will follow principles of Corbin and Strauss' (2015) approach to grounded theory, with an emphasis on identifying explicit links between people's perceived capacities for recall and rating, the strategies they use to execute recall and rating tasks, and the content of the measure instrument.

In these interviews, VPG will seek to collect data that reveals the ways that participants interact with concrete notions of time, severity, frequency, and difficulty in the context of questions asking about migraine experiences. VPG will also seek data regarding the strategies participants use to retrieve and characterize their experience in the context of the demand for these concrete parameters, and to select among responses or choose not to answer. Analysis of this data can then be used to support or contradict assumptions about appropriate recall and response options, and inform the selection of recall periods and response options that are best suited for the measure's intended purpose.

2.4.3. INTERVIEW METHODS

To develop additional insights into how people living with episodic and chronic migraine approach answering PROM items, VPG proposes to conduct 10 virtual interviews that focus on gathering data about perspectives on different recall time frames and response options for items related to the specific domains and concepts included in the MiCOAS draft measurement framework. Interviews will last approximately one hour and be conducted in accordance with a semi-structured interview guide (Appendix F). Interviews will be video-recorded for transcription and analysis; video recordings are required so that analysts may be certain which items and response options are being referred to in discussion. Interviews will be conducted virtually using the Microsoft Teams platform at a time convenient to the participant. Participants will be required to join using a computer or tablet so that they may view materials displayed on screen. Participants will not be required to be on camera, but may choose to turn their camera on if they wish. The interviewer will be on camera unless the participant prefers them to turn the camera off. A notetaker may also be used during interviews to support the interviewer in displaying on-screen content and recording participant selections. On-screen content will consist of slides that display questionnaire items and candidate response options (Appendix G).

The aims of these interviews are to systematically explore the following topics:

- The impact the recall time period may have when people are retrieving and characterizing information to respond to questions

- How people with migraine think about the tradeoffs inherent in responses based on recall time frame (i.e., given a specific item, what time frame seems easiest, most accurate, or most informative to people with migraine and why)
- The impact of response options on the way that people retrieve information and characterize their experiences
- How people with migraine view the benefits and drawbacks of using frequency vs. difficulty/severity responses for the concepts included in MiCOAS, including when they consider it valuable to collect both and why

2.4.4. Recruitment and Enrollment Procedures

Participants for this study will be recruited through a collaboration between VPG and CHAMP, an advocacy organization for people with headache, migraine, and cluster diseases. CHAMP will distribute study announcements through their website, social media, and other distribution channels to reach potentially eligible individuals. All announcements will direct individuals to a designated study webpage to access detailed study information and, if interested, complete an electronic screening questionnaire. The content across all study announcement channels will include consistent and concise introductory information highlighting key details of this study (Appendix A).

On the study's webpage, an electronic participant eligibility screener will be used to determine whether individuals meet the study eligibility criteria. The participant eligibility screener (Appendix B) will present questions based on the following inclusion and exclusion criteria:

Inclusion criteria:

- Be a resident of the U.S.
- Be between 18 and 75 years of age
- Report having been diagnosed by a healthcare professional
- Report being able to distinguish between a day with migraine and other types of headache days
- Report experiencing 4-26 migraine headache days per month
- Report experiencing limitations on physical or cognitive activities on at least 1 day over the last 3 months because of migraine
- Be comfortable reading and speaking in English
- Provide informed consent to participate in the study, which includes being willing to have the interview video recorded and transcribed

Exclusion criteria:

- Diagnosis of any other clinically significant health condition that might interfere with the person's ability to provide non-confounded descriptions of their experience, such as multiple sclerosis or dementia
- Reported alcohol or drug abuse over the past 3 months (not inclusive of medication overuse to treat migraine)

Individuals who do not meet all eligibility criteria will be immediately notified through the study web-based platform and thanked for their interest. Individuals who meet all eligibility criteria in the screener will be prompted to proceed to informed consent for study participation.

Eligible individuals will read and review the informed consent form (Appendix C) and, if they choose to participate, will provide their consent through the study's web-based platform. If an eligible person has questions regarding the study or the informed consent form or would like to discuss the study further before choosing to accept or decline participation, the individual may contact the research team directly (via phone or email listed on the form).

Completing informed consent will constitute enrollment as a study participant but does not guarantee that the individual will be contacted for an interview. Enrolled participants will be asked to complete the electronic Health and Demographic Information Form (Appendix D) and a short electronic form to provide limited contact information (Appendix E) and preferred contact timeframe to the research team. Contact information will only be used for contacting those individuals selected to participate in an interview.

Interview participants will be selected to represent a variety of demographic and health characteristics. Once eligible individuals complete all the enrollment steps, VPG will review eligibility and survey responses to select a diverse set of interview participants. Selected individuals will then be contacted for an interview by a member of VPG's study team. Interviews will be scheduled at times that accommodate participants' availability, time zones, and preferences for time of day. After an interview has been scheduled, the research team will contact each participant by their preferred method (email or phone), approximately 1 to 3 days prior to their scheduled interview, to remind the participant about the interview and reconfirm their availability. As needed, interviewers will also contact participants who do not join a scheduled interview to inquire about rescheduling.

2.4.5. Data Collection

The study data collection period will begin when the first participant has provided informed consent and end after the last participant has completed their interview.

2.4.5.1. Data Collection Instruments and Sources

No interventions, medical assessments, or tests are required for this study. Data sources and forms for the study are described in Table 1.

Table 1. Data Collection Instruments and Data Files

Document/Form	Purpose
Eligibility Screening Questionnaire (Appendix B)	To determine participant's study eligibility
Health and Demographic Information Survey (Appendix D)	To obtain participant's health and demographic information
Participant Contact Information (Appendix E)	To obtain participant's contact information for reconfirming eligibility, scheduling interview, and conducting the video interview
Interview Guide (Appendix F)	To guide the semi-structured interview about the PROM instrument
Interview video recordings and transcripts	To capture participant interview responses verbatim for analysis

2.4.5.2. PARTICIPANT COMPENSATION

Participants who complete an interview will be compensated with a $75 electronic Mastercard delivered by email.

2.4.5.3. INTERVIEW TRAINING AND MONITORING.

Interviewers will prepare by reviewing study aims, reviewing relevant FDA and International Society for Pharamacoeconomics and Outcomes Research guidance on interview procedures, closely studying the interview guide, and practicing with the virtual interview platform.

Interviewers will participate in mock interviews as part of their training. These interviews will also be used to refine the wording of interview questions and to test the virtual interview platform and logistics plan.

The qualitative study director will monitor the quality of interviews by reviewing recordings or transcripts. Monitoring will assess both interviewer adherence to best practices as well as the quality and comprehensiveness of data elicited during interviews. Quality issues with interviewers will be addressed through additional training. Issues with comprehensiveness of the data will be shared with the research team for decision making about whether and how to modify the interview guide.

2.4.5.4. PREPARATION OF TRANSCRIPTS

Audio from the interview recordings will be professionally transcribed. When transcripts are received, VPG will review the transcript for accuracy and remove any content that may serve to identify the interview participant, including but not limited to personal names or references to identifiable events.

2.4.6. ANALYSIS

Analysts will use both recordings and transcripts during analysis to accurately identify items, recall periods, and response options being discussed. Analysts will extract data from transcripts for each item that characterizes each participant's:

- Ability to recall experience over each time period and strategies used to retrieve information from memory
- Judgments about ease/challenge of recall, accuracy of recall, and inclusion or prioritization of selected experiences (e.g., based on recency or saliency)
- Strategies for using different response sets to answer items in connection with specific time periods
- Judgments or preferences related to the applicability of response sets for specific time periods

2.4.6.1. ASSESSING SUFFICIENCY OF DATA

In PROM development, saturation is a typical method for assessing sufficiency of interview data. Saturation is not a criteria for this study, however, because the interviews are highly structured. Instead, the research team will make an overall judgment on whether the collected data provides sufficient insight to be used as part of a justification of recall time period and response option selections. The research team will consider the item-level and topic-area levels of agreement among participants in making this judgment. If low levels of agreement are found across many topics or items, the research team will also make a judgment about whether additional data collection is likely to be useful.

3. REPORTING AND DISSEMINATION OF RESULTS

VPG will prepare a summary report of the study results. The report will comprise the following components: background and objectives, study design and methods, results, limitations, and discussion. The report will also include a set of recommendations for recall time periods and response options with an accompanying justification based on the study results.

3.1. POTENTIAL PUBLICATIONS AND PUBLICATION POLICY

The results of this study, with prior review from the FDA, may be submitted for publication in a scientific journal and/or for presentation at a medical or scientific conference. If published or presented, the results of this study will be described in such a way that confidential or proprietary information is not disclosed.

Selection of authors for any scientific publication(s) developed from this study will comply with the International Committee of Medical Journal Editors guidelines. Accordingly, authorship should be based on achieving all of the following 4 criteria:

1. Substantial contributions to the conception and design, or acquisition of data, or analysis and interpretation of data.
2. Drafting the article or revising it critically for important intellectual content.
3. Final approval of the version to be published.
4. Agreement to be accountable for all aspects for the work, thereby ensuring that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved.

All authors of a publication should meet all four criteria. Each author must agree to their inclusion in the list of authors. Resolution of scientific differences in the presentation or interpretation of study findings will be conducted along principles of honest scientific debate.

Individuals who may have contributed to this study but not sufficiently to qualify for authorship may be listed in the acknowledgements.

4. DATA MANAGEMENT

4.1. DATA STORAGE AND HANDLING

The data for all electronic forms completed by participants will be collected using the flexCOA® survey platform. flexCOA® is a proprietary electronic data collection platform owned by VPG that facilitates the distribution of surveys, measures, and questionnaires. flexCOA® is compliant with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and individual data collected within the system are encrypted and protected. Throughout the study, the VPG research team will regularly export study data from flexCOA® to the designated secure MiCOAS study folder.

The MiCOAS study folder will reside in secure, encrypted servers within VPG's information technology systems. Access to this folder will be restricted to the members of the VPG research team who are involved in this study. No participant-identifiable study data will be printed in hard copy. After study completion, VPG will securely archive all study participant-identifiable data for a period of 5 years, and then securely destroy the data consistent with current VPG standard operating procedures.

Recordings from participant interviews will be labeled with the participant's unique identification number and uploaded to the designated, secure MiCOAS study folder immediately after completion of each interview. Once the recording is confirmed as successfully stored in the study folder, the file will be deleted from the recording device. The recording for each study participant will be securely transferred for transcription through a credentialed file-sharing service restricted to interviewers and transcriptionists. When transcripts are completed, an analyst will review the transcript and redact any potentially identifying information, such as references to places, occupations, or events. Once the final de-identified transcript has been created, the recording shared with the transcriptionist will be securely destroyed. The de-identified interview transcripts will be uploaded to NVivo Windows for analysis. The NVivo Windows QDAS platform complies with HIPAA data security requirements.

4.2. DATA MONITORING AND QUALITY ASSURANCE

Prior to initiation of participant recruitment, quality checks will be performed on the electronically-collected data systems via user acceptance testing as performed by the research team. Any identified issues will be resolved. The research team will actively monitor the web-based screening data collection and review information entered by study participants when data is exported. In an effort to avoid missing data, key fields within each electronic data collection form will be marked as required before a study participant (or potential participant) can proceed to the next form or step in the data collection process. Certain questions will also be limited by pre-specified response options.

5. ETHICAL AND REGULATORY OBLIGATIONS

This study will be conducted in compliance with FDA and federal regulations for the protection of human subjects, the American Psychological Association code of ethics, and all local regulatory requirements applicable to non-interventional studies.

5.1. INSTITUTIONAL REVIEW BOARD

This study will be submitted to WCG IRB for review before initiation of any study activities. Study advertising and recruitment of potential participants will not begin until after written confirmation of IRB approval or determination of exemption is received.

5.2. INFORMED CONSENT

This study will be performed in accordance with ethical principles that are consistent with local and national applicable regulatory requirements. The consent form will describe the purpose of the study, data collection procedures, benefits and risks of participation, confidentiality measures to be taken, and participant rights. It will include study contact information, and a description of and contact for the IRB. Individuals will be encouraged to email or call the study contact with any questions they may have prior to consenting to participate in the study. Individuals will be able to take as much time as they need to consider their decision until enrollment in the study closes.

Prior to enrollment in this study, each person will be required to provide an electronically signed informed consent form to VPG through the flexCOA platform. Consented individuals will then be directed to complete their enrollment by filling out the electronic Health and Demographic Information Survey (Appendix D) and Participant Contact Information Form (Appendix E). Participants who complete all enrollment steps may then be contacted to schedule an interview. If important new information becomes available during the study, the consent form will be revised. Key informed consent elements, such as the right to withdraw at any time or to decline to answer questions, will be reconfirmed at the beginning of scheduled interviews.

Study participants will not receive any direct clinical benefits from their participation in this study. However, the information obtained from study participants is expected to provide a better understanding of people's experience with migraine and migraine treatment. Improving our understanding of their view on their condition and its treatment may help other people with migraine in the future. No physical or medical risks or burdens are expected to occur due to participants' involvement in this study. However, it is possible that participants may feel uncomfortable answering some of the interview questions, and during or after the interviews, participants may become more aware of the symptoms, impacts, or other factors related to migraine. Participants may also find the interview mentally tiring. Interviewers will be trained regarding the potential sensitivities of people with migraine and participants will be encouraged to talk with their healthcare professional about any medical questions or concerns.

5.3. CONFIDENTIALITY

VPG and Einstein will comply with regulatory requirements regarding the conduct of qualitative research, that does not involve the testing of a treatment or procedure. The study will be conducted in accordance with all applicable data privacy requirements. All participant data collected and processed for the purposes of this study will be managed by the research team with adequate precautions to ensure the confidentiality of the data, in accordance with applicable national and/or local laws and regulations governing personal data protection.

Participants' contact information will be provided directly by the participant to VPG and will be used only for the purposes of this study (i.e., to answer questions regarding the study, reconfirm eligibility, schedule the interview, conduct the interview, and send compensation for study participation). The study report and any publication or presentation of this study data will not contain any participant identifiable information and participant identity will remain confidential.

Personnel from the following organizations may examine the research study records: VPG, Einstein, regulatory agencies (e.g., FDA), and IRBs. Only research study staff directly involved in participant recruitment and data collection will know the identity of the participants, and all other study data retained for study analyses (descriptive quantitative data from questionnaire responses and interview transcripts) will be coded with a unique study ID and/or fully de-identified.

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APPENDIX A: STUDY OUTREACH ANNOUNCEMENTS

Section 1 – Email & eNewsletter

Dear CHAMP Community Member,

We're excited to share another opportunity to participate in an ongoing study for people who live with migraine. The study is sponsored by Vector Psychometric Group, LLC (VPG) through a grant from the United States Food and Drug Administration (FDA).

If you are between the ages of 18 and 75 and live in the United States, we invite you to see if you are eligible to participate.

In this study, the research team wants to learn how to make better questionnaires about migraine. The team will collect data about a migraine survey through online interviews. Interviewers will show you questions being considered for questionnaires and ask you how you would answer them.

If you are interested, please follow the link below to take a 5-minute survey to see if you are eligible for the study.

Please click here to see if you qualify for the study
[SCREENER URL]

If you are eligible, you will be asked to read more about the study and provide consent for your data to be used. If you provide consent, you

- Will be asked to complete a confidential online survey about your health and personal background.
- May be invited to take part in a 60 minute confidential interview at a time that works for you; interviews will take place online using Microsoft Teams meeting software

Taking part in this study is voluntary.

If you complete an interview, you will receive a $75 Mastercard e-gift card as a thank you for your time.

If you have any questions regarding the study, contact the VPG study coordinator at 301-392-7991 or by email at MiCOAS@vpgcentral.com

VPG specializes in conducting research to support the development and use of person-centered measures of health and well-being. CHAMP is proud to partner with VPG to recruit participants for this patient-centered study.

Your participation will make a difference for people with migraine. Thank you in advance for your interest in this study!

With appreciation,

The CHAMP Team

Section 2 – Social Media Posts

Facebook Post

Please help with an important new study for people living with migraine!

In this study, the research team wants to interview people with migraine. Interviews will take place online using Microsoft Teams meeting software. The interviewer will ask you to look at questions being considered for a migraine questionnaire and talk about how you would answer them.

Sharing your views will help researchers make better health measures for people with #migraine.

Put your personal migraine experience to good use to help others with migraine. See if you're eligible to participate in this new study: [SCREENER URL]

Targeted Facebook Posts [Optional]

Men

Are you a man who has migraine? We need you!

Researchers for a new study want to talk with men who live with migraine. Men are often left out of research on migraine. Sharing your time will help the research team better understand the real-world lives of men with #migraine. The team will use what they learn to create better ways to measure whether migraine treatments work for everyone.

The 60 minute phone interview is completely confidential. As thanks for your time, you will receive a $75 Mastercard e-card if you complete an interview.

If you live the U.S. and are 18-75 years of age, see if you're eligible to participate in this new study: [SCREENER URL]

BIPOC

Are you Black, Indigenous, or a Person of Color? Do you have migraine? Sharing your time will help the research team understand the real-world lives of BIPOC people who live with #migraine. The team will use what they learn to create better ways to measure whether migraine treatments work for everyone.

The research team in this study would like to talk to BIPOC individuals about their experiences living with migraine. The 60 minute phone interview is completely confidential. As thanks for your time, you will receive a $75 Mastercard e-card if you complete an interview.

If you live the U.S. and are 18-75 years of age, see if you're eligible to participate in this new study: [SCREENER URL]

Twitter Posts

Sharing your #migraine knowledge can make a difference! See if you're eligible to participate in a new, FDA-sponsored interview study to improve measures of how migraine treatment affects people's lives: [SCREENER URL]

Share your experiences with #migraine! A new FDA-sponsored study asks for 60 minutes of your time. We want to hear your views on a migraine questionnaire. See if you're eligible to participate in this new phone interview study: [SCREENER URL]

Participate in a new research study of how #migraine affects people's lives. Your voice will improve measurements in clinical studies so new treatments are assessed for what really matters. Check your eligibility to participate in a 60-minute virtual interview: [SCREENER URL]

APPENDIX B. ELIGIBILITY SCREENING QUESTIONNAIRE

[placeholder – same as prior study]

APPENDIX C: INFORMED CONSENT

PARTICIPANT CONSENT FORM

TITLE:	Patient Interviews on Recall and Response Options to Support Development of the Migraine Clinical Outcome Assessment System (MiCOAS)
PROTOCOL NO.:	MiCOAS UH3 2022-03 IRB Protocol TBD
SPONSOR:	Vector Psychometric Group, LLC Under a grant from the United States Food and Drug Administration (FDA) (#5UH3FD006795-04)
INVESTIGATOR:	R.J. Wirth, PhD 847 Emily Lane Chapel Hill, North Carolina 27516 United States
STUDY-RELATED PHONE NUMBER(S):	Lexy Bryant lexy.bryant@vpgcentral.com 301-392-7991 (24 hours) Rikki Mangrum rikki.mangrum@vpgcentral.com 919-893-9055

Why am I being contacted?

You are being invited to take part in a research study about people who have migraine headaches. If you participate, you will be one of about 10 participants in this study.

If you choose to participate, you:

- Will be asked to answer a 10-minute online survey about your background and health
- May be invited to participate in one interview that will last about 60 minutes

The main **benefit** of this research is that your participation will help scientists develop measures of the impact migraine has on people's lives. These measures will be used to evaluate how well treatments for migraine work. But, there is no direct benefit to you for participating.

The main **risk** of the research is that you may find the interview tiring.

Your participation is **voluntary**. Your alternative is to not participate. The decision to participate is up to you. You always have the right not to answer questions. You may also stop your participation at any time. If you do not want to participate or decide to stop participating, there will be no penalty or loss of benefit to which you are otherwise entitled.

More information about all these topics is provided below.

Why is this study being done?

The purpose of this study is to improve a draft questionnaire that measures migraine experience. This questionnaire asks about migraine symptoms and how migraine affects people's ability to do the things they want to do from day to day.

How will this study help people with migraine?

The information collected during this study will be used to improve the questionnaire. The questionnaire can then be used to understand whether treatments for migraine, such as medicines, are working as intended.

Who is paying for this study?

The United States Food and Drug Administration (FDA) is funding the study through grant number 5UH3FD006795-04.

Who is conducting this study?

Vector Psychometric Group, LLC, and Albert Einstein College of Medicine are conducting this study. In the rest of this document, Vector Psychometric Group will be called VPG.

What should I know about this research?

The study involves

- looking at the questionnaire during your interview
- talking with the interviewer about your thoughts about the measure survey

The study does not involve any medical treatments and will not affect your medical care in any way.

If you have any questions about the study after you read this form, please call or email the study contact listed at the top of this form. Ask all the questions you want before you decide about participating.

Taking part in this study is voluntary. It is your decision whether to participate at all times. No matter how you choose, there will be no penalty or loss of benefits to which you are otherwise entitled.

- You can choose not to take part at all
- You can agree to take part and later change your mind at any time

What are you asking me to do?

We are asking you to fill out a survey about your health and background. We may also ask you to take part in an interview to hear your thoughts on the draft measure.

The health and background survey will take about 10 minutes to fill out.

The interview will last about 60 minutes. The interview will take place through a video conferencing platform called Microsoft Teams. You will receive a unique, private link for your interview. We will ask you to use a computer or smart device so that you can see information the interviewer displays on screen. You do not have to be on camera for the interview, but can choose to use your webcam if you like.

The interview will be video-recorded and transcribed. The transcription will not include your name or personal details.

What do I do if I am interested in taking part in this research?

Taking part in the study requires a few steps.

1. **Consent to participate in the study**. The first step is completing this informed consent form.

   Take your time to read the form and ask any questions before giving your consent. You can reach out to the study contact listed at the top to ask any questions that you have about this study.

   If you want to participate, you should indicate your consent at the bottom of this form.

   Indicating consent to participate in the study does not waive your legal rights in any way. Your consent does not release VPG or any other institution involved in this study or in the review of this study from their legal and professional responsibilities to protect your identity and your personal information to the extent required by any applicable laws and regulations.

2. **Complete enrollment in the study**. Enrolling in the study involves filling out a survey of questions about your health and your background. After you fill out the survey, you may be contacted to schedule an interview. We may not be able to interview everyone who enrolls in the study.

The survey will ask about your health history and medications you use for migraine. It will also ask about your gender, race or ethnicity, education, and so on. We use this information to be sure that the people we interview are like all the different people who live with migraine.

You will also be asked to provide contact information, such as your name and telephone number or email address. The research team will use your contact information only for scheduling an interview and providing payment. No one will share your contact information outside the research team.

3. **Give permission for your interview to be video-recorded and transcribed**. Your interview will be video-recorded so we can create a transcript of the interview for analysis. This written copy of your exact words helps the research team be accurate in capturing what you say. The video recording also shows what was on-screen during the interview and we add that to the transcript, too. The transcript will not include your name or personal details.

   The interviewer will ask you to confirm your permission to record before starting the interview.

   If you do not want to give permission for your interview to be recorded and transcribed, you will not be able to participate in this study.

4. **Complete an interview**. If you are selected for an interview, VPG will contact you to schedule an interview appointment with a researcher from the study team. The interview will be scheduled at a time that works well for you. VPG will also contact you once, about 1 to 3 days ahead of time, to remind you about the interview. Scheduled interviews can be rescheduled at your request.

How will you protect my privacy?

Your privacy is very important to us, and we make every effort to protect you and your health information to the furthest extent possible. But there is a risk of loss of confidentiality when you participate in a research study.

There are several things we do to protect your privacy and respect the confidentiality of information you may share with us.

- **We store information in secure locations and limit the people who can access it.** We store all our data in secure, electronic files that can only be accessed by certain members of the research team. We will never use your name or identify you as an individual in any way in any reports, presentations, or publications of this study.

- **We don’t connect your name or contact information with your data**. To protect your identity, we use a study-specific identification number instead of your name or other personal

information. This number protects your identity and is used to label all information collected from you.

We keep your name and contact information separate from the interview transcript and survey responses. We only need this information to schedule your interview and provide payment, so we don't need to keep it with the study data.

- **Study staff with access to your personal data are bound by confidentiality rules**. If you participate in the study, the people who schedule or conduct your interview will know your name or personal details. The interview recording will be heard by the person who creates the transcript. These staff are bound by confidentiality rules and trained in how to maintain privacy and security of data.

- **We remove information that might help to identify you from your interview transcript**. We remove anything you or the interviewer may say during your interview that might be used to identify you. For example, you might say where you work or talk about how many children you have. When this happens, these details will be deleted from the transcript. Your transcript will then be combined with transcripts for all the other study participants for analysis.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for:

- Completing a survey about your background and your health
- Completing an interview if you are selected

Could being in this research hurt me?

There are no anticipated physical risks to participating in this study. The study involves completing a survey and taking part in a video interview.

There is a chance that you may find the interview too tiring. If that is the case, you can tell the interviewer that you are too tired to continue. You have the choice to stop your participation or to continue the interview at another time.

Will it cost me money to take part in this research?

There are no costs to you for participating in this study.

Will being in this research benefit me?

You may not receive any direct health benefits from participating in this study. This research study is not designed to diagnose, treat, or prevent any disease.

However, your contribution will help researchers better understand how to measure people's experience of migraine. This could lead to better ways of measuring the burden of migraine and the benefits of treatment.

Will I be paid for taking part in this research?

If you complete an interview, you will receive $75 as a thank you for your time. You will receive this payment as an electronic gift card (e.g., MasterCard or Visa) after you complete the interview.

Choosing to not answer some questions or to stop participating part way through the interview will not affect your payment.

What other choices do I have besides taking part in this research?

Your alternative is not to take part in this study.

What happens to the information collected for this research?

When this study is completed, we will write a report based on what we learn from all the study participants. This report will be shared with the FDA, who is the sponsor of this study, and with the public. The results may also be presented at scientific conferences or published in a research journal so that others can learn from this study. None of these reports or presentations will have any of your identifying data or report your results alone. They will report results that are combined among participants. Any quotes that are used will not include information that allows others to identify you.

The data from this study may be shared with other researchers directly involved in the conduct of this study, such as scientists from Albert Einstein College of Medicine. Study data may also be shared with authorities responsible for oversight of the study conduct such as the FDA, state regulatory agencies (if applicable), and Institutional Review Boards (IRBs), for the purposes of auditing this study to ensure data integrity and protection of study participants. We only share the data that does not include information that could identify you and information has been compiled from all study participants. However, not all parties who will have access to your information as part of this study are prohibited by federal law from further sharing it; therefore, the information once received by them, may no longer be protected by federal law.

There is a possibility that identifiers might be removed from the identifiable private information, and after such removal, the information may be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you.

Who can answer my questions about this research?

If you have any questions, concerns, complaints, or think this research has hurt you or made you sick after participating, please call or email the study contact listed at the top of this form. You may also contact the principal investigator.

This research study is being overseen by an IRB. An IRB is a group of people (scientists and non-scientists) who perform an independent review of research studies to ensure that they are ethical, fair, and safe. The goal of the IRB is to protect the rights and welfare of study participants. You may talk to WCG IRB at 855-818-2289 or researchquestions@wcgirb.com if:

- You have questions, concerns, or complaints that are not being answered by the study contact or principal investigator
- You cannot reach the study contact
- You want to talk to someone else about the research
- You have questions about your rights as a study participant

Can I be removed from this research without my approval?

The research team may remove you from this research without your approval. Possible reasons for removal include:

- If you are not able to keep your scheduled interview appointment
- If you decline to have your interview video recorded or transcribed
- If this study is cancelled by the sponsor, the FDA, or the IRB

What happens if I agree to be in this research, but I change my mind later?

You may withdraw your consent to participate at any time during this study. There will be no penalty or loss of benefits to which you are otherwise entitled if you withdraw from this study.

To withdraw consent from this study, please notify the study contact listed at the top of this form that you want to withdraw.

If you withdraw consent before participating in the interview, you will receive no compensation.

If you withdraw consent, no new data about you will be collected and none of your data will be analyzed. All data you provided will be destroyed.

If you do not withdraw consent, but do not complete all parts of the study, any completed data may be used in analysis.

Agree or disagree to participate

Signing below indicates that you have read and understood the information provided, and that you voluntarily **agree** to participate in this research study. You will be provided with a link to a website where you can complete the next steps.

If you **do not agree** to participate in this research study, then do not sign below.

I agree to participate in the MiCOAS interview study.

Print name:_____

Signature: _____

Date signed: _____

APPENDIX D: HEALTH AND DEMOGRAPHIC SURVEY

[placeholder – same as prior study]

APPENDIX E. PARTICIPANT CONTACT INFORMATION FORM

[placeholder – same as prior study]

APPENDIX F: 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.

MiCOAS Recall and Response Interview Guide

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

1. 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.

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

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

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

2. Thank you for sharing that with me!

3. 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.

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

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

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

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

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

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

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

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

i. For example…

1. Your typical experiences?
2. Your best or worst experiences?
3. Variations in what you experience?
4. Something else?

d. 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.

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

   a. IF YES:

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

      ii. 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.

   b. IF NO:

      *i. 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*

6. 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.

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

   i. 14 days?

   ii. 7 days?

   iii. 24 hours (if applicable)

      1. 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>?

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

   i. 14 days?

   ii. 7 days?

   iii. 24 hours (if applicable)

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

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

      i. Would be easiest for you to answer? [FEASIBILITY]

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

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

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

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

The interviewer will show applicable response options on screen.

8. 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.
    a. 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]
        i. Please explain
        ii. What difficulties might you have in choosing an answer from <the other response set>
    b. 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]
        i. Please explain
        ii. What difficulties might you have in choosing an answer from <the other response set>
    c. 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]
        i. Please explain
        ii. What difficulties might you have in choosing an answer from <the other response set> [DIFFICULTIES WITH RESPONSE SET]
9. 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
    a. 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]
        i. Participants can choose more than one; ask for elaboration
    b. Which response options would best? [PREFERRED RESPONSES]
        i. Participants can choose more than one; ask for elaboration

Alternate Questions for Items That Are Not Relevant to the Participant

10. Have you ever experienced this as part of migraine?

a. If NO: Go to next question.

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

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

   ii. *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.*

11. FOR QUESTIONS WITHOUT A "NOT APPLICABLE" OPTION:

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

       i. 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?

    b. How important would it be to you to have a response option like "I never experience this"?

End of Interview Questions

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

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

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

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

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

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

       i. 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 G. PROM INSTRUMENT MATERIALS

[place holder – consists of a slide deck]