Major Depressive Disorder (MDD) is a severe mental health disorder affecting 30% of the adult population, approximately 340 million people worldwide, and is a leading cause of disability, with disproportionate impact on women. Because depression typically occurs subjectively, and the severity of MDD symptoms is directly related to the degree of impairment that patients experience, the assessment of depressive symptoms is an essential endpoint for clinical studies, particularly where the clinical indicators will be limited. By conducting a preliminary experience with MDD through qualitative interviews, it is possible to better understand and document the specific depression-related concepts that are relevant to the patient, as well as understand the patient’s perspective of improvement in his or her condition.3,4 Ultimately, a well-developed instrument that has firmly established content validity (supported by qualitative data) will be expected to demonstrate greater sensitivity in clinical studies of treatment benefit.

Prior to conducting the qualitative interviews, a systematic review was conducted to evaluate existing depression assessment instruments5 as well as previously published qualitative data.6

The systematic review of qualitative data helped to inform the development of the interview guides. The systematic review of existing instruments helped to assist their content validity, measurement properties, and permitted an understanding of the extent to which existing measures were developed with direct input from patients. Systematic review of existing instruments could provide the basis for qualification or modification of the instrument.

OBJECTIVES:

- Complete qualitative elicitation and cognitive interviews with subjects diagnosed with MDD to support preliminary development of a patient-reported outcome (PRO) measure to assess treatment benefit in MDD clinical trials.

METHODS:

Study Population

- Recruitment was designed to enroll a diverse sample of patients similar to those who would be enrolled on the PRO instrument in future clinical trials of MDD treatments.
- No formal recruitment quotas were employed, each site recruited consecutive patients meeting the following criteria and MDD-treatment histories, as well as broad representation across demographic characteristics (e.g., race/ethnicity, age, sex, education level, marital status, and employment status).
- Subjects were recruited from 6 U.S. clinical sites (CT, NJ, OR, WA).

The eligibility criteria for the targeted interview population were designed to reflect common entry criteria for clinical trials in major depression:

- **Inclusion Criteria:** Males and females between the ages of 18 to 65, inclusive, who met DSM-IV-TR criteria for MDD; were being treated on an outpatient basis; were receiving antidepressant and MDD-treatment histories, as well as broad representation across demographic characteristics (e.g., race/ethnicity, age, sex, education level, marital status, and employment status).

- **Exclusion Criteria:** Current or past history of a personality disorder, a history of traumatic brain injury, substance use disorder, or current psychoactive medication treatment (e.g., benzodiazepines, major tranquilizers, antipsychotics, anti-hypertensive, or anti-epileptic drugs). Subjects were excluded if they met DSM-IV-TR criteria for MDD at the time of screening. Subjects were also excluded if they met DSM-IV-TR criteria for MDD at the time of screening. Subjects were also excluded if they met DSM-IV-TR criteria for MDD at the time of screening.

- Study enrollment (Table 1).

- **Demographic Characteristics**
  - Age: 18-65 years old
  - Gender: Male or female
  - Race/Ethnicity: White (Hispanic), Black (Non-Hispanic), Asian, Other (reported)
  - Years since onset of most recent MDE: mean [SD]; [range]
  - Graduation or Professional School: Yes/No
  - Employment Status: Employed/Unemployed
  - Marital Status: Single/Married
  - Children: 0-2
  - Years of Age at First MDD diagnosis: mean [SD]; [range]

- **Clinical Characteristics**
  - MDS Total Score at Screening: mean [SD]; [range]

- **Symptoms**
  - Physical Symptoms
  - Emotions/Mood
  - Sleep Disturbances
  - Cognitive Symptoms
  - Suicidal Ideation

- **Lived Experiences**
  - Sense of Self
  - Social/Role Functioning
  - Impairments of Daily Living
  - Physiological/Treatment
  - Psychological
  - Physical
  - Social
  - Emotional

- **Coping Strategies**
  - Cognitive
  - Emotional
  - Social

- **Coping Mechanisms**
  - Physical
  - Social/Role
  - Psychological

- **Depression Symptoms**
  - Physical
  - Emotional
  - Cognitive

- **Concept Elicitation (CE) Interviews**
  - Semi-structured qualitative interviews were conducted by trained research staff with a representative sample of adult MDD patients in the US who recently experienced a major depressive event.

- Interviews followed a pre-approved interview guide and used an open-ended approach to soliciting spontaneous reports of symptoms’impact/concepts.

- Subsequent interviews were conducted only if spontaneously reported by subjects.

- During the interviews, subjects were asked to rate the severity and level of bother or difficulty for reported symptoms and impacts.

- To guide item development, subjects were asked about the presence/absence, severity, frequency, or duration of specific concepts.

- A Saturation Grid was used to track symptoms and impacts expressed during the interviews and assess saturation of concept.

- Transcripts were summarized in cognitive interview transcripts.

- In parallel with the cognitive interview process, a translatability assessment was conducted.

- A semi-structured interview guide and a report card were used to evaluate the feasibility of the instrument.

- A total of 40 subjects participated in the CE interviews. They were diverse in age, gender, race/ethnicity, and education level.

- A total of 40 subjects participated in the CE interviews. They were diverse in age, gender, race/ethnicity, and education level.

- Exclusion Criteria: Current or past history of a personality disorder, a history of traumatic brain injury, substance use disorder, or current psychoactive medication treatment (e.g., benzodiazepines, major tranquilizers, antipsychotics, anti-hypertensive, or anti-epileptic drugs).

- Transcripts were analyzed in groups of 8 transcripts, and 97.5 to 99.1% agreement between raters was observed.

- Qualitative interviews have provided evidence for content validity.

- Cognitive interviews provided evidence that the instructions, items, and response options are comprehensive, easy to complete and are kept by the participants to complete the interviews in a clinical setting.

- Future qualitative studies will confirm the measurement properties of the SMDDS and support FDA qualification.

CONCLUSIONS:

- The SMDDS is a 35-item PRO measure intended for use as an end-item in MDD clinical trials to support medical product labeling.

- The SMDDS was developed in accordance with the FDA’s PRO Guidance and best practices.

- Qualitative interviews have provided evidence for content validity.

- Cognitive interviews provided evidence that the instructions, items, and response options are comprehensive, easy to complete and are kept by the participants to complete the interviews in a clinical setting.

- Future qualitative studies will confirm the measurement properties of the SMDDS and support FDA qualification.

FINANCIAL DISCLOSURES:

- For this research was provided by the following PRO consortium members: Abbott Inc; Bristol-Meyers Squibb; Eli Lilly and Company; Forest Laboratories; Janssen; Pfizer; Shire, proprietor of schemes and data regarding financial disclosures.

- Critical Path Institute’s PRO Consortium is supported by grant No. U54DD008583 from the United States Food and Drug Administration through an interagency agreement with the National Center for Advancing Translational Sciences, National Institutes of Health, through an interagency agreement with Science Foundation Arizona under Grant No. 5R05-13-08.