ASSESSING THE TRANSLATABILITY OF A NEW PATIENT-REPORTED OUTCOME MEASURE FOR MAJOR DEPRESSIVE DISORDER

Steven I. Blum, Sarah Basse, Kelly P. McCarrier, Stephen Joel Coons, Abhilasha Ramasamy, Nicholas Greco, Lucy Abraham, Mona L. Martin

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Background

- **The Critical Path Institute's (C-Path) PRO Consortium Depression Working Group consists of nine pharmaceutical member companies working together for the purpose of qualifying a patient-reported outcome (PRO) measure intended for use as a primary or key secondary endpoint to assess treatment benefit in major depressive disorder (MDD) clinical trials.**

- **The measure will need to comply with the US Food and Drug Administration's (FDA) PRO Guidance and will be qualified as fit for purpose through the FDA's Drug Development Tools (DDT) qualification process**

Background

- **Prior work of the Depression Working Group has included systematic literature reviews of previous qualitative research and existing depression measures, and qualitative instrument development including concept elicitation interviews, item generation and cognitive interviews.**

- **These steps have led to the development of a new 35-item PRO measure (Symptoms of Major Depressive Disorder Scale – SMDDS), which is intended for use as an endpoint in MDD clinical trials to support medical product labeling.**

- **During the final stages of qualitative development, a translatability assessment was conducted.**

Study Objectives

The primary objectives for conducting a Translatability Assessment (TA) were:

- to determine where difficulties would be encountered in subsequent translation efforts for the new PRO measure.

- to utilize that information toward improvement of the SMDDS items prior to the scale being finalized for quantitative assessment.

Methods

Five different languages were selected to represent four key language families:

- **French and Spanish (Indo-European, Romance Subgroup);**
- **German (Indo-European, Germanic subgroup);**
- **Chinese (Sino-Tibetan, Chinese subgroup);**
- **and Russian (Indo-European, Slavic Subgroup).**

Selection of Key Languages was based upon:

- **Regional representation**
- **Key language family representation**
- **Countries of interest to Working Group members for global clinical trials**

Methods (cont.)

An experienced translation consultant in each language was asked to:

- **review the text of each item, instruction segment, and response option in the preliminary measure**

- **assign a level of difficulty to indicate where problems were likely to be encountered if that text were to be selected for translation into their language**

- **comment on the possible solutions that might be used to render the item into their language and maintain conceptual equivalency**

Methods (cont.)

Translation consultants were also asked:

- **If it was possible to find commonly used language to reflect the concept in the draft text (y/n)**

- **If they felt it was possible to find language that does not have a dual meaning (y/n)**

- **If they could provide an equivalent idiomatic expression for the concept if the original English was idiomatic.**

Methods (cont.)

Difficulty Rating: (1) to (5)		Description
1 =	No difficulty	A more or less direct translation with the same meaning is possible
2 =	Slightly difficult	Some departure from a direct translation would be necessary to maintain concept equivalence.
3 =	Moderately difficult	A significant departure from a direct translation would be necessary to render the item into the target language.
4 =	Very difficult	Difficulty in finding an appropriate way to convey the concept. Even with a conceptual equivalent, there may still be some doubt about the intended meaning
5 =	Extremely difficult	represented a concept that would be extremely difficult or impossible to convey appropriately in the target language

Methods (cont.)

Difficulty Ratings were used in two ways:

(1) Individual items that had higher difficulty ratings across multiple languages were highlighted to review items and consider revisions

Items and Response Scales	French	German	Russian	Spanish	Chinese	Average Rating per Item
Title	1	1	3	1	1	1.4
Instruction	1	1	1	1	1	1
Item 1	2	2	1	1	1	1.4
Response Scale-items 1-17	1	2	3	1	3	2
Item 2	1	1	3	1	1	1.4
Item 3	1	2	2	3	1	1.8
Item 4	1	1	2	1	1	1.2
Item 5	1	3	1	1	1	1.4
Item 6	1	1	1	1	1	1
Item 7	1	1	1	1	1	1

Methods (cont.)

Item	Difficulty Ratings:	Can a translation in common language be found?	
Over the past 7 days, how much have you felt **useful**?	French: German: Russian: 3 Spanish: 1 Chinese: 1	French: Yes German: Yes Russian: Yes Spanish: Yes Chinese: Yes	**French:** "How much" would need to be translated as "how often" or "how much of the time" in order to better correspond to the response scale. **German:** "How much" would need to be translated as "how often" or "how much of the time" in order to better respond to the response scale. **Russian:** The word "useful" sounds too general for a Russian speaker "Useful" for what? For the society? For your family? I think this is the main difficulty for translation into Russian. **Spanish: No comments** **Chinese: No comments**

Difficulty Ratings were used in two ways:

(2) Item ratings were averaged for each language and the overall difficulty rating of the language was evaluated

	French	German	Russian	Spanish	Chinese
Average Rating per Language	1.51	1.61	1.46	1.46	1.12

Results: Overall Difficulty

For the Average Difficulty Ratings per language:

- **The highest average difficulty was found in German (1.61) and French (1.51), due largely to language structure rules and usage norms that prohibited direct translations.**
- **The lowest difficulty was found in Chinese (1.12)**
- **The middle difficulty scores were for Russian (1.46) and Spanish (1.46).**

Items contributing to high difficulty scores were those using more idiomatic language (e.g., *"keep your mind free of worrying thoughts"*).

Results: Heading/Title/Instructions

Heading/Title

- **It was recommended that the abbreviation of the scale (SMDDS) be included in the title in (English/Latin script) to ensure recognition of the measure.**

Instructions

- **No translation issues were identified for the instrument instructions.**

Results: Response Scales

Response Scales

- **Some issues with lack of unique wording (e.g. "Extremely" and "Very much" would be translated to the same term in German).**

- **Response Scales for some items had structural issues (e.g. Both Russian and Chinese would need to include the verb from the question in the response scale).**

Results: Item Stems

Item Stems

- **Translation difficulty scores identified potential issues in three items in the preliminary version of the SMDDS.**

- **When combined with the results of the cognitive interviewing process, revision of these items was recommended.**

Results: Revised Items

ORIGINAL ITEM:

Overall, in the past 7 days, how difficult was it for you to **keep your mind free of worrying thoughts**?

TRANSLATION ISSUE:

- French, German and Spanish would need to say "worries", since "worrying thoughts" has no direct translation into those languages. This ends up conveying a focus remarkably close to the "worry" item (Item 11).
- "Keep your mind free" is somewhat idiomatic to English, and problems would be found in Russian and German to translate it directly.

REVISED ITEM:

Overall, in the past 7 days, how difficult was it for you to **stop thinking about your problems**?

Results: Revised Items

ORIGINAL ITEM:

Over the past 7 days, how much have you **looked forward to things with enjoyment**?

TRANSLATION ISSUE
- This item received the highest average difficulty rating of all items (2. 4).
- "How much" is avoided in French and German to translate this item because it measures a non-countable construct (feeling like crying).
- Idiomatic phrases reflecting the same concept as "to look forward to" are found in all languages except Spanish (which would use a phrase like "awaited events with enthusiasm"). The suggested saying in French already refers to enjoyment, so "with enjoyment" would be redundant and therefore left out in French in order to match the English concept.

REVISED ITEM

Over the past 7 days, how much of the time have you **felt enjoyment**?

Results: Revised Items

ORIGINAL ITEM:

Over the past 7 days, how much have you felt **useful**?

TRANSLATION ISSUE

- This item received one of the highest difficulty ratings of all items (1.8).
- "How much" is avoided in French and German to translate this item because it measures a non-countable construct (feeling like crying).

REVISED ITEM

Over the past 7 days, how much of the time have you felt **useful**?

Conclusions

- **Translatability assessment was used to help identify and revise those items in the SMDDS, that might have presented challenges pertaining to translation and cross-cultural adaptation.**

- **Translatability assessment is a useful process to include in instrument development and should be conducted prior to the finalization of the measure when refinement in wording and changes to item structure are still feasible.**