REEVALUATING "DEPRESSED": UNRAVELLING THE LINGUISTIC AND CULTURAL COMPLEXITY IN CLINICAL OUTCOME ASSESSMENTS

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INTRODUCTION:

The objective of this study was to explore the term "depressed" within clinical outcome assessments (COAs) and to evaluate its interpretation across different linguistic and cultural contexts. Misinterpretations of such terminology can introduce biases, potentially compromising the validity of COAs.

To address this, we investigated the use of the term "depressed" across 18 languages and 40 countries. "Depressed" is often used to describe a patient's mental state, and can potentially point to persistent, extreme sadness, loss of interest, or other related symptoms, but its meaning can vary significantly based on cultural and linguistic nuances, as well as a COAs target constructs and condition.

Notably, in the PRO-CTCAE, "depressed" is listed as an unacceptable alternative to "sad" due to its stronger and more medically complicated connotations. This highlights the importance of accurately distinguishing between these terms in COAs.

Previous research has indicated that "depressed" may be a challenging term for patients to interpret consistently across languages; however, a comprehensive analysis focusing on this specific term in a diverse global context has not been conducted.

Here, we present findings from a qualitative analysis of patient responses, highlighting the diverse interpretations of "depressed" and proposing strategies for improving the linguistic validation of COAs to better capture patient experiences across cultures.

METHODS:

We performed a qualitative analysis of patient responses to the term "depressed" within clinical outcome assessments (COAs) across 18 languages and 40 countries. 200 adult (18 years or older) patients were surveyed using three open-ended probe questions during the course of cognitive debriefing of patient-reported outcome measures. The probe questions appear in Table 1:

Table 1: Probe questions and their corresponding respondent numbers

	Probe Question	N
1.	What does the word "depressed" mean to you?	138
2.	Do you think being "depressed" is equivalent to being sad?	143
3.	Do you think feeling "depressed" is equivalent to having "depression"?	135

These questions were included in data collection forms (DCFs) prepared by RWS Life Sciences and distributed to patients for completion. Cognitive debriefing interviews were conducted to gather spontaneous patient feedback on their interpretation of "depressed."

Qualitative analysis was performed on responses from 138 patients for the first question, 143 patients for the second, and 135 patients for the third. This analysis aimed to identify common themes and patterns in how "depressed" is understood across different languages and cultural contexts, with a focus on variations in meaning that could affect the validity of COAs.

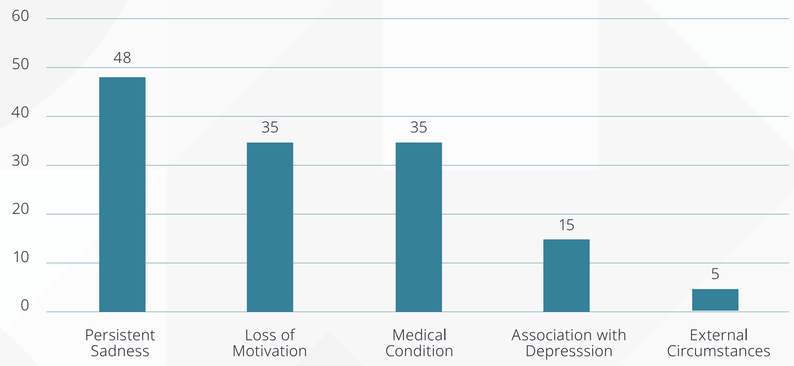
RESULTS:

Figure 1 and Table 2 summarize the thematic analysis of patient feedback (N=138) to Probe #1: "What does the word "depressed" mean to you?". Key themes included persistent sadness (N = 48), loss of motivation (N = 35), association with "depression" (N=15; which indexes conceptual overlap or ambiguity), and the view of "depressed" as a medical condition (N = 35). Additionally, a minority of respondents (N = 5) interpreted "depressed" in terms of material dissatisfaction or external circumstances, diverging from typical clinical or emotional definitions.

Table 2: Selected spontaneous feedback from participants, illustrating the thematic categories of persistent sadness, loss of interest, and medicalisation of the term "depressed."

Theme	Feedback
Persistent Sadness (n=48)	• Being depressed is like a disease, it is a permanent state of discouragement and sadness. (French-Belgium) • Depressed means feeling extremely and uncontrollably sad. (Spanish-Mexico) • Being depressed is being diagnosed and it's more intense and long-term and heavier than just being sad. (English-Australia)
Medical Condition (n=35)	• Depression is a mental state that prevents you from doing your usual activities. (Portuguese-Brazil) • Depression is a medical condition that you need a treatment and therapy to recover.(Spanish-Peru) • Depression is a disease in which one feels extremely and uncontrollably sad to a point in which there is lack of energy or motivation for most things. (Spanish-Mexico)
Association / Conceptual Overlap with "Depression" (n=15)	• Depression is a serious condition, when you're depressed you have constant sadness and low energy. (English-Australia) • Being depressed is the effect of having depression. Depression is normally an illness that makes a person lose interest in doing things, being sad and negative for long periods. (Spanish-USA) • Suffering from depression or simply sad, miserable. (Italian-Switzerland)
Loss of Motivation (n=35)	• It means not wanting to do anything, feeling super sad. (French-Canada) • Depressed is a person who is unmotivated, sad, but more than sad, it is a sadness so deep that he or she has no desire to do anything. (Spanish-Chile) • The word "depressed" points to the condition when your mental health is poor. It refers to the condition when you don't have a will to do things, and when your frame of mind is negative (Japanese-Japan)
External Circumstances (n=5)	• It's associated with not having this or that thing, the mobile, the trip overseas, the money. (Spanish-Colombia) • Depressed is being powerless to solve something that the person knows he/she can solve. (Spanish-Chile) • Depression is linked to the idea of family, social, and partnership contexts. (Spanish-Colombia)

Figure 1: This illustrates the distribution of thematic interpretations among patients regarding the term "depressed," highlighting the prevalence of associations with sadness, clinical depression, and other related concepts. The chart underscores the variability in understanding and the need for precise terminology in patient-reported outcomes.



Of the 143 patients who responded to Probe #2 ("Do you think being "depressed" is equivalent to being sad?"), 29 (20%) indicated equivalence. Figure 2 shows the distribution of responses to Probe #2 by language and country; furthermore, responses from 13/30 (43%) language-country pairs indicated some level of equivalence in interpretation. Figure 3 shows the distribution of patient feedback regarding the conceptual difference between "depressed" and "sad", where the primary categories are intensity, duration, the clinical nature of the condition (i.e., the need for a diagnosis), and the presence of other physical or emotional features.

Specifically, feedback generally indicated that being depressed is a more intense or severe condition, that it lasts longer than 'sadness', that it usually is accompanied by mental health care or an official diagnosis, and that it tends to be marked by additional physical (e.g., lethargy) or emotional (e.g., hopelessness; apathy) effects.

Figure 2: Distribution of responses to Probe #2 by language and country

Probe #2: Do you think being "depressed" is equivalent to being sad?

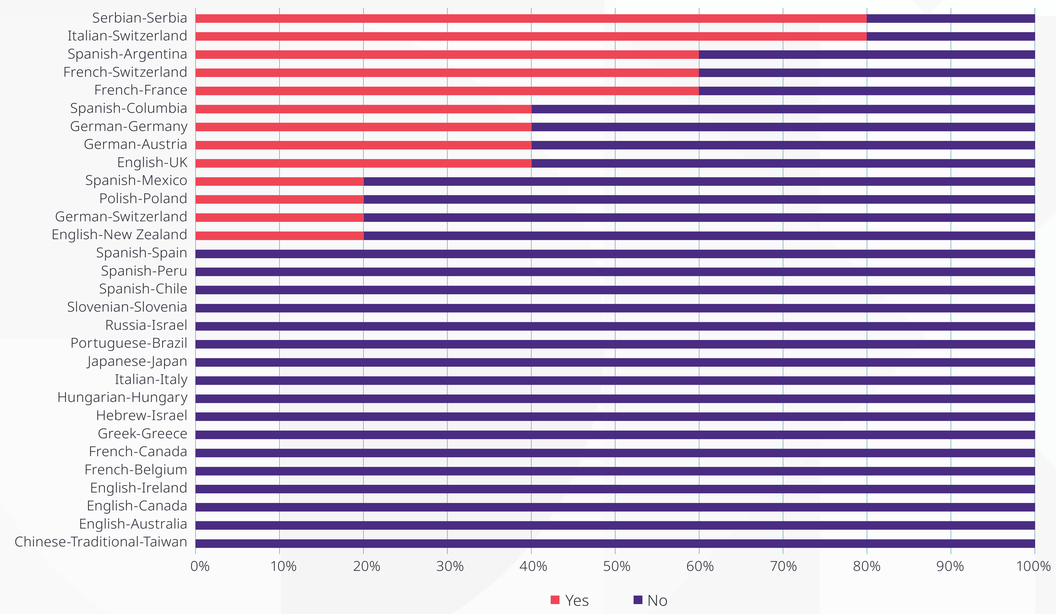
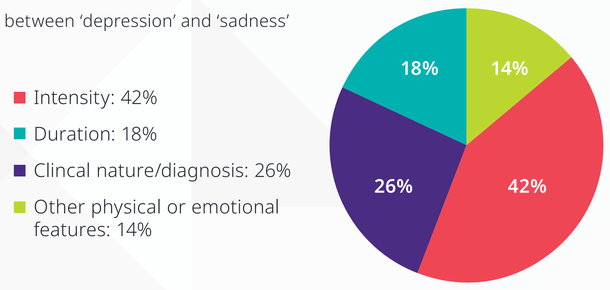


Figure 3: Thematic analysis of feedback to Probe #2

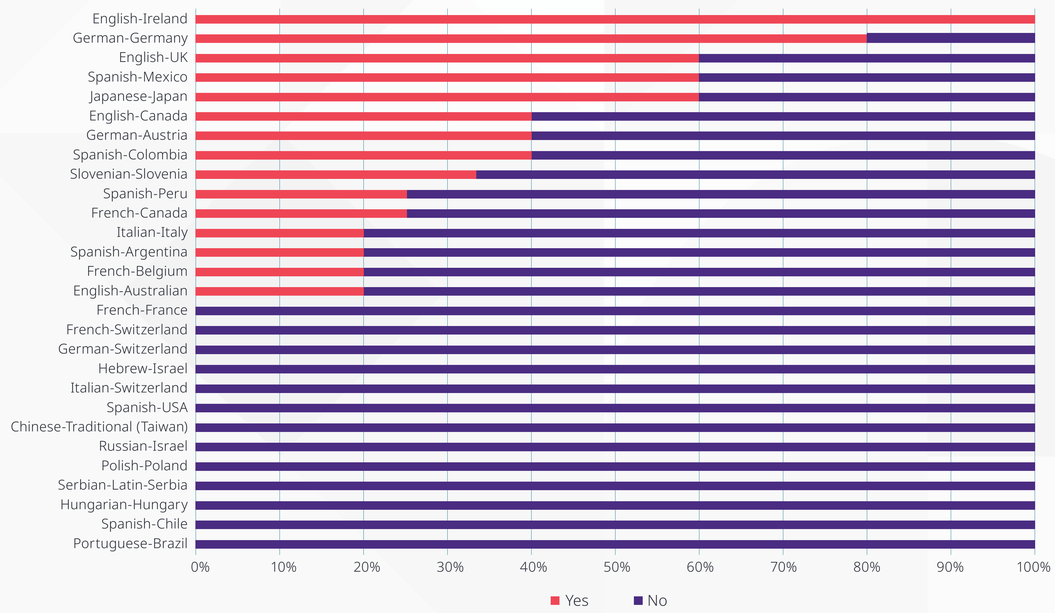
Patient feedback regarding the conceptual difference between 'depression' and 'sadness'



Of the 135 patients who responded to Probe #3 ("Do you think feeling 'depressed' is equivalent to having 'depression'?"), 31 (23%) indicated equivalence. This misunderstanding was most common among English-speaking respondents, with 53% (10/19) associating "depressed" with clinical depression. Figure 4 shows the distribution of responses to Probe #3 by language and country; responses from 14/28 (50%) language-country pairs analysed for this probe indicated some level of equivalence of interpretation.

Figure 4: Distribution of responses to Probe #3 by language and country.

Probe #3 Responses by Language and Country: Do you think feeling "depressed" is equivalent to having "depression"?



DISCUSSION

These results highlight significant variability in the interpretation of the term "depressed" across different cultural and linguistic contexts. Significant percentages of respondents equate "depressed" with "depression" or "sadness", which introduces potential biases and inaccuracies into clinical outcome assessments (COAs). This confusion is particularly notable in English-speaking regions, where "depressed" is frequently misunderstood as a clinical state rather than a persistent emotional condition, but is present in at least 50% of the language country pairs sampled here. Such misinterpretations can skew patient-reported outcomes and exacerbate regional health inequalities, affecting the reliability of symptom reporting and overall assessment validity.

CONCLUSIONS

To address these issues, COA developers should focus on concept elaboration by providing clear definitions and contextual examples of "depressed" as a persistent state of sadness rather than a temporary emotion. Incorporating cognitive debriefing feedback from diverse patient populations during instrument development can further refine understanding and ensure consistent interpretation, and importantly detect and allow for resolution of differential item functioning ahead of global administration. We further recommend continuous collection and evaluation of feedback on patient comprehension of COAs while they are in use, so that any issues or omissions (e.g., unintended differences in the interpretation of "depressed" across diverse patient groups) can be addressed in a timely fashion to preserve data integrity. By prioritising standardization and clarity of source wording, and considering linguistic and cultural factors affecting usage and comprehension for globally deployed COAs, developers can improve data accuracy and contribute to more equitable health outcomes across varied linguistic and cultural backgrounds.