

Cultural adaptation: translatability assessment and linguistic validation of the patient-reported outcome instrument for irritable bowel syndrome with diarrhea

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Background and objective: Following a 2009 US Food and Drug Administration guidance, a new patient-reported outcome (PRO) instrument was developed to support end points in multinational clinical trials assessing irritable bowel syndrome with diarrhea (IBS-D) symptom severity. Our objective was to assess the translatability of the IBS-D PRO instrument into ten languages, and subsequently perform a cultural adaptation/linguistic validation of the questionnaire into Japanese and US Spanish.

Materials and methods: Translatability assessments of the US English version of the IBS-D PRO were performed by experienced PRO translators who were native speakers of each target language and currently residing in target-language countries. Languages were Chinese (People's Republic of China), Dutch (the Netherlands), French (Belgium), German (Germany), Japanese (Japan), Polish (Poland), Portuguese (Brazil), Russian (Russia), Spanish (Mexico), and Spanish (US). The project team assessed the instrument to identify potential linguistic and/or cultural adaptation issues. After the issues identified were resolved, the instrument was translated into Spanish (US) and Japanese through a process of two forward translations, one reconciled translation, and one backward translation. The project team reviewed the translated versions before the instruments were evaluated by cognitive debriefing interviews with samples of five Spanish (US) and five Japanese IBS-D patients.

Results: Linguistic and cultural adaptation concerns identified during the translatability assessment required minor revisions, mainly the presentation of dates/times and word structure. During the cognitive debriefing interviews, two of five Spanish respondents misunderstood the term "bowel movement" to mean only diarrhea in the Spanish version. Consequently, the term was changed from "movimiento intestinal" to "evacuaciones". None of the Japanese respondents identified issues with the Japanese version.

Conclusion: The translatability of the IBS-D PRO instrument into ten target languages was confirmed, with only minor changes made to the translations of the instrument. The translation and linguistic validation into Spanish (US) and Japanese provide evidence that this instrument can be used in multinational trials and clinical settings.

Keywords: stool consistency, stool-form scale, translatability, IBS-D PRO instrument

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Introduction

Irritable bowel syndrome (IBS) is typically diagnosed using symptom-based diagnostic criteria, such as the Rome III criteria for IBS.^{1,2} Upon diagnosis, IBS is often subtyped into one of four categories, based on the predominant stool pattern: IBS with diarrhea

(IBS-D), IBS with constipation, IBS with mixed stool pattern, or unspecified IBS (insufficient stool consistency to be classified according to one of the other three subtypes).² Data suggest that ~75% of individuals change subtypes within a 1-year period.³

Following a 2009 US Food and Drug Administration guidance, a new patient-reported outcome (PRO) instrument was developed to support end points in multinational clinical trials assessing IBS-D symptom severity. For a new instrument to be used in global trials and clinical settings, it needs to be culturally adapted to the target patient population. Cultural adaptation – including translation and linguistic validation – is important, because it considers the target language and culture, medical culture, and conceptual equivalence of an instrument's wording, rather than simply the literally translated text.⁴ Prior to the actual translation of an instrument, a translatability assessment is often performed to help determine potential areas that require further clarification and issues that may occur during the translation process.⁵ During a formal translation process, various steps are taken to ensure cultural and linguistic equivalence between the source and target languages, including 1) defining the concepts of the instrument, 2) two forward and one backward translations, 3) cognitive debriefing to confirm acceptability and conceptual equivalence in the target language, and 4) documentation of the translation and validation process.⁴

The aim of this manuscript was to assess the translatability of the IBS-D PRO instrument into ten languages, and subsequently perform a cultural adaptation/linguistic validation of the questionnaire into US Spanish (a generic Spanish dialect spoken by the native speakers living in the US)⁶ and Japanese.

Objectives

The overall goal of this research was to translate the IBS-D PRO to be used in international clinical trials and clinical settings. To achieve this goal, two stages of work were identified: 1) translatability assessment and 2) linguistic validation.

The objective of the translatability assessment (stage 1) was to determine whether there would be any issues to attaining conceptually, culturally, and linguistically equivalent translations of the IBS-D PRO instrument text across ten different languages. The assessment specifically identified potential linguistic, sociolinguistic, or cultural issues that could emerge during the translation of words, phrases, idioms, and metaphors that are culturally anchored in the source language (ie, US English) and syntax (word order).

The objective of the formal and more comprehensive and rigorous translation and linguistic validation (stage 2) was to translate the instrument and confirm its conceptual

equivalence across cultures. Confirmation of equivalence was achieved by testing the translated text with patients within the target patient population and languages (Spanish [US] and Japanese [Japan]) through cognitive debriefing interviews.

Materials and methods

Design of the translatability assessment (stage 1)

The US English version of the PRO instrument (the IBS-D symptom diary and event log) was reviewed by experienced translatability evaluators who were residents of the ten countries and native speakers of the respective languages: Chinese (People's Republic of China), Dutch (the Netherlands), French (Belgium), German (Germany), Japanese (Japan), Polish (Poland), Portuguese (Brazil), Russian (Russia), Spanish (Mexico), and Spanish (US). This process was overseen by a translatability specialist with 13 years' experience in translatability assessment and linguistic validation, with a clinical psychology and psychometric background and cognitive debriefing training, as well as familiarity with International Society for Pharmacoeconomics and Outcomes Research (ISPOR) best practices, followed throughout the project.⁷

Each evaluator examined the source text and flagged any potential translatability issues by completing a translatability checklist. During the assessment, if a word or item would potentially present translation issues (eg, because of ambiguity), the evaluator (or the linguistic validation specialist) then defined in more detail or elaborated on the concept intended, so that the linguist knew which equivalent word to use in his/her translation. This study was performed in accordance with the ethical principles of the Declaration of Helsinki and are consistent with Good Clinical Practice and applicable regulatory requirements. Ethical approval for this study was not sought. All patients provided written informed consent prior to the start of the study.

Translatability assessment (stage 1)

The questionnaire focused on seven different aspects of translatability (ie, there were seven levels of analysis for each language), including concept elaboration, appropriateness of audience design, structure and design of an item, grammatical structure of an item, identification of idiomatic expressions, metaphors, and colloquialisms, evaluation of response choices, and any additional comments.

The questionnaire required each evaluator to flag any words or phrases that required additional concept information. If there were issues with an item, the evaluator was then required to provide further information to clarify the text. The appropriateness of the "audience design", which

is a sociolinguistic concept whereby certain text would be useful only if it were written (“designed”) appropriately for a specific target audience,⁸ was evaluated next. The evaluator provided information as to whether the text of an item was written appropriately for the target population.

The evaluator assessed the structure and design of each item and determined whether there were any missing response categories multiconcept (double-barreled) questions, double negatives, inconsistent use of words, etc, and whether there were any problems with syntax (ie, word order and/or sentence structure). The evaluator also reviewed the PRO instrument for any phrases anchored in the source language/culture that may be difficult to express in the target language. If issues were identified, the evaluator was to suggest strategies/text that would improve the translation to the target language.

The response choices in the questionnaire were also evaluated to identify any potential difficulties with translation, and the evaluator was to suggest strategies/text to resolve translation problems. The evaluator also provided details of any other issues that were not covered by the assessment strategy described earlier. After all of the linguistic and cultural issues that were identified during the translatability assessments were resolved by appropriate revisions to the text, the translation and linguistic validation/cultural adaptation stage was initiated.

Design of the translation and linguistic validation process (stage 2)

The translation and linguistic validation processes followed the recommendations of the ISPOR Patient-Reported Outcomes Translation and Linguistic Validation Good Research Practices Task Force.⁷

Following completion of the translatability assessments (ie, stage 1), the instrument was subjected to translation and linguistic validation into Spanish (US) and Japanese. For each language, three native-speaking translators (two forward translators, one backward translator) participated in the process. All of the translators had experience in several areas of the life sciences and worked independently on their respective steps of the translation and validation process. The translation and validation process consisted of two forward translations, one reconciled translation, and one backward translation. Upon completion of the process, clinical experts and project-team members reviewed the translations for accuracy and cultural appropriateness. The instruments were then evaluated by cognitive debriefing interviews with samples of five Spanish (US) and five Japanese IBS-D patients. The respondents for the cognitive interviews were native-speaking Spanish individuals living in the US, or native-speaking Japanese individuals living in Japan, mainly because these

Table 1 Translation and linguistic validation process

Source COA	Final linguistically validated COA instrument
1	Preflight TransPerfect reviews the source instrument and defines all concepts in a concept-definition document.
2	Dual forward translation Two native-speaking linguists of the target language independently perform forward translations, aiming for conceptual equivalence to the source and cultural appropriateness for the target country.
3	Reconciliation A third independent, native-speaking linguist compares the two forward translations, identifying any discrepancies or cultural differences to create a unified translation.
4	Backward translation A native-speaking (of English) linguist with fluency in the target language translates the reconciled document back into the source language using only the forward translation as source material.
5	Resolution of backward and forward translations A team consisting of native-speaking linguists (both of English and the target language), a quality manager, and a project manager resolve any discrepancies between the forward translation, backward translation, and source.
6	Clinician/medical review A clinician who practices in the relevant therapeutic area and is a native speaker of the target language provides feedback on the accuracy of all medical terminology.
7	Client in-country review/developer review The reconciled forward and backward translations are provided to the client or the developer for review. Comments are then assessed by TransPerfect’s linguistic team until all issues are resolved.
8	Cognitive interviewing Qualitative interviews are conducted with five to ten prescreened respondents who are representative of the study’s target population.
9	Final proofreading and delivery The finalized language is proofread by a native-speaking linguist of the target language. Once finalized, the files are delivered to the client.
10	Comprehensive final report TransPerfect authors a final report detailing all linguistic decisions made throughout the process, including cognitive interviewing results.

Abbreviation: COA, Clinical Outcomes Assessment.

were the most relevant languages to the sponsor's clinical trials performed in Japan and the US.

Steps in the translation and linguistic validation process (stage 2)

The translation and linguistic validation process is shown in Table 1. During the forward translation, the two translators for each language independently translated the IBS-D instrument into the respective target languages. The translators were provided with the original instrument and definitions of concepts, and were asked to focus on ensuring cultural relevance and conceptual equivalence of the item content, not just of literal translation. A third translator, who was also provided with the original instrument and definitions of concepts, examined the translated document item by item and selected the best word, phrase, or sentence between the two translations or provided an alternative option. This reconciliation (or harmonization) process addressed any discrepancies between the source language and the translations, any linguistic limitations, and any cultural differences in conveying the exact source meaning.

The translated documents were subsequently backward translated by a fourth translator in order to ensure the forward translation was successful and conceptually equivalent to the source. The backward translator was only provided with the reconciled forward translation, and had no access to the original instrument or the concepts. Following the backward translation, a fifth translator of the target language and subsequently a project manager reviewed the translated version for any discrepancies between the backward translation and the source. Any discrepancies were addressed to ensure conceptual equivalence.

A medical reviewer who was a native speaker of the target language was then consulted to review the translated version, to ensure that appropriate medical terminology was maintained. A project team review followed to ensure further the accuracy and appropriateness of the translated version. Any necessary changes were made to the forward and backward translations.

Five face-to-face cognitive debriefing interviews, each with one interviewer and one respondent, were performed for each of the translated, culturally adapted versions of the PRO instrument in the target language (ie, patients' native language) in order to confirm their content validity (ie, the extent to which the instrument [in this case, the IBS-D PRO] measured the concept of interest).⁵ The interviewers were trained by TransPerfect and were provided with appropriate guidelines prior to the interview. The respondents were recruited via physician referrals and patient-association

groups and meetings. They had been diagnosed with IBS, but IBS-D was not specifically confirmed. During the cognitive debriefing interviews, the respondents were asked to review and provide feedback on their understanding of the items and relevance of the concepts. Their responses were subsequently evaluated and categorized as stylistic (ie, preferential), objective (ie, a correction of a grammar/spelling mistake), or related to comprehension/cultural appropriateness.

Results

Translatability assessment: overall and country-by-country findings (stage 1)

The overall findings and recommended wording for improvements to the text are shown in Table 2. Among these findings, cultural issues, such as the presentation of dates and times, were identified by evaluators of nine of the ten languages included in the translatability assessment. Of the nine evaluators, all nine suggested that the time should be written as a 24-hour entry, since some countries do not use "am" or "pm", and that the date should be written in the standard format for each country. The idea of "abdominal pain" and "stomach pain" being separate symptoms/sensations was identified as requiring further clarification during the evaluators' concept elaboration, to allow for appropriate differentiation and adaptation into each language. The evaluators for the Chinese, Dutch, Portuguese, and Spanish (Mexico) assessments also noted issues with word structure and concept elaboration for the text "irritable bowel syndrome – diarrhea predominant (IBS-D) symptom-event log": half of these evaluators suggested that a hyphen should be added to the acronym between "diarrhea" and "predominant" for clarity; subsequently, one was added. Lastly, the evaluators of the Chinese, German, Polish, and Spanish (Mexico) languages also identified issues with the word "immediate", and suggested changing this to "urgent", as it is more appropriate in the context of IBS-D (eg, "How urgent was your need?").

The country-by-country findings are available in [Table S1](#). The evaluator for the translation into Spanish (US) did not identify any potential translatability issues. With regard to the images and descriptors, all of the evaluators perceived little or no room for misinterpretation or ambiguity. The linguistic and cultural issues highlighted earlier and in the tables were addressed by appropriate revisions to the text prior to initiation of the translation and linguistic validation of the Spanish (US) and Japanese (Japan) versions.

Table 2 Translatability assessment: summary of overall findings and recommendations

Source (English)	Comments	Suggested final English
Culture issues		
Four-item IBS-D Symptom-Event Log with stool descriptors and images of the Astellas Stool Form Scale	Several countries noted that the subject of the questionnaire can be embarrassing, but as this is to be used in a clinical setting, is appropriate.	
Irritable Bowel Syndrome – Diarrhea Predominant (IBS-D) Symptom-Event Log	To avoid confusion as to the location of the acronym, a hyphen should be added between “diarrhea” and “predominant” to ensure accurate understanding of the item.	Irritable Bowel Syndrome – Diarrhea-Predominant (IBS-D) Symptom-Event Log
Date (MM/DD/YYYY)	Allow dates to be entered in the standard format of the target country (eg, DD/MM/YYYY or YYYY/MM/DD).	
am or pm	Allow for time to be entered as a 24-hour entry if possible, as several cultures do not use “am” or “pm”.	
Concept elaboration		
How immediate was your need	Suggestion to either change “immediate” to “urgent” or ensure that this is explained in concept elaboration as an appropriate synonym. Also, a question mark should be added for accuracy.	How immediate (or urgent) was your need?
Which best describes what your bowel movement looked like	Add question mark for accuracy	Which best describes what your bowel movement looked like?
Irritable bowel syndrome - diarrhea predominant (IBS-D) daily symptom diary	To avoid confusion as to the location of the acronym, a hyphen should be added between “Diarrhea” and “Predominant” to ensure accurate understanding of the item.	Irritable bowel syndrome - diarrhea-predominant (IBS-D) daily symptom diary
The purpose of this diary is to collect some information about the symptoms of irritable bowel syndrome – diarrhea predominant (IBS-D) that you have experienced.	To avoid confusion as to the location of the acronym, a hyphen should be added between “diarrhea” and “predominant” to ensure accurate understanding of the item.	The purpose of this diary is to collect some information about the symptoms of irritable bowel syndrome – diarrhea-predominant (IBS-D) that you have experienced.
In the past 24 hours, on a scale of 0–10, how would you rate the severity of your stomach pain?	While not specifically noted in each country’s review, the idea of “abdominal pain” and “stomach pain” as separate sensations will need to be further explained during concept elaboration to allow for appropriate differentiation and adaptation into each language.	

Translation and linguistic validation: reconciliation of forward and backward translations and cognitive debriefing (stage 2)

There were a number of areas during the translation process that were identified in the Spanish (US) and Japanese versions of the instrument that required further revision. A summary of the key findings from the forward and backward translations is shown in Table 3.

Following the forward and backward translations, the cognitive debriefing interviews were conducted with five respondents for each language; their demographics are shown in Table 4. The sample covered a range of age and educational levels, as well as being as close as possible to a 50:50 sex representation. The five cognitive debriefing interviews conducted for the Spanish

(US) version identified additional areas requiring revision for clarity; a summary of the key areas is shown in Table 5.

Mainly, in the Spanish (US) version, although “bowel movement” had been translated literally during the forward and backward translations, two of five respondents misunderstood the term to include only diarrhea. As a result, the wording was changed throughout the instrument from “movimiento intestinal” to “evacuaciones”, which was better understood as having the meaning of “bowel movement”. All necessary revisions to the translated Spanish version were related to comprehension/cultural appropriateness. No areas requiring additional revision were identified for the Japanese version.

Discussion

Until recently, no validated PRO instrument existed to measure IBS-D symptoms in clinical trials that examine

Table 3 Key findings from the forward and backward translations

Spanish (US)					
Source	Reconciled forward translation	Backward translation	Reasoning for reconciliation	Updated forward translation	Updated backward translation
Soft chunks or clumps	Trozos o grupos compactos blandos	Soft compact pieces or groups	The forward translation and backward translation were revised to remove “compact”.	Trozos o grupos blandos	Soft chunks or groups
A little of the time	Pocas veces	A few times	The forward translation and backward translation were revised to reflect the source more accurately.	Durante muy poco tiempo	During little of the time
Some of the time	Algunas veces	Sometimes	The forward translation and backward translation were revised to reflect source more accurately.	Parte del tiempo	Some of the time
Japanese					
Source	Reconciled forward translation	Backward translation	Reasoning for reconciliation	Updated forward translation	Updated backward translation
Like marbles or hard rocks	ビー玉や小石のような形の便	Stool shaped like marbles or pebbles	The forward translation and backward translation were revised to match source more closely.	ビー玉や硬い小石のような便	Stool like marbles or hard pebbles
A single, solid, clumpy stool	1本の硬い塊状の便	One hard lump of stool	The forward translation and backward translation were revised to reflect “solid” for consistency.	1本の塊状の固形便	One solid lump of stool
Loose, mushy stool	柔らかくドロドロした軟便	Soft and mushy loose stool	The forward translation and backward translation were revised to remove “soft and” per source.	ドロドロした軟便	Mushy loose stool
No abdominal pressure	圧迫感なし	No pressure	The forward translation and backward translation were revised to add “abdominal”.	腹部圧迫感なし	No abdominal pressure

Table 4 Demographics of the cognitive debriefing-interview respondents

Spanish (US)					
Respondent	R1	R2	R3	R4	R5
Age (years)	83	47	57	39	55
Sex	Female	Female	Male	Female	Male
Diagnosis	IBS	IBS	IBS	IBS	IBS
Educational level (number of years)	15	13	14	6	9
Japanese					
Respondent	R1	R2	R3	R4	R5
Age (years)	28	20	32	35	42
Sex	Male	Male	Male	Female	Female
Diagnosis	IBS	IBS	IBS	IBS	IBS
Educational level (number of years)	16	14	16	14	16

Abbreviation: IBS, irritable bowel syndrome.

the efficacy of various IBS-D treatments. An IBS-D PRO instrument, the Astellas Stool Form Scale, was developed to assess clinical symptoms and stool form and consistency in clinical trials.⁹ This scale captures the continuum of stool consistency experienced by patients with IBS-D.¹⁰ In order for this instrument to be used in multinational trials and settings, it underwent translatability assessments for various target

languages prior to its translation and linguistic validation into Spanish (US) and Japanese.

A number of cultural issues were identified during the translatability assessments by evaluators of nine of the ten languages. These included the presentation of dates and times, word structure and concept elaboration for the text “irritable bowel syndrome – diarrhea predominant (IBS-D) symptom-event log”, difficulties understanding the word “immediate” to describe urgency, and the difference between sensations of “abdominal pain” and “stomach pain.” These issues, however, varied by country. The translatability assessment for each country led to some important changes in the IBS-D PRO instrument. Translatability assessments included European, South American, and Asian languages, which allowed for the identification of potential issues across a broad spectrum of additional languages.

Following the translatability assessments, the IBS-D PRO instrument underwent a rigorous translation and linguistic validation (cultural adaptation) process with a representative sample of the target patient population. Feedback from these reviews and cognitive debriefing interviews confirmed the validated translation of the instrument into Spanish (US) and Japanese. The respondents of both the languages easily

Table 5 Summary of the cognitive debriefing-interview analysis

Spanish (US)	Forward translation	Cognitive debriefing-response analysis	Linguistic feedback	Final forward translation	Final backward translation
The purpose of this event log is to collect some information about your bowel movements.	El propósito de este registro de eventos es recopilar información sobre sus movimientos intestinales.	R3 seemed to understand that he had to report every diarrhea event. When told that he had to report every bowel movement and asked what a bowel movement was, he said he did not know and that he thought it was diarrhea, but after being told that it meant "evacuation", he was able to paraphrase the item correctly. R4 said she did not understand what a bowel movement was, but when told it meant "evacuation," she paraphrased the item correctly.	Although the translation "movimiento intestinal" is the correct and appropriate translation of "bowel movement", this was changed to "evacuaciones", as two of five respondents misunderstood the term to mean only "diarrhea". This is an appropriate term that the respondents confirmed as understanding to have the meaning of "bowel movement" as well. The forward and backward translations were revised.	El propósito de este registro de eventos es recopilar información sobre sus evacuaciones.	The purpose of this event log is to compile information about your evacuations.
After every bowel movement, please fill out the date and time, and answer all of the following questions on that row.	Después de cada movimiento intestinal, complete la fecha y la hora y responda a todas las preguntas que aparecen a continuación en esa fila.	R1, R2, R4, and R5 reported no difficulty. R3 seemed to understand that he had to report every diarrhea event. When told that he had to report every bowel movement and asked what a bowel movement was, he said he did not know and that he thought it was diarrhea, but after being told that it meant "evacuation", he was able to paraphrase the item correctly. R4 said she did not understand what a bowel movement was, but when told it meant "evacuation", she paraphrased the item correctly.	Although the translation "movimiento intestinal" is the correct and appropriate translation of "bowel movement", this was changed to "evacuaciones", because one respondent misunderstood the term to mean only "diarrhea". This is an appropriate term, which the respondents confirmed as understanding to have the meaning of "bowel movement" as well. The forward and backward translations were revised.	Después de cada evacuación, complete la fecha y la hora y responda a todas las preguntas que aparecen a continuación en esa fila.	After each evacuation, complete the date and the time, and answer all of the questions that appear later on that row.
Smooth, a softer stool	Heces lisas, más blandas	R1, R3, R4, and R5 reported no difficulty. R2 found it difficult to understand the consistency expressed by this item.	The translation reflects the source, and the words used are simple and easy to understand, even for people with a low education level. In addition, a picture is shown. No revision suggested.	Heces lisas, más blandas	Smooth, softer stools
Soft chunks or clumps	Trozos o grupos blandos	R1, R3, R4, and R5 reported no difficulty. R2 reported no difficulty, but found that this item seemed like a combination of several things.	As none of the respondents showed any specific difficulty, no revision is needed.	Trozos o grupos blandos	Soft chunks or groups
Loose, mushy stool	Heces sueltas y flojas	R1, R3, R4, and R5 reported no difficulty. R2 did not understand the word "heces" (stools).	"Heces" is a correct translation of "stool." Even if a person does not understand the isolated word, when the word is given with so much context, even images, as in this case, it is not difficult at all to understand what the word means. No revision is suggested.	Heces sueltas y flojas	Mushy and loose stools

(Continued)

Table 5 (Continued)

Spanish (USA)	Forward translation	Cognitive debriefing-response analysis	Linguistic feedback	Final forward translation	Final backward translation
Watery and muddy	Acuosas y turbias	R1, R3, and R4 reported no difficulty. R2 did not understand the word "acuosas" (watery). R5 found the item difficult to understand, and did not know how to paraphrase it.	There seems to be some difficulty with the word "acuosas" (watery). Giving "aguadas" as a translation only could cause confusion, so for clarity the synonym is used in parentheses after.	Acuosas (aguadas) y turbias	Watery (watered down) and muddy
How immediate was your need?	¿Cuál fue su grado de urgencia?	R1, R2, R3, and R5 reported no difficulty. R4 reported no difficulty understanding the item, but said it was not well specified. When asked what she did not understand, she said "the degree of urgency". It was explained to her that it more or less means how much in a hurry you are when you have to evacuate. After that, she said she more or less understood it, and paraphrased it as "How much urge do you have to evacuate?"	While R4 expressed some confusion, the term is very clear, and adding the phrase at the end "to evacuate" would make the phrase more specific than the English source and the Japanese, which could cause discrepancies in conceptual equivalence. No revision should be made here.	¿Cuál fue su grado de urgencia?	What was your degree of urgency?
Which best describes what your bowel movement looked like?	¿Qué opción describe mejor el aspecto de su movimiento intestinal?	R1, R2, R3, and R5 reported no difficulty. R4 said she had no difficulty understanding, but when asked to paraphrase the item she said she did not understand it. When asked what she did not understand, she said "what is a bowel movement". She was told that it is another name for "evacuation", and when asked if she understood that she said she did and paraphrased the item correctly (What is the appearance every time you go to the toilet?).	Although the translation "movimiento intestinal" is the correct and appropriate translation of "bowel movement" this is changed to "evacuaciones" because one respondent misunderstood the term to mean only "diarrhea". This is an appropriate term which the respondents confirmed to understand as having the meaning of bowel movement as well. The FT and BT are revised.	¿Qué opción describe mejor el aspecto de su evacuación?	What option best describes the appearance of your evacuation?
For each question, please mark an X for the one answer most appropriate for that IBS-D symptom.	Para cada pregunta, marque con una X la respuesta más apropiada para ese síntoma del IBS-D.	R1, R2, R3, and R5 reported no difficulty. R4 reported difficulty understanding the item: she said she did not understand it.	R4 seemed to have difficulty, because this item was examined on its own, and out of context. Both the source and the translation are clear when the item is understood as the instructions for what comes below. No revision is needed.	Para cada pregunta, marque con una X la respuesta más apropiada para ese síntoma del IBS-D.	For each question, mark with an X the most appropriate answer for that symptom of IBS-D.
In the past 24 hours, on a scale of 0–10, how would you rate the severity of your abdominal pain?	Durante las últimas 24 horas, en una escala del 0 al 10, ¿cómo calificaría la intensidad de su dolor abdominal?	R1, R2, R3, and R5 reported no difficulty. R4 reported no difficulty understanding the item, but seemed to mistake "severity" (intensidad) for "frequency" (frecuencia).	The translation is clear and the word "intensidad" (severity) is a simple word and easy to understand, even for people with a low education level. As R4 must have simply mistakenly rephrased the wrong word, no revision is needed.	Durante las últimas 24 horas, en una escala del 0 al 10, ¿cómo calificaría la intensidad de su dolor abdominal?	During the last 24 hours, on a scale of 0 to 10, how would you rate the severity of your abdominal pain?

Spanish (US) Source	Forward translation	Cognitive debriefing-response analysis	Linguistic feedback	Final forward translation	Final backward translation
In the past 24 hours, on a scale of 0–10, how would you rate the severity of your abdominal pain?	Durante las últimas 24 horas, en una escala del 0 al 10, ¿cómo calificaría la intensidad de su dolor abdominal?	R1, R2, R3, and R5 reported no difficulty. R4 reported no difficulty understanding the item, but seemed to mistake “severity” (intensidad) for “frequency” (frecuencia).	The translation is clear and the word “intensidad” (severity) is a simple word and easy to understand, even for people with a low education level. As R4 must have simply mistakenly rephrased the wrong word, no revision is needed.	Durante las últimas 24 horas, en una escala del 0 al 10, ¿cómo calificaría la intensidad de su dolor abdominal?	During the last 24 hours, on a scale of 0 to 10, how would you rate the severity of your abdominal pain?
In the past 24 hours, on a scale of 0–10, how would you rate the severity of your stomach pain?	Durante las últimas 24 horas, en una escala del 0 al 10, ¿cómo calificaría la intensidad de su dolor estomacal?	R1, R2, R3, and R5 reported no difficulty. R4 reported no difficulty understanding the item, but seemed to mistake “severity” (intensidad) for “frequency” (frecuencia).	The translation is clear, and the word “intensidad” (severity) is a simple word and easy to understand, even for people with a low education level. As R4 must have simply mistakenly rephrased the wrong word, no revision is needed.	Durante las últimas 24 horas, en una escala del 0 al 10, ¿cómo calificaría la intensidad de su dolor estomacal?	During the last 24 hours, on a scale of 0 to 10, how would you rate the severity of your stomach pain?
In the past 24 hours, on a scale of 0–10, how would you rate the severity of your abdominal cramps?	Durante las últimas 24 horas, en una escala del 0 al 10, ¿cómo calificaría la intensidad de sus cólicos abdominales?	R1, R2, R3, and R5 reported no difficulty. R4 reported no difficulty understanding the item, but seemed to mistake “severity” (intensidad) for “frequency” (frecuencia).	The translation is clear, and the word “intensidad” (severity) is a simple word and easy to understand, even for people with a low education level. As R4 must have simply mistakenly rephrased the wrong word, no revision is needed.	Durante las últimas 24 horas, en una escala del 0 al 10, ¿cómo calificaría la intensidad de sus cólicos abdominales?	During the last 24 hours, on a scale of 0 to 10, how would you rate the severity of your abdominal cramps?
In the past 24 hours, on a scale of 0–10, how would you rate the severity of the pressure you felt in your abdomen?	Durante las últimas 24 horas, en una escala del 0 al 10, ¿cómo calificaría la intensidad de la presión que sintió en el abdomen?	R1, R2, R3, and R5 reported no difficulty. R4 reported no difficulty understanding the item, but seemed to mistake “severity” (intensidad) for “frequency” (frecuencia).	The translation is clear, and the word “intensidad” (severity) is a simple word and easy to understand, even for people with a low education level. As R4 must have simply mistakenly rephrased the wrong word, no revision is needed.	Durante las últimas 24 horas, en una escala del 0 al 10, ¿cómo calificaría la intensidad de la presión que sintió en el abdomen?	During the last 24 hours, on a scale of 0 to 10, how would you rate the severity of the pressure you felt in the abdomen?
In the past 24 hours, on a scale of 0–10, how bloated did you feel?	Durante las últimas 24 horas, en una escala del 0 al 10, ¿qué tan hinchado se sintió?	R1, R3, R4, and R5 reported no difficulty. R2 reported no difficulty, but she said it was not specified which body part the bloating applied to. She would have specified the area.	As none of the respondents showed any specific difficulty, no revision is needed. Also, translation is an accurate reflection of the source, and with the context it is understood that the area in question is the stomach/abdominal area.	Durante las últimas 24 horas, en una escala del 0 al 10, ¿qué tan hinchado se sintió?	During the last 24 hours, on a scale of 0 to 10, how bloated have you felt?
In the past 24 hours, did you have any accidents (lose control of your bowels)?	Durante las últimas 24 horas, ¿tuvo algún accidente (perdió el control de los intestinos)?	R1, R3, R4, and R5 reported no difficulty. R2 reported no difficulties, but when asked what the item meant for her she said “that the symptoms may become difficult to control”.	The translation is clear and none of the respondents reported difficulty, so no revision is needed.	Durante las últimas 24 horas, ¿tuvo algún accidente (perdió el control de los intestinos)?	During the last 24 hours, did you have any accident (lost control of the bowel)?

(Continued)

Table 5 (Continued)

Japanese Source	Forward translation	Cognitive debriefing-response analysis	Linguistic feedback	Final forward translation	Final backward translation
Date format (MM/DD/YYYY)	(年 (西暦) / 月 / 日)	R1 pointed out that the format of the date indicated here is different from the format of the example of date entry, but no confusion was reported. R4 pointed out that the four blanks to fill in the year come after the two blanks for month and day, and are not appropriate for Japanese, but reported no difficulties understanding the translation. R2, R3, and R5 reported no confusion.	R1 and R4 had no difficulties understanding the translation, yet they pointed out that the example and the blanks do not match the date format in this translation. Therefore, the example and the blanks for patients to fill in the dates in the questionnaire were updated to match the date format used in Japanese. No revision needed for this segment.	(年 (西暦) / 月 / 日)	(Y (AD)/M/D)
Like marbles or hard rocks	硬い、兔糞状の便	R2 and R4 felt it a little difficult to read the Chinese (Kanji) characters (“兔糞状”), but no confusion was reported. No difficulties reported by R1, R3, or R5.	While the kanji was a bit difficult for R4 to read, the accompanying image helps the patient to understand. Also, since no confusion was reported, there is no revision needed.	硬い、兔糞状の便	Hard, stool like a rabbit poo.
In the past 24 hours, how would you rate the severity of your abdominal cramps?	過去24時間の腹部痛 (腹部の刺すような鋭い痛み) の重症度を、0から10までの尺度で評価してください。	While R1, R2, R3, and R4 reported that it was difficult to read the Chinese (Kanji) characters (“疝痛”), no confusion leading to objective error in interpreting the meaning of the question was reported. No difficulties reported by R5.	Four of five patients reported that the kanji was difficult to understand. However, when this term was followed by an explanation in parentheses, all respondents were able to understand the term correctly. Therefore, no revision needed.	過去24時間の腹部痛 (腹部の刺すような鋭い痛み) の重症度を、0から10までの尺度で評価してください。	Please rate the severity of the abdominal cramp (stabbing, sharp pain in the abdomen) in the past 24 hours by the scale of 0 to 10.

Abbreviation: IBS-D, irritable bowel syndrome with diarrhea.

understood the items in the translated instrument, demonstrating conceptual and linguistic equivalence and cultural appropriateness. Only minor changes to the text were made for the term “bowel movement” (revised from “movimiento intestinal” to “evacuaciones”), which was cited as causing some confusion and misunderstanding.

The translatability assessment and cognitive debriefing interview processes were incorporated into the overall translation of the instrument, because literal translations potentially can pose problems with the validity and interpretability of the PRO measure.^{11,12} No significant modifications after changes made in accordance with the translatability assessments were required to improve the integrity and quality of the IBS-D PRO instrument in any of the languages evaluated. The usefulness of translatability assessments prior to the actual translation has previously been documented and is commonly accepted.¹³ Although it is often difficult to achieve conceptual and linguistic equivalence, as well as cultural appropriateness via the use of representative languages, similar findings were observed across all ten languages that were evaluated. The final translated versions of the instrument followed the ISPOR guidance for the translation, linguistic validation, and cultural adaptation of a PRO instrument for use in multinational trials and settings.^{7,14} The methodology used here (ie, the forward and backward translations, followed by cognitive debriefing interviews with native-speaking individuals of the target languages) is also consistent with the previously described methodology for translating other PRO instruments for use in multiple countries and languages.^{15–19}

Psychometric evaluation of the US English version of the PRO instrument had been previously performed and provided evidence that supports its psychometric validity (unpublished observation/manuscript in progress). Psychometric evaluation of the translated versions, however, has not yet been performed, and can be viewed as a limitation to this study; it is necessary to test whether the psychometric properties observed in the US English version are preserved in the Spanish (US) and Japanese versions. Another limitation is that the minimum standard of five respondents for each of the cognitive debriefing interviews was used. Additional testing with a larger sample would further strengthen the validation results.

Conclusion

In summary, the results of the translatability assessment reported here provide evidence that the IBS-D PRO is worded in a manner that is easily translated into numerous other languages. In addition, the linguistic validation results support the conceptual equivalence of the Spanish (US) and

Japanese translations of the IBS-D PRO instrument. These linguistically validated versions can be used in future research to assess their content validity and psychometric properties. These versions can also be used in multinational trials and studies to evaluate treatment benefit in IBS-D.

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Author contributions

LD-H, KL, AN, RA, BB, SZ, IG, and BZ contributed to the design of the study; LD-H, KL, BB, RA, and AP performed the research and participated in data acquisition; all authors were involved in the analysis/interpretation of the data and drafting or critically reviewing/revising the manuscript; and all authors approved the final version of the article. All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

Disclosure

AN, LD-H, IG, SZ, and BZ are employees of Astellas Pharma Inc. KL was an employee of Adelphi Values (formerly Mapi Values) at the time of the study, which was contracted by Astellas to work on IBS-D PRO instrument development. BB and RA are employed by Adelphi Values, and were contracted by Astellas to work on IBS-D PRO instrument development. BB and RA have also worked with other pharmaceutical companies on PRO development and validation projects over the previous 2-year period. AP is employed by TransPerfect, and was contracted by Astellas to work on the translatability assessments and linguistic validation. A US patent (application 13/274,040) is pending for the IBS-D daily symptom diary and symptom-event log (Astellas Stool Form Scale). The authors report no other conflicts of interest in this work.

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