The role of patient-reported outcomes (PRO) as primary endpoints in the evaluation of medicines approved with PRO claims

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OBJECTIVES: To review the drugs that used PRO as primary endpoints in the evaluation of their clinical efficacy and have been granted a PRO claim by the Food & Drug Administration (FDA) or the European Medicines Agency (EMA). METHODS: The PRO-labeled database, which centralizes medicinal products with a PRO claim, was searched using the keyword “primary endpoint”. Only drugs approved between January 1, 1995 and May 28, 2010 were included. RESULTS: A total of 303 (66%) out of 459 products included in the database were retrieved. Four were excluded because of a withdrawal notice (all EMA), 15 because they were approved before 1995, and two others because the endpoints were not clearly specified. In total, 282 products were analyzed (71 approved in Europe). They represented 81 different indications, with 47 products having more than one indication. The most frequent indications were: Pain (25 products), Rheumatoid Arthritis (25), Menopause (18), Parkinson’s disease (17), Epilepsy (15), Migraine disorders (13), Sleep disorders (12), Rhinitis Allergic Perennial, Seasonal (12), and Ankylosing Spondylitis (10). In total, 140 different PRO endpoints were listed. Seventy-seven percent of them were symptoms (e.g. pain, bowel movement, heartbeat symptoms, asthma symptoms, etc.). Function (e.g. physical function, functional impairment, etc.) represented only 5.7% of all endpoints. Health-related quality of life (HRQL) was a clear primary endpoint in only two products: Deloxetine (Urinary Incontinence) and Aliseide (Rhinitis Allergic Perennial and Seasonal). Both approvals were granted by the EMA in 2008 (after the first publication of the EMA and FDA guidances). CONCLUSIONS: Symptoms, as measured by patients, are a key criterion in the evaluation of medicines. Unsurprisingly, pain is the main indication in which the highest number of products with a PRO as a primary endpoint are approved. More sophisticated PRO endpoints, such as function or HRQL, are used less often.

Translation, linguistic validation and electronic administration in the Indian languages: A case study highlighting the special difficulties that exist at this intersection

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OBJECTIVES: Translation and linguistic validation of questionnaires for paper or electronic administration require similar processes. Both modalities share a common difficulty: how to best utilize existing processes to accommodate Indian languages. Working with Indian language instruments can be daunting, even without the compounded effect of managing both ePRO and linguistic validation together. This paper seeks to enumerate the challenges associated with the intersection of Indian languages, linguistic validation, and electronic administration and recommends the use of a specialized checklist to avoid escalating potential difficulties. METHODS: A case study was performed to explore the complexity of these processes. A Fibromyalgia e-diary and corresponding paper diary were translated into four Indian languages and three non-Indian languages with varying levels of linguistic difficulty. This allowed for a multidimensional analysis of issues faced in translation for ePRO versus paper administration, and translation for Indian versus non-Indian settings. RESULTS: During the translation validation, difficulties arose pertaining to font and formatting requirements, localization of colloquial terms and phrases and maintaining concept equivalence while respecting cultural appropriateness. Preparing an ePRO for use involves thorough analysis of existing instrument versions and possible modification of instructions, response sets or questionnaire format to accommodate technology or screen size limitations. A holistic approach of quality assurance should be employed, including multiple rounds of proofreading. When preparing an Indian language for electronic administration one must take even more care, accounting for the factors listed above as well as considering software font testing prior to production, and additional proofreading steps. CONCLUSIONS: Linguistic validation of ePRO questionnaires for use in Indian settings presents special challenges. Evidence suggests that additional consideration must be exercised early on in order to avoid compounded difficulties and delays later in the process. For such cases, the use of a checklist is recommended to assist in preempting future difficulties within the project.

Concept elaboration—an essential stage in the translation of PRO measures

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The ISPOR Principles of Good Practice paper for the translation of patient-reported outcome (PRO) measures describes concept elaboration within the scope of project preparation and emphasizes that the misinterpretation of items or concepts can result if the step is not undertaken. However, the paper does not discuss how to correctly perform concept elaboration or why it is an essential step in the translation process. Translation companies often harmonise their own translations with each other, but not with existing translations. Over time, a single measure may be translated by any number of companies. Wordings choices are often made by various translators and project managers without prior guidance—this can lead to wide variations. A concept elaboration document approved by the developer provides consistent clarification and guidance to promote harmonization across all language versions regardless of who is carrying out the work. Inconsistent wording choices across language versions can be due to misunderstandings as a result of ambiguous wording in the source text, misinterpretation of idioms or the influence of personal choice resulting in inconsistent use of alternative phrases for terms that are not directly translatable. Concept elaboration remedies these issues by providing a line-by-line analysis of the source text which clarifies ambiguous wording, provides alternative wording for items with no direct translations, and provides suitable equivalents of culture-bound concepts and provides guidelines on nuance, tone, and emphasis. Concept elaboration ensures that the text is fully understood by all translators before any translation work begins. It encourages standardised decision making for every language and allows the developer to exercise influence over the style and content of the translations even if they are unable to review each translation individually. For studies including developer reviews, these reviews should become more straightforward as the translations will have been carried out according to the developer’s guidance.