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 PROLabels database, which centralizes medicinal products with a PRO claim, was searched using the keyword “primary endpoint”. Only drugs approved between January 1, 1993 and May 32, 2010 were included. RESULTS: A total of 303 (66%) out of 459 products included in the database were retrieved. Four were removed 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), Rheumatoid Arthritis 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, heartburn 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: Duloxetine (Urinary Incontinence) and Alisade (Rheumatoid Arthritis Perennial and Seasonal). Both approvals were granted by the EMA in 2008 (after the first publication of the EMA and FDA guidelines). 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.

Comparison of methods for item generation and pretesting of five lymphoedema-specific health-related quality of life questionnaires

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OBJECTIVES: A systematic literature review identified four patient-reported outcome (PRO) measures that have been used in the assessment of quality of life for patients with upper limb lymphoedema. These are in addition to the author’s newly devised questionnaire. However the developers had all used different methods to devise the items with the final measures incorporating different items and domains. The objective was to compare the methods that had been used and review in the light of available guidance on best practice. METHODS: Review and tabulate the available information on each PRO regarding its development. Key aspects of the evaluation included specificity of target population, source of item generation, number of initial items generated, drafting of item/question wording, pretesting and defining the domains. RESULTS: Two of the five PROs had been developed to assess the quality of life of patients with upper or lower limb lymphoedema decreasing the specificity of the target population; two of the PROs did not use patients as the source for items relying on clinical aetiology; the number of items initially generated by the remaining three PROs were 98, 134 and 495, but none of the developers evaluated the point of saturation; different approaches were used for analyses of the items generated to create the initial draft of items/questions; not all PROs were pretested. Number of domains ranged from two to seven and number of items/questions in initial drafts ranged from 5 to 70. CONCLUSIONS: Each of the PROs measuring the same concept have been developed using different methods of generating the items and pretesting an initial draft of the PRO. To advance the field of measuring quality of life of lymphoedema patients, it will be important to establish which PROs have the best validity, that is, best reflects the impact of lymphoedema on their health and well-being.