Patient-Reported Outcome Measures (PROs): Overview and Relevance to Research on Nutrition

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Introduction to Patient-Reported Outcomes (PROs)

Definition of a PRO

Many aspects of medical conditions are known only by the patients themselves. A patient-reported outcome (PRO) instrument involves the report of health status coming directly from the patient without interpretation of the patient's response by a clinician, investigator, or anyone else.[1,2] Increasingly, clinical trials and other treatment outcome studies are relying on PRO measurement as primary outcomes or as instruments that can add information to clinical measures. For example, symptoms such as pain and fatigue can be assessed only via PRO measures. Consequently, a diverse range of symptom-based conditions such as migraine, overactive bladder, and major depression require PRO measures in order for healthcare providers to fully understand patients' experience of disease and treatment.

Use of PROs

PRO measures can be used to assess a broad range of patient characteristics, including both physical and psychological symptoms. For example, symptoms can be captured in terms of patient perceptions of severity or frequency. Many PRO measures assess the impact of treatments on functional domains such as work productivity, activities of daily living, social functioning, family relationships, and relationships with a significant other. Some PROs focus specifically on aspects of treatment, such as treatment satisfaction or preference for specific treatment attributes (eg, dosing, route of administration, or convenience).

PRO measures have been developed to assess health-related quality of life (HRQOL). Definitions of HRQOL vary widely, but two central aspects of this construct are inherent in most definitions. First, HRQOL is subjective, and therefore it should be assessed from the patient's perspective, which requires a PRO instrument. Second, HRQOL is a multidimensional construct that integrates a

broad range of outcomes. One definition that includes both of these components describes HRQOL as the subjective perception of the impact of health status, including disease and treatment, on physical, psychological, and social functioning.[3]

In addition to assessing efficacy in clinical trials and treatment outcome studies, PRO measures can serve many purposes. For example, PRO measures assessing patient preference, specific symptoms, or functional status can help differentiate between treatments that appear similar in terms of efficacy. Furthermore, by providing insight into the patient's experience, PRO measures can help clinicians, caregivers, policy-makers, and payers better understand medical conditions and treatments.

In clinical practice settings, the administration of PRO measures can help facilitate communication between clinicians and patients. PRO measures also can be used as screeners to identify patients who may need additional assessment or treatment, and clinics can use them to track patient progress and treatment effectiveness at their site.

Generic vs Condition-Specific PROs

PRO measures often are categorized as either generic or condition-specific.[4,5] Generic measures are designed for use among diverse populations with a broad range of medical conditions, and these instruments can also be used to characterize healthy samples without a particular medical condition. Commonly used generic PROs include the Short Form (36) (SF-36) Health Survey developed from the Medical Outcomes Study and the EQ-5D developed by the EuroQoL group. In contrast, condition-specific measures are relevant to a particular group of patients, and they have been developed to assess specific populations, quantify specific aspects of functioning, and examine the impact of particular medical conditions or treatments.

A substantial body of literature has focused on comparing generic and condition-specific measures, while identifying advantages of each. Compared with generic measures, the primary advantage of condition-specific measures is that they frequently are found to be more responsive to treatment-related change.[6-8] An advantage of generic PROs is that they can be used to compare among various populations, make comparisons to the general population, and estimate the relative impact of various medical conditions or treatments.[3,4,9,10] Because generic and condition-specific measures have different strengths and are conceptually distinct, it is often recommended that both types of instruments be administered as part of a complete assessment battery in treatment outcomes studies.[7,11,12]

PRO Measures Used in Research on Nutrition

The PRO measures and methods described thus far have been developed primarily in the context of pharmaceutical clinical trials and other treatment outcome studies. However, PRO measures also can be used to assess outcomes related to nutrition. Studies examining the impact of nutrition regimens or nutritional supplements usually focus primarily on non-PRO clinical outcomes such as body mass index, blood glucose levels, liver function, immune system response, muscle strength, energy intake, cholesterol levels, and vitamin levels. Awareness appears to be growing in nutrition-related literature that PROs can add important and unique information to these clinical measures. For example, PROs can supplement clinical outcomes by providing a direct indication of how patients feel and quantifying the real-world impact of nutrition on patients' lives. PRO measures also can reveal whether patients notice any meaningful improvement associated with nutrition-based interventions, as well as whether nutrition regimens or supplements have an impact on quality of life and functional status.

Generic PRO Measure Used in Nutrition Studies

The PRO measure most commonly used to assess outcomes in nutrition studies is the SF-36. This generic instrument assesses the patient's perceptions of health status in eight areas: physical functioning, social functioning, role limitations due to physical health problems, role limitations due to emotional problems, pain, mental health, vitality, and general health perceptions.[13] Several of these domain scores, such as vitality, can be expected to be particularly sensitive to changes in nutrition. With its broad psychological and physical domains, the SF-36 is often considered to be a measure of health-related quality of life (Figure).

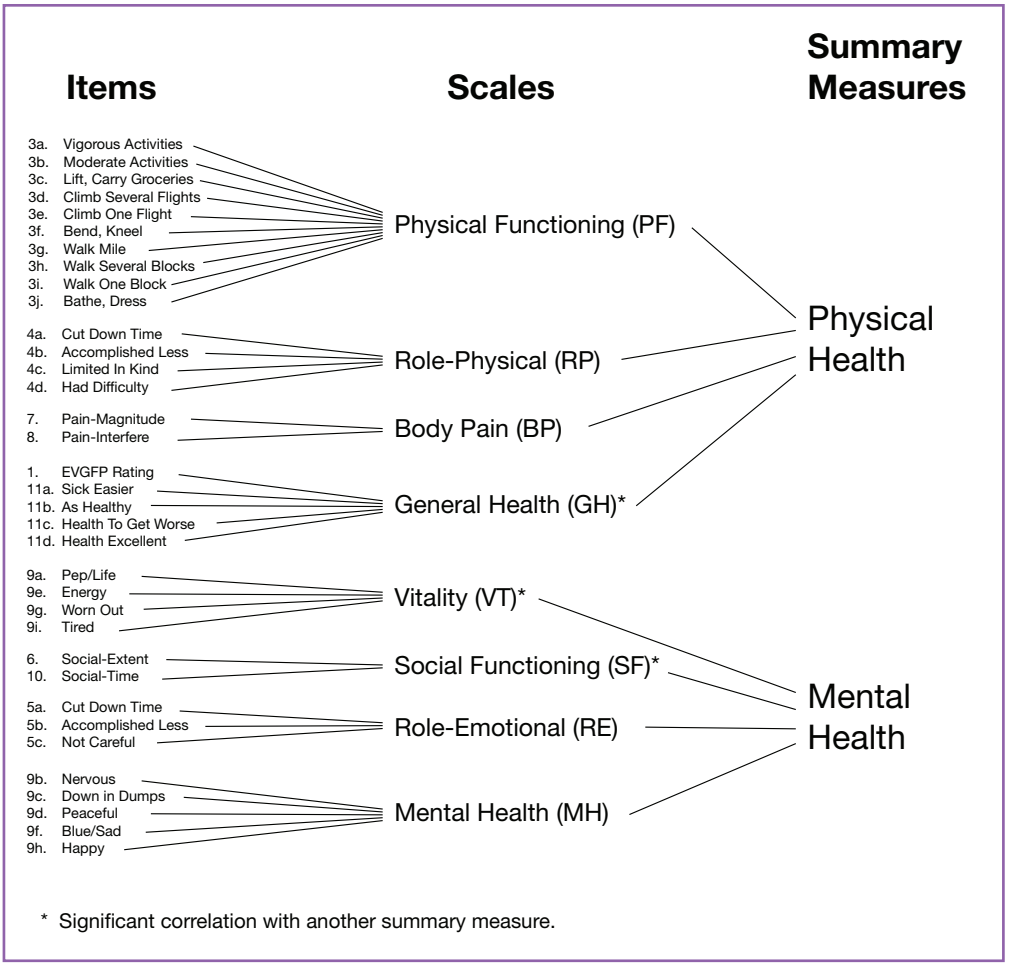

Figure. Domains of the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36).[13]
EVGFP=excellent, very good, good, fair, poor

The SF-36 has been used to assess outcomes for a range of nutrition interventions including dietary counseling and oral dietary supplements. These studies have been conducted in a range of patient subpopulations, including patients with depression, cancer, and chronic kidney disease, as well as in healthy individuals. Selected studies in which the SF-36 was used to assess outcomes of nutrition regimens or supplements are listed in Table 1.

Table 1. Selection of Studies Using a Generic PRO Measure Commonly Used in Nutrition Studies: The Medical Outcomes Study 36-Item Short Form Health Survey (SF-36)

Citation	Nutritional Variable or Content	Population, Treatment, or Medical Condition
Aghakhani et al.[14] 2012	Dietary counseling	Maintenance hemodialysis
Miller et al.[15] 2006	Oral nutritional supplement	Older adults following lower limb fracture
Neelemaat et al.[16] 2010	Transmural nutrition support (enriched diet, oral nutritional supplement, and dietitian consultations)	Malnourished elderly patients
Norman et al.[17] 2011	Oral nutritional supplement	Malnutrition associated with benign gastrointestinal disease
Persson et al.[18] 2007	Dietary counseling Liquid and multivitamin supplementation	Geriatric patients at risk of protein-energy malnutrition
Poppitt et al.[19] 2009	Omega-3 fish oil	Cardiovascular risk factors and mood in patients who had an ischemic stroke
Rondanelli et al.[20] 2011	Essential amino acid supplementation	Quality of life, amino acid profile, and strength in elderly patients
van Uffelen et al.[21] 2007	Vitamin supplement	Mild cognitive impairment

Condition-Specific PRO Measures Used in Nutrition Studies

A variety of condition-specific PRO measures also have been used to assess outcomes of nutrition studies. For example, outcomes associated with oral nutritional supplements have been assessed with depression-specific instruments (eg, Beck Depression Inventory) and cancer-specific instruments (eg, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 [EORTC QLQ-C30] and the Functional Assessment of Cancer Therapy-General) in studies conducted within these populations (Table 2). In all these studies, however, the PRO instrument was developed to assess outcomes related to the patient's medical condition rather than specific nutrition-related outcomes.

Table 2. A Selection of Condition-Specific PRO Measures Used in Nutrition Studies

Citation	PRO	Population or Medical Condition	Nutrition Variable or Content
Mantovani et al.[22] 2006	• EORTC QLQ-C30 • Appetite by VAS	Advanced cancer patients with cancer-related anorexia/ cachexia syndrome	• Diet with high polyphenols content • Antioxidant treatment • Vitamins E and C • Oral pharmaconutrition support
Rondanelli et al.[23] 2009	• Binge Eating Scale • Beck Depression Inventory (BDI-II) • Haber analogue scale to measure appetite	Healthy, overweight subjects	• Dietary supplement (N-oleyl-phosphatidylethanolamine and epigallocatechin-3-gallate formula)
Rondanelli et al.[24] 2010	• Geriatric Depression Scale (GDS) • Autonomy of eating (self-assessment) • Self-perception of health and nutrition	Elderly women with depression	• Omega-3 fatty acid supplementation (2.5 g/d of n-3 LCPUFAs, with 1.67 g of eicosapentaenoic acid and 0.83 g of docosahexaenoic acid)
Sugawara et al.[25] 2010	• Chronic Respiratory Disease Questionnaire (CRQ—Japanese version) • Borg dyspnea scale • 3-day dietary intake	Malnourished patients with COPD	• Nutritional supplementation (60% energy from carbohydrates, 25% energy from fat, and 15% energy from protein. Contains omega-3 PUFAs and vitamin A)
Wiese et al.[26] 2011	• Crohn's Disease Activity Index (CDAI) • Inflammatory Bowel Disease Questionnaire (IBDQ) • Daily diary (measures, bowel, abdominal pain, general well-being)	Patients with Crohn's disease	• Inflammatory bowel disease nutrition formula (fish oil, a fermentable prebiotic/fiber system, and increased levels of antioxidant vitamins and minerals)

VAS=visual analog scale, LCPUFA=long-chain polyunsaturated fatty acid, COPD=chronic obstructive pulmonary disease, PUFAs=polyunsaturated fatty acids

A Gap in the Literature: Nutrition-Specific PRO Measures

Patient-reported measures commonly are used in studies of nutrition regimens and nutritional supplements to assess and quantify food or supplement intake. These instruments are referred to by a variety of names, including food diaries, diet records, food-recall questionnaires, and supplement intake diaries. Some patient-reported measures designed specifically to assess the impact of obesity, diabetes, and other medical conditions are likely to be related to nutrition.[27]

However, only one nutrition-specific patient-reported measure is available from my review. This measure, called the Nutrition Screening Initiative (NSI) Checklist, was designed as a brief screener for identifying elderly respondents with nutrition problems. Despite the strengths of this instrument (which are described below), it was not designed to be used as a detailed outcome measure that would be sensitive to change in studies of nutrition regimens, treatments, or supplements. A nutrition-specific PRO measure focusing on detailed outcomes assessment could focus on aspects of patient health that are likely to be affected by nutrition regimens, dietary supplements, or various levels of nutrition-related health, including malnutrition. Compared with the commonly used generic and condition-specific PRO measures, a well-developed nutrition-specific PRO measure could be more sensitive to change in studies designed to assess outcomes of nutrition regimens and treatments.

Two "PRO by Proxy" Measures

Two clinician-reported measures were located that include items asking the clinician or study investigator to report their understanding of patients' perspective of their nutritional status. Although these items are not patient-reported per se, they are intended to assess the patient's subjective experience. Therefore, the items may be considered "PRO by proxy." However, responses should be interpreted with caution because the accuracy of clinicians' insight into patients' subjective experience is uncertain. Still, the successful implementation of these measures across studies suggests that a nutrition-specific PRO focused on the patient's experience of nutritional status could be a useful measurement tool.

The first of these two measures is the Mini Nutritional Assessment (MNA), which was designed to provide an overall indication of patients' nutritional status.[28,29] The instrument has been implemented in several studies. For example, it has been used to assess the nutritional status of elderly individuals receiving home care

services, the effect of omega-3 fatty acid dietary supplements in elderly women with depression, and the effect of amino acid dietary supplements in elderly patients.[20,24,30]

The MNA Short Form appears to be rated by clinicians or study investigators,[28] and therefore, it is not a PRO. However, it does include a brief attempt to assess patients' subjective perceptions of their own nutritional health. The MNA begins with assessment of more objective constructs including body measurements (eg, body mass index [BMI] and weight change), dietary assessment (eg, number of meals daily and type and amount of food), and general assessment (eg, medication and mobility). At the end of the questionnaire, two items focused on "self-assessment" are designed to capture patients' impressions of their own nutritional health. These items ask "Do they view themselves as having nutrition problems?" and "In comparison with other people, how do they consider their health status?"

A second measure that includes "PRO by proxy" items is the Malnutrition Inflammation Score (MIS), which was developed for patients treated with hemodialysis.[31] The instrument was developed for use in this population because malnutrition inflammation complex syndrome is common in maintenance hemodialysis patients. The 10 items of the MIS primarily include clinical items assessing objective content such as decreased fat stores or loss of subcutaneous fat, signs of muscle wasting, BMI, serum albumin, serum transferrin, and change in end dialysis dry weight. However, the instrument also includes several "PRO by proxy" items asking clinicians to rate the patient's subjective experience of gastrointestinal symptoms (eg, appetite, nausea, and vomiting) and functional status (eg, ambulation, feeling tired, and independent activities). The MIS has been used to assess outcomes associated with a range of dietary supplements such as omega-3 fatty acids and selenium.[32,33]

A Patient-Reported Screener

A true patient-reported measure of nutritional status, the NSI Checklist was developed as part of a national effort supported by more than 25 professional organizations. The goal of this initiative was to identify nutrition problems in the elderly and provide nutrition services to those with greatest nutrition-related health risks. The NSI Checklist is a 10-item patient-reported screening questionnaire that is intended to identify elderly people in need of nutrition intervention.[34,35] Items include "I eat fewer than two meals per day," "I don't always have enough money to buy the food I need," and "I am not always physically able to shop, cook and/or feed myself."

Based on responses to the 10 items, respondents are categorized as having low, moderate, or high nutritional risk. The instrument has demonstrated good sensitivity (ie, ability to detect people at risk) and specificity (ie, avoiding false positives). It has been used to assess nutritional status in a broad range of populations including patients with acute porphyria, mild cognitive impairment, and metabolic syndrome, as well as patients undergoing thoracic surgery.[36-39] The checklist also has been shown to be useful in various demographic groups, including a Hispanic rural sample and an inner-city African-American sample.[40,41] Despite the strengths of this measure, however, it may not be sensitive to change in a study assessing outcomes of nutrition regimens or nutrition-related treatments. The items primarily capture lifestyle issues that may be indicative of poor nutritional health, rather than aspects of the respondent's nutrition-related health status. Therefore, although the NSI Checklist appears to be a useful screener, researchers implementing this instrument must remember that it was not designed for the purpose of outcomes assessment.

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