OMERACT Quality-adjusted Life-years (QALY) Working Group: Do Current QALY Measures Capture What Matters to Patients?

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ABSTRACT. ***Objective.*** To understand the limitations with current patient-reported outcome measures (PROM) used to generate quality-adjusted life-years (QALY) in rheumatology, and set a research agenda.

Methods. Two activities were undertaken. The first was a scoping review of published studies that have used PROM to generate QALY in rheumatology between 2011 and 2016. The second was an interactive "eyeball test" exercise at Outcome Measures in Rheumatology 13 that compared subdomains of widely used generic PROM, as identified through the scoping review, to subdomains of the Assessment of SpondyloArthritis Health Index (ASAS-HI) condition-specific PROM for ankylosing spondylitis.

Results. The scoping review included 39 studies. Five different PROM have been used to generate QALY in rheumatology; however, the EQ-5D and Short Form 6 Dimensions (SF-6D) were used most frequently (in 32 and 9 of included studies, respectively). Special interest group participants identified energy/drive and sleep as 2 key subdomains of the ASAS-HI instrument that may be missed by the EQ-5D, and sexual function as potentially missed by the SF-6D. Participants also expressed concerns that aspects of the process of care and non-health outcomes may be missed. Three ways of incorporating additional subdomains were discussed, including using an alternative generic PROM, modifying an existing generic PROM with "bolt-on" subdomain(s), and generating societal weights for a condition-specific PROM.

Conclusion. Three priorities for future research were identified: understanding whether the EQ-5D and SF-6D identify what matters to patients with different rheumatic conditions, analyzing how much patients value process or non-health outcomes, and identifying which approaches to incorporating a greater number of subdomains into the QALY are being undertaken in other disease areas. (First Release March 15 2017; J Rheumatol 2017;44:1899–903; doi:10.3899/jrheum.161112)

Key Indexing Terms:
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Cost-effectiveness analysis is increasingly being used by policymakers to determine which drugs and technologies they will fund. This in turn affects which treatments are available to patients[1,2]. Quality-adjusted life-years (QALY) are the most widely used measure of benefit to assess the cost-effectiveness of drugs and technologies in healthcare[3]. QALY have been critical in justifying reimbursement for biologics in many countries[4], and will continue to be used

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while new treatments become available[5]. The QALY is a measure that considers both quality and length of life[6]. While length of life is relatively straightforward to measure, measuring "quality of life" is more challenging. In practice, this generally requires 2 components. The first is a system to describe quality of life, and the second is population weights that reflect societal preferences and are specific to that descriptive system.

The descriptive system of health is generally operationalized using a patient-reported outcome measure (PROM) that includes several subdomains that are relevant to health-related quality of life (HRQOL). PROM can be either generic, meaning that they are broadly applicable across different health conditions, or condition-specific, where the subdomains are more focused[7]. While each has potential advantages and drawbacks, generic PROM are most often used to generate QALY because they are comparable across conditions. The second component required to calculate QALY is population weights, which provide an indication of how much health states are valued. Population weights are generated through a large survey in a representative sample of the general population[8], and enable a value judgment to be made about whether, for example, living with reduced mobility is better (or worse) than living in pain. The resulting population weights provide scores for health states, on a 0–1 scale, where 0 corresponds to death and 1 corresponds to perfect health[9].

Generally speaking, generic PROM are more widely used as a descriptive system because population weights are available, whereas many condition-specific PROM would require these weights to be generated[10]. Generating weights can be expensive and difficult, which has led to various "mappings" from condition-specific PROM to generic PROM[11], though the accuracy of these algorithms is limited[12]. Importantly, previous research in rheumatology has shown that using different PROM results in different population weights[13,14]. National guidelines for economic evaluation recommend the use of generic PROM, such as the EQ-5D, because they are brief and applicable across all conditions[15]. However, there are concerns that generic PROM may miss aspects of HRQOL that are important to patients[16].

The QALY Working Group fits within several core areas of health as defined by the Outcome Measures in Rheumatology (OMERACT), including "Life Impact," "Death," and "Resource Use/Economical Impact."[17] The objective of the OMERACT QALY Special Interest Group (SIG) at OMERACT 13 in Whistler, British Columbia, Canada, was to build on previous work[18] and analyze the first component of the OMERACT Filter 2.0: Is the instrument a good match with the domain? The specific aim of this SIG was to understand the limitations with current instruments used to generate QALY in rheumatology research, and to set a future research agenda. This was accomplished through 2 activities:

1. A scoping review to identify which PROM are used to generate QALY in rheumatology, and
2. An interactive "eyeball test" exercise that compared subdomains of widely used generic PROM to subdomains of the Assessment of SpondyloArthritis Health Index (ASAS-HI) condition-specific PROM for ankylosing spondylitis (AS).

MATERIALS AND METHODS

A scoping review was undertaken to identify which PROM are currently being used to generate QALY in the rheumatology literature. An electronic search of PubMed and Embase was undertaken through OvidSP (Figure 1). To reflect the current literature, only studies published between 2011 and 2016 that used a PROM to generate QALY were included. Studies were excluded if they were dissertations, conference papers or reviews, not published in English, or the full text could not be obtained. Studies were reviewed independently by 2 reviewers (LT, NB) with disagreements resolved through discussion.

To identify subdomains of HRQOL that may be missed by the most widely used PROM, an interactive "eyeball test" was undertaken by attendees of the QALY SIG at OMERACT 13. Participants classified each of the subdomains from the ASAS-HI condition-specific PROM (for AS) as being "directly," "indirectly," or "not captured" by the most widely used PROM identified in the scoping review[19]. The ASAS-HI was chosen because it was developed with patients and considers a broad range of effects, including health, limitations in activities, and social participation. This exercise gave way to an open discussion among participants to identify future research priorities.

RESULTS

The primary literature search identified 776 studies from the online databases, of which 39 studies were included in the final analysis (Figure 1). Across the 39 included studies, 5 preference-based measures were used: the EQ-5D, the Short Form 6 Dimension (SF-6D), the 15D Instrument, the Health Utilities Index Mark 3, and the Quality of Well-Being Scale. The EQ-5D was used most frequently, having been measured in 32 studies across 5 rheumatic conditions. The SF-6D was the second most frequently used measure, with 9 studies measuring across 3 rheumatic conditions.

The 23 participants at the OMERACT SIG included methodologists (n = 8), clinicians (n = 13), and patients (n = 2). In comparing the ASAS-HI to the 2 most widely used PROM from the literature review, the EQ-5D and the SF-6D[20,21], participants identified energy/drive and sleep as 2 key subdomains that may be missed by the EQ-5D, and sexual function as potentially missed by the SF-6D (Table 1). While these may be identified indirectly by another subdomain, such as usual activities (EQ-5D), they may not be identified at all[22].

In discussing the implications for rheumatological conditions more broadly, participants expressed concerns that the generic PROM focused exclusively on health outcomes, and that patients may also value the process of care and non-health outcomes (such as economic self-sufficiency). It was suggested that in valuing these potential benefits, it would be important to understand whether patients would

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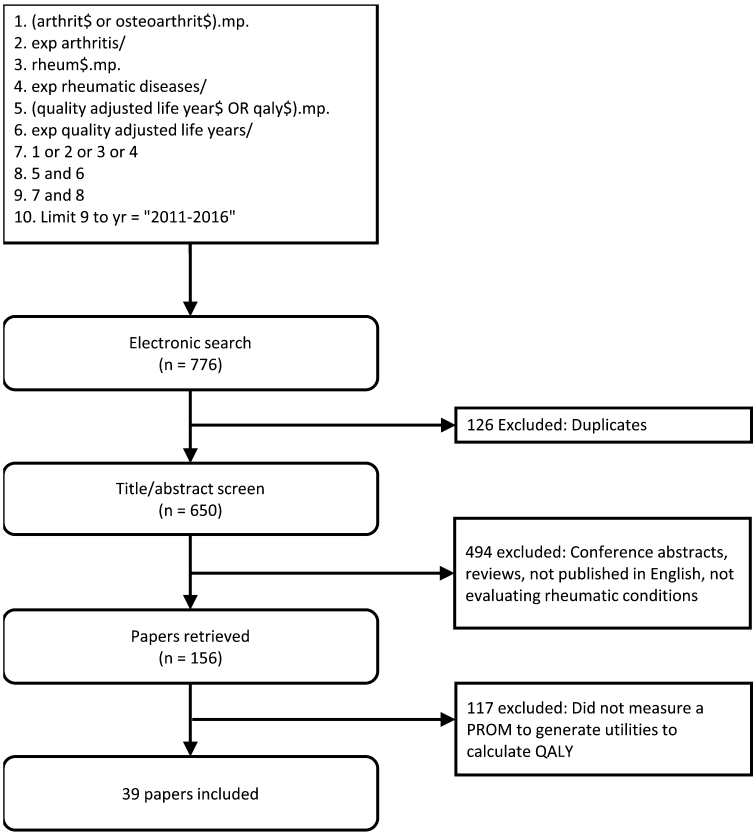

Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses diagram. QALY: quality-adjusted life-years; PROM: patient-reported outcome measure; exp: explode subject heading; mp: multipurpose.

trade health for them. Additional concerns were raised about whether the wording of levels of the EQ-5D and SF-6D fully identified the context of living with arthritis. On the mobility domain, for example, the levels do not distinguish between walking on flat ground and stairs or hills, and could fail to accurately represent the variability in symptoms on a day-to-day basis. Neither was it clear whether assistive devices, such as specialized footwear or gait aids, should be considered when describing health states.

Three potential ways to incorporate additional subdomains relevant to rheumatology into the QALY were discussed during the OMERACT working group. The first was to use an alternative generic PROM that is not currently being widely used, such as the Computerized Adaptive Tool-5 Domains[23]. A second approach was to modify an existing measure (e.g., EQ-5D) with "bolt-on" subdomain(s) that are currently missed, which have been done for sleep and vision[24,25]. The third approach was to generate a set of societal weights for an existing condition-specific PROM. While this can be done through "mapping," weights from a population survey can provide more accurate estimates[26]. Working group participants agreed that there is currently insufficient information to recommend one approach over another; however, there was a desire to undertake preliminary work to understand the value and feasibility of these approaches in rheumatology.

DISCUSSION

The QALY working group session at OMERACT 13 analyzed whether the instruments used to generate QALY in rheumatology are a good match with the domain. Through a scoping review and interactive "eyeball test" exercise, participants identified relevant subdomains of the ASAS-HI, which may be missed by the 2 most widely used PROM in rheumatologic trials (EQ-5D and SF-6D).

In the discussion that followed, OMERACT participants also expressed concerns about whether process and non-health outcomes can and should be incorporated into the QALY. There is evidence that rheumatology patients value process and non-health outcomes. For example, patients with rheumatoid arthritis have been shown to value autonomy and participation in shared decision making[27], mode of administration[28], ongoing disease management[29], how informed they are about the treatment[29], and their experience of care[30], including access to care and attitude of the provider.

Agencies that make reimbursement decisions recommend

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Table 1. The ASAS-HI domains according to the EQ-5D and SF-6D. Participants indicated which domains of the EQ-5D and SF-6D matched the questions of the ASAS-HI and how adequately they covered those questions: directly (++), indirectly (+), not (–), or unclearly (?). The results shown were the most common responses from the participants.

ASAS-HI Domain	ASAS-HI Item Description	EQ-5D		SF-6D	
		Most Relevant Domain	Coverage	Most Relevant Domain	Coverage
Pain	Pain sometimes disrupts my normal activities	Pain/discomfort	++	Pain	++
Maintaining a body position	I find it hard to stand for long	Pain/discomfort	+	Physical functioning	+
Moving around	I have problems running	Mobility	+	Physical functioning	+
Toileting	I have problems using toilet facilities	Self-care	++	Social functioning	+
Energy and drive	I am often exhausted	Usual activities	?	Vitality	++
Motivation	I am less motivated to do anything that requires physical effort	Anxiety/depression	+	Vitality, physical functioning	+
Sexual functions	I have lost interest in sex	Usual activities, anxiety/depression	?	Role limitation, mental health	?
Driving	I have difficulty operating the pedals in my car	Mobility, usual activities	+	Physical functioning	+
Community life	I am finding it hard to make contact with people	Usual activities	+	Social functioning	++
Moving around	I am not able to walk outdoors on flat ground	Mobility	++	Physical functioning	++
Handling stress	I find it hard to concentrate	Anxiety/depression	+	Mental health, vitality	+
Recreation and leisure	I am restricted in traveling because of my mobility	Mobility	++	Physical functioning	+
Emotional functions	I often get frustrated	Anxiety/depression	?	Mental health	+
Washing oneself	I find it difficult to wash my hair	Self-care	++	Physical functioning	+
Economic self-sufficiency	I have experienced financial changes because of my rheumatic disease	—	–	–	–
Sleep	I sleep badly at night	Usual activities	–	Vitality	+
Handling stress	I cannot overcome my difficulties	Anxiety/depression	+	Mental health	+

ASAS-HI: Assessment of SpondyloArthritis Health Index; SF-6D: Short Form 6 Dimensions.

the use of generic PROM to generate QALY[15,31]; however, they have also acknowledged in some cases that generic PROM may not be sufficiently sensitive to detect changes in HRQOL. In addition, some policymakers have expressed a desire to consider aspects of convenience of treatment in their decisions[32]. Thus, efforts are being made across disease areas, such as cancer, to incorporate additional health, non-health, and process subdomains into the QALY[33,34]. Participants at the QALY working group session expressed a desire for similar activities to be analyzed for rheumatic conditions. Based on the activities and discussion at OMERACT 13, three priorities for research were identified:

1. To understand to what extent the EQ-5D and SF-6D identify subdomains of HRQOL relevant to patients with different rheumatic conditions, and how their inclusion changes population weights for health states.
2. To analyze whether aspects of process or non-health outcomes matter to patients, and if so, see whether patients are willing to trade off these potential benefits against health outcomes.
3. To identify which approaches to incorporating additional (or different) subdomains into the calculation of the QALY are being undertaken in different disease areas.

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