



Patient Reported Outcome Measures (PROMs) in myeloma: are they fit for the future?

Full research report

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EXECUTIVE SUMMARY

PROMs are patient reported outcome data collection tools. They support the measurement of constructs (such as quality of life) from a patient perspective and may be used in both clinical practice and research. There are two types of PROM: disease-specific and generic. Disease-specific PROMs are tailored to the symptoms and impact of a condition. Generic PROMs consider more universal aspects of a condition or illness.

This report presents a literature review on the current landscape of PROMs in myeloma. It reports findings from Myeloma UK research with patients, clinicians, researchers, and pharmaceutical industry representatives on the challenges of PROM use in myeloma today and considers how future use of PROMs can be enhanced.

Our findings suggest that the principle of collecting and using patient-reported outcome data through PROMs is highly valued. However, in practice using, scoring, interpreting, and recording such data is complex. Our research found that PROMs are rarely used in myeloma clinical practice, primarily due to a lack of training and support for PROM use.

Although PROMs are being used more routinely in research, patients often struggle to complete the PROM questionnaires without support. Furthermore, we found that stakeholders and patients shared concerns about how suitable the PROMs used in the research setting are to capture outcomes that matter most to myeloma patients.

Our research encompassed focus groups with patients, all of whom were unfamiliar with PROMs. In their review of a selection of PROMs, patients found the language used in many tools to be vague and confusing, and some of the questions asked particularly within generic tools to be unreflective of myeloma experiences.

Patients wanted PROMs to reflect their experience of illness and to see clear explanation around how to complete the questions. The MyPOS and FACT-G were preferred over shorter, generic tools such as the EQ-5D-5L. This is unsurprising due to the MyPOS being developed specifically for myeloma patients.

Additionally, many patients found being asked questions about their psychosocial wellbeing validating and said that answering questions around sex, family, and other psychosocial concerns was helpful. Patients said that answering formal questions as part of a PROM could help them bring concerns over to their healthcare professional (HCP) in the future.

Although it is worrying that patient reported outcome data is not being systematically collected and recorded, it is clear that resourcing is a major challenge. If we are serious about collecting and acting on patient reported data we need to invest in training and infrastructure and create an environment which both encourages and facilitates the more effective use of PROMs in practice.

RECOMMENDATIONS

- There is a need for increased diversity in the testing phase of future PROMs. This would ensure new PROMs designed for use in myeloma are reflective of patients' differing backgrounds and experiences. Related to this is the need to engage myeloma patients early in the PROMs development process in order to capture meaningful data that are relevant to patients
- Researchers should systematically collect PROM data in addition to clinical data in myeloma clinical studies. PROM data can have an important function in evaluating treatment effectiveness in clinical trials and may subsequently inform decisions in the clinical setting. Trial sponsors should be encouraged to provide additional resource for the collection of PROM data
- Researchers, HCPs, and those involved in funding outcomes-based research should drive a shift away from relying on generic PROMs such as the EQ-5D-5L move towards condition-specific PROMs (such as the MyPOS in myeloma) in both clinical practice and research settings
- Regulatory and health technology assessment bodies should encourage and drive the collection of quality of life and health related quality of life data to support regulatory approval and reimbursement processes of myeloma treatments
- PROMs developers should ensure there is easily accessible guidance and training for individual PROMs. This should focus on how to select, use, interpret and implement PROMs
- A comprehensive online bank or database of myeloma PROMs should be developed to support tool selection and access. This database would be accessible, easy to use, and contain detail on tools and what constructs they measure. Such a facility could be developed by research organisations or pharmaceutical organisations in partnership with the third sector
- Investment in infrastructure and technology is necessary to support PROM use in routine clinical practice and research. This would support the routine collection of data which could be used both to improve understanding of individual patients' experiences and allow researchers access to existing data collected in a naturalistic environment
- NHS senior management teams should encourage HCPs and researchers to use currently available and validated PROMs (for example, the MyPOS in conjunction with others). Training and resources need to be made available so that HCPs and researchers feel comfortable using the tools and can act on data collected. Increased use and experience of acting on PROM data may further encourage patient trust in PROMs

INTRODUCTION

Myeloma is the second most common blood cancer (Jenal et al, 2007). Although sensitive to treatments such as chemotherapy, it remains incurable. Characteristics include lytic bone lesions, compression fractures, hypercalcemia, anaemia, and renal dysfunction (Sherman et al, 2008). Myeloma patients experience may experience numerous symptoms including pain, fatigue, and disrupted role functioning as well as side-effects from treatments.

Treatment advances in myeloma have increased survival from months to years for many patients (Osborne et al, 2012). However, although myeloma patients are living longer, they are also living with symptoms and treatment side-effects and concerns about their families and futures. Research suggests that myeloma patients have significant unmet supportive care needs (Molassiotis et al, 2011) and a higher burden of disease (Johnson et al, 2009) than many other cancers.

There is thus a need to understand the impact that myeloma has on individuals and the lived experience of the condition, so that outcomes in myeloma can be improved. One way to achieve this is for healthcare professionals (HCPs) and researchers to collect PRO (patient reported outcome) data using PROMs (patient reported outcome measures).

PROMs are carefully developed and tested questionnaires that capture patient reported outcomes. They are measurements “based on a report that comes directly from the patient about the status of a patient’s condition without amendment or interpretation of the patient’s response by a clinician or anyone else” (Salek, 2013). The use of a PROM is recommended when measuring a concept that is best known to the patient or best measured from the patient’s perspective (Salek, 2013). PROMs are important because, amongst other things, they assist clinicians to provide better and more patient-centred care and provide data for evaluating treatments, practices, and policies.

PROMs are commonly used to measure endpoints in clinical trials and as part of clinical practice and can measure a variety of constructs. Broadly there are two types of PROM: disease specific and generic. Disease specific PROMs are tailored to the symptoms and impact of a condition. Generic PROMs consider more universal aspects of a condition or illness.

Quality of life (QoL) and health related quality of life (HRQoL) are two important examples of constructs measured by PROMs. HRQoL is defined as the capacity to perform the usual daily activities for a person’s age and major social role. Thus, deviation from normalcy results in a reduced HRQoL (Doward and McKenna, 2004).

QoL, although similar, is a reflection of the way in which patients perceive and react to their health status and to other nonmedical aspects of their lives. QoL assessment tools explore whether or not an individual is able to fulfil his or her

needs (Doward and Mckenna, 2004). The primary reason for using QoL measures in clinical practice is to ensure that treatment plans and evaluations focus on the patient rather than the disease (Higginson and Carr, 2001).

Other tools focus on measuring the physical impact of illness, such as pain. Although many PROMs measure specific outcomes within specific conditions, other tools are multidimensional, looking at various constructs across a range of conditions.

PROMs are well used in some therapeutic areas, such as in hip or knee replacement surgeries. It is a requirement for organisations performing NHS-funded hip replacement, knee replacement, varicose vein or groin hernia surgery to collect PROMs data and submit that data to the Health and Social Care Information Centre. However, less is understood about the ways that PROMs should be used in myeloma. There is additionally little published literature on what tools should be used to assess constructs like QoL and HRQoL, and how data emerging from such assessment should be used.

This report therefore examines the published literature around PROMs in myeloma; reports on findings from in-depth consultation with expert stakeholders and patients on the future of PROMs in myeloma.

SECTION ONE: A REVIEW OF PROMS IN MYELOMA

This review examines the literature and explores the primary issues with PROM use in myeloma. It looks at what different PROMs exist and the different constructs they measure.

A targeted literature search was performed using the following databases: PubMed; PyschInfo; Web of Science; and Medline. The keywords searched were: myeloma AND PRO/M; patient reported outcomes; patient questionnaires; quality of life tools. Relevant articles were assessed for quality of evidence and included in the review. Questions put to the literature were:

1. What PROMs are being used in myeloma?
2. How are current PROMs currently perceived?
3. What guides the selection of PROMs in research and clinical practice?
4. What challenges and issues are there around current use?

What PROMs are used in myeloma?

Osborne et al (2012) conducted a systematic review of HRQoL tools in myeloma. These researchers found that the 'EORTC (European Organization for Research and Treatment of Cancer) - QLQ-C30' and its myeloma modules 'MY20 and MY24' were the most comprehensively validated instruments for assessing HRQoL in myeloma patients.

Other tools identified by Osborne et al (2012) were the FACT (Functional Assessment of Cancer Therapy) – An (anaemia); EORTC-QLQ-HDC19 (high dose chemotherapy module); FACT-BMT (bone marrow transplantation); SF-36 (medical outcome survey); SF-12 (medical outcome survey, shortened form); SEIQoL-DW (schedule for evaluation of individual quality of life); EQ-5D-5L; 15D; the Life ingredient profile; and the Quality of life index. Osborne et al (2012) found that such tools were mostly being used in research rather than in clinical practice. Some tools had also been developed primarily for research purposes.

Kvam et al (2009) additionally reviewed PROMs assessing HRQoL in randomised controlled trials (RCTs) in myeloma. These researchers identified 12 different instruments used for measurement of HRQoL in myeloma. Some tools identified in Osborne's (2012) examination of HRQoL appeared in Kyam's (2009) review.

Kyam et al (2009) found that seven of the 15 studies they identified used the EORTC QLQ-C30 questionnaire. This reflects the perceived suitability of the EORTC. Other PROMs not identified by Osborne et al (2012), but included in Kyam's (2009) review include: Spitzer's quality of life index (in Berenson et al, 1996); NHP (Nottingham Health Profile tool) and CLAS (Linear Analog Scale Assessment), (in Damaco et al, 2001); FACT (Functional Assessment of Cancer Therapy) - fatigue (in Hedenus et al, 2003); Multiple choice + global HRQoL (in Joshua et al, 1997); and the EORTC QLQ-C30 and FACT (in Lee et al, 2008).

Shaw et al (2016) reviewed the literature, looking at PROMs for assessing hematopoietic cell transplantation (HCT). Although not myeloma-specific, many of the PROMs in the review are relevant due to the high number of patients who receive HCT.

Shaw et al (2016) reviewed 114 studies, finding there to be 28 multi-item PROM measures used in two or more studies involving the HCT population. The measures most frequently used were the FACT-BMT (bone marrow transplant) in 28 studies, the EORTC QLQ-C30 in 26 studies, and the SF-36 in 26 studies. Only two other measures were used in 45 studies: the Sickness Impact Profile (SIP) and the Hospital Anxiety and Depression Scale (HADS). Such a review reflects what other studies have found: that the EORTC tool set is most frequently used within this population.

As discussed, Shaw's (2016) paper does not specify which PROMs were used in myeloma, but the set of tools identified within the paper is a useful insight into the domains measured within the population regardless: FACT-BMT; EORTC QLQ-C30; SF-36; Chronic GvHD Symptom Scale; COH (City of Hope) – QOL (BMT); FACT-G; POMS (SF) (profile of mood state) psychology; SLDS-C (BMT)-Satisfaction with Life, Domains Scale for Cancer; SF-12 ; Center for Epidemiological Studies (CES)-D (Depression); FAC-IT (Spiritual); BDI (Beck's Depression Inventory); RSCL (Rotterdam Symptom Checklist); Spielberger State Anxiety Scale; Cancer Rehabilitation Evaluation System (CARES-SF); NHP (Nottingham Health Profile); SDS (Symptom Distress Scale); HAP (Human Activity Profile); EORTC QLQ-HDC29 Piper Fatigue Scale; and the Coping Responses Inventory.

Allart et al (2013) also reviewed the literature, looking at PROMs used in haematological cancer. These researchers focused on QoL. They found papers using the following PROMs across haematology: EORTC-QLQ-C30; HADS; QHQ (anxiety); SCL-90-R (depression); HLoC self-esteem); SES; QoL-CS (personality); PMI (pain measurement index); SF-36; SEIQoL (general quality of life) ; MACS (mental adjustment to cancer); SEIQoL-DW (quality of life, short form) ; SF12; SOC-S; VAS (visual analogue scale); QoL-CS (quality of life, cancer survivors); FACIT-Sp-12-C (spiritual wellbeing); FACIT-G (functional assessment of cancer therapy general); and the EQ-5D-5L. Allart et al's (2013) review provides insight into the range of issues affecting myeloma patients and the tools available to measure them.

Sonnefeld et al (2013) also looked at HRQoL in myeloma. Aside from the previously mentioned tools, this review found use of the QLQ-CIPN20 (patient-reported chemotherapy-induced peripheral neuropathy); the FACT-Multiple

myeloma (disease-specific); the FACT-NTx (similar to the FACIT – Fatigue but with additional neurotoxicity parameters); and the EQ-5D-5L (a standardised generic HRQoL questionnaire).

Studies using PROMs outside of the tools already discussed are: Sherman et al (2008) using the Impact of events scale (cancer – specific stress) and the Satisfaction with life scale (overall life satisfaction); Wang et al (2015) using the MD Anderson Symptom Inventory MM module. This validated PROM measures symptom severity and the impact of symptoms on daily functioning. This tool has been used to assess various constructs in myeloma research; McDonald et al (2008) used the Roland-Morris Disability Questionnaire and the Visual Analog Scales for 'pain at rest' and 'pain with activity' to assess experiences vertebroplasty in myeloma patients; Kim et al (2016) used the Patient-Generated Subjective Global Assessment (PG-SGA) which measures weight loss, food intake, clinical symptoms, activities, and function to examine weight loss and malnutrition in myeloma patients; Tuchman et al (2015) used the Centre for Epidemiological Studies Depression Scale, the Pittsburgh Sleep inventory and the Brief pain inventory to measure depression, sleep and pain in their study of myeloma.

Finally, the European Haematology Association's scientific working group identify five quality of life and symptom assessment measures for use in myeloma. Their recommendations (EORTC – QLQ – MY20; the brief pain inventory; the McGill Pain questionnaire (short form); the Memorial Pain Assessment Card; and the comprehensive symptom profile – multiple myeloma) reflect the literature around PROMs in myeloma.

A myeloma-specific tool, which has recently been developed is the MyPOS. The MyPOS is a brief, comprehensive and acceptable tool that is reliable and valid on psychometric testing (Osborne et al, 2015). The MyPOS is ready to be used in both research and clinical decision making in the routine care of myeloma patients.

PROM tool and item banks

Aside from validated PROMs, there are opportunities for researchers and HCPs to create their own measures, using online databases to form multi-item measures.

The PROMIS (Patient Reported Outcomes Measurement Information System) is one such collection of PROM items. HCPs and researchers can tailor the constructs they wish to measure using PROMIS items, thus creating an adapted measure suitable for the construct they wish to measure.

Another bank of items is the National Cancer Institute's (NCI) PROM-CTCAE toolbox. The PROM-CTCAE is an online library comprising 124 items that assess different attributes (e.g. presence, frequency, severity, or interference with usual or daily activities). Wood et al (2013) used this system to select items for their study into physical and mental HRQoL in myeloma participants.

Such systems and online tools perhaps offer insight into the future of PROMs, showing how collections and online depositories are making it easier for patients, HCPs, and patients to use PROMs and record outcomes.

How are current PROMs in myeloma perceived?

Our review suggests that there are instruments available (such as the EORTC QLQ-C30 and QLQ-MY20) that capture symptom and impact domains in myeloma, with researchers such as Wisloff et al (2003) demonstrating that the QLQ-C30 is a reliable and valid instrument for the measurement of quality of life in patients with myeloma. However, others contest such tools as appropriate in all situations.

Osborne et al (2015) are amongst those who do not see the EORTC tools as appropriate in all situations. These researchers suggest that the EORTC-QLQ-C30 and its MY20 module were designed as research tools, with much of their validation taking place using myeloma patients recruited into clinical trials. Patients in trials are likely to be medically fitter than the average patient. This means that the populations that the PROMs were tested with were not necessarily clinically representative and as such the EORTC questionnaires may not always be well suited to clinical use (Osborne et al, 2015).

Wagner et al (2012) in a paper detailing the content validity of the FACT-MM (Functional Assessment of Cancer Therapy – myeloma) report a similar story. These researchers write that in developing the FACT-MM they recruited a small convenience sample from the USA. Additionally, patients who participated in the study were younger and higher-functioning than the general myeloma population. Thirty-eight percent of the sample were in remission and not receiving treatment and most were white. Thus, such participants may have under-reported disease-related symptoms and not fully represent the myeloma population.

Osborne et al's earlier (2013) study in QoL in myeloma also add that there is a tension in the design of questionnaires in the field of myeloma. These researchers write that, "existing questionnaires may not capture all that is important to QoL from the perspective of myeloma patients, and often miss items on health service factors or sexual function that are important to patients... [thus] further work is needed to develop or refine existing QoL tools for use in the clinical care of people with multiple myeloma" (Osborne et al, 2013, 2405). So, although tools exist, there is a need for further refinement.

The European Medicines Agency's (EMA) 2014 guidance paper on patient-reported outcome measures in oncology supports the need for the refinement of specialist PROMs for myeloma. The EMA document suggests that 'off-the-shelf' questionnaires may not be appropriate or specific enough to measure important outcomes in rare conditions, and that additional PROMs are required for accurate and complete assessment.

Trask et al (2013) presented a qualitative comparison of the EORTC QLQ-C30 and MY-20, FACT-MM, and MDASI-MM in relapsed/refractory myeloma patients. Findings from the study suggest that the EORTC QLQ-C30 and MY-20 capture the majority of symptoms reported by relapsed/refractory myeloma patients. Trask et al (2013) did however find that a gap in conceptual coverage was evident, which suggests that there remains room for improvement in assessing the experience of this patient population.

In clinical trials, Hamaker et al (2013) examined whether the outcome measures used in clinical trials in patients with haematological malignancies (including 11 myeloma trials) were relevant to elderly patient populations. The research was conducted in response to cancer research organisations and research cooperative groups urging for the development of cancer trials that address outcome measures most relevant to older patients. Hamaker et al (2013) argue that historically, older patients have been excluded from clinical trials. The researchers write that only 9% of patients enrolled in FDA registration trials were older than 75 years of age, whereas 31% of patients with cancer fall within that age group.

Hamaker et al (2013) found that progression-free survival or event-free survival was the most studied outcome, addressed in 94% of studies. Quality of life however, was only included as a primary or secondary objective in 24% of studies, while functional outcomes and cognitive functioning were only assessed in three studies each (6%). This research concluded that in clinical trials in haematological malignancies there is a focus on cancer-related outcome measures while patient-related factors such as quality of life or functional capacities are rarely included.

What guides the selection of PROMs in research and clinical practice?

Rahimi et al (2010), in their systematic review of PROM use in cardiovascular trials found that despite the continued rise in reporting of patient reported outcomes in cardiovascular trials, such data were still underused. The researchers conclude by reiterating the need for selection of more patient focused outcomes. However, what is less clear is how PROMs should be selected and for which circumstances.

Although it is perhaps obvious that PROMs should be selected based on the strength of their measurement properties (i.e., reliability, validity and responsiveness) in the population of interest, and on other key aspects including acceptability and interpretability, this may not always be the driver of PROM selection in practice.

Cella et al (2012) write that the selection of PROMs depends how well-documented the evidence of a PROM is to reflect certain measurement properties. These researchers add that, “measurement science relies on an iterative, accumulating body of evidence examining key properties in different contexts. Thus, it is the weight of the evidence that informs the evaluation of the appropriateness of a PROM. Older PROMs will have the benefit of having more evidence than more recent PROMs; yet the newer PROMs tend to have improved basic measurement properties that warrant attention” (Cella et al, 2012).

Luckett and King (2010) in their paper on choosing patient-reported outcome measures for cancer additionally reference the importance of peer review and validation but also provide more practical guidance. The guiding principles that Luckett and King (2010) suggest for choosing PROMs are to: “(1) always consider PROMs early in the design process within the context of other methodological decisions; (2) choose a primary PROM that is as proximal to the cancer and/or its treatment as will add to knowledge and inform practice; (3) identify candidate PROMs primarily on the grounds of scaling and content” (Luckett and King, 2010, 3149). This is a useful breakdown of the process of selecting a PROM for a cancer research study and these principles reflect other guidance which suggests that PROMs should be chosen on what they measure, on their reliability and validity constructs, and on their relevance to the study in question.

With respect to clinical development, a 2014 reflection paper on the use of PROM measures in oncology studies by the EMA provides rationale for including PROM assessment in the clinical development programme for oncology medicinal products. Authors of the report suggest that PROMs should be incorporated into studies if they can: provide data on patient functioning and well-being; add information on the clinical benefit of a therapy by complementing efficacy and safety data with patient-reported evaluation; assess the agreement between clinical reported endpoints and patient-reported endpoints; and provide information to facilitate more accurate future patient-HCP communication in terms of patients’ quality of life and the burden of treatment-related morbidities. The EMA report recommends that if a PROM can add this kind of data to the assessment of an oncological medicinal product then it merits incorporation into the clinical development process.

Although the EMA is not explicitly providing guidance on PROM selection here, the questions they outline may help clinical researchers choose the most relevant tool for the purpose of their study.

In addition to guidance from the literature, there are a number of resources available to aid selection of validated PROMs. The International Society for Quality of Life Research (ISOQOL) has published recommendations on the agreed minimum measurement property standards for PROMs. The Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) group have also produced a checklist for the evaluation of PROM measurement properties. Both sets of guidelines focus on constructs such as content validity, cross cultural validity, and interpretability.

What are the challenges of using PROMs in myeloma?

Interpretation and scoring

A related but separate issue to that of whether existing PROMs are fit for purpose is that of interpretation of PROM scores. Shaw et al (2016) write that little is known about how clinicians interpret or use PROM results from research studies in assessing their patients and recommending treatments. Issues with interpreting PROM results could mean that HCPs are perhaps not understanding, as fully as possible, what their patients' PRO data mean, due to misinterpretation of scores. Bausewein et al (2011), agree suggesting that a clear roadmap or uniform approach to measuring outcomes in clinical care and research is lacking. As a consequence, there are differences in the interpretation of results of studies.

Higginson and Carr (2001) suggest that part of the difficulty is that scores from quality of life measures in studies are often presented as means (averages). While this is useful in research, i.e. in testing one treatment against another, it is of less value in clinical practice. Higginson and Carr (2001) ask, at what point is a problem considered severe? Is it when the PROM score is above the mean? Or when scores are in the top quarter? Answers to such questions are difficult to answer and without clearer scoring guides, HCPs are perhaps less likely to use particular tools. There is little published literature surrounding this issue, but is explored later in this report in interviews with stakeholders.

Training

One way around improving interpretation is through training. Higginson and Carr (2001) suggest that training in the use of quality of life measures is something that is generally lacking in health education. Bausewein et al (2011) agree, finding that a lack of training and guidance was one of the main reasons HCPs in their study gave for not using PROMs. Although Bausewein et al's (2011) paper was not myeloma-specific, it is possible that reasons around the non-use of PROMs in palliative care apply in myeloma.

Access

Another issue in the accessibility of PROMs is around software and copyright barriers. Doward et al (2010) write that PROM selection is occasionally restricted by issues of availability. Bausewein's (2011) study additionally found that access was an issue, suggesting that some reasons for non-PROM use in clinical practice are due to registration barriers, language restrictions (e.g. tools not being translated), and cost constraints (e.g. fees for tools). Shaw et al (2016) add that in some cases, resulting PROM scores cannot be generated without access to paid-for scoring algorithms.

Additionally, Doward et al (2010) write that decisions around PROMs are based on familiarity rather than considerations of instrument relevance or quality.

The issue of PROM selection being based on familiarity rather than quality is not widely discussed. However, it raises a question over whether the frequent use of popular tools is partly due to proximity or familiarity with the tools than suitability.

Relevance and appropriateness

Related to issues around access are concerns around the relevance of PROMs. Osborne et al (2012) suggest that there are few studies that fully characterise the meaning of QoL from the perspective of myeloma patients.

Doward (2010), writing on PROMs in general, suggests that this issue may not be specific to myeloma. Doward (2010) explains that an important issue is the number of poorly designed PROMs, which are incapable of identifying changes in the construct measured in very mild or very severe patients (Doward et al, 2010). PROMs which are highly relevant to a patient group will maximise the quality of the data collected. However, irrelevant questionnaire content can alienate respondents, making them feel that their views are not fully appreciated.

In addition to alienating respondents in clinical practice, Bausewein et al (2011) suggest that in research, some studies using PROMs fail because researchers have used inappropriate measures without adequate responsiveness to change. Doward (2010) adds that poorly designed PROMs can lead to missing data; respondents may fail to answer questionnaires they consider irrelevant and disaffected respondents may take less care completing the questionnaire and miss additional questions in error. Generic scales, by definition, contain some questions that are irrelevant to specific patient groups and miss areas of particular importance (Doward et al, 2010).

Although researchers have identified problems with existing PROMs in myeloma, there is little other discussion of relevance around PROMs in myeloma, perhaps because of the few myeloma-specific tools available.

Literacy, language, and understanding

Cella et al (2012) writing on literacy, suggest that data collected from PROMs are only valid if the participants in a study can understand what is asked of them and can provide a response that reflects their experiences or perspectives. It is therefore important that developers of PROMs make sure the questions and response options are clear and easy to understand. Cella et al (2012) add that studies may require sampling based on race and ethnicity that reflects the prevalence of the condition in the study target population. PROMs therefore also need to be sensitive and appropriate across cultures.

Design: Closed vs open questions

One way in which some PROMs may capture missing issues is to incorporate free text space. Hajdarevic (2016), writing on prostate cancer, asks whether closed-ended questions in such questionnaires sufficiently capture patients' experiences. Their study looking at closed versus open questions in patient reported questionnaires found that participants who completed PROMs wished to say more than a response scale allowed. Foddy (1993) too, writes that research participants appreciate the opportunity to express themselves in their own words rather than choosing from a list of options.

Some tools incorporate free text space. They ask patients to write down their main concerns, rather than choosing from a selection of issues. This space intends to allow patients to express their experiences more freely.

However, there may be problems with free text in practice. Hajdarevic (2016) writes that open-ended questions can be expensive to produce and to score; they are not standardised; and there may be technical constraints in relation to handwriting, grammar, long words, and the amount of space available to write in.

New condition-specific PROMs

In response to the call for more specific and comprehensive PROMs in myeloma, UK researchers at King's College, London (Osborne et al, 2014) have developed and validated a myeloma-specific QoL tool, called the MyPOS. This tool has been developed specifically for use in clinical practice as opposed to other tools designed primarily for use in research settings. The MyPOS was developed to cover a wide range of areas important to patients that were found to be missing from previous PROMs. This tool is available and ready for implementation into clinical practice.

The European Hematological Association's scientific working group (EHA SWG) is also in the process of developing and validating a PROM for patients with haematological malignancies in clinical practice (project led by Dr Pushpendra Goswami, University of Hertfordshire). This tool aims to improve estimation of patients' symptom burden and other QoL issues, make sure these are addressed, and support understanding of these constructs in the clinic.

Conclusions

This narrative review shows that there are tools which work to assess patient outcomes in myeloma. However, there is limited information available on how PROMs are used in clinical practice and how effective they are in both clinical practice and research settings. It appears from the literature that there is a lack of consistency in selection and use of PROMs, and it is not clear what the drivers are from the published literature alone. The next stage of this project set out to develop our understanding of the issues highlighted by the literature.

SECTION TWO: STAKEHOLDER PERSPECTIVES ON PROMS IN MYELOMA

Fifteen stakeholders (clinicians, research nurses, researchers, pharmaceutical representatives, and those involved in clinical trials), selected for their expertise in PROMs in myeloma and cancer were invited to participate in this project. Alongside an invitation to participate, stakeholders were sent a discussion paper (see Appendix A) highlighting some of the issues around PROMs emerging from the literature.

The discussion paper asked participants to think about: the impact of PROMs; the advantages and disadvantages of generic and specific PROMs; PROM selection; and what the future of PROMs might look like. After being given two weeks to read the discussion papers, stakeholders were invited to interview.

Stakeholder interviews lasted around 30 minutes and were recorded and transcribed. Interviews were analysed using thematic analysis (Braun and Clarke, 2006) in NVivo. Thematic analysis is a method for identifying, analysing, and reporting patterns (themes) within data.

The rest of this chapter reports on the findings of this thematic analysis of stakeholder interviews.

The value of PROMs in providing a patient perspective

PROMs were perceived by many stakeholders to provide a useful patient perspective. There was consensus that PROMs give patients a chance to express their feelings and let HCPs and researchers know how they felt, and that this may not happen to the same degree without the tools. There was also a sense from some stakeholders that HCPs are not always a good judge of what is important in the lives of individual patients and how treatment and care might be affecting them and their families.

“Because I think that a lot of the research has shown that, actually, health professionals are not always a good gauge of what’s important in the lives of the individual or how something might be affecting them. So just a simple thing like neuropathy, if they have peripheral neuropathy and they can’t get dressed in the morning then that has massive implications on their care and who has to be involved with their care. It may seem quite small because they’re not having any other side-effects. So the treatment’s continuing and - so I’m not sure, sometimes, we’re always a good gauge of what concerns an individual has.”

– Nurse Researcher

“I think patients often feel that we don’t give them enough chance to actually express how they are. I think if they can actually - and that sometimes consultations can be very one-sided - so I think if they’ve actually got the opportunity within whatever outcome measure it is, to report how they’re feeling, and the symptoms they’re experiencing, and what their worries and concerns are, then I think they would find it beneficial.”

– Health Psychologist

It was also acknowledged that PROM questionnaires can work as reflective tools. One stakeholder reported that questions asked as part of the wider questionnaire can facilitate conversations that patients might not otherwise have with their HCP. This is important as without being explicitly asked about constructs such as emotional wellbeing, patients may not bring their concerns to those involved in their care. PROMs perhaps provide a platform for these conversations.

“What patients report to me is that they are asked questions through questionnaires or patient reported outcome measures of things they’ve not thought of before or get them to think about emotions, feelings, wellbeing aspects of that that they’ve never really considered. The outcome measures often act as a source of reflection for them.”

– Researcher

Those involved in clinical trials and health technology appraisals appraisals considered PROMs to be important for highlighting in a systematic way, patient preferences and experiences of side-effects. One researcher gave the example of how PROMs can provide insight as to why patients drop out of trials (e.g. intolerable side-effects) and why collecting this kind information is important.

“I think it’s particularly important, because it doesn’t just talk about how well patients are, whether they’re able to go back to work and so forth. But also if you - there have been studies in the past about, for instance, assessing patient preferences and side-effects of treatment, and what they found particularly difficult to cope with during the treatment. That may relate directly to adherence to a particular treatment. So if you’re not gathering this information, you just see that people are dropping off trials because they could not either tolerate or it just not for them for various reasons. You can really understand why that is. If a drug is making someone’s life unbearable, then they’re unlikely to be willing to take it.”

– Researcher

Another researcher discussed the merits of PROM data in policy making, referring to patient reported data as having the biggest potential impact on health policy.

“I think it has - I think patient reported outcome measures have the biggest impacts of any kind of data collection actually. They can influence policy most. If you have statistics and just percentages even, I think they’re very powerful in being able to change practice and policy. That’s not to say they’re always the best source of data but I think they probably have the most impact on the healthcare system. If you have a very clear statistic that this patient group has a certain dysfunction or whatever, that can be a very powerful thing and a very powerful tool that researchers and policy makers can use.”

– Health Psychologist

PROMs are thus perceived to be helpful in supporting understanding of patient experience and retention in trials and at a policy level. PROM data, if collected systematically, can be a powerful tool in influencing change.

Stakeholders agreed that PROMs are useful and necessary both in clinical practice and in the research and policy settings. However, there was acknowledgement that these tools are not perfect and that there is room for improvement.

Barriers to using PROMs in myeloma

HCP familiarity with using and interpreting PROMs

The first barrier to the use and application of PROMs within both clinical practice and research was whether PROMs are well understood enough to be helpful. There was a general feeling amongst some stakeholders that perhaps PROMs are used tokenistically and without an understanding of how they could add any real value to the assessment or care of patients.

“I think there is a common helplessness regarding what value these questionnaires really bring and whether the burden they place on the patient but also the healthcare professionals translates into ‘added value’.”

– Researcher

Additionally, there was concern that clinicians and other HCPs are not using the appropriate tools to measure the construct the HCP wishes to know more about.

“Sometimes people just pull out a questionnaire and say, right do that when they think of quality of life. But actually it’s not always quality of life questionnaires they’ve chosen or it’s not really measuring what they want to measure [in the end]. I think that is partly the same point that I made in the last question about not really understanding the science of psychometrics.”

– Clinician

There was additional concern from stakeholders that HCPs may not be familiar with how to instruct and help patients with the completion of PROMs and subsequently, how to interpret results.

“What does a score of 20 on a questionnaire really mean, how does this translate into clinical action and what supportive care interventions can be offered to help ameliorate this symptom? Equally, if a change of 5 points after these interventions is seen on the questionnaire, does this mean that the patient has improved so that the intervention can be considered a success?”

– Researcher

Although these concerns may be due to a lack of stakeholder knowledge of the range of tools available and scoring and interpretation skills, there are other explanations that provide us with insight into why using and interpreting PROMs might be challenging.

One researcher stated that she would like to see PROMs that provide scores that easily show whether an emerging score is worrisome, whether a clinical action needs to be taken, and what that action could be. She proposed that guidance around how to interpret and act on PROM scores could provide clinicians and other HCPs with a tangible reason for conducting a PROM questionnaire and a way of using data from the tool.

Interviews therefore supported the philosophy of PROMs but researchers and HCPs wanted more in the way of explanation and guidance for use.

“I’m happy with the PROMs that are available at the moment, I think it’s not a matter of improving them, it’s a matter of improving how to use them. That’s my personal opinion.”

– Clinician

PROM burden and relevance to patients

In addition to PROMs being difficult to use by HCPs due to scoring and interpretation issues, was the perception that PROMs can be burdensome to patients. Stakeholders spoke about some patients taking several hours to complete questionnaires. There was concern too that some questionnaires ask repetitive questions within complex scales which increases the burden on patients.

“I’m using a questionnaire at the minute and it has a seven point Likert scale on how true something is. So, it’s like very seldom true, seldom true, sometimes true and it’s just so complicated to present that to someone. It takes them 10 minutes just to get their head round what’s being asked in the Likert scale, never mind applying that to their experience. So, I think things like that can just be streamlined so that’s an easy thing to streamline but it’s just not thought about in the development stages because we are coming from this silo working: researchers who think ‘obviously it’s so easy’ because we get it, because we think it’s so easy.”

– Health Psychologist

Stakeholders spoke of it being necessary to sit with patients and explain questions in a clear way.

Another criticism of some PROMs was the perception that the tools are not sensitive enough to adequately capture the patient experience, in myeloma, and in cancer more generally. Stakeholders reported that some outcomes that patients actually want to discuss, for example, not being able to get on the bus due to pain, are not captured by existing PROMs.

“I am aware that certainly the EQ-5D-5L and even the updated one, the 5L, it doesn’t - it’s not sensitive enough really to capture especially the fatigue that’s associated with myeloma.”

– Researcher

“Imagine a patient going through 30-40 questions about pain using a complex scale. I’m not sure that’s really what they want to tell us.”

– Researcher

Related to this was a concern around action taken in response to PROM scores. One researcher who had previously conducted a piece of research around PROMs reported that some patients in her study questioned the clinical impact of PROMs. She reported:

“A common critique that was mentioned was the lack of clinical action taken by the clinical team in relation to high scores indicating symptom burden or problems in other areas. These participants said that they felt abandoned by their team and that completing these questionnaires was of no consequence for the issues they wanted help with being addressed.”

– Researcher

Findings from that project suggest that the reason why patients may have not acted on PROM scores was because the HCP teams did not themselves understand what to do with high scoring patients or how to make appropriate changes to care based on questionnaire outcomes. This highlights that more needs to be done to both address patient needs and, if PROMs are currently too complex, develop alternative ways to understand what issues are affecting patients with myeloma. The finding additionally highlights why PROMs are perhaps still underused within clinical practice.

More recently, however, condition specific tools have been developed which do appear to better capture the myeloma patient experience. One researcher spoke of the MyPOS as a tool that asks patients to report on more than just physical symptoms. He spoke of it as a multidimensional quality of life questionnaire that involves psychological, emotional, social, functional, and virtual impairment. This myeloma-specific tool has been validated and is ready for use in the clinical setting. The challenge is now to support HCPs working in the field to choose progressive tools such as the MyPOS over more familiar tools such as the EQ-5D-5L that have been used for many years.

Access to, familiarity with and availability of PROMs

Access, familiarity, and availability were all highlighted in the literature as barriers to the ways that PROMs are used within clinical practice and research. To develop our understanding of such barriers, stakeholders were asked what drives their selection of a PROM.

Many stakeholders suggested that tools were chosen based on what has been used and published previously.

“I think it is probably a mixture of cost and a Google presence. I would imagine that if you are starting a huge trial at a drug company you probably have experience of using certain measures - certain tools - and you would just use those again. Also I think probably a lot of people do - if you’re designing a smaller study or want to use the tool in your practice locally, you’re probably just going to do a Google search or a MEDLINE search to see what there is out there.”

– Clinician

Additionally, selections are made because of concepts such as loyalty to colleagues and career progression.

“People like the familiarity and people like using what they’ve used before and they have anecdotal evidence from their past careers and stuff of ones that they like and ones that they don’t like and will use them...there’s also obviously an issue of if you’re working for a professor or a researcher who has developed a measure, they’re going to use that measure so it gets more citations regardless of if there’s a more superior measure or if it’s lacking in validity or whatever, they would just use that one because it will help them career-wise. So, there is this conflict of interest in the choice.”

– Health Psychologist

Finally, interviews suggested that the expense of some PROMs limits their use in some universities or hospitals.

“Depending on the institution, how big they are and how well supported they are, if you have to pay for a particular PRO tool you’ll be unlikely to use it.”

– Researcher

Researchers spoke of sometimes using tools that were perhaps not entirely fit for purpose for measuring what really matters to the patients in question but rather for the purpose of comparing constructs across conditions. The EQ-5D-5L was a good example of this.

“The reason why we’re probably using it is that we can compare with other studies that have used these tools. So then can say we’ve found - we are finding the quality of life in the patient with myeloma in comparison with another population of patients with maybe another haematological cancer or maybe other cancer, or tumours, and so forth.”

– Researcher

The EQ-5D-5L is routinely used in health economic assessments of the cost-effectiveness of new treatments. Although stakeholders noted the disadvantages of the EQ-5D-5L, it has an established place within the reimbursement setting.

Influence of regulatory and HTA bodies on PROM selection

Related to this point around the reliance on established PROMs is an issue of regulatory influence.

“At the regulatory level, there is not enough impetus from the agencies like the FDA or the EMA that QoL results need to be included to drive treatment decision-making. Currently, they need to be included but data from these perspectives need not be brought together with primary endpoints. A difficult situation in the UK also arises from the fact that the EQ-5D-5L, a generic health utility index, is used to decide QALYs and therefore influence licensing and drug approval via the NHS for myeloma. It has been shown repeatedly in cancer and in myeloma that the EQ-5D-5L is too generic and crude a tool to sensitively capture change...one could therefore argue that the QoL of multiple myeloma patients is not adequately captured in these regulatory decisions.”

– Pharmaceutical Representative

Stakeholders familiar with the reimbursement setting agreed, stating that the sector’s dependence on the EQ-5D-5L is perhaps outdated, when more progressive or sensitive tools are now available which better capture constructs such as quality of life.

“I think the heavy focus that the HTA appraisal has on things like EQ-5D-5L it makes sense from an equality point of view because even though it’s not perfect it does allow you to compare across indications, but I think the - within the submission you can also present other health related quality of life measures. I just think maybe they could be given a little bit more attention than they currently are, especially in the clinical reviews of whatever treatment is under review. Because if we have good PROMs available that actually capture relevant outcomes of the population, then I do think that these need to be considered more in the clinical benefit of the drug. It goes above and beyond just response and survival.”

– Researcher

Although stakeholders wanted to see change coming from regulatory agencies such as the FDA and EMA regarding the use of PROMs in licensing and drug approval, it was acknowledged that this kind of change would be challenging.

Another problem that emerged at interview was a perception that patient views are not taken as seriously within the reimbursement setting.

Well, I think from the HTA perspective, I mean obviously there is room for the patient voice within the appraisal and NICE in particular engages with patients and invite them to meetings and invite them to submit statements as well. But sometimes there is a bit of a feeling that it's kind of - well like tokenism, do you know what I mean...I was at a NICE meeting the other day and there was a myeloma patient there who was very unemotive and very eloquent but you can see a few people just shutting down

– Pharmaceutical Representative

Although this researcher was discussing a patient voice, rather than systematically collected PROM data, there was still concern that patient perspectives have limited influence.

Research literacy

Stakeholders expressed concern over the research literacy that researchers or HCPs may assume when developing or asking patients to complete PROMs.

“I think it's - we assume that - because we've got a high research literacy as when we're - people who are familiar with questionnaires and research understand what's being asked. But if you're very naïve to research and you come in and you're given a questionnaire, you take that very seriously, the answers, and you think about things. So, it takes time and it often takes someone there, a researcher or a research nurse to explain what is being asked and how they should think about answering that question.”

– Research Nurse

This finding implies that we need to more critical of our own assumptions about what we think patients know and understand in order to work with them in understanding their needs. This does not mean that HCPs or researchers should need to explain every question or sit with a patient while they complete PROMs, but rather not assume an understanding of research methods or PROMs.

However, stakeholder interviews suggest that it is not just patients who find PROMs challenging. A clinician at interview speaks of psychometrics as the theory underpinning PROMs and scoring systems and that this technical form of measuring constructs, such as psychological wellbeing is not taught in health or medical degree programmes. Therefore, a lack of understanding around scoring and interpretation is perhaps to be expected.

“I suppose the possible reason might be the level of those designing the trials they may have a lack of familiarity with the use, a lack of familiarity with the science underpinning the use of quality of life questionnaires, because psychometrics is complicated and a science in its own right. A science quite separate actually from clinical sciences evaluating drugs...psychometrics is quite complicated and often isn't understood particularly well by even quite senior clinicians, because it's not really part of a medical training as such.”

– Clinician

One solution proposed was that rather than asking patients to complete long and potentially complex questionnaires, HCPs and researchers could ask up to three short and simple questions: what is important to you; what is your biggest concern at the moment; and what do you think we can do to try to help. These questions, although perhaps not a PROM in the traditional sense, could be a solution to those working in clinical practice who are not looking to collect large amounts of QoL data. If asked regularly, answers could build up a picture of the way that myeloma is impacting an individual.

Infrastructure and technology

Improving the infrastructure and technology around PROMs was also discussed as a way of resolving issues emerging from PROM questionnaires.

“Ideally we'd have a system where, for instance, the [PROM] data could be used in real time to address issues ongoing. With research at the moment it's very difficult to achieve this, but I'm thinking more of a clinical practice. If clinical teams were to use this real-time information it would enable them to act on any issue.”

– Researcher

“I think that would be a really good thing and then have those results on records that you can see if someone is - if their mood is low, you'll be able to track that. That only needs to be a one-item Patient Reported Outcome measure like the distress thermometer for example.”

– Researcher

Joined up, integrated systems that allowed HCPs and researchers to record and track PROM data was a common suggestion. A system like this might also facilitate conversations and learning around how to act on PROM scores and how to ensure such scores are informing clinical practice. A dedicated system for recording and tracking PROM scores might also make it more likely that PROM data would be recorded systematically and used in research.

In addition, an integrated system developed to connect both hospital and community staff and patients could support the collection of longitudinal data.

“A patient-reported outcome measure, if it is used for quality assurance or to understand the experience of patients with multiple myeloma, needs to be used over time. Only in this case can it be understood to be an “outcome measure” in the true sense.”

– Nurse / Researcher

Systematically tracking patient data from diagnosis, to treatment, through to periods of remission would provide HCPs and researchers with a detailed and holistic understanding of what is important to patients at different points in their illness. It would allow interventions and treatments to be tailored and patient-centred and it would allow researchers to use existing data rather than collecting their own in less naturalistic conditions.

However, a tracking system such as this would be both expensive and challenging to implement. It would require set up and maintenance costs, training, and additional time in clinics and other sessions. The collection of myeloma PROM data is not a requirement in the NHS and so, with already limited resources, this kind of collection system needs to be resourced.

Gaps in myeloma PROMs

The next set of themes that emerged from the analysis was around gaps in PROMs. A validated carers PROM, published longitudinal data, and guidance on use and implementation were common themes discussed by stakeholders.

A validated carers PROM

A recurring theme in the stakeholder interviews was the lack of a dedicated PROM for use with myeloma family members or other informal carers.

“One thing it doesn’t really take into account is that often for these patients their partners are their carers. So they’re thinking do I report the amount of time I spend with my wife or husband? I think sometimes they find that a little bit frustrating because there’s not a way to adequately report that a lot of their care will come from a family member.”

– Researcher

There was acknowledgement from many stakeholders that carers are impacted by myeloma and cancer and that their experience of illness is currently not being captured. One researcher reported that when carers feel supported, patients are

likely to benefit too. Thus, if carers are routinely asked how they are being affected by myeloma and that information is recorded and used to inform services for carers, then this will consequently benefit patients. A PROM developed for carers could facilitate patient-centred conversations and provide HCPs with a way of documenting myeloma's impact on the families of myeloma patients.

Published longitudinal data

Stakeholders identified that another aspect missing from the landscape is longitudinal data, referring to the lack of published research on PROMs and their use over time.

“In research, the patient experience, particularly how experiences change over time is often disregarded. So far, only one population-based longitudinal study has been published [Mols et al., 2012], involving a sample not defined by a particular treatment (as is the case in clinical trials), a disease phase (only newly diagnosed or relapsed/refractory patients included in the sample) or being treated in a centre. However, since HRQoL was only assessed at baseline and again after one year no data on the course of QoL over this year exists. This information would be crucial to understanding which patients are particularly burdened and in need of supportive care. It would allow identifying risk factors for doing poorly and needing more support.”

– Researcher

This lack of data is reflective of how PROMs are used clinically, with research nurses expressing concern around PROM data not being collected appropriately in the community. This highlights an issue that when patients leave hospital or a clinical trial they are not given the opportunity to self-report on issues that affect them in a formalised way. As monitoring appears to be confined to phases of treatment, there is a lack of valuable data about when patients are most burdened during their disease course.

Guidance on use and implementation

Partly related to missing longitudinal data is a lack of guidance on the way that PROMs should be selected, used, interpreted, and implemented. This is an issue that has emerged throughout this analysis of stakeholder interview data.

“There are no guidelines either for how to make a valid choice on which is the best one. So, there are guidelines for how to do a systematic review, guidelines for how to conduct a trial, but there are no guidelines for how to select an outcome measure.”

– Health Psychologist

This point highlighting the lack of guidance around the application of tools perhaps relates to what was discussed around the construction of tools in the academic setting. Stakeholders were frank in suggesting that researchers generating tools in academic settings generally direct their focus to concepts such as tool validity rather than concepts such as how the tool would function in a real world setting. Although the consensus was that stakeholders valued validated tools and tools that had been discussed in the literature, stakeholders who had worked in clinical practice or research settings were keen for more practical guidance on how tools should be used to address patient need.

Another common theme raised was the lack of focus on PROM implementation.

“Because the thing about it is, what happens, often, is you - there’s a lot of tools designed but nobody actually funds research for the implementation and follow up.”

– Researcher

“For implementation to be successful, PROMs need to be embedded fully into the clinical encounter and not be considered an add-on.”

– Researcher

Interviews suggested that there is comparatively little research on the implementation of existing PROMs.

“I think a lot of the tools are good but I think it’s just back to meaning in practice and training.”

– Researcher

Comprehensive PROMs database

The first suggestion proposed by several stakeholders was that a bank or database of PROMs would be helpful. This database would ideally be accessible, easy to use, and contain detail on tools and what constructs they measure.

“The way forward would be the construction of an item bank that can be used across settings, disease phases and even conditions, with items being calibrated on a common metric and that would therefore allow choosing short forms for different applications that can still be compared.”

– Researcher

“I think if there was some coherent database where you could access - you could type in fatigue and your cancer patient type - this may exist but I haven't found it...if it would bring up the validity and reliability, what exactly it's measuring and it would give you an online option or a paper option and then you could just use that.”

– Researcher

Although examples of such banks do exist (e.g. PROMIS), they are construct-specific e.g. fatigue and do not include specific tools in specific disease areas. Thus, a more comprehensive bank of tools that is regularly updated would be helpful in supporting PROM use in the future.

SECTION THREE: PATIENT PERSPECTIVES ON PROMS IN MYELOMA

The last phase of the project examined patient views of existing PROMs. Two groups of myeloma patients (one group in Scotland and one in England) were invited to review a selection of PROMs and answer questions on what they liked and disliked about each one.

Twelve participants were recruited. Participants all had a myeloma diagnosis and were members of the Myeloma UK Support Group Network. Four women and eight men participated. In line with the standard ethical practices, all participants were sent an information sheet in advance of the telephone interview and given an opportunity to ask questions about what taking part would involve.

The PROM questionnaires given to patient groups to review were the EQ-5D-5L, the FACT-G, the HADS, and the MyPOS. These tools were selected for patient review based on frequency of reference within the literature and by stakeholders. The MyPOS was additionally included as the only available myeloma-specific tool developed specifically for use in clinical practice. Each of the four PROMs were examined in turn by each focus group. Patients were asked what they liked, what could be improved, and what was missing from each tool. Focus group data was analysed using thematic analysis and using NVivo.

EQ-5D-5L-5L

The EQ-5D-5L-5L is a short and simple generic tool that can be used in the clinical and economic evaluation of health care. Although it has been designed for use in monitoring the health status of patient groups at different moments in time (for example pre and post treatment), it is, in the UK, mostly used in research and for HTA reimbursement decisions.

One recurring concern over this tool was that patients found the language vague.

“What does the word moderately mean?”

Patients generally did not like the terms of measurement used within this tool and preferred the clearer (numerical) rating scales of other tools. Some patients said that they would need support or clarification to understand the rating scales.

Patients also reported that the EQ-5D-5L did not pick up on key constructs which mattered to them.

“Something about pain relief works for me, pain relief doesn’t work for me. That would give a better clue as to what kind of impact it [the myeloma] is having.”

Additionally, the tool does not ask about activities of daily living which were important to some patients.

“The other thing is it makes the usual mistake of not saying are you in pain? Are you having trouble getting around? They are things that vary a lot for me. Sometimes I’m great I’m on the bicycle doing the shopping, whizzing around, sometimes I’m not. Which do I report? They’re both true.”

Although patients understood that the tool was designed to be a generic and quick questionnaire intended to elicit a snapshot perspective of how a patient is impacted by a condition, patients felt that the questions asked were not relevant to their myeloma. Patients wanted to see questions about their day-to-day activities and if they were working or coping. Additionally, some patients would have liked to have seen additional questions around psychological support in the EQ-5D-5L.

“There’s a little bit about anxiety and depression but not so much about do you feel supported or have enough friends and family and support.”

“Yeah...if you’re isolated that can have a big impact on your mood level.”

Although in practice it may be difficult to incorporate constructs such as psychological / psychosocial wellbeing into brief questionnaires such as the EQ-5D-5L, it is useful to note that patients wanted to engage with these kinds of questions.

In response to questions around what patients would like to see changed or added to the EQ-5D-5L, patients said that they would like more written explanation around what the purpose of the questionnaire was, to refer back to when completing. Although they acknowledged that a researcher or HCP would usually be present to explain this, patients cited problems with their memory and would prefer an introduction to the questions.

Additionally, some patients said that they would have liked to see free text boxes

underneath questions so that if they wished, they could expand on the answers provided in previous questions.

“I suppose you could put comment bit underneath it so that whatever you say then you can add a wee comment at the bottom.”

Other patients however were more sceptical of the use of data collected in free text boxes.

“I think - I wouldn't expect people to read all of - act on all of it. I would love to think people would have something to - my expectations are it's not going to happen.”

This scepticism from patients is perhaps not unfounded. Interview data from one stakeholder suggested that some HCPs do not know what to do with PROM scores and thus clinical action is not being taken in response to patient reported data emerging from PROMs. Again, this is worrying and highlights the need for better training in this area.

Overall, the EQ-5D-5L was acknowledged to be a quick tool that picked up on some of myeloma patients' concerns. However, many patients felt that this tool did not pick up on the primary constructs that mattered to them and that the scales within the tool were somewhat ambiguous.

FACT-G

The FACT-G (Functional Assessment of Cancer Therapy-General) is part of a series of quality of life questionnaires targeted to the measurement of chronic conditions. The FACT-G is a tool developed for use in patients with cancer. It is a 27-item compilation of general questions divided into four primary QoL domains: Physical Well-Being, Social/Family Well-Being, Emotional Well-Being, and Functional Well-Being.

Overall, patients were positive about this cancer-specific questionnaire. Patients reported that the questions felt relevant to their experiences of myeloma and picked up on some of their primary concerns.

“Yes, physical energy, nausea, attending to the needs of my family. It feels more relevant.”

Patients also preferred the rating scale contained within the FACT-G (i.e. a 0-4 numerical scale where 0 means not at all and 4 means very much) to that of the EQ-5D-5L. Patients liked the simplicity and explanation attached to answering the questions.

This PROM additionally asks about sex, which for some patients was important.

“I know [group member] was talking about it earlier but I think it is good that they ask about [sex] because it’s a part - it’s not just you. It’s your partner or your husband. I think it’s important to look at it as a couple because it does affect your relationship.”

The tool was perceived by some to take into account the wider context of myeloma which included family and friends, relationships, and psychosocial well-being. One patient said she had never been asked about these issues previously, especially sex, and it felt validating to have these issues acknowledged as being important. Some patients said that they would be more likely to bring emotional or sexual issues up with their HCP if they had been asked about them in a questionnaire such as the FACT-G.

Another question that some patients felt was validating was the question about thinking about death. Some patients discussed thinking about this when they were alone, but not talking about their fears or thoughts with HCPs.

“It’s a very valid question it’s going right to the heart of the matter. These are the sorts of things, moments, mostly we’re getting on with our lives but we have our moments, quiet moments in the middle of the night and these issues definitely come into the mind whether you want them to or not.”

The tool therefore has the potential to act as a facilitator of conversation, bringing subjects to the surface that might not otherwise be discussed. This is a useful finding, suggesting that even if HCPs are finding scoring and interpretation of PROM findings difficult, the tools themselves could work simply to encourage conversations with patients.

There was however critique of the language used in this tool, with patients questioning the meaning of statements within the PROM. The example below illustrates:

“I am bothered by side-effects. Does that mean I am suffering side-effects or does it mean the impact of side-effects?”

Again, it was clear that although PROMs, such as the FACT-G, are intended to be completed by patients, patients may still need some support or guidance to do so.

HADS

The Hospital Anxiety and Depression Scale (HADS) was developed to determine the levels

of anxiety and depression, a patient might be experiencing in hospital. The HADS is a generic fourteen item scale with seven items relating to anxiety and seven to depression. It is used in both research and clinical practice. Like the FACT-G, patients found the questions in the HADS to be broadly relevant to their experience.

“I think they are important questions nonetheless and I think - from our discussion earlier this morning I think as we were saying once you receive a diagnosis of cancer or myeloma it does change your outlook on life and it does affect many of these things.”

Some patients said that they had not been asked about feeling depressed or anxious, despite experiencing symptoms like panic attacks. The extract below highlights how on reflection this patient realised that his panic attacks were related to his stem cell transplant, yet at the time did not associate the two experiences.

“I think you probably pick up more - I mean no one's ever asked me, but I got panic attacks after my second transplant. No, I didn't actually really put the two together but I now know that's what it is, but no one ever asked me, so - but...it does need picking up and I probably do need my arm twisted.”

This patient also said that he would need his 'arm twisted' to acknowledge that he may have

some anxiety or other symptoms that may need addressed. The HADS, as with the other tools asking questions around the emotional experience of illness, was therefore perceived to be helpful in picking up issues that may not otherwise be discussed.

The final discussion around the HADS was again concerned with validation of their feelings and the idea that some patients had about being alive. Some patients felt as though they could not raise issues such as low mood because they were not important.

“I just think we tend to put up with a lot of patients because you think well what do you - you know, we're alive, we're lucky. You sort of forget that actually.”

Like the FACT-G, being asked about constructs such as anxiety and depression via tools

such as the HADS validated any negative or low feelings that they had. This experience of

patient validation through the use of PROMs is important as it may help to reduce stigma attached to illness and mental health.

MyPOS

The MyPOS is a quality of life PROM developed specifically for myeloma. It is part of the Palliative Outcome Scale set of measures developed by researchers in the UK. It has been developed specifically for clinical practice although it is being used in myeloma research. The PROM begins with a free text box asking patients to describe their main concerns.

Patients favoured this tool over the others in the set. It was perceived to be relevant to myeloma patients' concerns and capture effectively what it meant to live with and experience myeloma.

“Well I mean it covers the whole spectrum.”

When asked if any of the questions could be removed, patients said no. This was a positive finding in light of the literature suggesting that PROMs can be repetitive or burdensome for patients.

“Do you think anything we didn't really need to ask? Would you take anything out?”

“It all needs to be there.”

“Yep.”

“I think it's captured most aspects, hasn't it?”

When asked if there might be anything added to the questionnaire, some patients suggested that more could be asked of fatigue, and its associated effects.

“I still think you could ask a bit more about fatigue.”

“Yeah, there’s only...”

“It wasn’t really fatigue.”

“Weakness or lack of energy.”

“Yeah. I listed that as my first concern and then I found there wasn’t really a place to describe it.”

A further question around fatigue was the only suggestion that patients had to improve the design of the questionnaire.

Most patients liked the free text box at the beginning but additionally suggested that this could be moved to the end of the questionnaire. Patients said that questions within the PROM helped them to think about their concerns and that a space to expand on answers given to questions within the PROM would be useful.

One patient was visibly upset while discussing the MyPOS during the focus group. This was due to the PROM acknowledging some of the thoughts and feelings she had about her myeloma that had not been explored with her HCP. This once more highlights the importance of PROMs as a facilitator of difficult conversations and perhaps as a tool for guiding conversations in their own right.

Summary of patient perspectives

The focus group data suggest that most patients in our sample would be happy to complete PROMs and understood why the collection of such data by HCPs and researchers was important. Many patients found being asked questions about their psychosocial well-being validating and said that having these kinds of questions asked in a formal way, would help them bring such concerns to their HCPs in future.

Patients, however, wanted PROMs to reflect their experience of illness and they wanted to see clear explanation around how to complete the questions. PROMs such as the MyPOS and FACT-G were preferred over shorter, generic tools such as the EQ-5D-5L.

CONCLUSION

This review of PROMs reports the views of stakeholders working with PROMs and patients views on current PROMs used in myeloma. Findings suggest that both stakeholders and patients, in theory, understand why PROMs are important and why patient reported data should be being collected.

However, in practice using, scoring, interpreting, and recording such data is complex. Interviews suggested that PROMs are not being used in clinical practice due to staff having unmet training needs. It also emerged that none of the patients participating in the focus groups had previously been given a PROM to complete, highlighting the non-use of PROMs in myeloma.

Although it is worrying that patient reported outcomes data is not being systematically collected and recorded, it is clear that resourcing (the provision of training, staff costs, infrastructure) is the major challenge in facilitating PROM use. If we are serious about collecting and acting on patient reported data we need to create opportunities for PROMs to be used, across various settings.

If we are to take patient perspectives seriously, and use patient voices to address patient needs then we have to invest in people and in the technologies necessary to enable patient data to be collected and used to inform change.

Myeloma UK will continue to work in this area, using platforms such as Myeloma Academy to encourage and facilitate the use of the MyPOS in myeloma. We will additionally continue our work on understanding the myeloma patient experience so as to contribute to the evidence base and work to inform change at a policy level.

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APPENDIX A:

CONSULTATION QUESTIONS

Patient-reported outcomes in myeloma: are they fit for the future?

- 1.** Do you think existing PROMs capture the most important aspects of myeloma patient experience?
- 2.** Do you think that patients feel that their views are acknowledged and make a difference through the use of PROMs?
- 3.** What impact do you think data resulting from PROMs has in different settings: research, approval of treatments and clinical practice?
- 4.** Research suggests that although PROM use is rising in clinical trials, PROMs are still underused. Why do you think this is?
- 5.** What are your views on the advantages and disadvantages of generic vs myeloma-specific PROMs in research settings?
- 6.** What impact do you think current use (or non-use) of PROMs has on myeloma research?
- 7.** Research suggests that PROM selection may be restricted to issues of availability or familiarity rather than considerations of instrument relevance or quality. Is this an issue you are aware of?
- 8.** What do you think about the PROMs available in myeloma, and in cancer more widely?
- 9.** What do you think drives PROM selection (in research, trials and clinical practice)?
- 10.** How important is it that there is consistency in the use of PROMs?
- 11.** How would you want to see PROMs used in the future in myeloma?
- 12.** How could PROMs be made easier for you / stakeholders to use?
- 13.** What support and infrastructure do you think is needed to support selection and use of PROMs in myeloma?

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Myeloma UK is the only organisation in the UK dealing exclusively with myeloma. Our ultimate goal is to find a cure.

We are dedicated to myeloma patients – making sure they get access to the right treatment at the right time. We continually strive to improve standards of treatment and care through research, education and raising awareness of myeloma.

For more information about Myeloma UK, including details of our latest research and analysis, please visit myeloma.org.uk.

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